Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 429–437

TETRAHEDRON: *ASYMMETRY*

Synthesis of chiral calix[4]arenes bearing tartaric ester moieties

Hu-Shan Yuan and Zhi-Tang Huang *

Institute of Chemistry, The Chinese Academy of Sciences, Beijing, 100080, People's Republic of China

Received 6 November 1998; accepted 15 December 1998

Abstract

The synthesis of chiral calix[4]arenes with tartaric acid ester moieties has been achieved by the reactions of tartaric ester chloroacetates with calix[4]arenes in moderate yields. All the chiral calix[4]arene derivatives are in a cone conformation according to the ^{1}H NMR doublet–doublet pattern of the protons of the methylene groups between the phenol rings. The results of NMR and specific rotations indicate that the molecules have C_2 symmetry with asymmetric features.

1. Introduction

Calixarenes are macrocyclic compounds with defined cavities, having host–guest complexation properties similar to cyclodextrins. Compared with cyclodextrins, the parent calixarenes have limited chiral recognition abilities though they can be prepared on a large scale. In order to provide them with asymmetric features, many approaches have been applied to the chiral modifications of calixarenes.

Chiral calixarenes are classified into two categories which include those bearing the inherently chiral structure and those bearing chiral substituents. As to the former, it means that the molecules are built from the achiral phenol subunits. They owe their chirality to the fact that the molecules are not planar. The first example of optically resolved inherently chiral structure was reported by S. Shinkai et al. [1] The procedures involved the preparation of an asymmetrically conformationally rigidified backbone of calix[4]arene with a *meta*-substituent and the resolution of optical isomers by chiral HPLC. Other groups had also reported their work on the syntheses of inherently asymmetric structures, however, they have not yet been resolved to optical isomers.[2–4] When the substituents are asymmetrically arranged in one rigidified conformer of calixarene in the upper rim and/or lower rim, the inherent chirality can also be generated.[5–10] Recently, more challenging work was carried out to generate inherent chirality on the skeletons of calix[6]arene[11] and calix[8]arene,[12,13] but the severe limitation suffered by this inherent chirality still exists due to the difficulties met in the resolution of the racemates. Until now, the

* Corresponding author. Fax: 86-10-62559373; e-mail: huangzt@public.bta.net.cn

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00007-5

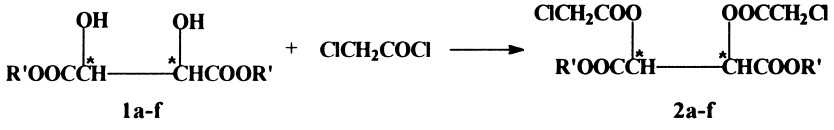
successful examples for optical resolution have been very limited.[1,7–9,11] It is noticeable that a recent report regarding the lipase-catalyzed transesterification of achiral calixarene provides a new way of synthesizing inherently chiral calixarenes with high enantiomeric excess.[14]

The second category of chiral calixarene, calixarenes bearing chiral substituents, appears to be preferable when chiral derivatizing agents are available to be introduced into the skeleton of calixarenes. Shinkai et al. first attained this kind of chiral calixarene compound by this idea.[15–18] Since then, amino acids,[19,20] sugars,[21–23] 1,1′-bi-2-naphthol,[24,25] glycidyl[26] and other chiral residues have been effectively attached to the platform of calixarenes and homotrioxacalix[3]arene. It is encouraging that the recognition,[27,28] separation[29] and analysis[30] of enantiomers with this kind of chiral calixarene have been accomplished recently. In order to find novel chiral calixarene derivatives with some specific properties, the present study describes the use of tartaric esters introduced into the lower rim of calix[4]arene derivatives.

2. Results and discussion

2.1. Synthesis of intermediates *2a–f*

The reactions of the esters of tartaric acid **1a–f** with chloroacetyl chloride afforded the useful intermediates **2a–f** in satisfactory yields (Scheme 1). The reaction was carried out at 0–5°C in the presence of pyridine to bind the hydrogen chloride formed in situ to inhibit the racemization of the unreacted **1**.



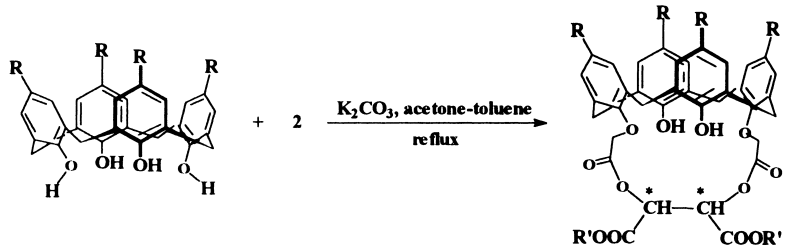
a: (L-),R'=Et; **b:** (L-), R'=n-Pr; **c:** (L-), R'=i-Pr;
d: (L-), R'=n-Bu; **e**: (D-), R'=Et; **f**: (D-), R'=i-Pr

Scheme 1.

2.2. Synthesis of *6–8*

Intermediates **2a–f** were intramolecularly distally connected to the lower rim of calix[4]arenes by the reactions of compounds **3–5** with **2a–f** in the presence of anhydrous K_2CO_3 in a mixture of anhydrous acetone and toluene to give the expected products **6–8** in moderate yields (Scheme 2). The reactants were refluxed for 48 hours under the protection of Ar. Although longer reaction times increased the yields slightly, some unknown side reactions resulted in a more complicated mixture which was not convenient to separate. In addition, dehydration of the base and solvent was indispensable to provide a better yield.

