Available online at www.sciencedirect.com
ScienceDirect
Coordination Chemistry Reviews 251 (2007) 546–553
COORDINATION CHEMISTRY REVIEWS
www.elsevier.com/locate/ccr

Review

Localizing molecular probes: Inclusion of Re(I) complexes in β-cyclodextrin

Drew Beck [a], Jason Brewer [a], Jennifer Lee [a], Dana McGraw [a], B.A. DeGraff [a,*], J.N. Demas [b,**]

[a] *Department of Chemistry, James Madison University, Harrisonburg, VA 22807, United States*
[b] *Department of Chemistry, University of Virginia, Charlottesville, VA 22901, United States*

Received 3 May 2006; accepted 2 August 2006
Available online 8 August 2006

Contents

Abstract

The inclusion of a series of luminescent Re(I) complexes in α- and β-cyclodextrin in water is described. The complex's general structure is $[L_2Re(CO)_3(4\text{-R-pyridine})][ClO_4]$ where L_2 represents the α-diimine ligands 2,2′-bipyridine or 1,10 phenanthroline. The R groups were selected to span a range of hydrophobicity from –H to $-(CH_2)_{12}CH_3$. These R's showed a variety of binding constants of the complexes to the hydrophobic interior of the β-cyclodextrin. Binding to β-cyclodextrin was accompanied by shifts in the emission λ_{max} to shorter wavelengths, and increases in both the excited state lifetime and luminescence quantum yield. No such effects were observed for α-cyclodextrin. The binding data could be fit by a simple two state model and binding constants ranged from 0.2 to 6.5 mM^{-1}. In contrast to previous studies, the mechanism responsible for the changes in photophysics is attributed to shielding the complexes from solvent interaction rather than from quenching by O_2. Solvent exposure experiments suggest that binding effectively blocks about half the solvent access to the chromophore.

Keywords: Luminescence; Cyclodextrins; Guest–host; Metal complexes

* Corresponding author. Tel.: +1 540 568 6673; fax: +1 540 568 7938.
** Corresponding author.
E-mail address: degrafba@jmu.edu (B.A. DeGraff).

0010-8545/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.ccr.2006.08.002

1. Introduction

1.1. Background

The design and characterization of molecular probes is an area that continues to attract considerable interest [1]. Because of their potential for exceptional sensitivity, luminescent materials have received considerable attention for use as molecular reporters and sensors [2,3]. While a variety of luminescent substances are available, probes based on luminescent transition metal complexes offer some significant advantages for a number of applications where long excited state lifetimes and near UV or visible light activation are important considerations. Within this class of substances, systems based on Ru(II), Os(II), Re(I), and Ir(III) have been most widely studied [4–7]. Complexes based on these metal ions can exhibit long excited state lifetimes, high quantum yields of emission, tunability of both absorption and emission through structural variation, and most importantly environmental sensitivity. This latter property usually occurs because of the environmental sensitivity of the metal-to-ligand-charge-transfer (MLCT) character of the lowest excited state. Luminescent complexes report on their environment through changes in excited state lifetime, emission maximum, and quantum yield.

The typical luminescent molecular probe consists of a sensing portion or chromophore and an equally important anchor or localization portion, although both functions can be assumed by a single ligand. The anchor function can be implemented through several approaches, including (1) actual covalent bonding of the probe to the region of interest or (2) use of some property such as hydrophobicity to attract the probe to the desired location. In many instances it is not desirable or possible to anchor the probe via an actual chemical bond. Thus, the need for reliable and predictable localization strategies based largely on intermolecular forces is apparent. Unfortunately, the mere act of anchoring/localizing a molecular probe can change its response characteristics, sometimes dramatically [8].

1.2. This work

Molecular probes based on $[L_2Re(CO)_3X]^+$ complexes where L_2 is a bidentate α-diimine ligand and X is largely a spectator ligand offer several attractive features. We have explored some of these materials previously and found long lifetimes, high quantum yields, and considerable environmental sensitivity [9]. We were interested in using the spectator ligand for the localization function and wanted to explore (1) how structural variation affected the strength of localization and (2) what effect being confined would have on the photophysical properties of the probe. We chose a series of substituted pyridines with a variety of alkyl and aryl substituents in the para or 4 position to provide the localization. These employed hydrophobicity to localize the complex in the target region. That region was the hydrophobic interior cavity of either α- or β-cyclodextrin (α-CD, β-CD). In many respects the luminescent probe resembles a jelly fish with only one tentacle. The luminophor is the body and will float above the tentacle which should be inserted into the CD cavity. Cyclodextrins are widely used as a host that mimics binding sites of biological materials, and they are also used to solubilize materials in such diverse applications as drug delivery and pollutant removal [10].

2. Experimental

2.1. Materials

The ligands used and our abbreviations are 2,2′-bipyridine (bpy), 1,10-phenanthroline (phen), pyridine (pyr), 4-methylpyridine (4-Mepyr), 4-ethylpyridine (4-Etpyr), 4-*tert*-butylpyridine (4-*t*Bupyr), 4-phenylpyridine (4-Phpyr), 4-(3-cyclohexen-lyl) pyridine (4-cHxpyr), 4-(3-phenylpropyl)pyridine (4-Phpropyr), and 4-(3-hydroxypropyl)pyridine (4-PrOHpyr). These materials were all obtained commercially from either GFS Chemical, Aldrich, or Rilley Tar and Chemical. They were all checked for purity with capillary glc and found to be at least 98% or better.

The α- and β-cyclodextrins (α-CD and β-CD) were obtained from Aldrich and used as received. Hplc grade H_2O was obtained from Fisher Scientific, while the D_2O was 99 atom% from Aldrich. Other solvents were reagent grade and used as received.

