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# Lithium Hexamethyldisilazide: A View of Lithium Ion Solvation through a Glass-Bottom Boat

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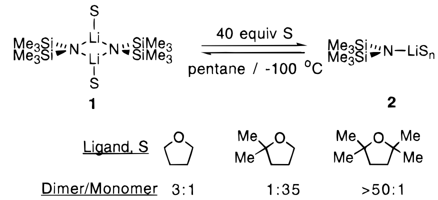
## Introduction

During the course of our investigations into organolithium structures and reactivities, we were drawn to lithium hexamethyldisilazide (LiHMDS; $(Me_3Si)_2NLi$) by its prominence as a selective Brönsted base in organic chemistry.[1] However, the synthetic importance of LiHMDS that had piqued our interest was soon overshadowed by the importance of LiHMDS as a vehicle to study the basic principles of lithium ion coordination chemistry.[2]

Understanding how solvation influences organolithium structure and stability (reactivity) is difficult due to (1) homonuclear and heteronuclear (mixed) aggregation, (2) the dual role of the solvents as both medium and ligand, (3) widely varying coordination numbers, (4) extremely rapid solvent exchanges, (5) competitive and cooperative (mixed) solvation in commonly employed solvent mixtures, and (6) the superposition of primary shell and secondary shell solvation.

To establish the tenor of this Account, we graphically illustrate the complex relationship of solvation and aggregation (eq 1): the monomer−dimer distribution of LiHMDS shows no obvious correlation with the perceived coordinating capacities of the solvents.[3] The NMR spectroscopic investigations described in this Account are targeted toward understanding such complex relationships. We will restrict the discussion to solution-phase studies; however, Williard has created a database from

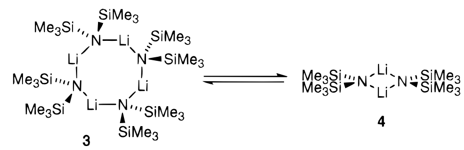



(1)

crystallographic investigations of LiHMDS worthy of its own Account.[4]

## A Legacy of T. L. Brown

Structural investigations of LiHMDS began auspiciously in the laboratory of T. L. Brown at the University of Illinois. In 1971, Kimura and Brown reported that LiHMDS exists as a tetramer−dimer mixture in hydrocarbons (eq 2) and as dimer−monomer mixtures in THF and $Et_2O$ (see eq 1).[5] Two decades later, with the aid of $^6$Li- and $^{15}$N-labeled



(2)

LiHMDS and much improved one- and two-dimensional NMR spectroscopic methods described in a previous Account,[6] we have now confirmed their conclusions in virtually every respect and extended their investigations to include upward of 100 additional ligands.[7−12]

## Ethers[5,7]

Reinvestigation of LiHMDS in hydrocarbons containing low concentrations of ethereal ligands led to an unprecedented and critically important result: free and dimer-bound ethereal ligands were observed on NMR spectroscopic time scales.[13,14] This offered a unique opportunity to address a host of fundamental and elusive issues relating to lithium salt solvation and aggregation. For example, the slow exchange made it possible to study the mechanism of ligand substitution. It became clear that slow ethereal solvent exchange had eluded detection in other organolithiums due to competing facile associative substitutions by strongly coordinating ligands such as THF and facile dissociative substitutions by weakly coordinating ligands such as $Et_2O$ (Scheme 1).

The presumption that THF is a better ligand than $Et_2O$, while widely accepted, would be difficult to defend with unassailable evidence.[15] Direct competitions of a range of ethereal ligands afforded clearer definitions of "strong" and "weak" by providing relative binding energies (eqs 3 and 4) that correlate well with the activation energies for dissociative ligand substitution (Table 1). As expected, THF is a stronger ligand than $Et_2O$ for the LiHMDS dimer, and methylation of THF (cf. eq 1) does, indeed, decrease the binding energy. Interestingly, the readily observable mixed solvates (**8**) are formed with little or no correlated solvation at the two (apparently insulated) lithium sites. Since

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Brett Lucht received a B.S. from the University of Puget Sound in 1991. He obtained a Ph.D. in 1996 from Cornell University working with David Collum and then moved to the University of California−Berkeley for postdoctoral research with T. Don Tilley. He is currently an assistant professor at the University of Rhode Island. His research at Rhode Island addresses the synthesis of novel polymers and structural, synthetic, and mechanistic investigations of organocuprates.

