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Solution Structures of Lithium Monoalkylamides (RNHLi)

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^{6}Li, ^{13}C, and ^{15}N NMR spectroscopic studies of lithiated monoalkylamides (RNHLi) reveal a range of structural types. Lithium *tert*-butylamide (*t*-BuNHLi) is a single oligomer, assigned as either a cyclic trimer or prismatic oligomer (tetramer, hexamer, or octamer). Lithium *N*,*N*-dimethylethylenediamine ($Me_2NCH_2CH_2NHLi$, LiDMEDA) is a prismatic higher oligomer (hexamer or octamer) of ill-defined stereochemistry. Variable-temperature NMR spectroscopic studies reveal several dynamic processes within the LiDMEDA oligomer. (*R*)-PhCH(NHLi)$CH_2N(CH_2)_4$ both in hydrocarbons and in hydrocarbons containing small concentrations of THF exists as a single D_2-symmetric tetramer whose symmetry properties allow for a complete structural and stereochemical assignment. The tetramer is converted to a cyclic dimer at elevated THF concentrations. A mixed dimer of *t*-BuNHLi and lithium phenylacetylide is readily characterized. A more complex mixed aggregate of (*R*)-PhCH(NHLi)$CH_2N(CH_2)_4$ and lithium phenylacetylide is shown to be a 4:2 mixed hexagonal prism.

Introduction

While the simplest protic lithium amide, $LiNH_2$, has played an important role in the development of organic chemistry,[1] contemporary organic chemists have not embraced protic lithium amides (RNHLi) or protic amine solvents. Admittedly, many organolithium reactions demand fully aprotic conditions, and a number of investigators (most notably Seebach and co-workers) have shown that protic amine byproducts derived from hindered lithium amides can be detrimental to reactions of enolates.[2] Nevertheless, there are many stabilized carbanions and related organolithium intermediates that can tolerate weakly protic conditions. Monoalkylamines and the corresponding protic lithium amides have assumed some importance in organolithium-mediated polymerizations,[3,4] epoxide cleavages,[5] and metalations.[6] Lithiated protic amides (or the corresponding amine−organolithium complexes) are beginning to find roles in asymmetric syntheses.[7−10]

While we have briefly investigated lithium amides under weakly protic conditions,[11] it is only recently that we began to appreciate some of the underlying structural and mechanistic issues.[12] Crystallographic studies indicate that, in contrast to the cyclic oligomer motif commonly found for lithium dialkylamides (R_2NLi),[13,14] the monoalkylamides readily form prismatic structures such as hexagonal prisms[15] ("drums") and octagonal prisms[16,17] (**2** and **3**, respectively). These results suggest structural relationships of lithium monoalkylamides

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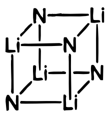

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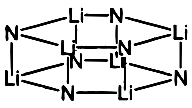

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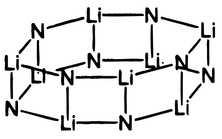

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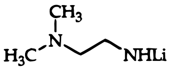

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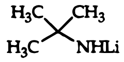

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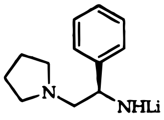

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with lithium enolates, lithium alkoxides, and alkyllithiums[18,19] that may prove mechanistically and synthetically important. We recently found that monoalkylamines bind quite strongly to lithium hexamethyldisilazide (LiHMDS) without proton transfer.[20] In contrast, potentially *chelating* monoalkylamines such as *N*,*N*-dimethylethylenediamine ($Me_2NCH_2CH_2NH_2$, DMEDA) are very strong ligands for LiHMDS, but they can also undergo proton transfer to afford complex mixtures including mixed aggregates containing $Me_2NCH_2CH_2NHLi$ (LiDMEDA, **4**).[12]

