

Synthesis and Characterization of Stearyl-Group-Terminated Dendrimers and Thermosensitivity of Their Toluene Solutions

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ABSTRACT: Stearyl-group-terminated poly(ester amide) dendrimers [PEAD (R)₃ and PEAD (R)₈] and a poly(amino amide) dendrimer [PAMAM (R)₄] were synthesized by the amidation of three, eight, and four terminated primary amino groups in poly(ester amine) dendrimers and a poly(amino amide) dendrimer with stearyl chloride. The dendrimer structures were characterized with IR and elemental analysis. The toluene solutions of the stearyl-group-termi-

nated dendrimers were thermosensitive. Not only did gels form in PEAD (R)₃, PEAD (R)₈, and PAMAM (R)₄-toluene solutions below 57.5, 60, and 49°C, respectively, but the content of toluene in the gels depended on the temperature, and a break existed at about 30°C. © 2005 Wiley Periodicals, Inc. *J Appl Polym Sci* 98: 341–346, 2005

Key words: dendrimers; solution properties; synthesis

INTRODUCTION

Dendrimers are molecules with a well-defined primary structure based on a hyperbranched, fractal-like motif emanating from a central core.¹ As a new class of macromolecules, they have been attracting great attention and have been identified as promising candidate materials for a wide variety of applications, including energy harvesting, drug delivery,² surfactants,³ catalysts,⁴ and nanocomposites,⁵ because of their unique properties that derive from their highly branched, monodisperse structure and globular, void-containing shapes. The functionalization of the external groups of dendrimers has proved a fruitful strategy for the preparation of a diversity of novel materials. Materials that may sensitively respond to a small change in external stimuli, such as the temperature, pH, ionic strength, light intensity, electric field, specific analyte, and antigen, are called smart materials, among which the temperature-sensitive ones have attracted extensive interest.⁶ However, typical traditional temperature-sensitive materials are linear poly(*N*-isopropylacrylamide) gel and its modified systems, and research in this field is primarily concentrated on aqueous systems.⁷ Dendrimers for smart materials have been mainly reported to be photosensitive, pH-sensitive, and so forth.^{8,9}

This article reports the synthesis and characterization of a series of stearyl-group-terminated dendrimers and the temperature sensitivity of their toluene solutions.

EXPERIMENTAL

Materials

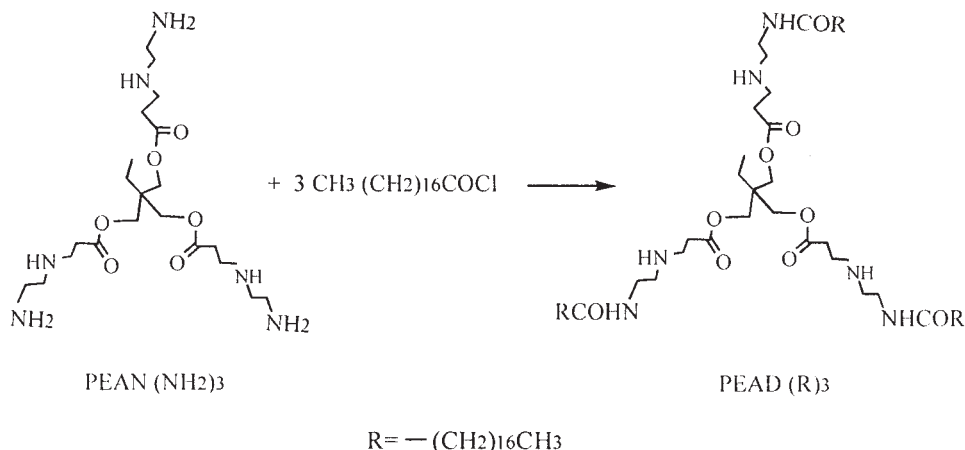
Poly(ester amine) dendrimers PEAN (NH₂)₃ and PEAN (acrylate)₈ and poly(amino amide) dendrimer PAMAM (NH₂)₄ were synthesized according to refs. 10, 11, and 12, respectively. Stearyl chloride (SC) was prepared according to the literature.¹³ Ethylenediamine (EDA) and methanol were supplied by the Third Reagent Co. of Shanghai (Shanghai, China) and purified by distillation before being used. Stearic acid was purchased from Nanxin Assistants Factory (Jiangsu, China). The other reagents were supplied by Shanghai Chemical Reagent Co. of Chinese Medicine (Shanghai, China) and used without further purification.