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**Scheme 1**

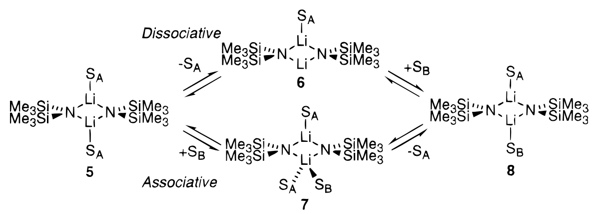



**Table 1. Experimentally Derived Free Energy of Activation for Ligand Exchange ($\Delta G_{act}°$) and Free Energy of Binding ($\Delta G_{solv}°$) on the LiHMDS Dimer**

| solvent, S | $\Delta G_{act}°$ | $\Delta G_{solv}°$ [a] |
|---|---|---|
| $Et_2O$ | 8.6 | 2.3 |
| *t*-BuOMe | 7.4 | 3.5 |
| THF | 10.8 | 0.0 |
| 2-MeTHF | 10.0 | 0.6 |
| 2,2-$Me_2$THF | 8.9 | 1.7 |
| *n*-BuOMe | 9.8 | 1.2 |
| *i*-PrOMe | 8.9 | 2.0 |
| THP | 10.6 | 0.3 |
| $Me_2$(Et)COMe | *b* | *b* |
| oxetane | *b* | −0.3 |

[a] $\Delta G_{solv}°$ (±0.3 kcal/mol) was determined relative to THF (0.0 kcal/mol) according to eqs 3 and 4. [b] Solvent exchange was rapid on the NMR time scales.

$$[(Me_3Si)_2NLi]_2(S_A)_2 + S_B \underset{-100\ °C}{\xrightleftharpoons{K_{solv},\ \Delta G_{solv}°}} [(Me_3Si)_2NLi]_2(S_A)(S_B) + S_A \quad (3)$$
$$\mathbf{5} \qquad \qquad \mathbf{8}$$

$$K_{solv} = [\mathbf{8}][S_A]/[\mathbf{5}][S_B] = \exp(-\Delta G_{solv}°/RT) \quad (4)$$

solvent mixtures are commonly employed in organolithium chemistry, understanding competitive and cooperative solvation is important.

The relative solvation energies ($\Delta G_{solv}°$, eq 4) provided a firm foundation upon which we could understand the mysterious solvent-dependent deaggregation in eq 1. By measuring the effect of solvent on the dimer−monomer aggregation energy ($\Delta G_{agg}°$, eqs 5 and 6), a plot of the $\Delta G_{solv}°$ vs $\Delta G_{agg}°$ *shows no correlation whatsoever* (Figure 1).

$$^1/_2[(Me_3Si)_2NLi]_2(S)_2 + (n-1)S \underset{\substack{(40\ \text{equiv S})\\ \text{pentane}\\ -100\ °C}}{\xrightleftharpoons{\Delta G_{agg}°,\ K_{agg}}} (Me_3Si)_2NLiS_n \quad (5)$$
$$\mathbf{1} \qquad \qquad \mathbf{2}$$

$$K_{agg} = [\mathbf{2}]/\{[\mathbf{1}]^{1/2}[S]^{n-1}\} = \exp(-\Delta G_{agg}°/RT) \quad (6)$$

We surmised that the scatter in Figure 1 arises from a poor correlation of monomer and dimer solvation and formulated the following model, shown below. As the steric demand of the solvent increases (e.g., $Me_2$THF in eq 1), significant solvent−amide interactions in dimer **1** would force deaggregation to monomer in a form of steric relief. As the steric demands of the solvent become extreme (e.g., $Me_4$THF), solvent−solvent interactions in monomer **9** would become dominant, forcing formation of the relatively unstable solvated dimer **9** by default.

