Separation Promoted by Molecular Recognition of a Core Engineered Macromolecular Nanocapsule

Decheng Wan,* Hongting Pu, and Xiangyu Cai

Institute of Functional Polymers, Key Laboratory of Advanced Civil Engineering Materials, College of Materials Science and Engineering, Tongji University, 1239 Siping Road, Shanghai 200092, P. R. China

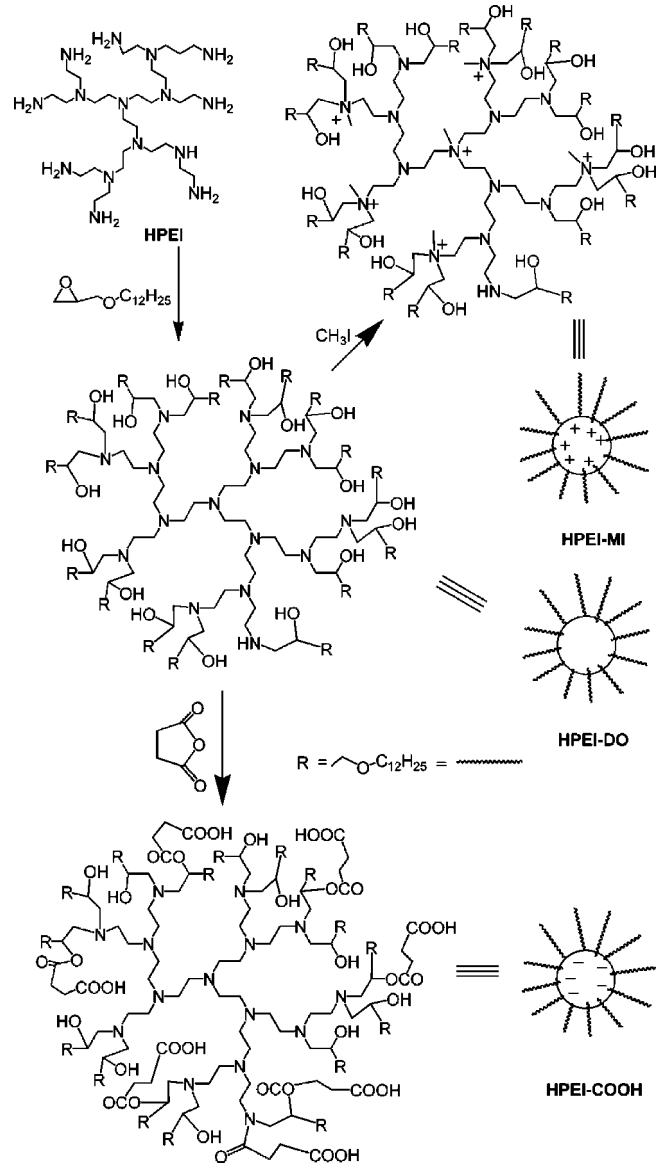
Received April 21, 2008
Revised Manuscript Received July 3, 2008

Introduction. Core−shell nanocapsule plays an increasingly important role in supramolecular host−guest chemistry.[1] Its encapsulation based on molecular recognition can greatly favor the guest solubility in a medium that is otherwise hardly or poorly soluble, thus its potential in biomedical and catalytic fields where solubilization, protection, and sequestering are desired. The noncovalent incorporation is related to a number of factors such as topological trapping, H-bonding interaction, hydrophobic interaction, electrostatic interaction, metal−ligand interaction, or a combination of them.[2] Additionally, it is suggested that a flexible core can considerably allow its polar and apolar groups to rearrange in a manner that is favorable for the accommodation of guest molecules.[3] Thus, the molecular design of a host that takes into account the electronic and geometric features of a guest becomes critical.

Unlike physically formed micelle, amphiphilc core−shell structured macromolecular nanocapsule (AMN) can be used in rigorous environments, but the ability of an AMN to release the entrapped guest is still a central issue. A generally encountered AMN has been found reluctant to release the locked-in guest due to its thick, compact, and incompatible shell, while a thin and less compact shell greatly reduces its encapsulating ability; moreover, even such a structurally compromised AMN can release but a fraction of the captured guest molecules. As an alternative strategy, a chemically labile shell can be adopted for triggered disruption and release of the guest.[4] Frequently, reversible and selective absorption/releasing under physical stimuli such as temperature, pH, or analytes are highly desired of an AMN.[5] However, up to now, only a few AMNs can combine efficient and selective encapsulating ability with physical reversibility.[2b,5a] On the other hand, selective encapsulation means potential in mixture separation, but knowledge in this field is still limited. Here in this communication, we show that without changing the core size of an AMN derived from hyperbranched polyethylenimine (HPEI), the engineering of the core can lead to enormous difference in guest-loading, guest-releasing, and guest-selecting ability due to the role of molecular recognition. This AMN can be a highly efficient and convenient tool in the field of mixture separation as well as a supramolecular host.

