

Synthesis and Spectroscopic Studies on Azo-Dye Derivatives of Polymetallic Lanthanide Complexes: Using Diazotization to Link Metal Complexes Together

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Lanthanide complexes have been widely used in a variety of imaging and assay related applications. In particular, gadolinium complexes have been used as contrast agents in magnetic resonance imaging,¹ while luminescent lanthanide ions are widely used in bioassay² and imaging.³ In such applications, it is important to be able to control the local environment around the metal and form kinetically stable complexes.⁴ For instance, in magnetic resonance imaging a complex should allow close approach and rapid exchange of water molecules, while retaining sufficient kinetic stability to be excreted intact. The case is altered for luminescence applications, since the excited states of lanthanide ions are quenched nonradiatively by vibrational harmonics of the O–H oscillator and it is therefore desirable to exclude water molecules from the inner sphere.⁵ Since electric dipole f–f transitions are Laporte forbidden and have very low extinction coefficients, sensitizing chromophores are often incorporated into the ligand structure: these can sensitize emission from the lanthanide excited state and lead to dramatic enhancement of the emission from the metal center.⁶ Energy transfer from the chromophore to the metal is usually mediated via the chromophore triplet state,⁷ though other mechanisms have also been shown to be viable in some complexes.^{8,9}

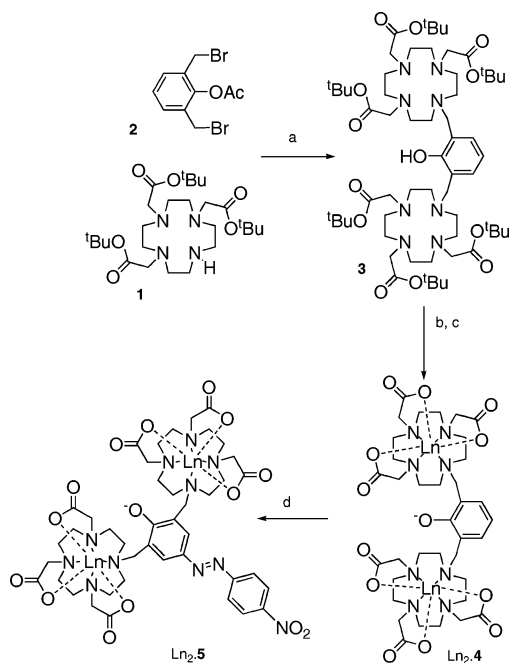
Kinetically stable complexes can also be used as building blocks for more complicated systems¹⁰ and can even be used in the preparation of heterometallic lanthanide complexes containing different lanthanide ions.¹¹

We now report how related bimetallic complexes can be linked together using diazotization reactions that generate a chromophore at the heart of the assembly, permitting visible light excitation of the bound lanthanide ions.

The synthesis of phenolic complexes suitable for reaction with diazonium salts is outlined in Scheme 1. Reaction of the well-known DO3A derivative¹² (**1**) with 2,6-bis(bromomethyl)phenoxy acetate (**2**) in the presence of cesium carbonate followed by aqueous workup yielded **3**. NMR revealed that cleavage of the phenoxy acetate ester had occurred under the reaction conditions, obviating the need for its subsequent removal.

Cleavage of the *tert*-butyl esters in trifluoroacetic acid unmasked both lanthanide binding sites, and treatment with lanthanide triflate salts resulted in the formation of bimetallic complexes [**Ln₂·4**][–] (Ln = Nd, Yb). Reaction of [**Ln₂·4**][–] with a 4-nitrophenyl diazonium salt in aqueous solution resulted in the formation of azo dyes [**Ln₂·5**][–] (Ln = Nd, Yb). These were purified using size selective dialysis tubing to separate any unreacted [**Ln₂·4**][–] from the product.

Scheme 1. Synthesis and Diazotization of Phenol Bridged Bis-Macrocycles and Their Complexes^a



^a Reagents and Conditions: (a) Cs₂CO₃, MeCN reflux, 72 h; (b) tfa, CH₂Cl₂, 48 h; (c) Ln(OTf)₃, MeOH, 50 °C, 48 h; (d) 4-nitroaniline, NaNO₂, HCl, 0 °C, 0.5 h.

As expected, azo dye formation results in a color change: the [**Ln₂·4**][–] complexes are colorless, while [**Ln₂·5**][–] complexes are deep red, owing to the increased conjugation between the phenolic oxygen donor and the nitro group acceptor.

All the complexes were found to be emissive in the near-IR region of the spectrum, and data fitted well to single exponential decays, suggesting that the conformers of the complex are in fast exchange on the luminescence time scale, unlike the case of an analogous complex with a 4-methyl substituent on the phenol bridge, for which double exponential behavior has been observed.¹³ Time resolved luminescence spectroscopy was used to establish the luminescence lifetimes of the complexes, and the number of inner sphere water molecules in the ytterbium complexes was determined from the luminescence decay constants in H₂O and D₂O using the formula

$$q = 1.0(k_{\text{H}_2\text{O}} - k_{\text{D}_2\text{O}} - 0.1)$$

where *q* is the number of bound water molecules at each ytterbium ion, and *k*_{H₂O} and *k*_{D₂O} are the observed rate constants in H₂O and

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D₂O, respectively (with units of μs^{-1}).¹⁴ No values were calculated based on neodymium luminescence owing to the large variations in lifetime with ligand structure in such systems.² The photophysical properties of the lanthanide complexes are shown in Table 1.