Measurements

High-efficiency liquid chromatography (HPLC) was performed on a Shimadzu LC-6A (Shimadzu Co., Japan) with a C₁₈ column (4.6 × 250 mm), a mixture of CH₃CN and H₂O (2:3 v/v) as an eluent (total flux = 0.7 mL/min), and 216 nm as the detection wavelength. IR spectra were carried out with a Magna 550 Fourier transform infrared spectrometer. Nuclear magnetic resonance (¹H-NMR and ¹³C-NMR) spectra were recorded on an Inova 400-MHz instrument with CDCl₃ as a solvent. Elemental analysis was carried out

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Scheme 1 Synthesis route of PEAD (R)₃.

with a Shimadzu EA-1110 CHNSO instrument (Shimadzu Co., Japan). Melting points were tested on an Electrochemical Engineering, Ltd., 8100 digital melting-point instrument.

Synthesis

Synthesis of poly(ester amide) dendrimer PEAD (R)₃ (C₇₅H₁₄₆N₆O₉; scheme 1)

SC (6.05 g, 0.020 mol) in 50 mL of *N,N*-dimethylformamide (DMF) was added dropwise to a solution of 2.25 g (0.005 mol) of PEAN (NH₂)₃ and 1.50 g (0.019 mol) of pyridine at room temperature. The reaction mixture was heated to 90°C for 10 h with stirring and then cooled and filtered; the filter cake was washed with acetone and water several times and recrystallized from chloroform three times to give PEAD (R)₃ as a white solid with an 82.4% yield.

mp: 166.3–167.3°C. IR spectra (KBr, cm⁻¹): 3302, 3082 (ν_{N-H}), 1647 (ν_{C=O}), 1555, 1242 (ν_{C-N}, δ_{N-H}), 2920, 2851 (ν_{CH2}, ν_{CH3}), 1470 (δ_{CH2}), 1385 (δ_{CH3}), 721 (δ_{(CH2)*n*}, *n* ≥ 4). ANAL. Calcd: C, 70.64%; H, 11.64%; N, 6.59%. Found: C, 70.60%; H, 11.75%; N, 6.96%.

Synthesis of poly(ester amide) dendrimer PEAD (R)₈ (C₂₂₂H₄₂₄N₁₈O₃₂; scheme 2)

Synthesis of poly(ester amine) dendrimer PEAN (NH₂)₈ (C₇₈H₁₅₂O₂₄N₁₈). EDA (108 g, 1.80 mol), 6.20 g (0.005 mol) of PEAN (acrylate)₈, and 7.70 mL of methanol were added to a 250-mL, three-necked flask equipped with a mechanical stirrer, a thermometer, and a condenser. The mixture was stirred well and warmed to 30°C for 24 h, methanol and most excess EDA were removed *in vacuo*, after the mixture was washed with ethyl acetate (10 g×3) and dried *in vacuo* at 30°C to obtain PEAN (NH₂)₈ as a light yellow, transparent, viscous, liquid product.