2.2. Ligand synthesis

Two ligands, 4-octylpyridine (4-*n*C_8pyr) and 4-tridecanylpyridine (4-*n*C_{13}pyr) were synthesized using standard butyl lithium/diisopropyl amine type procedures [11]. In a typical procedure 10 mmol of butyl lithium (2.5 M in hexane) were added to 100 ml of freshly distilled, from Na/benzophenone, THF at 0 °C containing 10 mmol of dry diisopropyl amine and the mixture stirred for 10 min under nitrogen. To the cooled mixture was then added 10 mmol of distilled 4-methylpyridine dissolved in 50 ml of dry THF. This addition was done over about 15 min and resulted in a deep blue/black solution. This solution was allowed to stir for about 30 additional minutes. To this solution was then added via a dropping funnel 10 mmol of the appropriate iodide (1-iodoheptane or 1-iodododecane) dissolved in 50 ml of dry THF. The addition typically took 30 min and was accompanied by loss of color. The resulting yellow solution was allow to stir and slowly warm to room temperature over a 4–5 h period. Standard workup resulted in an oil that was purified by column chromatography. Ligand purity was determined using capillary glc, and ligand structure was established by both H NMR and elemental analysis.

4-Octyl pyridine: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (dd, 2H, $J = 6.3, 2.8$), 7.93 (d, 2H, $J = 6.0$), 2.59 (t, 2H, $J = 8.0$), 1.62 (t, 2H, $J = 7.5$), 1.29 (m, 10H), 0.87_9 (t, 3H, $J = 7.0$). Anal. Calcd. for $C_{13}H_{21}N$: C, 81.59; H, 11.08; N, 7.33. Found: C, 82.08; H, 10.84; N, 7.08.

4-Tridecanylpyridine: ^{1}H NMR (400 MHz, $CDC1_3$): δ 8.47 (dd, 2H, $J = 6.3, 2.8$), 7.92 (d, 2H, $J = 6.0$), 2.58 (t, 2H, $J = 8.0$), 1.61 (t, 2H, $J = 7.8$), 1.29 (m, 20H), 0.87_8 (t, 3H, $J = 7.0$). Calcd. for $C_{18}H_{31}N$: C, 82.70; H, 11.94; N, 5.36. Found: C, 83.05; H, 11.23; N, 5.72.

2.3. Complex synthesis

The Re(I) complexes were synthesized from $Re(CO)_5Cl$ (Aldrich Chemical) as a starting material using a procedure reported earlier [9c]. All complexes were perchlorate salts and were purified by column chromatography. *WARNING: Perchlorates are potentially explosive and due care is required*. The absorption and emission spectra and lifetimes for those complexes already reported were in good agreement with those synthesized here [9]. All structures were verified by ^{13}C NMR, IR, and UV–vis spectra. Emission purity was established by lifetime measurements, i.e. a single lifetime in CH_2C1_2 and by an acceptable excitation spectra ratio [12], which was flat to within 3%.

Preparation of $Re(L_2)(CO)_3Cl$ complexes: Typically 100 mg of $Re(CO)_5Cl$ and a 10% molar excess of the appropriate ligand were placed in a 25 ml round bottom flask with ~8–10 ml of toluene. The mixture was heated to reflux with stirring until TLC (alumina plate, CH_2C1_2/CH_3CN (80%/20%) showed no remaining starting $Re(CO)_5Cl$; usually about 1.5 h. After removing the solvent, the resulting yellow solid was washed several times with diethylether to remove the excess ligand. Yields were typically >85% of TLC pure material.

Preparation of $[Re(L_2)(CO)_3(R\text{-pyridine})](ClO_4)$ complexes: Typically 100 mg of the appropriate $Re(L_2)(CO)_3Cl$ complex was placed in a round bottom flask with stir bar and the complex dissolved in just enough THF to assure homogeneity. This mixture was heated to reflux with stirring and then a molar equivalent of $AgClO_4$ in THF was added, followed by an excess of the appropriate pyridine derivative. A white powdery precipitate appears almost immediately. The reflux was continued until TLC (alumina plate, CH_2C1_2/CH_3CN (80%/20%) showed no remaining starting $Re(L_2)(CO)_3Cl$; usually <3 h. The reaction mixture was cooled, the AgCl removed by suction filtration and the solvent removed. The resulting yellow solid was purified via column chromatography using neutral alumina as the solid phase. The eluant was pure CH_2C1_2 at the start with increasing amounts of CH_3CN to isolate the desired product. The desired product was always the most abundant material with a characteristic yellow/green emission. The desired eluted fractions were combined, the solvent removed, and the solid dissolved in a minimum of CH_2C1_2. This concentrated solution was slowly dripped into a rapidly stirred excess of diethylether to produce the solid complex, which was isolated by suction filtration. The complexes were then characterized by ^{13}C NMR, IR, UV–vis, emission and lifetime measurements.

2.4. Complex characterization

$Re(bpy)(CO)_3Cl$: ^{13}C NMR (400 MHz, DMSO, ppm) (bpy) 124.52_9 128.09_1, 140.51_3, 153.15_2, 155.33_7; (CO's) 190.20_7, $197.99_1(2)$. I.r. (CO's) 2016.2 cm^{-1}, 1905.3 (shoulder) cm^{-1}, 1876.2 cm^{-1}.

$[Re(bpy)(CO)_3(pyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.57_7, 129.66_6, 142.00_3, 152.80_9, 154.69_9; (pyr) 127.54_4, 140.79_5, 156.60_3; (CO's) 192.49_1, $196.56_6(2)$. I.r. (CO's) 2027.9 cm^{-1}, 1946.2 (shoulder), 1922.9 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4\text{-}Mepyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.53_5, 129.63_1, 141.96_1, 152.04_3, 154.68_5; (pyr) 128.19_8, 153.58_9, 156.56_1; (CH_3) 20.93_5; (CO's) 192.57_5, $196.63_6(2)$. I.r. (CO's) 2027.9 cm^{-1}, 1946.2 (shoulder) cm^{-1}, 1928.7 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4\text{-}Etpyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.54_2, 129.63_1, 141.96_8, 152.26_8, 154.69_9; (pyr) 126.97_5, 156.59_6, 159.01_3; (CH_2) 28.40_3; (CH_3) 13.85_3; (CO's) 192.54_0, $196.65_7(2)$. I.r. (CO's) 2035.6 cm^{-1},1943.5 (shoulder) cm^{-1}, 1921.6 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$Re(bpy)(CO)_3(4\text{-}tBupyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.55_6, 129.62_4, 141.98_2, 152.27_5, 154.71_3; (pyr) 124.57_9, 156.63_8, 165.47_6; (C) 35.74_5; (CH_3 (3)) 29.90_7; (CO's) 192.54_0, $196.63_6(2)$. I.r. (CO's) 2027.9 cm^{-1}, 1928.7 (shoulder) cm^{-1}, 1911.2 cm^{-1}, (ClO_4^-) 1082.7 cm^{-1}.

