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Supramolecular Chirality

High Diastereoselection of a Dissymmetric Capsule by Chiral Guest Complexation**

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Abstract: *Encapsulation of chiral guests in the dissymmetric capsule* $\mathbf{1}\cdot\mathbf{4}BF_4$ *formed diastereomeric supramolecular complexes* $\mathbf{G}\subset\mathbf{1}\cdot\mathbf{4}BF_4$ *(**G**: guest). When chiral guests **2a–q** were encapsulated within the dissymmetric space of the self-assembled capsule* $\mathbf{1}\cdot\mathbf{4}BF_4$*, circular dichroism (CD) was observed at the absorption bands that are characteristic of the* π–π^* *transition of the bipyridine moiety of the capsule, which suggests that the P and M helicities of the capsule are biased by the chiral guest complexation. The P helicity of diastereomeric complex* (S)-$\mathbf{2l}\subset\mathbf{1}\cdot\mathbf{4}BF_4$ *was determined to be predominant, based on CD exciton coupling theory and DFT calculations. The diastereoselectivity was highly influenced by the ester substituents, such that benzyl ester moieties were good for improving the diastereoselectivity. A diastereomeric excess of 98% was achieved upon the complexation of **2j**. The relative enthalpic and entropic components for the distereoselectivity were obtained from a van't Hoff plot. The enthalpic components were linearly correlated with the substituent Hammett parameters* (σ_p^+)*. The electron-rich benzyl ester moieties generated donor–acceptor* π–π *stacking interactions with the bipyridine moiety, which resulted in a significant difference in energy between the predominant and subordinate diastereomeric complexes.*

Enantioselective molecular recognition is a ubiquitous, vital phenomenon in nature. An enzyme provides a binding pocket that is precisely configured for the shape of its substrate to ensure high enantioselectivity. This enantioselective recognition of chiral molecules has been a motive for the development of supramolecular chemistry by using designable platforms. Much effort has been devoted toward generating a chiral environment in which one component of a racemic mixture can be preferentially bound by employing steric and electronic interactions. A number of chiral host molecules based on cyclodextrins,[1] crown ethers,[2] cyclophanes,[3] and calixarenes[4] have been examined. In these systems, chiral auxiliaries are covalently installed to surround binding pockets.[5]

An alternative chiral space is produced by the self-assembly of achiral monomers. For example, Rebek and co-workers have demonstrated that a hydrogen-bonded dimeric capsule made up of two achiral monomers produces a dissymmetric space, in which a small chiral guest can be encapsulated in a diastereoselective fashion.[6] The enantiomers of the capsule are dynamically interconvertible through dissociation and recombination. When a chiral guest is captured, the chiral interior recognizes the shape of the chiral guest, which results in a difference in energy between the diastereomeric complexes. Coordination-driven self-assembly to build up a chiral cavity has also been reported by Raymond and co-workers.[7] In this case, a chiral guest was captured within the cavity, the chirality of which adapted to the guest shape; this led to diastereomeric complexes in 70% *de*. It is still challenging to achieve a high degree of diastereoselectivity in a dynamic system because the recognition process relies only on weak noncovalent interactions. Herein, we report the highly diastereoselective recognition of the dissymmetric self-assembled capsule $\mathbf{1}\cdot\mathbf{4}BF_4$ by virtue of the steric and electronic interactions between a guest and the interior of the cavity.

Our group has been working intensively on developing calixarene-based container molecules.[8] During these studies, the self-assembled capsule $\mathbf{1}\cdot\mathbf{4}BF_4$ has been discovered to encapsulate a variety of guest molecules and heterodimeric hydrogen-bonded pairs of carboxylic acids.[9] The D_4 symmetric capsule lacks a mirror plane and exists as a racemic mixture of two enantiomeric forms (Figure 1). When chiral guest **2** is encapsulated within capsule **1**, two diastereomeric isomers are formed. Guest **2** is positioned along the C_4 symmetry axis of the capsule, and its tumbling is constrained due to the steric requirements of the aromatic walls. The ester side chains of **2a–q** are placed near the resorcinarene upper ends of the capsule, which creates the close contact responsible for effective steric and electronic interactions with the bipyridyl moiety. These secondary interactions should lead to high diastereoselectivity of the dissymmetric capsule **1** with **2**.

