ACCOUNTS
of chemical research

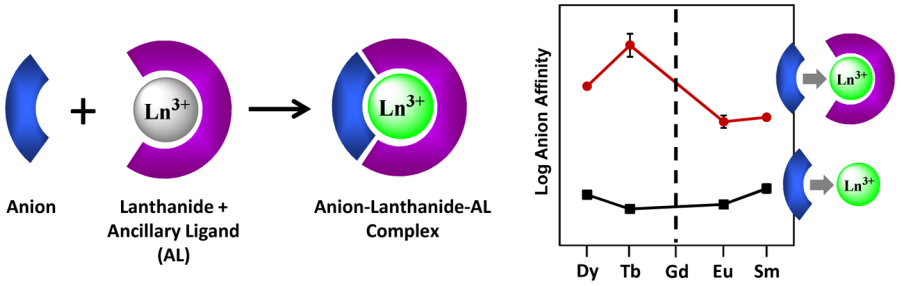
Enhancement of Anion Binding in Lanthanide Optical Sensors

MORGAN L. CABLE,[†] JAMES P. KIRBY,[§] HARRY B. GRAY,[*,‡] AND ADRIAN PONCE[*,†]

[†]*Jet Propulsion Laboratory, Pasadena, California 91109, United States, and*
[‡]*Beckman Institute, California Institute of Technology, Pasadena, California 91125, United States*

RECEIVED ON MARCH 5, 2013

CONSPECTUS



In the design of molecular sensors, researchers exploit binding interactions that are usually defined in terms of topology and charge complementarity. The formation of complementary arrays of highly cooperative, noncovalent bonding networks facilitates protein-ligand binding, leading to motifs such as the "lock-and-key". Synthetic molecular sensors often employ metal complexes as key design elements as a way to construct a binding site with the desired shape and charge to achieve target selectivity. In transition metal complexes, coordination number, structure and ligand dynamics are governed primarily by a combination of inner-sphere covalent and outer-sphere noncovalent interactions. These interactions provide a rich variable space that researchers can use to tune structure, stability, and dynamics.

In contrast, lanthanide(III)-ligand complex formation and ligand-exchange dynamics are dominated by reversible electrostatic and steric interactions, because the unfilled f shell is shielded by the larger, filled d shell. Luminescent lanthanides such as terbium, europium, dysprosium, and samarium display many photophysical properties that make them excellent candidates for molecular sensor applications. Complexes of lanthanide ions act as receptors that exhibit a detectable change in metal-based luminescence upon binding of an anion. In our work on sensors for detection of dipicolinate, the unique biomarker of bacterial spores, we discovered that the incorporation of an ancillary ligand (AL) can enhance binding constants of target anions to lanthanide ions by as much as two orders of magnitude.

In this Account, we show that selected ALs in lanthanide/anion systems greatly improve sensor performance for medical, planetary science, and biodefense applications. We suggest that the observed anion binding enhancement could result from an AL-induced increase in positive charge at the lanthanide ion binding site. This effect depends on lanthanide polarizability, which can be established from the ionization energy of $Ln^{3+} \rightarrow Ln^{4+}$. These results account for the order $Tb^{3+} > Dy^{3+} > Eu^{3+} \approx Sm^{3+}$. As with many lanthanide properties, ranging from hydration enthalpy to vaporization energy, this AL-induced enhancement shows a large discrepancy between Tb^{3+} and Eu^{3+} despite their similarity in size, a phenomenon known as the "gadolinium break". This discrepancy, based on the unusual stabilities of the Eu^{2+} and Tb^{4+} oxidation states, results from the half-shell effect, as both of these ions have half-filled 4f-shells. The high polarizability of Tb^{3+} explains the extraordinarily large increase in the binding affinity of anions for terbium compared to other lanthanides.

We recommend that researchers consider this AL-induced enhancement when designing lanthanide-macrocycle optical sensors. Ancillary ligands also can reduce the impact of interfering species such as phosphate commonly found in environmental and physiological samples.

Introduction

Lanthanide optical sensors have been developed for numerous applications[1−4] owing to their favorable properties, including large gaps between absorption and emission bands,[5,6] narrow emission lines,[7] resistance to photobleaching,[8] and long luminescence lifetimes.[9] We employed

Published on the Web 09/16/2013 www.pubs.acs.org/accounts
10.1021/ar400050t

TABLE 1. Lanthanide–Macrocycle–Dipicolinate Complex Photophysical Properties[a]

complex	Φ_L ($\times 10^{-3}$)[b]	ε_{Exp} (M^{-1} cm^{-1})[c]	Ln^{3+} ion resonance level (cm^{-1})
Sm(DO2A)DPA)$^-$	1.09 ± 0.03	4160 ± 10	Sm^{3+} $^4G_{5/2}$, 17 900
Eu(DO2A)(DPA)$^-$	7.51 ± 0.03	3369 ± 24	Eu^{3+} $^5D_0$, 17 264
Tb(DO2A)(DPA)$^-$	110 ± 2	2259 ± 10	Tb^{3+} $^5D_4$, 20 500
Dy(DO2A)(DPA)$^-$	7.87 ± 0.02	2832 ± 21	Dy^{3+} $^4F_{9/2}$, 21 100