$Re(bpy)(CO)_3(4\text{-}cHpyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.54_9, 129.62_4, 141.96_1, 152.42_3, 154.71_3; (pyr) 126.06_2, 156.62_4, 161.52_1; (c-hexene) 25.42_4, 28.81_8, 31.92_3, 39.76_4, 126.32_2, 127.79_0; (CO's) 192.55_4, $196.65_7(2)$. I.r (CO's) 2027.9 cm^{-1}, 928.7 (shoulder) cm^{-1}, 1911.2 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4\text{-}Phpyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.59_8, 129.65_9, 142.01_0, 153.01_3, 154.76_2; (pyr) 124.69_2, 151.93_8, 156.65_9; (phenyl) 128.00_2, 130.25_6, 131.50_0, 136.10_9; (CO's) 192.55_4,$196.61_6(2)$. I.r (CO's) 2032.1 cm^{-1},1935.4 (shoulder) cm^{-1}, 1916.6 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4\text{-}Phpropyr)]ClO_4$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.53_5, 129.63_1, 141.96_8, 152.20_5, 154.69_2; (pyr) 126.74_3, 156.59_6, 157.34_1; (phenyl) 127.48_1, 129.18_1, 142.53_7, 150.26_6; (CH_2) 31.92_3, 34.87_4, 35.52_0; (CO's) 192.56_1, $196.66_4(2)$. I.r (CO's) 2027.9 cm^{-1}, 1928.7 (shoulder) cm^{-1}, 1911.2 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4n\text{-}C_8pyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.53_5, 129.63_8, 141.96_8, 152.19_8, 154.70_6; (pyr) 127.45_3, 156.60_3, 157.88_2; (*n*-octyl) 14.22_5, 23.17_6, 29.51_3, 29.65_4, 29.71_7, 30.33_5, 32.34_5, 35.26_0; (CO's) 192.55_4, $196.65_7(2)$. I.r (CO's) 2027.9 cm^{-1}, 1928.7 (shoulder) cm^{-1}, 1911.9 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)3(4n\text{-}C_{13}pyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.56_3, 129.67_3, 142.00_3, 152.21_2, 154.70_6; (pyr) 127.46_0, 156.59_6, 157.85_4; (*n*-C_{13}) 14.28_8, 23.26_0, 29.56_3, 29.78_7, 29.93_5, 29.99_8, 30.13_9, 30.18_8, 30.20_9, 30.22_3, 30.35_6, 32.49_9, 35.28_9; (CO's) 192.55_4, $196.66_4(2)$. I.r (CO's) 2027.9 cm^{-1}, 1928.7 (shoulder) cm^{-1}, 1911.9 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

$[Re(bpy)(CO)_3(4\text{-}PrOHpyr)](ClO_4)$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (bpy) 125.54_9, 129.63_1, 141.96_1, 152.21_9, 154.70_6; (pyr) 127.53_0, 156.61_0, 157.55_9; (CH_2) 31.80_4, 33.23_0, 61.14_4; (CO's) 192.56_8, $196.66_4(2)$. I.r (CO's) 2027.9 cm^{-1}, 1928.7 (shoulder) cm^{-1}, 1911.2 cm^{-1}, (ClO_4^-) 1094.3 cm^{-1}, (OH) 3544.9 cm^{-1}.

$[Re(phen)(CO)_3Cl$: ^{13}C NMR (400 MHz, DMSO, ppm) (phen) 126.81_3, 128.01_4, 130.74_0, 139.60_7, 146.01_4, 153.77_1; (CO's) 190.17_1, $197.85_8(2)$. I.r. (CO's) 2016.2 cm^{-1}, 1922.9 cm^{-1}, 1887.8 cm^{-1}.

[Re(phen)(CO)$_3$(4-Phpropyr)]ClO$_4$: ^{13}C NMR (400 MHz, CD_3CN, ppm) (phen) 127.93_8, 128.95_7, 129.11_8(2), 132.09_7, 152.15_6; (pyr) 126.68_0, 155.34_5, 157.26_4; (phenyl) 127.33_4, 128.95_7, 142.47_4,147.36_4; (CH_2) 31.81_8, 34.77_6, 35.42_9; (CO's) 192.46_3, 196.57_3(2). I.r. (CO's) 2027.9 cm^{-1}, 1922.9 cm^{-1}, 1905.4 cm^{-1}, (ClO_4^-) 1088.5 cm^{-1}.

2.5. Equipment and procedures

Absorption spectra were taken with either a Hewlett-Packard 8452A diode array spectrometer or a Perkin-Elmer Lambda 2S spectrometer. Emission spectra were obtained using a Spex FluorMax fluorometer. The emission spectra, both regular and integrated, were background and instrument response corrected. The ratio of quantum yields for the bound and unbound forms was determined from the ratio of the appropriate corrected, integrated emission spectra. This ratio was also corrected for minor (>1%) differences in solution absorbance.

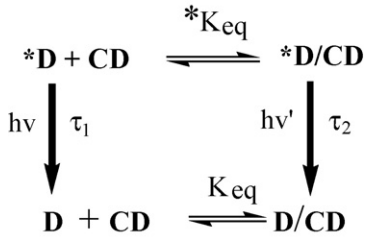
Lifetimes were measured using an apparatus consisting of an LSI nitrogen laser as the excitation source (λ = 337 nm). The sample compartment was of local design incorporating a Corion interference filter to remove plasma glow from the laser pulse, glass filters and saturated $NaNO_2$ to remove scattered laser light from the detector path, and an R928 PMT as detector. The decays were captured and averaged using a Hewlett-Packard 54502A digital scope and the data transferred via an HP-IB to a PC where it was processed using locally written software. At least 64 transients were averaged for each experiment. Unless specifically noted, all lifetimes refer to air saturated solutions.

