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Enantioselective detection of chiral phosphorescent analytes in cyclodextrin complexes

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Abstract

Inclusion complexes between camphorquinone (CQ) and cyclodextrins (CDs) in deoxygenated aqueous solutions are shown to exhibit relatively strong room temperature phosphorescence (RTP). Among the various CDs tested, α-CD showed the strongest RTP signals. Interestingly, these signals differed significantly for the two enantiomers of CQ; the phosphorescence lifetime of (+)-CQ was about four times longer than that of (−)-CQ, being 352 ± 16 and 89 ± 6 μs, respectively. This enantiomeric selectivity is attributed to a difference in dissociation rates (competing with the radiative emission process) for the diastereoisomeric inclusion complexes dealt with, which have a 2:1 stoichiometry (α-CD:CQ:α-CD). Time-resolved RTP detection using different delay times enables the determination of the two enantiomers in a mixture without involving a separation technique. The minimum detectable fraction of (+)-CQ in a 2 mM sample was 13%.

Keywords: Camphorquinone; Inclusion complex; Room temperature phosphorescence; Phosphorescence lifetime

1. Introduction

Available enantioselective detection methods, i.e. optical rotatory dispersion and circular dichroism, rely on the differential interaction of a stereoisomer with circularly polarized light. They are based on a differential measurement in the presence of a large background, which limits the sensitivity that can be achieved. Physical differences for the stereoisomers can be highlighted by turning them into diastereoisomers, but also for diastereoisomers conventional spectrochemical detection methods such as UV–vis absorption and fluorescence are usually not sufficiently selective. The determination of enantiomeric purity remains a major challenge in analytical chemistry. Most current methods are based on enantioselective separation techniques, such as chiral stationary phases in liquid chromatography and gas chromatography, and cyclodextrins (CDs) in capillary electrophoresis (CE) [1,2]. Recently, some enantioselective fluorescent sensors based on the formation of diastereoisomeric inclusion complexes with mandelic acid have been developed [3,4].

CDs are cyclic oligosaccharides, which in aqueous solutions can form cyclodextrin-analyte inclusion complexes with various types of compounds. The CDs used for analytical purpose are α-, β- and γ-CD, which contain six, seven, and eight glucose units, respectively. In recent years, derivatized CDs have also been widely used in analytical chemistry, for instance in CE [2,5].

Several reviews have discussed the spectroscopic effects of CDs and how these can be applied in analytical chemistry [6,7]. Under deoxygenated solvent conditions, CDs can enhance the room temperature phosphorescence (RTP) of various compounds such as 6-bromo-2-naphthol derivatives [8–11], polynuclear aromatic hydrocarbons [12,13], or acid–base indicators such as neutral red [14]. In the case of some exceptional, well-protected complexes strong RTP signals can even be observed without deoxygenation [15].

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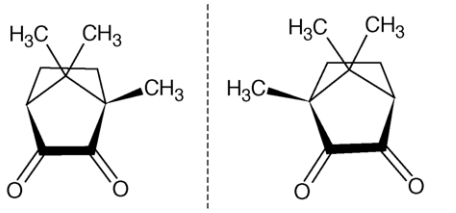

Fig. 1. Structure of the enantiomers of CQ.

Tran and Fendler [16] reported how CDs can be used to discriminate between (+)- and (−)-α-(1)-naphtylethylamine based on differences in fluorescence lifetimes. Studies using NMR spectra [17] as well as papers dealing with spectroscopic and photophysical investigations [18,19] also show the possibility of chiral discrimination by CDs for bicyclic compounds such as camphorquinone (CQ), the compound concerned with in the present paper. CQ is a chiral bicyclic 2,3-dione (see Fig. 1) and is widely used as photosensitizer for dental resin composites [20], or as photo-initiator for light-cure resin compositions [21,22] due to its photochemical reactivity upon excitation in the 400–500 nm range [23]. So far, its liquid-state room temperature phosphorescence spectra have been reported for nonpolar solvents as methylcyclohexane but not yet for aqueous CD solutions [24]; in aqueous solvents phosphorescence is hardly visible [18].

