

Cinnamoyl Shell-Modified Poly(amidoamine) Dendrimers

JINFENG WANG,¹ XINRU JIA,¹ HONG ZHONG,¹ HUIZHONG WU,¹ YOUYONG LI,¹ XIAOJIE XU,¹ MINGQIAN LI,¹ YEN WEI²

¹ Department of Polymer Science and Engineering, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, People's Republic of China

² Chemistry Department, Drexel University, Philadelphia, Pennsylvania 19104

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ABSTRACT: Poly(amidoamine)(PAMAM) dendrimers with a cinnamoyl shell were prepared by reacting full generation PAMAM dendrimers (G=3.0) with 2-chloroethanol and cinnamoyl chloride, which resulted in densely packed polymerizable unsaturated groups on the periphery. The cinnamoyl shell of the dendrimers dimerized when irradiated under a UV light by using 5-nitroacenaphthylene as an initiator in dilute dimethylformamide (DMF). FTIR, ¹H NMR, UV-Vis, SEC, and a viscosity test certified that the photocycloaddition of the cinnamoyl shell of the dendrimers took place within the molecules with the disappearance of double bond signals in the FTIR. ¹H NMR spectra as well as the intrinsic viscosity and polydispersity value of the products both before and after irradiation showed no difference. It was further found that the cinnamoyl shell-modified dendrimers possessed fluorescence property, and the fluorescence intensity became stronger when the shell was photocyclized under UV-irradiation. © 2000 John Wiley & Sons, Inc. *J Polym Sci A: Polym Chem* 38: 4147–4153, 2000
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INTRODUCTION

With the progress in the studies of dendrimer chemistry, attention is shifting towards the functionalization and application of these unique macromolecules.¹ An interesting subject is to introduce unsaturated groups on the dendrimer surface to obtain core-shell macromolecules or dendrimer-based materials. For example, Zimmerman et al.² have successfully synthesized cored dendrimers that is predicted as a “molding” process to form soluble endo-receptor for small molecules. Balogh et al.³ have presented their synthesis and characterization of dendrimer-coionic acetylene polymers in which the “soft” in-

ternal part is surrounded by a rigid and charged “crust.” Dvornic and his coworkers⁴ have described a family of radial layered copolymeric poly(amidoamine-organosilicon)(PAMAMOs) dendrimers that consist of a hydrophilic interiors and a hydrophobic exteriors. It is said that these materials can be applied as molecular “sponges” and “reactors,” protective or functional coatings on various substrates.

We have been interested in the synthesis of surface bonded or crosslinked dendrimers with particular attention focused on preparation and photocyclization of cinnamoyl shell poly(amidoamine) (PAMAM) dendrimers. As is well known, cinnamic acid and its derivatives are excellent photoactive resins. The photocyclization of them have been extensively studied.⁵ What concerns us is: (1) can the cinnamoyl shell of dendrimers be cyclized by irradiating under UV light in solution? (2) Can the cycloaddition reaction take place

Correspondence to: X. Jia (E-mail: xrjia@chemms.chem.pku.edu.cn)

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within the molecules? (3) What is the photochemical behavior of PAMAM dendrimers with a cinnamoyl shell?

In this article, we report the preparation, intramolecular photocycloaddition, and the fluorescence emission property of these cinnamoyl shell-modified PAMAM dendrimers.

EXPERIMENTAL

Materials

Ethylenediamine was dried with sodium hydroxide over night and distilled. Methyl acrylate was washed with 5% sodium hydroxide and distilled under reduced pressure. PAMAM dendrimers (G3.0) were synthesized according to the established procedure.⁶ Cinnamoyl chloride was prepared by reacting cinnamic acid with thionyl chloride. All organic reagents employed in this investigation are reagent quality. 5-Nitroacenaphthylene is a commercial product and used as received.