Compounds **6–8** are asymmetric due to the formation of the chiral sub-ring on the lower rim of calix[4]arenes. The stereogenic centers make the two methylenes attached to the same phenol ring non-equivalent. There are two signals for them in the ^{13}C NMR spectra of compounds **6–8**. It is noticeable that the signals of these protons appear to be two pairs of AB systems around 3.4 ppm and 4.2 ppm, and that the protons of the methylenes attached to the phenol oxygen show an AB system coupling pattern around 4.68 ppm. In addition, the introduction of the stereogenic center damages the planar symmetry of the phenyl rings, which results in 12 aromatic carbon signals appearing in the ^{13}C NMR



3 - 5 **6 - 8**

3, 6: R = H; **4, 7:** R = t-Bu; **5, 8:** R = $CH_2CH{=}CH_2$

Scheme 2.

spectra of compounds **6**–**8**. The two pairs of ^{1}H NMR doublet–doublets for the protons of the methylenes between the phenol rings indicate that compounds **6**–**8** bear only the cone conformation instead of other typical conformations (1,2-alternate, 1,3-alternate, and partial cone). Based on the above observations, it is concluded that compounds **6**–**8** are asymmetric molecules with C_2 symmetry in cone conformations.

3. Conclusion

In summary, the useful intermediates, tartaric ester chloroacetates **2a**–**f**, can be easily prepared by the reactions of chloroacetyl chloride with esters of tartaric acid **1a**–**f**. Attaching of these chiral fragments to the platforms of calix[4]arenes affords a new kind of chiral calix[4]arene derivatives **6**–**8**. All the structures rest on the data of microanalysis, IR, ^{1}H NMR, ^{13}C NMR and MS spectra. Further investigations on their molecular recognition properties and asymmetric auxiliary behavior are in progress.

4. Experimental

4.1. General

Melting points are uncorrected. Mass spectra were recorded on a Finnigan MAT 90, an AEI MS-50, and a KYKY-ZHP-5 mass spectrometer. IR spectra (liquid film and KBr tablet) were recorded on a Perkin–Elmer 782 spectrometer. NMR spectra were recorded on a Varian Unit-200 spectrometer. Specific rotations were measured on a Perkin–Elmer 241 MC polarimeter. Microanalyses were carried out by the Analytical Laboratory of the Institute.

*4.2. General procedure for the synthesis of compounds **2a**–**f***

A solution of 42 mmol of chloroacetyl chloride in 15 ml of chloroform was added dropwise into a mixture of 20 mmol of **1a**–**f**, 42 mmol of pyridine and 15 ml of chloroform at the ice bath temperature. After the addition, the mixture was stirred for an additional 5 h at room temperature. The resulting mixture was washed with brine three times, then the organic layer was dried over $MgSO_4$. Removal of the solvent under vacuum gave a sticky residue. After silica gel chromatographic separation (petroleum ether–ethyl acetate), a colorless oil was obtained for **2a**–**b** and **2d**–**e**, and crystals for **2c** and **2f** from petroleum ether.

*4.2.1. (2*R,*3*R*)-2,3-Di-(2-chloroacetoxy)-diethyl succinate* ***2a***

Yield, 85.2%; oil; $[\alpha]_D^{20}$ +10.1 (c, 7.9, EtOAc); IR (cm^{-1}) (film): 1775, 1765 (OCO); MS (FAB): 359 ($[M+1]^+$, 56). Anal. calcd for $C_{12}H_{16}Cl_2O_8$: C, 40.13, H, 4.49. Found: C, 40.18, H, 4.59. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.29 (t, *J*=7.6, 6H, C*H*$_3$), 4.19 (s, 4H, ClC*H*$_2$CO), 4.25 (q, *J*=7.6, 4H, OC*H*$_2$CH$_3$), 5.81 (s, 2H, C*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.8, 39.9, 62.6, 71.5, 164.6, 166.0.

*4.2.2. (2*R,*3*R*)-2,3-Di-(2-chloroacetoxy)-dipropyl succinate* ***2b***

Yield, 90.5%; oil; $[\alpha]_D^{20}$ +14.7 (c, 9.3, EtOAc); IR (cm^{-1}) (film): 1775, 1760 (OCO); MS (EI): 387 ($[M+1]^+$, 1). Anal. calcd for $C_{14}H_{20}Cl_2O_8$: C, 43.42, H, 5.21. Found: C, 43.40, H, 4.96. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.92 (t, *J*=5.6, 6H, C*H*$_3$), 1.64 (hex, *J*=5.6, 4H, CH$_2$C*H*$_2$CH$_3$), 4.17 (s, 4H, ClC*H*$_2$CO), 4.18 (t, *J*=5.6, 4H, OC*H*$_2$), 5.82 (s, 2H, C*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 9.9, 21.6, 39.9, 68.0, 71.5, 164.6, 165.9.

*4.2.3. (2*R,*3*R*)-2,3-Di-(2-chloroacetoxy)-di-(1-methylethyl) succinate* ***2c***

Yield, 84.0%; mp: 99–100°C; $[\alpha]_D^{20}$ +13.4 (c, 5.4, EtOAc); IR (cm^{-1}) (KBr): 1778, 1748 (OCO); MS (FAB): 387 ($[M+1]^+$, 20). Anal. calcd for $C_{14}H_{20}Cl_2O_8$: C, 43.42, H, 5.21. Found: C, 43.18, H, 5.19. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.22 (d, *J*=7.6, 6H), 1.30 (d, *J*=7.6, 6H, CH(C*H*$_3$)), 4.14, 4.20 (AB, *J*=12.0, 4H, ClC*H*$_2$CO), 5.08 (hep, *J*=7.6, 2H, C*H*(CH$_3$)), 5.80 (s, 2H, OC*H*CO); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.2, 21.3, 39.8, 70.8, 71.5, 164.0, 165.9.

