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Coordination Chemistry Reviews
171 (1998) 115–123

COORDINATION CHEMISTRY REVIEWS

Lanthanide-ion modified cyclodextrin supramolecules

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Accepted 19 November 1997

Contents

Abstract

A cyclodextrin appended with a lanthanide-ion macrocycle comprises a microscopic bucket that lights up when filled with mono- and bicyclic aromatics. This triggered luminescence response arises from an absorption-energy transfer-emission (AETE) process where blue light, absorbed by the aromatic, is transferred to the lanthanide ion to produce the emitting $^5D_0$ excited state of Eu^{3+} or the $^5D_4$ excited state of Tb^{3+} ion. Three supramolecule systems are presented, focusing on the design features that lead to the best luminescence response. © 1998 Elsevier Science S.A.

Keywords: Supramolecule; Cyclodextrin; Luminescence; Energy transfer; Lanthanide; Chemosensor; Aromatic hydrocarbon

1. Introduction

Supramolecules provide angstrom-sized architectures in which to control basic energy transduction processes that form the underpinning to a variety of potentially

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PII S0010-8545(98)00038-1

useful light-based applications. Photoactivated switches, electronic devices and molecule-based logic networks are now in the grasp of the supramolecular chemist [1–3]. Our interest in supramolecules centers on developing chemosensors featuring a photoactive center capable of emitting visible light and a docking site for a target analyte. In these supramolecules, the emitting center literally lights up when the analyte is recognized at the remote binding site [4–8]. Whereas most luminescence sensing schemes detect the presence of an analyte by quenching light emission from a photoactive site, our approach to chemosensor design has the advantage that a signal is produced against a dark background.

One important class of analytes to detect by a triggered luminescence approach is aromatic hydrocarbons. To date, most optical detection methods of these environmentally harmful pollutants rely on measuring their direct fluorescence [9]. Practically, laser-induced fluorescence approaches are problematic because the blue fluorescence of the aromatic must be deconvoluted from the blue fluorescence of other organic interferents. Recently, a triggered luminescence response scheme has been designed for large polycyclic aromatic hydrocarbons, which can displace fluorophores from DNA [10]. However, the low affinity of monocyclic (BTEXs — benzene, toluene, xylene, and ethyl benzene) and bicyclic (naphthalene and biphenyl) aromatics for DNA has prevented the detection of these important environmental toxins by this method. In view of these results, we sought to design a supramolecule that would bind small aromatics and, by manipulating the fundamental parameters governing energy flow within the supramolecule (i.e. the radiative, non-radiative and quenching rate constants), trigger a bright luminescence from a photoactive center upon their molecular recognition in the supramolecule environment.

Of the many diverse architectures considered for our chemosensor design, a properly modified cyclodextrin (CD) provides an ideal supramolecular template for the detection of mono- and bicyclic aromatics. Six, seven, or eight D-glucose units (α-, β-, and γ-CD, respectively) catenate in a head-to-tail arrangement to produce a miniature, water soluble bucket with a hydrophobic interior suitable for binding substrates such as aromatics. The CDs by themselves are inadequate chemosensing active sites because they do not possess a photoactive center. This problem is overcome by using the hydroxyl groups at the rim of the CD as sites of modification [11–13]. We settled on a lanthanide ion (Ln^{3+}) as a photoactive center because direct irradiation of the ion engenders little or no luminescence owing to the low absorbance ($<1\ M^{-1}\ cm^{-1}$) of the ^5D_J emitting state [14]. Yet, we suspected that, under the proper conditions, the aromatic hydrocarbon could absorb incident light and pass it on to the Ln^{3+} ion to indirectly excite the latent emitting center by an absorption-energy transfer-emission (AETE) process [2,15,16]. Luminescence may be intense as long as the rate of energy transfer from sensitizer to the Ln^{3+} ion is efficient. In this instance, docking of analyte would lead to a bright luminescence, heralding the presence of the aromatic in the supramolecule environment.

We now describe supramolecules with three different macropolycyclic Ln^{3+} ion binding sites appended to the bottom rim (primary hydroxyl side) of β-CD. As elaborated below, the intensity of the luminescence response for the three systems depends critically on the nature of the lanthanide-binding site.