Encapsulation studies with guests **2a–q** were carried out by ^{1}H NMR spectroscopy. Figure 2 displays the ^{1}H NMR spectrum of $\mathbf{2a}\subset\mathbf{1}\cdot\mathbf{4}BF_4$. The signals of the bound and unbound guests appeared independently at room temper-

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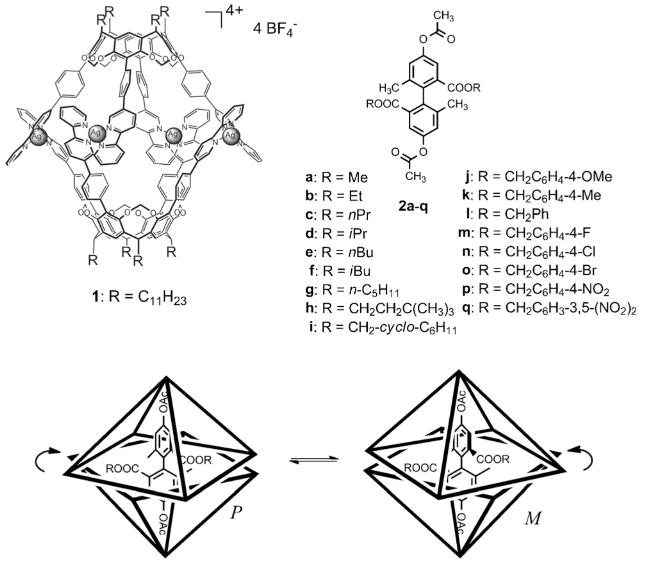

Figure 1. Self-assembled capsule $\mathbf{1}\cdot 4\,BF_4$, chiral guests **2a–q**, and a schematic representation of the stereoisomerism of $\mathbf{2}\subset\mathbf{1}$.

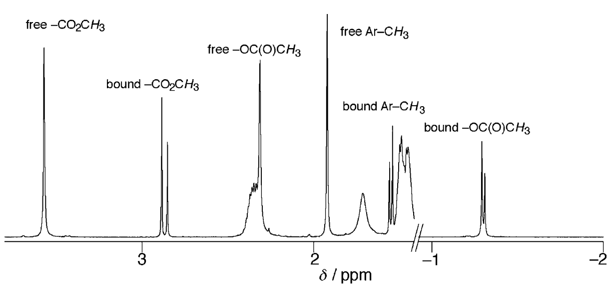

Figure 2. ^{1}H NMR spectrum of chiral guest **2a** in the presence of $\mathbf{1}\cdot 4\,BF_4$.

ature; this trait supported the suggestion that a sizeable kinetic barrier exists to the in-and-out exchange process of the guest to the capsule. The guest exchange between the bound and unbound states was confirmed with a 2D ROESY spectrum. The acetoxy methyl resonances appeared in a clear window above $\delta = 0$ ppm and were split into two sets of signals in a ratio of 3:2, which is demonstrative of the diastereomeric complexes (Figure 2). Large complexation-induced shifts (CIS) of the methyl resonances ($\Delta\delta = -3.60$ and -3.62 ppm) indicated that the acetoxy groups experienced a strong shielding effect, which could be rationalized by the fact that they were positioned deep inside the cavity surrounded by the eight aromatic rings of the cavitands. The methoxy and $ArCH_3$ groups also appeared as two sets of resonances with substantial upfield shifts ($\Delta\delta = -0.69$ and -0.72 ppm and $\Delta\delta = -0.36$ and -0.38 ppm for the $COOCH_3$ and $ArCH_3$ groups, respectively). Intermolecular NOE correlations between the methoxy resonance and the inner α-pyridyl and aromatic linker resonances place the methoxy groups in close proximity to the peripheral metal centers. Thus, the principal axis of the guest stays along the C_4 axis of the capsule, and the close contact of the ester groups to the chiral metal centers probably generates a steric interaction that results in a difference in energy between the diastereomers.

