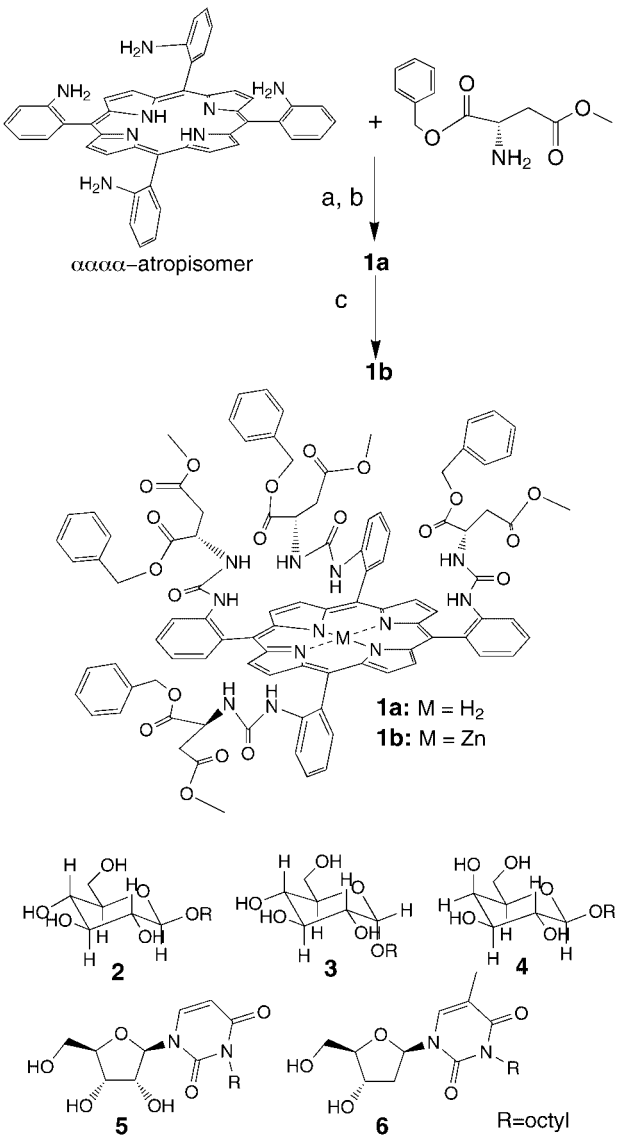
Molecular Recognition of Carbohydrates through Directional Hydrogen Bonds by Urea-Appended Porphyrins in Organic Media **

Yeon-Hwan Kim and Jong-In Hong*

Carbohydrate recognition through noncovalent interactions is one of the challenging goals of biomimetic and supramolecular chemistry.[1] This is partly because of the various cellular recognition processes of oligosaccharides on the cell surfaces,[2] and partly because of the 3D complexity, even in monosaccharide structures.[3] X-ray crystallographic analyses of sugar–protein complexes reveal that multiple hydrogen bonds are equatorially arranged in the hydrophobic protein cavity for effective intermolecular interactions.[4] Therefore, an effective approach to carbohydrate recognition is to surround the polar hydroxy groups of carbohydrates with complementary hydrogen-bonding receptor groups and introduce aromatic surfaces into the receptor against carbohydrate CH moieties. Despite considerable efforts in the development of artificial carbohydrate receptors, there have only been a few effective hydrogen-bonding and biomimetic carbohydrate-recognition systems in organic media reported to date.[5,6] Here we report novel porphyrin-based carbohydrate receptors with a complementary and convergent arrangement of hydrogen-bond donor and acceptor functionality, which show unusually high affinity and selectivity toward monosaccharides in chloroform and can tolerate significant amounts of hydroxylic cosolvents, in spite of an acyclic and flexible structure without a discrete hydrophobic cavity.[7]

Inspired by the X-ray crystal structures of protein–carbohydrate complexes, we designed receptors **1a** and **1b** (Scheme 1), in which four aspartate units are used as hydrogen-bond donors and acceptors and $\alpha\alpha\alpha\alpha$-5,10,15,20-tetrakis-(*o*-aminophenyl)porphyrin both as a π donor for CH–π interactions and as a rigid spacer for the convergent hydrogen-bonding groups (four urea groups) to be prearranged in favorable positions for sugar recognition above the porphyrin plane. These units were covalently connected by four urea linkages that were known to be strong H-bond donors. Therefore, multiple hydrogen bonds were possible in the inner cavity of the receptors. Compound **1a** was prepared by a reaction of α-benzyl-β-methyl protected aspartate and $\alpha\alpha\alpha\alpha$-5,10,15,20-tetrakis-(*o*-isocyanophenyl)porphyrin,[8] as shown in Scheme 1.[9a] Compound **1b** was prepared in quantitative yield by heating **1a** at reflux with $Zn(OAc)_2$ in a mixture of chloroform and methanol.[9b]