*4.2.4. (2*R,*3*R*)-2,3-Di-(2-chloroacetoxy)-dibutyl succinate* ***2d***

Yield, 84.6%; oil; $[\alpha]_D^{20}$ +15.2 (c, 6.3, EtOAc); IR (cm^{-1}) (film): 1775, 1758 (OCO); MS (FAB): 415 ($[M+1]^+$, 38). Anal. calcd for $C_{16}H_{24}Cl_2O_8$: C, 46.27, H, 5.83. Found: C, 46.57, H, 5.88. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.92 (t, *J*=7.1, 6H, C*H*$_3$), 1.34 (hex, *J*=7.3, 4H, C*H*$_2$CH$_3$), 1.60 (hex, 4H, *J*=5.7, C*H*$_2$CH$_2$CH$_3$), 4.18 (s, 4H, ClC*H*$_2$CO), 4.20 (t, *J*=6.1, 4H, OC*H*$_2$), 5.81 (s, 2H, C*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.2, 18.6, 30.1, 39.9, 66.2, 71.5, 164.6, 165.9.

*4.2.5. (2*S,*3*S*)-2,3-Di-(2-chloroacetoxy)-diethyl succinate* ***2e***

Yield, 87.3%; oil; $[\alpha]_D^{20}$ −10.4 (c, 2.9, EtOAc); IR (cm^{-1}) (film): 1775, 1758 (OCO); MS (FAB): 359 ($[M+1]^+$, 58). Anal. calcd for $C_{12}H_{16}Cl_2O_8$: C, 40.13, H, 4.49. Found: C, 40.41, H, 4.59. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.29 (t, *J*=7.6, 6H, C*H*$_3$), 4.18 (s, 4H, ClC*H*$_2$CO), 4.26 (q, *J*=7.6, 4H, OC*H*$_2$CH$_3$), 5.81 (s, 2H, C*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.9, 40.0, 62.7, 71.6, 164.7, 165.1.

*4.2.6. (2*S,*3*S*)-2,3-Di-(2-chloroacetoxy)-di-(1-methylethyl) succinate* 2f

Yield, 82.7%; mp: 99–100°C; $[\alpha]_D^{20}$ −13.2 (c, 4.1, EtOAc); IR (cm^{-1}) (KBr): 1778, 1745 (OCO); MS (FAB): 387 ($[M+1]^+$, 18). Anal. calcd for $C_{14}H_{20}Cl_2O_8$: C, 43.42, H, 5.21. Found: C, 43.38, H, 5.18. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.23 (d, *J*=7.6, 6H), 1.30 (d, *J*=7.6, 6H, CH(C*H*$_3$)$_2$), 4.15, 4.21 (AB, 4H, *J*=12.0, ClC*H*$_2$CO), 5.11 (hep, *J*=7.6, 2H, C*H*(CH$_3$)$_2$), 5.80 (s, 2H, OC*HCO*); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.3, 21.4, 39.9, 70.9, 71.6, 164.1, 166.0.

4.3. General procedure for the synthesis of compounds ***6–8***

A mixture of 1 mmol of **3**–**5**, 1.25 mmol of **2a**–**f**, 1 mmol of anhydrous K_2CO_3, and 2 mmol of KI in 25 ml of anhydrous acetone and 10 ml of toluene was refluxed under the protection of Ar for 48 h. After removal of solvent, chloroform (50 ml) was added to the residue and washed with brine three times, then dried over $MgSO_4$. After removal of chloroform, the crude product was purified by

silica gel chromatography (petroleum ether–dichloromethane–acetone), and the pure sample of **6–8** was recrystallized from dichloromethane and methanol.

4.3.1. (4′R,5′R)-25,27-Dihydroxy-26,28-(4′,5′-diethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6a***

Yield: 24.0%; mp: >300°C, $[\alpha]_D^{20}$ +25.8 (c 0.74, $CHCl_3$); IR (cm^{-1}): 3385 (OH), 1765, 1755 (OCO); MS (FD): 710 (M^+). Anal. calcd for $C_{40}H_{38}O_{12}$: C, 67.60, H, 5.39. Found: C, 67.39, H, 5.56. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.17 (t, *J*=5.3, 6H, C*H*$_3$), 3.37 (d, *J*=12.9, 2H), 3.47 (d, *J*=12.9, 2H), 4.22 (d, *J*=12.9, 2H), 4.23 (d, *J*=12.9, 2H) (ArC*H*$_2$Ar), 4.18 (q, *J*=5.3, 4H, OC*H*$_2$), 4.68, 4.80 (AB, *J*=16.9, 4H, OC*H*$_2$CO), 6.29 (s, 2H, OC*H*), 6.58–7.09 (m, 12H, Ar*H*), 8.07 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.8, 31.1, 31.5, 62.8, 71.3, 71.7, 118.8, 126.4, 127.0, 127.8, 128.4, 128,5, 129.1, 129.4, 133.0, 133.7, 149.8, 153.5, 165.7, 166.8.

4.3.2. (4′R,5′R)-25,27-Dihydroxy-26,28-(4′,5′-dipropoxycarbonyl-3′,6′-di-oxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6b***

Yield: 30.7%; mp: 283.5–285.0°C, $[\alpha]_D^{20}$ +27.1 (c 0.38, $CHCl_3$); IR (cm^{-1}): 3420 (OH), 1755, 1735 (OCO); MS (FD): 738 (M^+). Anal. calcd for $C_{42}H_{42}O_{12}$: C, 68.28, H, 5.73. Found: C, 68.31, H, 5.73. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.87 (t, *J*=5.3, 6H, C*H*$_3$), 1.57 (hex, *J*=5.4, 4H, C*H*$_2$CH$_3$), 3.35 (d, *J*=12.4, 2H, 3.46 (d, *J*=12.4, 2H), ArC*H*$_2$Ar), 3.96–4.26 (m, 8H, ArC*H*$_2$Ar, OC*H*$_2$CH$_2$), 4.67, 4.79 (AB, *J*=13.8, 4H, OC*H*$_2$CO), 6.32 (s, 2H, OC*H*), 6.58–7.08 (m, 12H, Ar*H*), 8.07 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 10.2, 21.8, 31.1, 31.5, 68.2, 71.3, 71.7, 118.8, 126.4, 126.9, 127.8, 128.4, 128.5, 129.1, 129.4, 133.0, 133.6, 149.8, 153.5, 165.7, 166.9.