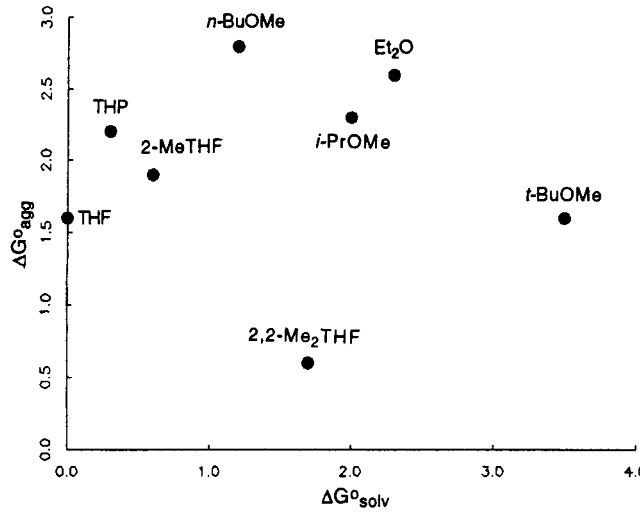
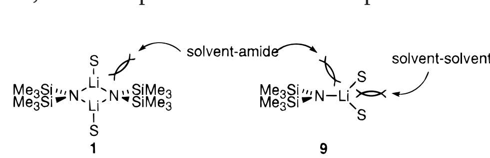



**FIGURE 1.** Plot of LiHMDS aggregation energies ($\Delta G_{agg}°$, eqs 5 and 6) vs dimer solvation energies ($\Delta G_{solv}°$, Table 1, eqs 3 and 4).

However, semiempirical calculations predicted that the




monomer and dimer solvation *enthalpies* ($\Delta H_{solv}°$) should correlate quite strongly. Further scrutiny revealed two fundamental flaws in our model: (1) Measuring the dimer−monomer equilibrium as a function of the solvent concentration (using a hydrocarbon cosolvent) showed that even hindered ethers afford tri- rather than disolvated monomer, while THF and oxetane afford appreciable concentrations of five-coordinate *tetrasolvated* monomers. (2) Variable-temperature studies revealed that the *enthalpies* of aggregation ($\Delta H_{agg}°$) are nearly equivalent and nearly zero for eight different ethereal ligands; the solvent dependence of the dimer−monomer mixtures stems from steric effects manifested in the solvent-dependent *entropies* of aggregation ($\Delta S_{agg}$).[16] Overall, we emerged with a self-consistent, albeit complex, model describing how ethereal solvents influence the aggregation states of LiHMDS.[17]

## Trialkylamines[8]

The coordination chemistry of trialkylamines is dominated by the steric hindrance of the splayed alkyl groups.[18] Even the least hindered trialkylamines coordinate weakly to the LiHMDS dimer and undergo facile dissociative ligand exchanges. They also readily afford a LiHMDS monomer reminiscent of $Me_2$THF (suggesting that the solvent−amide interactions in the dimer **1** are dominant). More hindered trialkylamines afford dimers due to dominant solvent−solvent interactions in the monomer (see **9**), as suggested for $Me_4$THF.

Monitoring the dimer−monomer equilibria as a function of amine concentrations revealed several unanticipated results: (1) LiHMDS in pentane showed a mono-

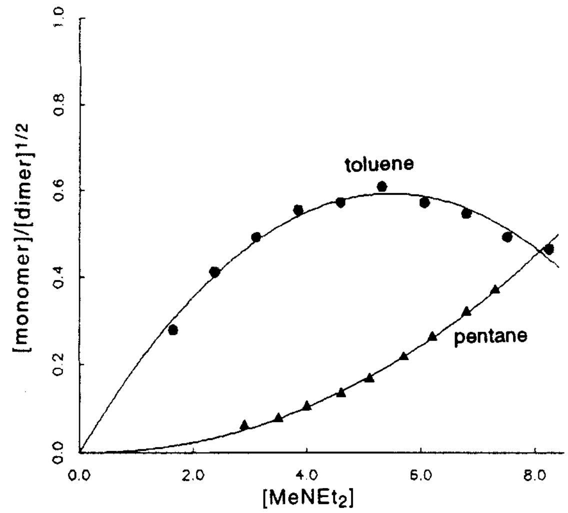



**FIGURE 2.** Plot of $[\text{monomer}]/[\text{dimer}]^{1/2}$ vs $[\text{MeNEt}_2]$ for 0.1 M LiHMDS at −80 °C in pentane (▲) and in toluene (●).