Non-aqueous solutions were prepared by simply dissolving the complex in the appropriate solvent to obtain an absorbance of ~0.1 at 337 nm. The aqueous solutions were prepared by stirring an excess of the complex with either pure H_2O or D_2O for about 1 h at room temperature. This solution was then filtered using Whatman #42 filter paper and the filtrate then passed through a Gelman Acrodisc with a 0.45 μm pore size. This saturated solution was then divided. To one portion was added sufficient solid α- or β-CD to make a 10 mM in CD stock solution. The two complex saturated stock solutions, with and without the CD, were then blended to obtain concentrations of CD ranging from 0 to 10 mM.

Deaerated solutions were prepared by purging the appropriate solution with solvent saturated Ar for at least 20 min. A lifetime measurement was then made and the solution purged again for an additional 5 min. If both lifetimes were within ±5%, adequate purging was assumed.

2.6. Data reduction and analysis

Lifetime data as a function of cyclodextrin concentration for each complex were analyzed using the simple 1:1 binding model shown below. Here the photon absorption is not shown. In this scheme D is the Re(I) complex, CD is α- or β-cyclodextrin and D/CD is the Re(I) complex bound to the cyclodextrin. τ_1 and τ_2 are the lifetimes of the unbound and bound form of the complex, respectively, and K_{eq} and $^*K_{eq}$ are the equilibrium constants for formation of the complex in the ground and excited state,



Scheme 1.

respectively. If the exchange rate for *D between the bound and unbound forms is slow compared to the decay of the excited state, then two distinct lifetimes are expected. This situation corresponds to the slow exchange limit. In this case K_{eq}, but not $^*K_{eq}$ is extracted from the lifetime variation with [CD]. The model, based on lifetime differences, is independent of exciting λ (Scheme 1).

In all cases, the decays with added CD could be fit to a two exponential expression of the form

$$I(t) = A_1 \exp\left(\frac{-t}{\tau_1}\right) + A_2 \exp\left(\frac{-t}{\tau_2}\right) \quad (1)$$

where A_1 and A_2 are the pre-exponential weighting factors and the τ's as discussed above. Because only two lifetimes, one of which was the free complex value, were required for each complex over the entire β-CD concentration range, we conclude that dynamically this system is in the slow exchange limit (i.e. the decay of the excited state is fast relative to the exchange process). Further, the unbound form always exhibited the shorter τ.

The decay data were fit to Eq. (1) using Genplot, a commercial non-linear least squares fitting package. For the stronger binding complexes, the two τ's were determined from the limiting decays in water and 10 mM CD respectively; at which point these complexes had reached a plateau. The optimal values for the A's were then determined with the τ's fixed at the appropriate limiting values. In all cases, good fits were obtained. For weaker binding complexes, A_1, A_2 and τ_2 were allowed to float when fitting with Eq. (1). Again, good fits were obtained and a consistent value for τ_2 as well as realistic values for A_1 and A_2.

The A's and, where necessary, τ_2 values obtained from fitting Eq. (1) were then used to determine the binding constants for the complex/cyclodextrin interaction using the following equation [13]:

$$\left(\frac{\phi_1}{\tau_1}\right)\left(\frac{\tau_2}{\phi_2}\right)\frac{A_2}{A_1} = K_{eq}[\beta - \mathrm{CD}] \quad (2)$$

where the subscripts 1 and 2 refer to the unbound and bound forms, respectively, ϕ's are the quantum yields whose ratio is found from the corrected integrated emission spectra, and the τ's are the limiting lifetimes for the complex free and fully bound. Plots of the Left Hand Side (lhs) of Eq. (2) versus the β-CD concentration were linear and the residuals randomly distributed around 0 for all complexes. For complexes with $K_{eq} > 1\ \mathrm{mM}^{-1}$, the plots plateaued at high β-CD concentration (10 mM). These results are again entirely consistent with the slow exchange limit.

3. Results

3.1. Photophysical changes on inclusion into β-CD

Table 1 presents some baseline photophysical properties of the complexes used. There are several trends that are germane to this study. First, for a given solvent, the emission λ_{max} is virtually independent of the R group in the 4 position of the pyridine or spectator ligand. Thus, the tether used has little effect on the MLCT energy of the complex and can be tailored for its anchoring properties without worry about the impact on the photophysical properties of the main chromophore. The same trend is also seen in the lifetimes, suggesting that the R group has minimal impact on the non-radiative rate (the radiative rate is assumed constant for a given series such as bpy or phen). The complexes do show modest solvatochromism, as is well known for Re(I) complexes [14]. However, the shift in MLCT energy with solvent is very modest. A much larger variation with solvent is noted for the lifetimes and this is attributed to changes in k_{nr} with solvent (*vide infra*). In this regard, H_2O is especially efficient in deactivation of the excited state, as has been observed for other metal complexes [15]. Note particularly, that Ar purging results in only a modest increase in the lifetime for the bpy complexes in water as the non-radiative rate is already large.

The typical effect of CD binding on the emission spectra of the complexes is illustrated in Fig. 1. The λ_{max} for the CD-bound complex is between the values of pure water and CH_2C1_2, a representative hydrophobic solvent, which is consistent with some type of solvent shielding by the inclusion into the β-CD. In addition, the quantum efficiency in deoxygenated water is increased by nearly a factor of 2 on binding, which was typical for the majority of the complexes studied. This, along with the pronounced increase in lifetime with addition of β-CD supports the assertions that (1) the complexes bind to β-cyclodextrin, (2) that such binding has a pronounced effect on the photophysical properties, and (3) that since only the pyr complex showed no evidence of binding the –R tethers are a critical component.

