Novel Cyclodextrin–Oligosiloxane Copolymers for Use as Stationary Phases to Separate Enantiomers in Open Tubular Column Supercritical Fluid Chromatography

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Five novel β- (or α-) cyclodextrin–hexasiloxane copolymers have been prepared by a seven- (or nine-) step process. A key step was the reaction of partially alkylated β- (or α-) cyclodextrin (**8**, **9**, or **10**) with *p*,*p*′-methylenebis(benzenesulfonyl chloride) to form a bissulfonate ester on the smaller rim of cyclodextrin. These bissulfonates were reacted with sodium *p*-(allyloxy)phenoxide followed by alkylation to form the peralkylated bis(allyloxyphenyl) β- (or α-) cyclodextrins **17–20**. β-Cyclodextrin bissulfonate ester **11** was also reacted with sodium azide followed by methylation, reduction, and acylation to form permethylated *N*,*N*′-bis[(allyloxy)benzoyl]-6^A,6^C-diamino-6^A,6^C-dideoxy-β-cyclodextrin (**24**). The bisalkenes were copolymerized with dodecamethylhexasiloxane by the hydrosilylation process to give the cyclodextrin-containing copolymers. The copolymeric phases provided excellent enantiomeric separation of a variety of chiral solutes in open tubular column supercritical fluid chromatography (SFC).

Introduction

The analytical separation of enantiomers has become very important in light of the interest in the resolution and enantiomeric purity of drugs.[1,2] The use of chiral stationary phases (CSPs) in chromatography is the most convenient method to determine enantiomeric purity.[3] Extensive separative work has been done using liquid (LC) and gas chromatography (GC) as reported in numerous reviews and books. Relatively little work has been reported on developing CSPs for supercritical fluid chromatography (SFC). The use of open tubular column SFC[4] to separate enantiomers is a good choice since SFC often provides faster separations and has higher efficiency than LC, and separations can be performed at lower temperatures than with GC.[5] Low-temperature separations are important for enantiomeric compounds because of increased chiral selectivity at lower temperature and reduced possibilities of thermal decomposition and racemization.

Various cyclodextrin derivatives have been used as chiral stationary phases for the capillary GC separation of a number of volatile racemates with very different structures. The state of the art in this field has recently been reviewed by Schurig and Nowotny.[6] Most of the stationary phases derived from cyclodextrin were prepared by diluting the relevant cyclodextrin derivative in polysiloxane in order to obtain selective chiral separations at temperatures below the melting point of the pure cyclodextrin derivative.[6] Generally speaking, these derivatives were peralkylated cyclodextrins, peralkylated hepta(trifluoracetyl)cyclodextrins, and the permethylated hydroxy ether derivatives of cyclodextrin.[7] A few stationary phases derived from cyclodextrin were prepared by chemically bonding permethylated alkenyl-β-cyclodextrin to a polysiloxane backbone by a hydrosilylation reaction.[8–10] These stationary phases provided good chiral separations when used in both capillary GC and SFC because they were thermally and chemically stable and had the excellent coating properties of the organic polysiloxanes.

We have recently reported new chiral copolymeric stationary phases composed of chiral organic and oligodimethylsiloxane units for capillary SFC. These new copolymeric phases provide excellent separation of a variety of enantiomeric diols.[11,12] We now report the preparation of a series of copolymers composed of cyclodextrin and polysiloxane units. These materials were synthesized by first preparing bis[*p*-(allyloxy)phenyl]-substituted peralkylated cyclodextrins (**17–20** and **24**) (Scheme I) and then forming copolymers **25–29** by a polyhydrosilylation reaction with an α,ω-dihydrooligosiloxane (Scheme II). A preliminary report of this work has been published.[13] These novel phases exhibit remarkable enantiomeric separation of a variety of chiral organic solutes, as will be reported later.[14] In this paper, the synthesis of these stationary phases is reported. Their