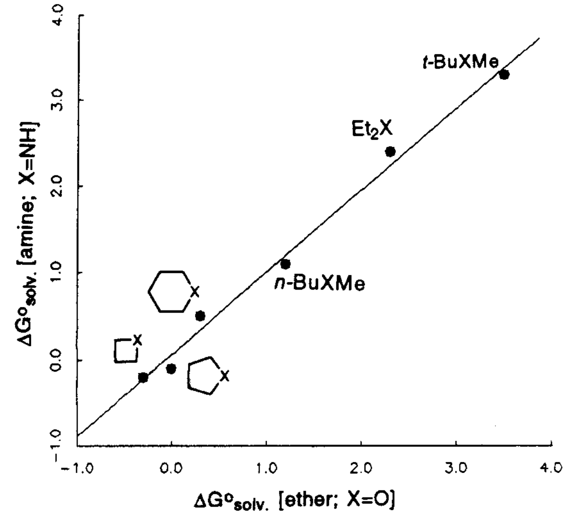



**FIGURE 3.** Plot of LiHMDS dimer solvation energies ($\Delta G_{\text{solv}}°$, eqs 3 and 4) for ethers vs amines (eqs 2 and 3). All solvents are referenced to THF at 0.0 kcal/mol.

tonic increase in monomer concentration with increasing amine concentration, fully consistent with the formation of trisolvated monomers. (2) *Disolvated* monomers can be observed in the slow solvent exchange limit in toluene as the cosolvent, but not pentane. (3) LiHMDS in amine/toluene solutions showed a marked—up to 10-fold—preference for monomers when compared to the analogous amine/pentane solutions as well as a maximum in the monomer concentration at intermediate amine concentrations (Figure 2). The only model that successfully fit the data included a toluene-solvated monomer, **10** (eq 7). However, these appear to be long-range effects ("me-

$$^{1}/_{2}(R_2NLi)_2(R_3N)_2 \rightleftharpoons \underset{\mathbf{10}}{R_2NLi(R_3N)_2(\text{toluene})} \rightleftharpoons R_2NLi(R_3N)_3 \quad (7)$$

dium effects"); mesitylene affords dimer−monomer mixtures that are indistinguishable from toluene, while alkenes and alkynes act like pentane. Similar aromatic solvent−cation interactions are being investigated by Dougherty.[19]

## Mono- and Dialkylamines[8]

The low basicity of LiHMDS allows for the complexation of protic amines without complicating proton transfers. Unhindered dialkylamines undergo associative exchanges on the LiHMDS dimer similar to their isostructural dialkyl ether counterparts. In fact, the similarities between dialkylamines and dialkyl ethers are extraordinary; competitive binding studies (see eqs 3 and 4) revealed that isostructural amines and ethers are virtually indistinguishable (Figure 3). The less hindered monoalkylamines (and $NH_3$) coordinate very strongly to the LiHMDS dimer but are difficult to investigate due to rapid associative ligand substitutions.

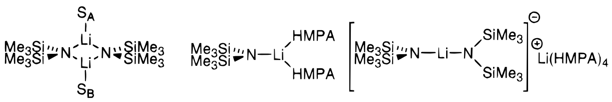
There have been several hints that monomers are disproportionately azaphilic. The amine-solvated LiHMDS dimer displays a greater tendency toward deaggregation to monomer. Since the isostructural dialkyl ethers and dialkylamines show indistinguishable affinities for the LiHMDS dimer, the monomers must be disproportionately stabilized by the amines. Similar azaphilicity of the monomer emerged from studies of polydentate ligands (below).

## Unsaturated Hydrocarbons[5,8]

Kimura and Brown reported that the tetramer−dimer equilibrium (eq 2) is sensitive to the choice of hydrocarbon solvent in a fashion that differs markedly from the amine/hydrocarbon mixtures described above.[5,20,21] Whereas LiHMDS in pentane or highly methylated aromatic solvents afford nearly equal proportions of tetramer and dimer, toluene and benzene afford only dimer. Kimura and Brown's suggestion that the aromatic $\pi$ systems coordinate to the dimer initially seems surprising; however, their hypothesis is supported by analogous behavior for more traditional ligands. A reinvestigation confirmed their observations and revealed that olefins and acetylenes also show substantial effects. While *cis*- or *trans*-2-pentene afford only slightly more dimer **4** than does pentane, 1-pentene functions much like toluene, affording almost exclusively dimer. Only a few equivalents of ethylene or 2-butyne in pentane are required to convert tetramer **3** completely to dimer **4**. Overall, the evidence supporting Li−$\pi$ interactions is fully self-consistent.[20] It is also interesting that such weak interactions can be probed through their influence on the aggregate equilibrium.