Surface Hydroxylation of PAMAM Dendrimers (G=3.0) (1)

Four grams (5.8×10^{-4} mol) PAMAM dendrimer (G3.0) and 40 mL dried DMF were added to a 100-mL three-necked flask equipped with a thermometer, a dropping funnel, and a condenser. The solution was stirred and warmed to 40 °C until it turned clear. After addition of 3 g anhydrous sodium hydrogen carbonate, a solution of 3 g (0.037 mol) 2-chloroethanol in 15 mL dried DMF was slowly dropped into the flask. The reaction mixture was stirred at 60 °C for 10 h. Thin-Layer Chromatographic (TLC) was used to observe the decrease of 2-chloroethanol with silicon G6.0 as a solid phase, ethyl acetate, and *n*-hexane (1 : 3–1 : 4) as eluant. The mixture was cooled to room temperature and filtered. The resulting filtrate was concentrated under reduced pressure, then dropped into carbon tetrachloride. Upon removing the solvent, the crude product was purified repeatedly by dissolving in methanol and evaporating the solvents under reduced pressure until a light brown powder **1** appeared. The powder was further purified by drying under 100 Pa at 40 °C for 48 h and obtained in 95% yield. FTIR: 1063, 3230–3550 cm^{-1} . ¹H NMR (DMSO-d₆, ppm) (new signals) δ 5.18(—OH), 3.94(—CH₂—O—), 2.82(—NCH₂—). ¹H NMR integration shows that 95% of —NH₂ reacted with 2-chloroethanol.

Preparation of Cinnamoyl Shell PAMAM Dendrimers (2)

To a 100-mL three-necked flask were introduced 2.0 g (1.7×10^{-4} mol) **1**, 40 mL dried DMF, and 3 mL triethylamine. The reaction mixture was stirred and heated to 40 °C. After **1** was totally dissolved in DMF, the solution of 1.83 g (0.011 mol) cinnamoyl chloride in 30 mL-dried DMF was slowly dropped into the flask. A slight exothermicity was observed. The reaction mixture was stirred at 50 °C for 10 h, cooled to room temperature, and put into refrigerator (–10 to –15 °C) overnight. The by-product, triethylamine hydrochloride, was filtered off. The filtrate was condensed using a rotary evaporator, then dropped into carbon tetrachloride. The resulting semisolid crude product was dissolved in methanol, then evaporating the solvents under reduced pressure. Repeating the procedure until the light brown powder **2** was obtained. The product was dried under 100 Pa at 40 °C for 48 h. Yield: 90%. FTIR [see Fig. 1(a)]: 3410, 3280, 3030, 1706, 1650, 1577, 710, 768 cm^{-1} . ¹H NMR (DMSO-d₆, ppm) [see Fig. 2(a)], new signals): δ 4.2–4.5 (—OCOCH₂—); 6.52–6.56 (—OCO—CH=CH—Ph); 7.57–7.61 (—OCO—CH=CH—Ph); 7.3–7.5, 7.6–7.9 (phenyl protons). ¹³C NMR(DMSO-d₆, ppm) (new signals) δ 65.62 (—CH₂—O—), 58.97 (—CH₂N—), 127.51, 128.44, 134.92 (phenyl), 118.43 (—OCOCH=CH—), 143.32 (—CH=CH—phenyl), and 165.49 (—OCO). By calculating from ¹H NMR integration of compound **2**, 90% of hydroxyl groups converted to cinnamoyl ester.

Photocycloaddition of 2

The modified dendrimers **2** and 5-nitroacenaphthylene with a weight ratio of 20 : 1 were dissolved in DMF. The concentration was controlled as low as 2 mg/mL to avoid intermolecular crosslinking. The mixture, which was charged in a glass tube, was degassed with several vacuum pump-nitrogen cycles, and then put into a water bath equipped with a stirrer, a UV-lamp, and a temperature-controlling system. The reaction mixture was irradiated (230 W cm^{-2}) at 25 ± 0.5 °C for different times. Then the mixture was transferred to a round flask to remove the solvent by a rotary vacuum dryer below 50 °C. The residue was dropped into carbon tetrachloride, and purified repeatedly by dissolving in methanol, then drove off the solvents. Finally, product **3** (a light brown powder) was dried under vacuum at 40 °C for 48 h.. The yield was in the range of 90–95%.

