

Solvation of Lithium Hexamethyldisilazide by *N,N*-Dimethylethylenediamine: Effects of Chelation on Competitive Solvation and Mixed Aggregation

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Received October 20, 1995

The high basicity of many organolithium species requires that alcohols, amines, and other protic functionalities within substrates and additives be masked by protection, peralkylation, or deprotonation.¹ However, there are a number of important organolithium derivatives for which aprotic conditions are not mandated.² Recent notable examples in which the presence of protic mono- and dialkylamines are particularly important in asymmetric chemistry include polyamine-catalyzed ketone alkylations,³ glycinamide alkylations,⁴ enolate protonations,⁵ lithium amide-modified cuprate additions,⁶ and polymerizations.⁷ Several groups have recently found that mono- and dialkylamines readily (and quite tenaciously) coordinate to the lithium hexamethyldisilazide (LiHMDS) dimer and monomer without concomitant proton transfer.⁸ We describe herein the complexation of LiHMDS by *N,N*-dimethylethylenediamine (Me₂NCH₂CH₂NH₂; DMEDA). The remarkable coordination chemistry is uniquely ascribable to the combined influence of the protic amine moiety and chelating capacity of the DMEDA.⁹

The ⁶Li and ¹⁵N NMR spectra of [⁶Li,¹⁵N]LiHMDS¹⁰ in 2:1 pentane–toluene mixtures at –110 °C show the LiHMDS unsolvated cyclic dimer (**1**) and the higher cyclic oligomer (**2**) described previously (Table 1).¹¹ The ⁶Li–¹⁵N resonance correlations affording Li–N connectivities were determined by single-frequency ¹⁵N decouplings.¹² Upon addition of 0.25 equiv of added DMEDA (per Li), we observe formation of mixed trimer **3**, mixed tetramer **4**, and mixed dimer **5** along with residual **1** and **2**. At 0.5 equiv of DMEDA, **4** and **5** are the only observable species. Trimer **3** displays a ⁶Li triplet,

Table 1. ⁶Li and ¹⁵N NMR Spectral Data of LiHMDS/DMEDA Solvates and Mixed Aggregates^a

compd	⁶ Li		¹⁵ N	
	δ (mult, J _{LiN}) ^b	(mult, J _{LiN}) ^c	δ (mult, J _{LiN}) ^b	δ ^c
1	0.64 (t, 3.7)		41.5 (q, 3.7)	
2	1.46 (t, 4.4)		44.9 (q, 4.5)	
3	–0.03 (d, 4.0)	(d, 3.9)	43.8 (mult)	<i>e</i>
	1.31 (t, 3.4)	(d, 3.8)	46.5 (q, 3.4)	
	2.30 (d, 3.9)	(d, 2.3)		
4	2.43 (d, 4.0)	(d, 2.7)	42.4 (q, 3.8)	16.5
	2.49 (d, 3.5)	(t, 4.0)		
5	2.44 (d, 3.5)	(d, 2.8)	42.1 (q, 3.6)	15.7
6	1.08 (d, 2.9)	(t, 2.4)	40.1 (mult)	15.0
	1.47 (t, 3.5)	(d, 4.3)	44.0 (q, 3.5)	21.6
	2.58 (d, 4.0)	(d, 2.6)		
7	1.60 (t, 3.3)	(d, 3.8)	38.2 (q, 3.3)	13.4
8	1.53 (d, 5.4)	(d, 3.8)	50.6 (t, 5.6)	17.5
	0.97 (d, 5.0) ^d		44.0 (t, 5.1) ^d	

^a Spectra were recorded on 0.1 M solutions of LiHMDS in 2:1 pentane/toluene at –110 °C. Coupling constants were measured after resolution enhancement. Multiplicities are denoted as follows: d = doublet, t = triplet, q = quintet, mult = multiplet. The chemical shifts are reported relative to 0.3 M ⁶LiCl/MeOH at –100 °C at (0.0 ppm) and neat Me₂Net (25.7 ppm). All *J* values are reported in hertz.

^b Spectra were recorded on samples with [⁶Li,¹⁵N]LiHMDS and [¹⁴N]DMEDA. ^c Spectra were recorded on samples with [⁶Li]LiHMDS and [¹⁵N]DMEDA. Couplings were poorly resolved in the ¹⁵N spectra. ^d Spectrum recorded with 5.0 equiv of DMEDA. ^e Resonance could not be located.