Results and Discussion. The preparation of the AMNs is outlined in Scheme 1. The reaction of epoxy compound with amine is known for mildness and efficiency; here the straightforward reaction of 2-dodecyloxymethyloxirane (DO) with HPEI ($M_n = 1 \times 10^4$, $M_w/M_n = 2.5$, degree of branch (DB) = 60%,[5e] Aldrich) leads to an amphiphilic AMN (HPEI-DO) with a highly polar core and a compact hydrophobic shell, accompanied by the simultaneous production of hydroxyl groups. The amines

Scheme 1. Outline of the Synthesis of AMNs with Different Core



can be further partly quaternized with methyl iodide, leading to an AMN (HPEI-MI) positively charged in core, or the hydroxyl groups of HPEI-DO can be transformed into carboxyl groups with succinic anhydride, leading to an AMN (HPEI-COOH) which can be negatively charged (at high pH) in the core. ^{1}H NMR analysis indicates that for HPEI-DO 86% of the HPEI amine protons are alkylated by DO, for HPEI-MI 40% of the amines is quaternized by methyl iodide, and for HPEI-COOH 40% of the OH groups are transformed into COOH groups (Figure s1, Supporting Information). All the AMNs are similar in that they are spherelike in shape with a hydrophobic shell and a hydrophilic core, and all are soluble in conventional apolar solvents such as chloroform, hexane, and diethyl ether. In sharp contrast, HPEI is soluble only in polar solvents such as water, methanol, and dimethylformamide. HPEI-COOH is negatively charged at high pH; as a result, upon mixing with the positively charged HPEI-MI, immediate precipitation in

* Corresponding author. E-mail: wandecheng@mail.tongji.edu.cn.

10.1021/ma800876r CCC: $40.75
Published on Web 10/11/2008

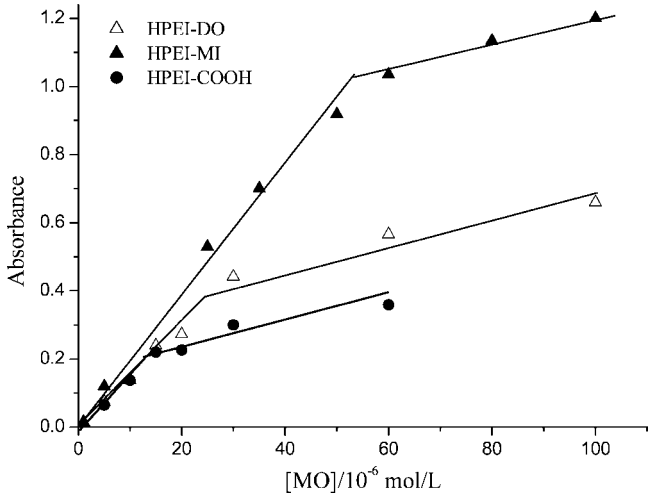


Figure 1. Determination of the saturated encapsulation of methyl orange (MO) by a chloroform solution of the AMN at 3.49×10^{-7} mol/L. The data are obtained from the UV−vis spectra.

chloroform appears, while several droplets of acetic acid result in a clear solution again.