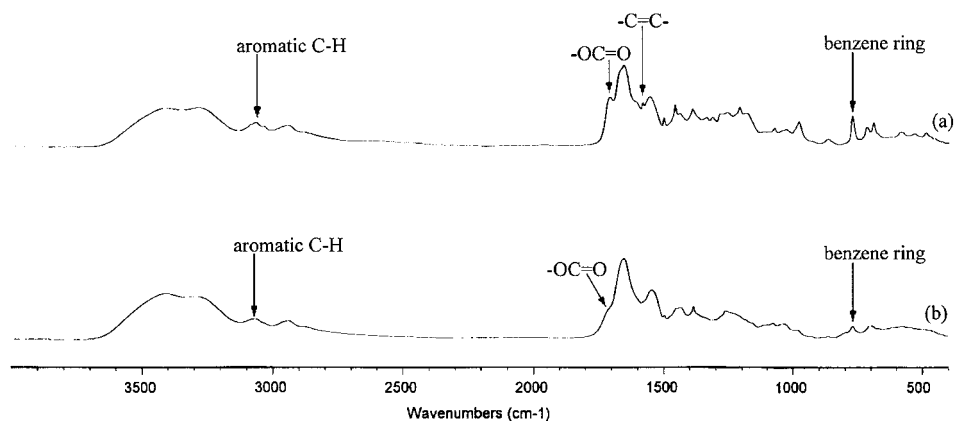


Figure 1. FTIR spectra of compounds **2** and **3**. (a) **2**, (b) **3**; D: dendrimer.

Characterizations

A UV light (GGZ1000-1 Hg lamp) was used for the photocyclization (230 W cm^{-2}). ^1H NMR, ^{13}C NMR spectra were obtained at room temperature in DMSO-d_6 using an ARX 400 apparatus. FTIR spectra were taken on a Nicolet Magna IR-750

spectrometer in a KBr powder-pressed pellet form. SEC was performed on a Waters 2410 instrument with a refractive index detector. DMF was used as the carrier solvent at a flow rate of 1.0 mL/min , and with narrow molecular weight distribution polystyrenes as the calibration standards. The viscosity measurements were carried out on an Ubbelohde viscometer at $25.0 \pm 0.1 \text{ }^\circ\text{C}$ in methanol. The intrinsic viscosities $[\eta]$ were determined by extrapolation of the reduced viscosities η_{sp}/c , determined at five different concentrations, to infinite dilution. The fluorescence spectra were recorded on a Hitachi F-4500 fluorescent spectrophotometer in DMF. UV-vis spectra were acquired on a UV-Visible scanning spectrophotometer (Shimadzu UV-2101 PC) at room temperature using methanol as the solvent. Molecular modeling software Cerius2 was used to simulate the molecular model at 300 K .

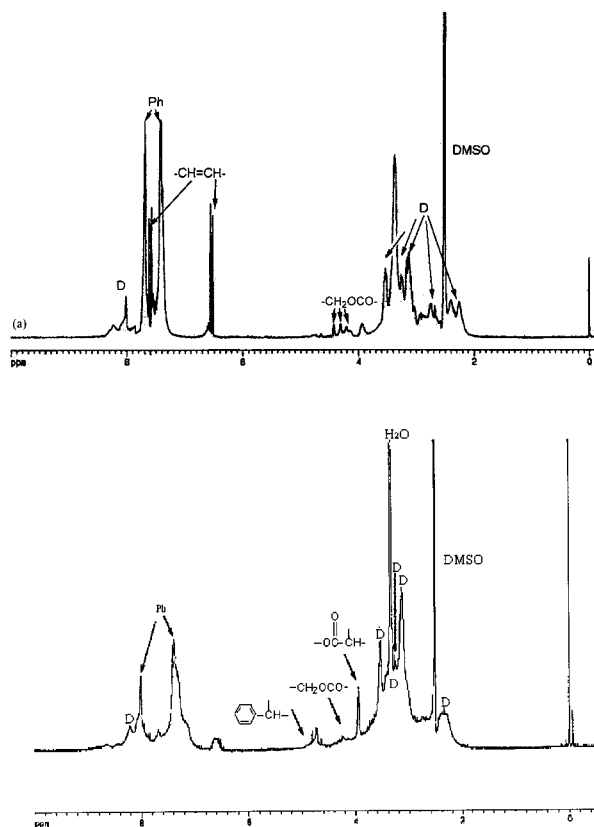


Figure 2. ^1H NMR spectra of compounds **2** and **3**. (a) **2**, (b) **3**; D: dendrimer.