To generate a sizeable difference in energy between the diastereomers, the intermolecular steric interactions between capsule $\mathbf{1}\cdot 4\,BF_4$ and the guest were tuned by modification of the ester substituents, through the synthesis of chiral guests **2a–q**. The binding constants (K_A and K_B) of the predominant and subordinate diastereomers were determined in competition experiments with 4,4′-diacetoxybiphenyl (K_a: 82 000 L mol^{-1})[9b] by using ^{1}H NMR spectroscopy at 298 K in [D$_1$]chloroform (Table 1). With the series of aliphatic esters **2a–i**, the stabilities of complexes $\mathbf{2a–i}\subset\mathbf{1}\cdot 4\,BF_4$ were influenced by the structure of the ester substituents. The encapsulation was facilitated by increased size of the aliphatic substituents, and the binding constant indicated saturation with the *n*-butyl ester **2e**. However, the larger aliphatic substituents of **2g–i** reduced the stability of the complexes. The guest encapsulation sets the alkyl substituents near the bipyridyl moiety. The close contact between the ester substituent and the bipyridyl moiety generates favorable CH–π interactions that probably give rise to extra stabilization of the complexes with substituents **2e**,**f**, whereas sizeable chains (in **2g–i**) are not preferred because of the serious steric interactions with the bipyridine moiety. However, the sizes and shapes of the ester substituents are not critical for the diastereoselectivities.

Table 1: Binding constants (K_A and K_B) for predominant and subordinate diastereomers and diastereomeric excesses (*de*) at 298 K in [D$_1$]chloroform.

Guest	K_A [L mol^{-1}]	K_B [L mol^{-1}]	*de* [%]	Guest	K_A [L mol^{-1}]	K_B [L mol^{-1}]	*de* [%]
2a	4656	3104	20	**2j**	158 652	1603	98
2b	2869	2347	10	**2k**	34 474	4701	76
2c	5582	2749	34	**2l**	44 761	5532	78
2d	2515	1976	12	**2m**	18 334	3755	66
2e	6037	6037	0	**2n**	9848	2778	56
2f	5702	2444	40	**2o**	8039	2680	50
2g	4760	3740	12	**2p**	350	150	40
2h	1076	717	20	**2q**	55	–	–
2i	1783	1783	0				

During the guest screening, excellent selectivity and stability for the encapsulation were accomplished by installing benzyl groups onto the ester substituents. A diastereoselectivity of 98 % *de* was achieved by the complexation of **2j**. Upon addition of **2j** into a chloroform solution of $\mathbf{1}\cdot 4\,BF_4$, two sets of acetoxy proton signals appeared at values higher than $\delta = 0$ ppm in a ratio of 99:1 and with appreciable binding constants. The electron-rich aromatic rings of the benzyl esters (**2j–l**) resulted in remarkable diastereoselectivities with high binding constants. In contrast, the introduction of electron-withdrawing groups onto the benzyl ester (**2m–p**) significantly reduced the diastereoselectivities and binding constants. The loading of two nitro groups onto the benzene rings greatly diminished the binding ability of **2q**. As a consequence of these results, it can be noted that the

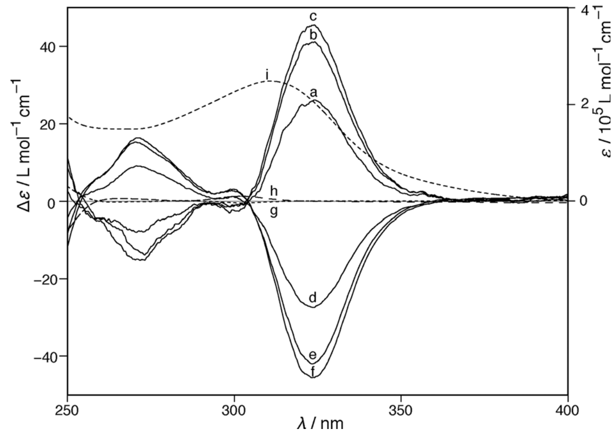

Figure 3. Circular dichroism spectra of capsule **1·4**BF$_4$ (9.00×10^{-5} mol L^{-1}) in the presence of chiral guests (*R*)-**2l** (a–c: 1.0, 2.0, and 3.0 equiv, respectively) and (*S*)-**2l** (d–f: 1.0, 2.0, and 3.0 equiv, respectively), (*R*)-**2l** alone (g), and (*S*)-**2l** alone (h), and the UV/Vis absorption spectrum of **1·4**BF$_4$ in chloroform at 298 K (i).

electronic features of the benzyl ester govern the *P* and *M* stereoisomerism.