Scheme 1. Synthesis of **1a** and **1b**: a) 20% phosgene in toluene, triethylamine (TEA), CH_2Cl_2; b) TEA, α-benzyl-β-methyl-aspartate, CH_2Cl_2; c) $Zn(OAc)_2$, $CHCl_3/CH_3OH$.

UV/Vis absorption spectra in chloroform, stabilized by 2% ethanol at 298 K, showed that the Soret bands of **1a** and **1b** underwent a red shift (1–2 nm) as **2**–**6** were bound in the inner space of the receptors (Supporting Information: Figure S1). The appearance of clear isosbestic points indicates the existence of two states, caused by the formation of a 1:1 complex. The relative binding affinities of **2**–**6** (**2** > **4** > **3** > **5** > **6**, with K_a values ranging from 700–65000) for the receptors **1a** and **1b** depend upon the number of equatorial hydroxy groups of the guests (Supporting Information: Table S1). A higher affinity to octyl β-D-glucoside, with its all-equatorial hydroxy groups, is caused by the appropriately arranged hydrogen-bonding sites of the receptors for **2**. It turns out that the inner space of the receptors is a pool of hydrogen bonding sites in which urea NH groups, strong hydrogen-bond donors, are positioned equatorially in a convergent manner.

For comparison of the receptors with other systems, we attempted to obtain the association constants in chloroform

[*] Prof. J.-I. Hong, Y.-H. Kim
School of Chemistry, College of Natural Sciences
Seoul National University
Seoul 151-747 (Korea)
Fax: (+82) 2-889-1568
E-mail: jihong@plaza.snu.ac.kr

[**] Financial support from CMDS (KOSEF) is gratefully acknowledged. Y.-H.K. thanks the Ministry of Education for the award of the BK 21 fellowship. We thank Dr. O. S. Lee for computational modeling. We also thank a referee for helpful suggestions.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

using fluorescence spectroscopy. On excitation at 420 nm, **1a** emits fluorescence between 620 nm and 690 nm (maximum at 649 nm). Compound **1b** emits between 540 nm and 690 nm (two maxima at 605 nm and 652 nm) on excitation at 430 nm. Addition of **2–6** to **1a** caused blue shifts (3–5 nm) with increasing emission intensity, and addition of **2–6** to **1b** led to a decrease of intensity and a slight blue shift of λ_{max} ($\approx$ 1 nm), unless a large excess of **2–6** was added (Supporting Information: Figure S2). The fluorescence titration data for **1b** at 605 nm as a function of the change in carbohydrate concentration fit well to a 1:1 binding isotherm before addition of many equivalents of **2–6**, and similar results were also obtained for **1a** (Figure 1). The apparent association constants for the formation of the complexes of the receptors and various carbohydrates are listed in Table 1. The selectivity trend is maintained, while the K_a value for **2** is raised to the high value of $2 \times 10^7\,\text{M}^{-1}$.

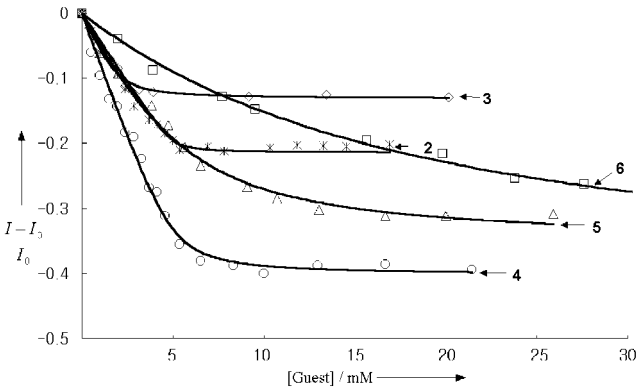


Figure 1. Experimental and calculated values for the fluorescence binding study of **1b**+(**2–6**). The solid line is the calculated curve; $[\mathbf{1b}] = 5 \times 10^{-6}$ M for **2** and **4–6**, and $[\mathbf{1b}] = 2.0 \times 10^{-6}$ M for **3**.