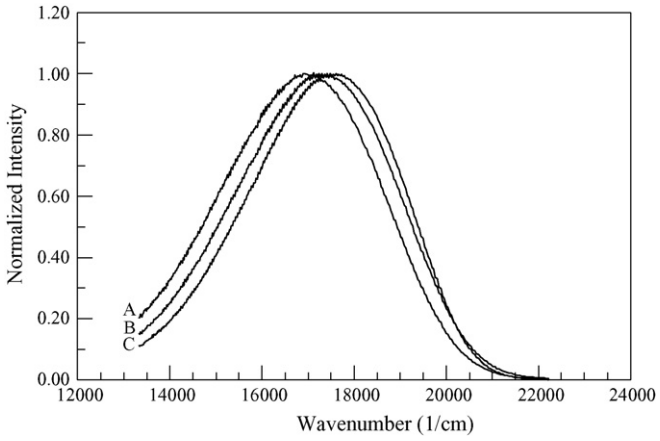


Fig. 1. Normalized corrected emission spectra of [Re(bpy)(CO)$_3$(4-phenylpyridine)][ClO_4] in water, A; 10 mM β-CD, B; CH_2C1_2, C. Samples were air saturated.

Table 1
Photophysical properties: emission maxima, luminescence lifetimes and oxygen quenching constants for [L_2Re(CO)$_3$(4-R-pyr)][ClO_4] complexes in various solvents at room temperature (~22 °C)

	Solvent	Emission λ_{max} (nm)	τ (ns), air saturated	τ (ns), Ar purged	k_q ($\times 10^{-8}$ M^{-1} s^{-1})
[Re(bpy)(CO)$_3$(4-R-pyr)][ClO_4]					
R=					
H–	CH_2Cl_2	554 ± 2	491	625	2.3
CH_3–	H_2O	568 ± 2	74	88	[a]
CH_3–	CH_2Cl_2	556 ± 2	449	564	2.4
C_2H_5–	H_2O	569 ± 2	80	82	[a]
C_2H_5–	CH_2Cl_2	556 ± 2	403	535	3.2
C_2H_5–	CH_3OH	576 ± 2	119	172	12.8
C_2H_5–	CH_3CN	580 ± 2	115	235	27.4
$(CH_3)_3C$–	H_2O	575 ± 2	82	94	[a]
$(CH_3)_3C$–	CH_2Cl_2	560 ± 2	407	535	3.1
$(CH_3)_3C$–	CH_3CN	580 ± 2	115	208	24.0
c-C_6H_9–	H_2O	572 ± 2	92	100	[a]
c-C_6H_9–	CH_2C1_2	555 ± 2	396	519	3.1
C_6H_5–	H_2O	571 ± 2	96	104	[a]
C_6H_5–	CH_2C1_2	556 ± 2	428	575	3.1
C_6H_5–$(CH_2)_3$–	H_2O	577 ± 2	89	96	[a]
C_6H_5–$(CH_2)_3$–	CH_2C1_2	557 ± 2	404	537	3.2
CH_3–$(CH_2)_7$–	H_2O	575 ± 2	83	85	[a]
CH_3–$(CH_2)_7$–	CH_2Cl_2	562 ± 2	397	518	3.1
CH_3–$(CH_2)_{12}$–	H_2O	573 ± 2	85	89	[a]
CH_3–$(CH_2)_{12}$–	CH_2Cl_2	558 ± 2	380	531	3.9
CH_3–$(CH_2)_{12}$–	CH_3CN	–	120	260	27.7
[Re(phen)(CO)$_3$(4-R-pyr)][ClO_4]					
C_6H_5–$(CH_2)_3$–	H_2O	561 ± 2	451	685	28.6
C_6H_5–$(CH_2)_3$–	CH_2Cl_2	545 ± 2	1182	2297	2.7

[a] No k_q reported due to the small differences in τ's for air saturated and purged water solutions.

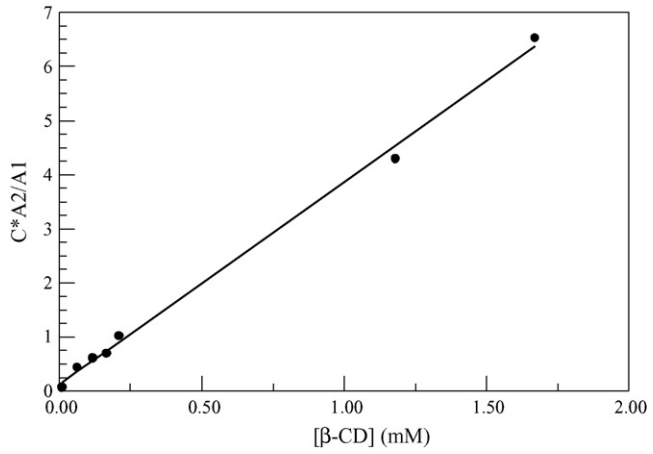


Fig. 2. Plot of lhs of Eq. (2) vs. β-CD concentration, where $C = (\phi_1/\tau_1)(\tau_2/\phi_2)$ for $[Re(bpy)(CO)_3(4\text{-}nC_8pyr)][ClO_4]$.

Aqueous solutions of all complexes with R > CH_3 showed significant lifetime increases with the addition of β-CD. Luminescent decays for complexes in solutions with no β-CD could be fit with a single exponential, while those with β-CD required two exponential terms, Eq. (1). Using limiting values for τ(unbound) = τ_1 and τ(bound) = τ_2 (vide supra), decays for the entire concentration range of added β-CD could be fit to Eq. (1). The *A*'s and τ's so determined were then used in Eq. (2) to determine the binding constant, K_{eq}. A typical plot is shown in Fig. 2.

