

Neutral Heteroleptic Lanthanide Complexes for Unravelling Host–Guest Assemblies in Organic Solvents: The Law of Mass Action Revisited

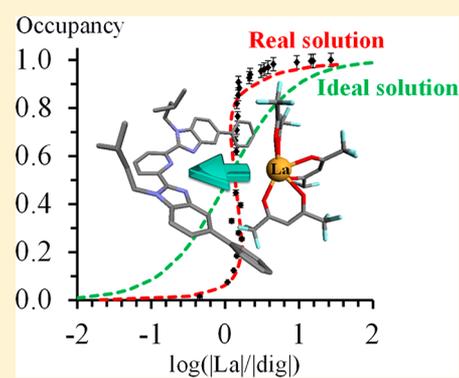
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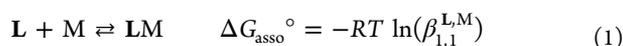
Supporting Information

ABSTRACT: The binding of lanthanide containers [Ln(β -diketonate)₃dig] [dig = 1-methoxy-2-(2-methoxyethoxy)ethane] to aromatic tridentate N-donor ligands (L) in dichloromethane produces neutral nine-coordinate heteroleptic [LLn(β -diketonate)₃] complexes, the equilibrium reaction quotients of which vary with the total concentrations of the reacting partners. This problematic drift prevents the determination of both reliable thermodynamic stability constants and intrinsic host–guest affinities. The classical solution theory assigns this behavior to changes in the activity coefficients of the various partners in nonideal solutions, and a phenomenological approach attempts to quantitatively attribute this effect to some partition of the solvent molecules between bulk-innocent and contact-noninnocent contributors to the chemical potential. This assumption eventually predicts an empirical linear dependence of the equilibrium reaction quotient on the concentration of the formed [LLn(β -diketonate)₃] complexes, a trend experimentally supported in this contribution for various ligands L differing in lipophilicity and nuclearity and for lanthanide containers grafted with diverse β -diketonate coligands. Even if the origin of the latter linear dependence is still the subject of debate, this work demonstrates that this approach can be exploited by experimentalists for extracting reliable thermodynamic constants suitable for analyzing and comparing host–guest affinities in organic solvents.



INTRODUCTION

Basic Thermodynamics of Host–Guest Assemblies: A Nontrivial Problem. Experimental coordination chemists with (or without) interest in lanthanide complexation reactions are determined to get reliable free-energy affinities $\Delta G_{\text{asso}}^{\circ}$ accompanying the association between a host ligand (L) and a guest metal container (M) occurring in a specific solvent according to eq 1.



The thermodynamic stability constant $\beta_{1,1}^{\text{L,M}}$, often unduly mixed by experimentalists with the equilibrium reaction quotient $Q_{1,1,\text{eq}}^{\text{L,M}}$ expressed in concentration units, is defined by the van't Hoff isotherm as the ratio of the activities (a_i^{aq}) of the various partners at equilibrium (left part of eq 2). Except for some rare cases where the activities can be monitored directly by selective electrodes or by vapor-pressure measurements, most experimental protocols consider the gathering of concentrations at equilibrium for the estimation of $\beta_{1,1}^{\text{L,M}}$. The introduction of activity coefficients γ_i , which transform mole fractions (x_i) or concentrations (c_i) into activities according to $a_i = \gamma_i x_i = \gamma_i (c_i/c^{\theta})$,¹ together with the standard concentration of the reference state c^{θ} ($c^{\theta} = 1 \text{ M}$) is used for the rest of this

contribution),² ensures an adequate procedure for estimating thermodynamic stability constants by using equilibrium reaction quotients $Q_{1,1,\text{eq}}^{\text{L,M}} = c_{\text{LM}}^{\text{eq}}/c_{\text{L}}^{\text{eq}}c_{\text{M}}^{\text{eq}}$ defined by the speciation expressed in molar concentration units (right part of eq 2).

$$\begin{aligned} \beta_{1,1}^{\text{L,M}} &= e^{-(\Delta G_{\text{asso}}^{\circ}/RT)} = \frac{a_{\text{LM}}^{\text{eq}}}{a_{\text{L}}^{\text{eq}}a_{\text{M}}^{\text{eq}}} = \frac{\gamma_{\text{LM}}}{\gamma_{\text{L}}\gamma_{\text{M}}} \frac{c_{\text{LM}}^{\text{eq}}/c^{\theta}}{(c_{\text{L}}^{\text{eq}}/c^{\theta})(c_{\text{M}}^{\text{eq}}/c^{\theta})} \\ &= \frac{\gamma_{\text{LM}}}{\gamma_{\text{L}}\gamma_{\text{M}}} Q_{1,1,\text{eq}}^{\text{L,M}} c^{\theta} \end{aligned} \quad (2)$$

Because coordination chemists are mainly focused on the determination of the stability constants (and their associated free-energy changes) by monitoring concentrations at equilibrium, eq 2 provides considerable difficulties because the activity coefficients are usually not accessible except for ideal solutions ($\gamma_i = 1$), where all intermolecular interactions are identical, a situation characterized by $\xi = 0$ within the frame of the classical solution model (ξ is a dimensionless parameter

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that estimates the energy of solute–solvent interactions relative to that of solvent–solvent and solute–solute interactions).¹ For chemical reactions involving ionic partners in solution, the Debye–Hückel limiting law provides a satisfying key because the activity coefficients of the ions only depend on their intrinsic charge and size and on the ionic strength of the mixture, a parameter that can be fixed by the addition of a large excess of dissociated nonreacting electrolytes. Even though the ratio $\gamma_{LM}/\gamma_L\gamma_M$ is unknown for charged partners at equilibrium, it corresponds to a constant for a fixed ionic strength. The equilibrium reaction quotient $Q_{1,1,\text{eq}}^{\text{L,M}} = c_{\text{LM}}^{\text{eq}}/c_{\text{L}}^{\text{eq}}c_{\text{M}}^{\text{eq}}$ estimated in concentration units (we take for granted the original choice of $c^\theta = 1$ M) is therefore proportional to the thermodynamic stability constant $\beta_{1,1}^{\text{L,M}}$ (eq 2). For these reasons, numerous equilibrium reaction quotients have been reported for the formation of charged coordination complexes in polar solvents, for which specific ionic strengths are duly mentioned.³ The situation becomes critical when association reactions are conducted (i) in a polar solvent in the absence of added polyelectrolytes or in a nonpolar (usually organic) solvent where the ionic strength cannot be fixed and (ii) when neutral partners are considered. A very rough, but instructive approach considers the classical solution theory for mastering the free-energy changes accompanying the mixing of two nonideal chemical components A and B, with the latter one being taken as the solvent (B, mole fraction x_B), while A (mole fraction $x_A = x_M + x_L + x_{LM}$) is assigned to the sum of the solute particles controlled by equilibrium (1). According to this hypothesis, the free energy of mixing $nRT[x_A \ln(a_A) + x_B \ln(a_B)]$ deviates from that of an ideal solution $nRT[x_A \ln(x_A) + x_B \ln(x_B)]$ by an excess enthalpic contribution $n\xi RTx_Ax_B$, which develops for n moles of the mixture when the solute–solvent (A–B) interactions differ from the solvent–solvent (B–B) and solute–solute (A–A) interactions ($\xi < 0$ means exothermic mixing and the dominance of favorable solute–solvent interactions, while the reverse situation characterizes $\xi > 0$).¹ Because $a_A = \gamma_A x_A$, the activity coefficient of the solute in a nonideal binary mixture finds a mathematical expression $\ln(\gamma_A) = \xi(x_B)^2 = \xi(1 - x_A)^2$ (Figure 1a), often referred to as the Margules equation,⁴ which finally leads to the solute activity $a_A = \gamma_A x_A = e^{\xi(1-x_A)^2} x_A$ (Figure 1b).

Using concentration units for diluted solutions ($x_B \geq 0.9$ and $c_B \gg c_{\text{L}}^{\text{eq}} + c_{\text{M}}^{\text{eq}} + c_{\text{LM}}^{\text{eq}}$), the mole fraction of the solute x_A in our “binary” mixture at equilibrium is given in eq 3 and its activity coefficient in eq 4.

$$x_A = \frac{c_{\text{L}}^{\text{eq}} + c_{\text{M}}^{\text{eq}} + c_{\text{LM}}^{\text{eq}}}{c_{\text{L}}^{\text{eq}} + c_{\text{M}}^{\text{eq}} + c_{\text{LM}}^{\text{eq}} + c_B} \simeq \frac{c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}}{c_B} \quad (3)$$

$$\gamma_A = \gamma_{\text{solute}} = \exp \left[\xi \left(1 - \frac{c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}}{c_B} \right)^2 \right] \quad (4)$$

Introducing eq 4 to eq 2 yields eq 5, where $Q_{1,1,\text{eq}}^{\text{L,M}}$ is the experimentally accessible reaction quotient, which is (very) often mistaken by coordination chemists for the thermodynamic stability constant $\beta_{1,1}^{\text{L,M}}$.

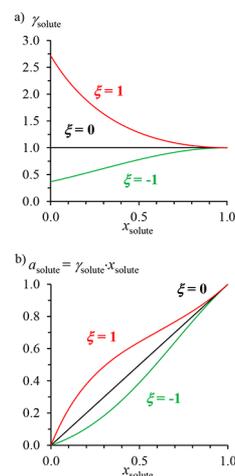
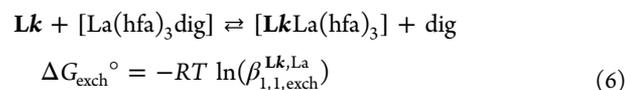


Figure 1. Plots of (a) activity coefficients γ_{solute} and (b) activities a_{solute} for a solute dispersed in a solvent in a binary mixture according to the Margules equation.⁴ ξ is the dimensionless parameter measuring the energy of the solute–solvent interactions relative to that of the solute–solute and solvent–solvent interactions.¹

$$\begin{aligned} \beta_{1,1}^{\text{L,M}} &= e^{-(\Delta G_{\text{asso}}^\circ/RT)} \\ &= \exp \left[-\xi \left(1 - \frac{c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}}{c_B} \right)^2 \right] \frac{c_{\text{LM}}^{\text{eq}}}{c_{\text{L}}^{\text{eq}}c_{\text{M}}^{\text{eq}}} c^\theta \\ &= \exp \left[-\xi \left(1 - \frac{c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}}{c_B} \right)^2 \right] Q_{1,1,\text{eq}}^{\text{L,M}} c^\theta \end{aligned} \quad (5)$$

Because (i) the sum $c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}$ varies during titration of the receptor L with an M guest and (ii) $\beta_{1,1}^{\text{L,M}}$ is a constant, eq 5 predicts that the reaction quotients recorded at equilibrium $Q_{1,1,\text{eq}}^{\text{L,M}} = c_{\text{LM}}^{\text{eq}}/c_{\text{L}}^{\text{eq}}c_{\text{M}}^{\text{eq}}$ will indeed change for various total concentrations of host and guest. It is therefore not so surprising that titrations of ligands L1–L3 with [La(hfa)₃dig] (eq 6), where hfa is the hexafluoroacetylacetonate anion (see Figure 2a), in dichloromethane systematically exhibit significant variations of the reaction quotients at equilibrium (Figure 2b),⁵ a trend previously noted for titrations of EDTA⁴⁻ (EDTA = ethylenediaminetetraacetic acid) with Ca²⁺ conducted in aqueous buffered solutions.⁶