two ⁶Li doublets (all of equal area), and two ¹⁵N quintets of equal area.¹³ Mixed tetramer **4** exhibits two ⁶Li doublets and an ¹⁵N quintet. Mixed dimer **5** displays a ⁶Li doublet and an ¹⁵N quintet. The existence of three discrete ⁶Li resonances of **3** suggests that the degenerate chelate exchange is slow on NMR time scales. In contrast, **5** undergoes a rapid chelate exchange. In addition, ¹⁵N NMR spectroscopy confirmed the presence of substantial [¹⁵N](Me₂Si)₂NH resulting from formation of Me₂NCH₂CH₂NHLi (LiDMEDA). Spectra of analogous mixtures of [⁶Li]LiHMDS and [¹⁵N']DMEDA (Me₂NCH₂CH₂¹⁵NH₂) display coupling consistent with the assigned structures of **3**–**5** (Table 1) and transannular coupling for **3** and **4** (*J* = 3.8 and 4.0 Hz, respectively) distinguishing them as ladders rather than cyclic oligomers.^{14,15}

Spectra of [⁶Li,¹⁵N]LiHMDS containing 0.75 equiv of DMEDA reveal three new species—mixed trimer **6**, disolvated dimer **7**, and chelated monomer **8**—in addition to **4** and **5**. At 1.0 equiv of DMEDA, only **7** and **8** remain. ⁶Li–¹⁵N heteronuclear multiple quantum correlation (HMQC) spectroscopy¹⁶ (Figure 1) established the resonance correlations. Mixed trimer **6** displays two ⁶Li doublets and a ⁶Li triplet (all of equal area) along with two new ¹⁵N quintets of equal area. While structure and spectroscopic properties of **6** are similar to those of **3**, the DMEDA concentration dependence shows **6** to be more highly solvated. In addition, mixtures of [⁶Li]LiHMDS and [¹⁵N']DMEDA reveal RNH₂–Li coupling (*J*_{Li–N} = 2.4 Hz) distin-

(13) We observe no appreciable change in the ⁶Li spectra upon broadband irradiation in the region corresponding to the protons of RNHLi (–2.0 ppm),¹⁷ indicating that ⁶Li–¹H coupling is not significant.

(14) There exist several species throughout the range of LiHMDS:DMEDA proportions whose low concentrations precluded their characterization.

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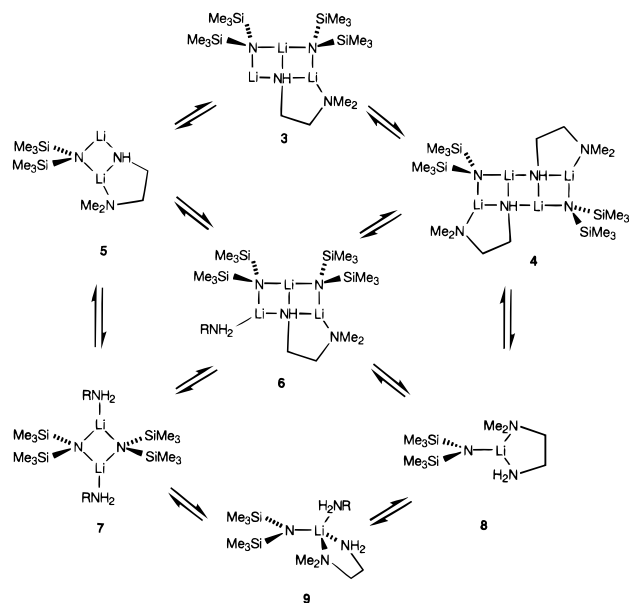
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guishing **6** as an amine solvate. Dimer **7** displays a ${}^6\text{Li}$ triplet and ${}^{15}\text{N}$ quintet, while monomer **8** shows a characteristic ${}^6\text{Li}$ doublet and ${}^{15}\text{N}$ triplet. The disappearance of all mixed aggregates containing LiDMEDA occurs concomitantly with the disappearance of resonances corresponding to $[\text{}^{15}\text{N}](\text{Me}_3\text{Si})_2\text{NH}$ in the ${}^{15}\text{N}$ NMR spectrum. Mixtures of $[\text{}^6\text{Li}]\text{LiHMDS}$ and $[\text{}^{15}\text{N}]\text{-DMEDA}$ display the anticipated coupling for **6–8**, including the $\text{RNH}_2\text{-Li}$ coupling in all three species as well as transannular coupling in **6** (Table 1).



At >1.0 equiv of $[\text{}^{15}\text{N}]\text{DMEDA}$, $\text{RNH}_2\text{-Li}$ coupling in dimer **7** and monomer **8** is lost due to rapid (associative)⁸ ligand substitution. Several lines of evidence implicate the formation of a highly solvated monomer (**9**): (1) The dimer:monomer ratio shows a marked DMEDA concentration dependence. (2) The ${}^6\text{Li}$ resonance corresponding to the monomer undergoes a significant (0.5 ppm) upfield shift with increasing amine concentration. (3) LiHMDS forms highly solvated monomers in the presence of simple monodentate amines.⁸ The dual role of DMEDA as a mono- and bidentate ligand in **9** seems reasonable, although a bis chelate analogous to $(\text{Me}_3\text{Si})_2\text{NLi}(\eta^2\text{-DME})_2$ ¹⁷ cannot be excluded.