During the investigations of LiHMDS/DMEDA we prepared and characterized LiDMEDA (**4**) in toluene/pentane.[12] However, complex spectroscopic properties forced us to defer full disclosure and discussion to a later date. We now describe ^1H, ^6Li, ^{13}C, and ^{15}N NMR spectroscopic studies of LiDMEDA as well as lithium *tert*-butylamide (*t*-BuNHLi, **5**)[16] and lithium amide **6**. We will also describe limited investigations of RNHLi–lithium acetylide mixed aggregates. We must confess that the unusually challenging problem of isolating protic lithium amides of sufficient purity precluded a more broadly based investigation.[21,22]

Table 1. NMR Spectroscopic Data[a]

compd	temp (°C)	$\delta(^6Li)$ (mult, J_{LiN})	$\delta(^{15}N)$ (mult, J_{LiN})
4[b]	−90	1.71(ddd, 4.3, 3.1, 1.7)	15.0 (br)[c]
4[b]	30	1.71 (dt, 4.3, 2.5)	*d*
5[e]	−90	2.34 (q, 3.3)	*d*
5[e]	−30	2.41 (q, 3.4)	47.7 (sp, 3.4)
5[e]	+30	2.49 (q, 3.5)	*d*
5[e]	+40	2.50 (br)	*d*
5[f]	−128	2.57 (q, 3.5)	*d*
5[g]	−128	2.79 (q, 3.5)	*d*
6a[e]	−95	1.72 (q, 3.3)	40.7 (br)
6a[e]	−60	1.74 (q, 3.2)	*d*
6a[e]	−30	1.92 (qn, 2.3)	*d*
6b[e]	−80	1.76 (d, 3.4)	52.5 (t, 3.3)
6a[h]	−115	2.38 (t, 4.5)	30.6 (qn, 4.6)
6b[h]	−115	2.34 (d, 2.3)	53.5 (t, 2.2)

[a] Spectra were recorded in 0.1 M solutions as listed below. Coupling constants (in Hz) measured after resolution enhancement. Multiplicities are denoted as follows: d = doublet, t = triplet, q = quartet, qn = quintet, sp = septet, br = broad mound. The chemical shifts are reported relative to 0.3 M $^6LiCl/MeOH$ at −90 °C (0.0 ppm) and neat Me_2NEt at −90 °C (25.7 ppm). [b] Spectrum recorded in d_8-toluene solution. [c] Spectrum recorded at −115 °C. [d] Spectrum not recorded. [e] Spectrum recorded in toluene solution. [f] Spectrum recorded in 2:1 pentane/toluene solution. [g] Spectrum recorded in 2.5 M Et_2O in pentane solution. [h] Spectrum recorded in 1:1 pentane/THF solution.

Table 2. NMR Spectroscopic Data[a]

compd	$\delta(^6Li)$ (mult, J_{LiN}), assignt	$\delta(^{15}N)$ (mult, J_{LiN}), assignt
17[b]	0.83 (d, 5.2)	67.3 (qn, 5.3)
18[c]	2.53 (t, 3.9), $Li_{\mathbf{A}}$	35.4 (br), $N_{\mathbf{A}}$
	2.02 (dd, 1.6), $Li_{\mathbf{B}}$	33.3 (br), $N_{\mathbf{B}}$
	1.35 (t, 4.1), $Li_{\mathbf{C}}$	
18[d]	2.56 (d, 2.6), $Li_{\mathbf{A}}$	53.6 (t, 2.6), $N_{\mathbf{C}}$
	2.04 (d, 2.7), $Li_{\mathbf{B}}$	51.8 (t, 2.6), $N_{\mathbf{D}}$
	1.39 (s), $Li_{\mathbf{C}}$	

[a] Spectra were recorded in 0.1 M solutions as listed below. Coupling constants (in Hz) measured after resolution enhancement. Multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, qn = quintet, br = broad mound. The chemical shifts are reported relative to 0.3 M $^6LiCl/MeOH$ at −90 °C (0.0 ppm) and neat Me_2NEt at −90 °C (25.7 ppm). [b] Spectra recorded in 1:1:1 pentane/toluene/THF solution at −115 °C. [c] Spectra recorded in 1:1 THF/toluene solution at −40 °C using **6a**. [d] Spectra recorded in 1:1 THF/toluene solution at −40 °C using **6b**.