Because (i) the stepwise appearance of free diglyme in solution exactly matches (stoichiometry 1:1) the complexation of Lk during the NMR titrations and (ii) [LkLa(hfa)₃] is the only complex characterized in the solid state and in solution,⁷ there is no ambiguity concerning the exclusive formation of 1:1 complexes in eq 6. In this situation, how may coordination chemists decide which one of the various reaction quotients collected in Figure 2b is pertinent for applying the van't Hoff equation, leading to the searched free-energy change $\Delta G_{\text{exch}}^\circ$ associated with equilibrium (6)? According to the classical solution theory, one expects $\gamma_{\text{solute}} \rightarrow 1$ for large concentrations of reacting partners (Figure 1), a situation impossible to reach in a diluted solution. On the other hand, working at infinite dilution should also fix the activity coefficients to constant values, but their considerable sensitivities to minor changes in

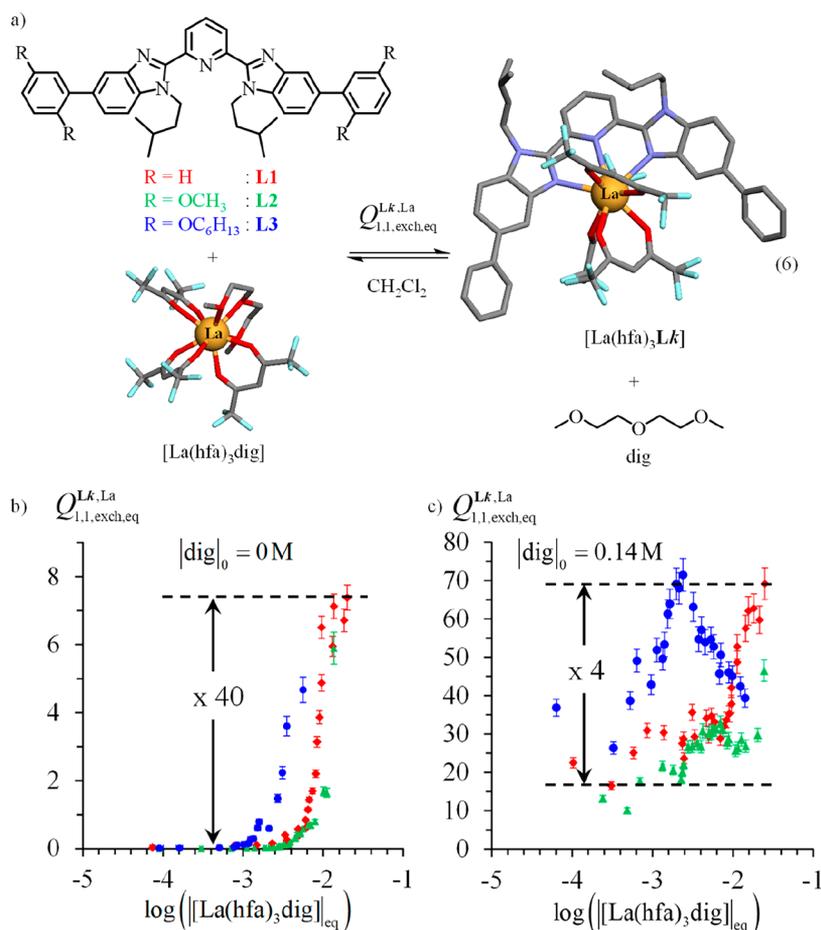


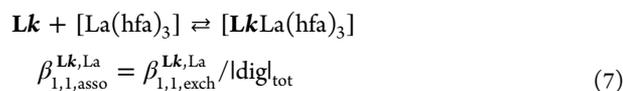
Figure 2. (a) Graphical illustration of the host–guest association involving the exchange of diglyme (dig) with tridentate ligands **L1–L3** around $[\text{La}(\text{hfa})_3]$ according to eq 6). Color code: C, gray; O, red; N, blue; F, light blue; La, orange. H atoms are omitted for clarity. Reaction quotients $Q_{1,1,\text{exch,eq}}^{\text{Lk,La}} = ([\text{LkLa}(\text{hfa})_3]_{\text{eq}}[\text{dig}]_{\text{eq}})/([\text{La}(\text{hfa})_3]_{\text{eq}}[\text{Lk}]_{\text{eq}})$ estimated during ^1H NMR titrations performed at total 10 mM host concentrations in the (b) absence and (c) presence of an excess (0.14 M) of diglyme. Color code: **L1**, red; **L2**, green; **L3**, blue.⁵

the composition of the mixture also make this approach precarious (Figure 1). We conclude that the systematic measurements of concentrations instead of activities during titration processes is a severe handicap, which finds a single acceptable key for the assembly of ionic partners in polar solvents where the ionic strength is fixed.

RESULTS AND DISCUSSION

Some Practical Attempts To Unravel the Thermodynamics of Host–Guest Assemblies in Solution. Whereas host–guest assemblies involving charged species can be satisfyingly modeled and understood thanks to the theory of the ionic atmosphere,¹ we are not aware of any comparable rationalization for related reactions conducted between neutral partners in poorly polar solvents. However, a simple look at the Margules equation plotted in Figure 1a suggests that γ_{solute} varies less when at least one member of the chemical entities under equilibrium can be fixed at high concentration, thus leveling out the change in the composition accompanying the complexation reaction. With this in mind, the titrations summarized in eq 6) were repeated, still using a 10 mM concentration of ligand receptors **L1–L3** but in the presence of a constant total concentration of 0.14 M diglyme, which is one of the products of the reaction. As anticipated, the variation of the novel equilibrium reaction quotients $Q_{1,1,\text{asso,eq}}^{\text{Lk,La}} = ([\text{LkLa}(\text{hfa})_3]_{\text{eq}}[\text{dig}]_{\text{tot}})/([\text{La}(\text{hfa})_3]_{\text{eq}}[\text{Lk}]_{\text{eq}})$ during the

titration is reduced by 1 order of magnitude (Figure 2c).⁵ For a fixed concentration of diglyme, eq 6 transforms into the conditional association process summarized in eq 7, which is reminiscent of equilibrium (1).



The plots of the occupancy factors $\theta_{\text{Lk}}^{\text{La}} = [\text{La}(\text{hfa})_3]_{\text{eq}}^{\text{bound}} / [\text{Lk}]_{\text{tot}}$ as a function of the free concentration of the $[\text{La}(\text{hfa})_3]$ guest (left part of eq 8) for the titrations of **L1–L3** conducted in $\text{CD}_2\text{Cl}_2 + 0.14 \text{ M}$ diglyme (diamonds in Figure 3a) indeed highlight only some minor shifts with respect to the theoretical binding isotherms (right part of eq 8) built by using a single thermodynamic constant $\beta_{1,1,\text{asso}}^{\text{Lk,La}} = (1/N) \sum_{i=1}^N (Q_{1,1,\text{asso,eq}}^{\text{Lk,La}})_i$ taken as the average of the N equilibrium reaction quotients determined along the titrations (dotted green traces in Figure 3a).⁵

$$\begin{aligned} \theta_{\text{Lk}}^{\text{La}} &= \frac{[\text{La}(\text{hfa})_3]_{\text{eq}}^{\text{bound}}}{[\text{Lk}]_{\text{tot}}} = \frac{[\text{La}]_{\text{tot}} - [\text{La}(\text{hfa})_3]_{\text{eq}}}{[\text{Lk}]_{\text{tot}}} \\ &= \frac{\beta_{1,1,\text{asso}}^{\text{Lk,La}} [\text{La}(\text{hfa})_3]_{\text{eq}}}{1 + \beta_{1,1,\text{asso}}^{\text{Lk,La}} [\text{La}(\text{hfa})_3]_{\text{eq}}} \end{aligned} \quad (8)$$

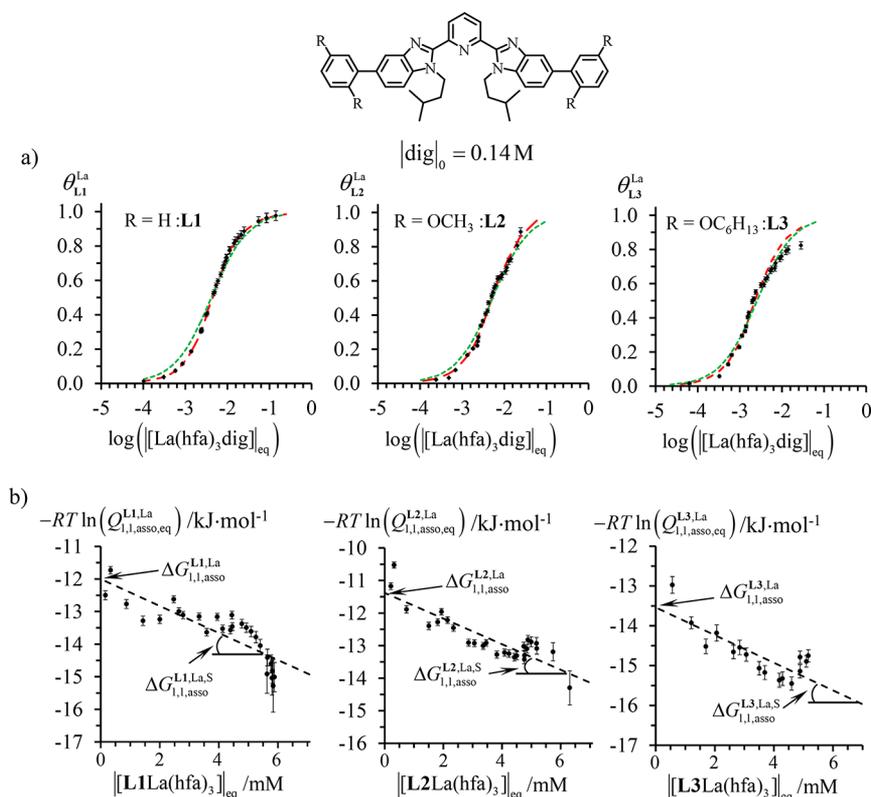


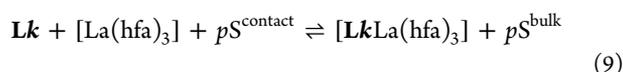
Figure 3. (a) Experimental (diamonds) and fitted (dotted green traces using eq 8; dashed red traces using eq 11) binding isotherms for the titration of **Lk** with $[\text{La}(\text{hfa})_3]\text{dig}$ in $\text{CD}_2\text{Cl}_2 + 0.14 \text{ M}$ diglyme at 298 K. (b) Dependences of the equilibrium reaction quotients $-RT \ln(Q_{1,1,asso}^{\text{Lk,La}})$ on the progress of the association reactions highlighting $\Delta G_{1,1,asso}^{\text{Lk,La}}$ and $\Delta G_{1,1,asso}^{\text{Lk,La,S}}$ according to eq 10.⁵