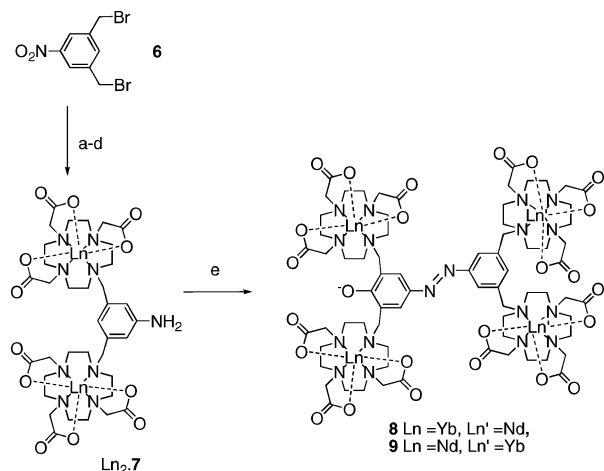
Table 1. Photophysical Properties of the Complexes^a

compound	$\lambda_{\text{em}}/\text{nm}$	$\tau_{\text{H}_2\text{O}}/\text{ns}$	$\tau_{\text{D}_2\text{O}}/\text{ns}$	q_{Yb}
Nd ₂ .4	1055	98	301	
Yb ₂ .4	980	1620	4510	0.3
Nd ₂ .5	1340	112	355	
Yb ₂ .5	980	1410	4020	0.4
Nd ₂ .7	1055	102	334	
Yb ₂ .7	980	1600	5310	0.3
8	980	1950	5120	0.2
8	1340	140	320	
9	980	1750	5170	0.3
9	1340	160	400	

^a All complexes exhibited emission following excitation at 337 nm. For [Ln₂.5][−] and **8** and **9**, excitation at 420 nm gave lifetimes within error of those given in the table.

Having prepared and studied bimetallic systems, we turned our attention to the preparation of heterotetrametallic arrays. Scheme 2 shows the synthetic strategy employed. The bis-macrocyclic **7** was prepared using an established procedure as shown in Scheme 2.¹⁵ Complexation with the lanthanide triflate yielded the bimetallic complexes Ln₂.7. Reaction of Ln₂.7 with sodium nitrite in dilute hydrochloric acid followed by addition of [Ln'.2.4][−] yielded the tetrametallic complexes **8** and **9**.

Scheme 2. Synthesis of Tetrametallic Complexes^a



^a Reagents and Conditions: (a) Cs₂CO₃, **1**, MeCN, reflux, 72 h; (b) tfa, CH₂Cl₂, 48 h; (c) Ln(OTf)₃, MeOH, 48 h; (d) N₂H₄, Pd/C, MeOH, 1 h; (e) NaNO₂, HCl, Ln'.2.4, NaOH, 0 °C, 0.5 h.

Both **8** and **9** were found to be luminescent; time-gated emission spectra are shown in Figure 1. The short-lived signals arising from neodymium emission dominate the early part of the luminescence spectrum (Figure 1a), and the ratio of the peaks at 1340 and 1055 nm for the two isomers clearly indicates that the neodymium centers are in different environments in the different complexes. Similarly, the later part of the luminescence (Figure 1b) shows the ytterbium signal after the overlapping neodymium emission has decayed. In this case the fine structure of the ²F_{5/2}–²F_{7/2} transition indicates differences in the ytterbium environment between **8** and **9**. Luminescence lifetimes and values for q_{Yb} are shown in Table 1. In this case lifetime measurements are less informative: **8** and **9** both exhibit low values for q_{Yb} despite the differences in ligand denticity in the octadentate and heptadentate sites in the molecule,

conceivably as a result of steric crowding in the tetrametallic complex inhibiting access by solvent to the metal center; indeed q_{Yb} for Yb₂.7 is the same as q_{Yb} for **9**, while q_{Yb} for Yb₂.5 is within error of that for **8**.

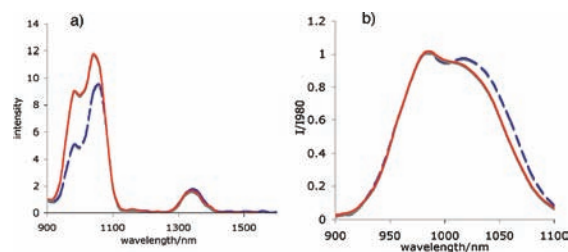


Figure 1. Time-gated emission spectra of D₂O solutions containing **8** (dashed line) and **9** (solid line): (a) in the period between 500 and 1000 ns after the laser pulse; (b) from 3 to 6 μs after the laser pulse, normalized at 980 nm.

The stability of systems such as these in the forcing conditions inherent to diazotization reactions is further evidence for the kinetic inertness of such complexes. This approach allows not only the preparation of heterometallic systems containing different lanthanide ions but also the simultaneous incorporation of a sensitizing chromophore.

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Supporting Information Available: Experimental procedures and characterization data for synthesis of compounds and complexes, absorption and (time-resolved) emission spectra of complexes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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