Communications to the Editor

Synthesis of Poly(*p*-phenylene) Having Phthalic Anhydride Moieties in the Main Chain and Its Conversion into Fluorescein Derivative

Jun-ichi Kadokawa,* Masakazu Suenaga, and Yoshiro Kaneko

Department of Nanostructured and Advanced Materials,
Graduate School of Science and Engineering, Kagoshima
University, Korimoto, Kagoshima 90-0065, Japan

Received April 6, 2008
Revised Manuscript Received April 29, 2008

Fully conjugated polymers have attracted much attention because of a large number of applications in electronic conductivity and optoelectronics.[1] Poly(*p*-phenylene) (PPP) is one of the most useful conjugated polymers for organic conducting materials and organic polymeric ferromagnets due to the planar conjugated π system, along with high strength, high heat resistance, and other structural unique properties.[2]

In recent years, considerable interest has been devoted to developing new fluorescence dye-based probes as the excellent sensors for biomolecules, being sensitive, fat-responding, and capable of affording high spatial resolution via microscopic imaging.[3] Among many fluorescence dyes, fluorescein is known to have a high quantum yield of fluorescence in aqueous solution and to be excitable at long wavelength.[4] Rhodamine is also a well-known fluorescence compound showing a great photostability,[5] which has been used as a very efficient laser dye for the red region of the visible spectrum. Over the years, a variety of fluorescein and rhodamine derivatives have been prepared and used as laser dyes, fluorescent detection, and fluorophore for labeling and sensing biomolecules.[6] Interestingly, both fluorescein and rhodamine can be prepared by the same kind condensation reaction using phthalic anhydride (PA) under acidic conditions. The reaction of PA with resorcinol gives fluorescein, whereas that with 3-aminophenol affords rhodamine.[7,8]

On the basis of the above viewpoints, we have been interested in the conjugated polymers containing the PA moieties in the main chain, e.g., the PPP with PA moieties, because such polymers are considered as good starting materials for the production of the fluorescein- or rhodamine-containing conjugated polymers by the above-mentioned condensation. The obtained polymers can be expected as the new photofunctional materials combining the conjugated polymer chains and the fluorescence dye groups. For the synthesis of the PPP derivative, one of the most general methods is the homo- or cross-coupling polymerization of the aromatic monomers having the reactive substituents at the *p*-positions.[9–12] In the case of this study, however, the difficulty for the preparation of the PPP with PA moieties by the coupling polymerization can be assumed, because the introduction of the substituents at the *p*-positions (C-3 and C-6) on an aromatic ring of PA is not common, attributed to the existence of an electron-withdrawing group, i.e., a carboxylic anhydride, at the *o*-positions of C-3 and C-6. Furthermore, even if such a desired monomer can be obtained, its coupling polymerization will not proceed well, because the coupling polymerization is generally performed under alkaline conditions, which certainly affects to cleave the carboxylic anhydride group. To the best of our knowledge, therefore, the PPP derivatives having the main chain bearing between the *p*-positions on the aromatic rings in PA moieties have hardly been prepared so far.

On the basis of the above considerations, we have designed other appropriate routes resulting in the PPP derivatives with PA moieties besides the coupling polymerization and consequently reached the polymer reaction method starting from poly(*p*-phenylene-1,3-butadienylene) (PPB), as shown in Scheme 1a. The first step is the introduction of the carboxylic anhydride groups in the main chain by the Diels−Alder reaction of PPB with maleic anhydride. Because the conjugated structure in the polymer chain is lost by the first reaction, its aromatization with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) is performed as the second step, giving rise to the desired PPP with PA moieties. Furthermore, the PPP derivative can be converted into the fluorescence dye-containing PPP. For example, the reaction with resorcinol will give the PPP having the fluorescein moieties in the main chain. In this communication, we would like to report the synthesis of the PPP with PA moieties according to the above synthetic route and its conversion into the fluorescein-containing PPP. For the PPB derivative as the starting polymer, we selected structure **1**, which had the long alkyl side chains (decyl groups) on the basis of the consideration for the solubility in the organic solvents. The PPB (**1**) was prepared by the Wittig reaction of the corresponding two monomers: a diacrolein[13–16] and a bis(phosphonium bromide)[13] under basic conditions (Scheme 2, top).[17–21]