Table 1. Average Free Energies $-RT \ln(\beta_{1,1}^{\text{Lk,La}})$ (eqs 8 and 12, Ideal Solutions) and Thermodynamic Parameters $\Delta G_{1,1}^{\text{Lk,La}}$ and $\Delta G_{1,1}^{\text{Lk,La,S}}$ (eq 10, Nonideal Solutions), Determined for the Titrations of **Lk** with $[\text{La}(\text{hfa})_3]\text{dig}$ in $\text{CD}_2\text{Cl}_2 + 0.14 \text{ M}$ Diglyme (eq 7, Columns 2–4) or in Pure CD_2Cl_2 (eq 6, columns 5–7)^a

host	$-RT \ln(\beta_{1,1,asso}^{\text{Lk,La}})/\text{kJ}\cdot\text{mol}^{-1}$	$\Delta G_{1,1,asso}^{\text{Lk,La}}/\text{kJ}\cdot\text{mol}^{-1}$	$\Delta G_{1,1,asso}^{\text{Lk,La,S}}/\text{kJ}\cdot\text{mol}^{-1}$	$-RT \ln(\beta_{1,1,exch}^{\text{Lk,La}})/\text{kJ}\cdot\text{mol}^{-1}$	$\Delta G_{1,1,exch}^{\text{Lk,La}}/\text{kJ}\cdot\text{mol}^{-1}$	$\Delta G_{1,1,exch}^{\text{Lk,La,S}}/\text{kJ}\cdot\text{mol}^{-1}$
L1	-13.2(6)	-12.2(1)	-305(22)	-4.6(2.1)	5.9(3)	-1615(50)
L2	-9.8(6)	-8.8(1)	-254(24)	-3.4(2.7)	5.6(3)	-1503(71)
L3	-9.5(8)	-9.0(1)	-285(36)	-3.9(2.4)	4.0(3)	-2020(92)
L7	-11.5(2)	-11.6(1)	16(9)	-7.8(2.1)	-1.7(2)	-729(27)

^aThe uncertainties are those obtained by least-squares fits using eqs 8 and 10.

Interestingly, Castellano and Eggers⁶ attempted to assign the change in the activity coefficients occurring during the titrations to some desolvation processes involving the solvent molecules in contact with the reactants and products. Their simple derivation postulates that a p subset of solvent molecules in second-sphere contact with the partners of the reactions (S^{contact}) possesses a specific chemical potential, which is different from that of the bulk solvent (S^{bulk}). In these conditions, the conditional association reaction (eq 7) transforms into equilibrium (9).



This approach has been rebutted recently with the support of sophisticated and probably irrefutable statistical thermodynamic arguments.⁸ In order to avoid any controversy, it is fair to mention here that an intuitive and simple balance of chemical potentials pertinent to equilibrium (9) led Castellano and Eggers to propose eq 10,⁶ which catches the variation of the activity coefficients, with the progress of the reaction

measured by the equilibrium concentration of the formed final $[\text{LkLa}(\text{hfa})_3]$ complex ($c_{\text{LM}}^{\text{eq}}$). The factor of proportionality is written as a free-energy change $\Delta G_{1,1,asso}^{\text{L,M,S}}$ assigned to some solvation effects accompanying the association reaction, which is not taken into account by the standard chemical potentials of the various species at equilibrium (for a detailed derivation, see Appendix 1 and ref 6).

$$-RT \ln(Q_{1,1,asso}^{\text{L,M}}) = \Delta G_{1,1,asso}^{\text{L,M}} + (c_{\text{LM}}^{\text{eq}}/c^\theta) \Delta G_{1,1,asso}^{\text{L,M,S}} \quad (10)$$

Empirical plots of $-RT \ln(Q_{1,1,asso}^{\text{Lk,La}})$ as a function of $[\text{LkLa}(\text{hfa})_3]_{\text{eq}}$ for titrations of L1–L3 in the presence of a constant excess of diglyme (0.14 M) indeed support approximate linear dependences predicted by eq 10 (Figure 3b), from which the thermodynamic free-energy changes $\Delta G_{1,1,asso}^{\text{Lk,La}}$ and correction factors $\Delta G_{1,1,asso}^{\text{Lk,La,S}}$ can be extracted (Table 1, columns 2–4).⁵ The rebuilt binding isotherms using the latter two fitted parameters in eq 11 slightly improve the matching with the experimental data (Figure 3a, dashed red traces).

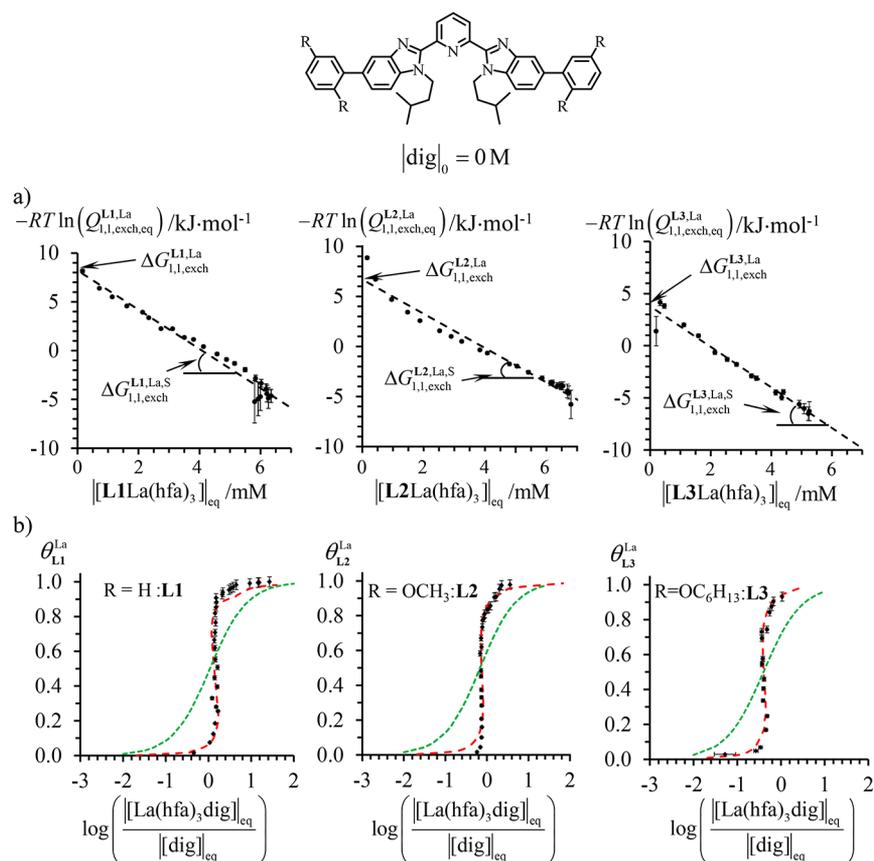


Figure 4. (a) Dependences of the equilibrium quotient reactions $-RT \ln(Q_{1,1,exch,eq}^{Lk,La})$ on the progress of the association reactions highlighting $\Delta G_{1,1,exch}^{Lk,La}$ and $\Delta G_{1,1,exch}^{Lk,La,S}$ according to eq 10. (b) Experimental (diamonds) and fitted (dashed green traces using eq 12; dashed red traces using eq 13) pseudobinding isotherms for the titration of **Lk** with $[La(hfa)_3]dig$ in CD_2Cl_2 at 298 K.⁵

$$\theta_{Lk}^{La} = \frac{[La(hfa)_3]_{eq}^{bound}}{[Lk]_{tot}} = \frac{Q_{1,1,asso,eq}^{Lk,La} [La(hfa)_3]_{eq}}{1 + Q_{1,1,asso,eq}^{Lk,La} [La(hfa)_3]_{eq}}$$

$$= \exp\left\{-\left[\Delta G_{1,1,asso}^{Lk,La} + [Lk]_{La(hfa)_3,eq} \Delta G_{1,1,asso}^{Lk,La,S}\right] / RT\right\} [La(hfa)_3]_{eq}$$

$$\left[1 + \exp\left\{-\left[\Delta G_{1,1,asso}^{Lk,La} + [Lk]_{La(hfa)_3,eq} \Delta G_{1,1,asso}^{Lk,La,S}\right] / RT\right\} [La(hfa)_3]_{eq}\right] \quad (11)$$

Related linear correlations between $-RT \ln(Q_{1,1,exch,eq}^{Lk,La})$ and $[Lk]_{La(hfa)_3,eq}$ were observed for the ligand-exchange reaction (eq 6) conducted in pure deuterated dichloromethane in the absence of a fixed concentration of diglyme (Figure 4a). Because the activity coefficients vary much more dramatically during the exchange process (compare Figure 2b for the exchange reaction with Figure 2c for the association reaction), the pseudobinding isotherms rebuilt with eq 12 and using a single average thermodynamic constant $\beta_{1,1,exch}^{Lk,La} = (1/N) \sum_{i=1}^N (Q_{1,1,exch,eq}^{Lk,La})_i$ (Table 1, column 5) are clearly not adapted (green traces in Figure 4b).

$$\theta_{Lk}^{La} = \frac{[La]_{tot} - [La(hfa)_3]_{eq}}{[Lk]_{tot}}$$

$$= \frac{\beta_{1,1,exch}^{Lk,La} ([La(hfa)_3]_{eq} / [dig]_{eq})}{1 + \beta_{1,1,exch}^{Lk,La} ([La(hfa)_3]_{eq} / [dig]_{eq})} \quad (12)$$

On the contrary, Castellano–Eggers' approach summarized in eq 10, where $\beta_{1,1,asso}^{Lk,La}$ is now replaced with $\beta_{1,1,exch}^{Lk,La}$ provides thermodynamic free-energy changes $\Delta G_{1,1,exch}^{Lk,La}$ and $\Delta G_{1,1,exch}^{Lk,La,S}$ (Table 1, columns 6 and 7) adapted to the satisfying reproduction of the experimental pseudobinding isotherms using eq 13 (Figure 4b, red traces).

$$\theta_{Lk}^{La} = \frac{Q_{1,1,exch,eq}^{Lk,La} [La(hfa)_3]_{eq}}{1 + Q_{1,1,exch,eq}^{Lk,La} [La(hfa)_3]_{eq}}$$

$$= \exp\left\{-\left[\Delta G_{1,1,exch}^{Lk,La} + [Lk]_{La(hfa)_3,eq} \Delta G_{1,1,exch}^{Lk,La,S}\right] / RT\right\} ([La(hfa)_3]_{eq} / [dig]_{eq})$$

$$\left[1 + \exp\left\{-\left[\Delta G_{1,1,exch}^{Lk,La} + [Lk]_{La(hfa)_3,eq} \Delta G_{1,1,exch}^{Lk,La,S}\right] / RT\right\} ([La(hfa)_3]_{eq} / [dig]_{eq})\right] \quad (13)$$

Note that the occupancy factors θ_{Lk}^{La} associated with the exchange reactions are plotted as a function of the ratio $[La(hfa)_3]_{eq} / [dig]_{eq}$ in eqs 12 and 13 because the concentration of diglyme is no longer constant.⁵