2. Lanthanide ion aza swing and cradle cyclodextrin supramolecules

Our chemosensing design strategy has been predicated on the photophysics of [2.2.1] cryptand lanthanide complexes. Coordination of light-absorbing substrates such as acetylacetonates (acac) or benzoate to $[(Ln \subset 2.2.1)]^{3+}$ (Ln = Eu or Tb) complexes enables energy to flow from the light-harvesting group to the photoactive Ln^{3+} ion. The AETE process in this case is efficient because the chelating arms of the substrate impose the close distance required for facile energy transfer [17]. For non-coordinating substrates such as aromatics, however, the cryptand supramolecule is a poor chemosensor because, free in solution, the energy collected by the aromatic is simply released (within nanoseconds) before it can be channeled to the encapsulated Ln^{3+} ion. Nonetheless, as described in Fig. 1, the [2.2.1] framework provides the basic template about which to design an aromatic chemosensor. The nitrogens of the macrocycle become available for attachment to the CD when the etherate arm (to give the aza macrocycle 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane) is removed from [2.2.1]. We initially sidestepped the issue of regiochemistry at the bottom of the CD cup by considering only a one-point attachment of the aza

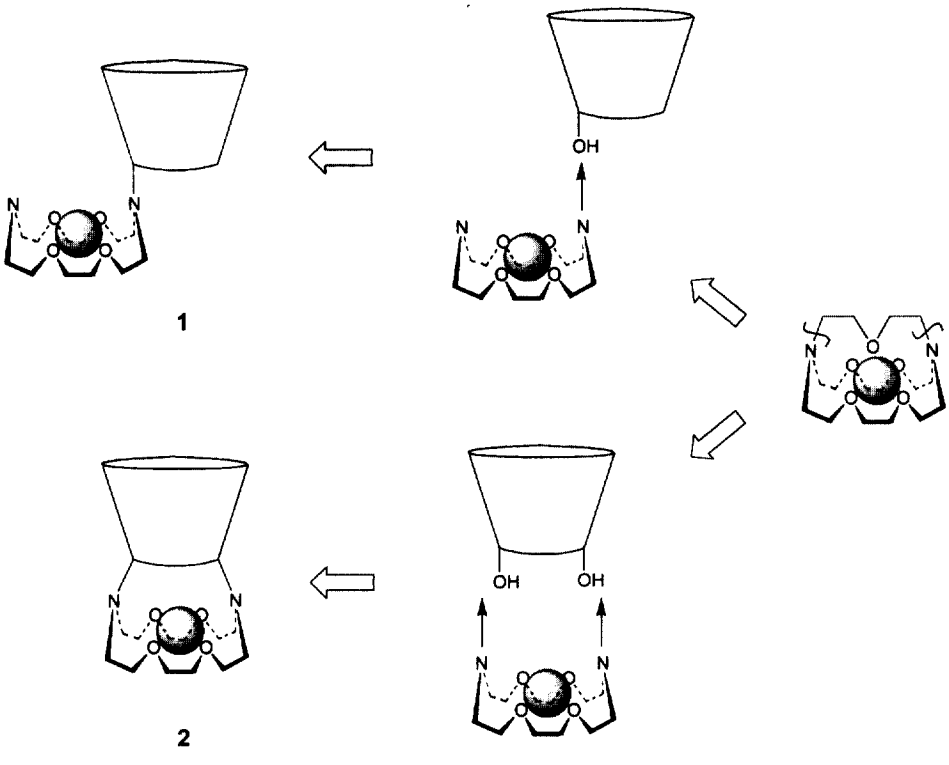

Fig. 1. Design strategies for the syntheses of β-CD (represented by the cup) modified with a luminescent lanthanide ion (shaded ball) residing in an aza ligand, derived from the [2.2.1] cryptand shown on the right-hand side of the figure.

macrocycle, where the pioneering work of Willner and Goren [18] pointed the way to the initial supramolecular design. Monosubstitution of a primary alcohol of β-CD with a tosyl group and subsequent replacement by the aza ligand yielded a modified CD capable of binding a Ln^{3+} ion, which was introduced from the nitrate salt to afford $[\beta\text{-CD}\cup{}^{1}(Eu\subset aza)]^{3+}$, $\mathbf{1}(Eu^{3+})$. Tethered at only one nitrogen, the $(Eu\subset aza)^{3+}$ macrocycle assumes a conformation that is swung away from the hydrophobic cup [19].

