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# Fluorescent pseudorotaxanes of a quinodicarbocyanine dye with gamma cyclodextrin

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A B S T R A C T

Spectrophotometric titration of buffered solutions of gamma cyclodextrin ($\gamma$CD) and 1,1′-diethyl,2,2′-dicarbocyanine (DDI) demonstrates extension of the known 1:2 host:guest complex to form a previously unreported 2:2 complex near the $\gamma$CD solubility limit. Though DDI is predominantly hosted as a non-fluorescent H-aggregate, both complexes exist in respective equilibria with two secondary complexes hosting unaggregated DDI as 1:1 and 2:1 complexes. The 2:1 complex exhibits significant fluorescence emission, with a quantum yield six times that of DDI in organic solvents, but ten times lower than that of an analogous indodicarbocyanine. Fragment Molecular Orbital calculations suggest that the 2:1 complex has the tail-to-tail conformation, and that solvent access to the dye strongly favors photoisomerization. In the host-guest complex, $\gamma$CD limits solvent access to the dye and hinders rotation of the quinolyl terminal groups, but nevertheless pairwise rotation of methine carbons within the $\gamma$CD cavity likely remains as a significant nonradiative relaxation pathway for the excited state.

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## 1. Introduction

As solution-phase fluorescent probes, the quinocyanine dyes are disappointing. Though they absorb light as strongly as their brighter indocyanine cousins, the basicity of their quinolyl terminal groups reduces the bond order of the outermost methine C–C bonds [1], predisposing their electronic structure toward bond length alternation [2], and nonradiative relaxation from the first excited singlet state by ultrafast rotation around a polymethine C–C bond [3–5]. Though unsuitable as fluorescent reporters, the quinocyanines may hold promise as components in molecular switching devices [6]. Polymer matrices doped with the vinylogous cationic quinocyanines 1,1′-diethyl-2,2′cyanine (PIC), 1,1′-diethyl-2,2′-carbocyanine (DCI), and 1,1′-diethyl,2,2′-dicarbocyanine (DDI) (Fig. 1) become increasingly electrically conductive as the length of the polymethine chain increases [7]. If photoisomerization occurs in dye-doped materials, it may permit rapid modulation of this conductivity by incident light [8], realizing a desirable characteristic of photonic information systems built of supramolecular nanostructures [9].

Logically, the greatest modulation in conductivity from a molecular switch would be expected if the photoisomerizable conductor were incorporated into, and oriented by, a linearly extendable dielectric nanotube [10] with a diameter large enough to allow for overlapping of the polymethine chains, but small enough to minimize parallel current paths. Self-assembly of nanotubes, templated around rodlike guests, have been reported [11–13] in solutions of the cyclic oligosaccharides $\beta$-cyclodextrin ($\beta$CD) and $\gamma$-cyclodextrin ($\gamma$CD). The extent to which photoisomerization remains possible in such nanocavities is uncertain [14]. The quinocyanines readily form host-guest complexes with $\gamma$CD [15,16], but the dye is generally incorporated as a non-fluorescent H-aggregate, so quantum yields have not been assessed as far as we know. Also, there is evidence that placing these dyes in viscous solvents [17,18] or polymer matrices of suitable Young's modulus [17,18] may reduce their photoisomerization yield.

Host-guest complexes of cyanine dyes with cyclodextrins are considered pseudorotaxanes since their formation is a reversible process driven by the displacement of high-energy water molecules from the cyclodextrin cavity [21]. Rotaxination is not always accompanied by spectral changes [22], but most cyanine/cyclodextrin adducts are distinguishable by absorbance spectroscopy [23,24]. Their equilibria have been titrated spectroscopically [25,26] using modifications of the Benesi-Hildebrand method [27], but this approach proved difficult in this work because of multiple equilibria and strongly overlapping spectral components. Various multivariate methods have been used to address these difficulties [25,26,28-30], including nonnegative matrix factorization (NMF) [31], the method used here.

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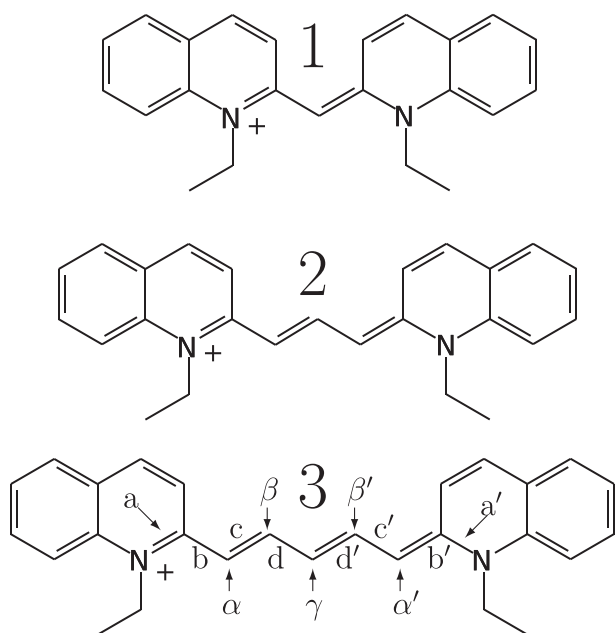*E-mail address:* john.silzel@biola.edu (J.W. Silzel).

**Fig. 1.** Dye structures of three vinylogous symmetric cationic quinocyanine dyes: 1,1′-diethyl-2,2′cyanine (PIC), 1,1′-diethyl-2,2′-carbocyanine (DCI), and 1,1′-diethyl,2,2′-dicarbocyanine (DDI), labeled 1, 2, and 3, respectively. Polymethine chain bonds and carbon atoms are labeled by lowercase roman and greek characters, respectively, see text.