Circular dichroism (CD) spectroscopy was informative for gaining an insight into the stereoselection of the diastereomeric complex **2l**$\subset$**1·4**BF$_4$. Induced CD was observed when the optically active guests (*R*)- and (*S*)-**2l** were encapsulated within the cavity. Figure 3 displays the UV/Vis absorption and CD spectra of **1·4**BF$_4$ in chloroform. An intense peak was observed in the absorption spectrum at 310 nm, which is assignable to a π–π* transition in the bipyridyl moiety of **1·4**BF$_4$. Upon addition of (*R*)-**2l**, induced plus-to-minus bisignate CD signals of **1·4**BF$_4$ emerged at 322 and 270 nm, respectively. The CD spectra with (*R*)-**2l** and (*S*)-**2l** exhibit a mirror-image relationship with respect to the line of $\Delta\varepsilon = 0$. The signal intensities at 322 nm were dependent on the concentrations of the guest, which indicates that the chiral guest complexation within the dissymmetric cavity resulted in a difference in energy between the *P* and *M* conformations and biased the population.

To determine the absolute stereochemistry of dissymmetric capsule **1·4**BF$_4$, a conformational search of complex **2l**$\subset$**1** was carried out by using the MacroModel V9.1 software.[10] Initial geometries of the complex were generated by a Low-Mode search,[11] and the resulting structures were optimized by using the MMFFs force field with GB/SA chloroform solvation treatment.[12] The most stable structure of complex (*S*)-**2l**$\subset$(*P*)-**1** is shown in Figure 4. The two benzyl groups of **2l** are located in one of the four open sides to create a π–π stacking interaction with the electron-deficient bipyridyl rings.

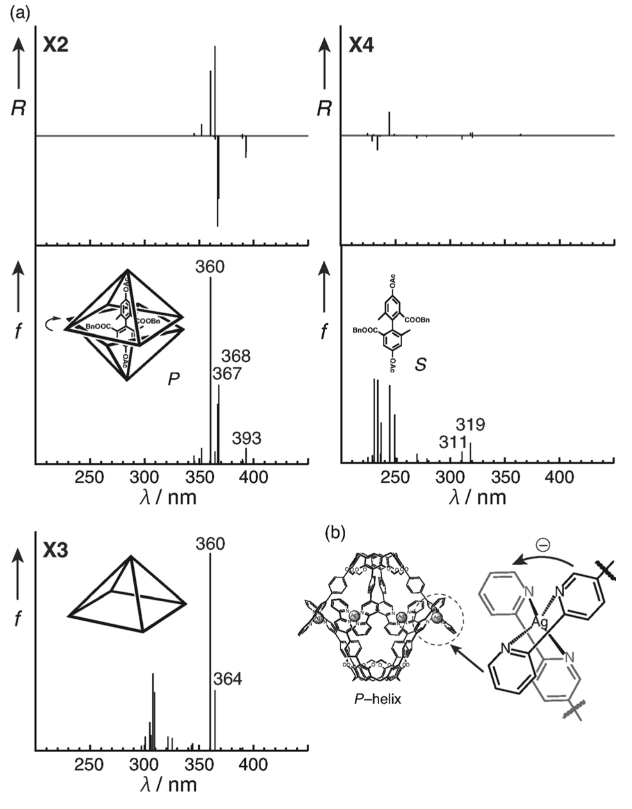

Figure 5. a) Theoretical absorption (bottom) and CD (top) spectra of **X2**, **X3**, and **X4**. Calculations were carried out by using the ZINDO/S Hamiltonian. b) Orientation of the bipyridyl moieties around the silver ion of the *P* helix of the capsule.

