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Fluorescence detection of conversion of phenolic Schiff bases to benzoxazoles

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Abstract

A fluorescence spectroscopic system for detecting conversion of phenolic Schiff bases to benzoxazoles has been developed. It demonstrated that the conversion of benzoxazoles from phenolic Schiff bases in presence of NaOH with UV light irradiation can be monitored by fluorescence changes of benzoxazoles in solution. It also revealed that solvents have great effects on both the velocity of conversion reaction and conversion yield. This assay system may be used to rapid screen and optimize reaction conditions on small scale.

Keywords: Fluorescence; Benzoxazole; Phenolic Schiff base; Conversion; Detection

1. Introduction

Spectroscopic monitoring of the progress of chemical reactions is an attractive area in chemistry due to rapid screening and efficient optimizing reaction conditions on a small scale [1–4]. Although many fluorogenic or chromogenic substrates exist to monitor cleavage reaction and formation reaction of carbon–carbon bond [5–10], the development of spectroscopic methods to monitor the progress of carbon–oxygen bond formation has lagged behind [11,12].

Benzoxazole derivatives are kind of important subunits in natural products since they exhibit biological activities [13–15], including anti-tumor, anti-microbial and anti-viral properties. There are many reports [16–19] on synthesis of benzoxazoles including the coupling of 2-aminophenols and carboxylic acid derivatives, and the oxidative cyclization of phenolic Schiff bases derived from the condensation of 2-aminophenols and aldehydes. In our previous work [20], we found that benzoxazole derivatives can be prepared by irradiating solution of phenolic Schiff bases, which derived from 2-aminophenols and aldehydes, in presence of NaOH with UV light and fluorescence appeared with conversion of phenolic Schiff base to benzoxazole. We suppose it is possible that the intramolecular carbon–oxygen bond formation of benzoxazoles can be monitored by fluorescence changes, and it may be useful to develop a system to detect the conversion of benzoxazoles in different conditions that could be used to rapid screening and optimize reaction conditions. The model compound employed to investigation was shown in Scheme 1.

2. Experimental

All phenolic Schiff bases and sample benzoxazoles examined in this paper were prepared according to reference [20]. Solvents were purified according to standard procedure before used. Absorption and fluorescence spectra were measured with an absorption spectrophotometer (Hitachi U-3010) and a fluorescence spectrophotometer (Hitachi F-2500), respectively.

3. Results and discussion

The absorption changes of **1a** in dichloromethane (DCM) with addition of NaOH were presented in Fig. 1. Addition of NaOH (0.05 M in methanol) to solution of **1a** in DCM produced a decrease of the band at 360 nm ($\varepsilon = 1.48 \times 10^4$) with a concomitant increase of two new ones at 410 nm ($\varepsilon = 8.1 \times 10^3$) and 270 nm ($\varepsilon = 1.72 \times 10^4$), respectively, which correspond to **1c** resulted from deprotonation of phenol. The new bands were

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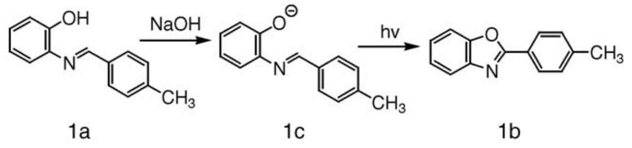


Scheme 1. Conversion reaction of model compound.

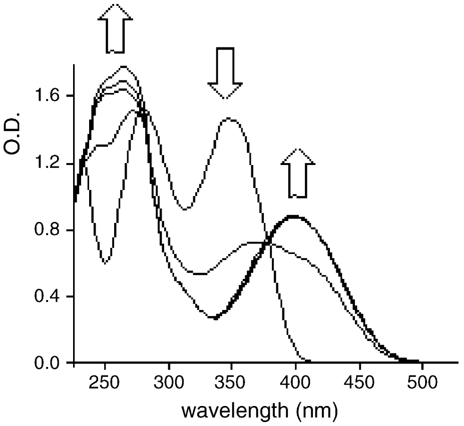


Fig. 1. Absorption changes of **1a** (1×10^{-4} M, DCM) with addiation of NaOH (0.05 M in MeOH, volume: 5, 10, 15, 20 μl).

not increased until a stoichiometric amount of NaOH (1 equiv) was added to the solution.