Although Eu^{3+} emission is insensitive to the addition of benzene to solutions of $(Eu\subset aza)^{3+}$, a weak red luminescence arises upon the addition of benzene to solutions of $\mathbf{1}(Eu^{3+})$ (intensity enhancement of 2 for ~440 ppm benzene). Excitation spectra and equilibrium constants reveal that the $^5D_0\rightarrow{}^7F_J$ transition of Eu^{3+} ion is triggered upon the molecular recognition of benzene in the hydrophobic interior of the CD cup [19,20]. These results are consistent with an AETE process in which the electronic energy from irradiated analyte residing in the CD cup is transferred to tethered $(Eu\subset aza)^{3+}$.

Although aromatic hydrocarbons trigger a red luminescence from **1**, the swing design is not optimized for the most efficient AETE process owing to the significant attenuation of energy transfer with distance ($1/r^6$ or e^{-ar} depending on the mechanism [21]). The obvious solution to the problem was to cradle the aza straps beneath the cup by the two-point attachment strategy depicted in Fig. 1. By following methods developed by Tabushi and coworkers [22–25], reaction of β-CD with a rigid rod tosylate (in this case, biphenyl-4,4′-disulfonyl chloride) produced a derivatized cyclodextrin that allowed us to tether the aza via both of its nitrogens to the (A,D) hydroxyl positions on the primary side of the CD cup [26]. As with $\mathbf{1}(Eu^{3+})$, $[\beta\text{-CD}\cup{}^{2}(Eu\subset aza)]^{3+}$ $[\mathbf{2}(Eu^{3+})]$ shows only very weak $^5D_0\rightarrow{}^7F_J$ luminescence upon direct excitation. Unlike the swing CD, however, the intensity of this luminescence was not triggered upon the addition of benzene or any other mono- or bicyclic aromatic hydrocarbon. Competitive binding experiments revealed that the attachment of the aza-binding site with a cradle regiochemistry greatly modifies the association of aromatic hydrocarbons to the interior of the CD cup, e.g. K_{assoc} for the $\mathbf{2}(Eu^{3+})\cdot$benzene complex is $<10\,M^{-1}$. Although the intrinsic energy transfer process should be more efficient in $\mathbf{2}(Ln^{3+})$, the diminished association of benzene to the CD cup limits the overall optical response from the supramolecule.

3. Charge-neutralized lanthanide ion cradle cyclodextrin supramolecules

Binding studies clearly revealed that the flaw in the design of the cradle CD was the presence of a 3+ positive charge at the bottom of the CD cup. Accordingly, we set out to design a charge compensating lanthanide ion-binding site. With the aza-binding site as a template, we undertook the synthetic strategy elaborated in Fig. 2. Three anionic moieties were introduced into the macrocycle by removing a (bis)etherate arm and replacing the central oxygen of the remaining strap with an amide. In this manner, we were able to introduce three carboxylates into the backbone of the lanthanide-binding site, while retaining connecting functionalities at the strap ter-

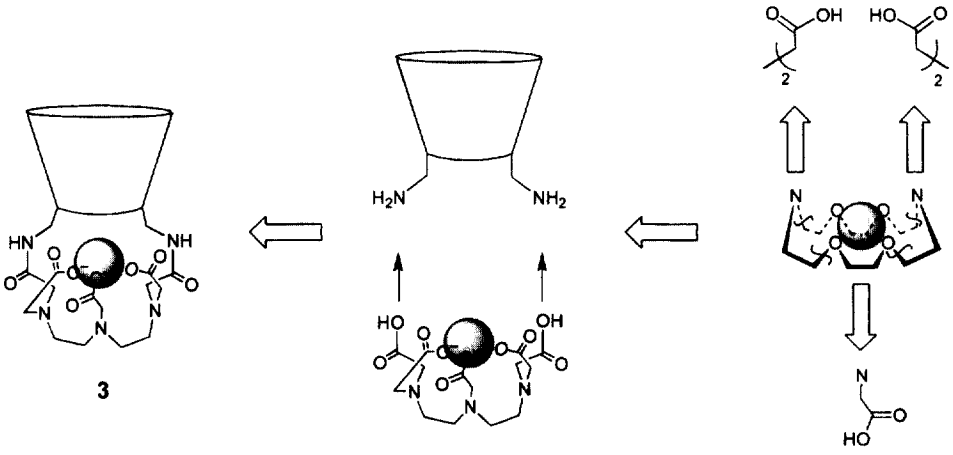

Fig. 2. Design strategy for the synthesis of β-CD modified with a neutral lanthanide-binding site in a cradle geometry.

mini. As with the synthesis of the $[\beta\text{-CD}\cup{}^{2}(\text{Eu}\subset\text{aza})]^{3+}$ cradle, the methods of Tabushi and coworkers were used to direct the (A,D) regiochemistry. The synthesis of CD modified with diethylenetriamine pentaacetic acid (DTPA) followed cleanly from A,D-diamino-β-CD and DTPA dianhydride [27]. Because low-lying carboxylate ligand-to-metal charge transfer excited states can interfere with AETE processes when the metal is Eu^{3+} [28], we chose the non-reducible Tb^{3+} as the lanthanide ion for this supramolecule.