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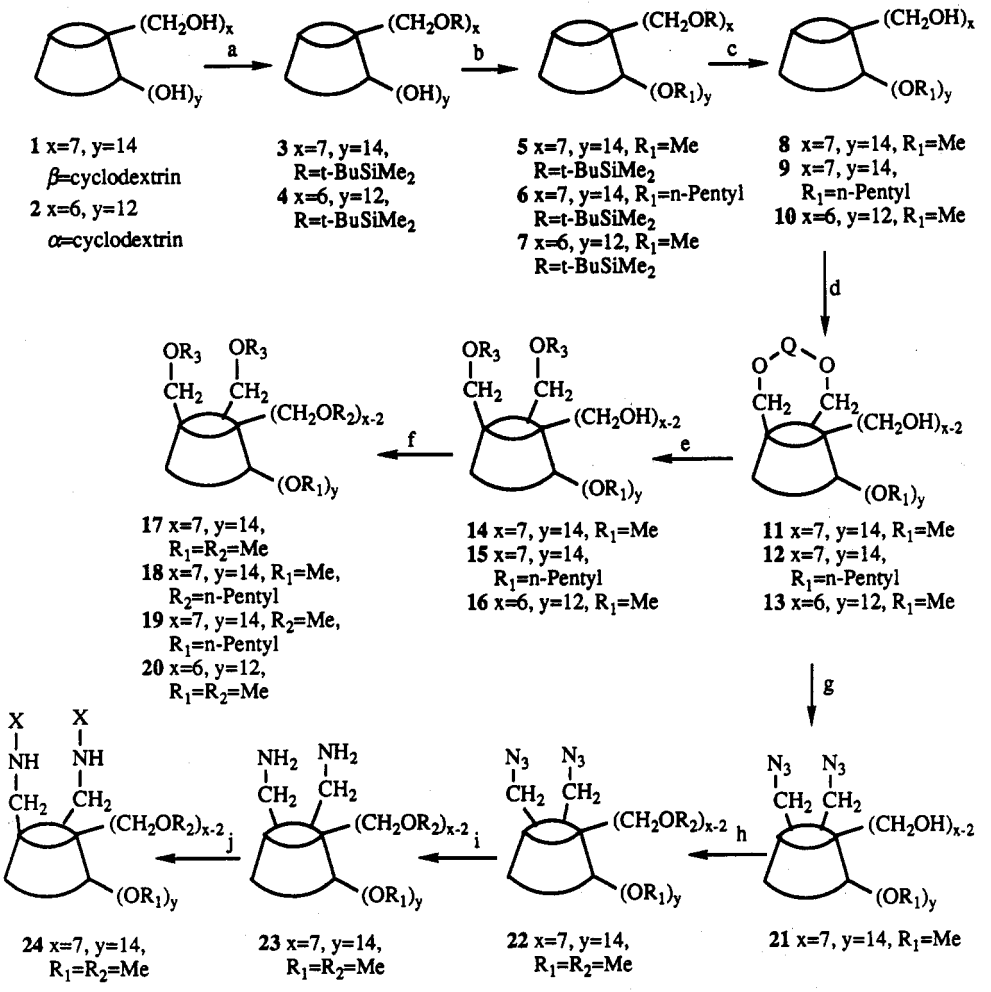
Scheme I.[a] Preparation of Bisallyl-Substituted Cyclodextrins 17–20 and 24



Q = p,p′-methylenebis(benzenesulfonyl); R_3 = p-(allyloxy)phenyl; X = p-(allyloxy)benzoyl

[a] Key: (a) t-BuSiMe$_2$Cl, imidazole, DMF; (b) NaH, MeI, DMF; (c) NH_4F, MeOH for **8** and **10**; (n-Bu)$_4$NF, THF for **9**; (d) p,p′-methylenebis(benzenesulfonyl chloride), pyridine; (e) sodium p-(allyloxy)phenoxide, DMF; (f) NaH, MeI, DMF; (g) NaN_3, DMF; (h) NaH, MeI, DMF; (i) H_2, PtO_2; (j) p-(allyloxy)benzoyl chloride, NEt_3, toluene.

utility in chromatography is shown by the separation of several racemic mixtures on one of the phases.

Results and Discussion

Bis[p-(allyloxy)phenyl]-substituted cyclodextrins **17–20** and **24** were prepared by the multistep sequence shown in Scheme I. Partially alkylated cyclodextrin derivatives **8**, **9**, and **10** were synthesized as reported.[15,16] Selectively protecting the primary hydroxy groups of cyclodextrin with *tert*-butyldimethylsilyl chloride was the first step, and then methylation of **3** and **4** with iodomethane or iodopentane and sodium hydride in DMF gave crystalline cyclodextrin derivatives **5**, **6**, and **7**, respectively. Ammonium fluoride was used to remove the silyl protecting groups[17] rather than tetrabutylammonium fluoride for the preparation of intermediates **8** and **10**. This modification avoided the usual tedious procedure to purify the O-desilylated crude product. Ammonium fluoride could not be used as a deprotecting reagent in the preparation of **9** because **6** was not soluble in methanol. Fortunately, tetrabutylammonium fluoride and tetrabutylammonium hydroxide were easily removed from the crude product by washing with methanol.

Bissulfonate esters **11–13** were prepared using p,p′-methylenebis(benzenesulfonyl chloride) as was used to make a similar bissulfonate of β-cyclodextrin.[18] The reaction of **8** or **9** with the bissulfonyl dichloride at 60 °C produced positional isomers 6^A,6^C- and 6^A,6^D-bissulfonate esters at a ratio of 85:15. This result is analogous to that reported by Tabushi and co-workers.[19] Purification of 6^A,6^C-bissulfonate ester was done by column chromatography. Dialkene-substituted cyclodextrins **14–16** were prepared by treating **11–13**, respectively, with an excess of p-(allyloxy)phenoxide in DMF at room temperature. The yield in DMF was 55–60%, but only 8–10% when the reaction was performed in THF at room temperature or at reflux. The bissulfonate ester of unsubstituted β-cyclodextrin could be prepared according to Tabushi's procedure,[18] but the bis[(allyloxy)phenyl] derivative of unsubstituted β-cyclodextrin could not be prepared by the reaction of this ester with sodium p-(allyloxy)-phenoxide under the same reaction conditions. In the