The interactions between the receptors and **2–6** were investigated by ^{1}H NMR spectroscopy. In $CDCl_3$, the formation of the complexes through multiple hydrogen bonds was shown by the significant downfield shifts of the signals for urea NH protons and the appearance of signals arising from carbohydrate protons in an abnormal upfield region, which may be attributed to the effect of the ring current of the porphyrin plane. In ^{1}H NMR spectroscopic reverse titrations, it was also found that addition of **1** to **2–4** induced upfield shifts of the signals for carbohydrate CH and OH protons (Supporting Information: Figure S3). However, the ^{1}H NMR titration spectra in $CDCl_3$ indicated saturation at about one equivalent carbohydrate and the motion of signals could not be analyzed by nonlinear least-squares curve fitting, maybe because of the large association constants in $CDCl_3$. Addition of **2–6** to **1** in $CDCl_3/CD_3OD$ (v/v, 10:1) showed distinct shifts of the other signals for **1**, despite the disappearance of the signals caused by the urea protons. This information means that complexation of pyranosides with the receptors remained effective in the presence of competing methanol and the association constants could be calculated by 1:1 nonlinear least-squares curve fitting (Table 2). The selectivity trend (**2** > **4** > **3**) was as before, and furanosides **5** and **6** were bound very weakly.

Molecular modeling revealed the plausibility of multiple hydrogen bonds in the complex of **1a** and **2**, in which all the hydroxy groups and the alkoxy oxygen of **2** were involved in the formation of hydrogen bonds as two donors (C=O···HO) and five acceptors (urea-NH···O), as shown in Figure S4 (Supporting Information).[10] In addition, the porphyrin plane is below two axial CH groups of **2**; this was confirmed by the upfield shifts of the CH-proton resonance signals of **2**. The complex of **1a** and **2** ($\Delta G° = -111.0$ kcal mol^{-1}) had a lower calculated conformation energy than that of **1a** and **3** ($\Delta G° = -108.8$ kcal mol^{-1}), which shows the same anomer-selective recognition for **2** as in the experimental result.[10]

Compound **1b** shows essentially distinct biphasic circular dichroism (CD) in the Soret region with negative Cotton effects at a short wavelength and positive Cotton effects at a longer wavelength (Figure 2). This biphasic CD seems to originate from the relative orientation of the aspartate carbonyl groups to the porphyrin[12] because one chiral aspartate group of **1b** is situated near the porphyrin plane through the formation of intramolecular hydrogen bonds between one aspartate β-carbonyl group and urea NH groups in the alternate position. This explanation was confirmed by the low-energy conformations based on the Monte Carlo conformation search, in which all the conformations found within 5 kcal above the lowest energy conformer show the same pattern of intramolecular hydrogen bonds (Supporting Information: Figure S5).[10] Interestingly, **1b** demonstrates chirality-specific CD signals on complexation with chiral carbohydrates; while the **1b**–L-glucoside complex gives an S-shaped CD band with decreased amplitude, **1b**–D-pyranoside complexes exhibit reversed S-shaped CD bands. We concluded that the intramolecular hydrogen bonds of the receptor were replaced by stronger intermolecular hydrogen bonds between the receptor and the guest, and therefore the relative orientations of the C–O and O–H moieties of the carbohydrate guest, which are located near the porphyrin plane, induced distinct biphasic CD spectra similar to the

Table 1. Binding constants (K_a [M^{-1}]) and free-energy change ($\Delta G°$ [kcal mol^{-1}]) calculated from fluorescence titrations of **1** with octyl pyranosides/furanosides **2–6** in chloroform[a] at 298 K.