The full structure of (*S*)-**2l**$\subset$(*P*)-**1** was reoptimized by the ONIOM2[13] (MX062X/6-31G:UFF) method. The ONIOM method divides (*S*)-**2l**$\subset$(*P*)-**1** into high- (encapsulated guest) and low- (host shell) level layers. Based on the geometry-optimized structure (**X1**), the calculated excitation and CD spectra of **X1** without silver ions (**X2**), the monomer unit of the host shell (**X3**), and the encapsulated guest only (**X4**) were obtained by using the ZINDO/S Hamiltonian, with the results shown in Figure 5 a. Relative to the results of the monomer **X3**, red-shifted transitions (393, 368, and 367 nm) were found in the calculated absorption spectra of the capsule **X2**; these transitions are assigned to

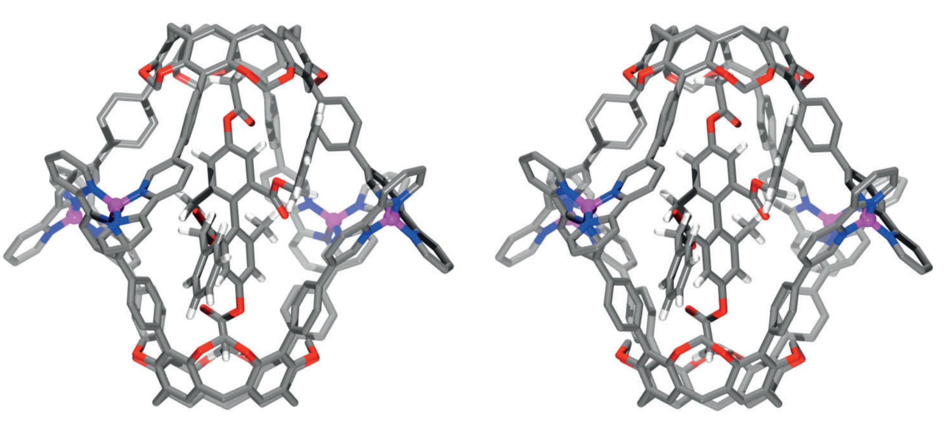

Figure 4. Stereoplot of the most stable structure of (*S*)-**2l**$\subset$(*P*)-**1**.

the long-axis-polarized π–π* transitions of the bipyridyl moiety of the host shell.[14] The CD intensities of these transitions were relatively strong. On the other hand, the calculated oscillator strengths and CD intensities were relativity weak in the spectra of the guest in the capsule (**X4**) and were calculated to be mostly in the shorter 230–250 nm region. Therefore, the observed CD signals in the 250–400 nm region can be assigned to supramolecular chirality of the host shell. In the calculated CD spectrum of **X2**, minus-to-plus signals were estimated; this result is consistent with that observed in ascending energy terms in the CD spectrum of (*S*)-**2l**$\subset$**1·4**BF$_4$ (Figure 3). The origin of the CD signal of (*S*)-**2l**$\subset$**1·4**BF$_4$ can then be explained by exciton coupling theory.[15] Two bipyridyl groups from the two monomer units constituting **1·4**BF$_4$ should be oriented in an anticlockwise (left-handed) screw arrangement around a silver ion (Figure 5b). When the two pyridyl moieties take left-handedness, the two calixarene units constituting the **1·4**BF$_4$ capsule arrange in a right-handed *P* helix. In other words, if the two calixarenes inversely arrange in a right-handed *P* helix in **1·4**BF$_4$, the CD signal in the longer wavelength region changes from minus-to-plus in ascending energy (left-handed for the two pyridine units). This occurs when **1·4**BF$_4$ encapsulates (*S*)-**2l**. Conversely, the plus-to-minus CD signal observed in the (*R*)-**2l**$\subset$**1·4**BF$_4$ spectrum (Figure 3) is consistent with a left-handed calixarene unit in **1·4**BF$_4$; that is, the (*R*)-**2l** guest induces a left-handed *M* helix of **1**.