In this work, spectroscopic titrations characterize two new pseudorotaxanes of the cationic quinocyanine dye 1,1′-diethyl,2,2′-dicarbocyanine (DDI, Fig. 1) that form near the aqueous solubility limit of γCD. Both complexes are fluorescent, allowing comparison of the quantum yield of DDI in the γCD complex with free DDI in water and organic solvents. These observations are compared with calculations performed using the Fragment Molecular Orbital (FMO) method to elucidate the nature of the host-guest complex and its excited state dynamics and assess the potential of this system to realize molecular switching.

## 2. Experimental Methods

Alpha cyclodextrin (αCD, CAS No. 10016-20-3, > 98%, Sigma Aldrich), Beta Cyclodextrin (βCD, CAS No. 7585-39-9 > 97%, Sigma-Aldrich), and Gamma Cyclodextrin (γCD, CAS No. 17465-86-0, > 98.0%, Tokyo Chemical Industry Co. Ltd.) were used as received. Linear dextrin (CAS No. 9004-53-9, molecular weight 162.07 g mol$^{-1}$) was obtained from Fisher Scientific. The quinocyanine dyes (Fig. 1) DDI (CAS No. 14187-31-6), DCI (CAS No. 605-91-4) and PIC (CAS No. 977-96-8) were obtained from Sigma Chemical Co. and used as received. All dyes were dissolved in dimethyl sulfoxide (DMSO) to give stable 1.0 mM stock solutions which was stored in the dark and added to γCD solutions immediately prior to spectroscopic studies, a protocol which left DMSO in the final solutions at a concentration of ≈1% by volume. Carbonate buffer (50.0 mM, pH 8.5) was chosen as the diluent for all CD solutions since this buffer is reported not to compete with other solutes for inclusion in the CD cavity [32,33]. Aqueous solutions were stored in darkness except when spectra were actually being measured.

Absorbance spectra were measured over a wavelength range from 400 nm to 1100 nm at a scan rate of 600 nm min$^{-1}$ using a Beckman Model DU-650 single-beam spectrophotometer with spectral bandwidth of 2 nm (FWHM). Absolute wavelength accuracy was verified to be ±1 nm over the measurement range using a NIST-traceable holmium oxide reference [34] (Starna Inc.). Disposable polystyrene semi-micro cuvettes (Fisher Scientific, 1.0 cm path length) were utilized for absorbance scanning.

Fluorescence emission spectra were acquired using a CCD-based laser induced imaging spectrofluorometer which has been described elsewhere [35,36]. This instrument features a vertical excitation beam aligned with the entrance slit of the detection optics so that the entire illuminated portion of the sample is viewed. For this work, the instrument was fitted with interchange-ableexcitation sources built around a 2 mW 635 nm diode laser (Quarton, Inc. VLM635-04) and a 4 mW 677 nm diode laser (Lasiris, Inc.). Fluorescence emissions were detected using an ISA CP-200 imaging spectrograph interfaced to a Peltier-cooled, front illumi-nated charge-coupled device (CCD) detector (EEV 576 × 384 pixel array, Princeton Instruments) operating at −10.0°C, affording inte-gration times of up to 2 min and a dispersion of 0.8 nm pixel$^{-1}$. This instrument was calibrated to a wavelength accuracy of ±1 nm using Hg emission lines. Quartz cuvettes (Beckman) were used.

## 3. Calculations

### 3.1. Spectroscopic Titrations

Absorbance spectra (n = 435 wavelengths) were obtained for each of m = 16 different samples representing different formal concentrations of γCD, and assembled column-wise to form an (nxm) data matrix **A**. Rank estimation and constrained nonnegative matrix factorization (NMF) of **A** by an iterative bilinear regression method gave a set of r nonnegative n-point spectral factors **σ** and corresponding nonnegative m-point concentration scores **χ**, where **A** = **σκχ**$^{\mathsf{T}}$, and **κ** is a diagonal scaling matrix. Assuming Beer-Lambert behavior, the columns of **σ** and **χ** are each respectively proportional to the extinction coefficients and concentrations of one of r different absorbing factors in the m sample mixtures. Rotational ambiguity in the NMF [37] was addressed by constraining the scores **χ** using an equilibrium model of host-guest complex formation. These calculations are described in Appendix A, and were implemented using the open-source Octave computing package [38].

### 3.2. Fragment Molecular Orbital Methods

Density functional theory (DFT) and time-dependent DFT (TD-DFT) find widespread application nowadays, but the quantum mechanical (QM) modeling *in toto* of molecular clusters of cyclodextrins, dyes, and the discrete solvent molecules necessary to reproduce complexation energetics is computationally expensive. The Fragment Molecular Orbital (FMO) method [39] reduces this cost by relying on the locality of electron correlation, applying conventional QM methods (RHF, DFT, or TD-DFT) piecewise to user-defined fragments comprising the molecular cluster, then iterating each fragment to self consistency in the electrostatic potential field of nearby fragments until the entire system is self-consistent. The accuracy of FMO increases with fragment size, but so does computational cost.

In this study, DDI was treated as a single ab-initio fragment, while γCD was fragmented into eight D-glucose units connected by glycosidic linkages modeled using the FMO "detached" covalent bond methodology. Solvation was by discrete water molecules, grouped into clusters by a nearest-neighbor algorithm. For ground state (GS) geometry optimization, a two-layer FMO calculation [40] was used which treated the γCD and water economically in one layer at the RHF 6-31G level of theory, but modeled DDI in a second layer that included diffuse orbitals and DFT at the B3LYP/6-31G* level. The B3LYP functional does not yield spectroscopic accuracy when applied to cyanines [41,42], but was selected because the other hybrid exchange/correlation functionals available in our FMO-GAMESS version (FMO Version 5.1 [43], GAMESS Version December