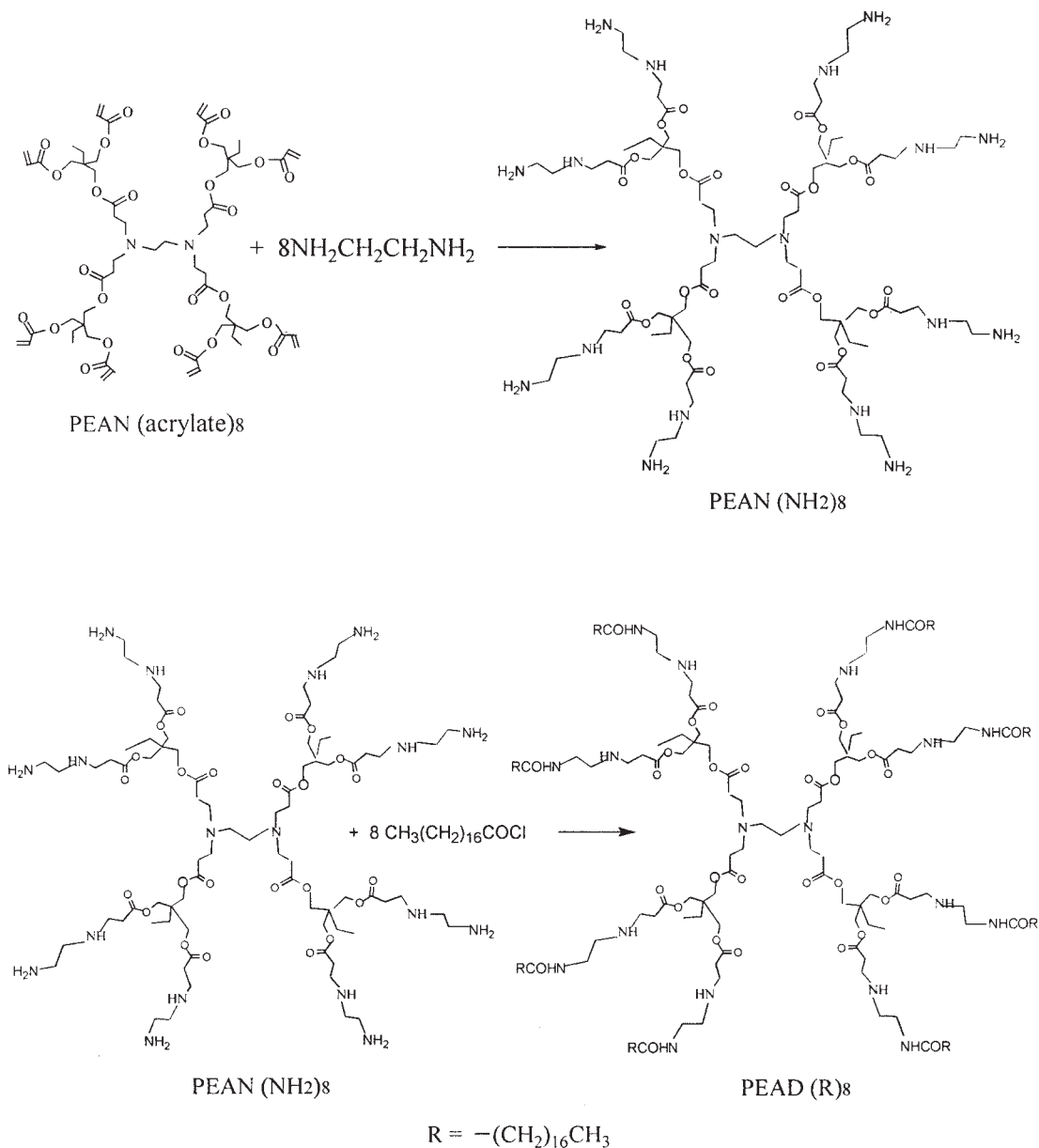
Yield: 8.07 g (0.0047 mol, 93.6%). Purity (HPLC): 98.4%. IR (KBr): 3295 (ν_{NH2}), 1644 (ν_{C=O}), 1385, 1115 (ν_{C-N}). ¹H-NMR (DMSO-*d*₆, δ): 0.75–0.79 (CH₃, 12H), 1.17–1.22 (CH₃*CH₂, 8H), 2.20 (CH₂COO, 8H, OCOCH₂, 16H), 2.28–2.31 [*CH₂N (CH₂)₂, 4H], 2.41 [CH₂N (*CH₂)₂, 8H], 2.53–2.56 (*CH₂NH₂, 16H), 2.62–2.68 (NH*CH₂CH₂NH₂, 16H), 3.07 (*CH₂NH, 16H), 3.25 (COOCH₂, 8H, CH₂OCO, 16H). ¹³C-NMR (DMSO-*d*₆, δ): 7.6 (CH₃), 21.3, 22.6 (*CH₂CH₃), 33.3 [*C (CH₂)₄], 36.0 (OOC*CH₂), 42.1, 43.3 (CH₂NH₂), 45.4 [CH₂N (*CH₂)₂], 49.0, 49.9 (OCOCH₂*CH₂), 51.3 [*CH₂N (CH₂)₂], 61.8 (OCH₂), 169.1, 171.5 (C=O). ANAL. Calcd: C, 54.29%; H, 8.82%; N, 14.62%. Found: C, 54.63%; H, 8.46%; N, 14.23%.