	2		**3**		**4**		**5**		**6**	
	K_a[b]	$-\Delta G°$	K_a	$-\Delta G°$	K_a	$-\Delta G°$	K_a	$-\Delta G°$	K_a	$-\Delta G°$
1a	$2(\pm 0.05$[c]$) \times 10^7$	9.87	$4(\pm 0.7) \times 10^6$	9.06	$9(\pm 0.4) \times 10^6$	9.51	$6(\pm 1) \times 10^5$	7.92	$2(\pm 0.3) \times 10^5$	7.25
1b	$2(\pm 0.05) \times 10^7$	10.00	$4(\pm 0.3) \times 10^6$	9.03	$5(\pm 0.8) \times 10^6$	9.17	$5(\pm 0.9) \times 10^5$	7.80	$7(\pm 0.5) \times 10^4$	6.59

[a] Used immediately after raising the pH with anhydrous K_2CO_3, $[\mathbf{1a}] = 2.5 \times 10^{-6}$ M for **2**, **3**, and **4**, 4.0×10^{-6} M for **5** and **6**, guest concentrations: 0.4–11 μM for **2**, 0.4–30 μM for **3**, and 0.6–11 μM for **4**, 0.6–18 μM for **5**, and 2–100 μM for **6**. $[\mathbf{1b}] = 5 \times 10^{-6}$ M for **2**, **4**, **5**, and **6**, 2.0×10^{-6} M for **3**. Guest concentrations: 0.5–17 μM for **2**, 0.4–20 μM for **3**, and 0.5–21 μM for **4**, 1–26 μM for **5**, and 2–79 μM for **6**. [b] Calculated using custom-written nonlinear least-square curve-fitting programs implemented within Sigmaplot version 4.01. [c] Standard deviations in K_a.

  0044-8249/02/11416-3072 $ 20.00+.50/0 *Angew. Chem.* **2002**, *114*, Nr. 16

Table 2. Binding constants (K_a [M^{-1}]), limiting change in chemical shift ($\Delta\delta$ [ppm]) of signals for benzylic H atoms and free-energy change ($\Delta G°$ [kcal mol^{-1}]) from ^1H NMR spectroscopic titrations of **1** with octyl pyranosides/furanosides **2**–**6** in $CD_3OD/CDCl_3$ (1:10) at 298 K.[a]

	2			**3**			**4**			**5**			**6**		
	K_a[b]	$\Delta\delta$	$-\Delta G°$	K_a	$\Delta\delta$	$-\Delta G°$	K_a	$\Delta\delta$	$-\Delta G°$	K_a	$\Delta\delta$	$-\Delta G°$	K_a	$\Delta\delta$	$-\Delta G°$
1a	340(9)	0.13	3.45	110(5)	0.14	2.78	140(13)	0.11	2.93	58(5)	0.11	2.40	NB[c]		
										>10000[d]	0.22	>5.45	6900(1600)[d]	0.19	5.23
1b	150(3)	0.05	2.97	59(1)	0.05	2.41	73(3)	0.05	2.54	NB[c]			NB[c]		
										>10000[d]	0.24	>5.45	1150(210)[d]	0.20	4.17

[a] [**1a**] is in the range 2.0–1.5 mM for titration with octyl pyranosides and in the range 0.8 to 0.7 mM for titration with octyl furanosides. The ^1H NMR spectrum of **1a** was independent of concentration within this range. Guest concentrations: 0.99–20 mM for **2**, 1.0–19 mM for **3**, 1.1–23 mM for **4**, 0.4–8 mM for **5**, and 0.4–6 mM for **6**. [**1b**] is in the range 1.5–1.0 mM for titration with octyl pyranosides and in the range 2.0–1.6 mM for titration with octyl furanosides. The ^1H NMR spectrum of **1b** was independent of concentration within this range. Guest concentrations: 0.79–33 mM for **2**, 2.0–33 mM for **3**, 1.2–33 mM for **4**, 0.8–16 mM for **5**, and 2.0–28 mM for **6**. [b] Standard deviations in K_a. [c] NB = No binding or very weak interaction in $CD_3OD/CDCl_3$. There is a very small chemical shift change during titration in this range and the binding constant is estimated to be $<10\,M^{-1}$. [d] In $CDCl_3$, in the range of [**1a**] = 1.54–2.0 mM, [**1b**] = 2.2–2.8 mM for titration with octyl furanosides. ^1H NMR spectra of **1** were independent of concentration within this range. Guest concentrations: 0.4–4.6 mM (for **1a**), 0.4–9.1 mM (for **1b**) of **5**, and 0.4–6.7 mM (for **1a**), 0.4–23 mM (for **1b**) of **6**.