The positive free-energy changes $\Delta G_{1,1,exch}^{Lk,La} > 0$ (Table 1, column 6) imply logically that the replacement of a tridentate O-donor ligand (diglyme) with a less electronegative tridentate N-donor ligand **Lk** around oxophilic trivalent lanthanides is thermodynamically unfavorable.⁹ The trend $\Delta G_{1,1,exch}^{L1,La} >$

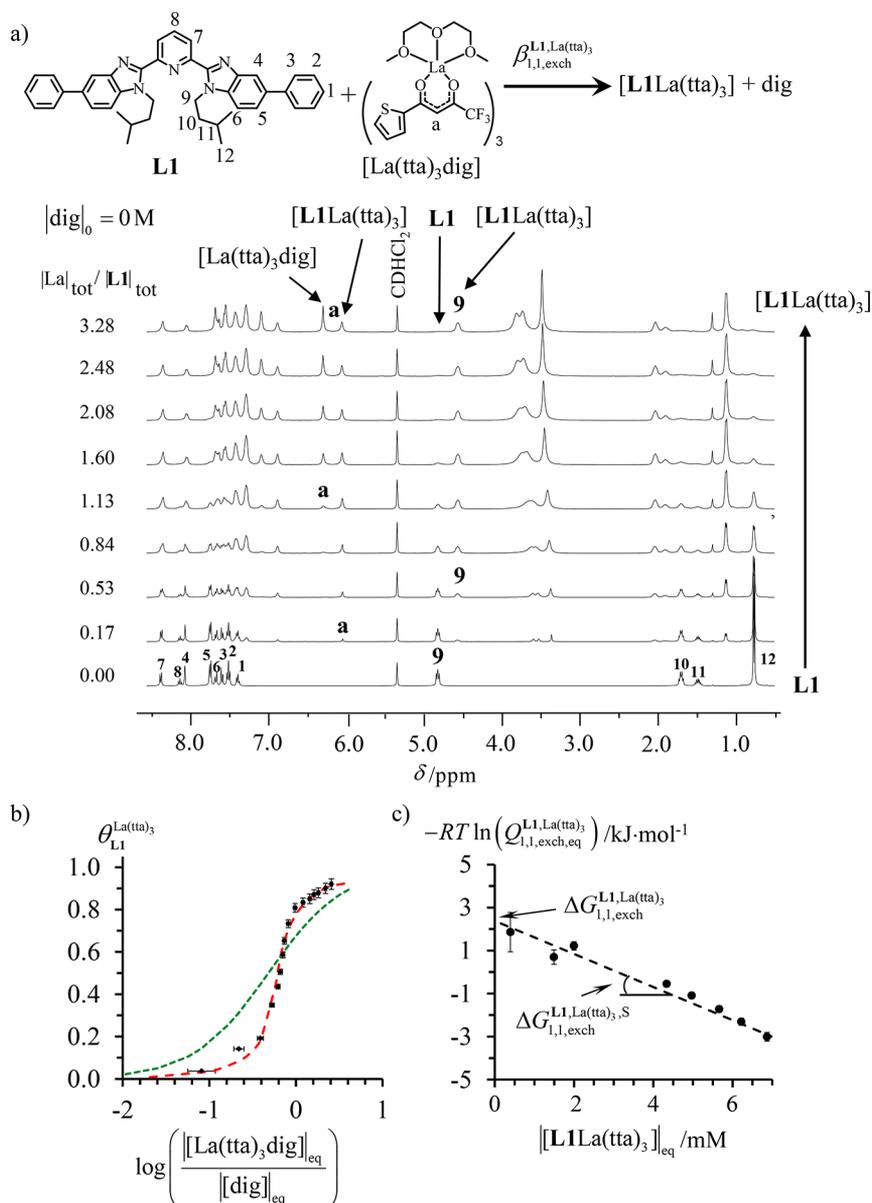


Figure 5. (a) ^1H NMR titration of **L1** with $[\text{La}(\text{tta})_3]\text{dig}$ in CD_2Cl_2 at 298 K with a numbering scheme ($8.3 \times 10^{-3} \leq |\text{L1}|_{\text{tot}} \leq 1.1 \times 10^{-2}$ M and $4.3 \times 10^{-4} \text{ M} \leq |\text{La}|_{\text{tot}} \leq 2.7 \times 10^{-2}$ M). (b) Experimental (diamonds) and fitted (dotted green traces using eq 12; dashed red traces using eq 13) pseudobinding isotherms. (c) Dependence of the equilibrium reaction quotients $-RT \ln(Q_{\text{L1,La}(\text{tta})_3}^{\text{L1,La}(\text{tta})_3})$ on the progress of the association reaction highlighting $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L1,La}(\text{tta})_3}$ and $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L1,La}(\text{tta})_3,\text{S}}$ according to eq 10.

$\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L2,La}} > \Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L3,La}}$ points to some minor, but specific, effects of the peripheral lipophilic chains on the energetic balance pertinent to the ligand-exchange process. In the presence of a constant and large excess of the leaving diglyme ligands, the energetic profiles $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La}} < 0$ (Table 1, column 3) reflect the affinity of the neutral lanthanide carrier $[\text{La}(\text{hfa})_3]$ for the entering tridentate **Lk** ligand. The associated trend $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L1,La}} < \Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L2,La}} \approx \Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L3,La}}$ is surprisingly reversed compared with that found for $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La}}$ which suggests some delicate balances in solvation processes affecting the lipophilic N-donor ligand upon changes in the nature of the solvent (pure dichloromethane for $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La}}$ and dichloromethane with 0.14 M diglyme for $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La,S}}$). Castellano–Eggers’ approach (eq 10) provides a second parameter $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La,S}}$ or $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La,S}}$ which is supposed to estimate the effect of the change in contact solvation. The data collected in Table 1 (columns 4 and 7) show huge negative values with no relationship with standard

solvation energies produced by dipole molecules immersed in a dielectric ($1\text{--}30 \text{ kJ}\cdot\text{mol}^{-1}$).¹⁰ We conclude that $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La,S}}$ or $\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{Lk,La,S}}$ cannot be interpreted in terms of simple contact solvation but that they mainly reflect the changes in the activity coefficients, a phenomenon that becomes crucial at high concentration because the $(c_{\text{eq}}^{\text{LM}}/c^\theta)\Delta G_{\text{L1,La}(\text{tta})_3}^{\text{L,M,S}}$ terms in eqn 10 become dominant and drive the quantitative replacement of diglyme with **Lk** at decimolar concentrations. Attempts to separate some pertinent enthalpic and entropic contributions using low-temperature NMR proved to be very delicate because of the technical limitations of our setup, which required a return to room temperature for opening of the NMR tube and the addition of one more crop of metal prior to restoration of the working temperature. The resulting scattered data are too imprecise to be exploited for the exchange process (equilibrium 6; see Figure S1 and Table S1). For the conditional association reaction (eq 7), the trends are more

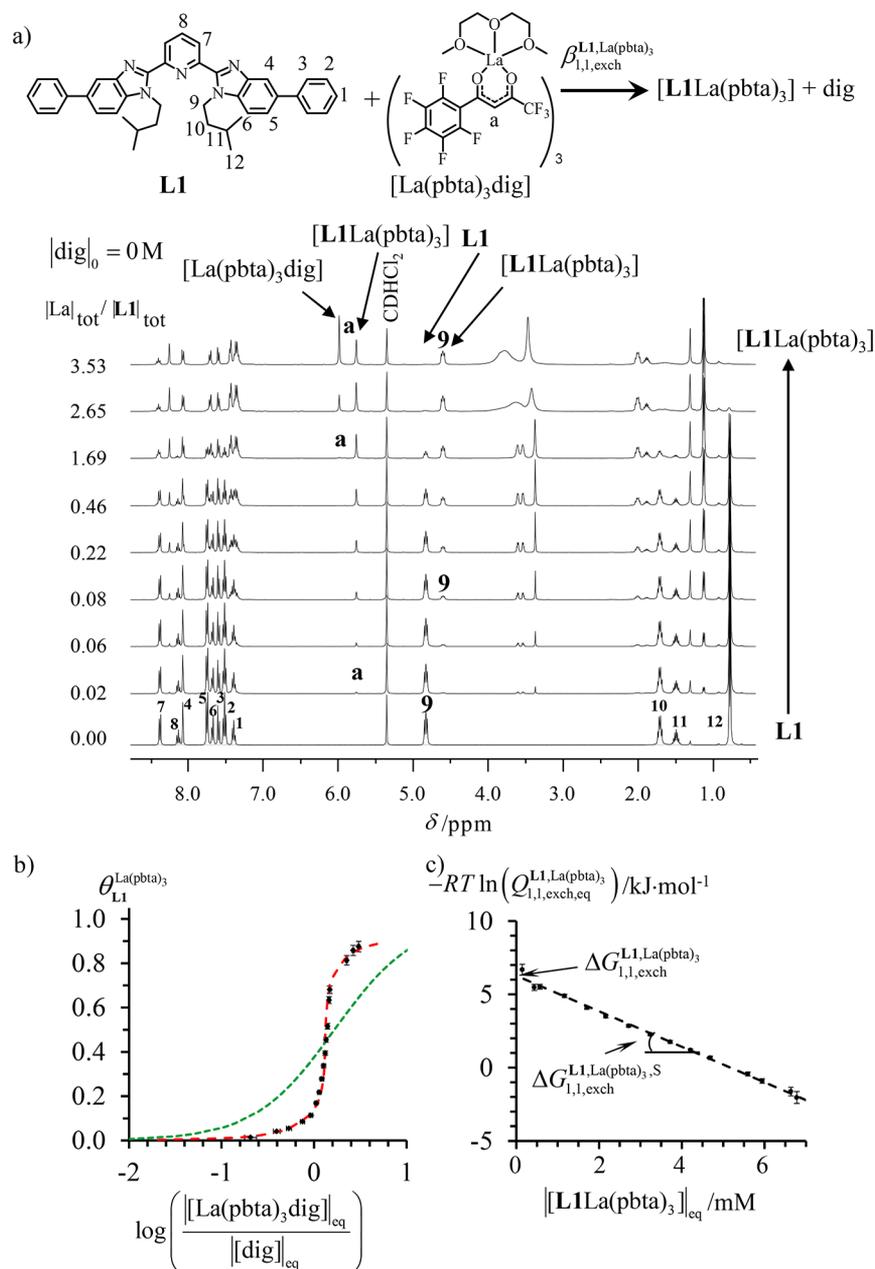


Figure 6. (a) ^1H NMR titration of **L1** with $[\text{La}(\text{pbta})_3\text{dig}]$ in CD_2Cl_2 at 298 K with a numbering scheme ($7.7 \times 10^{-3} \leq [\text{L1}]_{\text{tot}} \leq 1.1 \times 10^{-2}$ M and $1.8 \times 10^{-4} \text{ M} \leq [\text{La}]_{\text{tot}} \leq 2.7 \times 10^{-2}$ M). (b) Experimental (diamonds) and fitted (dotted green traces using eq 12; dashed red traces using eq 13) pseudobinding isotherms. (c) Dependence of the equilibrium reaction quotients $-RT \ln(Q_{1,1,\text{exch,eq}}^{\text{L1,La}(\text{pbta})_3})$ on the progress of the association reaction highlighting $\Delta G_{1,1,\text{exch}}^{\text{L1,La}(\text{pbta})_3}$ and $\Delta G_{1,1,\text{exch}}^{\text{L1,La}(\text{pbta})_3,\text{S}}$ according to eq 10.