In the present paper, it will be shown that liquid-state RTP in combination with the use of appropriate CDs provides a high selectivity between the optical isomers of a phosphorescent compound such as CQ, while absorption and fluorescence hardly show any difference. The phosphorescence lifetimes observed differ strongly, so that time discrimination for selective enantiomer detection is readily performed. It should be noted that CQ is used here as a model compound; the same method is expected to be applicable to a selected group of other chiral compounds that emit RTP in the liquid state, such as α-, β-unsaturated ketones (including the well-known testosterones) and chiral binaphthyl compounds. Furthermore, application of the RTP technique is not necessarily limited to phosphorescent analytes. In a separate study, we investigated the RTP of 1-bromonaphthalene in ternary complexes with β-CD and with (+)/(−)-menthol as analyte and demonstrated that RTP lifetimes can be used to discriminate between the non-phosphorescent menthol enantiomers (see accompanying paper [15]).

2. Experimental

2.1. Chemicals and samples

(±)-Camphorquinone ((±)-CQ), carboxymethylated-β-cyclodextrin (CM-β-CD, degree of substitution (d.s.) ∼ 3), α-cyclodextrin (α-CD) and (2-hydroxypropyl)-β-cyclodextrin (HP-β-CD, d.s. ∼ 0.6) were purchased from Fluka (Buchs, Switzerland). (1*R*)-(−)-Camphorquinone ((−)-CQ), (1*S*)-(+)-camphorquinone ((+)-CQ), β-cyclodextrin (β-CD), and γ-cyclodextrin (γ-CD) were purchased from Aldrich (Steinheim, Germany). All chemicals were used as received. Water used for the preparation of the solutions was purified through a Milli-Q system from Millipore (Bedford, MA, USA).

2.2. Instrumentation

An LS-50B luminescence spectrometer (Perkin-Elmer, Beaconsfield, UK) provided with a home-made set-up for continuous nitrogen deoxygenation of the solutions was used. For this purpose, the spectrophotometer was adapted for a special luminescence cuvette (Hellma Benelux BV, The Netherlands) with a cap, fitted with Teflon tubes, so that a low nitrogen flow through the sample could be maintained.

In order to remove interfering fluorescence from the phosphorescence spectra, a delay time of 0.10 ms was used (relatively long in order to fully reject scattered light from the pulsed excitation lamp); the gating time was typically 5.00 ms. For the lifetime measurements the gating time was fixed at 0.05 ms, while the delay time was varied from 0.10 to 1.40 ms. These values were chosen after exploratory measurements had shown that the lifetimes were in the 100–400 μs range.

2.3. Analytical procedure

Solutions of racemic CQ and separate enantiomers of CQ were prepared by dissolving in Milli-Q water, or in Milli-Q water with an appropriate amount of cyclodextrins (α-CD, β-CD, γ-CD, HP-β-CD, CM-β-CD) up to a final CQ concentration ranging from 0.5 to 5.0 mM. The CD concentrations were 10 mM for the initial comparison of the various CD's; in further studies the concentration of α-CD was varied over a 5–30 mM range and 20 mM for the lifetime measurements. In view of the photochemical reactivity of CQ, solutions were freshly prepared each day and kept in the refrigerator covered with aluminium foil until analysis. During the 10 min of nitrogen deoxygenation, which was found to be sufficient, the lamp of the spectrometer was kept off to avoid photodegradation, only to be switched on just before performing the measurements. Photodegradation was further avoided by using high spectral scan rates. Enantiomeric mixtures of CQ were made by mixing known amounts of single-enantiomeric stock solutions by weight. All data handling was done using Origin 6.1 from OriginLab Corporation.

3. Results and discussion

As expected [24], RTP of CQ in deoxygenated aqueous solution was extremely weak although not completely absent (see Fig. 2). However, in the presence of a 10 mM concentration of various cyclodextrins (α-CD, β-CD, γ-CD, HP-β-CD, CM-β-CD), an enhancement of the phosphorescence was ob-