These AMNs can absorb anionic, water-soluble dyes such as methyl orange (MO), Rose Bengal (RB), and Congo red (CR) via liquid−liquid extraction. For AMN at a given concentration in chloroform, the MOs in water can be completely and irreversibly transferred into the oil layer until a saturated point is satisfied. After saturation, extra MOs can be transported into the oil phase but is reversible; i.e., the extra MOs can be released when shaken with fresh water. Most probably, the extra MOs adhere to the AMN instead of being entrapped. The dye encapsulating ability is dependent on the concentration of the AMN: the lower the concentration of AMN, the higher the encapsulating ability (Figure s2 and Table 1, Supporting Information). For example, for HPEI-DO at 8.56×10^{-6} and 8.56×10^{-8} mol/L, the number of MOs encapsulated by one HPEI-DO molecule is 28 and 121 at the saturation point, respectively, indicating the HPEI-DO exists in cluster. Encapsulation at lower concentration (lower than 3.42×10^{-8} mol/L) becomes completely reversible, suggesting in this case the MOs adhere to the HPEI-DO rather than being entrapped; encapsulation of CR is no longer observed at this concentration (in contrast, at high concentration, irreversible encapsulation is observed). These results suggest that the encapsulation is due to the cluster of HPEI-DO rather than to its free entity. The dye-loading ability of the three AMNs is of enormous difference due to the core structure; Figure 1 shows the encapsulating ability of these AMNs at the same molar concentration of 3.49×10^{-7} mol/L.

Calculation indicates that, on average, each HPEI-DO nanocapsule can encapsulate 70.8 MOs at pH around 7; for HPEI-COOH, it is only 34.0 MOs, while for HPEI-MI, it is 143.0 MOs, which is a very high value. The difference in encapsulating ability is understandable if (1) the reversible protonation of amines by water and (2) ionic interaction between the dye and the nanocapsule are taken into account. The tertiary amine is known as a strong base; thus, the nitrogens of the AMNs are partially protonated by water even at pH = 8.[6] The protonation leads to a polar, cationic, and hydrophilic core, which is favorable for the encapsulation of anionic dyes, while deprotonation renders the cores hydrophobic, and as a consequence, dye release will occur. In fact, when the pH is adjusted to 12, HPEI-COOH and HPEI-DO expels any of the encapsulated MOs that no trace of MO can be detected in the oil layer by UV−vis measurement, while HPEI-MI still retains a fraction (17% of the saturated amount) of the MOs due to the existence of immobilized positive charges in the core (Figure s3, Supporting Information). The low encapsulating ability of HPEI-COOH should be related to the self-complementary ionic interaction between the anionic carboxylates and the cationic quaternized amines in its core.

As aforementioned, the pH-dependent encapsulation/releasing can be mainly attributed to ionic complementary host−guest interaction. As a direct concern, we wonder whether such a molecular recognition based on electrostatic interaction can be used in chemical separation. In this case, two issues need to be clarified: one is whether a cationic guest can be encapsulated by these AMNs, and the other is whether an encapsulated anionic guest can favor solubilization of a cationic guest. In fact, it has been reported that one guest could favor the solubility of another guest due to synergic effect.[2c] In our experiment, it is found either methylene blue (MB) or MO alone is insoluble in chloroform in the biphasic system of water/chloroform, but their mixture shows a rather high solubility in the chloroform; however, upon the addition of enough HPEI-DO, all the MBs migrate and reside in the water phase while all the MOs reside in the oil phase (Figure 2). Most probably, MB is solubilized in chloroform due to the cationic−anionic interaction with MO, but in the presence of HPEI-DO, the MOs are completely entrapped by HPEI-DO and can no longer solubilize MB, so MBs return to the water phase. Here MB is selected by us partly because the feature peaks of MO and MB in UV−vis spectra do not overlap. UV−vis (Figure 2) analysis proves that MB is 100% separated and MO can be 100% recovered (attention: only when "excessive" HPEI-DO is present can the solubilized MB completely return to the water layer; if there is not enough HPEI-DO in the system and thus MOs are not completely encapsulated, still a faction of MBs will stay in the oil due to the solubiliztion effect of MO; as a consequence, 100% separation will become impossible). It is also found that after the MOs are released the AMN solution can be reused for separation; the process is repeated times without any decrease in transportation ability even after 3 months. This property can be attributed to the chemical stability of the HPEI-DO.

It is worth noticing that this separation is based on a nonspecific interaction, which means this can be a general separation strategy. The separation of other hydrophilic mixture of RB/MB, CR/MB, is also carried out. It is found these mixtures can also be conveniently and effectively separated (Figure s4, Supporting Information). In both cases, the MB can be 100% separated, but the CR and RB cannot be completely released upon the increase of pH (RB can be completely released if the concentration of HPEI-DO is low enough). However, if it is noticed that the AMN can be repeatedly reused (Figure s5, Supporting Information), the incomplete release does not essentially influence the practical application. Among the three AMNs, HPEI-DO is recommended as the separation tool for its overall performance in guest encapsulating and guest releasing ability. Since HPEI-COOH will be negatively charged at high pH, it was once hoped to promote the release of anionic guest of CR and RB under high pH. Strangely, the releasing property does not improved but slightly decreased. This behavior strongly suggests that polarity of core also contributes to the encapsulation.