[a]Molar extinction coefficients (ε_{Exp}) are similar for all four complexes, but the luminescence quantum yield (Φ_L) of the terbium complex is much greater, due to strong coupling between the Tb^{3+} ion $^5D_4$ excited state and the DPA triplet state (26,600 cm^{-1}) and the absence of lower excited states that might quench emission (such as in the Dy^{3+} case). Data from ref 37. [b]0.1 M Tris buffer (pH 7.9), 25 °C, λ_{ex} = 280 nm, standardized to L-Trp reference. [c]0.1 M Tris buffer (pH 7.5), 22 °C, λ_{ex} = 280 nm.

sensitized terbium ion luminescence for the rapid detection of bacterial spores (endospores), which are the most resilient form of microbial life[10−21] and are used as biological indicators for sterility assurance.[22] Fast viability assessment of endospores is enabled by dipicolinic acid (DPA), a unique biomarker for endospores[23] that is present at high concentrations (10^8 DPA molecules per endospore)[24−27] and released in minutes during germination.[28] When DPA^{2-} binds to Tb^{3+}, the resulting luminescence is more than 3 orders of magnitude more intense than that of the terbium aqua ion,[23,29−31] allowing endospores to be imaged and enumerated with time-gated microscopy.[32,33] In our effort to further improve the terbium-dipicolinate luminescence assay, we discovered that incorporation of certain ancillary ligands (ALs) increases anion binding affinity to Tb^{3+} by approximately 2 orders of magnitude.

In sensitized lanthanide luminescence such as that seen with terbium dipicolinate, a chromophore absorbs and transfers energy to a lanthanide cation (usually Tb^{3+} or Eu^{3+}), circumventing the selection rules that disfavor *f*–*f* excitation (Table 1).[34−36] Dipicolinate is an effective absorber of UV radiation ($\varepsilon_{280\ nm} \sim 2800\ M^{-1}\ cm^{-1}$),[37] owing to strongly allowed electronic transitions in the aromatic pyridine ring. Since the lowest triplet excited state of DPA is well matched energetically to the lowest emitting level of Tb^{3+}, the dipicolinate complexes exhibit greatly enhanced (sensitized) luminescence (Figure 1).[38] In addition, these complexes have luminescent lifetimes in the micro- to millisecond range,[39,40] a property that makes it possible through time-gated techniques to reduce nanosecond fluorescence from interferents common in environmental samples.[6,40]

Although the use of "free" Tb^{3+} for bacterial spore detection is rapid and straightforward, it has several weaknesses, including sensitivity to anionic interferents that can outcompete dipicolinate, and Tb^{3+}-bound water molecules that reduce excited state populations by nearly an order of magnitude through nonradiative decay.[37] To eliminate the potential for solvent quenching and reduce susceptibility to interferents, we explored the use of a hexadentate AL to

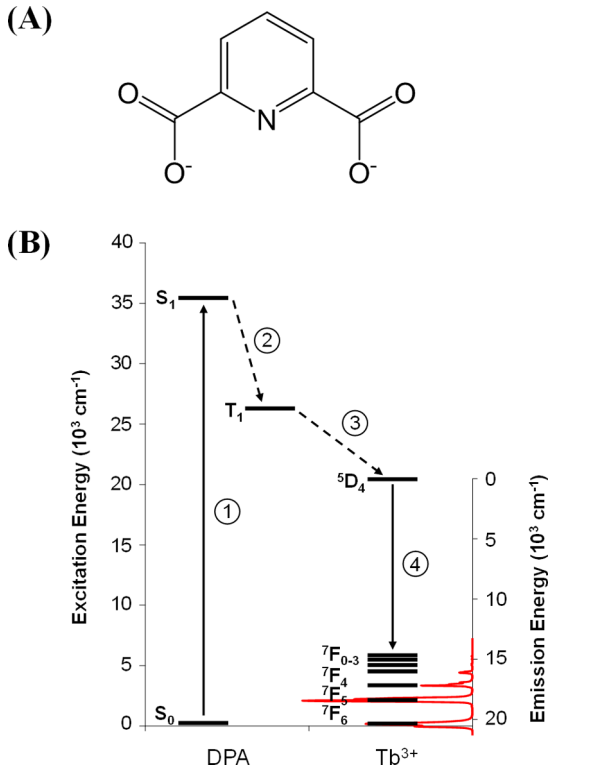


FIGURE 1. (A) Structure of dipicolinate (DPA). (B) Sensitized luminescence of terbium dipicolinate. (1) UV excitation populates a singlet excited state (S_1) of DPA, which undergoes (2) intersystem crossing to a triplet excited state (T_1) of the ligand, (3) energy transfer to the emitting level ($^5D_4$) of the Tb^{3+} ion, and finally (4) radiative decay to the Tb^{3+} ground state manifold ($^7F_0$-$^7F_6$), observed in the emission spectrum (red).