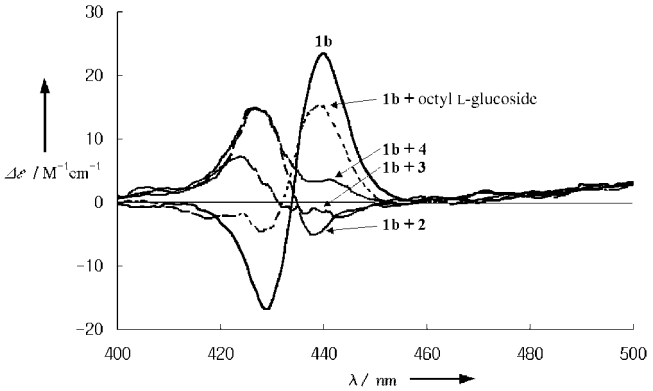


Figure 2. Circular dichroism induced in receptor **1b** by various carbohydrates in $CHCl_3$ at 25 °C. [**1b**] = 5×10^{-6} M, [**2**] = [**3**] = [**4**] = [octyl L-glucoside] = 2×10^{-3} M.[11]

results reported by Shinkai and co-workers and Mizutani et al.[13] Therefore, the receptors are not only effective binding agents for monosaccharides but also act as a sensitive CD probe for their chirality determination.

Finally, the extraction of native carbohydrates into nonpolar organic media containing the receptor yields further valuable information about the carbohydrate recognition of the receptors. When **1b** was sonicated with an excess of carbohydrates (glucose, galactose, and mannose) in $CHCl_3$, significant quantities of the carbohydrate could be detected by ^1H NMR spectroscopy after re-extraction into D_2O. No carbohydrate was detected in a control run in the absence of **1b**, except for trace galactose. These results show that organic-insoluble carbohydrates can be transported into an organic phase by the receptor. The extractabilities or affinities of hexoses for the receptor decreased in the same order as in the binding of organic-soluble carbohydrates to the receptors: glucose > galactose > mannose.[6q] The binding of natural carbohydrates to **1b** makes it possible that urea-appended porphyrin receptors with a well-defined hydrophobic cavity may bind them effectively, even under aqueous conditions (Supporting Information: Figure S6).

In summary, urea-appended porphyrins with convergent multiple hydrogen-bonding sites were found to be the most effective binding agent for pyranosides in chloroform among the carbohydrate receptors known to date, and still very effective even in the presence of hydroxylic cosolvents. The current system is an excellent example of how the combination of a rigid platform (porphyrin skeleton) and acyclic, flexible, yet preorganized polar groups (urea groups), aligned in a rigid plane, enables three-dimensional recognition of carbohydrates through the formation of a hydrophobic cavity and a suitable arrangement of hydrogen bonding sites. Such results look very promising as urea groups in the $\alpha\alpha\alpha\alpha$-positions of the porphyrin can be used to create strong hydrogen-bonding motifs for carbohydrate recognition and further adjusted to act as versatile receptors by introducing polar groups with H-bond donors and acceptors and/or hydrophobic groups.

Received: February 28, 2002
Revised: June 3, 2002 [Z18784]

[1] a) A. P. Davis, R. S. Wareham, *Angew. Chem.* **1999**, *111*, 3160–3179; *Angew. Chem. Int. Ed.* **1999**, *38*, 2978–2996; b) Y. Aoyama in *Comprehensive Supramolecular Chemistry, Vol. 2* (Eds.: J. L. Atwood, J. E. D. Davis, D. D. MacNicol, F. Vögtle), Pergamon, Oxford, **1996**, pp. 279–307.

[2] S. Hokomori, *Pure Appl. Chem.* **1991**, *63*, 473–482; A. Kobata, *Acc Chem. Res.* **1993**, *26*, 319–324.

[3] N. Sharon, H. Lis, *Science* **1989**, *246*, 227–234; N. Sharon, H. Lis, *Sci. Am.* **1993**, *268*(1), 74–81.

[4] R. U. Lemieux, *Chem. Soc. Rev.* **1989**, *18*, 347–374; F. A. Quiocho, *Pure Appl. Chem.* **1989**, *61*, 1293–1306; W. I. Weiss, K. Drickamer, *Annu. Rev. Biochem.* **1996**, *65*, 441–473.