Interestingly, a mixture of anionic dyes can also be efficiently separated. For example, to an aqueous solution of MO/CR, HPEI-DO in chloroform is added, and the CR is preferentially transported to the oil layer. Under optimized conditions, the CR is 100% transported, leaving the MO intact in the water and can be 100% separated, indicating the separation is highly efficient. Figure 3

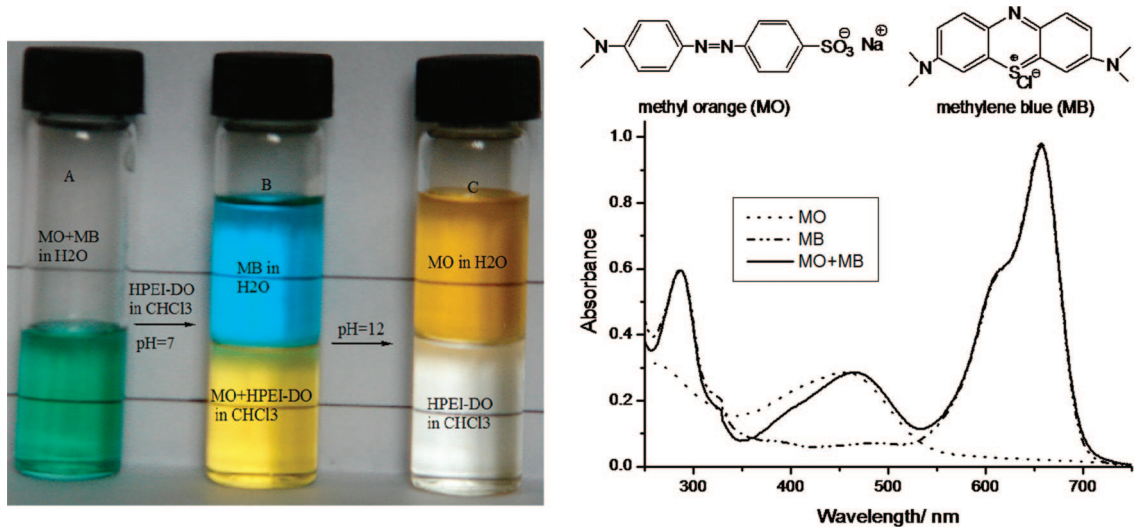


Figure 2. HPEI-DO aided separation of MB and MO. (left) The mixture of MO and MB appears green in water (A), and MB is completely separated because the MO can be exclusively entrapped by the added HPEI-DO in $CHCl_3$ at pH = 7 (B); after removal of the MB-containing water layer, the residual oil is shaken with fresh water at pH = 12, and the entrapped MO can be 100% recovered (C). (right) UV−vis spectra of the mixture of MO + MB and the separated MO and MB.

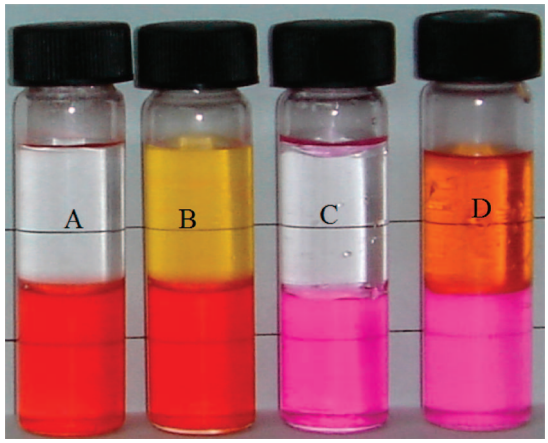


Figure 3. Selective encapsulation of anionic dyes by HPEI-DO in biphasic system of water/chloroform: (A) HPEI-DO solution saturated by CR; (B) after addition of MO with shaking and phase balancing; (C) HPEI-DO solution saturated by RB; (D) after addition of MO with shaking and phase balancing.