chelate Tb^{3+} and complete the inner coordination sphere when DPA is bound. In the process, we discovered a more general AL-induced enhancement of anion binding. In this Account, we review our work on AL-enhanced lanthanide-ion optical sensors for detection of dipicolinate and other biologically relevant anions. We show that ALs can enhance analyte binding affinity by 1−2 orders of magnitude across an isostructural series of lanthanide complexes.

Ancillary Ligand-Induced Enhancement

Ancillary Ligand Binding. Choosing an appropriate ancillary ligand for lanthanide-based sensors transforms the

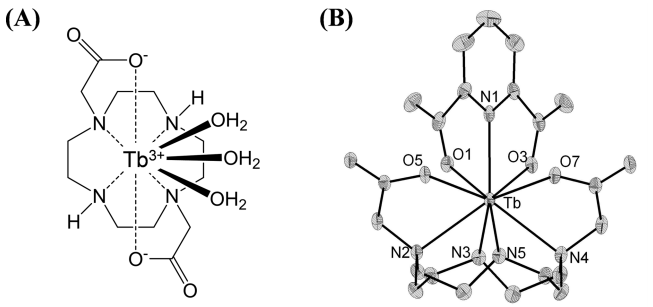


FIGURE 2. Dipicolinate receptor site is Tb^{3+} with the DO2A ancillary ligand. (A) Structure of $[Tb(DO2A)(H_2O)_3]^+$. (B) Thermal ellipsoid plot (50% probability) of the $[Tb(DO2A)(DPA)]^-$ ternary complex with the DO2A ligand in the Tb^{3+} lower hemisphere and dipicolinate in the upper hemisphere. Hydrogens omitted for clarity. Reprinted with permission from ref 49. Copyright 2007 American Chemical Society.

lanthanide ion into a sensing complex. Ancillary ligands with reactive pendant moieties can also act as synthons for appending sensing complexes to solid substrates.[1,41,42] The AL must bind to the lanthanide with high affinity to reduce solvent quenching, yet also leave a binding site available for the target analyte. Thus, the stability/denticity of the ligand, and the size/geometry of the binding pocket it generates, are key parameters when choosing an AL.

Macrocyclic ligands, which have a semirigid backbone ring structure and variable ring diameter and functionalization, have a hydrophilic metal-ion binding cavity that is shielded from the environment by its lipophilic envelope.[43−45] Many macrocyclic ligands bind lanthanide ions with extraordinary selectivity and stability,[46] and resultant complexes are highly water-soluble, kinetically inert at neutral pH, and cell-permeable.[47,48] We selected DO2A (1,4,7,10-tetraazacyclododecane-1,7-bisacetate) as the ancillary ligand of choice[49] with the goal of improving bacterial spore detection based on Tb^{3+}-DPA luminescence (Figure 2).

Dipicolinate Binding. To verify that DO2A does not hinder dipicolinate binding to Tb^{3+}, we measured binding affinities (eq 1, K_a') by competition assay,[50] and compared results across the luminescent lanthanide ions Dy^{3+}, Eu^{3+}, Tb^{3+}, and Sm^{3+}.

$$[Ln(DO2A)(H_2O)_3]^+ + DPA^{2-} \overset{K_a'}{\rightleftharpoons} [Ln(DO2A)(DPA)]^- + 3H_2O \quad (1)$$

The assay revealed an AL-induced enhancement of dipicolinate binding affinity by about an order of magnitude for $[Ln(DO2A)]^+$ as compared to the Ln^{3+} aqua ion, and almost 2 orders of magnitude for Tb^{3+} (Figure 3).[37] As chelation in lanthanide complexes is typically dominated by electrostatic interactions,[1,7] an increase in