## Phosphoryl Ligands[9,10]

In an early investigation of LiHMDS, we found that hexamethylphosphoramide (HMPA) in THF solution[9] affords a variety of HMPA-solvated cyclic dimers **11**−**13**, monomer **14**, and ionized dimer (triple ion) **15**. Most strikingly, despite HMPA's reputation for deaggregating organolithiums, the formal dimer−monomer ratio re-




**11**; $S_A = S_B$ = THF **14** **15**
**12**; $S_A$ = HMPA, $S_B$ = THF
**13**; $S_A = S_B$ = HMPA

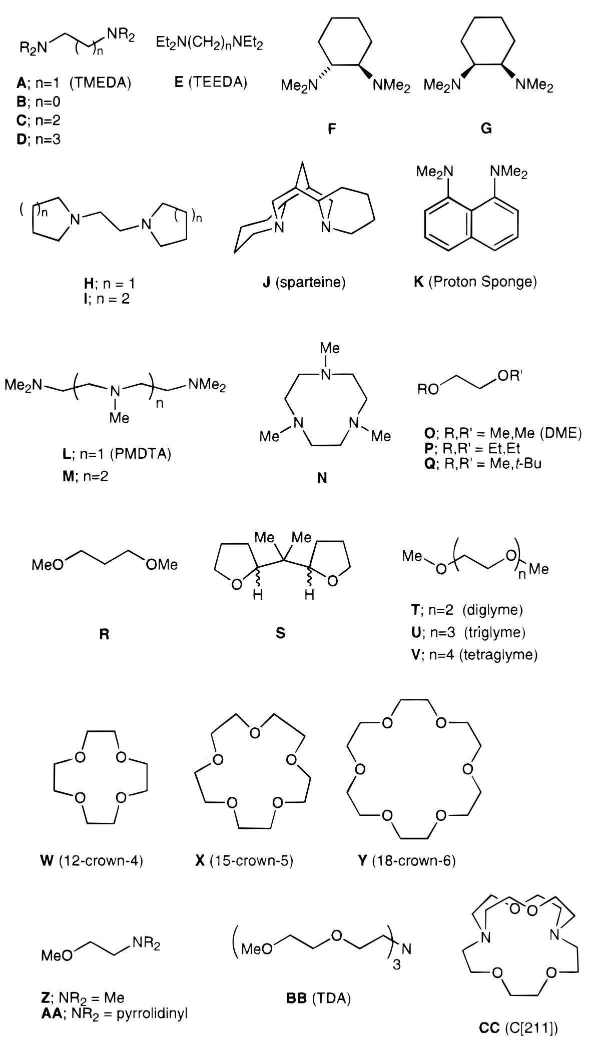
mains nearly unchanged, even at high HMPA concentration, where **14** and **15** are the two observable forms.[22]

Recent studies of several phosphates as possible replacements for the highly carcinogenic HMPA uncovered some interesting mixed solvation effects.[10] $EtO_3P{=}O$/toluene solutions of LiHMDS contain dimer at low $EtO_3P{=}O$ concentration and exclusively monomer at high $EtO_3P{=}O$ concentration; triple ions analogous to **15** are notably absent. Investigation of LiHMDS/$EtO_3P{=}O$ mixtures in various THF/pentane mixtures revealed strongly [THF]-dependent dimer−monomer mixtures, implicating mixed solvated monomers, $(Me_3Si)_2NLi(O{=}POEt_3)_2(THF)_n$. Reinvestigation of LiHMDS/HMPA at variable THF concentrations[10] revealed a relative per-lithium THF solvation number in the order dimer < monomer < triple ion. Quantitative studies indicated that the triple ion **15** also includes at least two THF's per lithium—*four THF's per* $^{+}$*Li(HMPA)*$_4$ *cation*. Two additional observations clarify the role of the THF: (1) The relative stability of the HMPA-solvated triple ion is highly dependent upon the structure of the ethereal cosolvent, following the order oxetane > THF > 2-MeTHF > $Et_2O$. (2) An analogous LiHMDS monomer−triple ion equilibrium in which the triple ion differs only by having a $^{+}Li(crown)_2$ counterion (see eq 10, below)[11] shows no dependence on the structure or concentration of the ethereal cosolvent. Consequently, it appears that the four additional ethereal ligands are associated with the $^{+}Li(HMPA)_4$ in a sterically sensitive secondary solvation shell. An analogous secondary solvation shell was invoked in the context of rate studies of *N*-alkylations of $Ph_2NLi$, manifesting an extraordinary seventh-order [THF] dependence.[23] Although speculative, the model has considerable implications about the role of secondary solvation effects, cooperative solvation effects, and the structure of metal ions in relatively nonpolar, aprotic media.[2]