Prior to carrying out the synthetic experiments from **1** by Scheme 2, an attempt for the preparation of the model compounds (**4** and **5**) by the same reaction steps was made as shown in Scheme 1b to confirm whether the synthesis of the desired PPP with PA moieties according to Scheme 1a was possible. The compounds can be considered as the analogue for the unit structures of the desired polymers. Diels−Alder reaction of *trans,trans*-1,4-diphenyl-1,3-butadiene (**2**) with maleic anhydride[22,23] followed by the aromatization[24,25] gave **4** in 47.7% yield (overall). Furthermore, the reaction of **4** with resorcinol was conducted in the presence of methanesulfonic acid in 1,2-dichloroethane,[7,26] giving rise to 3,6-diphenylfluorescein (**5**) in 69.8% yield. On the basis of the results of the above model reactions, we judged that the synthesis of the PPP with PA moieties and the conversion into the fluorescein-containing PPP could be achieved according to Scheme 1a.

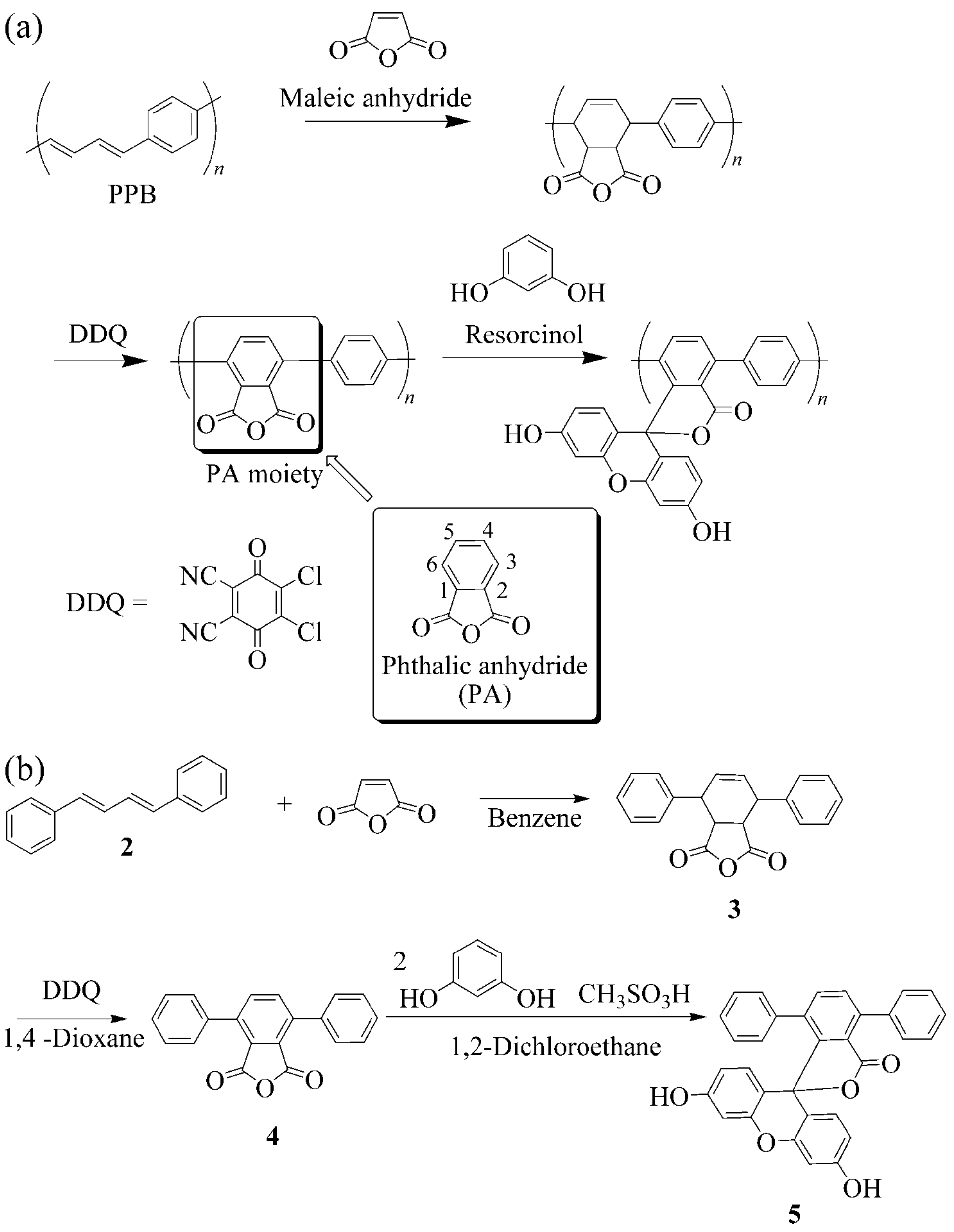
Diels−Alder reaction of **1** (M_n = 5900, M_w/M_n = 1.48, by