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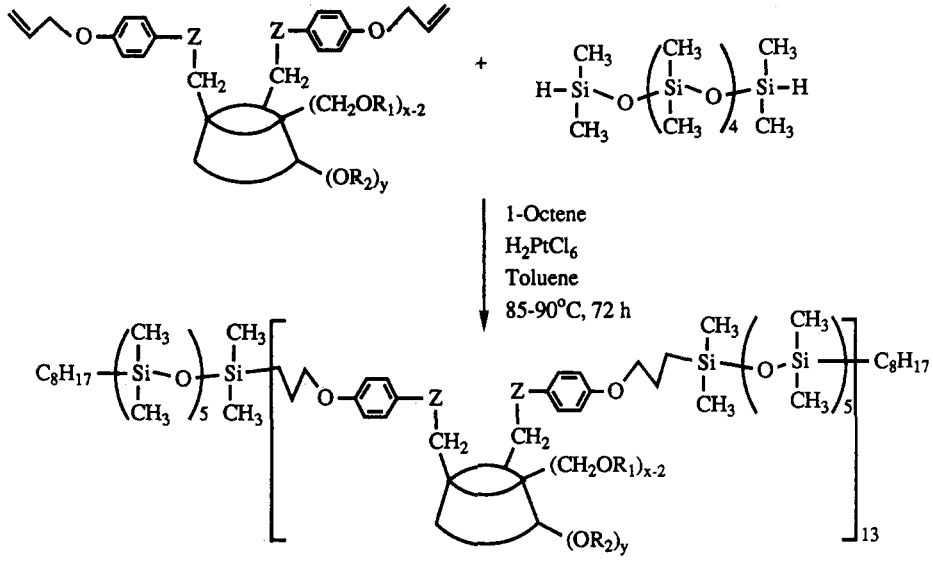
Scheme II. Preparation of Cyclodextrin–Hexasiloxane Copolymers



copolymer	x	y	R_1	R_2	Z
25	7	14	Me	Me	O
26	7	14	Pentyl	Me	O
27	7	14	Me	Pentyl	O
28	6	12	Me	Me	O
29	7	14	Me	Me	-CONH-

latter case, we obtained mainly one product that did not contain the (allyloxy)phenyl arm on the rim of β-cyclodextrin, and it was not β-cyclodextrin as determined by TLC. This crude product has not been purified further, but the product could be 3,6-dehydro-β-cyclodextrin as reported by Stoddart and co-workers.[20] Cyclodextrins **14–16** were alkylated using iodomethane or iodopentane and sodium hydride to yield the peralkylated bis[(allyloxy)-phenyl]-β-cyclodextrins **17–20**.

Diazidoheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (**21**) was obtained by treating **11** with azide anion in DMF at 120 °C. Diazidopermethyl-β-cyclodextrin **22** was prepared by the methylation of **21** with iodomethane and sodium hydride. Hydrogenation of **22** at 50 psi H_2 for 4 days in the presence of platinum oxide at room temperature gave diaminoheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (**23**) as reported by Tabushi and co-workers for the preparation of diamino-β-cyclodextrin.[21] The reaction of **23** with *p*-(allyloxy)benzoyl chloride and triethylamine in toluene gave permethylated *N*,*N*′-bis[*p*-(allyloxy)benzoyl]-6^A,6^C-diamino-6^A,6^C-dideoxy-β-cyclodextrin (**24**).

Copolymers **25–29**, shown in Scheme II, were synthesized by the hydrosilylation of **17–20** and **24** with dodecamethylhexasiloxane in a manner similar to that reported.[11] Preliminary testing of some of these phases has been done using capillary SFC with CO_2 as a carrier. For example, copolymer **25** was coated on a 5 M × 50 μM i.d. fused silica column with a film thickness of about 0.25 μM as

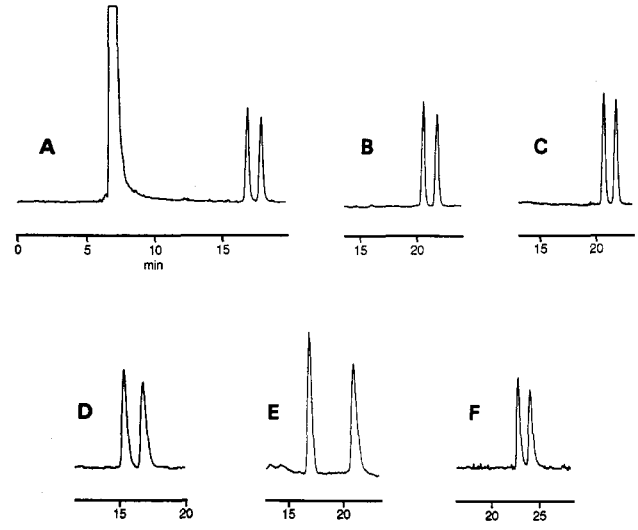


Figure 1. SFC separation of the enantiomers of diethyl tartrate (A), 2-phenylcyclohexanol (B), 1-phenylethanol (C), ibuprofen (D), pantolactone (E), and 1,2-diphenyl-1,2-ethanediol (F) on phase 25. Conditions are given in the text.

reported.[12] Typical separations were accomplished using a density program such as from 0.30 g mL^{-1} at a rate of 0.010 g mL^{-1} min^{-1} after a 1-min isopycnic period. Enantiomer separations were observed for chiral diols, monoalcohols, lactones, and carboxylic acids containing aromatic substituents. Figure 1 shows the separations of diethyl tartrate (A), 2-phenylcyclohexanol (B), 1-phenylethanol (C), ibuprofen (D), pantolactone (E), and 1,2-diphenyl-1,2-ethanediol (F) using the above column. Other

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enantiomeric pairs have been resolved using these copolymers,[14] indicating a broad application range for this phase.

Experimental Section

Proton and carbon NMR spectra were recorded at 200 MHz. Heptakis[6-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-methyl]-β-cyclodextrin (**5**),[16] heptakis[6-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-pentyl]-β-cyclodextrin (**6**),[22] and hexakis[6-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-methyl]-α-cyclodextrin (**7**)[15] were prepared as reported.