3.2. Evaluation of binding constants

The information obtained from fitting Eq. (2) and other relevant parameters for the various complexes are presented in Table 2. The binding of the complexes to β-CD can be detected through both lifetime and emission intensity changes for all the *R*'s > CH_3. No changes of any kind in the lifetime, emission maxima, or quantum yield, were observed with up to 10 mM β-CD for the parent unsubstituted pyridine, 4-R = H, complex with either bpy or phen as the chromophoric ligand. With 4-R = CH_3, there is some evidence for binding in that β-CD does enhance the emission quantum yield by about 23%, which was well outside experimental error. However, no detectable changes in lifetime or emission maxima were seen for this complex. As expected, the binding of the complexes to the β-CD becomes stronger as the hydrophobicity of the 4-R group increases, at least up to a point. The K_{eq}'s for binding found here are of a similar magnitude to those seen in earlier studies involving Ru(II) [10c,16] and Re(I) [9a] complexes.

Table 2
Summary of binding constants, quantum yield ratios, and life time ratios for $[L_2Re(I)(CO)_3(4\text{-R-pyr})][ClO_4]$ complexes in aqueous β-CD at ~22 °C

	K_{eq} $(mM)^{-1}$	ϕ_f (bound)/ϕ_f (unbound)	τ (bound)/τ (unbound)
L_2 = bpy, R=			
–H	0	1.0	1.0
$-CH_3$	[a]	1.23	1.16
$-C_2H_5$	0.224	1.66	1.68
$-(CH_2)_2-CH_2OH$	0.364	1.61	1.37
-*t*-C_4H_9	6.46	1.82	1.81
c-C_6H_9	5.51	1.78	1.61
c-C_6H_9/D_2O	5.86	1.57	1.46
$-C_6H_5$	0.725	1.80	1.78
$-(CH_2)_3-C_6H_5$	1.32	1.42	1.38
$-(CH_2)_7-CH_3$	3.73	1.24	1.26
$-(CH_2)_{12}-CH_3$	[b]	1.13	1.20
L_2 = phen, R=			
$-(CH_2)-C_6H_5$	1.90	1.26	1.28

[a] Not determined due to insufficient differences in lifetimes.
[b] Not determined due to very low complex solubility in water.

In addition to the main trend in K_{eq} with hydrophobicity, a number of interesting facets are revealed by the data. In addition to the gross size of the hydrophobic group, its geometry is also an important consideration as shown by the large increase seen for *t*-butyl as compared to ethyl. The substitution of two methyls for two hydrogens on ethyl results in a 30-fold increase in K_{eq}. A comparison of the cyclohexene and phenyl groups is both interesting and puzzling. Using water solubility as a proxy for hydrophobicity, we expect the two to have a similar hydrophobic character [17] and the planar aspect of the phenyl would suggest easier insertion into the β-CD cavity. The cyclohexene is a bent plane and why it binds about eight times better is not altogether obvious. K_{eq} is a ratio of forward and reverse rates and one might suggest that the insertion or forward rate is similar for both. However, the releasing process is hindered for the bent group as it can "catch" on the internal OH's of the cavity as it tries to leave. The result, not unlike barbs on a fishhook, is a reduced rate of exit and a higher binding constant. Interestingly, addition of a propyl linkage between the pyridine and the phenyl results in a rough doubling of the binding, though still inferior to the *t*-butyl group.

That the binding constants are not higher for the longer alkyl chain groups such as R = $-C_8H_{17}$ is a surprise. However, with the longer alkyl chain the β-CD unit is likely, on average, quite far from the chromophore (vide infra), and its impact is muted. This means a somewhat less accurate determination of the binding constant and it may be that the K_{eq}'s for these groups are not that different. The CD-chromophore distance reaches an extreme with the R = $-(CH_2)_{12}CH_3$ group, which should surely bind, but which may be so long that the CD does not interact with the chromophore and does not significantly affect the photophysics other than a slight increase in the quantum yield. This same muting effect as the length of the tether increases beyond a certain point was observed in earlier work [9a]. Comparison of the $\phi_{bound}/\phi_{unbound}$ or $\tau_{bound}/\tau_{unbound}$ ratios for phenyl versus propylphenyl shows that even though the propylphenyl binds more readily, the impact on the brightness and lifetime is muted by the greater average distance between the β-CD and the chromophore.

An interesting comparison involves the binding constants for R = ethyl, 3-hydroxypropyl and *t*-butyl. Given the nearly 30-fold increase in binding between R = $-C_2H_5$ and R = $-C(CH_3)_3$, one would reasonably expect a ~5–10-fold increase for R = $-CH_2CH_2CH_3$. However, our complex has an –OH in the terminal position and the unfavorable interaction between the hydrophillic OH group of the R and the hydrophobic CD cavity

for R = –$CH_2CH_2CH_2OH$ limit the increase to about 60% compared to R = –C_2H_5.

The ratios of bound to unbound quantum yields and lifetimes track each other closely as shown in Table 2, suggesting that changes in k_{nr} are responsible for the increased lifetimes and luminescence efficiencies for the bound form. The ratio of ϕ_f(bound)/ϕ_f(unbound) × τ(unbound)/τ(bound) yields the ratio of k_r's for the bound and unbound forms. This ratio is ∼1 (within 15%) for all the complexes studied. Thus, whatever protective function the β-CD is playing, the mechanism involves reduction of one or more nonradiative energy loss channels. That k_r is little affected by binding is not unexpected [18].

Two complexes, 4-*t*Bupyr and 4-cHxpyr, which bind well to β-CD, were tried with α-CD to see if similar changes in the photophysics occurred. In the range of 0–10 mM of α-CD, no change in either lifetime or quantum yield could be detected. We cannot say whether binding simply did not occur or that binding occurred but did not result in observable changes. Given the high sensitivity of the luminescence to CD binding, we favor the former on intuitive grounds, but the question is open at this point.