[5] Studies in aqueous or partially aqueous media: a) Y. Aoyama, Y. Tanaka, H. Toi, H. Ogoshi, *J. Am. Chem. Soc.* **1988**, *110*, 634–635; b) Y. Aoyama, Y. Tanaka, S. Sugara, *J. Am. Chem. Soc.* **1989**, *111*, 5397–5404; c) Y. Kikuchi, K. Kobayashi, Y. Aoyama, *J. Am. Chem. Soc.* **1992**, *114*, 1351–1358; d) K. Kobayashi, Y. Asakawa, Y. Kato, Y. Aoyama, *J. Am. Chem. Soc.* **1992**, *114*, 10307–10313; e) R. Yanagihara, Y. Aoyama, *Tetrahedron Lett.* **1994**, *35*, 9725–9728; f) J. C. Morales, S. Penades, *Angew. Chem.* **1998**, *110*, 673–676; *Angew. Chem. Int. Ed.* **1998**, *37*, 654–657; g) T. D. James, K. Sandanayake, S. Shinkai, *Angew. Chem.* **1996**, *108*, 2039–2050; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1911–1922; h) A. Sugasaki, M. Ikeda, M. Takeuchi, S. Shinkai, *Angew. Chem.* **2000**, *112*, 3997–4000; *Angew. Chem. Int. Ed.* **2000**, *39*, 3839–3842; i) I. Hamachi, T. Nagase, S. Shinkai, *J. Am. Chem. Soc.* **2000**, *122*, 12065–12066; j) M. Bielecki, H. Eggert, J. C. Norrild, *J. Chem. Soc. Perkin Trans. 2* **1999**, 449–455; k) C. J. Davis, P. T. Lewis, M. E. McCarroll, M. W. Read, R. Cueto, R. M. Strongin, *Org. Lett.* **1999**, *1*, 331–334; l) P. T. Lewis, C. J. Davis, L. A. Cabell, M. He, M. W. Read, M. E. McCarroll, R. M. Strongin, *Org. Lett.* **2000**, *2*, 589–592; m) O. Rusin, V. Král, *Chem. Commun.* **1999**, 2367–2368;

  0044-8249/02/11416-3073 $ 20.00+.50/0

n) V. Král, O. Rusin, J. Charvátová, P. Anzenbacher, Jr., J. Fogl, *Tetrahedron Lett.* **2000**, *41*, 10147 – 10151; o) N. Sugimoto, D. Miyoshi, J. Zou, *Chem. Commun.* **2000**, 2295 – 2296.

[6] Studies in polar or apolar organic media: a) R. P. Bonar-Law, A. P. Davis, B. A. Murray, *Angew. Chem.* **1990**, *102*, 1497 – 1499; *Angew. Chem. Int. Ed. Engl.* **1990**, *30*, 1407 – 1409; b) A. P. Davis, R. S. Wareham, *Angew. Chem.* **1998**, *110*, 2397 – 2400; *Angew. Chem. Int. Ed.* **1998**, *37*, 2270 – 2273; c) R. Liu, W. C. Still, *Tetrahedron Lett.* **1993**, *34*, 2573 – 2576; d) P. B. Savage, S. H. Gellman, *J. Am. Chem. Soc.* **1993**, *115*, 10448 – 10449; e) C.-Y. Huang, L. A. Cabell, E. V. Anslyn, *J. Am. Chem. Soc.* **1994**, *116*, 2778 – 2792; f) R. P. Bonar-Law, J. K. M. Sanders, *J. Am. Chem. Soc.* **1995**, *117*, 259 – 271; g) J. Cuntze, L. Owens, V. Alcazar, P. Seiler, F. Diederich, *Helv. Chim. Acta* **1995**, *78*, 367 – 390; h) S. Anderson, U. Neidlein, V. Gramlich, F. Diedrich, *Angew. Chem.* **1995**, *107*, 1722 – 1725; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1596 – 1599; i) U. Neidlein, F. Diederich, *Chem. Commun.* **1996**, 1493 – 1494; j) A. Bähr, A. S. Droz, M. Püntener, U. Neidlein, S. Anderson, P. Seiler, F. Diederich, *Helv. Chim. Acta* **1998**, *81*, 1931 – 1963; k) D. K. Smith, A. Zingg, F. Diederich, *Helv. Chim. Acta* **1999**, *82*, 1225 – 1241; l) A. Bähr, B. Felber, K. Schneider, F. Diederich, *Helv. Chim. Acta* **2000**, *83*, 1346 – 1376; m) T. Mizutani, T. Murakami, N. Matsumi, T. Kurahashi, H. Ogoshi, *J. Chem. Soc. Chem. Commun.* **1995**, 1257 – 1258; n) G. Das, A. D. Hamilton, *Tetrahedron Lett.* **1997**, *38*, 3675 – 3678; o) M. Inouye, T. Miyake, M. Furusyo, H. Nakazumi, *J. Am. Chem. Soc.* **1995**, *117*, 12416 – 12425; p) M. Inouye, K. Takahashi, H. Nakazumi, *J. Am. Chem. Soc.* **1999**, *121*, 341 – 345; q) M. Inouye, K. J. Chiba, H. Nakazumi, *J. Org. Chem.* **1999**, *64*, 8170 – 8178; r) J. M. Coterón, F. Hacket, H.-J. Schneider, *J. Org. Chem.* **1996**, 61, 1429 – 1435; s) M. Mazik, H. Bandmann, W. Sicking, *Angew. Chem.* **2000**, *112*, 562 – 565; *Angew. Chem. Int. Ed.* **2000**, *39*, 551 – 554; t) M. Mazik, W. Sicking, *Chem. Eur. J.* **2001**, *7*, 664 – 670; u) H.-J. Kim, Y.-H. Kim, J.-I. Hong, *Tetrahedron Lett.* **2001**, *42*, 5049 – 5052.

