Polymer Bulletin 44, 79–84 (2000)

Polymer Bulletin

Fluorescent chemosensor for metal ions using a polymer having pendant pyridylbenzoxazole groups

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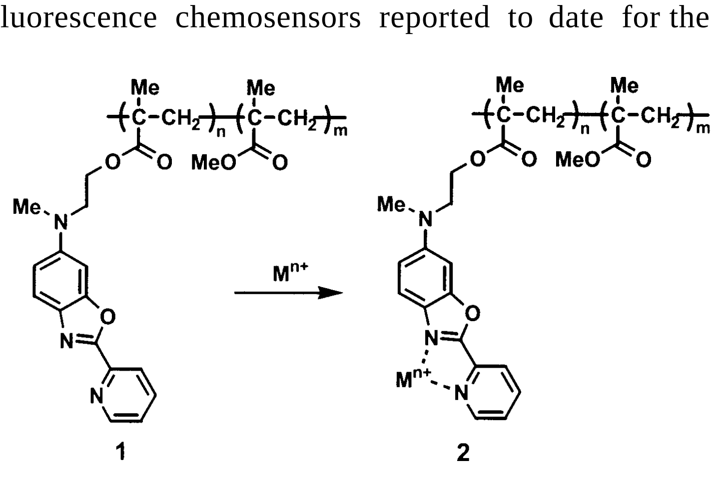
Received: 2 November 1999/Revised version: 19 December 1999/Accepted: 22 December 1999

Summary

A polymer having fluorescent pyridylbenzoxazole groups has been prepared for the purpose of detecting of metal ions. Metal ions such as Co^{2+} , Ni^{2+}, Cu^{2+} and Fe^{2+} were found to coordinate with the bipyridyl-like fluorescent benzoxazole chromophores. Among the metal ions investigated, the Fe^{2+} ion was shown to be the most effective in terms of its fluorescence quenching ability. The addition of a metal scavenger 2,2'-dipyridyl to the metal ion-quenched polymer solution resulted in the recovery of the fluorescence.

Introduction

In a conjugated aromatic system, the nature of fluorescence is often greatly affected by substituents. A strong fluorescence, in general, is observed when an aromatic compound has structurally extended π-conjugation and electron donor substituents such as hydroxy or amino groups at both ends of the conjugation. The fluorescence of the molecule, however, drastically decreases if one of the electron-donor substituents is replaced by a strong electron-withdrawing substituent such as nitro group. Complex formation of a fluorescent chromophore with metal ions also can affect the nature of the fluorescence. When the changes of fluorescence caused by chelation of metal ions are significant and detectable, the chromophore can be used as a fluorescent chemosensor. The majority of fluorescence chemosensors reported to date for the detection of metal ions are either crown ether or their analogs.[1-3] In order to extend the scope of the metal ion chemosensor from crown ether-based systems to other sensory units,[4-5] we have designed a polymer which has fluorescent pyridybenzoxazole moieties as pendant groups. The design strategy for the



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polymer chemosensor we now present in this report is as follows. The polymer **1** has a 2,2'-dipyridyl-like benzoxazole chromophore. Since 2,2'-dipyridyl is a good metal scavenger, pyridybenzoxazole group of the polymer **1** also should have the ability to coordinate metal ions. Accordingly, it is expected that the fluorescence of the chromophore would be altered and detected by an emission spectroscopy.

Results and Discussion

The synthetic sequences employed in the preparation of monomer **8** are shown in Figure 1. Benzoxazole derivatives are, in general, prepared by a prior formation of an *o*-hydroxy amide through condensation of an *o*-aminophenol with an acid chloride at low temperature, followed by thermal cycloaddition at high temperature.[6] In the cyclization step which requires high temperature some unwanted side reactions often occur. In order to avoid this limitation, we have developed mild reaction conditions for the formation of the benzoxazole ring. Thus, protection of the hydroxyl group of 5-fluoro-2-nitrophenol (**3**) followed by aromatic substitution with (2-methylamino)ethanol provided the alcohol **5** in good yield. Conversion of **5** to pyridybenzoxazole **7** was achieved in three steps. Removal of the protecting group and reduction of nitro group by hydrogenation followed by further treatment with 4-pyridinecarboxaldehyde gave the imine intermediate **6**. The intermediate **6**, then, was subjected to oxidative cyclization with lead acetate at room temperature to provide a benzoxazole chromophore **7** in high yield (80% from **5**). No purifications were necessary for the deprotection, imine formation, and cyclization steps. Conversion of the pyridylbenzoxazole **7** to the desired monomer **8** was achieved by treatment with methacryloyl chloride.

