Improved design of inherently chiral calix[4]arenes as organocatalysts†

Seiji Shirakawa‡ and Shoichi Shimizu*

Received (in Montpellier, France) 18th November 2009, Accepted 11th February 2010
First published as an Advance Article on the web 18th March 2010
DOI: 10.1039/b9nj00685k

Improvement of the design of inherently chiral calix[4]arenes as organocatalysts was accomplished *via* the introduction of a diarylmethanol structure. Novel, inherently chiral calix[4]arenes bearing a tertiary amine or a quaternary ammonium moiety, together with a diarylmethanol moiety, were synthesized from previously reported chiral calix[4]arene amino acid derivatives in an optically pure form. These chiral calix[4]arenes were applied to asymmetric reactions as organocatalysts, and a positive effect of the diarylmethanol structure on enantioselectivity was observed.

Introduction

Calixarenes have been widely used as three-dimensional molecular platforms for the design of artificial molecular receptors, owing to the ready availability of cheap starting materials and the facile modification of the calixarene structure at both the wide and narrow rims.[1]

Interest in the chemistry of chiral calixarenes has increased in recent years due to their importance in the development of new chiral receptors for asymmetric recognition. This provides a potent tool for understanding the stereochemistry of biochemical systems. Hence, many chiral calixarenes containing chiral residues at either the wide or narrow rim have been prepared as chiral receptors[2] and catalysts.[3] A more challenging and attractive approach to the introduction of chirality is to make the calixarene "inherently" chiral by creating an asymmetric array of achiral substituents on the calixarene skeleton.[4] For the past two decades, many inherently chiral calixarenes have been prepared, and some of them have been resolved into individual enantiomers.[5] In spite of these efforts, only a few examples of enantiomeric recognition[6] and asymmetric catalysis[7–10] with inherently chiral calixarenes have been reported. These limited results might arise from the difficulties associated with both the design of a synthetic route to functionalized, inherently chiral calixarenes and the separation of the synthesized chiral calixarenes into optically pure enantiomers.

We recently developed a novel and efficient method for the synthesis of inherently chiral calix[4]arenes containing aminophenol structures, which were then applied to asymmetric reactions as organocatalysts.[8] Inherently chiral calix[4]arenes have traditionally been synthesized as racemates. Each of the calixarenes is then resolved into optically pure enantiomers. In these reports, we succeeded in the separation of the enantiomers of chiral calixarenes. However, tedious screening of the separation methods for each of the chiral calixarenes was needed to obtain them enantiomerically pure. To solve this problem, more recently, we reported the design and synthesis of an inherently chiral calix[4]arene amino acid[11] as a chiral building block for subsequent transformation into various types of inherently chiral calix[4]arene.[9] In this study, an optically pure, inherently chiral calix[4]arene amino alcohol was prepared by the separation of a diastereomeric mixture of the calix[4]arene amino acid derivatives **1a** and **1b**, bearing a (*R*)-BINOL moiety. Separated **1a** and **1b** were easily transformed into different types of inherently chiral calix[4]arenes, **2a** and **3a**, in optically pure forms. Calix[4]arenes **2a** and **3a** were applied to asymmetric reactions as organocatalysts, and high catalytic efficiencies with low enantioselectivities were observed. In the present study, for the design of more effective chiral catalysts that are able to use chiral building blocks **1a** and **1b** for synthesis, we planned the introduction of a diarylmethanol structure into the calix[4]arene. Such diarylmethanol structures are often seen in efficient chiral catalysts, such as α,α-diarylprolinols[12] and TADDOLs[13] (Fig. 1). Herein, we report the synthesis of novel, inherently chiral calix[4]arenes containing a diarylmethanol structure, and the beneficial effect of the diarylmethanol structure on its enantioselectivity as an organocatalyst in asymmetric reactions.[14]

Results and discussion

Synthesis of inherently chiral calix[4]arenes 2b and 3b

The requisite chiral calix[4]arene **2b** (Fig. 2) could be prepared by the arylation of the ester moiety of **1a** and **1b** with an aryllithium (Scheme 1). Initially, we tried to introduce the phenyl groups as aryl substituents by the treatment of **1a** or **1b** with PhLi. Unfortunately, the desired product was unstable, presumably due to the lesser stability of the diarylmethanol moiety as a part of the "tri"-arylmethanol structure. To stabilize the diarylmethanol moiety, we next tried the introduction of 4-(trifluoromethyl)phenyl groups, which contain an electron-withdrawing group on the phenyl ring, by the treatment of **1a** and **1b** with the corresponding aryllithium. The desired chiral calix[4]arene, **2b** (Ar = 4-CF_3–C_6H_4), was

Department of Applied Molecular Chemistry, College of Industrial Technology, Nihon University, Narashino, Chiba, 275-8575, Japan. E-mail: shimizu.shouichi@nihon-u.ac.jp; Fax: +81 47 474 2579; Tel: +81 47 474 2568

† Electronic supplementary information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra of **2b** and **3b**, characterization data and HPLC chromatograms for products of the asymmetric reactions. See DOI: 10.1039/b9nj00685k

‡ Present address: Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8502, Japan.