RESULTS AND DISCUSSION

Photocycloaddition

It is believed that cinnamic acid and its derivatives in liquid media generally undergo photoisomerization instead of photocyclization when electronically excited by near-ultraviolet light,⁷ while for the solid state, photocyclization is the only reaction pathway.⁸ Rennert et al.⁹ reported that dicinnamate esters in dilute solution photocyclize to form cyclobutane derivatives in good yields. They studied the competing reactions of electronically excited 1,3-trimethylene dicinnamate, and provided an effective method to attain the requisite distance for the photoisomeriza-

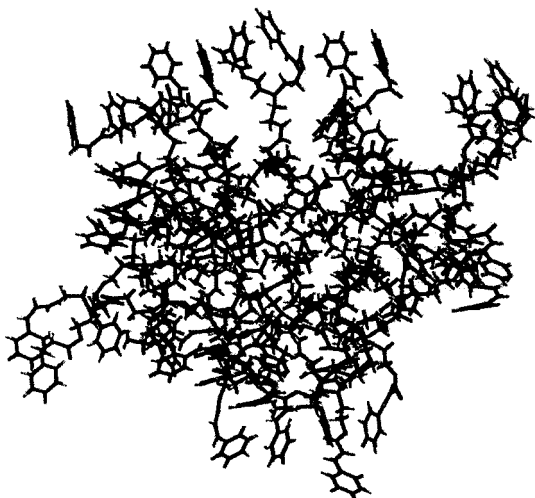
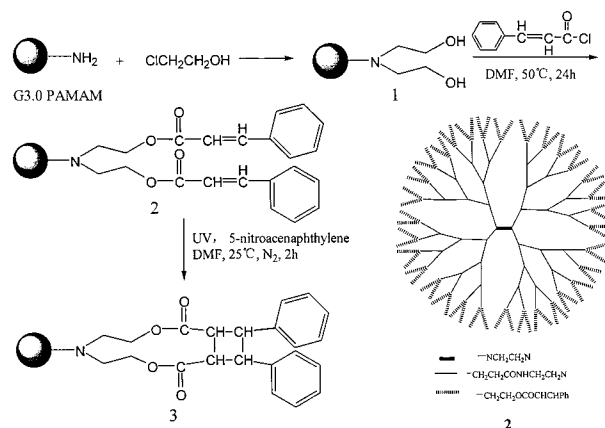


Figure 3. One of the optimal conformations of the molecule **2**.

tion to occur. Here, we introduce densely packed cinnamoyl units at the dendrimer periphery, which provides highly localized concentrations of both excited and ground-state cinnamoy species. Could the photocyclization reaction take place in this system? To get the conformation information about **2**, the molecular model was simulated using the Cerius2 software. We performed molecular dynamics simulation using Cvff95 Force Field in constant NVE condition. The total simulation steps were 200,000 in units of a 1-fs simulation step, and the simulation temperature was 300 K. Figure 3 shows one of the optimal conformations of **2**. It is seen that the molecule adopted nearly a globular structure with a radius value of 2–2.5 nm, and the outside groups were well distributed in all directions. The distance between the closest double bonds was 5.3–7.5 Å. From the molecular simulation result, it can be predicted that the distance between the adjacent groups and the high local concentration of cinnamoyl groups within the dendrimer molecules make the intramolecular photocyclization more likely to occur.

UV-initiated reaction was performed in dilute DMF. The concentration of the modified dendrimers in DMF was controlled as low as possible to avoid intermolecular crosslinking. Comparison of the FTIR, ^1H NMR spectra of **2** and the product **3** confirmed the occurrence of double-bond addition. It shows that the absorption at 1577 cm^{-1} for $\text{C}=\text{C}$ stretching was missing [see Fig. 1(b)]. This can be further evidenced by ^1H NMR spectrum [see Fig. 2(b)]. The strong signals of vinyl protons



Scheme 1. Preparation and photocyclization of cinnamoyl shell-modified G3.0 PAMAM dendrimers.

at 6.52–6.56 ppm and 7.57–7.61 ppm almost disappeared. Meanwhile, the new signals that are assigned to the cyclic $-\text{OCO}-\text{CH}<$ and $>\text{CH}-\text{Ph}$ shows at 3.87–3.95 and 4.72–4.81 ppm (see Scheme 1). The result indicates that the photocycloaddition occurs as the main reaction.

