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Chiral discrimination of quinine and quinidine based on notable room temperature phosphorescence lifetime differences with γ-cyclodextrin as chiral selector

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Abstract

Upon addition of small amount of bromocyclohexane (BrCH), quinine (QN) and quinidine (QD) display strong room temperature phosphorescence (RTP) in γ-cyclodextrin (γ-CD) solution without deoxygenation. The associated phosphorescence decay curves can be best fitted to biexponential patterns and quite different RTP lifetimes are obtained for QN (86.9 and 12.5 ms) and QD (12.1 and 4.17 ms), indicating a distinct chiral discrimination of γ-CD toward this pair of pseudo-enantiomers. The corresponding association constants evaluated for QN/γ-CD/BrCH and QD/γ-CD/BrCH are 3.47×10^5 and 4.67×10^4 L mol^{-1}, respectively. It can be inferred that their different ability to form complexes with the chiral γ-CD is accounted for the notable difference in RTP lifetimes between QN and QD.

Keywords: Quinine; Quinidine; Room temperature phosphorescence; Chiral discrimination; Lifetime

1. Introduction

The chiral recognition is of great importance in many different fields including chemistry, biology, pharmaceutical, medical and life science, etc. Various methods such as capillary electrophoresis, chromatographic (HPLC and thin-layer chromatography) and spectroscopic techniques have been used for chiral separation and recognition [1–6]. In the spectroscopic detection methods, fluorescence lifetime resolution based on either time-domain or frequency-domain has been demonstrated to be a powerful technique for the analysis of chiral molecules. Based on phase modulation fluorescence lifetime measurement, quinine and quinidine can be resolved without chemical separation [7]. As an important complementary method of fluorescence sensing, room temperature phosphorimetry (RTP) gives much more advantages, e.g., large Stokes shift, good selectivity and especially longer and easily measurable triplet lifetimes. However, only recent RTP technique has been employed for chiral analysis [8,9]. In deoxygenated aqueous solutions [8], the complexes of two camphorquinone (CQ) enantiomers with α-cyclodextrin exhibited strong and different RTP signals. And the phosphorescence lifetime of (+)-CQ was about four times longer than that of (−)-CQ, which enabled the determination of the two enantiomers in a mixture without involving a separation procedure. Wei et al. [9] also reported the alteration of phosphorescence lifetimes of QN and QD by adding chiral modifiers. The lifetime difference, however, was less than 15% and not large enough. In addition, the observation of RTP required deoxygenation in the above-mentioned reports.

As a highly organized host media, cyclodextrins (CDs) have been used to induce RTP under aerated conditions with a third component as a space regulator [10–16]. Owing to their chiral cavities, CDs have also been widely used as chiral selector in chiral separation and recognition [1–3,17–20]. In the present paper, we investigated the RTP of QN and QD in γ-CD aqueous solution without deoxygenation and demonstrated that γ-CD can

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be used as a chiral selector to increase RTP lifetime differences between QN and QD by altering their photophysical properties.

2. Experimental

2.1. Reagents

Quinine (QN) and quinidine (QD) were purchased from Alfa Aesar Reagent Company. α-CD, HP-β-CD, Me-β-CD and γ-CD were kindly presented by Wacker Co. and used as received. Absolute ethyl alcohol (≥99.7%) and bromocyclohexane (BrCH, ≥98.0%) were purchased from Beijing Chemicals Factory. Stock solutions of QD and QN were prepared in ethanol at 1×10^{-2} M. Double distilled water was used throughout.

2.2. Apparatus

Phosphorescence measurements were performed on Cary Eclipse Fluorescence Spectrophotometer (Varian Co.) equipped with a pulse xenon lamp. The samples were excited at 330 nm and the phosphorescence signal was monitored at 503 nm. The excitation and emission slit widths were set at 10 and 20 nm, respectively.

The delay time of 0.10 ms was used in order to remove interfering fluorescence and scattering light from the phosphorescence spectrum, and the gate time was selected as 5.0 ms. For the lifetime measurements the initial delay time was set at 0.06 ms while the gate time is typically set at 7.0 ms. The phosphorescence lifetime values were obtained by fitting the RTP decay curves to a mono- or bi-exponential curve.