$[\text{}^6\text{Li}]\text{LiDMEDA}$ ¹⁸ provided additional structural information. Mixtures of $[\text{}^6\text{Li}, \text{}^{15}\text{N}]\text{LiHMDS}$ and $[\text{}^6\text{Li}]\text{LiDMEDA}$ show only **3–5**, confirming the neutral (nonlithiated) DMEDA solvation of **6–9**. Addition of DMEDA to mixtures of $[\text{}^6\text{Li}, \text{}^{15}\text{N}]\text{LiHMDS}$ and $[\text{}^6\text{Li}]\text{LiDMEDA}$ affords **6–9** along with free (uncomplexed) LiDMEDA. Addition of >1.0 equiv of $(\text{Me}_3\text{Si})_2\text{NH}$ to solutions of LiDMEDA affords **7** and **8**.

The structural complexity in LiHMDS/DMEDA and LiHMDS/LiDMEDA mixtures obscures several remarkable trends in solvation and aggregation. Since mixtures of LiHMDS and

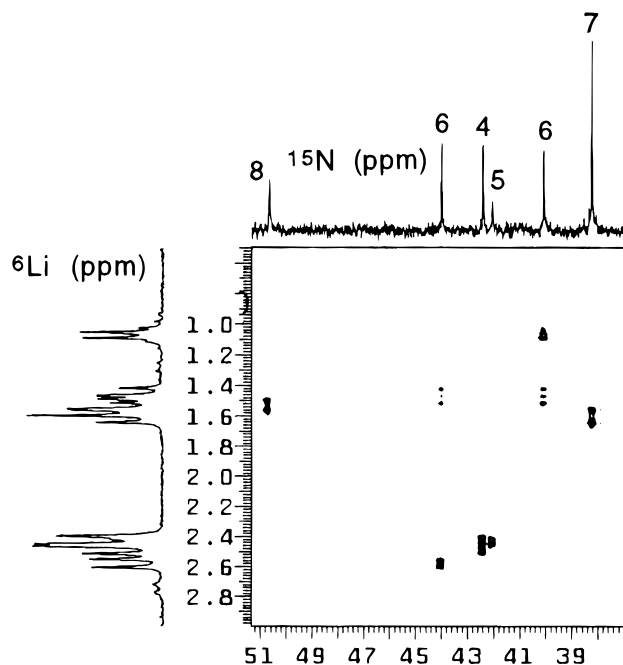


Figure 1. ${}^6\text{Li}\text{-}{}^{15}\text{N}$ HMQC spectrum of 0.10 M $[\text{}^6\text{Li}, \text{}^{15}\text{N}]\text{LiHMDS}$ in 2:1 pentane/toluene with 0.75 equiv of DMEDA. The left and upper traces are the corresponding one-dimensional ${}^6\text{Li}$ and ${}^{15}\text{N}$ $\{^6\text{Li}, ^1\text{H}\}$ NMR spectra, respectively.

standard monoalkylamines afford solvated monomers and dimers,^{8a} 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.¹⁹ We suspect that the confusing behavior of protic diamine-solvated enolates recently described by Vedejs and co-workers may stem from similar equilibria;⁵ preliminary ${}^6\text{Li}$ NMR spectroscopic studies of lithium enolate/DMEDA are supportive.¹⁷ We also find that other di- and trialkylated diamines afford seemingly analogous spectral complexity, possibly offering insights into the chemistry of unimetal superbases.²⁰ Detailed accounts of these additional investigations may be reported in due course.

Acknowledgment. We thank the National Institutes of Health for direct support of this work. B.L.L. thanks the National Institutes of Health for a predoctoral fellowship. We also acknowledge the National Science Foundation Instrumentation Program (CHE 7904825 and PCM 8018643), the National Institutes of Health (RR02002), and IBM for support of the Cornell Nuclear Magnetic Resonance Facility.

Supporting Information Available: ${}^6\text{Li}$ and ${}^{15}\text{N}$ NMR spectra of LiDMEDA and LiHMDS-LiDMEDA complexes (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA953517X

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(18) LiDMEDA was isolated as an air-sensitive, thermally stable crystalline solid. Multinuclear NMR spectroscopy reveals a single, highly symmetric aggregate (possibly a hexagonal prism related to that observed by Williard and co-workers).⁸ However, the spectra recorded on $[\text{}^6\text{Li}, \text{}^{15}\text{N}]\text{-LiDMEDA}$ display unusual features that cannot be adequately discussed in this communication.

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