Synthesis of PEAD (R)₈. SC (3.51 g, 11.6 mmol) in 15 mL of DMF was added dropwise to a solution of 1.00 g (0.58 mmol) of PEAN (NH₂)₈ and 0.80 g (10.1 mmol) of pyridine at room temperature. The reaction mixture was heated to 90°C for 30 h with stirring; the crude product was obtained in the same way as PEAD (R)₃ and recrystallized from dimethyl sulfoxide to give product PEAD (R)₈ as an off-white solid with a 55.4% yield.

mp: 154.9–157.3°C. IR (KBr): 3302, 3086 (ν_{N-H}), 1640 (ν_{C=O}), 1559, 1250 (ν_{C-N}, δ_{N-H}), 2920, 2851 (ν_{CH2}, ν_{CH3}), 1470 (δ_{CH2}), 1385 (δ_{CH3}), 741 (δ_{(CH2)*n*}, *n* ≥ 4). ANAL. Calcd: C, 69.16%; H, 11.01%; N, 6.54%. Found: C, 69.22%; H, 11.51%; N, 6.25%.

Synthesis of poly(amino amide) Dendrimer PAMAM (R)₄ (C₉₄H₁₈₄N₁₀O₈; scheme 3)

SC (4.70 g, 0.016 mol) in 30 mL of DMF was added dropwise to a solution of 1.00 g (0.002 mol) of PAMAM (NH₂)₄ and 0.79 g (0.010 mol) of pyridine at room temperature. The reaction mixture was heated to 80°C for 12 h with stirring; the crude product was obtained in the same way as PEAD (R)₃ and recrystallized from DMF three times to give PAMAM (R)₄ as a white solid with an 84.2% yield.



Scheme 2 Synthesis route of PEAD (R)₈.

mp: 165.8–167.3°C. IR (KBr): 3302, 3086 ($\nu_{\text{N-H}}$), 1644 ($\nu_{\text{C=O}}$), 1559, 1250 ($\nu_{\text{C-N}}$, $\delta_{\text{N-H}}$), 2920, 2851 (ν_{CH_2} , ν_{CH_3}), 1470 (δ_{CH_2}), 1385 (δ_{CH_3}), 721 ($\delta_{(\text{CH}_2)_m}$, $n \geq 4$). ANAL. Calcd: C, 71.39%; H, 11.65%; N, 8.86%. Found: C, 70.76%; H, 11.97%; N, 8.43%.

Preparation and property test of the thermosensitive gels

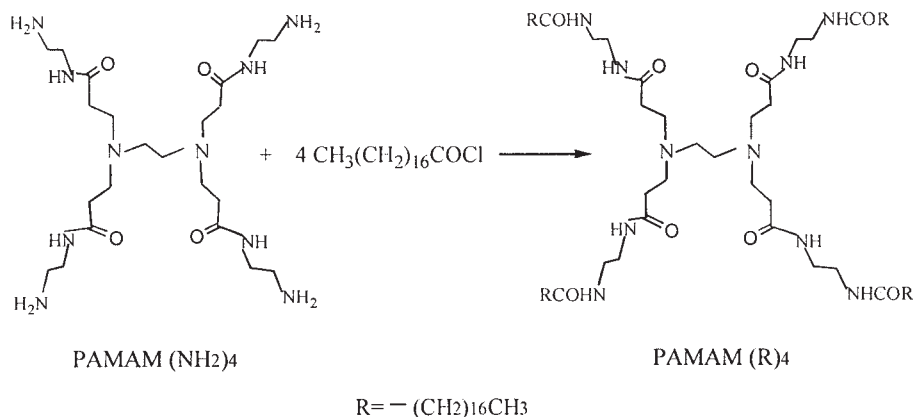
Stearyl-group-terminated dendrimers (2.0 g) in 38 mL of toluene were heated to dissolve completely and then separated into two parts. The one was cooled at a rate of 2°C/min, and the temperature at which dendrimer–toluene gels formed suddenly was observed. The other was cooled to 10°C at the same rate and