4.3.3. (4′R,5′R)-25,27-Dihydroxy-26,28-(4′,5′-di-1-methylethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6c***

Yield: 20.4%; mp: 278.0–280.0°C, $[\alpha]_D^{20}$ +21.5° (c 0.5, $CHCl_3$); IR (cm^{-1}): 3410 (OH), 1745, 1730 (OCO); MS (FD): 738 (M^+). Anal. calcd for $C_{42}H_{42}O_{12}$: C, 68.28, H, 5.73. Found: C, 67.76, H, 5.68. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.13 (d, *J*=6.1, 6H), 1.21 (d, *J*=6.1, 6H, CH(C*H*$_3$)$_2$), 3.35 (d, *J*=11.8, 2H), 3.47 (d, *J*=11.8, 2H), 4.18 (d, *J*=11.8, 2H), 4.24 (d, *J*=11.8, 2H, ArC*H*$_2$Ar), 4.67, 4.77 (AB, *J*=16.5, 4H, OC*H*$_2$CO), 5.09 (hep, *J*=6.1, 2H, OC*H*Me$_2$), 6.26 (s, 2H, OC*H*), 6.59–7.06 (m, 12H, Ar*H*), 8.07 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.1, 21.5, 31.1, 31.5, 71.0, 71.5, 71.6, 118.7, 126.4, 126.8, 127.8, 128.4, 128.5, 129.1, 129.3, 132.9, 133.6, 149.7, 153.4, 165.2, 166.8.

4.3.4. (4′R,5′R)-25,27-Dihydroxy-26,28-(4′,5′-dibutoxycarbonyl-3′,6′-di-oxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6d***

Yield: 24.8%; mp: 252.5–254.5°C, $[\alpha]_D^{20}$ +23.5 (c 0.21, $CHCl_3$), IR (cm^{-1}): 3410 (OH), 1758, 1540 (OCO); MS (FD): 766 (M^+). Anal. calcd for $C_{44}H_{46}O_{12}$: C, 68.91, H, 6.06. Found: C, 68.77, H, 6.06. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.79 (t, *J*=5.0, 6H, C*H*$_3$), 1.29 (hex, *J*=7.1, 4H, C*H*$_2$), 1.52 (quin, *J*=7.1, 4H, C*H*$_2$), 3.36 (d, *J*=11.5, 2H), 3.45 (d, *J*=11.5, 2H, ArC*H*$_2$Ar), 4.00–4.30 (m, 8H, OC*H*$_2$, ArC*H*$_2$Ar), 4.67, 4.78 (AB, *J*=15.0, 4H, OC*H*$_2$CO), 6.31 (s, 2H, OC*H*), 6.53–7.05 (m, 12H, Ar*H*), 8.07 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.5, 18.8, 30.3, 31.1, 31.5, 66.6, 71.3, 71.7, 118.8, 126.3, 126.9, 127.8, 128.4, 128.5, 129.1, 129.4, 132.9, 133.6, 149.7, 153.5, 165.8, 166.8.

4.3.5. (4′S,5′S)-25,27-Dihydroxy-26,28-(4′,5′-diethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6e***

Yield: 23.8%; mp: >300°C, $[\alpha]_D^{20}$ −24.9 (c 0.37, $CHCl_3$); IR (cm^{-1}): 3400 (OH), 1765, 1755 (OCO); MS (MALDI-TOF): 710 (M^+). Anal. calcd for $C_{40}H_{38}O_{12}$: C, 67.60, H, 5.39. Found: C, 67.67, H, 5.77. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.17 (t, *J*=5.3, 6H, C*H*$_3$), 3.36 (d, *J*=12.9, 2H), 3.47 (d, *J*=12.9, 2H), 4.22 (d, *J*=12.9, 2H), 4.23 (d, *J*=12.9, 2H) (ArC*H*$_2$Ar), 4.18 (q, *J*=5.3, 4H, OC*H*$_2$), 4.68, 4.80 (AB, *J*=16.9, 4H, OC*H*$_2$CO), 6.28 (s, 2H, OC*H*), 6.58–7.09 (m, 12H, Ar*H*), 8.07 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.6, 31.2, 31.5, 62.8, 71.3, 71.7, 118.8, 126.4, 127.0, 127.8, 128.4, 128,5, 129.2, 129.4, 133.0, 133.7, 149.8, 153.5, 165.7, 166.8.

4.3.6. (4′S,5′S)-25,27-Dihydroxy-26,28-(4′,5′-di-1-methylethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene ***6f***

Yield: 21.9%; mp: 278.0–279.0°C, $[\alpha]_D^{20}$ −23.0 (c 0.27, $CHCl_3$); IR (cm^{-1}): 3410 (OH), 1745, 1730 (OCO); MS (MALDI-TOF): 738 (M^+). Anal. calcd for $C_{42}H_{42}O_{12}\cdot 0.25CH_2Cl_2$:[31] C, 66.53, H, 5.62. Found: C, 66.32, H, 5.48. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.12 (d, *J*=6.1, 6H), 1.22 (d, *J*=6.1, 6H, CH(C*H*$_3$)$_2$), 3.35 (d, *J*=11.8, 2H), 3.47 (d, *J*=11.8, 2H), 4.18 (d, *J*=11.8, 2H), 4.24 (d, *J*=11.8, 2H), (ArC*H*$_2$Ar), 4.67, 4.77 (AB, *J*=16.5, 4H, OC*H*$_2$CO), 5.08 (hep, *J*=6.1, 2H, OC*H*Me$_2$), 6.28 (s, 2H, OC*H*), 6.59–7.06 (m, 12H, Ar*H*), 8.06 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.2, 21.5, 31.1, 31.5, 71.0, 71.5, 71.7, 118.8, 126.4, 126.9, 127.8, 128.5, 128.6, 129.1, 129.4, 133.0, 133.6, 149.8, 153.4, 165.3, 166.8.