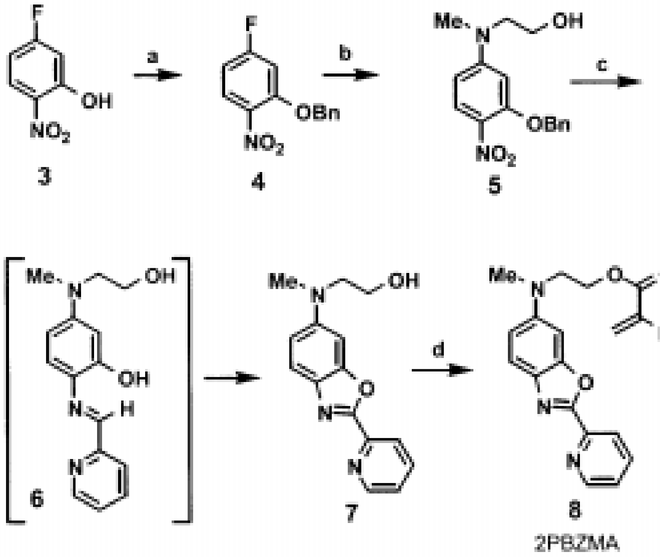


Figure 1. Synthesis of pyridylbenzoxazole monomer **8**. a) benzyl bromide, K_2CO_3, DMF, 100 ℃, 3 h, 83%. b) 2-(methyamino)ethanol, K_2CO_3, DMF, 100 ℃, 3 h, 85%. c) (i) H_2, 10% Pd/C, THF, 25 ℃, 12 h; (ii) 2-pyridine carboxaldehyde, THF, 25 °C, 3 h; (iii) $Pb(OAc)_4$, THF, 25 ℃, 3 h, 69% from **5**. d) methacryloyl chloride, TEA, THF, 25 ℃, 12 h, 74%.

Copolymerization of the monomer **8** with methyl methacrylate (MMA) was carried out with 1:1 molar feed ratio in 1-methyl-2-pyrrolidinone (NMP) using 2,2'-azobis (isobutyronitrile) (AIBN) as a radical initiator. The copolymer **1**, after precipitation into methanol was obtained as yellow powder in a 61% yield. The polymer **1** has an average molecular weight (Mw) of 24,000 with a polydispersity of 1.50. The composition of the