warmed again at a rate of 2°C/min to examine the dependence of the toluene content in the gels on the temperature. The gels were kept for 24 h thermostatically at a certain temperature and weighed. The content of toluene in the gels was calculated according to the formula $(M_w - M_d)/M_d \times 100\%$, where M_d is the mass of the stearyl-group-terminated dendrimer and M_w is the mass of the gel.

RESULTS AND DISCUSSION

Synthesis of the stearyl-group-terminated dendrimers

Stearyl-group-terminated dendrimers PEAD (R)₃, PEAD (R)₈, and PAMAM (R)₄ were synthesized by the



Scheme 3 Synthesis route of PAMAM (R)₄.

amidation of amino-group-terminated dendrimers PEAN (NH₂)₃, PEAN (NH₂)₈, and PAMAM (NH₂)₄ with SC. The effects of some factors on the yields of the products were investigated.

Molar ratio of SC and NH₂-terminated dendrimer

From the chemical reaction equation, the theoretical molar ratios of SC to PEAN (NH₂)₃, PAMAM (NH₂)₄, and PEAN (NH₂)₈ are 3, 4, and 8. However, Figure 1 shows that the theoretical molar ratio leads to low yields of stearyl-group-terminated dendrimers, especially PEAD (R)₈. An excess of SC raises the yields of the products because every amino group in the NH₂-terminated dendrimers is afforded new reaction opportunities. The more amino groups the NH₂-terminated dendrimers contain, the more excess of SC is needed. However, for each NH₂-terminated dendrimer there exists an appropriate amount of SC, corresponding to molar ratios of 4 [SC/PEAN (NH₂)₃], 8

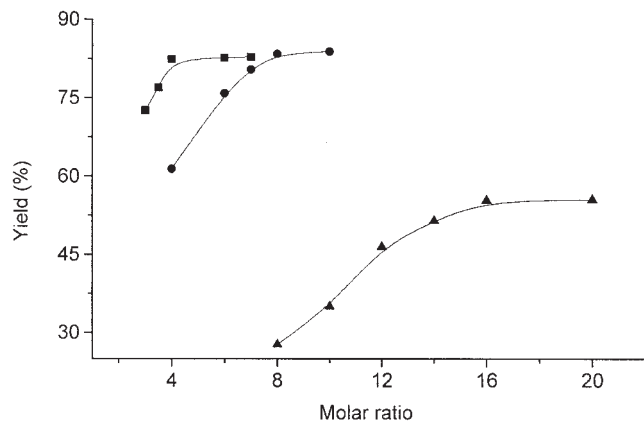


Figure 1 Effects of the molar ratio of raw materials on the yields of stearyl-group-terminated dendrimers: (■) SC/PEAN (NH₂)₃ (temperature = 90°C, time = 10 h), (●) SC/PAMAM (NH₂)₄ (temperature = 80°C, time = 12 h), and (▲) SC/PEAN (NH₂)₈ (temperature = 90°C, time = 30 h).

[SC/PAMAM (NH₂)₄], and 16 [SC/PEAN (NH₂)₈], above which the yields of stearyl-group-terminated dendrimers increase very slowly.

