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Water-Soluble Knedel-like Structures: The Preparation of Shell-Cross-Linked Small Particles

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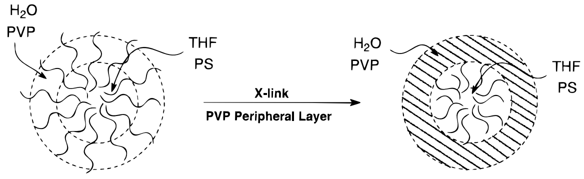
There is currently great interest in the preparation and study of new classes of polymeric materials. This interest is largely based upon the potential that these materials hold for new and advanced physical, chemical, and mechanical properties. Specifically, the design and synthesis of novel macromolecular architectures (e.g., stars,[1] dendrimers,[2−4] hyperbranched,[5] macrocycles,[6] rotaxanes,[7] two-dimensional sheets,[8] etc.) has successfully created products possessing unusual behavior, in comparison to traditional linear polymers. Dendrimers have received considerable attention as globular structures that can be prepared with controlled functionality. For example, encapsulation has been demonstrated for rigid sphere[9] and micellar[10] dendrimers, which can act as carrier systems. Many other biochemical and materials applications have also been targeted. However, some of the difficulties associated with dendrimers are their costly and time-consuming syntheses as well as their limited growth. As reported herein, we have designed a method for the preparation of low-polydispersity globular macromolecules bearing unique structure and functionalization, composed of an immobile but permeable cross-linked peripheral layer and a mobile non-cross-linked core region. Such structures resemble dendrimers by having a large number of peripheral functionalities, a penetrable core, and globular shape, but are capable of larger scale production and nanometer-size diameters in only three synthetic steps. The method simply involves a combination of linear polymer synthesis and self-assembly, and the resulting shell-cross-linked knedel-like[11] (SCK) particles appear to be a hybrid between dendrimers, hollow spheres, latex particles, and block copolymer micelles.



2
Organized into micelles
(in 2.5 : 1, H_2O : THF)

1
Knedel SCK

Figure 1. Schematic representation of the basic approach for the formation of SCK's. Micellization of amphiphilic **2** is followed by cross-linking through the styrenyl side chains located in the peripheral aqueous layer to yield **1**.

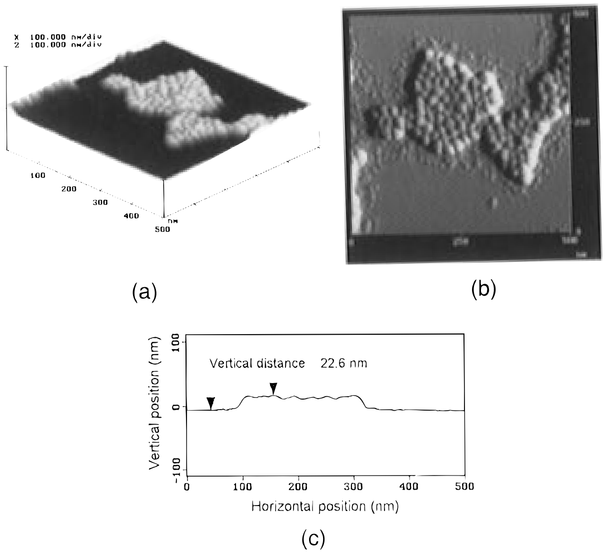


Figure 2. Tapping mode AFM images of monolayer aggregates of SCK's, **1**, on mica: (a) 3D rendering of a surface profile; (b) "error signal" AFM image of the surface shown in part a;[19] (c) vertical profile of the aggregate shown in part a.

The micellar organization of block copolymers composed of blocks with different solubility properties is well-known to occur when the block copolymer is placed into a selective solvent system at the appropriate concentration.[12] The morphology of the micellar aggregates has been shown to differ depending upon the block copolymer block lengths and concentration.[13] The unique design of the SCK synthesis is that the incorporation of cross-linkable functional groups along the peripheral block of the micelle allows for polymerization of the exterior[14] layer (Figure 1) and gives stability to the micellar assembly.[15] This results in the novel SCK's, **1**, where each of the core polymer chains are covalently-attached to the cross-linked, web-like shell. The method of preparation is also extremely attractive because the rigidity, reactivity, size, shell thickness, core diameter, penetrability, and stability of the structures may be easily controlled through variation of the cross-link density, the cross-linkable-block length, and the composition and properties of the block copolymers.

To demonstrate the synthesis, a block copolymer of polystyrene and poly(4-vinyl pyridine), PS-*b*-PVP, was prepared by anionic polymerization under argon, in which the PS block was of $M_w = 4900$, $M_w/M_n = 1.14$ (from GPC based on polystyrene standards) and the PVP block was of $M_w = 5800$ (based on ^1H NMR, due to GPC column affinity problems). In this case, the PS serves as the hydrophobic block and PVP is quaternized to generate the hydrophilic block and to introduce the cross-linkable group. Reaction of the PS-*b*-PVP with *p*-(chloromethyl)styrene proceeds in tetrahydrofuran with the addition of increasing amounts of methanol as the extent of the formation

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(1) Martin, M. K.; Ward, T. C.; McGrath, J. E. In *Anionic Polymerization*: McGrath, J. E., Ed.; ACS Symposium Series 166; American Chemical Society: Washington, DC, 1981; pp 557-580.