4.3.7. (4′R,5′R)-5,11,17,23-Tetra-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-diethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***7a***

Yield: 19.3%; mp: >300°C; $[\alpha]_D^{20}$ +26.6 (c 1.12, $CHCl_3$); IR (cm^{-1}): 3433 (OH), 1765, 1755 (OCO); MS (FD): 934 (M^+). Anal. calcd for $C_{56}H_{70}O_{12}$: C, 71.92, H, 7.55. Found: C, 71.74, H, 7.17. ^{1}H NMR ($CDCl_3$), δ (ppm) 1.15 (s, 18H, C(C*H*$_3$)$_3$), 1.18 (t, *J*=7.0, 6H, OCH$_2$C*H*$_3$), 1.22 (s, 18H, C(C*H*$_3$)$_3$), 3.31, (d, *J*=12.6, 2H), 3.39 (d, *J*=12.6, 2H), 4.22 (d, *J*=12.6, 2H), 4.23 (d, *J*=12.6, 2H, ArC*H*$_2$Ar), 4.18 (q, *J*=7.0, 4H, OC*H*$_2$CH$_3$), 4.63, 4.73 (AB, *J*=16.4, 4H, OC*H*$_2$CO), 6.25 (s, 2H, C*H*), 6.97–7.06 (m, 8H, Ar*H*), 7.88 (s, 2H, O*H*). ^{13}C NMR ($CDCl_3$), δ (ppm) 13.8, 31.1, 31.6, 31.8, 32.2, 33.7, 34.2, 62.7, 71.2, 71.7, 125.2, 125.3, 125.8, 126.1, 126.4, 127.3, 132.7, 133.3, 141.1, 147.9, 148.1, 151.0, 165.8, 167.1.

4.3.8. (4′R,5′R)-5,11,17,23-Tetra-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-dipropoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***7b***

Yield: 25.5%; mp: 285–286°C, $[\alpha]_D^{20}$ +22.2 (c 0.12, $CHCl_3$); IR (cm^{-1}): 3430 (OH), 1765, 1755 (OCO); MS (FD): 962 (M^+). Anal. calcd for $C_{58}H_{74}O_{12}$: C, 72.32, H, 7.74. Found: C, 72.33, H, 7.56. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.87 (t, *J*=8.0, 6H, C*H*$_3$), 1.14 (s, 18H, *t*-Bu), 1.23 (s, 18H, *t*-Bu), 1.59 (hex, *J*=5.5, 4H, C*H*$_2$CH$_3$), 3.31 (d, *J*=13.3, 2H), 3.40 (d, *J*=13.3, 2H), 4.00 (d, *J*=13.3, 2H), 4.23 (d, *J*=13.3, 2H), (ArC*H*$_2$Ar), 4.19 (t, *J*=5.4, 4H, OC*H*$_2$CH$_2$), 4.63, 4.74 (AB, *J*=15.1, 4H, OC*H*$_2$CO), 6.25 (s, 2H, OCH), 6.97–7.07 (m, 8H, Ar*H*), 7.89 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 10.2, 21.7, 31.1, 31.6, 31.9, 32.2, 33.7, 34.2, 68.2, 71.2, 71.7, 125.2, 125.3, 125.8, 126.1, 126.4, 127.2, 132.7, 133.2, 141.1, 147.8, 148.2, 151.0, 165.8, 167.1.

4.3.9. (4′R,5′R)-5,11,17,23-Tetra-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-di-1-methylethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]-arene* ***7c***

Yield: 27.0%; mp: 287.5–289.0°C, $[\alpha]_D^{20}$ +22.7 (c 0.47 $CHCl_3$); IR (cm^{-1}): 3430 (OH), 1765, 1745 (OCO); MS (FD): 962 (M^+). Anal. calcd for $C_{58}H_{74}O_{12}$: C, 72.32, H, 7.74: Found: C, 72.35, H, 7.27.

^{1}H NMR ($CDCl_3$): δ (ppm): 1.03 (s, 18H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.05 (d, *J*=6.0, 6H), 1.23 (d, *J*=6.0, 6H, $CH(CH_3)_2$), 3.29 (d, *J*=12.0, 2H), 3.40 (d, *J*=12.0, 2H), 4.14 (d, *J*=12.0, 2H), 4.22 (d, *J*=12.0, 2H, $ArCH_2Ar$), 4.62, 4.73 (AB, *J*=18.0, 4H, OCH_2CO), 5.08 (hep, *J*=6.0, 2H, $OCHMe_2$), 6.24 (s, 2H, OC*H*), 6.96–7.06 (m, 8H, Ar*H*), 7.90 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.2, 21.5, 31.1, 31.6, 31.8, 32.2, 33.7, 34.2, 70.9, 71.4, 71.6, 125.2, 125.3, 125.8, 126.1, 126.3, 127.2, 132.7, 133.2, 141.0, 147.8, 148.1, 151.0, 165.2, 167.1.