Heptakis(2,3-di-*O*-methyl)-β-cyclodextrin (8). A solution of the compound **5** (7.20 g, 3.4 mmol) and NH_4F (5.27 g, 0.14 mol) in 125 mL of CH_3OH was refluxed for 24 h and concentrated. Ethyl acetate (100 mL) was added to the residue and the mixture was filtered through a 2-cm pad of silica gel. The filtrate was concentrated and the residue was purified by column chromatography on silica gel ($CHCl_3$–CH_3OH/8:1, then $CHCl_3$–CH_3OH–H_2O/50:10:1) to give 4.30 g (95%) of **8**: mp 153–154 °C (lit. mp 168–172 °C);[16] $[\alpha]^{25}_D$ +137.9° (*c* 1.40, $CHCl_3$) (lit. $[\alpha]^{24}_D$ +176°);[16] ^1H NMR ($CDCl_3$) δ 5.13 (d, *J* = 3.2 Hz, 7 H, H-1), 4.41 (s, OH), 4.10–3.10 (m, 84 H); ^{13}C NMR δ 99.35 (C-1), 82.68 (C-4), 82.38 and 82.11 (C-2,3), 72.82 (C-5), 61.68 (C-6), 62.01 and 58.99 (OCH_3). Anal. Calcd for $C_{56}H_{98}O_{35}$: C, 50.52; H, 7.42. Found: C, 50.36, H, 7.60.

Heptakis(2,3-di-*O*-pentyl)-β-cyclodextrin (9). A mixture of 40.0 g (13.7 mmol) of **6**, 500 mL of THF, and 96 mL of 1 M $(C_4H_9)_4NF$ in THF (96 mmol) was refluxed for 24 h. The solvent was evaporated, the residue was washed with CH_3OH to remove $(C_4H_9)_4NF$ and $(C_4H_9)_4NOH$, and then the residue was dissolved in $CHCl_3$. The organic layer was washed with water and dried ($MgSO_4$). The solid that formed after concentration was purified on column chromatography ($CHCl_3$–CH_3OH/15:1) to give 24.7 g (85%) of **9**; mp 213–215 °C; $[\alpha]^{25}_D$ +105.8° (*c* 1.7, $CHCl_3$) (lit. $[\alpha]^{22}_D$ +108.9°);[22] ^1H NMR ($CDCl_3$) δ 5.10 (d, *J* = 3.2 Hz, 7 H), 4.40 (s, 7 H, OH), 4.09–3.35 (m, 63 H), 3.19 (dd, J_1 = 3.2 Hz, J_2 = 6.7 Hz, 7 H), 1.73–1.43 (m, 28 H), 1.43–1.08 (m, 56 H), 0.87 (t, *J* = 6.5 Hz, 42 H); ^{13}C NMR δ 98.3, 81.0, 80.8, 79.2, 73.1, 74.4, 72.1, 28.8, 28.7, 23.3, 23.1, 14.5. Anal. Calcd for $[C_{16}H_{30}O_5]_7$: C, 63.55; H, 10.00. Found: C, 63.37; H, 9.84.

Hexakis(2,3-di-*O*-methyl)-α-cyclodextrin (10). Compound **7** (30.60 g, 16.8 mmol) and 18.61 g (0.50 mol) of NH_4F were refluxed in 500 mL of CH_3OH for 24 h. **10** was isolated as described above for **8** using column chromatography ($CHCl_3$–CH_3OH/8:1 and then $CHCl_3$–CH_3OH–H_2O/50:10:1) to give 17.3 g (90%) of **10**: mp 214–216 °C (lit. mp 215–218 °C);[15] $[\alpha]^{25}_D$ +142.7° (*c* 1.50, $CHCl_3$) (lit. $[\alpha]^{26}_D$ +170.0°);[15] ^1H NMR ($CDCl_3$) δ 5.03 (d, *J* = 3.2 Hz, 6 H), 4.94 (s, OH), 4.18–3.92 (m, 6 H), 3.87–3.68 (d, *J* = 6.5 Hz, 12 H), 3.68–3.30 (m, 48 H), 3.22–3.02 (dd, J_1 = 3.2, J_2 = 6.8 Hz, 6 H); ^{13}C NMR δ 99.7 (C-1), 82.7, 82.5, 82.3 (C-2,3,4), 73.5 (C-5, 62.5 (C-6), 62.2, 58.6 (MeO).