2.3. Procedures

Typically, appropriate amount of stock solutions of QN or QD was transferred into a 10 mL comparison tube and then proper volumes of γ-CD and BrCH solution were added. The mixed solution was diluted to the final 5 ml with double distilled water and shaken thoroughly. The working solutions were left to equilibrate for 40 min at room temperature and then were transferred into a 1 cm standard quartz cell with a cover to measure the phosphorescence spectra and phosphorescence lifetimes.

3. Results and discussion

3.1. Phosphorescence spectra of QN and QD

No RTP signals were observed in individual γ-CD solutions in the presence of oxygen. Upon addition of BrCH, both QN and QD produced strong RTP in γ-CD solution under nondeoxygenated conditions, indicating the formation of a three-component inclusion complex, namely, γ-CD/QN (QD)/BrCH. Fig. 1 shows RTP excitation and emission spectra of QN and QD. As expected, they exhibited very similar spectrum profiles, with maximum emission at 503 nm and excitation peak was at 231, 276 and 330 nm. 330 nm was used for all the lifetime and intensity measurements. Furthermore, the RTP intensity was linear with the concentration of QN or QD in the range of 2.00×10^{-6} to 8.00×10^{-5} M ($R^2 = 0.9969$) and 8.00×10^{-6} to 1.00×10^{-4} M ($R^2 = 0.9811$). The limits of detection are 1.93×10^{-6} M for QN and 6.69×10^{-7} M for QD, respectively.

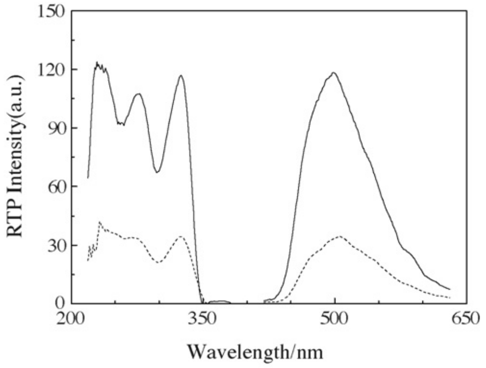

Fig. 1. Phosphorescence excitation and emission spectra of QN (—) and QD (···) ([QN] = [QD] = 8×10^{-5} M; [γ-CD] = 18 mM; $V_{\mathrm{BrCH}} = 4$ μL in 5 mL).

As comparative investigations, the experiments were also performed in other CDs systems including α-CD, β-CD, HP-β-CD and Me-β-CD, but no RTP of QD or QN was observed, indicating the sizes of these CDs are too small to include QN or QD while γ-CD can easily form inclusion complexes with QN or QD.

3.2. Effect of pH on RTP intensity

It is well known that the spectroscopic properties of cinchona alkaloid are pH-sensitive. As can be seen in Fig. 2, in the presence of BrCH and γ-CD, the RTP intensity of QN increased gradually with increasing pH and leveled off at pH 6.5. RTP intensity of QD, however, was relatively insensitive to pH and reached a plateau at pH 6. The following experiments were performed at the pH of the working solution, namely pH 7.6.

3.3. Selection of both γ-CD and BrCH concentrations.

The influences of γ-CD concentration and BrCH concentration on the phosphorescence intensity of QN and QD were investigated. In the presence of BrCH, RTP intensity increased

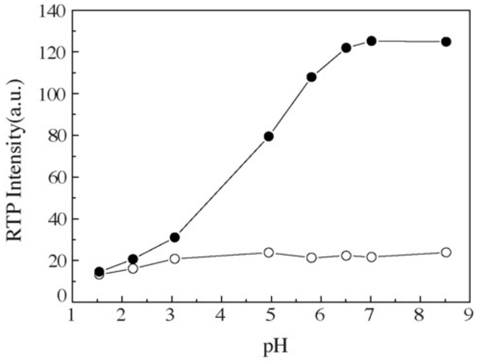

Fig. 2. Effect of pH on the phosphorescence intensity of QN (●) and QD (○) ([QN] = [QD] = 8×10^{-5} M; $V_{\mathrm{BrCH}} = 4$ μL in 5 mL).