## Polydentate Ligands[11,12]

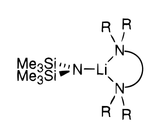
The perennial interest in polyamine[24] and polyether[25] ligands stems from their dramatic effects on organolithium structures and reactivities.[24,26] Nevertheless, precisely how chelating ligands influence structure and stability of lithium salts is still elusive. Most investigations either focus upon a restricted number of ligands for a given lithium salt or suffer from ambiguities surrounding the lithium salt structure and ligand stoichiometry.[27,28] We took steps to remedy this situation by investigating LiHMDS solvated by a range of acyclic and cyclic polyethers, polyamines, and cryptands (Chart 1).[11] Insights into solvation numbers, mechanisms of ligand substitution, relative binding energies, and ligand-dependent aggregation energies are complemented by an overall rich structural diversity.

**Chart 1**




## Diamines

Treatment of LiHMDS with low concentrations of diamines **A**−**K** affords chelated monomer **16** to the exclusion of solvated dimer or more highly solvated monomer. Relative binding energies (Table 2) determined by direct



**16a-k**; diamine = **A-K**

competition (eq 8) or by competition with THF (eq 9) revealed several trends.

$$(Me_3Si)_2NLi{-}L_1 + L_2 \xrightleftharpoons{K_{eq}(1)} (Me_3Si)_2NLi{-}L_2 + L_1 \quad (8)$$

$$^1/_2[(Me_3Si)_2NLi]_2(THF)_2 + L \xrightleftharpoons{K_{eq}(2)} (Me_3Si)_2NLi{-}L + THF \quad (9)$$

(1) Five-membered rings are strongly preferred over six-membered rings, as documented by Klumpp[29] and Reich.[14b] The four- and seven-membered chelates do not form.

(2) Nearly equivalent binding of TMEDA (**A**) and the more sterically congested TEEDA (**E**) suggests that LiH-

**Table 2. Relative LiHMDS Monomer Binding Free Energies($\Delta G_{solv}°$, Eqs 8 and 9) and Ligand Exchange Activation Free Energies ($\Delta G_{act}°$)**

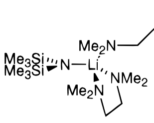
| solvent (Chart 1) | $\Delta G_{solv}°$ [a] | $\Delta G_{act}°$ |
|---|---|---|
| **A** (TMEDA) | 0.0 | 10.1 |
| **C** (TMPDA) | 1.0 | 11.5 |
| **E** (TEEDA) | 0.3 | 15.2 |
| **F** (*trans*-TMCDA) | −1.3 | 16.6 |
| **G** (*cis*-TMCDA) | 0.6 | 14.7 |
| **H** | −0.6 | 15.7 |
| **I** | −0.1 | 16.3 |
| **J** (sparteine) | −0.5 | 19.1 |
| **L** (PMDTA) | −2.8 | 14.4 |
| **M** (HMTTA) | −2.2 | 13.9 |
| **N** | −2.0 | 16.9 |
| **S** | 0.2 | <8.0 |
| **T** (diglyme) | −0.1 | <8.0 |
| **U** (triglyme) | −0.1 | <8.0 |
| **V** (tetraglyme) | −0.2 | <8.0 |
| **W** (12-crown-4) | −1.0 | <8.0 |
| **X** (15-crown-5) | −0.9 | <8.0 |
| **Y** (18-crown-6) | −0.1 | <8.0 |
| **BB** (TDA) | −1.5 | <8.0 |

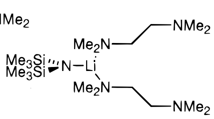
[a] Approximated error: ±0.3 kcal/mol. Energies determined relative to TMEDA in toluene-$d_8$ at −100 °C (0.0 kcal/mol).

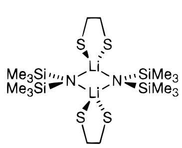
MDS is not sufficiently hindered to attain what Brown[30] refers to as the "minimum steric threshold" required to detect differences in ligand bulk. The high affinity of sparteine is especially interesting in light of its steric demand as well as its importance in organic synthesis.[31] The capacity of diamines to cause deaggregation may be as much a function of congestion in the dimers as stabilization of the monomers.[7,27]

(3) The relative binding constants (eqs 8 and 9) once again revealed the relative stabilization of amine-solvated monomers by toluene when compared with pentane. While the approximate 10-fold change in the binding constant may not seem large, Beak and co-workers reported a 5-fold increase in enantioselectivity of *sec*-BuLi/sparteine-mediated metalations upon changing from pentane to toluene cosolvent[32] that seems *very* large.