$6^A,6^C$-[Di-*O*-*p,p'*-methylenebis(benzenesulfonyl)]heptakis(2,3-di-*O*-methyl)-β-cyclodextrin (11). A solution of **8** (5.99 g, 4.5 mmol) in 1000 mL of dried pyridine was heated under N_2, and 80 mL of pyridine was distilled to remove traces of water. The solution was cooled to rt, and *p,p'*-methylenebis(benzenesulfonyl chloride) (2.0 g, 5.4 mmol) was added slowly. The mixture was stirred until the solid dissolved completely, and then it was heated to 60 °C for 3 h. The mixture was cooled, and pyridine was removed by vacuum distillation (0.2 mm, $T < 40$ °C). The residue was partitioned between $CHCl_3$ and water. The organic layer was separated, dried, and concentrated. The residue was subjected to column chromatography ($CHCl_3$–CH_3OH/20:1) to give 1.90 g (26%) of **11**; mp 180–181 °C; $[\alpha]^{25}_D$ +161.3° (*c* 1.31 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.86 (m, 4 H), 7.52 (m, 4 H), 5.15 (m, 7 H), 4.09 (s, 2 H), 3.97–2.90 (m, 84 H), 2.09 (s, OH); ^{13}C NMR δ 147.2, 134.6, 133.1, 130.3, 130.1, 129.5, 129.1, 100.2, 99.5, 98.7, 82.7, 82.4, 82.1, 81.9, 81.8, 81.7, 81.6, 81.5, 81.4, 81.2, 81.1, 73.5, 72.5, 72.3, 72.1, 69.8, 69.6, 62.8, 62.1, 62.0, 61.6, 61.5, 61.1, 59.5, 59.1, 58.8, 58.7, 30.2. Anal. Calcd for $C_{69}H_{106}O_{39}S_2$: C, 51.04; H, 6.58. Found: C, 50.84; H, 6.47.

$6^A,6^C$-[Di-*O*-*p,p'*-methylenebis(benzenesulfonyl)]heptakis(di-*O*-pentyl)-β-cyclodextrin (12). Cyclodextrin derivative **12** was prepared as above for **11** from 21.12 g (5.7 mmol) of **9**, 1000 mL of dry pyridine, and 2.51 g (6.87 mmol) of *p,p'*-methylenebis(benzenesulfonyl chloride). Column chromatography required $CHCl_3$–CH_3OH/100:1 as eluant to give 3.59 g (26%) of amorphous **12**: mp 85–88 °C; $[\alpha]^{25}_D$ +94.7° (*c* 1.76, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.87, 7.77 (d, *J* = 8.7 Hz, 4 H), 7.43, 7.37 (d, *J* = 8.7 Hz, 4 H), 5.20–4.97 (m, 7 H), 4.54–3.28 (m, 65 H), 3.28–3.02 (m, 7 H), 1.68–1.40 (m, 28 H), 1.40–1.07 (m, 56 H), 0.96–0.70 (m, 42 H); ^{13}C NMR δ 147.2, 133.3, 130.2, 130.0, 129.5, 128.8, 100.8, 99.2, 98.6, 98.4, 97.9, 81.3, 81.0, 80.9, 80.8, 80.6, 80.5, 74.3, 74.1, 72.6, 72.5, 72.4, 72.3, 72.2, 72.1, 69.8, 62.8, 62.7, 30.8, 30.6, 30.3, 29.0, 28.8, 23.4, 23.2, 14.7. Anal. Calcd for $C_{125}H_{218}O_{39}S_2$: C, 62.32; H, 9.12. Found: C, 62.40; H, 9.33.