Results

The ^{15}N-labeled amines were prepared using literature protocols[12,23−25] as described in the Supporting Information. Lithium amides **4**−**6** were prepared using multiply recrystallized $[^6Li]n$-BuLi[26] and were recrystallized from pentane. The NMR spectra were recorded using methods described previously.[27] We routinely record ^{15}N NMR spectra with proton decoupling. The ^6Li spectra were also recorded with concurrent irradiation of the N–H proton resonances (δ −1.0 to −3.0 ppm) due to significant Li–H coupling[28] observed in some

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(21) We isolated several other $[^6Li]RNHLi$, where R is a saturated alkyl group without a pendant chelating moiety. Unfortunately, none exhibited appreciable solubility in hydrocarbons and were not studied further. $[^6Li,^{15}N]PhNHLi$ was isolated using commercially available $[^{15}N]$aniline. The ^6Li NMR spectra of 0.1 M solutions in toluene with 1.0, 5.0, or 10 equiv of THF do not display $^6Li–^{15}N$ coupling.

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Table 3. Single-Frequency ^{6}Li{^{15}N} Decoupling to Determine the Structure of 18[a]

	δ(Li$_A$)	δ(Li$_B$)	δ(Li$_C$)
^{6}Li resonance	2.53	2.02	1.35
6a no irradiation	t, 3.9	dd, 1.6	t, 4.1
6a N$_A$ irradiated	t, 3.7	d, 1.7	s
6a N$_B$ irradiated	s	d, 1.7	t, 3.9
6b no irradiation	d, 2.6	d, 2.7	s
6b N$_C$ irradiated	d, 2.9	s	s
6b N$_D$ irradiated	s	d, 2.3	s

[a] Spectra were recorded in 0.1 M 1:1 THF/toluene solution at −40 °C. Multiplicities are denoted as follows: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, br = broad mound. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −90 °C (0.0 ppm) and neat Me$_2$NEt at −90 °C (25.7 ppm).

Table 4. NMR Spectroscopic Data: Mixed Aggregates with [^{6}Li,^{13}C]Lithium Phenylacetylide[a]

compd	δ(^{6}Li) (mult, J_{LiC})	δ(^{13}C) (mult, J_{LiC})
17[b]	0.86 (d, 7.4)	143.4 (qn, 7.5)
18[c]	2.54 (d, 4.3) 2.00 (d, 8.9) 1.37 (d, 3.4)	134.7 (m)

[a] Spectra were recorded in 0.1 M solutions as listed below. Coupling constants (in Hz) measured after resolution enhancement. Multiplicities are denoted as follows: d = doublet, qn = quintet. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −90 °C (0.0 ppm) and the toluene methyl resonance at −90 °C (20.4 ppm). [b] Spectra recorded in 1:1:1 toluene /pentane/THF solution at −115 °C. [c] Spectra recorded in 1:1 toluene/THF solution at −90 °C.

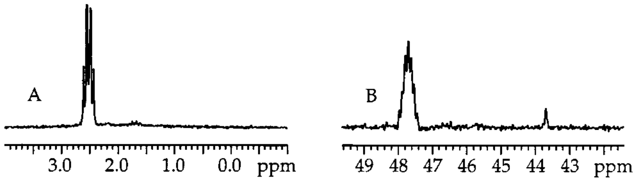
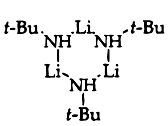


Figure 1. (A) ^{6}Li NMR spectrum of 0.1 M [^{6}Li,^{15}N]*t*-BuNHLi in toluene at −30 °C. (B) ^{15}N{^{1}H} NMR spectrum of 0.1 M [^{6}Li,^{15}N]*t*-BuNHLi in toluene at −30 °C.

instances.[12] The spectral data are summarized in Tables 1−4.