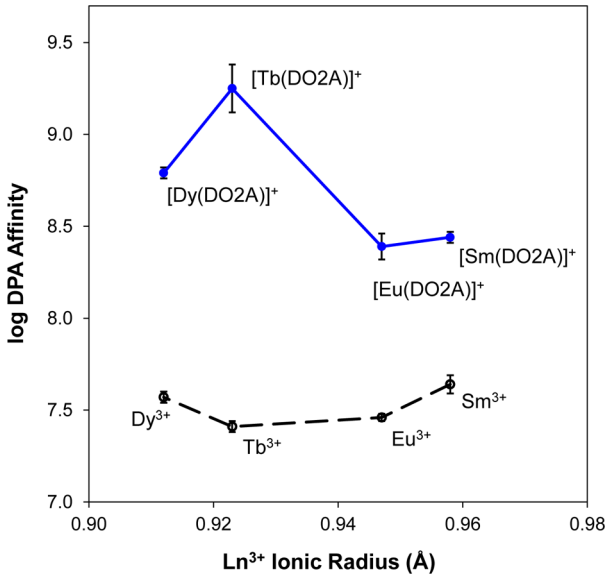


FIGURE 3. Dipicolinate binding affinities for DO2A complexes (blue) and aqua ions (black) depend on Ln^{3+} ionic radii. Adapted with permission from ref 37. Copyright 2009 American Chemical Society.

binding affinity of dianionic DPA^{2-} to the less-electropositive $[Ln(DO2A)]^+$ complex was contrary to expectations based on bulk electrostatics. Clearly, the traditional net charge model is insufficient to account for the behavior of dipicolinate with lanthanide ions in the presence of the DO2A ancillary ligand.

AL-Induced Gadolinium Break. The binding affinity enhancement imparted by DO2A is lanthanide-dependent, and especially pronounced between Tb^{3+} and Eu^{3+}, which juxtapose Gd^{3+} in the series. This phenomenon, known as the "gadolinium break,"[51] has emerged from various studies of stability constants across the lanthanide series, such as those with acetate and anthranilate,[52] as well as in investigations of hydration enthalpy,[53] vaporization energy,[54] viscosity,[55] molar entropy,[56] and enzyme inhibition properties (Figure 4).[57] Consistent with past potentiometric work,[58] binding affinities of DPA^{2-} to Ln^{3+} aqua ions were relatively uniform and did not exhibit any gadolinium break. Lifetime measurements of DO2A-chelated complexes indicated no differences in average hydration state,[49] and crystal structures show no significant changes in bond lengths or angles.[37] Most likely, the property causing the gadolinium break effect is also responsible for the increase in binding affinity, both being induced by binding of DO2A.

We sought to determine if this effect was unique to our lanthanide-DO2A-dipicolinate system, and found several lanthanide/ligand/analyte systems exhibiting the same AL-induced enhancement (Table 2).[59−64] In each case,

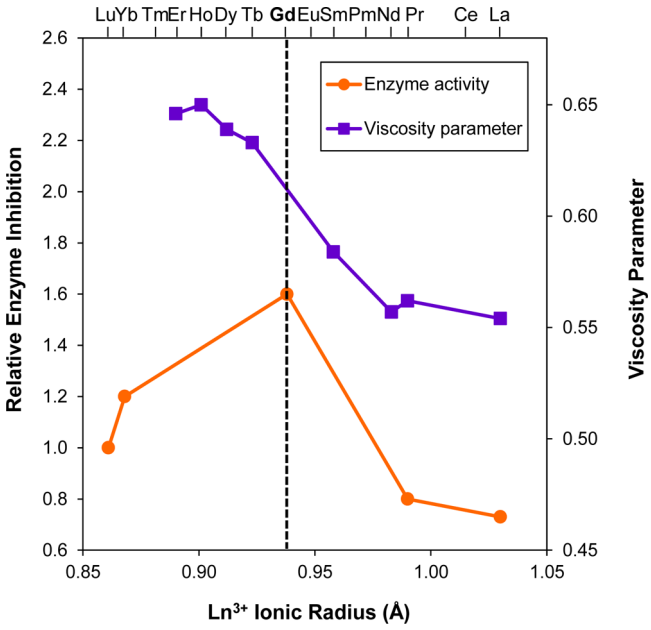


FIGURE 4. Two examples of the gadolinium break (dotted line). Enzyme activity (ref 57) is inhibited by Mg^{2+} binding to NAD(P)+ malic enzyme in the presence of 20 μM Ln^{3+}. Viscosity parameter is for an aqueous solution of 1.0 M $LnCl_3$ at 25 °C (ref 55).