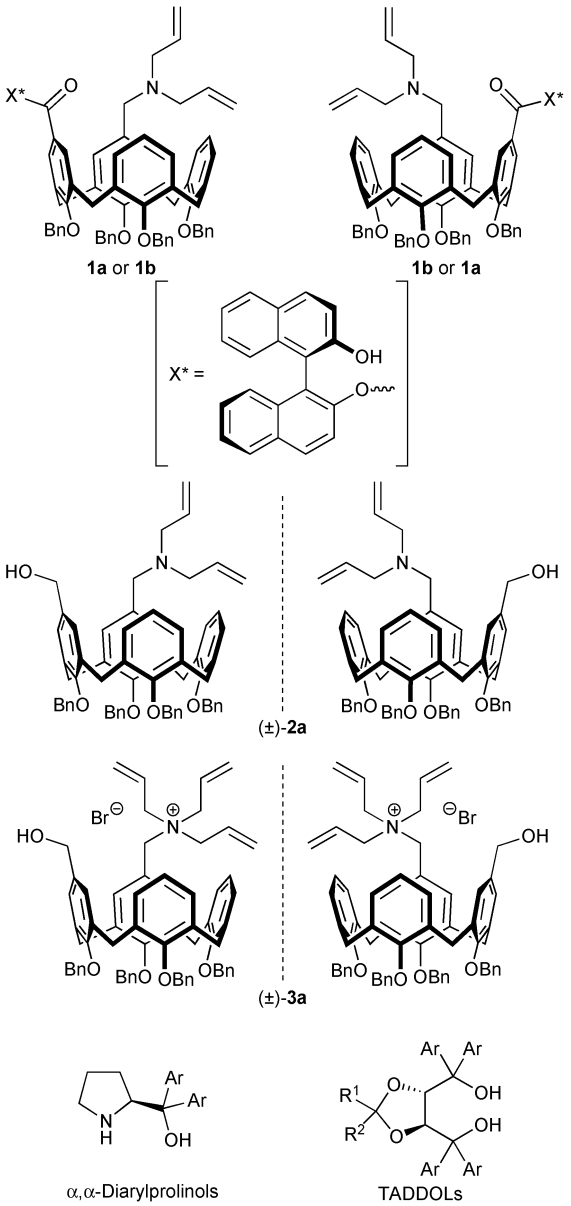


Fig. 1 Chiral catalysts with a diarylmethanol structure.

obtained in good yields (72–74%) with high stability of the compound. Furthermore, a chiral calix[4]arene containing a quaternary ammonium moiety, **3b** (Ar = 4-CF_3–C_6H_4), was prepared *via* the *N*-alkylation of chiral calix[4]arene **2b** (Ar = 4-CF_3–C_6H_4). The optical rotations of (+)-**2b** and (−)-**2b**, and (+)-**3b** and (−)-**3b** showed similar values with opposite signs (Scheme 1), and the circular dichroism (CD) spectra of the enantiomers of **2b** and **3b** showed mirror images (Fig. 3), which definitively proves they are a pair of enantiomers.

The NMR spectra of **2b** and **3b** provided encouraging structural evidence. The ^{1}H NMR spectrum of **2b** showed a set of four AB systems for the methylene bridges of the calix[4]arene at 4.23, 4.17, 4.09 and 4.07 ppm for the axial protons, and at 3.35, 3.21, 2.73 and 2.71 ppm for the equatorial protons. The ^{13}C NMR spectrum showed peaks at 31.38 (3 peaks overlapped) and 31.27 ppm for the four pertinent carbons. The ^{13}C NMR chemical shift values, and the ^{1}H and ^{13}C NMR

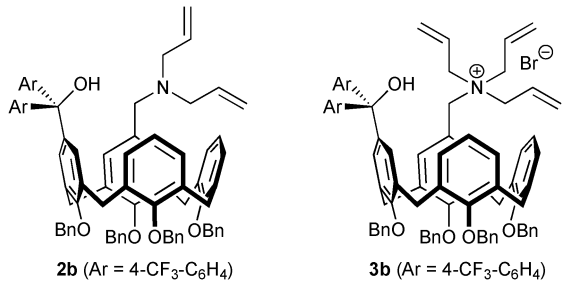
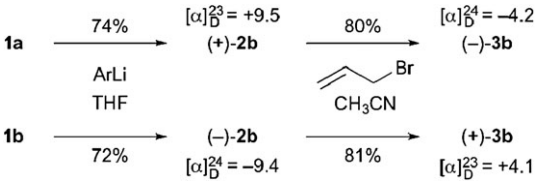


Fig. 2 Inherently chiral calix[4]arenes with a diarylmethanol structure.



Scheme 1 The synthesis of inherently chiral calix[4]arenes **2b** and **3b**.

