Cyclodextrin Complexes

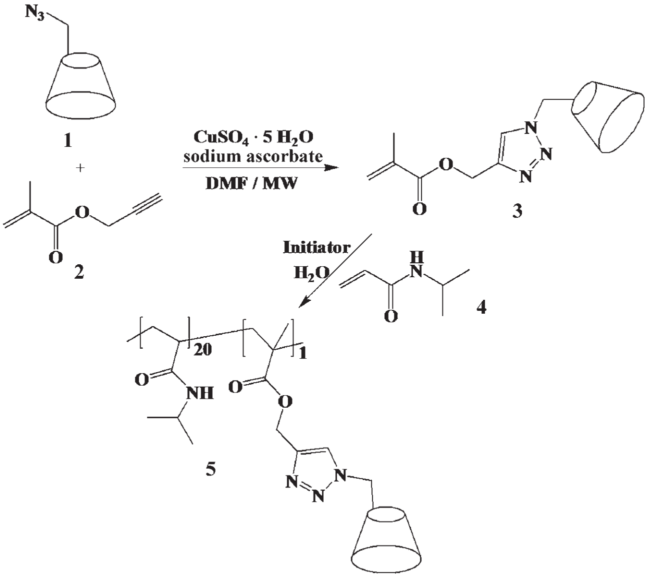
DOI: 10.1002/anie.200704995

# Pseudopolyanions Based on Poly(NIPAAM-*co*-β-Cyclodextrin Methacrylate) and Ionic Liquids

*Sadik Amajjahe, Soowhan Choi, Maricica Munteanu, and Helmut Ritter**

Cyclodextrins (CD) have gained much attention because of their ability to form inclusion complexes in aqueous solutions.[1] Herein we describe the synthesis of cyclodextrin-containing polymers by 1,3-dipolar cycloaddition. This type of click reaction is not only devoid of side reactions, but also provides access to complex structures in high yields. The process is experimentally simple and has enormous scope.[2]

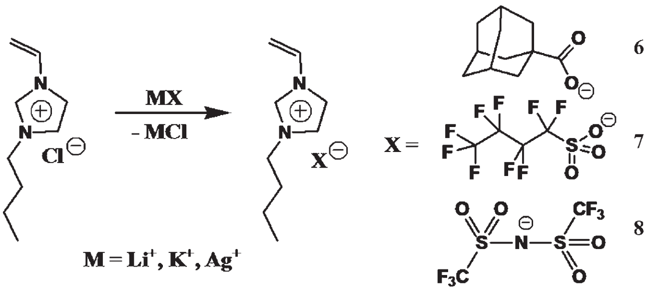
We investigated the influence of different ionic liquids as guests on the lower critical solution temperature (LCST) and hydrodynamic volume of copolymers consisting of *N*-isopropylacrylamide (NIPAAM) and methacrylated CD. The triazole-CD-containing methacrylate **3** was obtained by a click-type reaction of propargyl methacrylate **2** with CD-azide **1** under microwave-assisted reaction conditions.[3] The monomer **3** and NIPAAM **4** were radically copolymerized in a molar ratio of 1:20 using a water-soluble azo initiator in an aqueous medium (Scheme 1). The number-average molar mass ($M_n$) of the obtained copolymer **5** was about 16000 $\mathrm{g\,mol^{-1}}$ according to GPC measurements, using polystyrene as standard. The copolymer **5** was further characterized by $^1$H NMR spectroscopy, turbidity measurements, and dynamic light scattering (DLS).



*Scheme 1.* Synthesis of the CD-NIPAAM copolymer. MW = microwave.

The temperature-dependent solubility of aqueous solutions of copolymer **5** was investigated by monitoring changes of transparency as a function of temperature. Copolymer **5** had a slightly increased LCST at 36 °C, which is about 3 °C higher than that of homopoly(NIPAAM).[4] This increased value is caused by the influence of hydrophilic CD components in the copolymer, which leads as expected to an increased water solubility in comparison to the corresponding homopolymer of NIPAAM.[5]

The attached CD rings suggest that the copolymer **5** can form supramolecular polyelectrolyte-type structures through host–guest interactions with suitable ionic guests. To test this assumption, turbidity measurements were carried out. We used three ionic liquids[6] (ILs) **6–8** to investigate their influence on the LCST values of copolymer **5**. The ionic liquids were synthesized by alkylation of *N*-vinylimidazole, followed by exchange of the anions (Scheme 2). In recent model studies, we evaluated the complex stabilities and stoichiometries of these ionic liquids **6**, **7**, and **8** with CD (Table 1).[7] Until now, mainly adamantyl guests have been reported to form exceptionally stable complexes with CD.[8]



*Scheme 2.* Synthesis of the three vinylimidazolium ionic liquids (IL) with the anions **6**, **7**, and **8**.

