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

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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 ($Me_2NCH_2CH_2NH_2$; 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 ^{15}N NMR spectra of [^6Li,^{15}N]LiHMDS[10] 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 $^6Li-^{15}N$ resonance correlations affording Li−N connectivities were determined by single-frequency ^{15}N 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, two ^6Li doublets (all of equal area), and two ^{15}N quintets of equal area.[13] Mixed tetramer **4** exhibits two ^6Li doublets and an ^{15}N quintet. Mixed dimer **5** displays a ^6Li doublet and an ^{15}N 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, ^{15}N NMR spectroscopy confirmed the presence of substantial [^{15}N]$(Me_3Si)_2NH$ resulting from formation of $Me_2NCH_2CH_2NHLi$ (LiDMEDA). Spectra of analogous mixtures of [^6Li]LiHMDS and [$^{15}N'$]DMEDA ($Me_2NCH_2CH_2{}^{15}NH_2$) 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]

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

	^6Li		^{15}N	
cmpd	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)	*e*
	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
9	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 Me_2NEt (25.7 ppm). All J values are reported in hertz. [b] Spectra were recorded on samples with [^6Li,^{15}N]LiHMDS and [^{14}N]DMEDA. [c] Spectra were recorded on samples with [^6Li]LiHMDS and [^{15}N]DMEDA. Couplings were poorly resolved in the ^{15}N spectra. [d] Spectrum recorded with 5.0 equiv of DMEDA. [e] Resonance could not be located.

Spectra of [^6Li,^{15}N]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. $^6Li-^{15}N$ heteronuclear multiple quantum correlation (HMQC) spectroscopy[16] (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 ^{15}N 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 [$^{15}N'$]DMEDA reveal RNH_2-Li coupling (J_{Li-N} = 2.4 Hz) distin-

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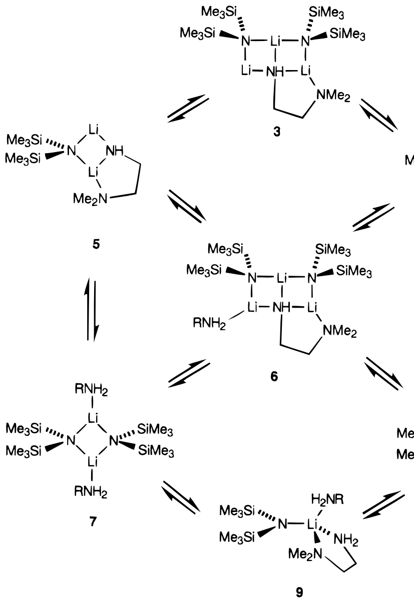
guishing **6** as an amine solvate. Dimer **7** displays a ^{6}Li triplet and ^{15}N quintet, while monomer **8** shows a characteristic ^{6}Li doublet and ^{15}N triplet. The disappearance of all mixed aggregates containing LiDMEDA occurs concomitantly with the disappearance of resonances corresponding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



At >1.0 equiv of [^{15}N′]DMEDA, RNH$_2$−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}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 (Me$_3$Si)$_2$NLi-(η^2-DME)$_2$[17] cannot be excluded.

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

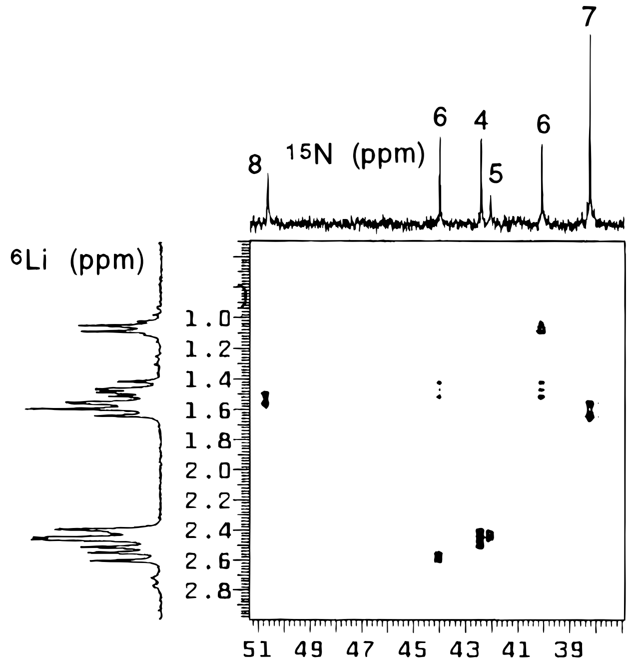


Figure 1. ^{6}Li−^{15}N HMQC spectrum of 0.10 M [^{6}Li,^{15}N]LiHMDS in 2:1 pentane/toluene with 0.75 equiv of DMEDA. The left and upper traces are the corresponding one-dimensional ^{6}Li and ^{15}N {^{6}Li,^{1}H} NMR spectra, respectively.

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Supporting Information Available: ^{6}Li and ^{15}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.

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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 [^{6}Li,^{15}N]-LiDMEDA display unusual features that cannot be adequately discussed in this communication.

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