---

* Corresponding author: e-mail kadokawa@eng.kagoshima-u.ac.jp; fax +81 99 285 3253.

10.1021/ma800771h CCC: $40.75

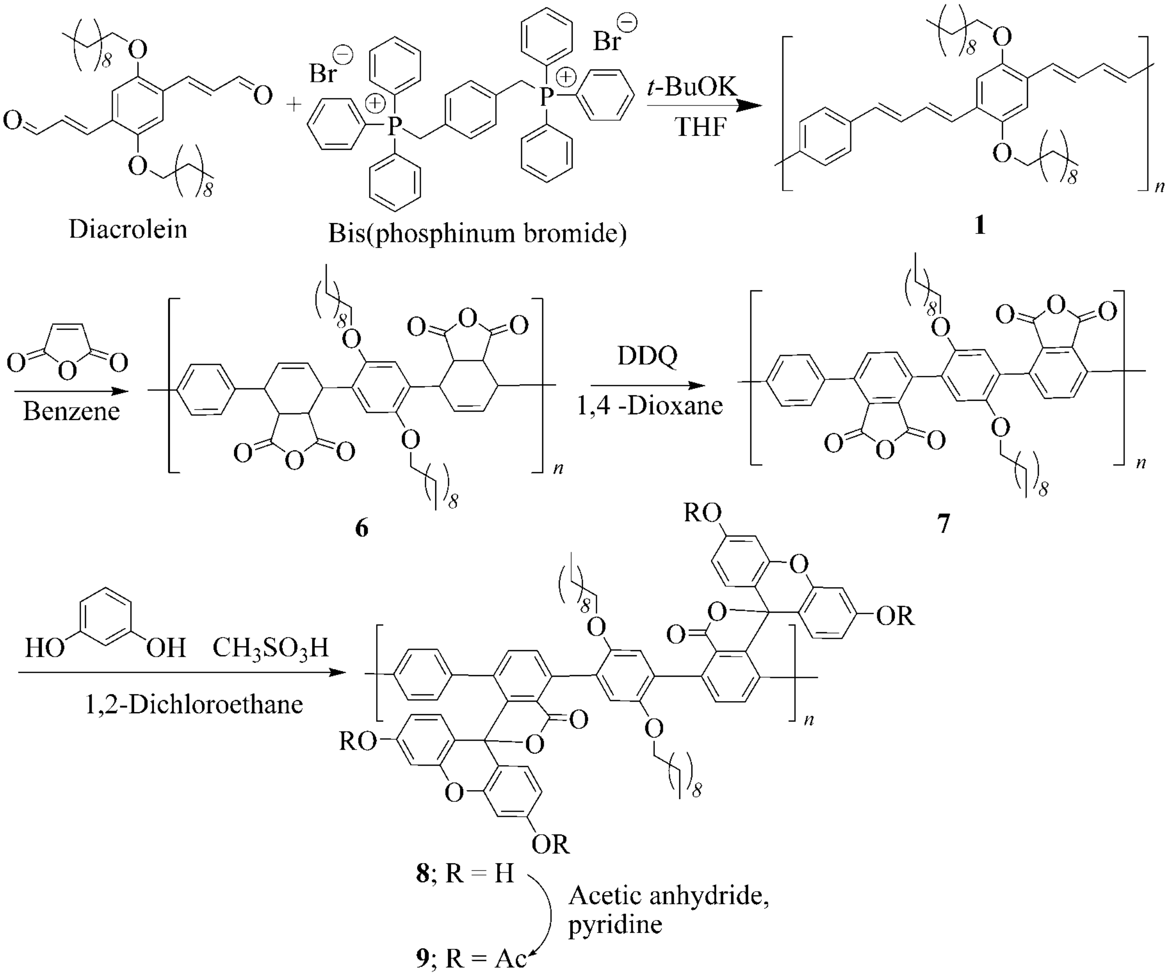
Scheme 1. Synthetic Design for Poly(*p*-phenylene)s Having Phthalic Anhydride and Fluorescein Moieties (a) and Synthesis of Model Compounds 4 and 5 (b)