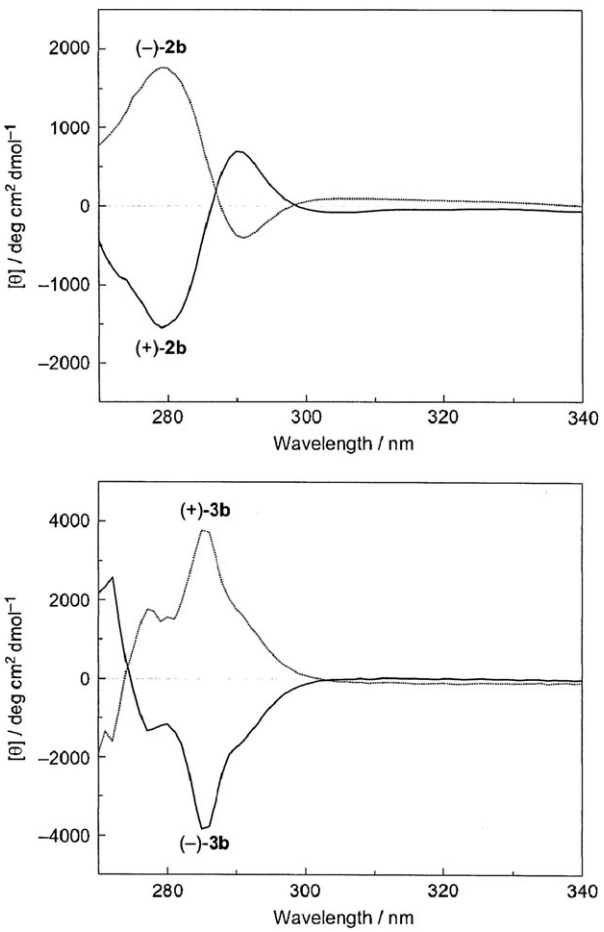


Fig. 3 The CD spectra of enantiomers of calix[4]arenes **2b** and **3b** in $CHCl_3$.

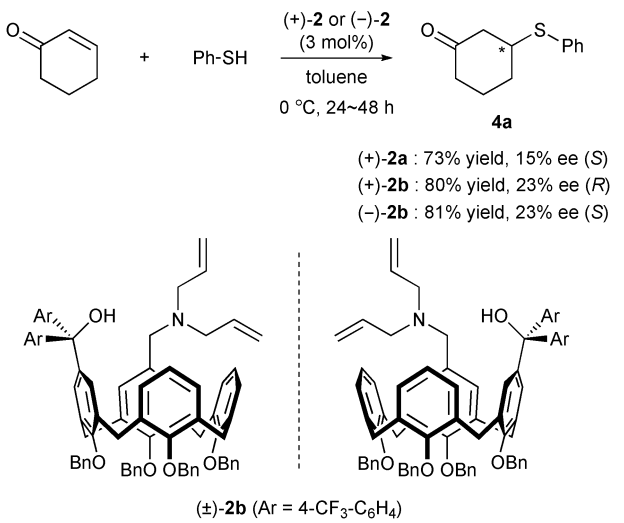
spectral patterns indicate that **2b** is present in the cone conformation[15] and that it possessed inherent chirality. The NMR spectra of **3b** showed a similar tendency.

Asymmetric reactions catalyzed by inherently chiral calix[4]arenes 2 and 3

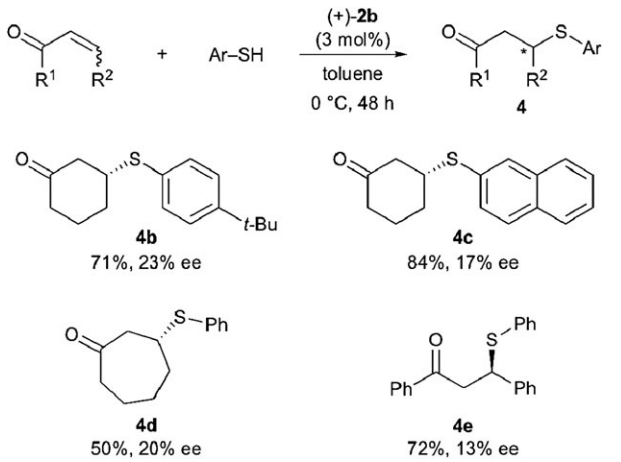
The application of inherently chiral calixarenes as chiral catalysts is a worthy challenge in organic synthesis. However, the reported examples of asymmetric catalysis with inherently chiral calixarenes have been quite limited.[7–10] Recently, we reported the use of chiral calix[4]arene **2a** as an organocatalyst to efficiently promote the Michael addition reaction of thiophenol[16] with a low enantioselectivity (15% ee, Scheme 2).[9b] To improve the enantioselectivity, we employed chiral calix[4]arene **2b**, containing a diarylmethanol structure, for the Michael addition reaction of thiophenol. Pleasingly, a positive effect of the additional diaryl group was observed, and product **4a** was obtained in 23% ee with good yield (Scheme 2). Of course, the observed enantioselectivity was still moderate. However, this result indicates the direction that the design of more efficient, inherently chiral calixarene catalysts should take.

Other substrates for Michael addition reactions catalyzed by **2b** were also examined, and selected examples are shown in Scheme 3. Substituted thiophenols could be applied to the reaction system to give products **4b** and **4c** in good yield with moderate enantioselectivity (17–23% ee). Another cyclic enone, with a different ring size, and an acyclic enone were also applied to the reaction, giving products **4d** and **4e** with moderate enantioselectivity (13–20% ee).