TABLE 2. Analyte Binding Affinities[a]

ligand[b]	analyte	$\Delta \log K^c$	ref
$DO2A^{2-}$	dipicolinate	0.8−1.8	37
$EDTA^{2-}$	picolinate	0.2−1.5[d]	59, 60
DO3A L_1	lactate	0.8−1.5[e]	61, 62
DO3A L_2	acetate	0.1−1.4[e]	62, 63

[a]Table reprinted from ref **64**, Copyright 2011, with permission from Elsevier. [b]DO3A L_1 = (*SSS*)-1,4,7-tris[1-(1-phenyl)ethylcarbamoylmethyl]-1,4,7,10-tetraazacyclododecane. DO3A L_2 = (*SSS*)-1,4,7-tris[1-(1-phenyl)ethylcarbamoylmethyl]-10-methyl-1,4,7,10-tetraazacyclododecane. [c]$\Delta \log K = \log K_a' - \log K_a$. [d]$\log K_a$: 0.1 M KNO_3, 25 °C; $\log K_a'$: 0.5 M $NaClO_4$, 25 °C. [e]$\log K_a$: 0.1 M $NaClO_4$, 20 °C; $\log K_a'$: 0.1 M collidine/HCl, 21.8 °C, pH 7.4.

employing an AL improved binding affinity of the oxyanion analyte (picolinate, acetate and lactate) by roughly an order of magnitude, regardless of the type (cyclic or linear), denticity, or net charge of the AL. One of these studies, which compared two heptadentate macrocyclic AL complexes of Tb^{3+} and Eu^{3+}, noted an increase in binding affinity of the terbium complex for acetate, bicarbonate, and phosphate, in comparison to the europium complex (the effect is about the same as observed for dipicolinate, Figure 5).[62] This difference in binding affinities was not seen when the AL was absent—again, evidence of the gadolinium break induced by binding of the ancillary ligand. As with the dipicolinate system, no differences in hydration states were detected in lifetime measurements. The authors attributed the affinity trend to a divergence of pK_a for the two complexes. However, if the pK_a of the europium complex were lower than

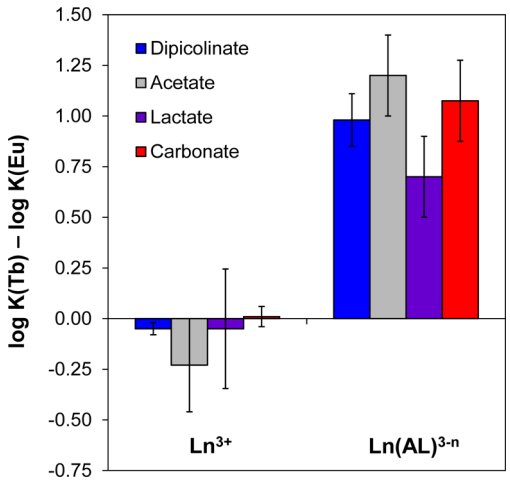


FIGURE 5. Differences in binding affinities of various Tb^{3+} and Eu^{3+} complexes for dipicolinate, acetate, lactate and carbonate analytes. DPA values from ref 37; all others from refs 62 and 63**.**

that of the terbium complex, the presence of a population of hydroxylated species in the former case would reduce the overall binding affinity. Moreover, we have found no evidence for such a hydroxylated species in our pH dependence studies.[37] As this model does not account for our findings, we turn to perturbations of Ln^{3+} electronic structure as a possible way to explain the AL-induced enhancement.

The ability of an AL to tune the electronic structure of Ln^{3+} ions depends on (i) the structure and electronegativity of the AL, and (ii) the lanthanide ion polarizability. In the case of DO2A, six electron-withdrawing groups bind to the Ln^{3+} ion on one hemisphere, causing a shift in electron density from the Ln^{3+} ion toward DO2A. This creates greater electropositive character on the opposite side of the lanthanide where the analyte binds. Hence, the *local* charge at the analyte binding site of the $[Ln(DO2A)]^+$ complex may be even greater than that of the Ln^{3+} aqua ion, despite a lower net charge (1+ versus 3+), which explains the increase in dipicolinate binding affinity when DO2A is added. This model explains not only the increase in binding affinity observed in our lanthanide-DO2A-dipicolinate system, but also the progressively increasing affinity of a lanthanide ion for multiple dipicolinate species. The first dipicolinate binds to the Ln^{3+} aqua ion ($\log K_1 = 6.98$), where the nine solvent molecules are evenly distributed about the coordination sphere and the electron density is uniform. After the first DPA binds, the electron density around the lanthanide shifts and presents a more electropositive area for the second DPA molecule, causing an increase in binding affinity ($\log K_2 = 7.9$) despite a decrease in net complex charge (+3 to +1).[65] This same trend has been observed for acetate, in that the formation