GPC with chloroform using polystyrene standards) with maleic anhydride (2.08 equiv for **1**) was carried out in benzene at a refluxing temperature (Scheme 2, middle). The product was isolated as a fraction insoluble in methanol (yield; 80.6%), and its ^{1}H NMR and IR data were as follows: ^{1}H NMR ($CDCl_3$): δ 0.7−1.0 (CH_3, 3H), 1.0−1.6 ($CH_3(CH_2)-$, 28H), 1.6−2.0 (CH_2CH_2O, 4H), 3.5−4.5 (CH_2O, $-CH-CH-C{=}O$, 12H), 6.0−8.0 (CH=CH, aromatics, 10H). IR (KBr): 1782.1, 1851.5 cm^{-1} (C=O of cyclic anhydride). In the ^{1}H NMR spectrum, the appearance of new signals due to methine protons (CH−CH−C=O), which were overlapping with the signal of CH_2O, strongly supported the formation of nonconjugated main chain by Diels−Alder reaction. Furthermore, the IR spectrum exhibited the typical carbonyl absorptions due to the five-membered cyclic anhydride. The above analytical results fully suggested the structure **6** of the product. The M_n value was determined by GPC measurement with chloroform using polystyrene standards to be 6700 with $M_w/M_n = 1.33$.

Then, the aromatization of the main chain in **6** was performed using 4.02 equiv of DDQ at 60 °C in 1,4-dioxane. Figure 1a shows the ^{1}H NMR spectrum ($CDCl_3$) of the isolated product as a fraction insoluble in methanol (yield 60.4%), and the signals' assignments are as follows: δ 0.7−1.0 (CH_3), 1.0−1.6 ($CH_3(CH_2)_7-$, 28H), 1.6−2.0 (CH_2CH_2O, 4H), 3.7−4.2 (CH_2O 4H), 6.7−8.1 (aromatics, 10H). The disappearance of the signals due to CH=CH as observed at around δ 6 in the ^{1}H NMR spectrum of **6** indicates the occurrence of the perfect aromatization, which is also supported by decreasing the intensity of the signal at around δ 4 in comparison with other signal intensities after the reaction. The aromatization caused the conversion of CH−CH−C=O into C=C−C=O, resulting in the disappearance of the methine signals overlapping with the CH_2O signal at around δ 4 in the ^{1}H NMR spectrum of **6**. The carbonyl absorptions due to the five-membered cyclic anhydride (1774.4 and 1851.5 cm^{-1}) were maintained in the IR spectrum of the aromatization product, indicating that this reaction did not affect the carboxylic anhydride group. The M_n value determined by GPC was 6500 with $M_w/M_n = 1.51$. The above

Scheme 2. Synthesis of Poly(*p*-phenylene-1,3-butadienylene) (1) by the Wittig Reaction (Top), Diels−Alder Reaction and Aromatization for Synthesis of Poly(*p*-phenylene) 7 with Phthalic Anhydride Moieties (Middle), and Conversion of 7 into Poly(*p*-phenylene) 8 Having Fluorescein Moieties and Its Acetylation (Bottom)



analytical data can be taken to support that we have successfully synthesized the desired PPP (**7**) with PA moieties according to the synthetic route in Scheme 2.