[7] Similar tetraureas were previously synthesized and used as anion receptors by Burns and co-workers; R. C. Jagessar, M. Shang, W. R. Scheidt, D. H. Burns, *J. Am. Chem. Soc.* **1998**, *120*, 11684 – 11692.

[8] a) J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Long, W. T. Robinson, *J. Am. Chem. Soc.* **1975**, *97*, 1424 – 1439; b) J. S. Lindsey, *J. Org. Chem.* **1980**, *45*, 5215.

[9] a) **1a**: ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = -2.66$ (s, 2H; imide-NH), 2.57 (d, $J = 4.1$ Hz, 8H; CHCH_2CO$_2$CH$_3$), 3.25, (s, 12H; CHCH$_2$CO$_2$CH_3), 4.49 (m, 4H; PhCH$_2$O$_2$CCHCH$_2$CO$_2$CH$_3$), 4.97 (s, 8H; PhCH_2O$_2$CCHCH$_2$CO$_2$CH$_3$), 6.82 (br, 4H; urea-NH), 7.23–7.35 (m, 24H; benzyl-ArH and *meso*-phenyl-ArH), 7.48 (d, $J = 7.7$ Hz, 4H; *meso*-phenyl-ArH), 7.73 (t, 4H, $J = 8.1$ Hz; *meso*-phenyl-ArH), 7.90 (s, 4H; urea-NH), 8.47 (d, $J = 8.1$ Hz, 4H; *meso*-phenyl-ArH), 8.66 ppm (br, 8H; β-pyrrolic-CH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): $\delta =$ 36.84, 49.82, 52.16, 66.98, 116.76, 121.97, 128.53, 128.87, 129.18, 129.91, 131.59, 132.40, 136.49, 140.05, 155.95, 171.50, 171.95 ppm; MALDI-TOF MS: m/z: 1727.8 [MH$^+$];b) **1b**: ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 2.5$ (br, 8H; CHCH_2CO$_2$CH$_3$), 3.24, (s, 12H; CHCH$_2$CO$_2$CH_3), 4.41 (m, 4H; PhCH$_2$O$_2$CCHCH$_2$CO$_2$CH$_3$), 4.95 (s, 8H; PhCH_2O$_2$CCHCH$_2$CO$_2$CH$_3$), 6.78 (br, 4H; urea-NH), 7.22–7.32 (m, 24H; benzyl-ArH and *meso*-phenyl-ArH), 7.49 (s, 4H; urea-NH), 7.58 (d, $J = 6.3$ Hz, 4H; *meso*-phenyl-ArH), 7.71 (t, 4H, $J = 8.0$ Hz; *meso*-phenyl-ArH), 8.39 (d, $J = 8.4$ Hz, 4H; *meso*-phenyl-ArH), 8.61 ppm (dd, $J = 11.6$, 4.5 Hz, 8H; β-pyrrolic-CH); ^{13}C NMR (75 MHz, CDCl$_3$): $\delta = 36.72$, 49.60, 52.17, 67.68, 116.01, 123.23, 123.61, 128.48, 128.78, 128.90, 129.82, 131.96, 132.11, 134.96, 135.41, 139.74, 150.55, 150.64, 155.72, 171.76 ppm; MALDI-TOF MS: m/z: 1790.7 [MH$^+$].