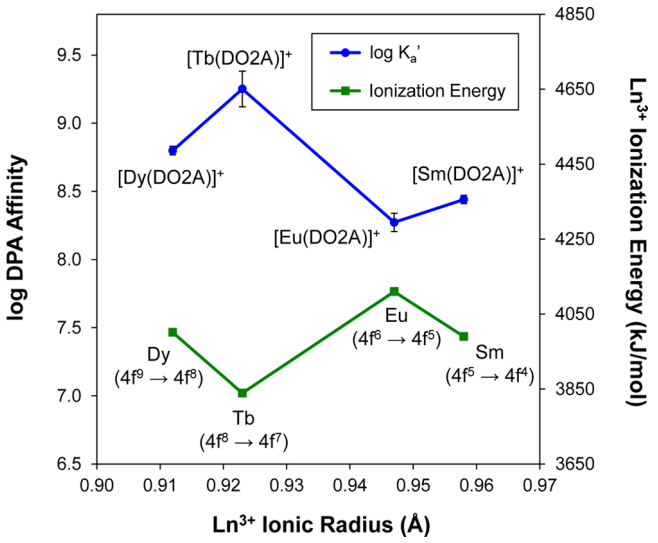


FIGURE 6. Relationship of AL-induced enhancement to $Ln^{3+} \rightarrow Ln^{4+}$ ionization energy (see ref 7).

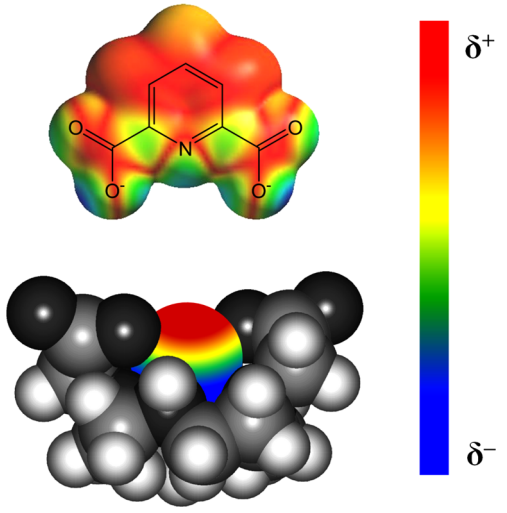


FIGURE 7. Electron density map of the highest occupied molecular orbital (HOMO) for dipicolinate, with blue as highest electron density and red as lowest. Chelation of the DO2A ancillary ligand shifts the electronic structure of the Tb^{3+} ion such that the hemisphere exposed in the binding site is more electropositive (red). Dipicolinate electron density map generated using Titan molecular modeling software; Tb^{3+} electron density map is an estimate.

rate constant of the bis-acetato complex is greater than that for the monoacetato complex.[66] This proposed shift in electron density also is consistent with the general oxophilic nature of lanthanide ions.[67]

The AL-induced increase in binding affinity is different for each lanthanide, because lanthanide ions have different polarizabilities. Lanthanide polarizability can be established from ionization energy—in this case, the energy required to remove an electron from the Ln^{3+} ion. As shown in Figure 6, the observed trend in dipicolinate binding affinity follows the corresponding $Ln^{3+} \rightarrow Ln^{4+}$ ionization energies very closely. The Tb^{3+} ion has the lowest ionization energy of all lanthanides investigated, owing to the fact that Tb^{4+} has an exactly half-filled 4*f*-shell and is unusually stable.[7] Accordingly, Tb^{3+} is particularly polarizable and susceptible to perturbation by an electronegative ancillary ligand. Conversely, for europium the exactly half-filled 4*f*-shell occurs in the Eu^{2+} ion, meaning Eu^{3+} has a greater electron affinity compared to Tb^{3+} and the $Eu^{3+} \rightarrow Eu^{4+}$ ionization energy is high. This results in lower Eu^{3+} polarizability, and lower susceptibility to AL-induced binding enhancement. Evidence for the high electron affinity of Eu^{3+} compared to Tb^{3+} can be seen in more rapid H/D exchange of secondary amides in Eu complexes,[68] as well as lower pK_a values in coordinated waters of Eu-aqua species.[69] This polarizability variation in lanthanide ions is most likely compounded by differences in electron distribution of the 4*f*-shell. Quadrupole approximations of Tb^{3+} and Dy^{3+} both depict equatorially expanded quadrupole moments of the *f*-electron charge cloud, suggesting lower axial electron density than Sm^{3+} and Gd^{3+}, which were axially elongated and spherical, respectively (Eu^{3+} has a J = 0 ground state and could not be modeled).[70] This *f*-electron density anisotropy difference between Tb^{3+}/Dy^{3+} and Sm^{3+}/(and presumably Eu^{3+}) could account for the relatively large AL enhancements of Tb^{3+} and Dy^{3+} complexes. The observed AL-induced gadolinium break therefore appears to be a manifestation of the half-shell effect, where the lanthanide ions with the lowest ionization energies are amenable to the largest AL-induced enhancements in analyte binding affinity.

In summary, we can account both for the AL enhanced binding affinity and the lanthanide-dependence of that enhancement. Chelation of the ancillary ligand leads to a shift in electron density, making the binding site more electropositive and therefore more attractive to the negatively charged dipicolinate analyte (Figure 7). Further, the increase in binding affinity does not match the trend lanthanide ionic radius, but instead follows the gadolinium break due to the half-shell effect.