$6^A,6^C$-[Di-*O*-*p,p'*-methylenebis(benzenesulfonyl)]hexakis(2,3-di-*O*-methyl)-α-cyclodextrin (13). Compound **10** (9.05 g, 7.97 mmol) was stirred in 500 mL of pyridine with 2.91 g (7.97 mmol) of *p,p'*-methylenebis(benzenesulfonyl chloride) at 60 °C for 3 h. Product **13** was isolated as described for **11**. Column chromatography of the residue gave 1.85 g (16%) of **13**; mp 181–183 °C; $[\alpha]^{20}_D$ +127.7° (*c* 4.52, $CHCl_3$); ^1H NMR δ 7.98–7.77 (m, 4 H), 7.70–7.52 (m, 4 H), 5.02 (d, *J* = 3.1 Hz, 6 H), 4.28–2.90 (m, 74 H); ^{13}C NMR δ 147.4, 147.3, 134.6, 133.3, 130.4, 130.1, 129.6, 100.9, 100.8, 100.6, 100.5, 100.4, 83.0, 82.9, 82.7, 82.5, 82.4, 82.2, 82.0, 81.6, 81.5, 81.3, 72.6, 69.7, 69.2, 62.4, 62.3, 62.2, 58.6, 58.5, 58.3, 30.2. Anal. Calcd for $C_{61}H_{92}O_{34}S_2$·1.5$CHCl_3$: C, 46.55; H, 5.84. Found: C, 46.64; H, 5.71.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]heptakis(2,3-di-*O*-methyl)-β-cyclodextrin (14). A solution of *p*-(allyloxy)phenol (5.73 g, 38.2 mmol) and 0.97 g (38.2 mmol) of sodium hydride in 100 mL of THF was refluxed for 30 min. A solid formed after concentration and this was added to a solution of 6.21 g (3.82 mmol) of **11** dissolved in 100 mL of DMF. The above solution was stirred at rt for 24 h. After concentration, the residue was partitioned between 200 mL of $CHCl_3$ and 100 mL of water. The organic layer was separated, dried, and concentrated. The crude product was subjected to column chromatography ($CHCl_3$–CH_3OH/20:1) to give 3.46 g (57%) of **14**: mp 145–147 °C; $[\alpha]^{25}_D$ +137.7° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.91–6.74 (m, 8 H), 6.02 (m, 2 H), 5.31 (m, 4 H), 5.07 (m, 7 H), 4.45 (m, 4 H), 4.35–3.30 (m, 77 H), 3.30–3.01 (m, 7 H); ^{13}C NMR δ 153.5, 153.3, 134.0, 117.9, 116.1, 115.9, 99.4, 99.2, 99.1, 99.0, 82.6, 82.4, 82.2, 82.1, 82.0, 81.8, 80.8, 80.7, 80.6, 73.0, 72.7, 72.6, 72.4, 71.4, 69.8, 68.5, 62.4, 62.1, 62.0, 61.9, 61.8, 61.6, 59.2, 59.0, 58.9. Anal. Calcd for $C_{74}H_{114}O_{37}$: C, 55.70; H, 7.20. Found: C, 55.78; H, 7.24.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]heptakis(2,3-di-*O*-pentyl)-β-cyclodextrin (15). A solution of **12** (0.80 g, 0.33 mmol) and sodium *p*-(allyloxy)phenoxide (0.57 g, 3.3 mmol) in 50 mL of DMF was stirred at rt for 24 h. The solvent was removed under reduced pressure and then was partitioned between $CHCl_3$ and water. The organic layer was separated, dried, and concentrated. The product was chromatographed ($CHCl_3$–CH_3OH/100:1) to give 0.41 g (52%) of **15**; mp 83–85 °C; $[\alpha]^{25}_D$ +93.6° (*c* 0.89, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.91–6.67 (m, 8 H), 6.02 (m, 2 H), 5.45–4.83 (m, 11 H), 4.50–4.31 (m, 74 H), 1.79–1.45 (m, 28 H), 1.45–1.10 (m, 56 H), 1.04–0.72 (m, 42 H); ^{13}C NMR δ 153.4, 134.2, 117.7, 116.1, 116.0, 99.0, 98.5, 98.2, 97.8, 97.5, 80.8, 80.7, 80.1, 74.9, 74.3, 74.0, 72.9, 72.6, 72.0, 71.8, 71.4, 68.2, 62.9, 62.1, 30.7, 30.4, 28.9, 28.7, 23.3, 23.1, 14.6. Anal. Calcd for $C_{130}H_{226}O_{37}$: C, 65.57; H, 9.57. Found: C, 65.37; H, 9.36.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]hexakis(2,3-di-*O*-methyl)-α-cyclodextrin (16). Compound **16** was prepared as above for **14** from 1.75 g (1.22 mmol) of **13**, 50 mL of DMF, and 12.2 mmol of sodium *p*-(allyloxy)phenoxide to give 0.95 g (56%) of **16**: mp 129–131 °C; $[\alpha]^{25}_D$ +134.1° (*c* 1.48 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.92–6.73 (m, 8 H), 6.13–5.90 (m, 2 H), 5.45–5.19 (m, 4 H), 5.16–4.91 (m, 6 H), 4.50–4.38 (m, 4 H), 4.38–3.36 (m, 66 H), 3.29–3.02 (m, 6 H); ^{13}C NMR δ 153.8, 153.7, 153.5, 134.2, 118.0, 116.4, 116.3, 116.1, 100.0, 99.8, 82.9, 82.8, 82.7, 82.6, 82.4, 82.2, 82.1, 73.2, 71.2, 70.0, 69.8, 62.9, 62.4, 58.7, 58.6. Anal. Calcd for $C_{66}H_{100}O_{32}$: C, 56.40; H, 7.17. Found: C, 56.03; H, 7.17.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-methylheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (17). NaH (95%, 240 mg, 7.95 mmol) was added at 0 °C to a solution of **14** (240 mg, 0.16 mmol) in 20 mL of DMF. The mixture was stirred

(22) König, W. A.; Icheln, D.; Runge, T.; Pforr, I.; Krebs, A. *J. High Resolut. Chromatogr.* **1990**, *13*, 702.

