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Binding of Diamines to *n*-Butyllithium Dimers: Relative Solvation Energies and Evidence of Correlated Solvation

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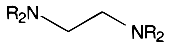
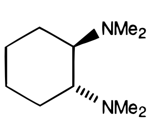
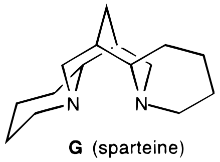
Polyamines such as *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) have had an enormous impact within organolithium chemistry.[1,2] However, despite extensive structural and mechanistic studies,[2,3] it is still not clear how chelating ligands influence organolithium structure and reactivity.[3] As part of an effort to understand structure−reactivity relationships in organolithium chemistry, we have been investigating the role of TMEDA and related chelating ligands.[4] We describe herein spectroscopic investigations of *n*-butyllithium (*n*-BuLi) solvated by an assortment of vicinal diamines.[5,6] These studies reveal highly ligand-dependent solvation energies and correlated solvation effects.



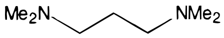
A; $NR_2 = NMe_2$ (TMEDA)
B; $NR_2 = NEt_2$ (TEEDA)
C; $NR_2 = N(CH_2)_4$
D; $NR_2 = N(CH_2)_5$



F (TMCDA)



G (sparteine)



E (TMPDA)

^{13}C NMR spectra of toluene-d_8 solutions containing freshly recrystallized[7] [^{6}Li]*n*-BuLi (0.10 M) and a diamine (**A**−**G**; 0.10−0.40 M)[8] reveal that a single structural form (>20:1) exists at −70 °C in each case. The α ^{13}C resonances display multiplicities (quintets, $J_{^6\mathrm{Li}-^{13}\mathrm{C}} = 7-8$ Hz) and chemical shifts (11.8−15.1 ppm) characteristic of cyclic dimers (**1A**−**1G**).[5] The free and coordinated diamines could be observed in the slow exchange limit by ^{13}C NMR spectroscopy in some instances.[9] The corresponding ^{6}Li NMR spectra display a single resonance in each case.[10a] Samples containing molar excesses of two diamines display two new ^{6}Li resonances of a heterosolvate, $(n\text{-BuLi})_2SS'$, along with one or both homosolvates, $(n\text{-BuLi})_2S_2$ and $(n\text{-BuLi})_2S'_2$ (Figure 1).[10b]

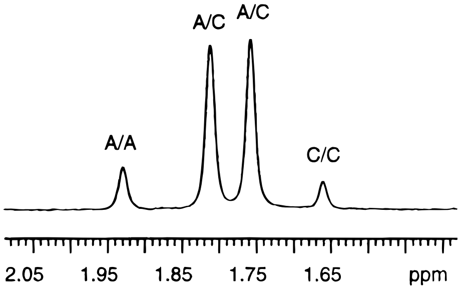
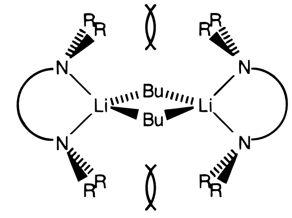


Figure 1. ^{6}Li NMR spectrum of a 0.10 [^{6}Li]*n*-BuLi/toluene-d_8 solution containing 0.6 equiv of TMEDA (**A**) and 0.6 equiv of 1,2-dipyrrolidinoethane (**C**) at −100 °C. Labels refer to homosolvated (**A**/**A** = **1A** and **C**/**C** = **1C**) and heterosolvated (**A**/**C**) *n*-BuLi dimer (**1**).