The obtained **7** was converted into the fluorescein-containing PPP (**8**) by the reaction with resorcinol (8 equiv for **7**) in the presence of methanesulfonic acid in 1,2-dichloroethane at 40 °C (Scheme 2, bottom). The product was isolated as a fraction insoluble in water and purified further by reprecipitation into diethyl ether (yield 57.0%). The isolated polymer was soluble in DMSO and DMF but insoluble in chloroform. Figure 1b shows the ^{1}H NMR spectrum of the isolated product in DMSO-d_6 with the following signals' assignments: δ 0.5−0.8 (CH_3, 6H), 0.8−2.0 ($CH_3(CH_2)_8$−, 32H), 3.8−4.2 (CH_2O, 4H), 6.0−8.2 (aromatics, 22H), 8.5−10.5 (OH, 4H). The observation of the signals at the lower magnetic field (around δ 6−7) compared with the general aromatic region (δ 7−8), which are reasonably assignable to the aromatic protons of the xantene structures, indicates the formation of the fluorescein moieties in the main chain. The existence of the fluorescein moieties is also supported by the appearance of OH signals in Figure 1b, which have disappeared by addition of D_2O in the NMR sample. The conversion of the PA moieties into the fluorescein moieties in the polymer was also supported by the IR spectrum of the product, in which the carbonyl absorptions due to the carboxylic anhydride group disappeared, whereas the new carbonyl absorption ascribable to the lactone structure in the fluorescein appeared at 1728.1 cm^{-1}. All the above analytical results indicate that the reaction of **7** with resorcinol took place to give the PPP (**8**) having the fluorescein moieties. However, the exact functionality of the fluorescein moieties in the PPP main chain of the product could not be calculated by the ^{1}H NMR or IR spectrum.

For the further confirmation of the structure of **8**, therefore, the acetylation of the product was performed using acetic anhydride and pyridine (Scheme 2, bottom).[27,28] After the general work-up procedure, the acetylated product **9** was isolated as a fraction insoluble in methanol. The isolated material was soluble in chloroform, and thus, the M_n value was estimated using the same GPC equipment as that used for the above-mentioned polymers to be 7980 with M_w/M_n = 1.75. The integrated ratio of two methyl signals due to the acetyl and decyl groups, the functionality of the fluorescein moieties in the polymer was calculated to be 94.0%. This value also indicated the good functionality of the PA moieties in **7**.

The fluorescence spectrum of **8** (Figure 2a) shows an emission maximum peak at 486 nm in acetone by excitation at 440 nm, which is ascribed to the $\pi-\pi^*$ transition of the conjugated main chain, whereas no obvious emission peak was not observed in the fluorescence spectrum of **5** excited at the same wavelength in acetone (data not shown). Because it has been well-known that the fluorescein derivatives exhibit strong fluorescent signals at higher pHs, i.e., under alkaline conditions, attributed to the conjugating structure by ring opening, the fluorescence spectra of **8** and **5** were also measured after the addition of triethylamine