Lanthanide Sensor Design

AL-induced enhancement is a new tool in lanthanide-based sensor design, supplementing traditional approaches based primarily on energy-level matching, steric constraints and net complex charge. For example, many Eu^{3+} complexes have been developed as sensors because the lowest emitting level of europium is lower in energy than that of terbium

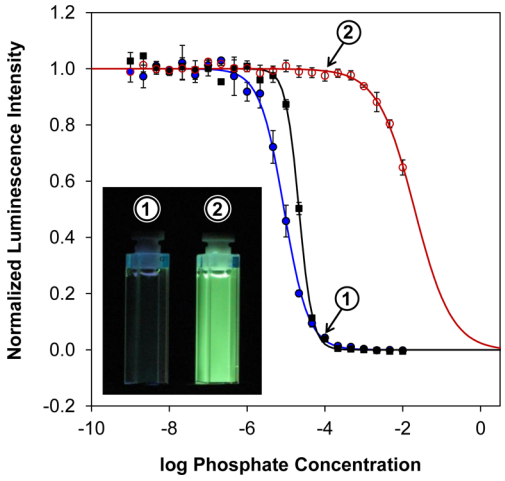


FIGURE 8. Effect of phosphate on $[Tb(DO2A)(DPA)]^-$ (red) and $[Tb(DPA)]^+$ (blue), 100 nM in 0.1 M MOPS, pH 7.3. DO2A mitigates phosphate interference up to mM levels, an improvement of more than 3 orders of magnitude compared to Tb^{3+} alone, and over 2 orders of magnitude better than the traditional solution of aluminum chloride (black), here at 1000x to $[Tb(DPA)]^+$. Inset: The difference conferred by DO2A is striking, even by eye. At 0.1 mM phosphate, luminescence of $[Tb(DO2A)(DPA)]^-$ at right (2) is clearly visible in a quartz cuvette illuminated by a UV lamp, whereas that of $[Tb(DPA)]^+$ at left (1) is almost entirely quenched. Reprinted in part with permission from ref 37. Copyright 2009 American Chemical Society.

(Table 1), and therefore some analytes act as more efficient chromophores for Eu^{3+} than for Tb^{3+};[71−76] the ground state of europium is also nondegenerate, making interpretation of emission spectra (such as determining a change in hydration state) much easier for this lanthanide.[1,77] However, for cases where these factors are not critical, the binding affinity may be increased by up to an order of magnitude by simply replacing Eu^{3+} with Tb^{3+}.

The binding affinity increase of anions to AL complexes containing Tb^{3+} can aid significantly in mitigating interfering species, as evidenced by the remarkable resistance of $[Tb(DO2A)(DPA)]^-$ to phosphate and other cationic and anionic interferents (Figure 8).[37] Lanthanide/AL combinations that previously might have been omitted in sensor development should be considered in the new context of the AL-induced enhancement effect. In particular, the ligand-induced gadolinium break makes it very attractive to use Tb^{3+} as the lanthanide ion of choice, because in this case AL-induced polarization will lead to the greatest increase in binding affinity.

Further improvements in analyte binding affinity can be achieved by careful design of the ancillary ligand. The most effective ancillary ligands will maximize the number of electron-withdrawing groups such that, upon Ln^{3+} chelation in one hemisphere, a more electropositive binding site will be generated in the other hemisphere. Such considerations must be tempered by other design constraints, such as binding site geometry, donor ligand polarizability,[78] secondary noncovalent interactions (π-stacking, hydrogen bonding, etc.),[79] and overall complex reactivity. However, exploitation of AL-induced enhancement should hasten the development of sensitive, selective lanthanide-based sensors.

In certain cases, AL-induced enhancement may take precedence over other binding site design considerations such as binding site topology. We explored development of lanthanide-based sensors for catecholamines, "fight-or-flight" hormones released in response to stress.[80] Deficiency or overproduction of these hormones has been linked to Parkinson's disease, degenerative cardiovascular and neurotic disorders, and carcenoid and neuroendocrine tumor formation.[81,82] Catecholamines such as dopamine (DA), epinephrine (Epi), and norepinephrine (NE) are known to chelate metal ions in bidentate fashion when deprotonated,[83,84] so they are excellent candidates for detection via sensitized lanthanide luminescence.[85] As DA, Epi, and NE are bidentate and Tb^{3+} is 9-coordinate, we predicted that a heptadentate ligand, DO3A (1,4,7,10-tetraazacyclododecane-1,4,7-trisacetate), would generate the optimal receptor site. However, hexadentate DO2A produced a more luminescent complex in all cases. Other examples of AL/analyte denticity mismatches include those of hexadentate EDTA with salicylate, 4-aminosalicylic acid, and 5-fluorosalicylic acid, all of which are bidentate,[86] as well as our work with DO2A and salicylurate, an aspirin metabolite.[87] In this last case, we were able to achieve a detection limit of <2 mg/L salicylurate in urine without modifications to the DO2A ligand, demonstrating that AL-induced enhancement can improve analyte binding in complex biological fluids without the need to follow a strict "lock-and-key" approach. Ancillary ligand selection should not be limited by traditional binding site strategies.