The very weak $^5D_4 \rightarrow {}^7F_J$ emission observed from aqueous solutions of $\mathbf{3}(Tb^{3+})$, when the metal ion is directly excited, is markedly enhanced in the presence of mono- and bicyclic aromatic hydrocarbons. The luminescence intensity increases monotonically with the concentration of aromatic hydrocarbon, reaching an asymptotic limit that is specific to the analyte. The plot shown in Fig. 3 shows this result. A 10% increase in the intensity of the supramolecule when benzene is present in 200 ppm is contrasted by a ~4000% intensity enhancement when biphenyl is present at concentrations of only 10 ppm. The increase in emission intensity with added substrate is accompanied by the appearance of bands in the excitation spectra that are energetically coincident with the absorption maxima of the aromatics. This spectroscopic result is a signature of the indirect excitation of the $^5D_4$ excited state of Tb^{3+} by the aromatic via a unimolecular AETE process. As expected, when the CD is absent, the luminescence intensity from the native $[\text{Tb}\subset\text{DTPA}]$ complex is weak and insensitive to the concentration and the absorption cross-section of the aromatic. The smaller triggered luminescence response of $\mathbf{3}(Tb^{3+})$ toward benzene as compared to biphenyl reflects the smaller association constant of the $\mathbf{3}(Tb^{3+})\cdot$ benzene complex and the smaller absorption cross-section of the monocyclic aromatic.

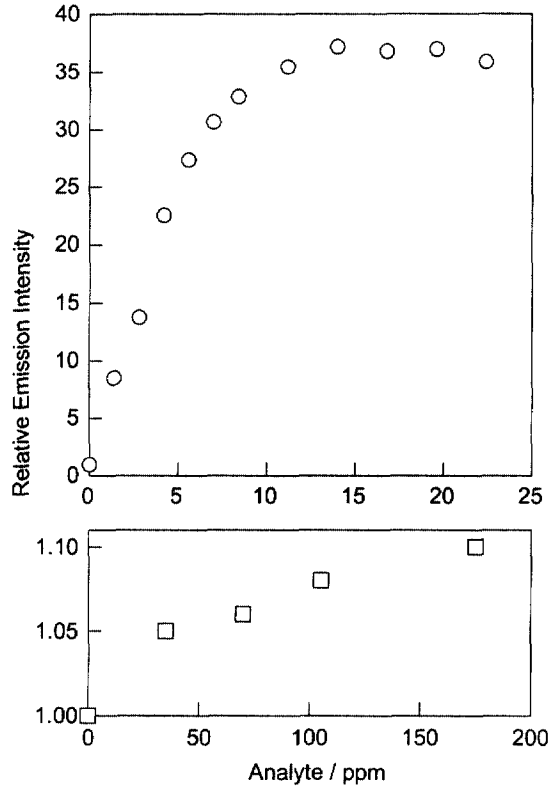

Fig. 3. Relative Tb^{3+} emission intensity ($\lambda_{det}=544$ nm) from aqueous solutions of **3**, [β-CD∪^{2}(Ln⊂DTPA)], in the presence of biphenyl (○) and benzene (□).

4. Mechanism of the AETE process in the DTPA cradle supramolecule

We have studied the mechanism of the AETE process of Ln^{3+} complexes of **3**(Ln^{3+}) by time-resolved spectroscopy [29]. The energy resulting from the prompt absorption of light by biphenyl included in **3**(Tb^{3+}) appears at the $^5D_4$ state in 12 μs. The green luminescence of the Tb^{3+} ion subsequently decays with its natural lifetime of 1.6 ms. To gain further insight into the photophysics, we have augmented these time-resolved studies with a similar investigation of **3**(Gd^{3+}). Because the Gd^{3+} triplet excited state is too high in energy to accept energy from the biphenyl donor, the **3**(Gd^{3+}) complex provides a reference for the supramolecule photophysics in the absence of energy transfer to the Ln^{3+} ion. A comparison of the luminescence decay kinetics for biphenyl associated to the **3**(Tb^{3+}) and **3**(Gd^{3+}) complexes leads to the model depicted in Fig. 4. The AETE process is initiated upon absorption of an incident photon to produce the $^1\pi\pi^*$ excited state of biphenyl. The lanthanide facilitates intersystem crossing to the triplet whereupon energy transfer occurs to produce the $^5D_4$ excited state of the Tb^{3+} ion. Energy transfer calculations yield a