(2) Tomalia, D. A.; Naylor, A. M.; Goddard, W. A., III. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 138.

(3) Ardoin, N.; Astruc, D. *Bull. Soc. Chim.* **1995**, *132* (9), 875.

(4) *Advances in Dendritic Macromolecules*; Newkome, G. R., Ed.; JAI Press: Greenwich, CT, 1994−5; Vol. 1−2.

(5) Kim, Y. H. *Adv. Mater.* **1992**, *4*, 764.

(6) Gan, Y.; Zoller, J.; Hogen-Esch, T. E. *Polym. Prepr.* **1993**, *34* (1), 69.

(7) Shen, Y. X.; Gibson, H. W. *Macromolecules* **1992**, *25*, 2058.

(8) Stupp, S. I.; Son, S.; Lin, H. C.; Li, L. S. *Science* **1993**, *259*, 59.

(9) Jansen, J. F. G. A.; Janssen, R. A. J.; de Brabander-van den Berg, E. M. M.; Meijer, E. W. *Adv. Mater.* **1995**, *7* (6), 561.

(10) Hawker, C. J.; Wooley, K. L.; Fréchet, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1287.

(11) (Note: knedel is a Polish word to describe a food of meat surrounded by a dough layer; pronounced k•nĕd′ ‘l).

(12) Qin, A.; Tian, M.; Ramireddy, C.; Webber, S. E.; Munk, P.; Tuzar, Z. *Macromolecules* **1994**, *27*, 120.

(13) Zhang, L.; Eisenberg, A. *Science* **1995**, *268*, (June 23), 1728.

(14) For reference to the linking-together of the head groups of small molecule surfactants, see: Paleos, C. M.; Malliaris, A. *J. Macromol. Sci., Rev. Macromol. Chem. Phys.* **1988**, *C28* (3−4), 403.

(15) For somewhat related work see: Procházka, K.; Baloch, M. K. *Macromol. Chem.* **1979**, *180*, 2521. Ishizu, K.; Saito, R. *Polym.-Plast. Technol. Eng.* **1992**, *31* (7&8), 607. Guo, A.; Liu, G.; Tao, J. *Macromolecules* **1996**, *29*, 2487.

(16) An approximate aggregation number of 250 chains/SCK was calculated from the SCK diameter, density of 1 g/mL, and the estimated molecular weight of **2** (*ca*. 15000 g/mol).

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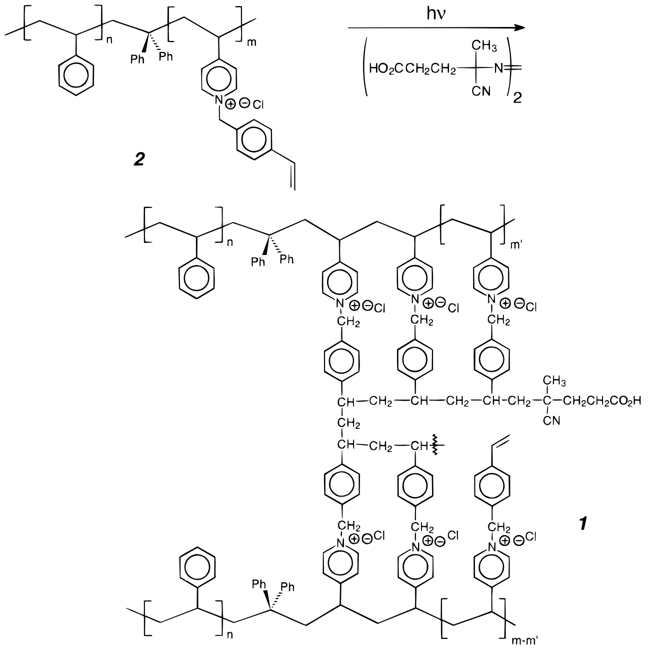
Scheme 1. The Cross-Linking Reaction of the Styrenyl Side Chain Groups of the Poly(4-vinyl pyridine) Block of the Amphiphilic Block Copolymer **2**, Initiated by the Photolytic Degradation of 4,4′-Azobis(4-cyanovaleric acid) as the Water-Soluble Radical Initiator, To Yield the SCK's, **1**



of the quaternized pyridinium salts increases. Precipitation into hexane affords **2** as a green powder. Solubilization of **2** in a mixture of 30% THF/H_2O at a concentration of 10^{-5} M results in the formation of micelles. The THF is then removed by evaporation.