precise and probably reliable for $\Delta G_{1,1,\text{asso}}^{\text{Lk,La}}$ (see Figure S2 and Table S2), which are characterized by slightly unfavorable enthalpy changes ($\Delta H_{1,1,\text{asso}}^{\text{Lk,La}} \geq 0$). The opposite entropic contributions ($-T\Delta S_{1,1,\text{asso}}^{\text{Lk,La}} \ll 0$) are responsible for the driving force leading to nonnegligible lanthanide-ligand association ($\Delta G_{1,1,\text{asso}}^{\text{Lk,La}} < 0$) at room temperature, a mechanism in line with the compensation model popularized during the early 1980s by Choppin for rationalizing lanthanide complexation in aqueous solution.¹¹

Applying the “Contact-Solvent Correction” Patch to the Binding of Nonsymmetrical $[\text{La}(\beta\text{-diketonate})_3]$ Guests to Tridentate Receptors **L1–**L3**.** After exploration of the systematic lipophilic changes in the ligands **L1**–**L3**, the nature of the lanthanide containers was varied by using the

nonsymmetrical $[\text{La}(\text{tta})_3\text{dig}]$ (Htta = 2-thenoyltrifluoroacetone; Figure 5a) and $[\text{La}(\text{pbta})_3\text{dig}]$ (Hpbta = perfluorophenyltrifluoroacetone; Figure 6a) complexes, with the structure of the latter being isostructural with that recently reported for $[\text{Eu}(\text{pbta})\text{dig}]$ (see Figure S3 and Tables S3–S7).¹² Again, a simple look at the experimental binding isotherms extracted from the ^1H NMR titrations of **L1**–**L3** with these nonsymmetrical lanthanide containers in pure dichloromethane [equilibrium (6); Figures 5b, 6b, and S4 and S5] or in dichloromethane containing 0.14 M diglyme [equilibrium (7); Figure S6] unambiguously shows that they obey eq 10, thus leading to approximately linear dependences of the logarithms of the equilibrium reaction quotients on the concentrations of the $[\text{LkLaX}_3]$ adducts ($X = \text{tta}, \text{pbta}$; Figures 5c and 6c). The

Table 2. Average Free Energies $-RT \ln(\beta_{1,1}^{Lk,LaX_3})$ (eqs 8 and 12) and Thermodynamic Parameters $\Delta G_{1,1}^{Lk,LaX_3}$ and $\Delta G_{1,1}^{Lk,LaX_3,S}$ (eq 10), Determined for the Titrations of *Lk* with $[La(X)_3]dig$ ($X = tta, pbta$) in $CD_2Cl_2 + 0.14$ M Diglyme

host/guest	$-RT \ln(\beta_{1,1}^{Lk,La})/kJ\cdot mol^{-1}$	$\Delta G_{1,1,asso}^{Lk,La}/kJ\cdot mol^{-1}$	$\Delta G_{1,1,asso}^{Lk,La,S}/kJ\cdot mol^{-1}$	$-RT \ln(\beta_{1,1,exch}^{Lk,La})/kJ\cdot mol^{-1}$	$\Delta G_{1,1,exch}^{Lk,La}/kJ\cdot mol^{-1}$	$\Delta G_{1,1,exch}^{Lk,La,S}/kJ\cdot mol^{-1}$
L1/tta	-10.4(6)	-8.8(1)	-463(16)	-2.5(1)	3.0(2)	-848(30)
L2/tta	<i>b</i>	<i>b</i>	<i>b</i>	-0.2(2)	4.6(1)	-973(15)
L3/tta	<i>b</i>	<i>b</i>	<i>b</i>	3.0(1)	7.0(3)	-1510(122)
L1/pbta	-12.8(2)	-12.3(1)	-100(24)	0.6(2)	6.2(1)	-1197(24)
L2/pbta	-9.3(9)	-8.4(2)	-524(69)	-0.3(2)	6.0(1)	-1368(18)
L3/pbta	<i>b</i>	<i>b</i>	<i>b</i>	-1.8(2)	4.6(2)	-2080(80)

^aThe uncertainties are those obtained by least-squares fits of eqs 8 and 10. ^bToo small affinities for being analyzed by NMR at 10 mM concentrations.

associated thermodynamic free-energy changes $\Delta G_{1,1,exch}^{Lk,LaX_3}$ and $\Delta G_{1,1,exch}^{Lk,LaX_3,S}$ for the exchange reaction ($CH_2Cl_2 + 0$ M diglyme) and $\Delta G_{1,1,asso}^{Lk,LaX_3}$ and $\Delta G_{1,1,asso}^{Lk,LaX_3,S}$ for the conditional association reactions ($CH_2Cl_2 + 0.14$ M diglyme) are gathered in Table 2 and can be directly compared with those previously reported for the symmetrical $[Ln(hfa)_3]dig$ container (Table 1).

While the magnitude of the contact-solvent corrections, which take into account the change in the activity coefficients, is difficult to rationalize (column 7 in Tables 1 and 2), the exchange free energies extrapolated at infinite dilutions (column 6 in Tables 1 and 2) are all positive and do not largely vary ($3.0 \leq \Delta G_{1,1,exch}^{Lk,LaX_3} \leq 7.0$ $kJ\cdot mol^{-1}$) whatever the choice of ligands or lanthanum containers. The Born–Haber thermodynamic cycle built in Figure 7 and summarized in eq 14 is well-suited for clarifying this observation.

$$\Delta G_{1,1,exch,sol}^{Lk,LaX_3} = \Delta G_{1,1,exch,gas}^{Lk,LaX_3} + \Delta_{solv} G_{dig}^0 - \Delta_{solv} G_{[LaX_3]dig}^0 + \Delta_{solv} G_{[LkLaX_3]}^0 - \Delta_{solv} G_{Lk}^0 \quad (14)$$

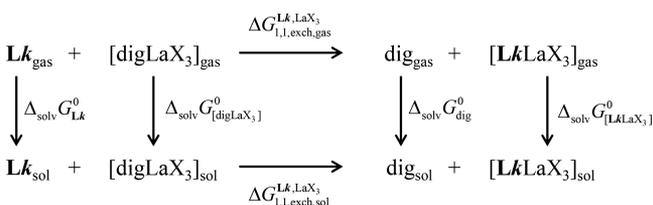


Figure 7. Thermodynamic cycle for ligand exchanges around $[La(X)_3]$ containers ($X = hfa, tta, pbta$).

For a given lanthanide container $[LaX_3]$, the gas-phase contribution $\Delta G_{1,1,exch,gas}^{Lk,LaX_3}$ is not expected to vary significantly because peripheral substitution on going from L1 to L3 has little, if any, inductive effect on the basicity of the N-donor atoms of the entering tridentate ligands. With the contribution of $\Delta_{solv} G_{dig}^0 - \Delta_{solv} G_{[LaX_3]dig}^0$ being independent of the nature of the ligands, the Born–Haber cycle summarized in eq 14 can be abridged to give eq 15.

$$\Delta G_{1,1,exch,sol}^{Lk,LaX_3} = \Delta_{solv} G_{[LkLaX_3]}^0 - \Delta_{solv} G_{Lk}^0 + \text{constant} \quad (15)$$

The variable solvation energies of the neutral dipolar molecules *Lk* and $[LkLaX_3]$ can be estimated with the help of the Onsager equation, which predicts a μ^2/R_H^3 dependence (μ is the dipole moment of the particle, and R_H is the radius of a spherical cavity cut from the dielectric when a spherical solute is immersed into the solvent).¹³ Because of the much larger dipole moments calculated for the $[LkLaX_3]$ complexes ($13.1 \leq \mu \leq 14.9$ D) compared with those of the free *Lk*

ligands ($1.5 \leq \mu \leq 3.4$ D),^{10,12} $\Delta_{solv} G_{[LkLaX_3]}^0$ (-10 to -20 $kJ\cdot mol^{-1}$) dominates $\Delta_{solv} G_{Lk}^0$ (-1 to -2 $kJ\cdot mol^{-1}$) by 1 order of magnitude. With this in mind, eq 15 predicts that the changes in $\Delta_{solv} G_{[LkLaX_3]}^0$ control those of $\Delta G_{1,1,exch,sol}^{Lk,LaX_3}$ along the ligand series for a given lanthanide container. Consequently, the only minor changes computed recently¹⁰ for the total pseudospherical volumes and electric dipoles accompanying specific ligand substitution on going from L1 to L3 fully justify the limited variation of $\Delta G_{1,1,exch,sol}^{Lk,LaX_3}$ observed in solution (column 6 in Tables 1 and 2).

Considering the alternative situation, for which different lanthanide containers are connected to the same tridentate ligand *Lk*, the situation is more complicated because the Born–Haber cycle in eq 14 translates into eq 16, which contains three variable contributions.

$$\Delta G_{1,1,exch,sol}^{Lk,LaX_3} = \Delta G_{1,1,exch,gas}^{Lk,LaX_3} + \Delta_{solv} G_{[LkLaX_3]}^0 - \Delta_{solv} G_{[LaX_3]dig}^0 + \text{constant} \quad (16)$$

The dipole moments of the lanthanide containers $[La(hfa)_3]dig$, $[La(pbta)_3]dig$, and $[La(tta)_3]dig$ decrease in the order hfa (7.7 D) > pbta (6.7 D) > tta (4.6 D), whereas those of $[L1La(hfa)_3]$, $[L1La(pbta)_3]$, and $[L1La(tta)_3]$ are more scattered (hfa, 13.8 D; pbta, 13.1 D; tta, 14.9 D).¹² With these numbers in hand, the pertinent difference $\Delta_{solv} G_{[LkLaX_3]}^0 - \Delta_{solv} G_{[LaX_3]dig}^0$ found in eq 16 is systematically negative and maximizes its favorable contribution according to the order tta \ll hfa \approx pbta if we reasonably assume similar sizes for $[L1La(X)_3]$. We therefore expect more favorable free energies of exchange for the $[La(tta)_3]$ container, a trend roughly obeyed in Tables 1 and 2 (column 6).

Extending the “Contact-Solvent Correction” Patch to Successive Host–Guest Assemblies in Solution. The detailed thermodynamic investigation of the association of monotridentate ligands L1–L3 with the $[La(X_3)]dig$ container in dichloromethane demonstrated that the equilibrium quotient reaction $Q_{1,1,asso,eq}^{L,M}$ may be an ambiguous reporter of the thermodynamic stability constants $\beta_{1,1,asso}^{L,M}$. Irrespective of the chemical origin of the dependence of the equilibrium reaction quotients on the advance of the association reactions (change in the activity coefficients according to the classical solution theory and/or consequences of contact-solvent molecules on the chemical potential of the solvent), the empirical eq 10, $-RT \ln(Q_{1,1,asso,eq}^{L,M}) = -RT \ln(\beta_{1,1,asso}^{L,M}) + (c_{eq}^{L,M}/c^0) \Delta G_{1,1,asso}^{L,M,S}$, proposed by Castellano and Eggers⁶ satisfyingly correlates these two parameters, thus leading to a specific free-energy change at infinite dilution $\Delta G_{1,1,asso}^{L,M} = -RT \ln(\beta_{1,1,asso}^{L,M})$.