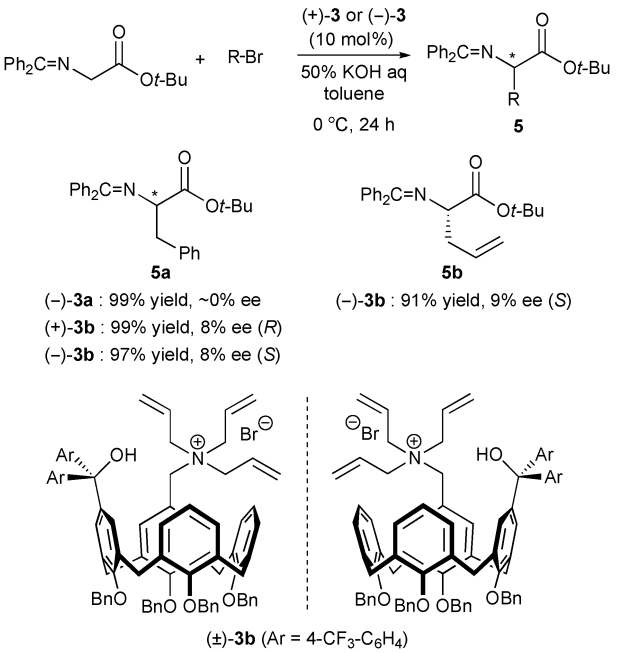
For the past decade, asymmetric phase-transfer catalysis, based on the use of chiral quaternary ammonium salts as catalysts, has become a topic of great scientific interest.[17] Inherently chiral calix[4]arenes **3**, containing a quaternary ammonium moiety, were applied to asymmetric reactions as chiral phase-transfer catalysts. To test the effect of a diarylmethanol structure in catalyst **3**, they were applied to the asymmetric alkylation of a glycine derivative (Scheme 4).[18,19] Thus, the asymmetric alkylation of a glycine derivative with benzyl bromide in a toluene–50% aqueous KOH biphasic system under the influence of **3a** gave the corresponding phenylalanine derivative **5a** in excellent yield with almost no



Scheme 2 The effect of the catalyst structure in the Michael addition reaction of thiophenol.



Scheme 3 Asymmetric Michael addition reactions of thiophenols catalyzed by (+)-**2b**.



Scheme 4 Asymmetric alkylations of a glycine derivative catalyzed by **3** under phase-transfer conditions.

enantioselectivity. On the other hand, the reaction under the influence of **3b** gave product **5a** in excellent yield with a low, but certain, chiral induction (8% ee). Allylation of a glycine derivative was also examined and gave allylglycine derivative **5b** in excellent yield with 9% ee.

Conclusions

In the present study, we present the design and synthesis of inherently chiral calix[4]arenes containing a diarylmethanol structure. Calix[4]arenes **2b** and **3b** were applied to asymmetric reactions as a chiral base catalyst and as a chiral phase-transfer catalyst, respectively. The effect of the diaryl group of **2b** and **3b** in the asymmetric reactions was examined, and a positive effect on enantioselectivity was observed. The

asymmetric induction observed for the reaction remained moderate; however, we believe that this result indicates the direction that the design of more efficient, inherently chiral calixarene catalysts should take.

Experimental

General

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$. Tetramethylsilane (TMS) served as the internal standard (0 ppm) for ^{1}H NMR, and $CDCl_3$ served as the internal standard (77.0 ppm) for ^{13}C NMR. IR spectra were measured with a Jasco FT/IR-700 spectrometer. Circular dichroism (CD) spectra were measured with a Jasco J-820 spectrometer. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter. High performance liquid chromatography (HPLC) was performed on a Hitachi 655 liquid chromatograph. Analytical thin-layer chromatography (TLC) and column chromatography were carried out on pre-coated silica gel 60 F_{254} glass plates (E. Merck) and with silica gel 60 (spherical 0.040–0.100 mm, Kanto), respectively. Tetrahydrofuran (THF) was freshly distilled from Na–benzophenone.

5-(*N*,*N*-Diallylaminomethyl)-11-hydroxy-{di[4-(trifluoromethyl)phenyl]}methyl-25,26,27,28-tetrabenzyloxycalix[4]arene (2b)