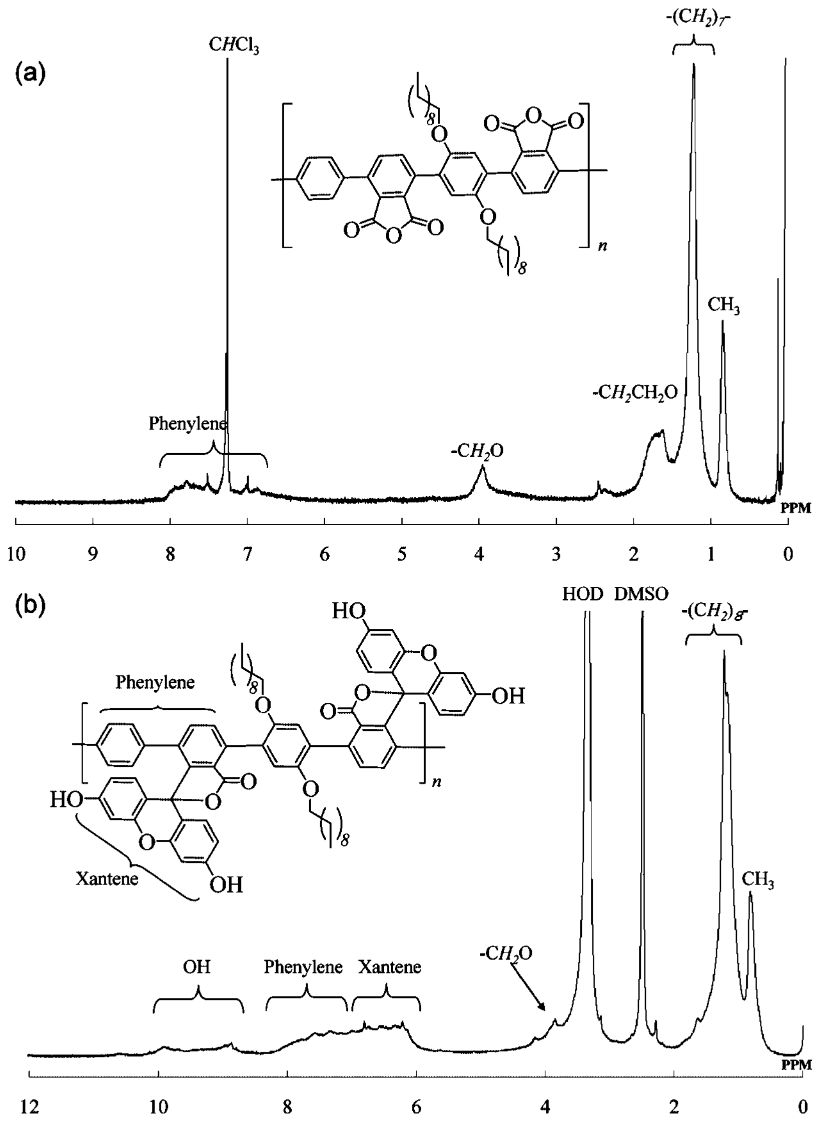


Figure 1. ^{1}H NMR spectra of **7** (CDCl$_3$) (a) and **8** (DMSO-d_6) (b).