The UV-vis spectra of **2** and **3** at different irradiation times were recorded to obtain more information about the double-bond reactions. The relationship between the spectral violet shift and the irradiation time is shown in Figure 4. It can be seen that the spectral violet shift was over 13 nm in 3 h. After this period, it reached equilibrium, although the irradiation lasted 7.5 h. It is well known that one reason for the spectral violet shift is the decrease of the double bond. The UV-Vis result indicated that the reaction oc-

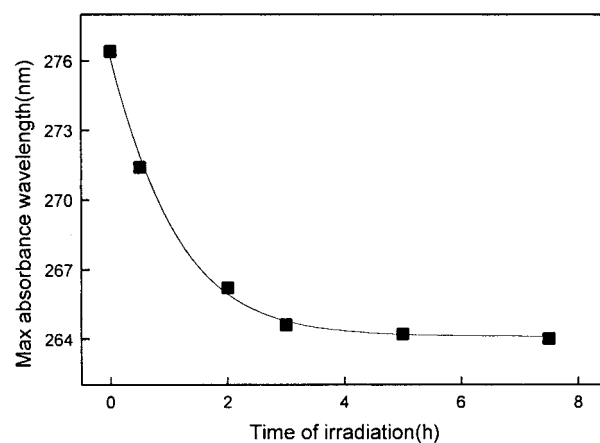


Figure 4. The maximum UV absorbance wavelength at different irradiation time; solvent: methanol; [chromophore] = 1.74×10^{-4} mol/L.

Table I. The Intrinsic Viscosity, Hydrodynamic Radii, and Polydispersity of **2** and **3**

| Sample | $[\eta]^a$ (dL/mg) | r_η^a (nm) | r_m^b (nm) | M_n^c | M_w/M_n^c | M_c^d |
|----------|-----------------------|--------------------|-----------------|---------|-------------|---------|
| 2 | 4.9×10^{-3} | 2.43 | 2–2.5 | 15,673 | 1.11 | 18,420 |
| 3 | 4.8×10^{-3} | 2.41 | 2–2.5 | 17,664 | 1.17 | 18,420 |

^a From Ubbelohde viscometer measure.

^b Determined from molecular simulation.

^c By SEC analysis relative to narrow molecular weight polystyrene.

^d Theoretical-calculation value.

curred rapidly in 3 h. From ¹H NMR integration, we know 80–85% double bonds disappeared after irradiation. Reasonably, the double bonds could not totally disappear because of the following: (1) the dendrimers with three-dimension spherical shape has branches in all directions. Each branch could take different forms, which may be extended or backfolded in the solvent,¹⁰ as the exterior chain of the modified dendrimers can be considered as flexible. The complex conformation makes some arms difficult to react because it is difficult to find adjacent double bonds in the dendrimer interior; (2) “C=C” double bonds possess *trans* and *cis* conformations, and these conformations can be interconvertible with enough energy supply. Under the conditions we used in this reaction, a few double bonds probably did not have suitable conformation and lost reaction activity; (3) there are defects in the molecules, because each step of the modified reactions could not reach 100% conversion. These defect positions make some double bonds isolated, and remain unreacted after irradiating.

To identify whether the reaction occurred intramolecularly or intermolecularly, we used Ubbelohde viscometer to measure the intrinsic viscosity of **2** and **3**. The intrinsic viscosity values of **2** and **3** were 4.9×10^3 dL/g and 4.8×10^3 dL/g, respectively (Table I). The hydrodynamic radii were calculated based on the intrinsic viscosity data by using the Einstein equation¹¹ as follows:

$$R\eta = \{3M[\eta]/10\pi N_A\}^{1/3} \quad (1)$$

where N_A is Avogadro's constant, M is molecular weight (the theoretical molecular weight of **2** and **3** are used in the calculation), and $[\eta]$ is the intrinsic viscosity obtained from the experiment. The hydrodynamic radii of **2** and **3** were 2.4 and 2.3 nm (Table I), which corresponded with the radii values of 2–2.5 nm obtained from the molec-

ular dynamics simulation. As a comparison, we have also modified PAMAM dendrimers with an itaconate shell and tried to make the surface double bonds crosslinked intramolecularly under the same conditions as mentioned above. The FTIR and ¹H NMR spectrum demonstrated the disappearance of double bonds. But the intrinsic viscosity of irradiated products became higher than the unirradiated. Therefore, it can be concluded that the double bonds of cinnamoyl groups linked within the dendrimer molecules, because if the intermolecular crosslinking had happened, the molecular volume would have been enlarged greatly, which was bound to cause an increase of the intrinsic viscosity.