To a solution of 1-bromo-4-(trifluoromethyl)benzene (4.5 mmol) in THF (15 ml) was added *n*-BuLi (4.0 mmol, 1.5 M in hexane) at −78 °C under an argon atmosphere, and the mixture was stirred for 15 min at this temperature. The resulting solution of aryllithium was then transferred to solutions of **1a** or **1b**[9] (0.50 mmol) in THF (15 ml) *via* a cannula at −78 °C under an argon atmosphere, and the mixture was stirred for 30 min at this temperature. The mixtures were then warmed to 0 °C and stirred for 2 h. The reaction mixtures were quenched with 0.2 N HCl aq. (30 ml). After the removal of THF by evaporation, the organic material was extracted with $CHCl_3$ (3 × 10 ml). The organic extracts were washed with sat. aq. $NaHCO_3$ and dried over $MgSO_4$. Evaporation of solvents and purification of the residue by column chromatography on silica gel ($CHCl_3$/AcOEt = 1/0 to 10/1 as eluent) afforded (+)-**2b** ($[\alpha]_D^{23}$ +9.5 (*c* 1.8, $CHCl_3$)) and (−)-**2b** ($[\alpha]_D^{24}$ −9.4 (*c* 1.6, $CHCl_3$)) in 74 and 72% yields, respectively: R_f 0.26 ($CHCl_3$/AcOEt = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$/ppm) 7.12–7.39 (m, 24H), 6.94–7.04 (m, 5H), 6.86 (d, *J* = 1.5 Hz, 1H), 6.47–6.66 (m, 6H), 6.16 (d, *J* = 2.3 Hz, 1H), 5.94 (d, *J* = 2.2 Hz, 1H), 5.76–5.86 (m, 2H), 5.08–5.18 (m, 8H), 4.72–4.82 (m, 4H), 4.23 (d, *J* = 13.2 Hz, 1H), 4.17 (d, *J* = 13.2 Hz, 1H), 4.09 (d, *J* = 13.2 Hz, 1H), 4.07 (d, *J* = 13.2 Hz, 1H), 3.35 (d, *J* = 13.1 Hz, 1H), 3.21 (d, *J* = 13.1 Hz, 1H), 2.90–3.00 (m, 6H), 2.73 (d, *J* = 13.3 Hz, 1H), 2.71 (d, *J* = 13.3 Hz, 1H) and 2.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$/ppm) 155.21, 155.16, 154.96, 153.95, 149.76, 138.70, 137.57, 137.47, 137.29, 137.22, 136.42, 136.31, 136.15, 135.46, 134.55, 134.40, 134.29, 133.78, 132.79, 130.38, 130.28, 129.58, 129.48, 129.30, 128.91, 128.84, 128.62, 128.53, 128.45, 128.25, 128.17, 128.10, 127.86, 127.72, 127.59, 127.52, 125.51, 124.54, 124.50, 124.44, 124.41, 122.81, 122.66, 122.25, 117.68 (Ar–*C*, *C*H=*C*H$_2$, and *C*F$_3$), 80.69 (Ar$_2$*C*OH), 77.12, 76.84, 75.89, 75.46 (Ph*C*H$_2$O), 57.05 (Ar*C*H$_2$N), 56.15 (N*C*H$_2$CH=CH$_2$), 31.38 and 31.27 (Ar*C*H$_2$Ar); IR 3571, 3063, 3031, 2920, 2868, 1458, 1326, 1124, 1068, 983, 765 and 698 cm^{-1}. Anal. calc. for $C_{78}H_{67}F_6NO_5 \cdot H_2O$: C, 76.14; H, 5.65; N, 1.14. Found: C, 75.94; H, 5.59; N, 1.14%.

5-Hydroxy{di[4-(trifluoromethyl)phenyl]}methyl-11-(*N*,*N*,*N*-triallylammoniomethyl)-25,26,27,28-tetrabenzyloxycalix[4]arene bromide (3b)

A mixture of (+)-**2b** or (−)-**2b** (0.20 mmol) with allyl bromide (1.0 mmol) in CH_3CN (5.0 ml) was heated at 80 °C for 8 h. Evaporation of CH_3CN and purification of the residue by column chromatography on silica gel ($CHCl_3$/MeOH = 100/1 to 10/1 as eluent) afforded (−)-**3b** ($[\alpha]_D^{24}$ −4.2 (*c* 1.1, $CHCl_3$)) and (+)-**3b** ($[\alpha]_D^{23}$ +4.1 (*c* 0.85, $CHCl_3$)) in 80 and 81% yields, respectively: R_f 0.24 ($CHCl_3$/MeOH = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$/ppm) 7.42–7.51 (m, 8H), 7.14–7.35 (m, 20H), 6.92–6.99 (m, 2H), 6.78–6.84 (m, 3H), 6.50 (d, *J* = 1.9 Hz, 1H), 6.26–6.38 (m, 3H), 6.11 (s, 1H), 5.71–5.81 (m, 4H), 5.59–5.63 (m, 6H), 5.13 (d, *J* = 11.7 Hz, 1H), 5.12 (d, *J* = 11.8 Hz, 1H), 5.03 (d, *J* = 11.6 Hz, 1H), 5.02 (d, *J* = 11.9 Hz, 1H), 4.72–4.83 (m, 4H), 4.65 (d, *J* = 13.0 Hz, 1H), 4.26 (d, *J* = 13.4 Hz, 1H), 4.18 (d, *J* = 13.4 Hz, 1H), 4.13 (d, *J* = 13.7 Hz, 1H), 4.09 (d, *J* = 13.7 Hz, 1H), 3.88 (d, *J* = 13.0 Hz, 1H), 3.78 (d, *J* = 6.8 Hz, 6H), 3.01 (d, *J* = 13.6 Hz, 1H) and 2.83 (d, *J* = 13.8 Hz, 1H + 1H + 1H); ^{13}C NMR (100 MHz, $CDCl_3$/ppm) 156.70, 155.56, 154.97, 154.56, 151.62, 150.81, 140.67, 137.33, 137.19, 137.15, 137.01, 136.67, 136.16, 135.99, 135.55, 135.33, 135.17, 134.13, 133.64, 131.08, 130.15, 129.49, 129.20, 129.11, 129.06, 128.65, 128.59, 128.46, 128.39, 128.28, 128.19, 128.09, 128.04, 127.98, 127.94, 127.84, 127.74, 127.13, 125.63, 124.86, 124.40, 124.37, 122.91, 122.29, 122.06, 120.66 (Ar–*C*, *C*H=*C*H$_2$, and *C*F$_3$), 80.69 (Ar$_2$*C*OH), 77.24, 76.80, 75.91, 75.55 (Ph*C*H$_2$O), 63.69 (Ar*C*H$_2$N), 61.31 (N*C*H$_2$CH=CH$_2$), 31.31 and 31.25 (Ar*C*H$_2$Ar); IR 3292, 3062, 3031, 2922, 2869, 1459, 1326, 1164, 1120, 1068, 981 and 699 cm^{-1}. Anal. calc. for $C_{81}H_{72}BrF_6NO_5 \cdot 3H_2O$: C, 70.12; H, 5.67; N, 1.01. Found: C, 70.21; H, 5.58; N, 1.03%.