*4.3.10. (4′*R,*5′*R*)-5,11,17,23-Tetra*-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-dibutoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***7d***

Yield: 10.5%; mp: 229.5–231.5°C, $[\alpha]_D^{20}$ +22.2 (c 0.11, $CHCl_3$); IR (cm^{-1}): 3430 (OH), 1765, 1750 (OCO); MS (FD): 990 (M^+). Anal. calcd for $C_{60}H_{78}O_{12}$: C, 72.70, H, 7.93. Found: C, 72.66, H, 7.97. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.78 (t, *J*=6.5, 6H, CH_3), 1.12 (s, 18H, *t*-Bu), 1.23 (s, 18H, *t*-Bu), 1.29 (hex, *J*=7.2, 4H, CH_2CH_3), 1.52 (quin, *J*=5.5, 4H, CH_2), 3.30 (d, *J*=12.6, 2H), 3.40 (d, *J*=12.6, 2H), ($ArCH_2Ar$), 4.00–4.29 (m, 8H, $ArCH_2Ar$, OCH_2), 4.63, 4.73 (AB, *J*=16.5, 4H, OCH_2CO), 6.27 (s, 2H, OC*H*), 6.84–7.02 (m, 8H, Ar*H*), 7.89 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 13.5, 18.8, 30.4, 31.1, 31.7, 31.8, 32.3, 33.7, 34.2, 66.6, 71.2, 71.7, 125.2, 125.3, 125.8, 126.1, 126.3, 127.2, 132.7, 133.3, 141.1, 147.9, 148.0, 151.0, 166.0, 167.0.

*4.3.11. (4′*S,*5′*S*)-5,11,17,23-Tetra*-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-di-ethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* 7e

Yield: 20.9%; mp: >300°C; $[\alpha]_D^{20}$ −25.8 (c 0.6, $CHCl_3$) ; IR (cm^{-1}): 3430 (OH), 1765, 1755 (OCO); MS (MALDI-TOF): 934 (M^+). Anal. calcd for $C_{56}H_{70}O_{12}$: C, 71.92, H, 7.55. Found: C, 71.60, H, 7.37. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.15 (s, 18H, $C(CH_3)_3$), 1.18 (t, *J*=6.3, 6H, OCH_2CH_3), 1.22 (s, 18H, $C(CH_3)_3$), 3.31, (d, *J*=12.6, 2H), 3.39 (d, *J*=12.6, 2H), 4.22 (d, *J*=12.6, 2H), 4.23 (d, *J*=12.6, 2H, $ArCH_2Ar$), 4.18 (q, *J*=6.3, 4H, OCH_2CH_3), 4.63, 4.73 (AB, *J*=16.4, 4H, OCH_2CO), 6.25 (s, 2H, C*H*), 6.97–7.06 (m, 8H, Ar*H*), 7.88 (s, 2H, O*H*). ^{13}C NMR ($CDCl_3$), δ (ppm) 13.8, 31.1, 31.6, 31.9, 32.2, 33.7, 34.2, 62.7, 71.3, 71.7, 125.2, 125.3, 125.8, 126.1, 126.5, 127.3, 132.7, 133.3, 141.2, 147.9, 148.2, 151.0, 165.8, 167.1.

*4.3.12. (4′*S,*5′*S*)-5,11,17,23-Tetra*-tert-*butyl-25,27-dihydroxy-26,28-(4′,5′-di-1-methylethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***7f***

Yield: 30.0%; mp: 289.0–290.0°C (dec.), $[\alpha]_D^{20}$ −24.5 (c 0.54 $CHCl_3$); IR (cm^{-1}): 3420 (OH), 1760, 1745 (OCO); MS (MALDI-TOF): 962 (M^+). Anal. calcd for $C_{58}H_{74}O_{12}$: C, 72.32, H, 7.74. Found: C, 72.44, H, 7.80. ^{1}H NMR ($CDCl_3$), δ (ppm): 1.03 (s, 18H, *t*-Bu), 1.22 (s, 18H, *t*-Bu), 1.05 (d, *J*=6.0, 6H), 1.23 (d, *J*=6.0, 6H) ($CH(CH_3)_2$), 3.29 (d, *J*=12.0, 2H), 3.40 (d, *J*=12.0, 2H), 4.14 (d, *J*=12.0, 2H), 4.22 (d, *J*=12.0, 2H, $ArCH_2Ar$), 4.62, 4.73 (AB, *J*=18.0, 4H, OCH_2CO), 5.08 (hep, *J*=6.0, 2H, $OCHMe_2$), 6.23 (s, 2H, OC*H*), 6.96–7.06 (m, 8H, Ar*H*), 7.89 (s, 2H, O*H*); ^{13}C NMR ($CDCl_3$), δ (ppm): 21.2, 21.5, 31.1, 31.6, 31.8, 32.2, 33.7, 34.2, 70.9, 71.4, 71.6, 125.2, 125.3, 125.8, 126.1, 126.3, 127.2, 132.7, 133.3, 141.1, 147.8, 148.1, 151.0, 165.2, 167.1.