The free energies for exchange of free and monomer-bound diamines fall into two distinct ranges (Table 2) which roughly correlate with two different mechanisms. Unhindered ligands undergo a rate-limiting ligand association via a disolvated monomer such as **17** or **18**. Hindered ligands show a LiHMDS concentration depen-


**17**

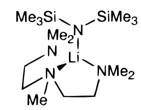

**18**

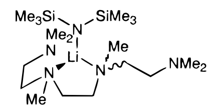

**19**

dence implicating a *rate-limiting association of two LiHMDS monomers* to form a dimer such as **19**. As a consequence of the two associative mechanisms, the binding energies and exchange rates of the ligands do not correlate.

## Polyamines

*N,N,N′,N″N″*-Pentamethyldiethylenetriamine (PMDTA, **L**) affords a four-coordinate monomer **20** showing restricted rotation about the Li−N bond akin to that observed previously.[33] The corresponding tetraamine **M** (**21**) offers no advantages over PMDTA. The cyclic triamine **N** (**22**) is inferior to PMDTA as a ligand for the LiHMDS monomer. The "macrocyclic effect"[25] falls short of expectation on several occasions (see below).


**20**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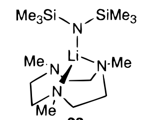
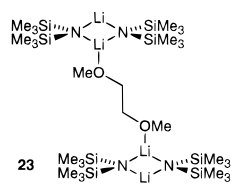
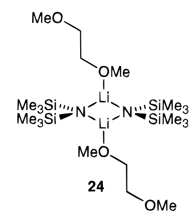
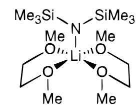

**22**

## Polyethers

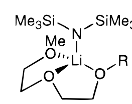
The LiHMDS−polyether complexes show a considerable structural diversity. Vicinal diethers such as DME (**O**) afford complex equilibria containing $\eta^1$-solvated dimers **23** and **24**, DME-linked oligomers, and chelated monomer **25**. The reluctance of DME to afford chelated LiHMDS

**23**


**24**



**25**

dimers is supported by both crystallographic and computational studies of Williard and co-workers.[4] The stability of five-coordinate monomer **25** is consistent with crystallographic studies showing that DME can promote high-coordinate lithium[34] and spectroscopic investigations showing that LiHMDS monomer may exist as a five-coordinate tetrasolvate in THF or oxetane.[7] Diglyme, triglyme, and tetraglyme (**T**, **U**, and **V**, respectively) afford $\eta^3$-solvated monomers **26**−**28**.



**26**; R = Me
**27**; R = $CH_2CH_2OMe$
**28**; R = $(CH_2CH_2O)_2Me$

The relative free energies for binding polyethers to the LiHMDS monomer (Table 2) are generally lower than those for their polyamine counterparts, corroborating similar findings of Klumpp[29] and Reich.[14b] This may seem self-evident from the higher Bronsted basicity of amines; however, recall that the LiHMDS dimers do not display enhanced azaphilicities.[8]

LiHMDS−crown ether mixtures contain crown-solvated monomer **31** along with triple ions bearing either one or two crown ethers per lithium counterion (**29** and **30**, respectively).

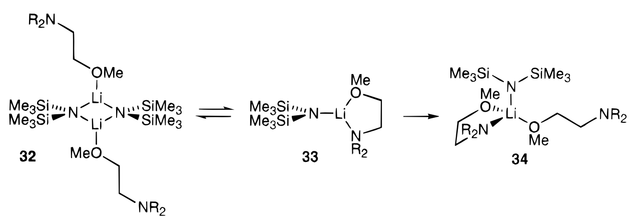
$$\underset{\mathbf{29}}{[(Me_3Si)_2N{-}Li{-}N(SiMe_3)_2]^-//^+LiL} \overset{L}{\rightleftharpoons} \underset{\mathbf{30}}{[(Me_3Si)_2N{-}Li{-}N(SiMe_3)_2]^-//^+LiL_2} \rightleftharpoons \underset{\mathbf{31}}{(Me_3Si)_2N{-}Li{-}L} \quad (10)$$