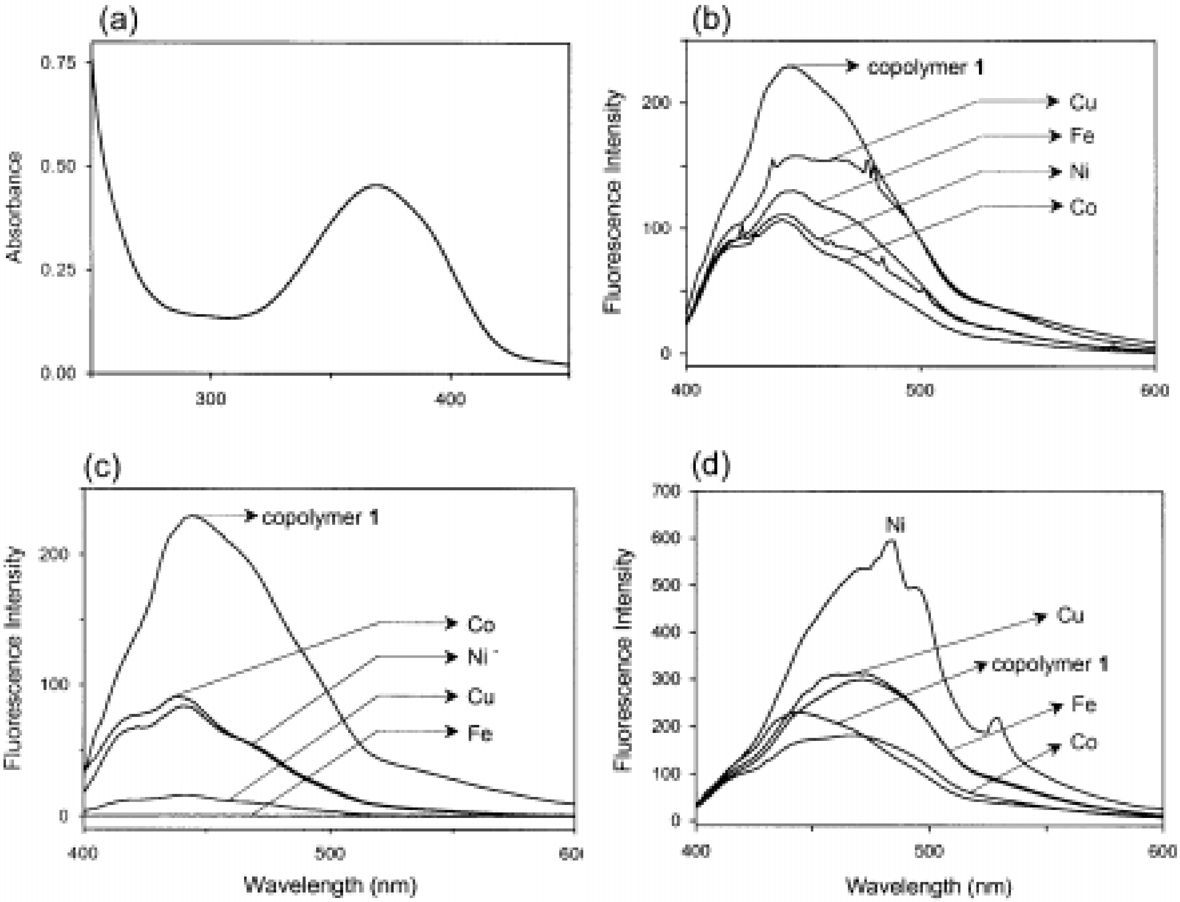


Figure 2. A UV spectrum of 1 x 10^{-7} M of the polymer **1** in $CHCl_3$ (a); fluorescence emission spectra of 1 x 10^{-7} M of the polymer **1** in $CHCl_3$ in the presence of metal ions (final concentration of the metal ions: 1 x 10^{-5} M (b) and 1 x 10^{-1} M (c)); after adding 2,2'-dipyridyl (final concentration: 1 x 10^{-3} M) to the solution from figure (b) containing the polymer-metal ion complex (d).

obtained copolymer **1** was confirmed to have a 4:6 ratio between pyridylbenzoxazole monomer and MMA unit by NMR and UV spectroscopic analysis.

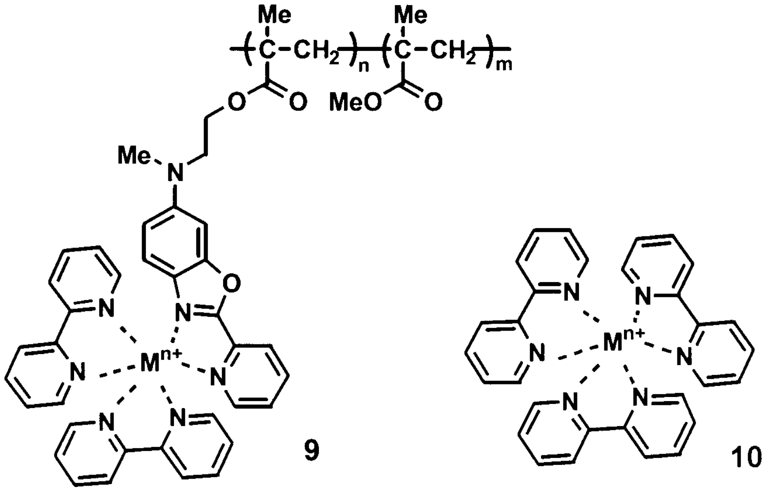
The polymer prepared as described above has a maximum absorption wavelength at 369 nm in chloroform solution due to the pyridylbenzoxazole groups (Figure 2 (a)). In order to investigate the possibility and degree of fluorescence quenching by metal ions, fluorescence intensity of a solution containing the polymer (1 x 10^{-7} M based on the benzoxazole chromophore) in chloroform was monitored by adding various metal ions (Figure 2 (b) and (c)). As shown in Figure 2 (a) and (b), the fluorescence intensity of the polymer solution decreased in the presence of metal ions such as Co^{2+}, Ni^{2+}, Cu^{2+} and Fe^{2+}. The degree of fluorescence quenching, however, was dependent on the metal ions added. At a lower concentration (1 x 10^{-5} M) of metal ions, the fluorescence quenching effect by Ni^{2+} and Co^{2+} ions was larger than that achieved by Cu^{2+} and Fe^{2+} ions (Figure 2 (b)). At a higher concentration (1 x 10^{-1} M) of metal ions, the effect of fluorescence quenching by metal ions was reversed (Figure 2 (c)). Thus, approximately 90% of the fluorescence intensity decreased in the presence of the Cu^{2+} ion at this concentration. Complete disappearance of fluorescence of the solution was monitored when Fe^{2+} ion was present.