General procedure for the catalytic asymmetric Michael addition reactions catalyzed by (+)-2 or (−)-2

To a solution of (+)-**2** or (−)-**2** (0.0075 mmol) and 2-cyclohexen-1-one (0.25 mmol) in toluene (1 ml) was added thiophenol (0.30 mmol) at 0 °C under an argon atmosphere, and mixture was stirred for 48 h at this temperature. The reaction was quenched with 0.2 N aq. HCl (2 ml), and the organic materials extracted with $CHCl_3$ (2 × 3 ml). The organic solution was washed with water (5 ml) and dried over $MgSO_4$. Evaporation of solvents and purification of the residue using flash chromatography on silica gel afforded the Michael addition product. The enantioselectivity of the product was determined using chiral HPLC analysis, and the absolute configuration was determined by comparison of the HPLC retention time with the reported times and/or by comparison of the observed optical rotation with the reported values.[16]

General procedure for the catalytic asymmetric alkylation catalyzed by (+)-3 or (−)-3

To a solution of (+)-**3** or (−)-**3** (0.0050 mmol) and *tert*-butyl glycinate benzophenone Schiff base (0.050 mmol) in toluene (0.50 ml)–50% aq. KOH solution (0.20 ml) was added benzyl bromide (0.060 mmol) at 0 °C under an argon atmosphere, and the mixture stirred for 24 h at this temperature. The reaction was diluted with water (3 ml), and the organic materials extracted with $CHCl_3$ (2 x 3 ml). The organic solution was washed with water (5 ml) and dried over $MgSO_4$. Evaporation of solvents and purification of the residue using flash chromatography on silica gel afforded an alkylation product. The enantioselectivity of the product was determined using chiral HPLC analysis, and the absolute configuration was determined by comparison of the HPLC retention time with the reported times and/or by comparison of the observed optical rotation with the reported values.[18]

References

1 For representative reviews on calixarenes, see: (*a*) C. D. Gutsche, *Calixarenes*, Monographs in Supramolecular Chemistry, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, UK, 1989; (*b*) *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Topics in Inclusion Science 3, ed. J. Vicens and V. Böhmer, Kluwer, Dordrecht, The Netherlands, 1991; (*c*) S. Shinkai, *Tetrahedron*, 1993, **49**, 8933; (*d*) M. Takeshita and S. Shinkai, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 1088; (*e*) V. Böhmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713; (*f*) A. Pochini and R. Ungaro, *Comprehensive Supramolecular Chemistry*, ed. F. Vögtle, Pergamon Press, Oxford, UK, 1996, vol. 2, pp. 103–142; (*g*) C. D. Gutsche, *Calixarenes Revisited*, Monographs in Supramolecular Chemistry, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, UK, 1998; (*h*) A. Ikeda and S. Shinkai, *Chem. Rev.*, 1997, **97**, 1713; (*i*) *Calixarenes in Action*, ed. L. Mandolini and R. Ungaro, Imperial College Press, London, UK, 2000; (*j*) *Calixarenes 2001*, ed. Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, Kluwer, Dordrecht, The Netherlands, 2001; (*k*) N. Morohashi, F. Narumi, N. Iki, T. Hattori and S. Miyano, *Chem. Rev.*, 2006, **106**, 5291; (*l*) D. M. Homden and C. Redshaw, *Chem. Rev.*, 2008, **108**, 5086.

2 (*a*) Y. Kubo, S. Maeda, S. Tokita and M. Kubo, *Nature*, 1996, **382**, 522; (*b*) E. Pinkhassik, I. Stibor, A. Casnati and R. Ungaro, *J. Org. Chem.*, 1997, **62**, 8654; (*c*) R. K. Castellano, C. Nuckolls and J. Rebek, Jr., *J. Am. Chem. Soc.*, 1999, **121**, 11156; (*d*) L. J. Prins, F. D. Jong, P. Timmerman and D. N. Reinhoudt, *Nature*, 2000, **408**, 181; (*e*) B. Botta, D. Subissati, A. Tafi, G. Della Monache, A. Filippi and M. Speranza, *Angew. Chem., Int. Ed.*, 2004, **43**, 4767; (*f*) Y.-S. Zheng and C. Zhang, *Org. Lett.*, 2004, **6**, 1189; (*g*) S. Cherenok, A. Vovk, I. Muravyova, A. Shivanyuk, V. Kukhar, J. Lipkowski and V. Kalchenko, *Org. Lett.*, 2006, **8**, 549; (*h*) C. Bonini, L. Chiummiento, M. Funicello, M. Teresa Lopardo, P. Lupattelli, A. Laurita and A. Cornia, *J. Org. Chem.*, 2008, **73**, 4233.

3 (*a*) G. Arnott, H. Heaney, R. Hunter and P. C. B. Page, *Eur. J. Org. Chem.*, 2004, 5126; (*b*) C. Gaeta, M. De Rosa, M. Fruilo, A. Soriente and P. Neri, *Tetrahedron: Asymmetry*, 2005, **16**, 2333; (*c*) G. Arnott and R. Hunter, *Tetrahedron*, 2006, **62**, 992; (*d*) A. Quintard, U. Darbost, F. Vocanson, S. Pellet-Rostaing and M. Lemaire, *Tetrahedron: Asymmetry*, 2007, **18**, 1926; (*e*) A. Marson, Z. Freixa, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Eur. J. Inorg. Chem.*, 2007, 4587.