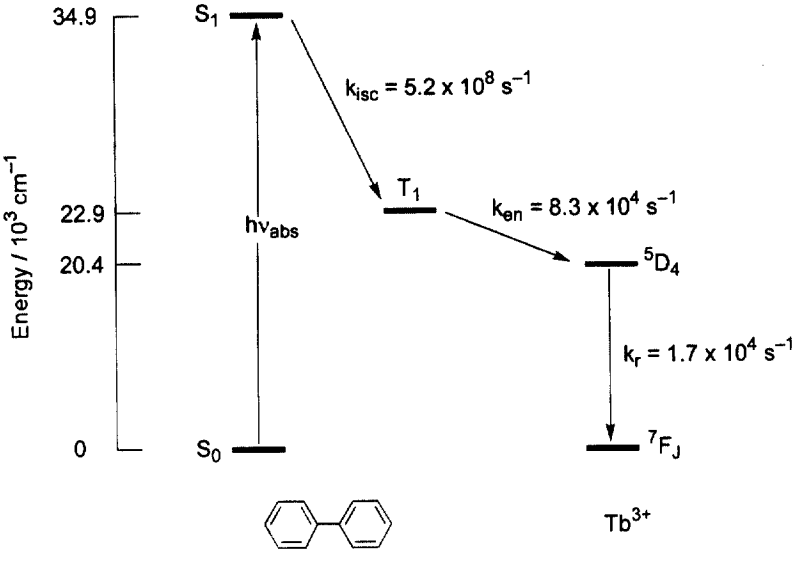

Fig. 4. Energy scheme with measured rate constants for the AETE process of the binary complex formed between **3**(Tb^{3+}) and biphenyl.

donor–acceptor distance consistent with the ~5 Å distance between biphenyl and Tb^{3+} ion as measured from energy minimized molecular models of the **3**(Tb^{3+})·biphenyl complex.

The scheme depicted in Fig. 4 is not unique to **3**(Tb^{3+}). That the triplet excited state represents a staging area for energy transfer is an emerging trend in the photophysics of many other lanthanide ion supramolecules. For instance, the Tb^{3+} and Eu^{3+} complexes of modified calix[4]arenes also undergo AETE via the triplet excited state of donors [30–32]. These results, taken together with the systems described here, serve to emphasize the role of the lanthanide ion to open a conduit for energy flow in such supramolecular assemblies. In addition to the obvious importance of the Ln^{3+} ion as the emitting center in the AETE process, the Ln^{3+} ion also provides a mechanism to produce a long-lived donor excited state from which energy transfer may occur. In the absence of this heavy atom effect, the singlet excited state of the aromatic would return to its ground state before energy transfer could be enacted. By channeling the singlet to a long-lived triplet, ample time is provided for the slower energy transfer process to effectively compete with the fast natural radiative and non-radiative processes of the analyte.

5. Conclusions

Mono- and bicyclic aromatics may be detected by a triggered luminescence response when the chemosensor is a properly designed supramolecule featuring an aromatic binding site and proximate emitting center. In the systems described here,

light absorbed by the aromatic is delivered to the emitting state of a lanthanide ion by an AETE process. Three factors govern the overall luminescence response: (1) association of the aromatic to the supramolecule; (2) the absorption cross-section of the aromatic; and (3) the distance for energy transfer from the aromatic to the emitting center. The design of supramolecule **3** is superior to those embodied by **1** and **2** because the short distance needed for efficient energy transfer in the AETE process is imposed by attaching the DTPA at the (A,D) glucose sites of a β-CD and because the three carboxylates of the DTPA cradle neutralize terbium's positive charge, which otherwise interferes with the inclusion of a neutral, apolar guest into the hydrophobic CD cavity.

Acknowledgements

The research on optical supramolecule architectures is sponsored by the Air Force Office of Scientific Research (F49620-98-1-0203) with additional support provided by the National Science Foundation Materials Research Science and Engineering Center (DMR-9400417). DGN would like to thank Jeffrey May for his wisdom and insight in the design and function of large architectures and Paul Smith, Chris Hayes and Harry Roy for their craftsmanship and diligence in taking re-design issues of large architectures from concept to reality.

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