1 A-G

In principle, the relative binding constants for a two-step ligand substitution (K_1 and K_2, eq 1) and the equilibrium constants for the complete ligand exchange (K_{tot}) could be determined for any pair of diamines by competing the two diamines for complexation to the *n*-BuLi dimer (eqs 2−4). However, the homosolvate containing two inferior ligands cannot always be observed, allowing only K_1 to be determined. To obtain K_2 and K_{tot}, the two ligands are competed under conditions in which the total ligand concentration is in only slight excess to the *n*-BuLi concentration. The low total ligand concentration forces the coordination of *both* ligands irrespective of the relative ligand binding affinities. This allows $(n\text{-BuLi})_2S_2$, $(n\text{-BuLi})_2S'_2$, and $(n\text{-BuLi})_2SS'$ to be observed concomitantly and K' to be determined from eqs 5 and 6. K_2 and K_{tot} can then be calculated with eqs 7 and 8. Formally, K' is a measure of the extent that solvation is correlated. However, if only statistical factors are considered, then $K' = 4$ and $K_1 = 4K_2$.[11] Consequently, we define a new constant, K_{corr}, according to eq 9 to describe *nonstatistical* preferences for heterosolvation. If there is no steric or electronic communication between the bound diamines, then $K_{\mathrm{corr}} = 1$. Nonstatistical preferences for the hetero- or homosolvates would be reflected by $K_{\mathrm{corr}} \neq 1$. The key equilibrium constants (K_{corr},

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[8] For leading bibliographies to diamines **A**−**G**, see ref 4.

[9] Free and coordinated ligand could not be completely resolved for ligands **E**, **F**, and **G**.

[10] (a) Dimer **1G** displays two resonances in a nearly 1:1 ratio, consistent with two possible orientations of the sparteines. (b) On occasion, one of the two heterosolvate ^{6}Li resonances was obscured by the resonance of the homosolvate. Adjustments of the ligand concentration confirm the location of the missing resonance, which could then be accounted for in the resonance integrations.

[11] For the proper treatment of statistical factors, see: Benson, S. W. *J. Am. Chem. Soc.* **1958**, *80*, 5151. For additional leading references to statistical contributions in "redistribution reactions", see: Fay, R. C.; Lowry, R. N. *Inorg. Chem.* **1974**, *13*, 1309.

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Table 1. Relative Binding Constants and Free Energies of Solvation by Diamines **A**−**G** to *n*-BuLi Dimer **1**

		K_{corr}[b]						
ligand	K_{tot} ($\Delta G°_{\mathrm{tot}}$)[a]	**A**	**B**	**C**	**D**	**E**	**F**	**G**
TMEDA (**A**)	1 (0)	1						
TEEDA (**B**)	2.2×10^{-4} (2.9)	30	1					
DpyrE (**C**)	0.75 (0.1)	33	*c*	1				
DpipE (**D**)	6.9×10^{-4} (2.5)	110	*c*	0.90	1			
TMPDA (**E**)	1.2×10^{-3} (2.3)[d]	1.0	0.65	2.1	2.5	1		
(*R*,*R*)-TMCDA (**F**)	5.7 (−0.6)	1.1	13	20	50	1.1	1	
(−)-sparteine (**G**)	7.1×10^{-3} (1.7)	4.5	0.20	0.93	0.15	0.65	0.60	1

[a] Relative binding constants (K_{tot}) and binding energies ($\Delta G°_{\mathrm{tot}}$, kcal/mol) of diamines (S′) relative to TMEDA (S) were determined according to eqs 7 and 8 by competing TMEDA (**A**) against diamines **B**−**G** and are estimated to be ±10%. [b] Correlated binding constants (K_{corr}) were determined according to eqs 5−9 by competing combinations of ligands **A**−**G** as described in the text. [c] Complete overlap of the resonances of the homosolvates precluded determination of K_{corr}. [d] Exchange broadening was significant for *n*-BuLi/TMPDA/TMEDA. K_{tot} of TMPDA was determined by competing TMPDA (**B**) against TEEDA (**C**).