The guest-induced helicities of **1·4**BF$_4$ with chiral guests (*R*)-**2a–q** were assessed by using CD spectroscopy. The molar circular dichroism values (Δε) and dissymmetric factors (*g*) at 324 nm were evaluated when the cavity of **1·4**BF$_4$ was fully occupied by (*R*)-**2a–q**. Table 2 shows the Δε and *g* values and the helicity of the capsule, as determined by the sign of the Δε value at 324 nm. The aliphatic ester substituents of (*R*)-**2a–i** had a limited participation in the helical induction. The guest complexation for (*R*)-**2b–g** resulted in negative Δε values, which indicated that the *P* helicity was predominant, whereas (*R*)-**2a,h** promoted the *M* helicity with a positive Δε value. The *n*-butyl and cyclohexyl substituents in (*R*)-**2e,i** had no effect on the helical induction. In contrast, guests (*R*)-**2j–o** displayed intense Δε values with positive signs and led to *M* helicity. The electron-withdrawing nitro group in (*R*)-**2p** caused a negative CD sign, which resulted in *P* helicity. Thus, it is obvious that the electronic features of the benzyl ester substituents influence the helicity of the capsule.

Table 2: Molar circular dichroism ($\Delta\varepsilon_{324\,\text{nm}}$ [L mol^{-1} cm^{-1}]), predominant helicities, and dissymmetric factors (g/10^{-4}) of capsule **1·4**BF$_4$ in the presence of chiral guests (*R*)-**2a–q** in chloroform at 298 K.

Guest	Δε	Helicity	*g*	Guest	Δε	Helicity	*g*
2a	16.16	*M*	0.80	**2j**	84.34	*M*	4.16
2b	−5.23	*P*	−0.26	**2k**	28.75	*M*	1.42
2c	−29.14	*P*	−1.44	**2l**	45.03	*M*	2.22
2d	−20.11	*P*	−0.99	**2m**	27.06	*M*	1.33
2e	0.0	–	0.0	**2n**	15.60	*M*	0.77
2f	−30.73	*P*	−1.51	**2o**	14.88	*M*	0.73
2g	−19.65	*P*	−0.97	**2p**	−12.89	*P*	−0.64
2h	9.42	*M*	0.46	**2q**	–	–	–
2i	0.0	–	0.0				

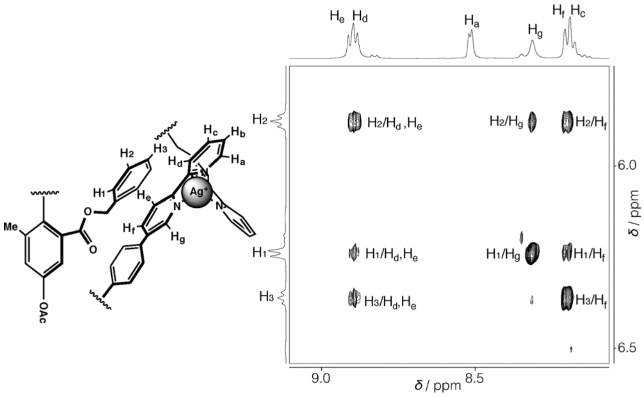

Figure 6. Structural representation of the π–π stacking interaction between the guest side chain and the bipyridyl moieties of **1·4**BF$_4$ (left) and the intermolecular NOE correlations (right).

A detailed structure consideration of complex **2l**$\subset$**1·4**BF$_4$ was carried out by using 2D NMR techniques. Figure 6 shows the intermolecular NOE correlations between the aromatic protons of the benzyl ester and the bipyridiyl protons (H1/H$_{\text{d–g}}$, H2/H$_{\text{d–g}}$, H3/H$_{\text{d–f}}$), which suggest that the aromatic rings remain stacked on the bipyridyl moiety. In fact, the aromatic protons of the benzyl ester experienced shielding effects that led to significant upfield shifts of $\Delta\delta = -0.89$, -1.40, and -0.92 ppm for H$_1$, H$_2$, and H$_3$, respectively. Thus, a significant contribution from the intermolecular aromatic stacking interactions probably drives the diastereoselectivities.

In order to gain insight into the diastereoselection, van't Hoff plots were carried out, which showed the diastereoselectivities to be dependent on temperature. Ratios of the diastereomers for complexes **2j–p**$\subset$**1·4**BF$_4$ were measured at various temperatures. Plotting of the ratios of the $\ln(K_A/K_B)$ value versus the $1/T$ value resulted in a very good linear correlation, to produce the relative enthalpic and entropic contributions between the diastereomeric pairs. The diastereoselectivities were enthalpy driven and entropy opposed (Table 3). Plots of the enthalpic components versus the substituent Hammett constants (σ_p^+)[16] produce a good linear correlation ($R^2 = 0.926$), which indicates that strongly electron-donating substituents enhance the diastereoselectivity of the complexes. Thus, the electron-donating aromatic

Table 3: Hammett parameters (σ_p^+), $\Delta\Delta G^\circ_{303\,\text{K}}$, $\Delta\Delta H^\circ$, and $\Delta\Delta S^\circ$ for the diastereomeric pairs.