Reaction temperature

The fact that the yields of PEAD (R)₃, PAMAM (R)₄, and PEAD (R)₈ are 51.0, 20.1, and 1.5% at 30°C and the yield of PEAD (R)₈ is notably lower than that of PEAD (R)₃ and PAMAM (R)₄ at the same temperature (Fig. 2) indicates that complete amidation becomes more and more difficult with the number of amino groups on the periphery of the dendrimer increasing. On the other hand, the yields of PEAD (R)₃, PAMAM (R)₄, and PEAD (R)₈ continuously increase when the reaction temperature rises from 30 to 110°C, and for each stearyl-group-terminated dendrimer, there exists a temperature, that is, 90°C for PEAD (R)₃ and PEAD

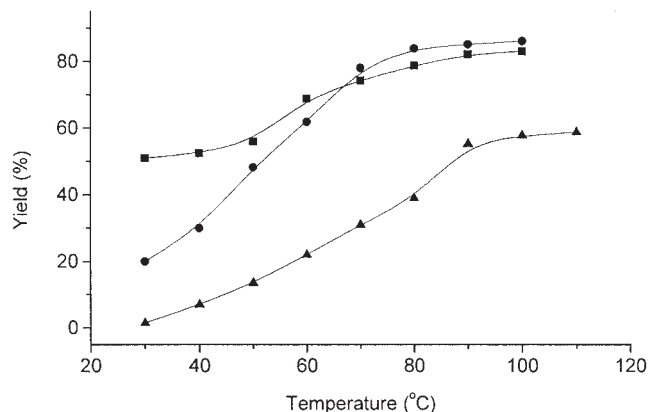


Figure 2 Effects of the reaction temperature on the yields of stearyl-group-terminated dendrimers: (■) PEAD (R)₃ [molar ratio of SC to PEAN (NH₂)₃ = 4, time = 10 h], (●) PAMAM (R)₄ [molar ratio of SC to PAMAM (NH₂)₄ = 8, time = 12 h], and (▲) PEAD (R)₈ [molar ratio of SC to PEAN (NH₂)₈ = 16, time = 30 h].

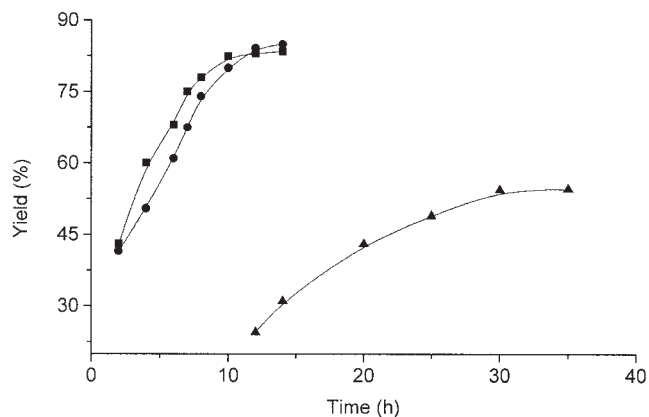


Figure 3 Effects of the reaction time on the yields of stearyl-group-terminated dendrimers: (■) PEAD (R)₃ [molar ratio of SC to PEAN (NH₂)₃ = 4, temperature = 90°C], (●) PAMAM (R)₄ [molar ratio of SC to PAMAM (NH₂)₄ = 8, temperature = 80°C], and (▲) PEAD (R)₈ [molar ratio of SC to PEAN (NH₂)₈ = 16, temperature = 90°C].

(R)₈ and 80°C for PAMAM (R)₄, over which the yields of the dendrimers trend toward stability.

Reaction time

Figure 3 shows that when the reaction time is prolonged, the yields of PEAD (R)₃, PAMAM (R)₄, and PEAD (R)₈ increase rapidly at first and then almost no longer change after a reaction for a certain period of time. The stearyl-group-terminated dendrimers PEAD (R)₃ and PAMAM (R)₄ exhibit similar relationship between the yields and reaction time and yields over 80.0% at 10 h, whereas the yield of PEAD (R)₈ is only 24.5% at 12 h. A reaction for 30 h gives a 55.4% yield of PEAD (R)₈. The results show again that the complete amidation becomes more and more difficult with the number of amino groups on the periphery of the dendrimer increasing. The appropriate reaction times for PEAD (R)₃, PAMAM (R)₄, and PEAD (R)₈ are 10, 12, and 30 h, respectively.