Table 1. Equilibrium constants of the polymer **1** with various metal ions measured at 25 ℃ in chloroform.

metal ion	K_{eq} (M^{-1})
Co^{2+}	1.87
Ni^{2+}	2.14
Cu^{2+}	6.78 x 10^2
Fe^{2+}	1.95 x 10^3

Titration experiments with individual metal ions allowed us to calculate the equilibrium constants (K_{eq}) and are presented in Table 1. When an excess amount of a metal scavenger 2,2'-dipyridyl was added to the polymer solution containing metal ion (1 x 10^{-5} M), an increase of fluorescence intensity was observed (Figure 2 (d)). Interestingly, an addition of dipyridyl to metal ion-quenched polymer solution resulted in not only an increase of the fluorescence but also a bathochromic shift of maximum emission wavelength. It is, presumably, because 2,2'-dipyridyl forms a complex with the already existing metal-benzoxazole chromophore as in **9**. Under similar conditions, dipyridyl-metal ion complex without the benzoxazole chromophore as in **10** showed no fluorescence at all.

In summary, a polymer having pendant pyridylbenzoxazole groups has been prepared. The bipyridyl-like fluorescent benzoxazole chromophore of the polymer was shown to coordinate with various metal ions. The fluorescence intensity of the polymer solution was altered in the presence of metal ions. Among the metal ions investigated, the Fe^{2+} was shown to be the most effective in terms of its fluorescence quenching ability. Addition of a metal scavenger 2,2'-dipyridyl to the metal ion-quenched polymer solution resulted in recovery of the fluorescence. The strategy described above for a fluorescent chemosensor should be useful in the design of new polymer chemosensors.



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Experimental

General

^{1}H NMR spectra were recorded on a Varian Gemini 2000 (200MHz) spectrometer using $CDCl_3$ as a solvent. (Chemical shifts are reported in ppm relative to tetramethylsilane, which was used as an internal standard.) UV spectra were recorded on a Shimadzu UV-

240 spectrophotometer. Fluorescence intensity of all samples was measured with ISS Inc. K2 fluorometer. Melting points were recorded by using a Griffin Mel-Temp capillary melting point apparatus. Column chromatography was performed with Merck-EM type 60 (230-400 mesh) adsorbents.

Materials

5-Fluoro-2-nitrophenol, 2-(methylamino)ethanol, 10 % palladium on carbon, 2-pyridinecarboxaldehyde, benzyl bromide, methyl methacrylate (MMA) and methacryloyl chloride were purchased from Aldrich. MMA was distilled before use. 2,2'-Azobisisobutyronitrile (AIBN) as a radical initiator was recrystallized from ethanol before use. Other reagents were used as received.

4: To a solution of 94.3 g (0.60 mol) of 5-fluoro-2-nitrophenol (**3**) in 200 mℓ of DMF was added 82.9 g (0.60 mol) of potassium carbonate and 136.8 g (0.8 mol) of benzyl bromide. The resulting mixture was stirred at 100 °C for 3 h, filtered and the filtrate was diluted with diethyl ether. The organic layer was washed with water and dried with anhydrous magnesium sulfate. Concentration followed by vacuum distillation (142-146 °C/0.1 torr) of the residue gave 123.1 g (83%) of yellow solid product **4**. m.p: 55-56 °C; ^{1}H-NMR ($CDCl_3$) δ = 5.18 (s, 2H), 6.66-6.87 (m, 2H), 7.32-7.49 (m, 5H), and 7.94 (d, 1H). Anal. Cald. for $C_{13}H_{10}N_1O_3F_1$(247.23): C, 63.16 %; H, 4.08 %; N, 5.67 %; O, 19.41 %; F, 7.68 %. Found: C, 63.50 %; H, 4.09 %; N, 5.21 %.