4. Discussion

4.1. Comparison with prior work

In previous studies of the interaction of metal complexes with β-CD there was clearly an oxygen shielding effect with the Re complexes studied [9a]. Indeed, the limiting lifetimes for the complexes at high β-CD concentration approached those observed without added β-CD but with vigorous nitrogen purging. Clearly that cannot be the mechanism for the observed changes in the present study. Bound lifetimes and quantum yields well exceed those for carefully purged samples but without added β-CD. In addition the fractional τ change for air saturated versus nitrogen purged Re(bpy) complexes was between 0.08 and 0.10. For those complexes with $K_{eq} > 2$, at 10 mM β-CD where virtually all the complex is bound, the fractional change for air saturated and nitrogen purged was also between 0.08 and 0.10. We suggest that the mechanism in this case is protection from solvent quenching. Water is well known to be an efficient deactivator of the excited state, primarily through the O–H vibration [19]. Indeed, many complexes have significantly longer τ's in D_2O compared with H_2O, which is direct evidence for OH quenching. Our complexes are no exception in that for the complex with R = cyclohex-2-ene, τ = 92 ns for the H_2O while for D_2O, τ = 148 ns, both for aerated solutions. If our model is correct, then the impact of protection by β-CD from the solvent should be greater for a given complex in H_2O than in D_2O. That is indeed the case as the limiting τ's (complete binding at 10 mM β-CD) for the R = cyclohex-2-ene complex are 148 and 219 ns for air saturated H_2O and D_2O, respectively. Thus, the percentage increase in τ on binding is 62% and 48%, respectively. This finding supports our suggestion that providing protection from the solvent is the major mode of action by the β-CD. This is also supported by the finding that decreases in k_{nr} account for observed changes in lifetime and quantum yield.

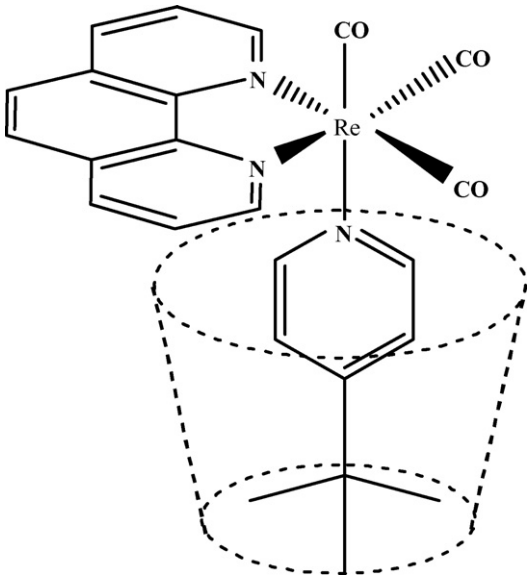


Fig. 3. Schematic of β-CD binding to the anchor ligand, a 4-alkylpyridine.

4.2. Solvent quenching model

While shielding from oxygen quenching by the β-CD is not a significant effect for the majority of this series, it may be important with longer lived complexes. The short lifetimes for the majority of the complexes reported here and the limited solubility of oxygen in water reduce the impact of oxygen quenching and allow the effects of solvent quenching to be observed.

The question arises as to how the β-CD can provide protection to the chromophore when it is bound to a spectator ligand. Very simple molecular mechanics modeling shows that these Re(I) complexes resemble a one tentacled jelly fish. When the β-CD, which resembles a lamp shade accepts the anchor R group, the β-cyclodextrin can be drawn up close to the body of the complex and effectively shields the underside of the complex from solvent interaction. Fig. 3 shows a representation of the binding of β-CD to the anchor ligand of the complex. This picture is supported by the *F* number calculated for the R = cyclohex-2-ene complex. Previously, we have shown that one can estimate the fraction of the complex that is exposed to an aqueous environment by calculating a ratio of lifetimes called the *F* number [20]. The expression used is

$$F = \frac{(\tau_{H,bound})^{-1} - (\tau_{D,bound})^{-1}}{(\tau_{H,unbound})^{-1} - (\tau_{D,unbound})^{-1}} \quad (3)$$

where the subscripts H and D refer to H_2O and D_2O. If both the bound and unbound forms experience the same local environment then the *F* number is 1, while an $F \sim 0$ implies that the bound form is completely protected from the water solvent. For our system with R = cyclohex-2-ene, the *F* value is 0.53. This implies that bound form experiences about 1/2 the water exposure of the unbound form, in good agreement with our physical picture of the protective mechanism for β-CD. Simple molecular mechanics modeling also suggests that the steric requirement for CD inclusion by our two bulkiest R groups for which good binding is observed is between 4.3 A for *t*-butyl and 4.9 A for the

cyclohexene R groups. This is well within the cavity dimension for β-CD of 6.0–6.4 A [21]. However, the bipyridine requires about 9.3 A and cannot be well shielded by direct inclusion. Thus, protection of the chromophoric portion of the complex must be indirect and a portion of the included complex remains exposed to both solvent and oxygen. In the complexes reported here, their rather short lifetime and the modest oxygen solubility in water allows the solvent quenching to dominate.

5. Conclusions

For complexes of the type $[L_2Re(CO)_3(4R\text{-}L')][ClO_4]$, where L′ is not the chromophoric ligand, suitable localizing, based on hydrophobic interaction, can be affected by judicious choice of the R group. When R is chosen for its hydrophobic qualities, then facile inclusion into β-CD of a typical guest–host nature is observed. The binding is strong and the binding constants reflect the relative hydrophobicity of R and also its spatial structure. A 30-fold variation in binding was observed for the series used here. It is possible to localize the probe using the hydrophobic pocket of the host, yet allow the chromophoric portion of the molecule to experience the environment external to host.

Recent work on luminescent metal complexes as sensors suggests that lifetime measurements are more reliable than intensity measurements as they are less sensitive to deterioration of the optical system, photobleaching of the sensor material, or fouling of the device when placed in a real application [22]. The relatively long lifetimes of many metal complexes allows the use of simpler lifetime instrumentation than is required for the much shorter lived organic sensors. This salutary feature comes at a price in that long lived metal complexes are subject to oxygen quenching and this is a significant effect for which some type of correction must be applied. This work suggests that there may be a lifetime window in which oxygen quenching is a minimal problem, yet lifetime measurements can still be made employing relative inexpensive equipment. However, since many sensor applications involve water as the host solvent, one must be aware that solvent quenching may be important and that by proper sequestering of the complex solvent problems can be minimized while retaining essential sensor functions.