To get more evidence on the intramolecular cyclization, size-exclusion chromatography (SEC) was used to observe the polydispersity of **2** and **3**. The results from SEC may not reflect the accurate molecular weights because of the specific shape of dendrimers relative to the random coil polystyrene standards, but it is a convenient technique for determining the polydispersity of the dendrimers.¹² The M_n and polydispersity of **2** and **3** are also shown in Table I. The polydispersity values of **2** and **3** were 1.11 and 1.17, respectively, which supported the conclusion of intramolecular photocycloaddition. However, the polydispersity of 1.11 and 1.17 are large for a supposedly pure compound. This may be due to the fact that each dendrimer molecule experienced a different reaction.

We attempted to use MALDI-TOF Mass Spectrometer to characterize the two compounds **2** and **3**, but failed because we could not find a suitable substrate. We also tried to get the dimensions of **2** and **3** using laser light scattering with the wavelength of 541.5 nm. Because of the strong luminance of these two compounds, the data are considered to be inaccurate.

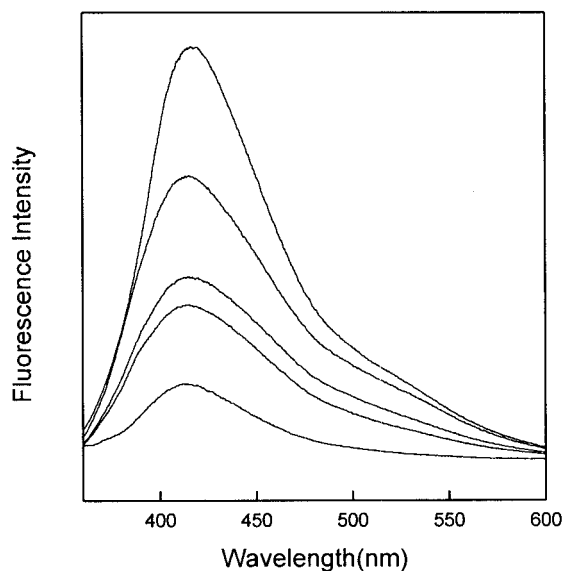


Figure 5. The fluorescence intensity for different irradiation time (bottom to top): 0, 0.5, 2, 3, 7.5 h; $\text{Ex}=348$ nm; $[\text{chromophore}]=1.74 \times 10^{-3}$ mol/L.

Fluorescence Behavior of 2 and 3

Interestingly, we found both compounds **2** and **3** show fluorescence, although PAMAM and cinnamic acid do not have such a property. Furthermore, the fluorescence intensity increased with more double bonds disappearing (see Fig. 5).

In general, rigid and planar structures promote fluorescence.¹³ The principal effect of increasing molecular rigidity is to decrease the interaction between fluorescent substance and solvent molecules or other solute molecules, and this minimizes the energy transfer, and therefore enhances fluorescence. By comparing the structure of **2** with **3** (see Scheme 1), it is clear that the formation of cyclic structure in **3** results in the increase in rigidity, which causes the increase in the fluorescence intensity.

Another explanation for the increase of the fluorescence intensity after photocyclization is the "structural self-quenching effect" (SSQE) of compound **2**. SSQE phenomena have been reported and explained by Li et al.¹⁴ The coexistence of the electron-accepting carbon-carbon double bond adjacent to carbonyl and electron-donating phenyl ring in compound **2** causes the formation of the exciplex and thus quenches the fluorescence. To clarify that the carbonyl carbon-carbon double bond does act as electron acceptors in the exciplex formation, the fluorescence quenching of **3** was carried out by use of electron-deficient compounds

such as AN (acrylonitrile), FN (fumaronitrile), and TCNQ (7,7,8,8-tetracyanoquinodimethane) as quenchers. As an example, the fluorescence spectra of compound **3** in DMF in the presence of varying concentrations of FN is shown in Figure 6.