[10] MacroModel 7.0 with modified MM2 force field. 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.

[11] Compound **1b** does not exist in dimeric or oligomeric forms below $\approx$ 1 mM concentration; this was inferred from the ^{1}H NMR dilution titration of urea-appended porphyrins in CDCl$_3$. In addition, chiral urea-appended porphyrin analogues without carbonyl groups did not exhibit distinct biphasic CD in the Soret region. Therefore, the distinct CD signs do not originate from the exciton coupling between porphyrins. While approximately symmetrical, the shape of the CD spectrum of **1b** is similar to that obtained from the coupling of two porphyrins, and is also similar to induced CD spectra from the coupling of a porphyrin and aspartate C=O groups.[12a] Induced CD spectra from the coupling of a porphyrin and C=O groups do not have to be symmetrical, as revealed by Mizutani et al.[12a] Furthermore, a relatively unsymmetrical shaped biphasic CD spectrum of **1b** was obtained in the high-resolution CD spectrum of **1b**.

[12] Mizutani et al. reported that the intermolecular complex between a porphyrin derivative and dimethyl aspartate exhibited a distinct biphasic CD in the Soret region, and this originated from the coupling between the transition moment of the two carbonyl chromophores of dimethyl aspartate and that of the porphyrin chromophore; a) T. Mizutani, T Murakami, T. Kurahashi, H. Ogoshi, *J. Org. Chem.* **1996**, *61*, 539 – 548; b) T. Mizutani, T. Ema, T. Yoshida, T. Renné, H. Ogoshi, *Inorg. Chem.* **1994**, *33*, 3558 – 3566; c) T. Mizutani, T. Ema, T. Yoshida, Y. Kuroda, H. Ogoshi, *Inorg. Chem.* **1993**, *32*, 2072 – 2077.

[13] The unsymmetrical biphasic CD spectral shape is similar to that observed for porphyrin–carbohydrate complexes; a) T. Imada, H. Kijima, M. Takeuchi, S. Shinkai, *Tetrahedron Lett.* **1995**, *36*, 2093 – 2096; b) T. Imada, H. Kijima, M. Takeuchi, S. Shinkai, *Tetrahedron* **1996**, *52*, 2817 – 2826; c) T. Mizutani, T. Kurahashi, T. Murakami, N. Matsumi, H. Ogoshi, *J. Am. Chem. Soc.* **1997**, *119*, 8991 – 9001.

Micelles and Hollow Nanospheres Based on ε-Caprolactone-Containing Polymers in Aqueous Media**

Xiaoya Liu, Ming Jiang,* Shuli Yang, Mingqing Chen, Daoyong Chen, Cheng Yang, and Kang Wu

Motivated by the great range of potential applications, the development of polymeric nanostructures has witnessed great progress in the last decade.[1] Among the target materials, polymeric hollow nanospheres are especially interesting and are in great demand because of their ability to encapsulate large quantities of guest molecules, particularly those with functionalities within the inner cavity.[2] The most studied procedures[3] for preparing polymeric hollow nanospheres from block copolymer precursors involves many steps: preparing micelles in the selective solvents, cross-linking of the micellar corona, and removing the core by chemical degradation. However, further development has been limited by the preparation of block copolymers containing both cross-linkable and degradable blocks.

We have been attempting to produce polymeric micelles in which only hydrogen bonds, rather than covalent bonds, connect the core and shell.[2e,4] As a significant advance in a "block-copolymer-free" strategy for preparing micelles, we

[*] Prof. M. Jiang, Prof. X. Liu, Prof. D. Chen
The Key Laboratory of Molecular Engineering of Polymers
Ministry of Education of China, Fudan University
Shanghai 200433 (China)
Fax: (+86) 21-6564-0293
E-mail: mjiang@fudan.edu.cn
Prof. X. Liu, S. Yang, Prof. M. Chen, Prof. C. Yang, K. Wu
School of Chemical & Material Engineering
Southern Yangtze University
Wuxi, Huihe Road 170, 214036 (China)

[**] The National Natural Science Foundation of China (NNSFC, Nos. 29992590 and 50173006) and Ministry of Education of China is acknowledged for supporting this research.

  0044-8249/02/11416-3074 $ 20.00+.50/0