Acknowledgements

We wish to thank the National Science Foundation (CHE 97-26999), the Petroleum Research Fund (29550-B3), and the Dreyfus Foundation (Senior Mentor Program) for their generous support.

References

[1] (a) J.R. Lakowicz (Ed.), Topics in Luminescence Spectroscopy. Probe Design and Chemical Sensing, vol. 4, Plenum Press, New York, 1994;
(b) O.S. Wolfbeis, J. Mater. Chem. 15 (2005) 2657.
[2] (a) O.S. Wolfbeis (Ed.), Fiber Optic Chemical Sensors and Biosensors, CRC Press, Boca Raton, FL, 1991;
(b) A.P. de Silva, H.Q.N. Gunaratne, T. Gunnlaugsson, A.J.M. Huxley, C.P. McCoy, J.T. Rademacher, T.E. Rice, Chem. Rev. 97 (1997) 1515;
(c) J.N. Demas, B.A. DeGraff, Anal. Chem. 71 (1999) A793;
(d) J.N. Demas, B.A. DeGraff, J. Chem. Ed. 74 (1997) 690 (and other articles in that issue).
[3] J.N. Demas, B.A. DeGraff, Coord. Chem. Rev. 211 (2001) 317.
[4] Y. Amao, Microchim. Acta 143 (2003) 1 (review).
[5] O.S. Wolfbeis, Anal. Chem. 76 (2004) 3269 (review).
[6] (a) C. Malins, H.G. Glever, T.E. Keyes, J.G. Vos, W.J. Dressick, B.D. MacCraith, Sens. Actuators B 67 (2000) 89;
(b) M. Montalti, S. Wadhwa, W.Y. Kim, R.A. Kipp, R.H. Schmehl, Inorg. Chem. 39 (2000) 76;
(c) H.-F. Ji, Y. Shen, J.P. Hubner, B.F. Carroll, R. Schmehl, J.A. Simon, K.A. Schanze, Appl. Spectrosc. 54 (2000) 856.
[7] S.G. Schulman, O. Wolfbeis (Eds.), Molecular Luminescence Spectroscopy: Methods and Applications: Part 2., John Wiley & Sons, New York, 1988.
[8] K.A. Kneas, W. Xu, J.N. Demas, B.A. DeGraff, Appl. Spectrosc. 51 (1997) 1346 (and references therein).
[9] (a) L. Sacksteder, M. Lee, J.N. Demas, B.A. DeGraff, J. Am. Chem. Soc. 115 (1993) 8230;
(b) G.A. Reitz, J.N. Demas, B.A. DeGraff, E.M. Stephens, J. Am. Chem. Soc. 110 (1988) 5051;
(c) A. LouAnn Sacksteder, A.P. Zipp, E.A. Brown, J. Streich, J.N. Demas, B.A. DeGraff, Inorg. Chem. 29 (1990) 4335.
[10] (a) D. Ducheme (Ed.), Cyclodextrins and Their Industrial Uses, Editions de Sante, Paris, 1987;
(b) K. Uekama, M. Otagiri, Crit. Rev. Ther. Drug Carrier Syst. 3 (1987) 1;
(c) W. Xu, A. Jain, B.A. Betts, B.A. DeGraff, J.N. Demas, J. Phys. Chem. A 106 (2002) 251;
(d) W. Sliwa, T. Girek, Heterocycles 60 (2003) 2147;
(e) F. Hapiot, S. Tillory, E. Monflier, Chem. Rev. 106 (2006) 767.
[11] D.L. Ciana, I. Hamachi, T.J. Meyer, J. Org. Chem. 54 (1989) 1731.
[12] L. Sacksteder, J.N. Demas, B.A. DeGraff, Inorg. Chem. 28 (1989) 1787.
[13] S.W. Snyder, PhD Thesis, University of Virginia, Charlottesville, 1988.
[14] (a) M.S. Wrighton, D.L. Morse, J. Am. Chem. Soc. 96 (1974) 998;
(b) P.J. Giordano, S.M. Fredericks, M.S. Wrighton, D.L. Morse, J. Am. Chem. Soc. 100 (1978) 2257;
(c) P.J. Giordano, M.S. Wrighton, J. Am. Chem. Soc. 101 (1979) 2888.
[15] (a) J.V. Caspar, T.J. Meyer, J. Am. Chem. Soc. 105 (1983) 5583;
(b) J. Van Houten, R.J. Watts, J. Am. Chem. Soc. 98 (1976) 4853.
[16] J.I. Cline III, W.J. Dressick, J.N. Demas, B.A. DeGraff, J. Phys. Chem. 89 (1985) 94.
[17] http://www.inchem.org/documents/icsc/icsc/eics0015.htm and http://www.oecd.org/dataoecd/39/51/33649424.pdf
[18] (a) J.V. Caspar, B.P. Sullivan, E.M. Kober, T.J. Meyer, Chem. Phys. Lett. 91 (1982) 91;
(b) J.V. Casper, E.M. Kober, B.P. Sullivan, T.J. Meyer, J. Am. Chem. Soc. 104 (1982) 630.
[19] (a) W.D. Horrocks Jr., Meth. Enzymol. 226 (1993) 495;
(b) W.D. Horrocks Jr., D.R. Sudnick, Acc. Chem. Res. 14 (1981) 384;
(c) W.D. Horrocks Jr., D.R. Sudnick, Science 206 (1979) 1194;
(d) W.D. Horrocks Jr., D.R. Sudnick, J. Am. Chem. Soc. 101 (1979) 334;
(d) S. Salama, F.S. Richardson, J. Phys. Chem. 84 (1980) 512.
[20] B.L. Hauenstein Jr., W.J. Dressick, S.L. Buell, J.N. Demas, B.A. DeGraff, J. Am. Chem. Soc. 105 (1983) 4251.
[21] W. Saenger, Angew. Chem. Int. Ed. Engl. 19 (1980) 344.
[22] J.R. Lakowicz, Principles of Fluorescence Spectroscopy, 2nd ed., Kluwer Academic/Plenum Publishers, New York, 1999.