for 1 h at 0 °C, 24 h at rt, and then cooled to 0 °C. CH_3OH was added to decompose the excess hydride. The mixture was concentrated, and the residue was partitioned between $CHCl_3$ and water. The organic layer was separated, washed successively with water, aqueous $Na_2S_2O_3$, and water, dried, and concentrated. Column chromatography ($CHCl_3$–CH_3OH/200:1) of the product gave 222 mg (83%) of **17**: mp 125–126 °C; $[\alpha]^{25}_D$ +143.4° (*c* 0.96, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.74 (m, 8 H), 5.93 (m, 2 H), 5.24 (m, 4 H), 5.03 (m, 7 H), 4.32 (m, 4 H), 4.22–3.00 (m, 99 H); ^{13}C NMR δ 153.4, 153.3, 133.9, 117.7, 115.9, 115.8, 99.6, 99.5, 99.3, 82.5, 82.2, 81.1, 80.8, 80.6, 71.7, 71.4, 71.3, 70.9, 69.7, 62.0, 61.9, 61.8, 59.4, 59.3, 59.2, 59.0, 58.9, 58.8. Anal. Calcd for $C_{79}H_{124}O_{37}$: C, 56.96; H, 7.50. Found: C, 57.11; H, 7.71.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-pentylheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (18). A solution of **14** (0.60 g, 0.38 mmol) and NaH (95%, 0.48 g, 19 mmol) was stirred at rt for 2 h. The mixture was cooled to 0 °C and iodopentane (4.47 g, 23 mmol) was added dropwise. The mixture was stirred at 0 °C for 1 h and at rt for 24 h. After concentration under vacuum, the residue was partitioned between $CHCl_3$ and water. The organic layer was separated, washed twice with water, dried ($MgSO_4$), and concentrated under vacuum. The crude product was purified by column chromatography (benzene–C_2H_5OH/95:5) to give 0.34 g (48%) of **18** as white crystals: mp 80–82 °C; $[\alpha]^{25}_D$ +118.8° (*c* 0.97, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.90–6.68 (m, 8 H), 6.12–5.85 (m, 2 H), 5.44–4.97 (m, 11 H), 4.48–4.31 (m, 4 H), 4.26–2.87 (m, 94 H), 1.75–1.39 (m, 10 H), 1.39–0.99 (m, 20 H), 0.99–0.65 (15 H); ^{13}C NMR δ 153.5, 133.8, 118.0, 116.2, 116.1, 100.0, 99.8, 99.4, 82.9, 82.8, 82.5, 81.0, 80.2, 72.1, 72.0, 71.9, 71.0, 69.0, 68.2, 62.1, 59.0, 58.8, 30.0, 29.0, 23.1, 14.7. Anal. Calcd for $C_{99}H_{164}O_{37}$: C, 61.09; H, 8.49. Found: C, 61.18; H, 8.59.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-methylheptakis(2,3-di-*O*-pentyl)-β-cyclodextrin (19). Compound **19** was prepared as **17** above from 0.40 g (0.17 mmol) of **15**, 30 mL of DMF, 0.10 g (95%, 4.2 mmol) of NaH, and 0.31 mL (5.04 mmol) of CH_3I to give 0.11 g (25%) of **19** as an oil; $[\alpha]^{25}_D$ +99.7° (*c* 1.07, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.90–6.69 (m, 8 H), 6.13–5.89 (m, 2 H), 5.47–5.00 (m, 11 H), 4.53–4.37 (m, 4 H), 4.32–3.02 (m, 85 H), 1.75–1.46 (m, 28 H), 1.46–1.12 (m, 56 H), 1.04–0.77 (m, 42 H); ^{13}C NMR δ 153.7, 134.0, 117.8, 116.0, 98.9, 98.7, 98.6, 98.4, 81.0, 80.8, 80.6, 79.2, 74.5, 72.0, 71.8, 71.6, 71.5, 71.4, 71.2, 69.9, 69.6, 68.7, 68.5, 59.5, 59.4, 30.7, 30.4, 28.9, 28.7, 23.3, 23.1, 14.6. Anal. Calcd for $C_{135}H_{236}O_{37}$: C, 64.01; H, 9.46. Found: C, 63.73; H, 9.55.

$6^A,6^C$-[Di-*O*-*p*-(allyloxy)phenyl]-$6^B,6^D,6^E,6^F$-tetra-*O*-methylhexakis(2,3-di-*O*-methyl)-α-cyclodextrin (20). Compound **20** was prepared as **17** above from 0.9 g (0.64 mmol) of **16**, 30 mL of DMF, 0.37 g (95%, 15.4 mmol) of NaH, and 1.1 mL (18.4 mmol) of CH_3I to give 0.71 g (76%): mp 82–84 °C; $[\alpha]^{25}_D$ +150.2° (*c* 1.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.93–6.69 (m, 8 H), 6.15–5.90 (m, 2 H), 5.47–5.17 (m, 4 H), 5.14–4.90 (m, 6 H), 4.52–4.37 (m, 4 H), 4.28–2.90 (m, 84 H); ^{13}C NMR δ 153.5, 153.4, 134.0, 118.0, 117.9, 116.1, 115.9, 115.8, 100.6, 100.4, 98.2, 82.8, 82.7, 82.6, 82.5, 81.9, 81.8, 71.7, 71.5, 71.4, 69.9, 69.6, 62.3, 62.2, 59.4, 59.3, 58.5, 58.4. Anal. Calcd for $C_{70}H_{108}O_{32}$: C, 57.52; H, 7.45. Found: C, 57.24; H, 7.37.

$6^A,6^C$-Diazido-$6^A,6^C$-dideoxyheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (21). A solution of **11** (2.33 g, 1.43 mmol) in 50 mL of DMF and 1.12 g (17.2 mmol) of NaN_3 was stirred at 120 °C for 100 min. After cooling to 60 °C, the mixture was concentrated under vacuum. The residue was partitioned between $CHCl_3$ and water. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated. The product was purified by column chromatography ($CHCl_3$–CH_3OH/10:1) to give 1.62 g (81%) of **21**: mp 134–136 °C; $[\alpha]^{25}_D$ +151.8° (*c* 1.18, $CHCl_3$); IR 2101 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 5.09 (m, 7 H), 4.10–3.05 (m, 89 H); ^{13}C NMR δ 99.2, 99.0, 98.9, 98.8, 82.4, 82.1, 82.0, 81.9, 80.5, 79.6, 72.7, 72.6, 72.5, 71.5, 62.2, 62.1, 62.0, 61.9, 61.8, 61.7, 59.4, 59.2, 59.1, 59.0, 58.9, 52.2. Anal. Calcd for $C_{56}H_{96}N_6O_{33}$: C, 48.69; H, 7.01. Found: C, 48.45; H, 7.07.