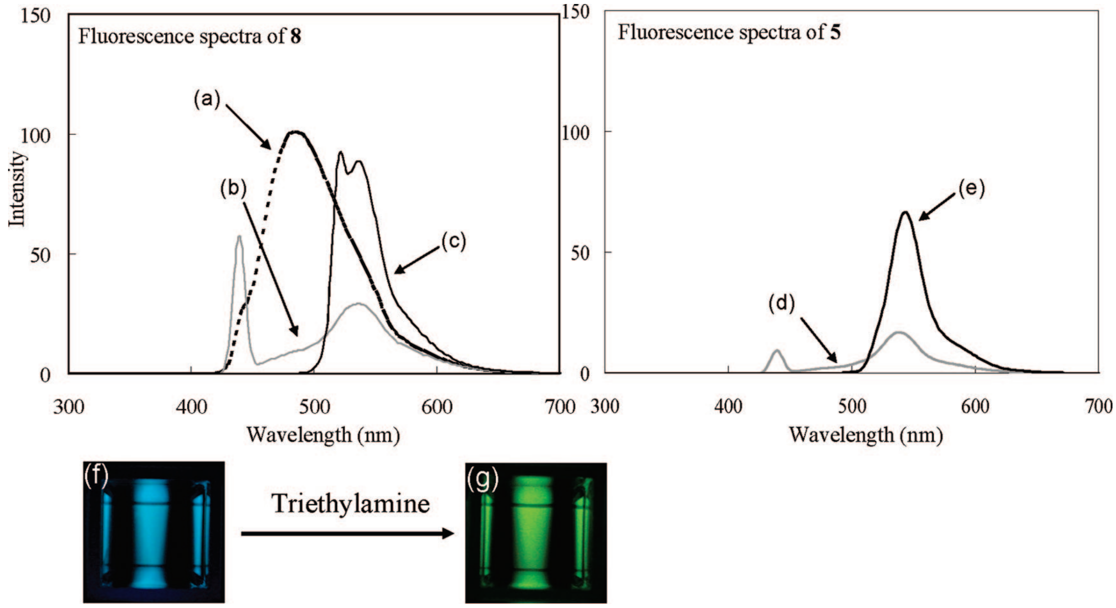


Figure 2. Fluorescence spectra of **8** (left) and **5** (right) (c = 0.2 mmol/L): (a) excited at 440 nm in acetone, (b, d) excited at 440 nm in triethylamine/acetone (0.05% v/v), (c, e) excited at 520 nm in triethylamine/acetone (0.05% v/v); fluorescence photographs of **8** excited at 440 nm in acetone (f) and excited at 520 nm in triethylamine/acetone (0.05% v/v) (g).

(0.05% v/v) to the above sample in acetone. Consequently, these spectra exhibit the fluorescence of maxima peaks at 536 and 544 nm, respectively, by excitation at 520 nm, as shown in Figure 2c,e, typically attributed to the emission of the fluorescein moiety excited at such the long wavelength. By excitation at 440 nm, both the spectra of **8** and **5** in triethylamine/acetone also exhibit maxima peaks at 536 and 538 nm (Figure 2, b and d, respectively) although the intensities of the peaks are lower than those excited at 520 nm.[29] In Figure 2b, the polymer emission due to the $\pi-\pi^*$ transition of the conjugated main chain is not obviously observed even by excitation at 440 nm unlike Figure 2a, indicating that the energy transfer from the excited polymer chain to the fluorescein moiety in **8** may occur. Because the broad emission of the PPP chain centered at 486 nm as observed in Figure 2a is overlapping with the wavelength of the typical excitation for the fluoresceins, such as 520 nm. The detailed study on the evaluation for the probable occurrence of the energy transfer is now in progress in our research group. In the fluorescence spectra of **8** and **5** excited at the long wavelength, i.e., 520 nm in acetone only, the emission peak due to the fluorescein moiety was not detected (data not shown). In conclusion of the above fluorescence measurements, the incorporation of the fluorescein moiety into the PPP main chain appeared as the fluorescence property that exhibits two different emissions in one polymer molecule, due to both the conjugated polymer chain and the fluorescein unit. Actually, Figure 2f shows the fluorescence photograph of **8** in acetone excited at 420 nm, and the color is actually changed in the fluorescence photograph (Figure 2g) excited at 520 nm after addition of triethylamine.

In conclusion, we have reported the synthesis of the PPP (**7**) having PA moieties by the polymer reaction method from the PPB (**1**). The first step was Diels–Alder reaction of **1** with maleic anhydride for the introduction of the carboxylic anhydrides to give **6**. Then, the aromatization of **6** was performed using DDQ to produce the desired polymer **7**. Furthermore, **7** was converted into the fluorescein-containing PPP (**8**) by the reaction with resorcinol in the presence of methanesulfonic acid. The fluorescence spectrum of **8** in acetone showed the emission maximum at 486 nm excited at 420 nm and, after addition of triethylamine in the sample solution, **8** exhibited the fluorescence spectrum with the emission maximum at 536 nm by excitation at 520 nm.