*4.3.13. (4′*R,*5′*R*)-5,11,17,23-Tetra-allyl-25,27-dihydroxy-26,28-(4′,5′-di-ethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***8a***

Yield: 16.2%; mp: 184.0–185.0°C; $[\alpha]_D^{20}$ +27.9 (c 0.78 $CHCl_3$); IR (cm^{-1}): 3410 (OH), 1765, 1753 (OCO); MS (FD): 870 (M^+). Anal. calcd for $C_{52}H_{54}O_{12}$: C, 71.71, H, 6.25. Found: C, 71.65, H, 6.41. ^{1}H NMR ($CDCl_3$), δ (ppm) 1.18 (t, *J*=5.5, 6H, CH_3), 3.10–3.25 (m, 8H, $=CHCH_2$), 3.27 (d, *J*=14.0, 2H), 3.37 (d, *J*=14.0, 2H), 4.20 (d, *J*=14.0, 2H), 4.21 (d, *J*=14.0, 2H, $ArCH_2Ar$), 4.14 (q, *J*=5.5, 4H,

OCH_2CH$_3$), 4.61, 4.73 (AB, J=15.5, 4H, OCH_2CO), 4.95–5.08 (m, 8H, CH_2=), 5.71–6.06 (m, 4H, =CH), 6.27 (s, 2H, OCH), 6.83 (s, 8H, ArH), 7.96 (s, 2H, OH); ^{13}C NMR (CDCl$_3$), δ (ppm): 13.9, 31.2, 31.5, 39.3, 39.7, 62.8, 71.2, 71.8, 115.0, 115.8, 126.9, 127.8, 128.5, 128.6, 129.1, 129.3, 129.9, 133.0, 133.6, 137.2, 137.4, 138.2, 148.4, 151.6, 165.7, 166.8.

*4.3.14. (4′*R*,5′*R*)-5,11,17,23-Tetra-allyl-25,27-dihydroxy-26,28-(4′,5′-di-propoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***8b***

Yield: 17.7%; mp: 170.0–171.0°C, [α]$_D^{20}$ +27.6 (c 0.14, CHCl$_3$); IR (cm^{-1}): 3390 (OH), 1755 (OCO); MS (FD): 898 (M$^+$). Anal. calcd for $C_{54}H_{58}O_{12}$: C, 72.14, H, 6.50. Found: C, 72.18, H, 6.18. ^{1}H NMR (CDCl$_3$), δ (ppm): 0.86 (t, J=8.3, 6H, CH_3), 1.57 (hex, J=7.2, 4H, CH_2CH$_3$), 3.10–3.25 (m, 8H, =CHCH_2), 3.27 (d, J=13.0, 2H), 3.37 (d, J=13.0, 2H) (ArCH_2Ar), 3.95–4.25 (m, 8H, ArCH_2Ar, OCH_2CH$_2$), 4.61, 4.73 (AB, J=16.5, 4H, OCH_2CO), 4.95–5.12 (m, 8H, =CH_2), 5.74–6.01 (m, 4H, =CH), 6.27 (s, 2H, CH), 6.82 (s, 8H, ArH), 7.97 (s, 2H, OH); ^{13}C NMR (CDCl$_3$), δ (ppm): 10.1, 21.7, 31.1, 31.5, 39.3, 39.7, 68.2, 71.2, 71.7, 115.0, 115.7, 126.8, 127.7, 128.4, 128.5, 129.0, 129.3, 129.8, 133.0, 133.6, 137.2, 137.4, 138.3, 148.4, 151.6, 166.7, 166.9.

*4.3.15. (4′*R*,5′*R*)-5,11,17,23-Tetra-allyl-25,27-dihydroxy-26,28-(4′,5′-di-1-methylethoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***8c***

Yield: 15.6%; mp: 200.0–201.0°C, [α]$_D^{20}$ +25.2 (c 0.8, CHCl$_3$); IR (cm^{-1}): 3410 (OH), 1759, 1735 (OCO); MS (FD): 898 (M$^+$). Anal. calcd for $C_{54}H_{58}O_{12}$: C, 72.14, H, 6.50. Found: C, 72.31, H, 6.42. ^{1}H NMR (CDCl$_3$), δ (ppm): 1.14 (d, J=6.0, 6H), 1.22 (d, J=6.0, 6H, CH(CH_3)$_2$), 3.28 (d, J=15.0, 2H), 3.39 (d, J=15.0, 2H), 4.14 (d, J=15.0, 2H), 4.19 (d, J=15.0, 2H, ArCH_2Ar), 3.14–3.25 (m, 8H, =CHCH_2), 4.62, 4.71 (AB, J=18.0, 4H, OCH_2CO), 5.01–5.13 (m, 10H, =CH_2, OCHMe$_2$), 5.82–5.93 (m, 4H, CH=), 6.27 (s, 2H, OCH), 6.85 (s, 8H, ArH), 8.00 (s, 2H, OH); ^{13}C NMR (CDCl$_3$), δ (ppm): 21.2, 21.5, 31.1, 31.6, 39.3, 39.7, 70.9, 71.4, 71.7, 115.0, 115.8, 126.8, 127.8, 128.5, 128.6, 129.1, 129.3, 129.8, 133.0, 133.6, 137.2, 137.4, 138.3, 148.3, 151.6, 165.2, 166.9.

*4.3.16. (4′*R*,5′*R*)-5,11,17,23-Tetra-allyl-25,27-dihydroxy-26,28-(4′,5′-di-butoxycarbonyl-3′,6′-dioxa-2′,7′-dioxooctylene)-dioxycalix[4]arene* ***8d***

Yield: 9.6%; mp: 75.0–76.0°C, [α]$_D^{20}$ +24.3 (c 5.3, CHCl$_3$); IR (cm^{-1}): 3400 (OH), 1755 (OCO); MS (FD): 926 (M$^+$). Anal. calcd for $C_{56}H_{62}O_{12}$: C, 72.55, H, 6.74. Found: C, 72.52, H, 6.71. ^{1}H NMR (CDCl$_3$), δ (ppm): 0.81 (t, J=6.0, 6H, CH_3), 1.30 (hex, J=6.5, 4H, CH_2), 1.54 (quin, J=6.0, 4H, CH_2), 3.15–3.24 (m, 8H, =CHCH_2), 3.29 (d, J=12.0, 2H), 3.39 (d, J=12.0, 2H, ArCH_2Ar), 4.06–4.24 (m, 8H, OCH_2, ArCH_2Ar), 4.63, 4.72 (AB, J=15.0, 4H, OCH_2CO), 5.00–5.05 (m, 8H, =CH_2), 5.81–5.92 (m, 4H, =CH), 6.31 (s, 2H, OCH), 6.84 (s, 8H, ArH), 7.99 (s, 2H, OH); ^{13}C NMR (CDCl$_3$), δ (ppm): 13.8, 19.2, 30.7, 31.5, 31.9, 39.7, 40.1, 66.9, 71.6, 72.1, 114.9, 115.7, 126.5, 127.4, 128.3, 128.8, 128.9, 129.8, 133.1, 133.5, 137.3, 137.4, 138.5, 148.3, 151.4, 165.6, 166.8.