Amount of DMF

DMF is the solvent in the amidation reaction. From Figure 4, we can see that there is an optimum amount of DMF in the reaction systems at which the yields of products PEAD (R)₃, PAMAM (R)₄, and PEAD (R)₈ are maximum.

Characterization of the stearyl-group-terminated dendrimers

The structures of the stearyl-group-terminated dendrimers have been characterized by IR and elemental analysis. The IR spectra in Figure 5 can be analyzed as follows: 3302 and 3082 (3086) cm⁻¹ are peaks of N—H

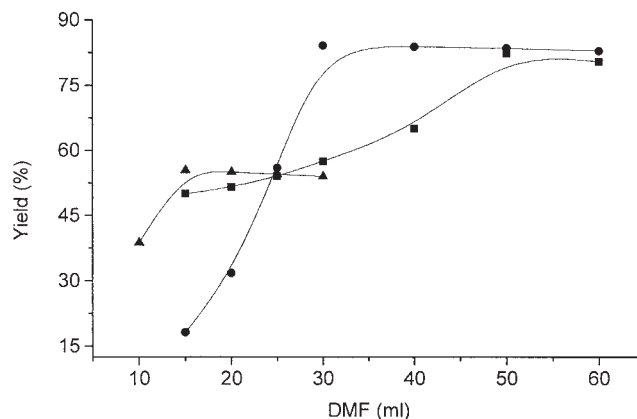


Figure 4 Effects of the amount of DMF on the yields of stearyl-group-terminated dendrimers: (■) PEAD (R)₃ [molar ratio of SC to PEAN (NH₂)₃ = 4, temperature = 90°C, time = 10 h], (●) PAMAM (R)₄ [molar ratio of SC to PAMAM (NH₂)₄ = 8, temperature = 80°C, time = 12 h], and (▲) PEAD (R)₈ [molar ratio of SC to PEAN (NH₂)₈ = 16, temperature = 90°C, time = 30 h].

in secondary amide; 1647 (1644 and 1640) cm⁻¹ is the peak of C=O in secondary amide; 1555 (1559) and 1242 (1250) cm⁻¹ are the combination bands of the stretching vibration of C—N and the bending vibration of N—H; 2920 and 2851 cm⁻¹ are associated with the stretching vibration of C—H in CH₂ and CH₃; the 1470- and 1385-cm⁻¹ peaks are related to the scissor vibration of C—H in CH₂ and the bending vibration of C—H in CH₃, respectively; and 721 (741) cm⁻¹ is characteristic of the (CH₂)_n (n ≥ 4) group. The peaks in Figure 5 are consistent with the expected ones for stearyl-group-terminated poly(ester amide)s PEAD

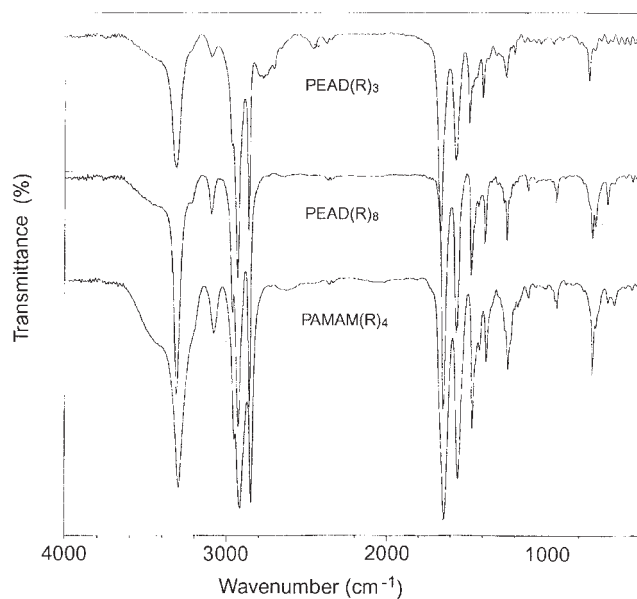


Figure 5 IR spectra of stearyl-group-terminated dendrimers.