L = 12-crown-4, 15-crown-5, or 18-crown-6

Consequently, *higher* crown ether concentrations afford *lower* triple ion concentrations, possibly explaining a reported *inverse* correlation of conductivity with crown ether concentration.[35] Quantitative binding studies indicate that the "macrocyclic effect" [25]—the enhanced binding of the crown ethers compared to the acyclic polyglymes—adds only 0.7–0.9 kcal/mol of stabilization to the LiHMDS monomer. The capacities of chelating ligands to coordinate the LiHMDS monomer and solvent-separated lithium cation do not strongly correlate. Overall, the structural variations underscore the potential dangers of using empirical observations (such as conductivity) to determine crown ether binding affinities and highlight the merits of the gas-phase binding studies.[36]

## Aminoethers

Vicinal amino ethers **Z** and **AA** manifest properties intermediate to those of the corresponding diamines and diethers. They afford a mixture of $\eta^1$-solvated LiHMDS dimer **32** and chelated monomer **33** at <1.0 equiv per Li and more highly solvated monomer **34** at elevated ligand concentrations. While the dimer is reminiscent of DME,



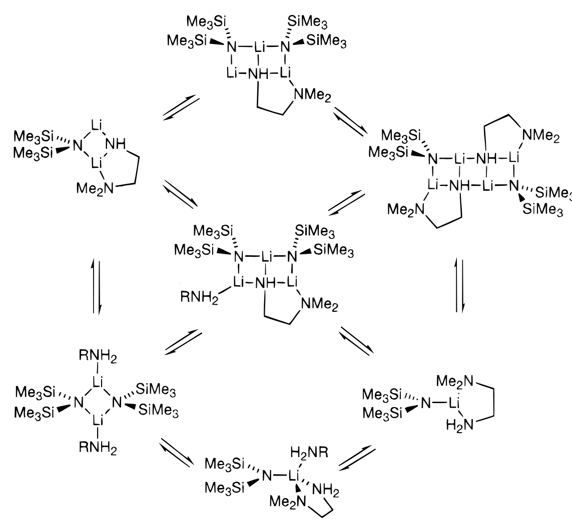
the formation of LiHMDS monomer, even at <1.0 equiv per Li, is more reminiscent of the diamines. Cryptand **CC** affords triple ion analogous to **29**, with a simple ion pair appearing only at elevated cryptand concentrations. Previous studies of lithiated hydrazones uncovered a similar reluctance of the anionic triple ion fragments to forfeit the second $Li^+$ to the C[211] ligand.[37] Interestingly, the acyclic aminoether ligand TDA (**BB**) functions like a crown ether or cryptand affording substantial concentrations of triple ion at a fraction of the cost.

## Protic Diamines

Protic diamines have shown a growing importance in asymmetric synthesis.[38] Treating LiHMDS with *N,N*-dimethylethylenediamine ($Me_2NCH_2CH_2NH_2$, DMEDA) reveals a remarkable coordination chemistry that is uniquely ascribable to the combined influence of the protic amine moiety and the chelating capacity of the DMEDA (Scheme 2).

The structural complexity in LiHMDS/DMEDA mixtures obscures several surprising trends in solvation and aggregation. Since mixtures of LiHMDS and standard monoalkylamines afford solvated monomers and dimers,[8] the transmetalation of DMEDA and resulting mixed aggregates attest to the importance of the chelate effect. The disappearance of mixed aggregates at elevated DMEDA concentrations underscores the sensitive balance between the stabilizing influences of mixed aggregation and solvation.[39] The complex behavior of protic diamine-solvated enolates described by Vedejs and co-workers may stem from similar equilibria.[40]

**Scheme 2**



## Conclusion

In principle, a better understanding of lithium ion solvation could lead to new reagents for organic synthesis, improved anionic polymerizations, or superior electrolytes for rechargeable lithium batteries. In fact, we submit that the plethora of ligand-dependent empirical observations salted throughout the literature cannot possibly provide substantial mechanistic insights in the absence of such detailed structural information. While we have certainly not resolved all structural details of the LiHMDS coordination sphere, the structural diversity observed for LiHMDS underscores the ambiguities affiliated with less structurally illuminating systems. Moreover, the insights gained from the LiHMDS structural and binding studies may be transferrable to other systems. Of course, during efforts to choose or design ligands for lithium, one must first ascertain whether one's goal is best attained through strongly binding or weakly binding ligands.[27] This is not as simple as it sounds.

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