Stabilization of the micellar organization and generation of **1** is then accomplished by the addition of a water-soluble radical initiator, 4,4′-azobis(4-cyanovaleric acid), to the reaction mixture and irradiation at 254 nm for 24 h (Scheme 1). Therefore, the cross-linking is through polymerization of the styrenyl side chain groups, and only occurs in the peripheral aqueous layer of the micelles.

Before cross-linking, freeze-dried micelles of **2** are not water-soluble, but are soluble in a mixture of water and THF. The ^{1}H NMR spectrum of **2** in a D_2O/THF-d_8 solvent system displays resonances for protons of the entire copolymer. Although the SCK's appear to remain in solution within D_2O after cross-linking, no resonances are observable by ^{1}H NMR. Interestingly, only the resonances for polystyrene are observed following addition of THF-d_8 to the D_2O solution of **1**, thus confirming the cross-linking within the PVP block, the permeability of the outer PVP shell, and the mobility of the polystyrene core. Presumably, it is only the polystyrene of the core that is being solubilized, since no resonances for the PVP are observed. Once **1** is dried or freeze-dried, it is no longer soluble in previous solvents, for example H_2O, H_2O/THF, methanol, or methanol/methylene chloride, even upon sonication. The loss of apparent solubility may be due to further cross-linking or intermolecular cross-linking that can occur in the solid state because of the presence of remaining radical initiator. Alternatively, the lack of solubility may be due to a change in the surface groups upon solvent removal. Experiments using lyoprotectants (e.g., sugars) are being investigated.

Fluorescence studies using pyrene in water determined the critical micelle concentration of **2** to be 2×10^{-7} M. A detectable cmc was not found for **1**, which along with solubility properties and ^{1}H NMR observations confirms that cross-linking did indeed occur.

Two glass transition temperatures were observed for **1** at 103 and 129 °C, indicating the presence of two domains for the polystyrene and PVP blocks; the T_g's of **2** were observed at 102 and 132 °C.

The size and shape of the SCK's was determined by tapping mode atomic force microscopy (AFM). As shown in Figure 2, the structures are approximately spherical with diameters of *ca.* 23 nm[16] and narrow size distribution. SCK's deposited on mica exhibited a tendency to organize into relatively regular aggregates, similar to those observed for polymer latex particles.[17] Due to the distribution of sizes, the aggregates showed only short-range "order" resembling local hexagonal packing of perfectly spherical monodisperse motifs. The ability of **1** to form monolayers of such aggregates indicates that cross-linking of the exterior layer proceeds only through intramicellar polymerization with little or no intermicellar reaction. This observation is consistent with the apparent retention of water-solubility for **1**. In addition, the presence of the PVP on the surface of **1** is supported by preliminary contact mode AFM studies, which indicate that under the lateral force exerted by the AFM probe tip, the surface deforms more easily than the surface of PS latex particles.

In conclusion, micellar organization of amphiphilic block copolymers followed by intramicellar cross-linking of the peripheral block has lead to the preparation of a new material possessing a unique macromolecular architecture. Characterization of solubility properties, solution-state ^{1}H NMR spectra, fluorescence studies, DSC measurements, and AFM images have confirmed the knedel-like, aqueous-soluble, amphiphilic, shell-cross-linked structure. Further characterization by solid-state NMR is currently in progress. The SCK's may find application in the removal of hydrophobic contaminants from aqueous solutions, and since they resemble hollow-sphere polymers, they may be used in applications as varied as recording materials, hydraulic fluids, or delivery processes where diffusion from a mobile solvating core through a uniform shell thickness[18] is desirable. Other potential applications include catalysis, phase transfer reactions, solvation, coatings, fillers and reinforcement agents for plastics, chromatography, etc.

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Supporting Information Available: Experimental details for the synthesis of **1** and **2**; ^{1}H NMR spectra of PS-*b*-PVP, **1** and **2**; plot of pyrene excitation spectral data for **2**; pyrene excitation spectra for **1** and **2**; and procedures for the AFM measurements (7 pages). See any current masthead page for ordering and Internet access instructions.

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(17) Sommer, F.; Duc, T. M.; Pirri, R.; Meunier, G.; Quet, C. *Langmuir* **1995**, *11*, 440.

(18) Pekarek, K. J.; Jacob, J. S.; Mathiowitz, E. *Nature* **1994**, *367*, 258.

(19) Under ideal circumstances the amplitude of oscillation of an AFM cantilever ("error signal") should be constant during scanning and equal to a setpoint value (e.g. 85% of "free" amplitude throughout our experiments). Due to a finite response time of the instrument this condition is not satisfied when the probe encounters the areas of rapidly changing height. Thus the maps of cantilever oscillation amplitude enhance the edges of surface features and are useful to identify the features on the images with large range of depth. With this respect they are similar to highpass-filtered images, but they are free of artifacts introduced by digital filtering procedures.