However, in coordination and supramolecular chemistry, the consideration of a single equilibrium is rare and eq 10 leads to

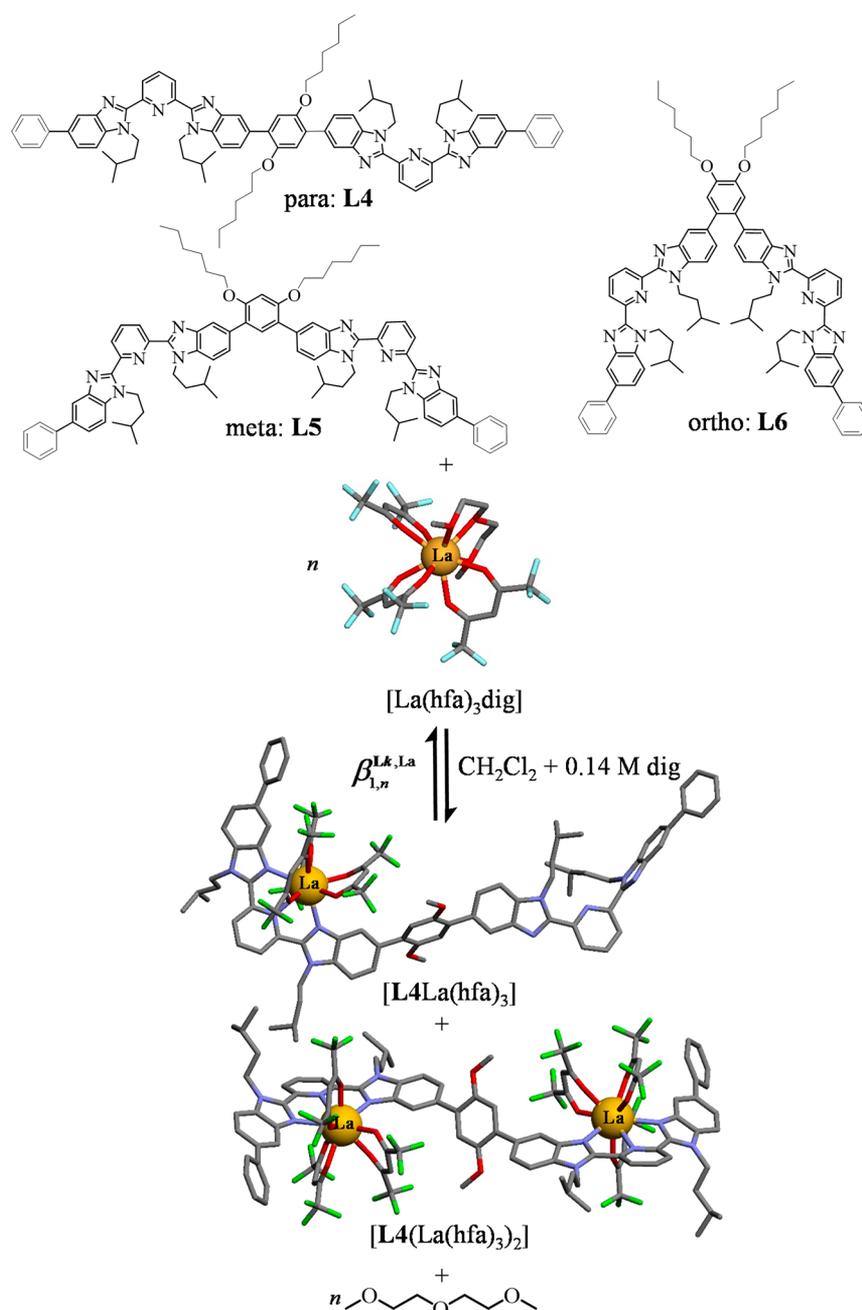
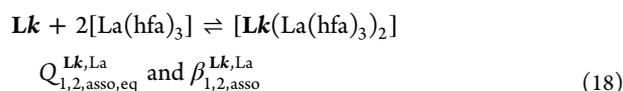
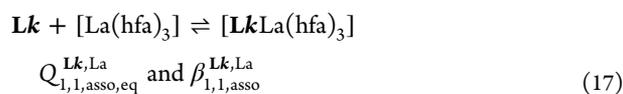


Figure 8. Host–guest association for the connection of ditridentate ligands **L4–L6** to $[\text{La}(\text{hfa})_3]$ containers.

major inconsistencies when, for instance, the ditridentate ligands **L4–L6** successively fix two $[\text{La}(\text{hfa})_3]$ guests in $\text{CH}_2\text{Cl}_2 + 0.14 \text{ M diglyme}$ to give $[\text{LkLa}(\text{hfa})_3]$ or $[\text{Lk}(\text{La}(\text{hfa})_3)_2]$ (eqs 17 and 18 and Figure 8).¹⁰



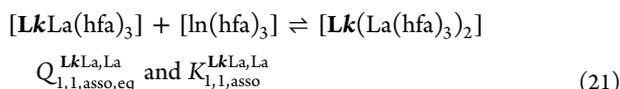
Application of eq 10 to equilibria (17) and (18) provides

$$\begin{aligned} \Delta G_{1,1,\text{asso}}^{\text{Lk,La}} &= -RT \ln(\beta_{1,1,\text{asso}}^{\text{Lk,La}}) \\ &= -RT \ln(Q_{1,1,\text{asso,eq}}^{\text{Lk,La}}) \\ &\quad - ([\text{LkLa}(\text{hfa})_3]_{\text{eq}}/c^\theta) \Delta G_{1,1,\text{asso}}^{\text{Lk,La,S}} \end{aligned} \quad (19)$$

$$\begin{aligned} \Delta G_{1,2,\text{asso}}^{\text{Lk,La}} &= -RT \ln(\beta_{1,2,\text{asso}}^{\text{Lk,La}}) \\ &= -RT \ln(Q_{1,2,\text{asso,eq}}^{\text{Lk,La}}) \\ &\quad - ([\text{Lk}(\text{La}(\text{hfa})_3)_2]_{\text{eq}}/c^\theta) \Delta G_{1,2,\text{asso}}^{\text{Lk,La,S}} \end{aligned} \quad (20)$$

Because G is a state function, standard thermodynamics require that the free-energy change $\Delta G_{1,1,\text{asso}}^{\text{LkLa,La}} = -RT \ln(K_{1,1,\text{asso}}^{\text{LkLa,La}})$ associated with the fixation of the second $[\text{La}(\text{hfa})_3]$ container to $[\text{LkLa}(\text{hfa})_3]$ (eq 21) is given by the

difference between the two cumulative processes $\Delta G_{1,1,asso}^{LkLa,La} = \Delta G_{1,2,asso}^{Lk,La} - \Delta G_{1,1,asso}^{Lk,La}$



In ideal solutions, the equilibrium reaction quotients strictly mirror the thermodynamic stability constants, and eq 22 holds.

$$\Delta G_{1,1,asso}^{LkLa,La} = -RT \ln(K_{1,1,asso}^{LkLa,La}) = -RT \ln(Q_{1,1,asso,eq}^{LkLa,La})$$

$$= -RT \ln(Q_{1,2,asso,eq}^{Lk,La} / Q_{1,1,asso,eq}^{Lk,La}) \quad (22)$$

For nonideal solutions, the use of eqs 19 and 20 gives eq 23

$$\Delta G_{1,1,asso}^{LkLa,La} = -RT \ln(K_{1,1,asso}^{LkLa,La})$$

$$= -RT \ln(Q_{1,2,asso,eq}^{Lk,La} / Q_{1,1,asso,eq}^{Lk,La})$$

$$- (|Lk(La(hfa)_3)_2|_{eq} / c^\theta) \Delta G_{1,2,asso}^{Lk,La,S}$$

$$+ (|LkLa(hfa)_3|_{eq} / c^\theta) \Delta G_{1,1,asso}^{Lk,La,S} \quad (23)$$

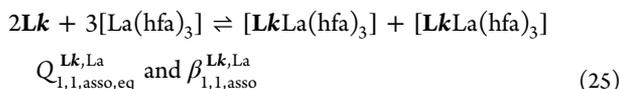
which is close, *but not equal*, to the application of Castellano–Eggers’ approach (eq 10) to equilibrium (21) summarized in eq 24.

$$\Delta G_{1,1,asso}^{LkLa,La} = -RT \ln(K_{1,1,asso}^{LkLa,La})$$

$$= -RT \ln(Q_{1,2,asso,eq}^{Lk,La} / Q_{1,1,asso,eq}^{Lk,La})$$

$$- (|Lk(La(hfa)_3)_2|_{eq} / c^\theta) \Delta G_{1,1,asso}^{LkLa,La,S} \quad (24)$$

The unacceptable discrepancy between eqs 23 and 24 originates from the contribution of contact solvation, which considers different corrections for the formation of $[Lk(La(hfa)_3)_2]$ depending on the “mechanism” of its formation, either from Lk and two $[La(hfa)_3]$ containers [equilibrium (18) and eq 20] or from $[LkLa(hfa)_3]$ and one $[La(hfa)_3]$ container [equilibrium (21) and eq 24]. This limitation can be overcome by considering the sum of the two cumulative complexation reactions in equilibrium (25) because the relative fractions of each formed complex $[LkLa(hfa)_3]$ and $[Lk(La(hfa)_3)_2]$ during the titration procedure are now associated with their specific contact solvation correction in eq 26. Now, the Born–Haber cycle $\Delta G_{2,3,asso}^{Lk,La} = \Delta G_{1,1,asso}^{Lk,La} + \Delta G_{1,2,asso}^{Lk,La}$ is obeyed (see eqs 19, 20, and 26).



$$\Delta G_{2,3,asso}^{Lk,La} = -RT \ln(\beta_{2,3,asso}^{Lk,La})$$

$$= -RT \ln(Q_{2,3,asso,eq}^{Lk,La})$$

$$- (|LkLa(hfa)_3|_{eq} / c^\theta) \Delta G_{1,1,asso}^{Lk,La,S}$$

$$- (|Lk(La(hfa)_3)_2|_{eq} / c^\theta) \Delta G_{2,1,asso}^{Lk,La,S} \quad (26)$$

Mathematically speaking, eq 26 corresponds to the equation of a plane in a three-dimensional $(|LkLa(hfa)_3|_{eq}; |Lk(La(hfa)_3)_2|_{eq}; -RT \ln(Q_{2,3,asso,eq}^{Lk,La}))$ Cartesian frame (Figures 9 and S7 and S8). Bilinear least-squares fits of the titration data collected¹⁰ for the titrations of L4–L6 with $[La(hfa)_3]_{dig}$ in $CH_2Cl_2 + 0.14$ M diglyme provide total free-energy changes