shows that to a biphasic solution of HPEI-DO, which is saturated by CR, addition of MO under vigorous shaking does not lead to transportation of MO to the oil or the release of CR to the water (monitored by UV−vis), indicating the encapsulation is highly selective. On the contrary, if the HPEI-DO-entrapped MOs are exposed to aqueous CR, any of the MO is expelled to the water phase by CR that no MOs can be detected in the oil layer. In the above experiment, if the CR is replaced by RB, the separation is still feasible but less efficient; minor RBs are released to water, and minor MOs (8% molar fraction of RB) enter the oil. Or to a MO-saturated chloroform solution of HPEI-DO, addition of aqueous RBs cannot expel all the MOs into water; minor (<8%) MOs retain in the oil phase. Because CR and RB are larger in size than MO, the above experiments prove that the selective encapsulation is not due to the shape/size of the guest or due to the shell compact of HPEI-DO, but due to the host−guest binding strength, perhaps because MO is with single anion while CR and RB is with double anions.

The encapsulating ability of HPEI-DO seems to be insensitive to its shell compactness; for HPEI with 30−86% alkylated by DO, the encapsulating ability on MO is almost the same in molar number (Table 2, Supporting Information), indicating the shell compactness play a minor role in guest selection, but when the ratio of alkylation is 15% or lower, encapsulating ability is greatly reduced.

In conclusion, the amphiphilic core−shell structured macromolecular nanocapsule reported here combines several merits on mixture separation: highly selective encapsulation of a guest from its mixture and the pH-responsive releasing of the encapsulated guest; the repeatedly reusable property and adaptability to a wide range of mixtures, which may be useful in chemical and biological separation and favorable for energy-saving applications.

Supporting Information Available: Synthesis and ^{1}H NMR data of the macromolecular nanocapsule, UV−vis spectra, mixture separation, dependence of encapsulating ability on concentration, and structure of macromolecular nanocapsule. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) For reviews, see: (a) Frechet, J. M. J.; Tomalia, D. A. *Dendrimers and Other Dendritic Polymers*; Wiley: West Sussex, 2001. (b) Baars, M. W. P. L.; Meijer, E. W. *Top. Curr. Chem.* **2000**, *210*, 131–182, and references therein.

(2) (a) Sunder, A.; Kramer, M.; Hanselmann, R.; Mulhaupt, R.; Frey, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 3552–3555. (b) Kramer, M.; Kopagzynska, M.; Krause, S.; Haag, R. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2287–2303. (c) Liu, C. H.; Gao, C.; Yan, D. Y. *Macromolecules* **2005**, *39*, 8102–8111. (d) Scott, R. W. J.; Wilson, O. M.; Crooks, R. M. *J. Phys. Chem. B* **2005**, *109*, 692–704. (e) Zimmerman, S. C.; Lawless, L. J. *Top. Curr. Chem.* **2001**, *217*, 95–120.

(3) Liu, M.; Kono, K.; Frechent, J. M. J. *J. Controlled Release* **2000**, *65*, 121–131.

(4) For example, see: Shi, L. J.; Berkland, C. *Macromolecules* **2007**, *40*, 4635–4643.

(5) (a) Kramer, M.; Stumbe, J.-F.; Turk, H.; Krause, S.; Komp, A.; Delineau, L.; Prokhorona, S.; Kautz, H.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 4252–4256. (b) Gil, E. S.; Hudson, S. M. *Prog. Polym. Sci.* **2004**, *29*, 1173–1222. (c) Chaterji, S.; Kwon, I.; Park, K. *Prog. Polym. Sci.* **2007**, *32*, 1083–1122. (d) Chen, Y.; Shen, Z.; Pastor-Perez, L.; Frey, H.; Stiriba, S. E. *Macromolecules* **2005**, *38*, 227–229. (e) Liu, H. J.; Chen, Y.; Zhu, D. D.; Shen, Z.; Stiriba, S. E. *React. Funct. Polym.* **2007**, *67*, 383–395. (f) Baars, M. W. P. L.; Kleppinger, R.; Koch, M.; Yeu, S. L.; Meijer, E. W. *Angew. Chem., Int. Ed.* **2000**, *39*, 1285–1288. (g) Barrs, M. W. P. L.; Froehing, P. E.; Meijer, E. W. *Chem. Commun.* **1997**, 1959–1960.

(6) Behr, J.-P. *Chimia* **1997**, *51*, 34–36.

MA800876R