Guest	σ_p^+	$\Delta\Delta G^\circ$ [kcal mol^{-1}]	$\Delta\Delta H^\circ$ [kcal mol^{-1}]	$\Delta\Delta S^\circ$ [cal mol^{-1} K^{-1}]
2j	−0.778	−1.68	−3.8 ± 0.1	−7.2 ± 0.7
2k	−0.311	−1.10	−2.94 ± 0.03	−6.1 ± 0.1
2l	0.000	−1.12	−2.80 ± 0.05	−5.6 ± 0.1
2m	−0.073	−0.92	−2.72 ± 0.07	−6.0 ± 0.1
2n	0.114	−0.78	−2.70 ± 0.05	−6.4 ± 0.1
2o	0.150	−0.74	−2.66 ± 0.05	−6.4 ± 0.1
2p	0.790	0.55	−1.07 ± 0.05	−5.5 ± 0.1

ring of the benzyl ester prefers to be in close contact with the electron-deficient bipyridyl moiety in a π–π stacking conformation. Accordingly, the predominant diastereomer receives greater enthalpic benefits that originate from the donor–acceptor interaction. This electrostatic interaction acting at the host periphery is a considerable determinant for the diastereoselectivity.

In conclusion, high diastereoselectivity of the dissymmetric capsule was achieved by chiral guest encapsulation. Surprisingly, an excellent selectivity of 98% *de* was attained. The helical sense of the self-assembled capsule was determined based on CD exciton coupling theory, molecular mechanics, and DFT calculations. A negative CD sign at 324 nm established a *P* helicity of the capsule. A detailed structure study of $\mathbf{2l}\subset\mathbf{1}\cdot\mathbf{4}\,\mathrm{BF}_4$ revealed that the benzyl ester moiety is positioned on the bipyrydyl moiety with attractive π–π stacking interactions. The difference in energy between the *P* and *M* conformations was determined by the steric and electronic interactions found at the periphery of the capsule: electron-donating groups strongly improved the diastereoselectivity, whereas electron-withdrawing group did not. These results might provide a rational means for the development of a molecular machine that manipulates chiral information encoding in a supramolecular structure.

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[1] a) C. J. Easton, S. F. Lincoln, *Chem. Soc. Rev.* **1996**, *25*, 163–170; b) E. Rizzarelli, G. Vecchio, *Coord. Chem. Rev.* **1999**, *188*, 343–364; c) K. Kano, *J. Phys. Org. Chem.* **1997**, *10*, 286–291.

[2] a) D. J. Cram, R. C. Helgeson, L. R. Sousa, J. M. Timko, M. Newcomb, P. Moreau, F. De Jong, G. W. Gokel, D. H. Hoffman, L. A. Domeier, S. C. Peacock, K. Madan, L. Kaplan, *Pure Appl. Chem.* **1975**, *43*, 327–349; b) G. W. Gokel, W. M. Leevy, M. E. Weber, *Chem. Rev.* **2004**, *104*, 2723–2750; c) X. X. Zhang, J. S. Bradshaw, R. M. Izatt, *Chem. Rev.* **1997**, *97*, 3313–3361.

[3] a) P. S. Dieng, C. Sirlin, *Int. J. Mol. Sci.* **2010**, *11*, 3334–3348; b) T. H. Webb, C. S. Wilcox, *Chem. Soc. Rev.* **1993**, *22*, 383–395; c) C. Seel, F. Vögtle, *Angew. Chem.* **1992**, *104*, 542–563; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528–549.