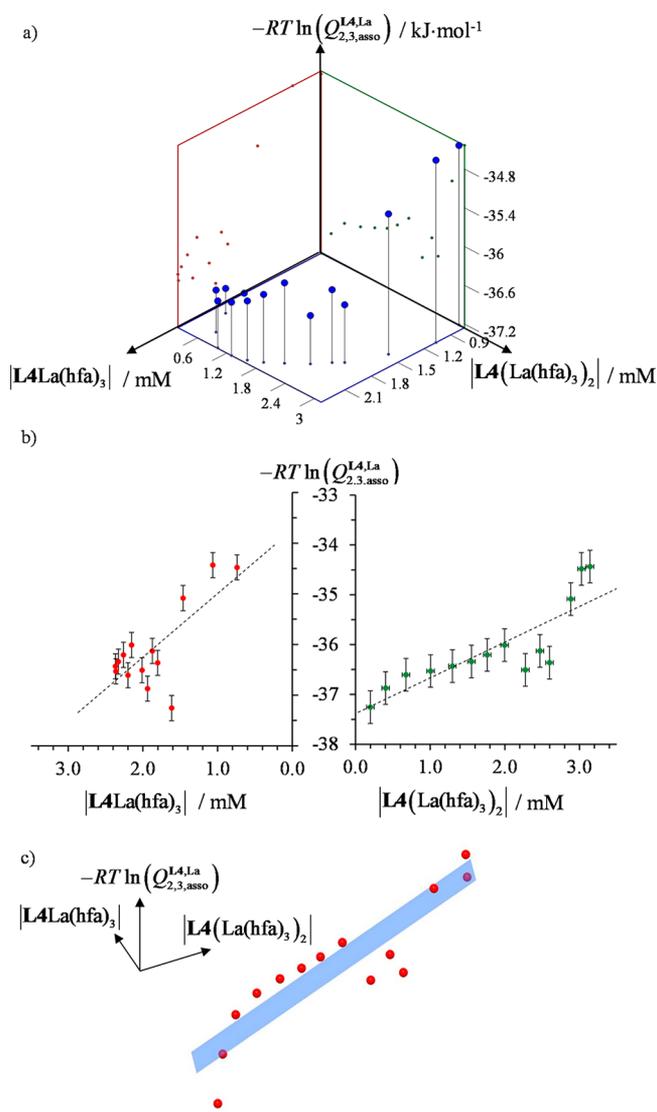


Figure 9. Plots of (a) $-RT \ln(Q_{2,3,asso}^{L4,La})$ as a function of $[L4La(hfa)_3]_{eq}$ and $[L4(La(hfa)_3)_2]_{eq}$ according to eq 26. (b) Projections onto the $[L4(La(hfa)_3)_2]_{eq} = \text{constant}$ plane (left) and $[L4La(hfa)_3]_{eq} = \text{constant}$ plane (right). (c) Projection roughly orthogonal to the best least-squares plane (shown in blue) for the titration of L4 with $[La(hfa)_3]_{dig}$ in $CH_2Cl_2 + 0.14$ M diglyme (298 K).

and “solvation” corrections $\Delta G_{1,1,asso}^{Lk,La,S}$ and $\Delta G_{1,2,asso}^{Lk,La,S}$ gathered in Table 3.

The fitted binding isotherms rebuilt using eq 27 are shown as red traces in Figure 10 and do not display major improvements compared with the previously reported fits¹⁰ taking the constant activity coefficients for granted (green dotted traces in Figure 10).

Table 3. Free-Energy Changes $\Delta G_{2,3,asso}^{Lk,La,0}$ and Associated Contact Solvation Variations $\Delta G_{1,1,asso}^{Lk,La,S}$ and $\Delta G_{1,2,asso}^{Lk,La,S}$ (eq 26) for the Titration of Lk with $[La(hfa)_3]_{dig}$ in $CH_2Cl_2 + 0.14$ M Diglyme (298 K)

	L4	L5	L6
$\Delta G_{2,3,asso}^{Lk,La,0} / \text{kJ} \cdot \text{mol}^{-1}$	-36.1(8)	-32.2(7)	-43.3(8)
$\Delta G_{1,1,asso}^{Lk,La,S} / \text{kJ} \cdot \text{mol}^{-1}$	-514(351)	552(282)	1190(357)
$\Delta G_{1,2,asso}^{Lk,La,S} / \text{kJ} \cdot \text{mol}^{-1}$	525(144)	-378(100)	559(158)

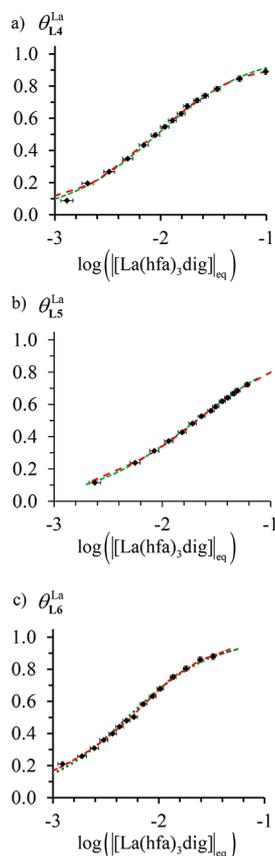
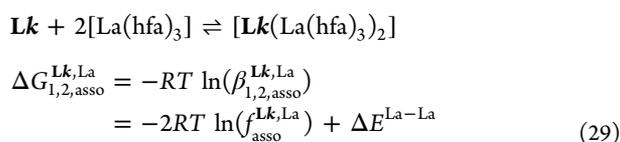
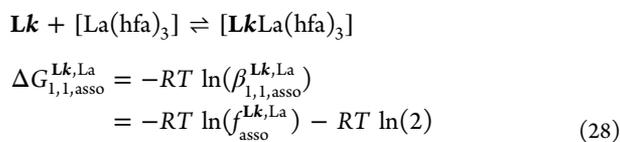


Figure 10. Experimental (diamonds) and fitted (dashed red traces using eq 27) binding isotherms for the titrations of (a) L4, (b) L5, and (c) L6 with $[La(hfa)_3]dig$ in $CH_2Cl_2 + 0.14$ M diglyme (298 K). The green dotted traces correspond to previous fits assuming fixed activity coefficients as reported in ref 10.

$$\theta_{Lk}^{La} = \frac{[LkLa(hfa)_3]_{eq} + 2[Lk(La(hfa)_3)_2]_{eq}}{2[Lk]_{tot}} \quad (27)$$

When standard thermodynamics is followed (i.e., $\Delta G_{1,2,asso}^{Lk,La} = \Delta G_{1,2,asso}^{Lk,La} + \Delta G_{1,1,asso}^{Lk,La}$), the introduction of contact-solvent corrections for multiple successive complexation processes (eqs 17 and 18) performed in excess of diglyme does not improve significantly the thermodynamic analysis (Figure 10). Consequently, the cooperativity factors for the successive binding of two $[La(hfa)_3]$ to L4 [$\Delta E^{La-La} = 0.1(2)$ $\text{kJ}\cdot\text{mol}^{-1}$], L5 [$\Delta E^{La-La} = 1.15(5)$ $\text{kJ}\cdot\text{mol}^{-1}$], and L6 [$\Delta E^{La-La} = -0.8(2)$ $\text{kJ}\cdot\text{mol}^{-1}$]¹⁰ deduced from the simple site-binding model applied in the absence of contact-solvent corrections (eqs 28 and 29) are reliable ($f_{asso}^{Lk,La}$ is the intrinsic affinity, and ΔE^{La-La} is the closest-neighbor intersite interaction).¹⁰



Deciphering Lipophilicity as a Major Issue for Programming Host–Guest Assemblies in Solution.

Having now in hand a safe procedure for analyzing the intrinsic affinities of lanthanide containers for tridentate binding sites, it is worth questioning the unsolved stepwise decrease of the latter parameter with the length of the oligomeric host (Figure 11).^{10,14} The logarithmic dependence

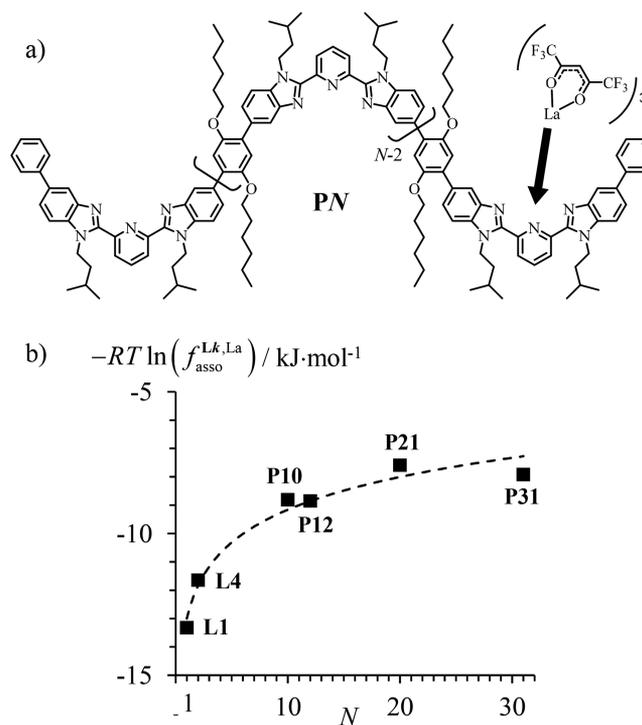


Figure 11. (a) Chemical structures and (b) Intrinsic association free energies $-RT \ln(f_{asso}^{Lk,La})$ for equilibrium (7) using monomeric ligand L1 ($N = 1$), dimer L4 ($N = 2$), and polymers PN ($N = 10, 12, 20$, and 31) with $[La(hfa)_3]$ (N is the number of available tridentate binding sites; $CD_2Cl_2 + 0.14$ M diglyme, 298 K).^{10,14}

of $-RT \ln(f_{asso}^{Lk,La})$ on the increasing size (N) of the multitridentate oligomers (Figure 11b) was tentatively assigned in ref 10 to the balance of the solvation energies, which is controlled by the systematic freezing of rotational degrees of freedom accompanying complexation of the entering metals to the receptors to give the target metallopolymers $\{PN[La(hfa)_3]_n\}$ ($1 \leq n \leq N$). However, a simple look at PN shows that the amount of lipophilic chains also linearly grows with the number of binding sites N and may therefore offer an alternative explanation, which is supported by the decrease of the affinities of the tridentate binding site for $[La(hfa)_3]$ on going from L1 [no lipophilic hexyloxy chains; $\Delta G_{1,1,asso}^{L1,La} = -RT \ln(f_{asso}^{L1,La}) = -12.2(1)$ $\text{kJ}\cdot\text{mol}^{-1}$] to L3 [four lipophilic hexyloxy chains; $\Delta G_{1,1,asso}^{L3,La} = -RT \ln(f_{asso}^{L3,La}) = -9.0(1)$ $\text{kJ}\cdot\text{mol}^{-1}$]. Interestingly, the intrinsic affinity $\Delta G_{1,1,asso}^{L4,La} = -RT \ln(f_{asso}^{L4,La}) = -11.6(1)$ $\text{kJ}\cdot\text{mol}^{-1}$ of the dimeric ligand L4, which possesses two binding sites separated by a phenyl spacer bearing two hexyloxy chains, lies between those of L1 and L3.