By irradiation with 254 nm light, the absorption bands at 410 and 270 nm of **1c** decreased along with the increase of new absorption band at 300 nm ($\varepsilon = 1.49 \times 10^4$), which attributed to the benzoxazole **1b,** as shown in Fig. 2. Comparing the longest band of **1b** with that of **1a** and **1c** found that the longest band of **1b** was blue-shifted as much as 60 nm (360–300 nm) and 110 nm (410–300 nm), respectively.

A fluorescence spectrophotometer was employed to detect the conversion reaction of **1b** from **1c**. It was found that no fluorescence emission was detected for both **1a** and **1c** with excitation wavelength of 360 and 410 nm, respectively, in DCM. The fluorescence emission was, however detected when the solution of **1c** was irradiated with UV light and using an excitation wavelength of 310 nm. Moreover, the fluorescence intensity was increased with increase of irradiation time of the solution **1c** (Fig. 3), and the fluorescence intensity maximum (2460) was obtained with 7 min irradiation of the solution **1c**. It indicated that **1b**, resulted from **1a** in presence of NaOH with UV light irradiation, exhibited fluorescence emission, and the fluorescence intensity was increased with increase the concentration of **1b** in solution till the conversion reaction was performed completely.

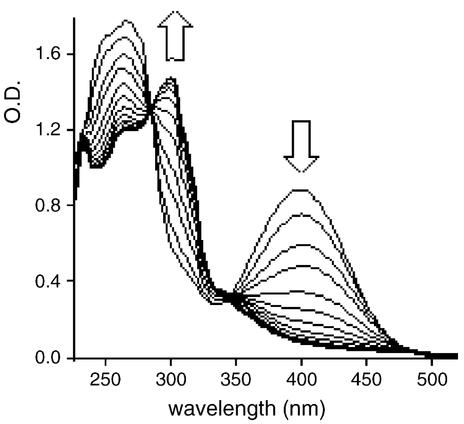


Fig. 2. Absorption changes of **1c** (1×10^{-4} M, DCM) with UV light irradiation (periods: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300 s).

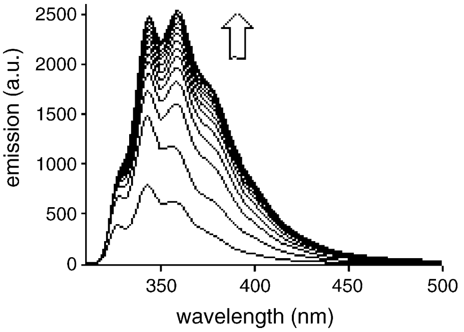


Fig. 3. Fluorescence intensity changes of **1b** ($\lambda_{ex} = 300$ nm) resulted from **1c** (1×10^{-4} M, DCM) with UV light irradiation (periods: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300 s).

Next, we turn our attention to examine the application of this system to measure the conversion yield of benzoxazole. It is well known that fluorescence intensity has close relation with concentration of compound and the fluorescence intensity increases with increase of concentration of compound. It is possible, therefore, that the conversion yield of benzoxazole can be calculated by comparing the fluorescence intensity maximum of benzoxazole with that of sample benzoxazole in the same condition. In order to test the possibility and reliability of this method, sample **1b**, used as standard, was prepared according to the paper [20] and isolated in yield 74%. It was found that the fluorescence intensity maximum of sample **1b** (1×10^{-4} M, DCM) is 3500. Comparing the fluorescence intensity maximum of **1b** (2470) with that of sample **1b** (3500) in same condition found that the conversion yield of benzoxazole resulted from phenolic Schiff base was about 71% (2470/3500 = 71%). This result was nearly agreement with the conversion yield of sample **1b** (74%).

Because the reaction medium has an effect on both the velocity of the conversion reaction and the conversion yield, the conversion of **1c** to **1b** under a variety of solvents including DCM, acetonitrile, toluene, ethanol and cyclohexane was investigated. It was found that the conversion of **1c** to **1b** was performed in all solvents above although the reaction time (Fig. 4) and conversion yield (Fig. 5) were different. The conversion of **1c** to **1b** was performed very well in acetonitrile and in DCM, it took 14 and 7 min, respectively, to finish the conversion reaction, and the conversion yields were 76% and 71%, respectively. When the conversion of **1c** to **1b** was carried out in cyclohexane solution, it took 22 min to finish the reaction and the yield was 59%. Comparison of the results above found that the conversion of **1c** to **1b** took much time and was lower yield in cyclohexane than in acetonitrile and in DCM.