4 (*a*) V. Böhmer, D. Kraft and M. Tabatabai, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1994, **19**, 17; (*b*) H. Otsuka and S. Shinkai, *Supramol. Sci.*, 1996, **3**, 189; (*c*) A. Dalla Cort, L. Mandolini, C. Pasquini and L. Schiaffino, *New J. Chem.*, 2004, **28**, 1198.

5 (*a*) S. Pappalardo, S. Caccamese and L. Giunta, *Tetrahedron Lett.*, 1991, **32**, 7747; (*b*) S. Shinkai, T. Arimura, H. Kawabata, H. Murakami and K. Iwamoto, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2429; (*c*) K. Iwamoto, H. Shimizu, K. Araki and S. Shinkai, *J. Am. Chem. Soc.*, 1993, **115**, 3997; (*d*) H. Otsuka and S. Shinkai, *J. Am. Chem. Soc.*, 1996, **118**, 4271; (*e*) T. Jin and K. Monde, *Chem. Commun.*, 1998, 1357; (*f*) J. K. Browne, M. A. McKervey, M. Pitarch, J. A. Russell and J. S. Millership, *Tetrahedron Lett.*, 1998, **39**, 1787; (*g*) N. Morohashi, N. Iki, T. Onodera, C. Kabuto and S. Miyano, *Tetrahedron Lett.*, 2000, **41**, 5093; (*h*) S. Caccamese, A. Bottino, F. Cunsolo, S. Parlato and P. Neri, *Tetrahedron: Asymmetry*, 2000, **11**, 3103; (*i*) D. Hesek, Y. Inoue, M. G. B. Drew, P. D. Beer, G. A. Hembury, H. Ishida and F. Aoki, *Org. Lett.*, 2000, **2**, 2237; (*j*) Y.-D. Cao, J. Luo, Q.-Y. Zheng, C.-F. Chen, M.-X. Wang and Z.-T. Huang, *J. Org. Chem.*, 2004, **69**, 206; (*k*) F. Narumi, T. Hattori, W. Yamabuki, C. Kabuto and H. Kameyama, *Tetrahedron: Asymmetry*, 2005, **16**, 793; (*l*) R. Miao, Q.-Y. Zheng, C.-F. Chen and Z.-T. Huang, *J. Org. Chem.*, 2005, **70**, 7662; (*m*) V. I. Boyko, A. Shivanyuk, V. V. Pyrozhenko, R. I. Zubatyuk, O. V. Shishkin and V. I. Kalchenko, *Tetrahedron Lett.*, 2006, **47**, 7775; (*n*) A. V. Yakovenko, V. I. Boyko, O. Danylyuk, K. Suwinska, J. Lipkowski and V. I. Kalchenko, *Org. Lett.*, 2007, **9**, 1183; (*o*) Z.-X. Xu, C. Zhang, Q.-Y. Zheng, C.-F. Chen and Z.-T. Huang, *Org. Lett.*, 2007, **9**, 4447; (*p*) V. I. Boyko, A. V. Yakovenko, Y. I. Matvieiev, O. I. Kalchenko, O. V. Shishkin and V. I. Kalchenko, *Tetrahedron*, 2008, **64**, 7567; (*q*) F. Narumi, N. Matsumura, N. Sasagawa, K. Natori, T. Kajiwara and T. Hattori, *Tetrahedron: Asymmetry*, 2008, **19**, 1470; (*r*) Z.-X. Xu, C. Zhang, Y. Yang, C.-F. Chen and Z.-T. Huang, *Org. Lett.*, 2008, **10**, 477; (*s*) M. Paletta, M. Klaes, B. Neumann, H.-G. Stammler, S. Grimme and J. Mattay, *Eur. J. Org. Chem.*, 2008, 555; (*t*) V. I. Boyko, Y. I. Matvieiev, M. A. Klyachina, O. A. Yesypenko, S. V. Shishkina, O. V. Shishkin and V. I. Kalchenko, *Tetrahedron*, 2009, **65**, 4220; (*u*) Z.-X. Xu, Z.-T. Huang and C.-F. Chen, *Tetrahedron Lett.*, 2009, **50**, 5430; (*v*) M. A. Kliachyna, O. A. Yesypenko, V. V. Pirozhenko, S. V. Shishkina, O. V. Shishkin, V. I. Boyko and V. I. Kalchenko, *Tetrahedron*, 2009, **65**, 7085.

6 (*a*) K. Araki, K. Inada and S. Shinkai, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 72; (*b*) F. Narumi, T. Hattori, N. Matsumura, T. Onodera, H. Katagiri, C. Kabuto, H. Kameyama and S. Miyano, *Tetrahedron*, 2004, **60**, 7827; (*c*) J. Luo, Q.-Y. Zheng, C.-F. Chen and Z.-T. Huang, *Tetrahedron*, 2005, **61**, 8517.

7 Inherently chiral calixarenes containing other chiral residues have been applied to asymmetric reactions as chiral ligands or catalysts. See: (*a*) C. Dieleman, S. Steyer, C. Jeunesse and D. Matt, *J. Chem. Soc., Dalton Trans.*, 2001, 2508; (*b*) Z.-X. Xu, G.-K. Li, C.-F. Chen and Z.-T. Huang, *Tetrahedron*, 2008, **64**, 8668.