*Table 1:* Stability constants, $\Delta H$ and $T\Delta S$ values of **6**, **7**, and **8** with CD at 25 °C.

| IL anion | $K_s$[a] [kJ mol$^{-1}$] | $-\Delta H$ [kJ mol$^{-1}$] | $T\Delta S$ [kJ mol$^{-1}$] |
|---|---|---|---|
| **6** | 5300 | 9.75 | 11.52 |
| **7** | 21000 | 23.51 | 1.18 |
| **8** | 8100 | 32.25 | −9.92 |

[a] Determined by microcalorimetric titrations.

---

[*] S. Amajjahe, Dr. S. Choi, M. Munteanu, Prof. Dr. H. Ritter
Institut für Organische Chemie und Makromolekulare Chemie II
Heinrich-Heine-Universität Düsseldorf
Universitätsstrasse 1,40225 Düsseldorf (Germany)
Fax: (+49) 211-8115-840
E-mail: h.ritter@uni-duesseldorf.de

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

However, in our studies, we could show conclusively that the fluorinated anions **7** and **8** have a high tendency to form inclusion complexes with CD (Table 1).

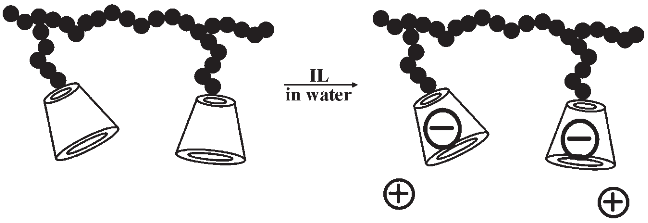
As shown in Table 2, the cloud points (LCST) of the aqueous NIPAAM-CD copolymer **5** change significantly with ILs **6**, **7**, and **8** as guest molecules. The LCST values of complexed copolymers **5** increase after addition of ionic guest molecules **6** and **7**. This increased hydrophilicity of pseudo-polyanions results from the free carboxylate (IL **6**) and sulfonate (IL **7**) groups, which are preferentially located in the aqueous phase and therefore responsible for these increased LCST values of 43 °C and 53 °C, respectively.

*Table 2:* LCST of copolymer **5** and its complexes with **6**, **7**, and **8** in water.

| Polymer | 5 | 5+6 | 5+7 | 5+8 |
|---|---|---|---|---|
| LCST [°C][a] | 36 | 43 | 53 | 34 |

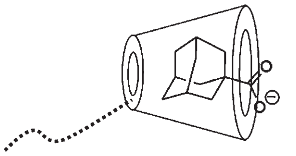
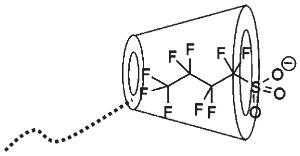
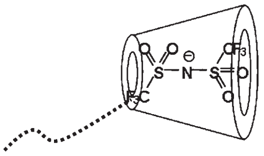
[a] Determined by turbidity measurements.

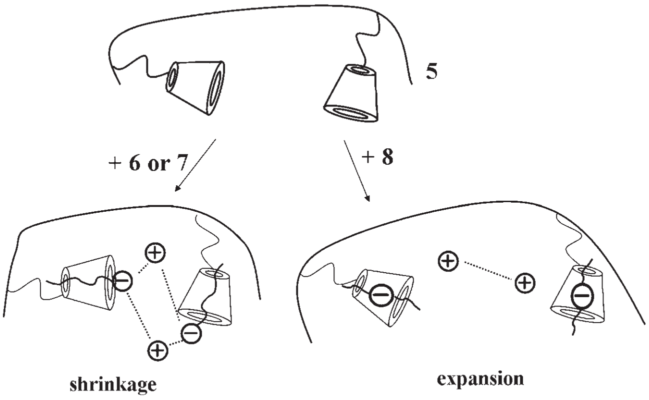
Complexation of the bis(trifluoromethylsulfonyl)imide anion **8** leads to a compound in which the hydrophobic trifluoromethylsulfonyl group is preferentially located in the centre of the CD-cavity, leading to a decreased LCST value. The cloud points of the copolymer **5** decrease with increasing hydrophobicity of the ionic liquids, as expected (Table 2).[4] This observed influence of ILs on the LCST values is a result of the complexation of negatively charged guests in CD cavity. In other words, starting from a neutral polymer, we obtained a pseudopolyanion (Scheme 3).



*Scheme 3.* Generation of pseudopolyanions.

*Table 3:* Determination of hydrodynamic diameter of the complexes of **5** with **6**, **7** and **8** at 25 °C in water.

| System | | Diameter [nm] |
|---|---|---|
| **5** | | 15.1 |
| **5+6** |  | 11.5 |
| **5+7** |  | 9.8 |
| **5+8** |  | 16.5 |



*Scheme 4.* Intramolecular interactions of guest molecules (IL **6** and IL **7**) with covalently bonded CD lead to shrinkage with IL anions **6** and **7** (left), or to expansion of the polymer chains with IL **8** (right) For details, see text.