It was worth noting that when toluene was used as solvent. It is found that the conversion reaction took 8 min for **1b** to

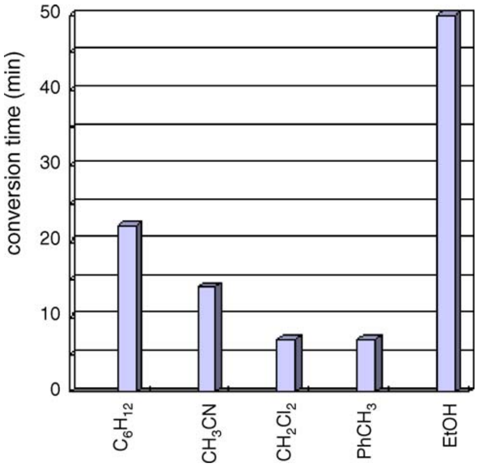


Fig. 4. The conversion time of **1b** from **1c** in different solvents.

achieve the fluorescence intensity maximum but the conversion yield was less than 10%, as shown in Figs. 4 and 5. Further investigations showed that the fluorescence intensity of **1b** increased with increasing irradiation time of **1c** before 8 min, but decreased with longer irradiation. It indicated that **1b** in toluene probably occurred degradation with longer irradiation although the mechanism is not clear.

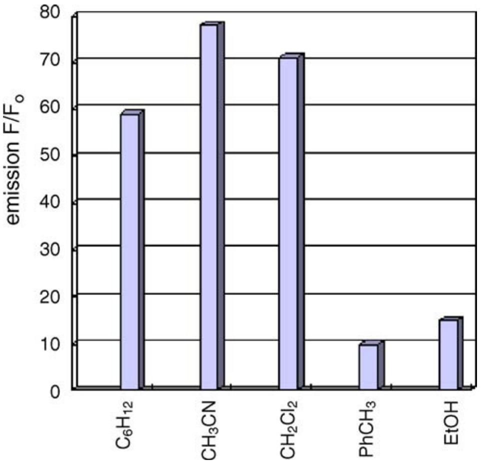


Fig. 5. The ratio of fluorescence intensity of **1b** to that of sample **1b** (F/F_0) in different solvents.

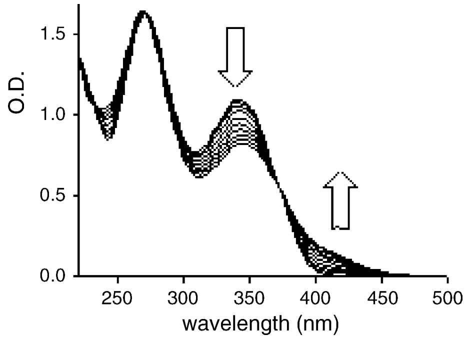


Fig. 6. Absorption changes of **1a** (1×10^{-4} M, EtOH) with addiation of NaOH (0.05 M in MeOH, volume: 0, 5, 10, 15, 25, 35, 45, 55, 65, 75 μl).

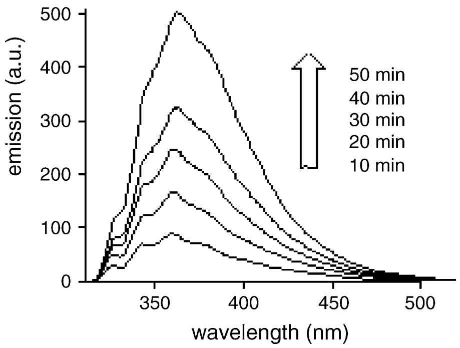
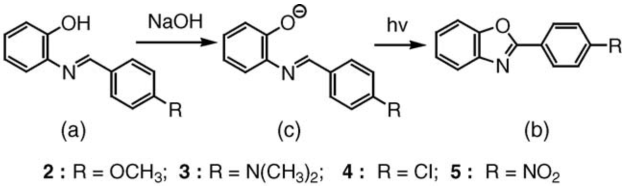


Fig. 7. Fluorescence intensity changes of **1b** (1×10^{-4} M, DCM) in absence of NaOH with UV light irradiation (periods: 10, 20, 30, 40, 50 min).