$6^A,6^C$-Diazido-$6^A,6^C$-dideoxy-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-methylheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (22). A solution of **21** (2.10 g, 1.50 mmol) in 150 mL of DMF was treated with 1.89 g (95%, 75 mmol) of NaH, followed by 8 mL (128 mmol) of CH_3I. The mixture was treated as in the preparation of **17** above to give 1.20 g (55%) of **22**: mp 85–87 °C; $[\alpha]^{25}_D$ +148.5° (*c* 1.48, $CHCl_3$); IR 2101 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 5.04 (m, 7 H), 3.95–3.26 (m, 92 H), 3.20–3.03 (m, 7 H); ^{13}C NMR δ 99.8, 99.7, 99.4, 98.9, 82.6, 82.4, 82.2, 81.9, 80.8, 80.7, 80.5, 71.7, 71.4, 71.3, 61.9, 61.8, 59.4, 59.2, 59.0, 58.9, 52.5. Anal. Calcd for $C_{61}H_{106}N_6O_{33}$: C, 50.48; H, 7.36. Found: C, 50.21; H, 8.05.

$6^A,6^C$-Diamino-$6^A,6^C$-dideoxy-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-methylheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (23). A solution of **22** (0.97 g, 0.66 mmol) in 50 mL of ethanol containing 50 mg of platinum oxide was shaken at room temperature for 4 days under hydrogen (50 psi). The mixture was filtered through a Celite 545 pile and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by column chromatography ($CHCl_3$–CH_3OH–H_2O/50:10:1) to give 0.38 g (41%) of **23**: mp 107–108 °C; $[\alpha]^{25}_D$ +137.2° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.02 (m, 7 H), 3.93–3.25 (m, 92 H), 3.17–3.00 (m, 7 H), 2.67 (s, 4 H); ^{13}C NMR δ 99.4, 99.2, 99.1, 98.6, 82.9, 82.4, 82.1, 81.9, 81.8, 81.7, 81.5, 81.0, 80.6, 80.5, 80.4, 72.0, 71.8, 71.5, 71.4, 71.2, 61.9, 61.7, 61.6, 59.6, 59.5, 59.4, 59.2, 59.0, 58.8, 42.7. Anal. Calcd for $C_{61}H_{110}N_2O_{33}\cdot 4H_2O$: C, 49.79; H, 8.08. Found: C, 49.75; H, 7.64.

$6^A,6^C$-Bis[[*p*-(allyloxy)benzoyl]amino]-$6^A,6^C$-dideoxy-$6^B,6^D,6^E,6^F,6^G$-penta-*O*-methylheptakis(2,3-di-*O*-methyl)-β-cyclodextrin (24). A solution of *p*-(allyloxy)benzoyl chloride (216 mg, 1.08 mmol) in 30 mL of toluene was added dropwise to a stirring solution of 0.38 g (0.27 mmol) of **23** and 0.11 g (1.08 mmol) of $(C_2H_5)_3N$ in 30 mL of toluene at rt over 1 h. The mixture was stirred 24 h at rt. The mixture was diluted with 150 mL of toluene and washed twice with water. The organic layer was dried ($MgSO_4$) and concentrated. The residue was subjected to column chromatography (C_6H_6–C_2H_5OH/20:1, then 15:1) to give white solid **24** (0.33 g, 71%); mp 118–120 °C; $[\alpha]^{25}_D$ +107.6° (*c* 1.60, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.67, 7.62 (d, J = 6.9 Hz, 4 H), 7.06 (s, 2 H), 6.95–6.59 (m, 4 H), 6.06–5.80 (m, 2 H), 5.40–5.12 (m, 4 H), 5.12–4.90 (m, 7 H), 4.56–4.36 (m, 4 H), 4.15–2.94 (m, 99 H); ^{13}C NMR δ 167.3, 161.7, 161.3, 133.1, 132.9, 131.8, 129.3, 129.1, 127.4, 118.5, 188.3, 114.9, 114.8, 114.5, 99.3, 99.2, 99.1, 82.7, 82.5, 82.4, 82.3, 82.2, 82.1, 81.9, 80.8, 71.7, 71.5, 71.4, 71.3, 69.2, 69.1, 62.1, 62.0, 61.9, 61.8, 59.8, 59.4, 59.1, 59.0, 58.9, 58.7. Anal. Calcd for $C_{81}H_{126}N_2O_{37}$: C 56.57; H, 7.38. Found: C, 56.27; H, 7.94.

General Procedure for the Preparation of Cyclodextrin–Oligosiloxane Copolymers 25–29. A typical synthetic procedure is given for copolymer **25**. **17** (70 mg, 0.042 mmol), 1,1,3,3,5,5,7,7,9,9,11,11-dodecamethylhexasiloxane (19.5 mg, 0.045 mmol), 1 μL (0.73 mg, 0.0065 mmol) of 1-octene (for endcapping), and 5 mL of toluene were placed in a 50-mL Teflon centrifuge tube. Parafilm was placed around the cap to keep out moisture. The mixture was left in an oil bath at 85–90 °C for 1 h. Then 8 μL of 1% H_2PtCl_6 (in THF–C_2H_5OH) was added. The mixture was stirred at 85–90 °C for 72 h. The toluene was evaporated in a stream of N_2. The residue was dissolved in 10 mL of CH_2Cl_2, and 10 mL of CH_3OH was added followed by 10 mL of water. The mixture was centrifuged and the water layer was removed. This process was repeated three more times. The CH_2Cl_2 was evaporated and the residue was dried under vacuum for 10 h at 60 °C to give 0.13 g (81%) of **25**. The IR spectrum of the copolymer had no peak at 2154 cm^{-1} (Si–H). The proton NMR spectrum of **25** indicated the structure shown in Scheme II. The other copolymers were prepared in a like manner.

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