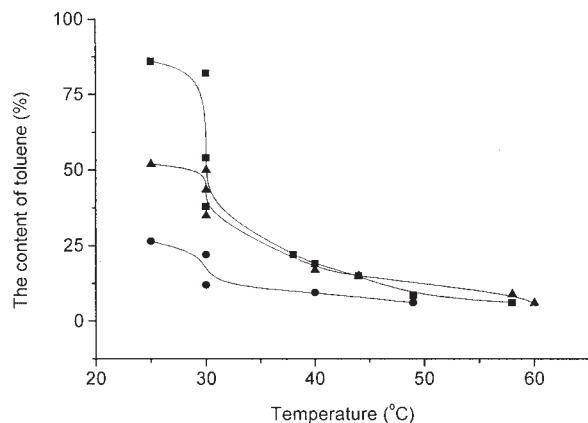


Figure 6 Dependence of the toluene content in the dendrimer-toluene gels on the temperature: (■) PEAD (R)₃, (●) PAMAM (R)₄, and (▲) PEAD (R)₈.

(R)₃ and PEAD (R)₈ and poly(amino amide) dendrimer PAMAM (R)₄. The results of elemental analysis show that the experimental data for C, H, and N correspond to the theoretical ones. IR spectra and elemental analysis indicate that stearyl-group-terminated poly(ester amide)s PEAD (R)₃ and PEAD (R)₈ and poly(amino amide) dendrimer PAMAM (R)₄ were successfully synthesized

Thermosensitivity of the stearyl-group-terminated dendrimers

The stearyl-group-terminated dendrimers (2.0 g) in 38 mL of toluene were completely dissolved at 80°C. When three parts of dendrimer-toluene solutions were cooled at a rate of 2°C/min, PEAD (R)₃, PEAD (R)₈, and PAMAM (R)₄ dendrimer-toluene gels appeared suddenly at 57.5, 60, and 49°C, respectively. This result suggests that the dendrimer-toluene solutions have thermosensitivity.

To examine the dependence of the toluene content in the dendrimer-toluene gels on the temperature, three other parts of dendrimer-toluene solutions were cooled to 10°C at a rate of 2°C/min and warmed again at the same rate; the results are shown in Figure 6. The toluene content in the gels decreases as the temperature increases.

This can be explained as follows: the similar molecular polarity leads to the formation of dendrimer-toluene gels. At a low temperature, the stearyl groups on the periphery of poly(ester amide) and poly(amino amide) dendrimers may be possibly folded partially, and the topology of the dendrimer molecules is relatively stable because the Brownian motion of the molecules is not very strong. We can suppose that the partially folded dendrimer molecules just have good affinity to toluene molecules. Consequentially, the gels

hold much toluene; when the temperature is raised, the extension of stearyl groups reduces the polarity of the dendrimer molecules, and strong Brownian motion makes the topology of the dendrimer molecules constantly change. These two aspects weaken the affinity between the dendrimer and toluene molecules, and the gels release toluene. The sudden change of the dendrimer-toluene affinity results in a break release of toluene, which corresponds to the abrupt turn around 30°C on the curves in Figure 6. The ability to suddenly release toluene, explained by the reduced percentage of the toluene content in the dendrimer-toluene gels around 30°C, is in the order of PEAD (R)₃ > PEAD (R)₈ > PAMAM (R)₄, and this indicates that the thermosensitivity of poly(ester amide) dendrimers is better than that of poly(amino amide) dendrimers, and the thermosensitivity decreases when the generation of the dendrimer increases.

The properties of temperature-sensitive gels make it possible for gels to absorb solvents at low temperatures and liberate them at high temperatures; as a result, not only is the solution concentrated, but the gels gain rebirth.

CONCLUSIONS

Stearyl-group-terminated dendrimers PEAD (R)₃, PEAD (R)₈, and PAMAM (R)₄ were synthesized and characterized. The dendrimer-toluene solutions had thermosensitivity; that is, gels formed when the solutions were cooled to a certain temperature. Furthermore, the content of toluene in the gels depended on the temperature, and an abrupt change occurred at about 30°C.

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