Acknowledgements

We are grateful to the National Natural Science Foundation of China for the financial support.

References

1. Shinkai, S.; Arimura, T.; Kawabata, H.; Murakami, H.; Araki, K.; Iwamoto, K.; Matsuda, T. *J. Chem. Soc., Chem. Commun.* **1990**, 1734–1736.
2. Casabianca, H.; Royer, J.; Satrallah, A.; Taty-C A, Vicens, J. *Tetrahedron Lett*. **1987**, *28*, 6595–6596.
3. Reddy, P. A.; Gutsche, C. D. *J. Org. Chem*. **1993**, *58*, 3245–3251.
4. Verboom, W.; Bodewes, P. J.; van Essen, G.; Timmerman, P.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *Tetrahedron* **1995**, *51*, 499–512.
5. Pappallardo, S.; Giunta, L.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B. *J. Org. Chem*. **1992**, *57*, 2611–2624.
6. Iwamoto, K.; Yanagi, A.; Arimura, T.; Matsuda, T.; Shinkai, S. *Chem. Lett*. **1990**, 1901–1904.
7. Iwamoto, K.; Shimizu, H.; Araki, K.; Shinkai, S. *J. Am. Chem. Soc.* **1993**, *115*, 3997–4006.
8. Pappallardo, S.; Caccamese, S.; Giunta, L. *Tetrahedron Lett*. **1991**, *32*, 7747–7750.
9. Ferguson, G.; Gallagher, J. F.; Giunta, L.; Neri, P.; Pappallardo, S.; Parisi, M. *J. Org. Chem*. **1994**, *59*, 42–53.
10. Böhmer, V.; Wolff, A.; Vogt, W. *J. Chem. Soc., Chem. Commun*. **1990**, 968–970.
11. Otsuka, H.; Shinkai, S. *J. Am. Chem. Soc*. **1996**, *118*, 4271–4275.
12. Geraci, C.; Piattelli, M.; Neri, P. *Tetrahedron Lett.* **1996**, *37*, 7627–7630.
13. Ikeda, A.; Suzuka, Y.; Shinkai, S. *Tetrahedron: Asymmetry* **1998**, *9*, 97–105.
14. Browne, J. K.; McKervey, M. A.; Pitarch, M.; Russell, J. A.; Millership, J. S. *Tetrahedron Lett*. **1998**, *39*, 1789–1790.
15. Arimura, T.; Edamitsu, S.; Shinkai, S.; Manabe, O.; Muramatsu, T.; Tashiro, M. *Chem. Lett*. **1987**, 2269.
16. Shinkai, S.; Arimura, T.; Satoh, H.; Manabe, O. *J. Chem. Soc., Chem. Commun*. **1987**, 1495.
17. Arimura, T.; Kawabata, H.; Matsuda, T.; Muramatsu, T.; Satoh, H.; Fujio, K.; Manabe, O.; Shinkai, S. *J. Org. Chem*. **1991**, *56*, 301–306.
18. Ikeda, A.; Nagasaki, T.; Shinkai, S. *J. Phys. Org. Chem*. **1992**, *5*, 699–710.
19. Peña, M. S.; Zhang, Y.; Thibodeaux, S.; McLaughlin, M. L.; de la Peña, A. M.; Warner, M. *Tetrahedron Lett*. **1996**, *37*, 5841–5844.
20. Takeshita, M.; Inokuchi, F.; Shinkai, S. *Tetrahedron Lett*. **1995**, *36*, 3341–3344.
21. Marra, A.; Dondoni, A.; Sansone, F. *J. Org. Chem*. **1996**, *61*, 5155–5158.
22. Li, Z. J.; Huang, Z. T. *Chin. Chem. Lett*. **1997**, *8*, 369–372.
23. Dondoni, A.; Kleban, M.; Marra, A. *Tetrahedron Lett*. **1997**, *38*, 7801–7804.
24. Kubo, Y.; Maruyama, S.; Ohhara, N.; Nakamura, M.; Tokita, S. *J. Chem. Soc., Chem. Commun*. **1995**, 1727–1728.
25. Pinkhassik, E.; Stibor, I.; Casnati, A.; Ungaro, R. *J. Org. Chem*. **1997**, *62*, 8654–8659.
26. Neri, P.; Bottino, A.; Geraci, C.; Piattelli, M. *Tetrahedron: Asymmetry* **1996**, *7*, 17–20.
27. Kubo, Y.; Maeda, S.; Tokita, S.; Kubo, M. *Nature* **1996**, *382*, 522–524.
28. Park, B. S.; Knobler, C. B.; Eid Jr., C. N.; Warmuth, R.; Cram, D. J. *Chem. Commun*. **1998**, 55–56.
29. Peña, M. S.; Zhang, Y.; Warner, I. M. *Anal. Chem*. **1997**, *69*, 3239–3242.
30. Grady, T.; Harris, S. J.; Smyth, M. R.; Diamond, D.; Hailey, P. *Anal. Chem*. **1996**, *68*, 3775–3782.
31. This compound includes some methylene chloride molecules, which are hardly removed. The 0.25 CH_2Cl_2 is calculated from the chlorine content analysis.