It was also worth noting that when the conversion reaction of **1c** to **1b** was performed in ethanol (EtOH), different result was obtained. It showed the conversion reaction of **1c** to **1b** was very slowly (more than 50 min) and conversion yield was less than 15% after irradiating 50 min. Further investigations showed that free phenolic anion **1c**, formed easily in other solvents above, probably could not be formed in EtOH solution with addition of NaOH solution because of the hydrogen bond between phenol and EtOH. The absorption changes of **1a** in EtOH with addition of NaOH solution was presented in Fig. 6. It was found that the absorption band at 360 nm was decreased very slowly with addition of NaOH solution, and no distinguished new band, like in Fig. 1, appeared. As shown in Figs. 4 and 5, the conversion reaction of **1a** to **1b** took much longer time to complete and conversion yield was much lower in EtOH than in DCM. The longer conversion time and lower conversion yield of **1a** in EtOH suggested that the free phenolic anion maybe necessary intermediate for photoconversion of benzoxazole from phenolic Schiff base. In order to confirm this suggestion, the conversion reaction of **1a** in DCM without adding NaOH solution was carried out. Upon irradiation with UV light, it was found that **1a** converted into **1b** very slowly in DCM in absence of NaOH, and about 14% (500/3500 = 14%) conversion yield was obtained after 50mim irradiation (Fig. 7). This result was similar to that in EtOH.

To test the application of this system to conversion reaction of other benzoxazoles with different substitute groups, phenolic Schiff bases with electron-donating and electron-acceptor substitutes (**2a**–**5a**) were employed to study (Scheme 2). The result of benzoxazoles **2b**–**5b** obtained from **2c** to **5c** demonstrated that phenolic Schiff bases with both electron-donating and electron-acceptor groups can also be converted to benzoxazoles in solution in presence of NaOH with UV light irradiation



2 : R = OCH_3; **3 :** R = $N(CH_3)_2$; **4 :** R = Cl; **5 :** R = NO_2

Scheme 2. Benzoxazoles derived from phenolic Schiff bases.

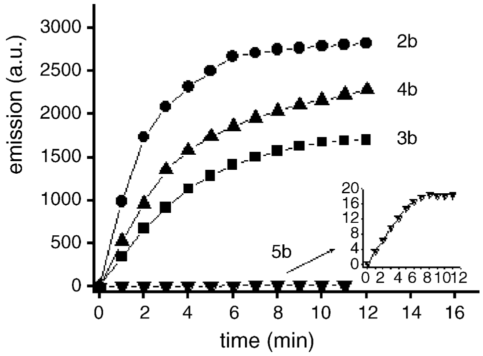


Fig. 8. Plot of fluorescence intensity changes of benzoxazoles **2b**–**5b** (1×10^{-4} M, DCM) against irradiation time.

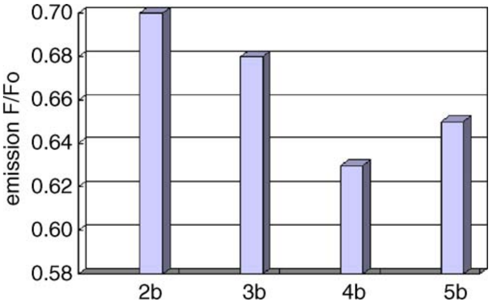


Fig. 9. The ratio of fluorescence intensity of **2b**–**5b** to that of samples **2b**–**5b** (F/F_0) in DCM.

although the fluorescence intensity of benzoxazoles were different with different substitute group. Comparing the velocities of the conversion reaction of benzoxazoles possessing electron-donating and electron-acceptor (Fig. 8) found that no significant differences in the velocity of the conversion reactions were observed among them. Over 95% of conversion reactions have been finished within 10 min when **2a**–**5a** were in DCM with UV light irradiation, and 63–70% conversion yields were obtained by comparison the maximum fluorescence intensity of **2b**–**5b** with those of samples **2b**–**5b** (Fig. 9) in same condition. That is agreement with the results of reported [20]. When other solvents above were employed, the results of conversions of **2b**–**5b** from **2a**–**5a** were similar with that of the case of **1b**.

4. Conclusions

In summary, we have demonstrated fluorescence monitoring of the conversion of benzoxazoles from phenolic Schiff bases in presence of NaOH with UV light irradiation. Solvents make great effects on both the velocity of conversion reaction and conversion yield. This assay system may be used to screen and optimize reaction conditions on small scale.

Acknowledgement

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