Supporting Information Available: Experimental procedures for synthesis of **1**–**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Yamamoto, T.; Hayashida, N. *React. Funct. Polym.* **1998**, *37*, 1.
(2) Cianga, I.; Hepuzer, Y.; Yagci, Y. *Macromol. Symp.* **2002**, *183*, 145.
(3) Bissell, R. A.; de Silva, A. P.; Gunarathe, H. Q. N.; Lynch, P. L. M.; McCoy, C. P.; Maguire, G. E. M.; Sandanayake, K. R. A. S. In *Fluorescent Chemosensors for Ion and Molecule Recognition*; Czarnik, A. W., Ed.; ACS Symposium Series 538; American Chemical Society: Washington, DC, 1993; Chapter 9.
(4) Sun, W.; Gee, K. R.; Klaubert, D. H.; Haugland, R. P. *J. Org. Chem.* **1997**, *62*, 6469.
(5) Drexhage, K. H. *Laser Focus* **1973**, *9*, 35.
(6) Haugland, R. P. *Handobook of Fluorescent Probes and Research Products*, 9th ed.; Probes, Inc.: Eugene, 2002.
(7) Silcoff, E. R.; Sheradsky, T. *New J. Chem.* **1999**, *23*, 1187.
(8) Scala-Valéro, C.; Doizi, D.; Guillanmet, G. *Tetrahedron Lett.* **1999**, *40*, 4803.
(9) Yurteri, S.; Cianga, I.; Degirmenci, M.; Yagci, Y. *Polym. Int.* **2004**, *53*, 1219.
(10) Yamashita, Y.; Kaneko, Y.; Kadokawa, J. *Polym. Bull.* **2007**, *58*, 635.
(11) Cianga, I.; Hepuzer, Y.; Yagci, Y. *Polymer* **2002**, *43*, 2141.
(12) Yamashita, Y.; Kaneko, Y.; Kadokawa, J. *Eur. Polym. J.* **2007**, *43*, 3795.
(13) Wang, B.; Wasielewski, M. R. *J. Am. Chem. Soc.* **1997**, *119*, 12.
(14) Monte, A. P.; Marona-Lewicka, D.; Parker, M. A.; Wainscott, D. B.; Nelson, D. L.; Nichols, D. E. *J. Med. Chem.* **1996**, *39*, 2953.
(15) Kuhnert, N.; Rossignolo, G. M.; Lopez-Periago, A. *Org. Biomol. Chem.* **2003**, *1*, 1157.
(16) Lüttringhaus, A.; Schill, G. *Chem. Ber.* **1960**, *93*, 3048.
(17) Sonoda, Y.; Kaeriyama, K. *Polymer* **1992**, *33*, 2437.
(18) Jiang, B.; Yang, S.-W.; Jones, W. E., Jr *Chem. Mater.* **1997**, *9*, 2031.
(19) Takagi, K.; Nishikawa, N.; Kunisada, H.; Yuki, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3927.
(20) Liao, L.; Ding, L.; Karasz, F. E.; Pang, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 303.
(21) The PPB derivative was also prepared by the other method besides the Wittig reaction: Chujo, Y.; Sasaki, Y.; Kinomura, N.; Matsumi, N. *Polymer* **2000**, *41*, 5047.
(22) Landelle, H.; Godard, A.-M.; Laduee, D.; Chenu, E.; Robba, M. *Chem. Pharm. Bull.* **1991**, *39*, 3057.
(23) Abu-Yousef, I. A.; Hay, A. S. *Synth. Commun.* **1999**, *29*, 291.
(24) Olsen, R. K.; Shao, R. *J. Org. Chem.* **1996**, *61*, 5852.
(25) Vessels, J. T.; Janicki, S. Z.; Petillo, P. A. *Org. Lett.* **2000**, *2*, 73.
(26) Ueno, T.; Urano, Y.; Setsukinai, K.; Takakusa, H.; Kojima, H.; Kikuchi, K.; Ohkubo, K.; Fukuzumi, S.; Nagano, T. *J. Am. Chem. Soc.* **2004**, *126*, 14079.
(27) Sun, W.-C.; Gee, K. R.; Klaubert, D. H.; Haugland, R. P. *J. Org. Chem.* **1997**, *62*, 6469.
(28) Tanaka, K.; Miura, T.; Umezawa, N.; Urano, Y.; Kikuchi, K.; Higuchi, T.; Nagano, T. *J. Am. Chem. Soc.* **2001**, *123*, 2530.
(29) The fluorescence spectra of a standard fluorescein in triethylamine/acetone (0.05% v/v) also exhibited the emission peaks at 540 nm by excitation at 520 nm and at 534 nm by excitation at 440 m. The intensity of the latter peak was much lower than that of the former peak.

MA800771H