5: To a solution of 123.1 g (0.5 mol) of **4** and 56.3 g (0.75 mol) of 2-(methylamino)ethanol in 200 mℓ of DMF was added 51.83 g (0.38 mol) of potassium carbonate. The resulting mixture was heated at 100 °C for 3 h, poured into 1 L of water. The yellow precipitate was collected, dried and dissolved in THF. Precipitation into hexane provided 128.4 g (85 %) of the product **5**. m.p: 104-106 °C; ^{1}H NMR ($CDCl_3$) δ = 2.41 (s, 1H), 3.03 (s, 3H), 3.50 (t, 2H), 3.77 (t, 2H), 5.13 (s, 2H), 6.10-6.22 (m, 2H), 7.27-7.50 (m, 5H), and 7.88 (d, 1H); Anal. Cald. for $C_{16}H_{18}N_2O_4$ (302.33): C, 63.57 %; H, 6.00 %; N, 9.27 %. Found: C, 63.50 %; H, 6.09 %; N, 9.21 %.

7: A mixture of 4.05 g (13.4 mmol) of **5** and 0.8 g of 10 % Pd/C in 40 mℓ of THF stirred under hydrogen at 25 °C for 12 h. The catalyst was removed by filtering and to the filtrate was added 1.6 g (13.9 mmol) of 2-pyridinecarboxaldehyde. The resulting solution was stirred at 25 °C for 3 h. Lead acetate (8.8 g, 19.8 mmol) was slowly added to the solution and the mixture was vigorously stirred at 25 °C for 3 h. Removal of lead diacetate followed by flash column chromatography (silica gel, THF) gave 2.48g (69% from **5**) of the product **7** as yellow solid. m.p: 107-110 °C; ^{1}H NMR ($CDCl_3$) δ = 2.98 (s, 3H), 3.52 (t, 2H), 3.85 (t, 2H), 6.80 (m, 1H), 6.89 (m, 1H), 7.37 (m, 1H), 7.53 (d, 2H), 7.80 (m, 1H), 8.21 (d, 1H), 8.72 (d, 1H); ^{13}C NMR ($CDCl_3$) δ = 39.4, 55.8, 59.8, 94.0, 111.6, 120.3, 122.6, 124.7, 132.8, 137.0, 146.3, 149.4, 150.1, 152.8, and 158.4.

8: The benzoxazole intermediate **7** (2.40 g, 8.92 mmol) was dissolved in 100 mℓ of methylene chloride and to the solution was added 1.87 g (17.8 mmol) of methacryloyl chloride and TEA (3.0 mℓ, 21.55 mmol). The mixture was stirred at 25 °C for 12 h, poured into water and extracted with methylene chloride. The organic layer was dried and subjected to silica gel column chromatography (EtOAC/hexane=1/3) to yield 2.32 g (77%) of the monomer **8**. m.p: 58-60 °C; λmax (CHCl$_3$) = 370 mn; ^{1}H NMR (CDCl$_3$): δ = 1.88 (s, 3H), 3.05 (s, 3H), 3.71 (t, J = 5.9 Hz, 2H), 4.35 (t, J = 5.9 Hz 2H), 5.51 (s, 1H), 6.03 (s, 1H), 6.85 (m, 1H), 6.95 (m, 1H), 7.36 (m, 1H), 7.51 (m, 1H), 7.83 (m, 1H), 8.24 (m, 1H), and 8.76 (m, 1H); ^{13}C NMR (CDCl$_3$) δ = 17.9, 38.9, 51.3, 61.4, 93.4, 110.8, 120.2, 122.4, 124.5, 125.8, 132.5, 135.7, 136.7, 146.1, 148.4, 149.8, 152.8, 159.1, and 167.1.

Copolymer 1 P(2PBZMA/MMA): A solution containing monomer **8** (0.5 g, 1.48 mmol), MMA (0.15 g, 1.49 mmol), AIBN (9.7 mg) and 2.5 mℓ of NMP in an ampoule was subjected to repeated freeze-thaw cycles before the ampoule was sealed under vacuum. The sealed ampoule was heated at 65 °C for 40 h. After polymerization, the product was precipitated into methanol and dried to give 0.39 g (61 %) of **1** as yellow powder.

Polymer-Metal Complex Formation. CuCl$_2$, FeCl$_2$, NiCl$_2$ and CoCl$_2$ are used as metal ions. Polymer-metal complex solutions used for optical measurements were prepared by mixing a polymer solution (2.7 mℓ) in CHCl$_3$ and a metal ion solution (0.3 mℓ) in CH$_3$OH at room temperature. Final concentration of the polymer was 1 x 10^{-7} M and the metal ion was either 1 x 10^{-5} M or 1 x 10^{-1} M.

Acknowledgment:

Support for this effort by Korea Ministry of Science and Technology through KIST program (2V00363) is greatly appreciated.

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