K_1, K_2, and K_{tot}) are summarized in Table 1. K_{tot} is scaled relative to TMEDA (S = TMEDA, S′ = diamine).

$$(n\text{-BuLi})_2\mathrm{S}_2 + 2\mathrm{S}' \xrightleftharpoons{K_1} (n\text{-BuLi})_2\mathrm{SS}' + \mathrm{S} + \mathrm{S}' \xrightleftharpoons{K_2} (n\text{-BuLi})_2\mathrm{S}'_2 + 2\mathrm{S} \quad (1)$$

$$K_1 = \{[(n\text{-BuLi})_2\mathrm{SS}'][\mathrm{S}]\}/\{[(n\text{-BuLi})_2\mathrm{S}_2][\mathrm{S}']\} \quad (2)$$

$$K_2 = \{[(n\text{-BuLi})_2\mathrm{S}'_2][\mathrm{S}]\}/\{[(n\text{-BuLi})_2\mathrm{SS}'][\mathrm{S}']\} \quad (3)$$

$$K_{\mathrm{tot}} = K_1K_2 = [(n\text{-BuLi})_2\mathrm{S}'_2][\mathrm{S}]^2/[(n\text{-BuLi})_2\mathrm{S}_2][\mathrm{S}']^2 \quad (4)$$

$$(n\text{-BuLi})_2\mathrm{S}_2 + (n\text{-BuLi})_2\mathrm{S}'_2 \xrightleftharpoons{K'} 2(n\text{-BuLi})_2\mathrm{SS}' \quad (5)$$

$$K' = \{[(n\text{-BuLi})_2\mathrm{SS}']^2\}/\{[(n\text{-BuLi})_2\mathrm{S}_2][(n\text{-BuLi})_2\mathrm{S}'_2]\} \quad (6)$$

$$K' = K_1/K_2 \quad (7)$$

$$K_{\mathrm{tot}} = (K_1)^2/K' \quad (8)$$

$$K_{\mathrm{corr}} = K'/4 \quad (9)$$

While the steric and electronic properties of a ligand influence the strength of the metal−ligand interactions, these intrinsic properties do not supersede ligand−substrate and ligand−ligand interactions. For example, the strongly correlated binding reflected in K_{corr}—*up to 100-fold*—attests to the importance of ligand−ligand interactions (see **1A**−**G**). Although stabilization of the heterosolvates may be fostered by bulky ligands such as TEEDA, the negative correlation—the anomalous stabilization of the homosolvates—found for several sparteine/ligand combinations implicates complex relationships. It is instructive to further consider what the relative binding constants *do not* reveal. For example, one might infer that K_1 values for the substitution of a single TMEDA by a variety of ligands (**B**−**G**) would provide a systematic view of lithium ion affinities. However, each binding constant includes contributions from transannular ligand−TMEDA interactions that are unique to that particular pair. If one uses the data in Table 1, K_1 values can be standardized to any of the ligands; however, the relative values will depend markedly upon the choice of standard ligand. Alternatively, one might be tempted to employ K_{tot} as a measure of inherent binding affinity. Once again, however, the transannular ligand−ligand interaction in each homosolvate is unique. This serves as a reminder that ligand binding constants are influenced by the ancillary ligands within the complexes.[12]

The highly correlated solvation effects described herein are sobering in light of the enormous number of organolithium reactions carried out in mixtures of polyamines and ethereal solvents. The choice of both the diamine and the cosolvent has been largely empirical. However, ethereal solvents undoubtedly display variable tendencies to displace diamines from lithium. Strong correlation effects would also render the displacement of the first diamine substantially more facile than the second. For example, recent studies by Beak and co-workers reveal that *i*-PrLi in sparteine/$\mathrm{Et_2O}$ exists as a mixed-solvated dimer with only one coordinated sparteine.[13] Such correlated solvation of organolithium reactants will, by definition, influence the rates and mechanisms of subsequent reactions.[14] Correlated solvation can also occur in the rate-limiting transition structures bearing the disolvated *n*-BuLi dimer fragment,[15] which makes cogent mechanistic models very difficult to construct. We certainly hope to unravel the complex effects of correlated solvation on organolithium structures, reaction mechanisms, and reaction rates in due course.[16]

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Supporting Information Available: ^{6}Li and ^{13}C NMR spectra of *n*-BuLi and a general experimental protocol (20 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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