[4] a) A. Sirit, M. Yilmaz, *Turk. J. Chem.* **2009**, *33*, 159–200; b) V. Böhmer, D. Kraft, M. Tabatabai, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *19*, 17–39; c) Y.-S. Zheng, J. Luo, *J. Inclusion Phenom. Macrocyclic Chem.* **2011**, *71*, 35–56; d) S.-Y. Li, Y.-W. Xu, J.-M. Liu, C.-Y. Su, *Int. J. Mol. Sci.* **2011**, *12*, 429–455.

[5] a) S. E. Gibson, M. P. Castaldi, *Chem. Commun.* **2006**, 3045–3062; b) J. Zhou, Y. Tang, *Chem. Soc. Rev.* **2005**, *34*, 664–676; c) T. W. Bell, N. M. Hext, *Chem. Soc. Rev.* **2004**, *33*, 589–598.

[6] a) J. M. Rivera, T. Martín, J. Rebek, Jr., *Science* **1998**, *279*, 1021–1023; b) C. Nuckolls, F. Hof, T. Martín, J. Rebek, Jr., *J. Am. Chem. Soc.* **1999**, *121*, 10281–10285; c) J. M. Rivera, S. L. Craig, T. Martín, J. Rebek, Jr., *Angew. Chem.* **2000**, *112*, 2214–2216; *Angew. Chem. Int. Ed.* **2000**, *39*, 2130–2132; d) J. M. Rivera, T. Martín, J. Rebek, Jr., *J. Am. Chem. Soc.* **2001**, *123*, 5213–5220.

[7] A. V. Davis, D. Fiedler, M. Ziegler, A. Terpin, K. N. Raymond, *J. Am. Chem. Soc.* **2007**, *129*, 15354–15363.

[8] a) T. Haino, H. Araki, Y. Yamanaka, Y. Fukazawa, *Tetrahedron Lett.* **2001**, *42*, 3203–3206; b) T. Haino, Y. Yamanaka, H. Araki, Y. Fukazawa, *Chem. Commun.* **2002**, 402–403; c) T. Haino, J. Seyama, C. Fukunaga, Y. Murata, K. Komatsu, Y. Fukazawa, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 768–770; d) T. Haino, C. Fukunaga, Y. Fukazawa, *Org. Lett.* **2006**, *8*, 3545–3548; e) T. Haino, M. Yanase, C. Fukunaga, Y. Fukazawa, *Tetrahedron* **2006**, *62*, 2025–2035; f) T. Haino, H. Fukuoka, M. Katayama, Y. Fukazawa, *Chem. Lett.* **2007**, *36*, 1054–1055; g) T. Haino, H. Fukuoka, H. Iwamoto, Y. Fukazawa, *Supramol. Chem.* **2008**, *20*, 51–57.

[9] a) T. Haino, M. Kobayashi, M. Chikaraishi, Y. Fukazawa, *Chem. Commun.* **2005**, 2321–2323; b) T. Haino, M. Kobayashi, Y. Fukazawa, *Chem. Eur. J.* **2006**, *12*, 3310–3319; c) T. Haino, K. Fukuta, H. Iwamoto, S. Iwata, *Chem. Eur. J.* **2009**, *15*, 13286–13290.

[10] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440–467.

[11] I. Kolossváry, W. C. Guida, *J. Am. Chem. Soc.* **1996**, *118*, 5011–5019.

[12] D. Qiu, P. S. Shenkin, F. P. Hollinger, W. C. Still, *J. Phys. Chem. A* **1997**, *101*, 3005–3014.

[13] S. Dapprich, I. Komáromi, K. S. Byun, K. Morokuma, M. J. Frisch, *J. Mol. Struct. THEOCHEM* **1999**, *461*, 1–21.

[14] N. Kobayashi, S. Minato, T. Osa, *Makromol. Chem.* **1983**, *184*, 2123–2132.

[15] N. Kobayashi, A. Muranaka, J. Mack, *Circular Dichroism and Magnetic Circular Dichroism Spectroscopy for Organic Chemists*, RSC, Cambridge, **2012**.

[16] a) H. C. Brown, Y. Okamoto, *J. Am. Chem. Soc.* **1958**, *80*, 4979–4987; b) Y. Okamoto, H. C. Brown, *J. Org. Chem.* **1957**, *22*, 485–494; c) S.-H. Chiu, K.-S. Liao, J.-K. Su, *Tetrahedron Lett.* **2004**, *45*, 213–216.