The hydrodynamic diameters of copolymer **5** without guests, and copolymer **5** with charged guest molecules included, were measured by DLS (Table 3). Surprisingly, the results indicate that polymer **5** has a larger mean coil size than that of its complexes with IL **6** and **7**. In both cases (**5**+**6** and **5**+**7**), the negative charges of the anions are in contact with the water phase, owing to the hydrophobic cavity of CD. A possible reason for this situation is the increasing ionic strength, which leads to some intramolecular interactions between the CD-complexed anions and the cations in solution, resulting in a largely reduced intra- and intermolecular repulsion of the chains. These attractive forces obviously lead to a decrease of the hydrodynamic diameter of the complexes **5**+**6** and **5**+**7** (Scheme 4). We can thus conclude that electrostatics override entropy effects.[9]

In contrast, the hydrodynamic diameter of the complex **5**+**8** slightly increases in comparison to the pure copolymer **5** (Scheme 4), owing to incorporation of the anion group of guest monomer **8** into the CD ring. Furthermore, as shown in Table 1, the entropy of the complex-formation process of IL **8** with CD is very negative, which indicates that a noncoordinating character of the covered anion dominates. Thus, the cation–cation repulsion plays a major role and determines the extended polymer coil structure.

The light-scattering results are consistent with the outcomes of the turbidity measurements. The complexes **5**+**6** and **5**+**7** are more hydrophilic than the pure copolymer **5**, resulting in an increase of the LCST. A decrease in hydrodynamic diameter is due to counterion effects. In case of IL **8**, a lower cloud point was obtained, because the ions are covered by the CD ring and therefore spatially separated from the cation. A higher hydrodynamic diameter is a result of electrostatic repulsion between the cations. These results are due to the delocalized negative charge of the anion of **8**.

Thus, the inclusion of ionic liquids into the cavity of a neutral copolymer consisting of NIPAAM and methacrylated CD generate a new type of polyelectrolyte, so-called pseudopolyanions. This result may open a new field of research in the area of polyelectrolytes. One important application would be in the field of hydrogels. The shrinkage and expansion behavior of cyclodextrin-containing networks could be controlled by supramolecular interaction of the CD components with ionic liquids. Moreover, the solubility behavior of CD-containing polymers could be controlled by complex formation.

## Experimental Section

**5**: Monomer **3** (0.174 g, 1.4 mmol, 0.118 mg) was added to a solution of NIPAAM **4** (0.100 g, 0.07 mmol) in 0.7 mL $H_2O$. The solution was flushed with argon for 15 min, and the initiator VA-044 (2,2′-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride) (0.03 mmol) was added under argon atmosphere. After stirring at 50 °C overnight, the copolymers were separated from the hot reaction mixture by filtration and dried under vacuum.

Characterization and further synthetic procedures are given in the Supporting Information.

Received: October 29, 2007
Revised: November 30, 2007

**Keywords:** cyclodextrins · host–guest systems · ionic interactions · ionic liquids · polymers

---

[1] a) A. Harada, M. Furue, S. Nozakura, *Macromolecules* **1976**, *9*, 701 – 704; b) G. Wenz, B.-H. Han, A. Müller, *Chem. Rev.* **2006**, *106*, 782 – 817.
[2] a) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem.* **2002**, *114*, 2708 – 2711; *Angew. Chem. Int. Ed.* **2002**, *41*, 2596 – 2599; b) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem.* **2001**, *113*, 2056 – 2075; *Angew. Chem. Int. Ed.* **2001**, *40*, 2004 – 2021; c) P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Frechet, K. B. Sharpless, V. V. Fokin, *Angew. Chem.* **2004**, *116*, 4018 – 4022; *Angew. Chem. Int. Ed.* **2004**, *43*, 3928 – 3932.
[3] S. W. Choi, M. Munteanu, H. Ritter, unpublished results.
[4] a) M. Heskins, J. E. Guillet, *J. Macromol. Sci. Chem.* **1968**, *2*, 1441 – 1455; b) O. B. Ptitsyn, A. K. Kron, Y. Y. Eizner, *J. Polym. Sci. Part C* **1968**, *16*, 3509 – 3517; c) H. G. Schild, *Prog. Polym. Sci.* **1992**, *17*, 163 – 249.
[5] H. Ritter, O. Sadowski, E. Tepper, *Angew. Chem.* **2003**, *115*, 3279 – 3281; *Angew. Chem. Int. Ed.* **2003**, *42*, 3171 – 3173; Corrigendum: H. Ritter, O. Sadowski, E. Tepper, *Angew. Chem.* **2005**, *117*, 6253; *Angew. Chem. Int. Ed.* **2005**, *44*, 6099.
[6] P. Bonhôte, A.-P. Dias, N. Papageorgiou, K. Kalyanasundaram, M. Grätzel, *Inorg. Chem.* **1996**, *35*, 1168 – 1178.
[7] S. Amajjahe, H. Ritter, *Macromolecules*, 2008, 47, 716 – 718.
[8] M. V. Rekharsky, Y. Inoue, *Chem. Rev.* **1998**, *98*, 1875 – 1917.
[9] C. Gao, S. Leporatti, S. Moya, E. Donath, H. Möhwald, *Chem. Eur. J.* **2003**, *9*, 915 – 920.