8 (*a*) S. Shirakawa, A. Moriyama and S. Shimizu, *Org. Lett.*, 2007, **9**, 3117; (*b*) S. Shirakawa, A. Moriyama and S. Shimizu, *Eur. J. Org. Chem.*, 2008, 5957; (*c*) S. Shirakawa, T. Kimura, S. Murata and S. Shimizu, *J. Org. Chem.*, 2009, **74**, 1288.

9 (*a*) S. Shirakawa, Y. Tanaka, T. Kobari and S. Shimizu, *New J. Chem.*, 2008, **32**, 1835; (*b*) S. Shirakawa and S. Shimizu, *Eur. J. Org. Chem.*, 2009, 1916.

10 R. Mao, Z.-X. Xu, Z.-T. Huang and C.-F. Chen, *Sci. China, Ser. B*, 2009, **52**, 8668.

11 For the synthesis of achiral calixarene amino acids, see: (*a*) F. Sansone, L. Baldini, A. Casnati, E. Chierici, G. Faimani, F. Ugozzoli and R. Ungaro, *J. Am. Chem. Soc.*, 2004, **126**, 6204; (*b*) L. Baldini, F. Sansone, G. Faimani, C. Massera, A. Casnati and R. Ungaro, *Eur. J. Org. Chem.*, 2008, 869; (*c*) J.-A. Richard, M. Pamart, N. Hucher and I. Jabin, *Tetrahedron Lett.*, 2008, **49**, 3848.

12 A. Lattanzi, *Chem. Commun.*, 2009, 1452.

13 (*a*) D. Seebach, A. K. Beck and A. Heckel, *Angew. Chem., Int. Ed.*, 2001, **40**, 92; (*b*) H. Pellissier, *Tetrahedron*, 2008, **64**, 10279.

14 For representative reviews on organocatalysts, see: (*a*) P. I. Dalko and L. Moisan, *Angew. Chem., Int. Ed.*, 2004, **43**, 5138; (*b*) J. Seayad and B. List, *Org. Biomol. Chem.*, 2005, **3**, 719; (*c*) A. Berkssel and H. Gröger, *Asymmetric Organocatalysis—From Biomimetic Concepts to Applications in Asymmetric Synthesis*, Willy-VCH, Weinheim, 2005; (*d*) *Enantioselective Organocatalysis*, ed. P. I. Dalko, Willy-VCH, Weinheim, 2007.

15 C. Jaime, J. de Mendoza, P. Prados, P. M. Nieto and C. Sánchez, *J. Org. Chem.*, 1991, **56**, 3372.

16 (*a*) H. Hiemstra and H. Wynberg, *J. Am. Chem. Soc.*, 1981, **103**, 417; (*b*) K. Suzuki, A. Ikegami and T. Mukaiyama, *Bull. Chem.*

Soc. Jpn., 1982, **55**, 3277; (*c*) F. Wang and M. Tada, *Agric. Biol. Chem.*, 1990, **54**, 2989; (*d*) M. Ostendorf, S. van der Neut, F. P. J. T. Rutjes and H. Hiemstra, *Eur. J. Org. Chem.*, 2000, 105; (*e*) M. Ostendorf, J. Dijkink, F. P. J. T. Rutjes and H. Hiemstra, *Eur. J. Org. Chem.*, 2000, 115; (*f*) M. Saito, M. Nakajima and S. Hashimoto, *Tetrahedron*, 2000, **56**, 9589; (*g*) J. Skarzewski, M. Zielinska-Blajet and I. Turowska-Tryk, *Tetrahedron: Asymmetry*, 2001, **12**, 1923; (*h*) P. McDaid, Y. Chen and L. Deng, *Angew. Chem., Int. Ed.*, 2002, **41**, 338.

17 For recent reviews on asymmetric phase-transfer catalysis, see: (*a*) M. J. O'Donnell, *Acc. Chem. Res.*, 2004, **37**, 506; (*b*) B. Lygo and B. I. Andrews, *Acc. Chem. Res.*, 2004, **37**, 518; (*c*) T. Ooi and K. Maruoka, *Angew. Chem., Int. Ed.*, 2007, **46**, 4222; (*d*) T. Hashimoto and K. Maruoka, *Chem. Rev.*, 2007, **107**, 5656; (*e*) K. Maruoka, *Asymmetric Phase Transfer Catalysis*, Wiley-VCH, Weinheim, 2008.

18 (*a*) M. J. O'Donnell, W. D. Bennett and S. Wu, *J. Am. Chem. Soc.*, 1989, **111**, 2353; (*b*) B. Lygo and P. G. Wainwright, *Tetrahedron Lett.*, 1997, **38**, 8595; (*c*) E. J. Corey, F. Xu and M. C. Noe, *J. Am. Chem. Soc.*, 1997, **119**, 12414; (*d*) T. Ooi, M. Kameda and K. Maruoka, *J. Am. Chem. Soc.*, 1999, **121**, 6519; (*e*) T. Ooi, M. Kameda and K. Maruoka, *J. Am. Chem. Soc.*, 2003, **125**, 5139.

19 For a calixarene-based chiral phase-transfer catalyst with a chiral residue, see: S. Bozkurt, M. Durmaz, M. Yilmaz and A. Sirit, *Tetrahedron: Asymmetry*, 2008, **19**, 618.