The nonsymmetrical monomeric ligand L7 (Figure 12a and Scheme 1) with two lipophilic hexyloxy chains thus represents the missing link for assigning the thermodynamic trend depicted in Figure 11 either to the larger size of the molecular receptor or to the larger amount of lipophilic hexyloxy chains brought by the disubstituted *p*-phenylene spacers as N

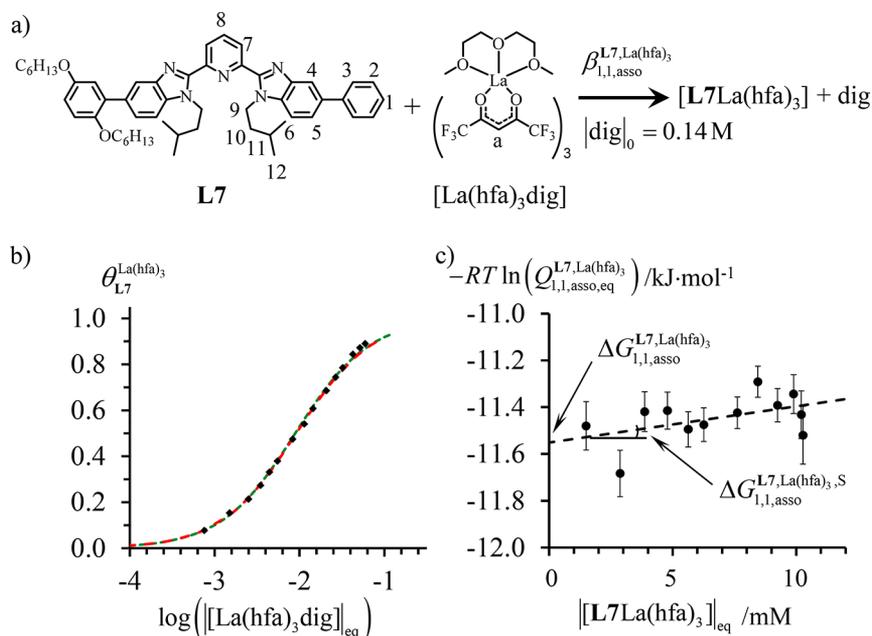
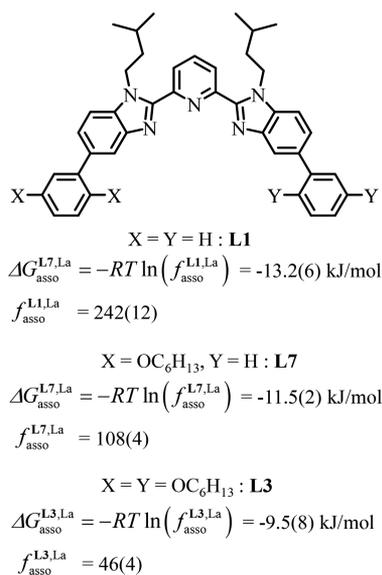


Figure 12. (a) Association reaction between the nonsymmetrical ligand L7 and [La(hfa)₃]dig. (b) Experimental (diamonds) and fitted (dotted green traces using eq 8; dashed red traces using eq 11) binding isotherms for the titration of L7 with [La(hfa)₃]dig in CD₂Cl₂ + 0.14 M diglyme at 298 K. (c) Dependence of the equilibrium reaction quotients $-RT \ln(Q_{1,1,asso,eq}^{L7,La(hfa)_3})$ on the progress of the association reaction highlighting $\Delta G_{1,1,asso}^{L7,La(hfa)_3}$ and $\Delta G_{1,1,asso}^{L7,La(hfa)_3,S}$ according to eq 10.

Scheme 1. Intrinsic Binding Affinities of Monomeric Ligands L1, L3, and L7 for La(hfa)₃ in CD₂Cl₂ + 0.14 M Diglyme at 298 K



increases. The tricky synthesis of L7 is reported in Appendix 2. ¹H NMR titrations of L7 with [La(hfa)₃]dig conducted in the absence of diglyme (Figure S9) and in the presence of an excess (0.14 M) of diglyme (Figures 12 and S10) indeed gave $\Delta G_{asso}^{L7,La} = -RT \ln(f_{asso}^{L7,La}) = -11.5(2) \text{ kJ}\cdot\text{mol}^{-1}$ (Table 1), a value intermediate between those found for the related monomeric ligand without a lipophilic chain (L1) and that with four chains (L3). Moreover, the $\Delta G_{asso}^{L7,La}$ found for the nonsymmetrical monomeric ligand L7 exactly fits $\Delta G_{asso}^{L4,La} = -11.6(1) \text{ kJ}\cdot\text{mol}^{-1}$, where two related tridentate sites are connected in the dimeric ligand L4.

We conclude that the surprising logarithmic dependence observed for the intrinsic affinity on the length of the polymer (Figure 11b) does not originate from the increasing number of connected binding sites as originally thought,¹⁰ but it is the result of the reduced intrinsic affinities of the tridentate binding units for La(hfa)₃ when peripheral lipophilic 1,4-dihexyloxyphenyl substituents are connected to the distal benzimidazole rings (Scheme 1). In other words, the lipophilic ligand L3 may be considered as a valuable model of the binding sites in the bulk of the linear polymers PN, whereas L7 is well-suited for modeling the terminal sites of these polymers. However, ligand L1 is not pertinent for modeling any of the binding sites in polymer PN.

CONCLUSIONS

The host–guest assemblies between the neutral lanthanum carriers [La(β-diketonate)₃] and the tridentate N-donor binding sites found in ligands L1–L7 unambiguously rely on nonideal solute–solution mixtures in dichloromethane. The additional nonelusive enthalpic contribution to the mixing entropy modeled by the classical solution theory predicts that the equilibrium reaction quotients Q_{eq} deduced from molar speciation in solution (i) significantly deviate from the thermodynamic equilibrium constants β and (ii) depend on the total concentrations of the hosts and guests (eq 5). These previsions were experimentally confirmed by systematic NMR titrations (Figure 2). For an analytical chemist, this behavior is usually assigned to some changes in the activity coefficients γ_i , and only setting them to a fixed value during the complete titrations is acceptable for restoring standard binding isotherms reminiscent of those observed in ideal solutions ($\gamma_i = 1$). This situation is common for reactions involving ionic partners in polar solvents, and the Debye–Hückel approach demonstrates that a large and constant ionic strength ensures constant activity coefficients. For host–guest associations involving neutral partners, rough consideration of the classical solution

theory limited to binary mixtures combined with the Margules equation (summarized in eq 5) suggests that setting one of the partners of the reaction at a large and constant concentration should restore proportionality between the thermodynamic stability constant β and equilibrium reaction quotients Q_{eq} . We therefore decided to set the concentration of diglyme (dig) at 0.14 M for our association reactions summarized in eq 6, which corresponds to sufficient excess for considering the concentration of this partner of the reaction as dominant and constant during the NMR titrations of ligands L1–L7 with $[\text{La}(\beta\text{-diketonate})_3\text{dig}]$ containers. In these conditions, only minor drift could be detected between the ideal binding isotherms (dashed green traces in Figures 3a, 10, and 12) and the experimental occupancy factors (black diamonds in these figures). We therefore recommend this approach for the easy collection of conditional stability constants pertinent to association processes involving neutral partners in nonideal solutions. When working with pure solvents with no excess of a given partner of the reaction in solution, the fluctuation of the activity coefficients with the evolution of the nonideal mixtures prevents extraction of the pertinent stability constants from the various equilibrium reaction quotients (see, for instance, the green traces in Figures 4b, 5b, and 6b). On the basis of some interesting and chemically intuitive considerations of the solvent reorganization processes, which accompany the host-guest assembly depicted in eq 9, Castellano and Eggers⁶ proposed that deviation from the ideality estimated by $RT\xi[1 - (c_{\text{L}}^{\text{tot}} + c_{\text{M}}^{\text{tot}} - c_{\text{LM}}^{\text{eq}}/c_{\text{B}})]^2$ in eq 5 in terms of free energy could be modeled using a simple linear correction $\Delta G^{\text{S}}c_{\text{LM}}^{\text{eq}}$ in eq 10 (Appendix 1). ΔG^{S} thus stands for some additional changes in the solvent-solute contact interactions, which are not taken into account by the chemical potential of the pure solvent and partners. The empirical application of eq 10 to the NMR titrations of monomeric ligands L1–L3 and L7 indeed shows roughly linear plots between $-RT \ln(Q_{\text{eq}})$ and $c_{\text{LM}}^{\text{eq}}$ (Figures 4a, 5c, 6c, and 12), a behavior paralleled in two dimensions when using ditridentate ligands L4–L6 with two available binding sites (Figure 9). This gives access to the free-energy change $\Delta G_{1,1}^{\text{L,M}}$ at infinite dilution ($c_{\text{LM}}^{\text{eq}} \rightarrow 0$), which is related to a thermodynamic equilibrium constant $\beta_{1,1}^{\text{L,M}} = e^{-\Delta G_{1,1}^{\text{L,M}}/RT}$, together with a second parameter ΔG^{S} , which measures the sensitivity of the activity coefficients to the exact composition of the nonideal mixture. The often huge experimental values estimated for ΔG^{S} (hundreds to thousands of kilojoules per mole in Tables 1 and 2) prevent its interpretation as a straightforward balance of solvation energies brought by the replacement of the reactants with products during the chemical reaction because the Onsager equation returns a maximum of a few tens of kilojoules per mole for the solvation energies of these complexes and ligands in dichloromethane.¹⁰ Whatever its theoretical justification, ΔG^{S} can be considered by experimental coordination chemists as a constant specific to a given solvent and a specific reaction, which transforms the equilibrium reaction quotients $Q_{1,1,\text{eq}}^{\text{L,M}}$ obtained by speciation at equilibrium into a single thermodynamic constant at infinite dilution $\beta_{1,1}^{\text{L,M}}$. This approach restores some pertinent comparisons between the intrinsic affinities recorded for various ligands (Scheme 1) and different lanthanide containers (Table 2) in a given solvent. It is probably worth mentioning here that the addition of external chemical species, not involved in the chemical reaction, is expected to change the magnitudes of $\Delta G_{1,1}^{\text{L,M}}$ and ΔG^{S} because the nature of the

solvent has changed. However, there is no reason for inducing any significant reduction of the fluctuation of the activity coefficients during the titrations. This statement was confirmed by repeating the ¹H NMR titrations of L1–L3 in dichloromethane by adding 0.2 M of either benzene (Figure S11) or NBu₄PF₆ (Figure S12), which indeed showed no smoothing in the change of the activity coefficients of the reacting partners (Tables S8 and S9).

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.9b00755.

Derivation of eq 10 (Appendix 1), synthesis of ligand L7 (Appendix 2), tables of crystal data, geometric parameters, and thermodynamic data, and figures showing molecular structures, ¹H NMR titrations, and thermodynamic binding isotherms (PDF)

Accession Codes

CCDC 1902650 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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