The Stern-Volmer quenching rate constants were calculated by using the Stern-Volmer equation¹⁵

$$I_0/I_q = 1 + K_{sv}[Q]. \quad (2)$$

Stern-Volmer plots for the fluorescence quenching of the compounds **3** by AN, PN, and TCNQ are depicted in Figure 7. The K_{sv} values were 2.54, 24.0, and $2.8 \times 10^3 \text{ M}^{-1}$ when using AN, FN, and TCNQ as quenchers, respectively. The quenching efficiency of AN, FN, and TCNQ increases in the order of their polarities, as reported by Li et al.¹⁴

CONCLUSIONS

In summary, PAMAM ($G=3.0$) dendrimers with a cinnamoyl shell were prepared by two-step reactions. The intramolecular bonding of the modified PAMAM dendrimers was successfully carried out in dilute DMF under UV-irradiating by using 5-nitroacenaphthylene as an initiator. From the similarity of the intrinsic viscosity and the poly-

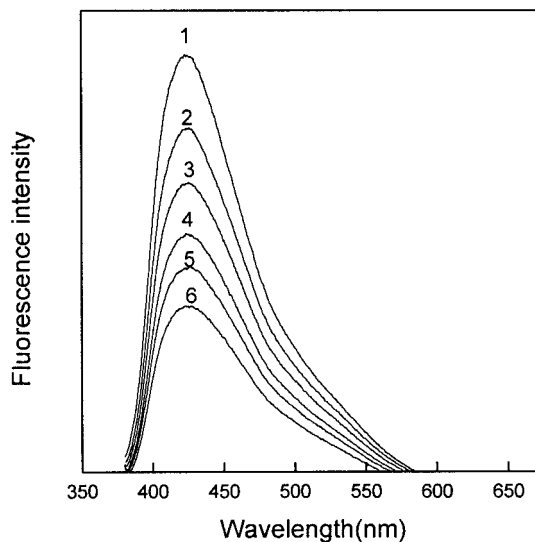


Figure 6. Fluorescence spectra of **3** in DMF in presence of varying concentration of FN (10^{-2} mol/L): (1) 0, (2) 0.91, (3) 1.80, (4) 2.86, (5) 3.75, (6) 4.73; $\text{Ex}=370$ nm; $[\text{chromophore}]=1.74 \times 10^{-3}$ mol/L.

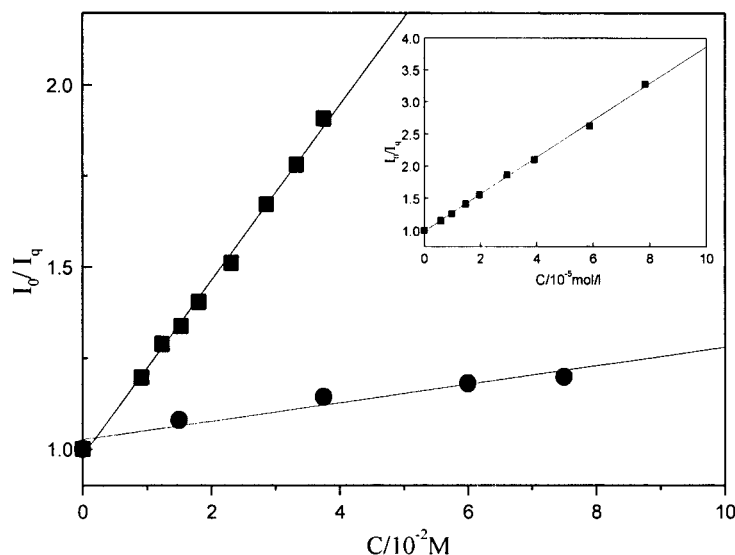


Figure 7. Stern–Volmer plots for fluorescence quenching of **3** by PN (■), AN (●), and TCNQ (inset) in DMF; $\text{Ex}=370\text{ nm}$; $[\text{chromophore}]=1.74 \times 10^{-3}\text{ mol/L}$.

dispersity between **2** and **3**, it can be concluded that the reaction occurred within the molecules. The double bonds reacted rapidly in a period of 2–3 h with a yield of 80–85%, which was indicated by UV-Vis spectrometer and $^1\text{H NMR}$ integration. Both the unirradiated cinnamoyl shell-modified compounds and the irradiated products were found to possess fluorescent property. The fluorescent intensity of the latter was stronger, and the fluorescent intensity increased with the decreasing of double bond groups.

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