Concluding Remarks

We have shown that ancillary ligands can greatly enhance anion analyte binding in lanthanide-based sensors. Upon binding of the AL, electronegative chelating moieties induce anisotropy in the electronic structure of the lanthanide ion, generating a more electropositive binding site for the analyte and enhancing binding affinity. This AL-induced enhancement has been observed in all luminescent lanthanides for aromatic and nonaromatic analytes with ancillary ligands of varying denticity and charge. The binding affinity

of the analyte is improved by approximately 1 order of magnitude for Eu^{3+}, Sm^{3+}, and Dy^{3+} complexes, and approaching 2 orders of magnitude for Tb^{3+} complexes. This effect is governed by lanthanide ion polarizability and follows the gadolinium break trend, as evidenced by the binding affinity correlation with Ln^{3+} ionization energy. The Tb^{3+} ion has the lowest ionization energy and consequently the greatest polarizability, and thus exhibits the strongest response to AL-induced enhancement. In addition to improved analyte binding affinity, use of well-matched ALs can also mitigate interference of environmental or physiological contaminants.

We dedicate this Account to the memory of Michael Day, a wonderful colleague and great friend. The authors would also like to acknowledge helpful comments by the reviewers of this manuscript. The research was carried out at the Jet Propulsion Laboratory, California Institute of Technology, under contract with the National Aeronautic and Space Administration and was sponsored by NASA's Astrobiology and Planetary Protection Programs (A.P., J.P.K.), the Department of Homeland Security's Chemical and Biological Research & Development Program (A.P.), and the NASA Graduate Student Research Program (M.L.C.). Work at Caltech was supported NIH Grant DKO19038 and the Arnold and Mabel Beckman Foundation.

ABBREVIATIONS

AL, ancillary ligand; DA, dopamine; DO2A, 1,4,7,10-tetraazacyclcododecane-1,7-bisacetate; DO3A, 1,4,7,10-tetraazacyclododecane-1,4,7-trisacetate; DPA, dipicolinic acid; DTPA, diethylenetriaminetetraacetic acid; EDTA, ethylenediaminetetraacetic acid; Epi, epinephrine; NE, norepinephrine; UV, ultraviolet.

BIOGRAPHICAL INFORMATION

Morgan L. Cable earned her Ph.D. in Chemistry from the California Institute of Technology in 2010, where she investigated various lanthanide-based receptor sites for the detection of bacterial spores. As a NASA Postdoctoral Fellow (2010−2013) and currently as a technologist in the Imaging Spectroscopy group at the NASA Jet Propulsion Laboratory, Morgan's work continues to focus on organic/biomarker detection strategies, through both in situ and remote sensing techniques.

James Patrick "J.P." Kirby received his Ph.D. from Michigan State University in 1997. He was a postdoctoral fellow at the University of California, Berkeley from 1997 to 2000 and is currently a Senior Scientist with the Planetary Science Institute. His research interests include life detection technology development and analytical science instruments for planetary science and terrestrial extreme environments.

Harry Gray is the Arnold O. Beckman Professor of Chemistry and the Founding Director of the Beckman Institute at the California Institute of Technology. In 1961, after graduate work in inorganic chemistry at Northwestern University and postdoctoral research at the University of Copenhagen, he joined the chemistry faculty at Columbia University, where he investigated the electronic structures and reactions of inorganic complexes. In 1966, he moved to Caltech, where for over 40 years he has been working on problems in biological inorganic chemistry and inorganic photochemistry.

Adrian Ponce manages the Higher Education Office at NASA's Jet Propulsion Laboratory, and is a Visiting Associate faculty at the California Institute of Technology. His interests include lanthanide-based sensor development and astrobiology research. He received his Ph.D. in Chemistry from Caltech in 2000 for research in electron transfer, and since then invented an Anthrax Smoke Detector for biodefense and Germinable Endospore Biodosimetry for sterility assurance, which are being commercialized by his startup, Verrix, LLC. (http://ponce.caltech.edu).

FOOTNOTES

*To whom correspondence should be addressed. E-mail: hbgray@caltech.edu (H.B.G.); Adrian.Ponce@jpl.nasa.gov (A.P.).
The authors declare no competing financial interest.
The manuscript was written by all authors. All authors have given approval to the final version of the manuscript.
§J.P.K.: Planetary Science Institute, Tucson, AZ 85719.

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