***t*-BuNHLi.** ^{6}Li{^{1}H} NMR spectra recorded on 0.1 M solutions of [^{6}Li,^{15}N]*t*-BuNHLi (**5**) in toluene at −30 °C display a single sharp 1:3:3:1 quartet resulting from coupling to three magnetically equivalent ^{15}N nuclei (Figure 1, Table 1). The analogous ^{15}N{^{1}H} NMR spectrum reveals a septet resulting from coupling to three magnetically equivalent ^{6}Li nuclei. These spectroscopic properties are consistent with any one of three behaviors: (1) the cyclic trimer **7** in the limit of rapid intraaggregate site exchange,[29−31] (2) the cubic tetramer **8** in the limit of slow intraaggregate site exchange, or (3) the prismatic hexamer **9** or octamer **10** (recently characterized crystallographically by Mulvey and coworkers)[16] in which the coupling to the neighboring nuclei around the perimeter of the drum and along the vertical struts of the drum are equivalent by coincidence.



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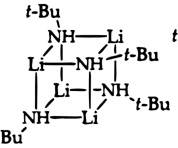

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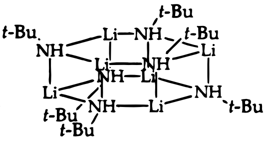

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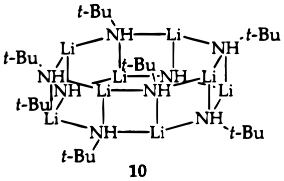

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We probed the assignment of *t*-BuNHLi as prismatic oligomers (**8**−**10**) by variable-temperature NMR spectroscopy. Although each ^{6}Li nucleus would be coupled to only three neighboring ^{15}N nuclei at any given instant, a rapid intraaggregate exchange could allow for coupling to all ^{15}N nuclei, resulting in a ^{6}Li quintet for the cube **8**, a septet for hexamer **9**, or a nonet for octamer **10**. The change in multiplicity would be accompanied by a statistical reduction in the coupling constant due to the diminished residence time.[29,31] Such properties are observed for lithium amide **6** (described below). However, warming the probe fails to cause the ^{6}Li quartet of [^{6}Li,^{15}N]*t*-BuNHLi to change multiplicity. At 40 °C the quartet broadens (reversibly) into a broad signal, consistent with the onset of rapid interaggregate exchange. We cannot exclude the possibility that the broadening results from the rapid intraaggregate exchange of octamer **10**, in which the nine-line multiplet with a small coupling (approximately 1.3 Hz) might be obscured.

We also explored the assignment of the *t*-BuNHLi aggregate as cyclic trimer **7** with coupling of all ^{6}Li nuclei to all ^{15}N nuclei resulting from rapid intraaggregate exchange. The 3.4 Hz coupling observed in the ^{6}Li quartet coincides with the statistically weighted 5 Hz coupling expected for a cyclic trimer.[13,32] In this instance, one would expect the quartet to simplify to a triplet in the low-temperature limit due to slowing of the intraaggregate exchange. Indeed, we observed such spectral behavior for the cyclic trimer of lithium diethylamide.[31] However, no such simplification is observed in either 2:1 pentane−toluene or 2.5 M Et$_2$O−pentane solutions at −128 °C (described below). Therefore, trimer **7** and prismatic oligomers **8**−**10** cannot be excluded at this time. We have chosen *not* to rely upon potentially misleading molecular weight measurements in an effort to resolve the ambiguity.

Spectroscopic studies of [^{6}Li,^{15}N]*t*-BuNHLi in the presence of ethereal ligands afforded mixed results. In

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(30) Intraaggregate exchange was observed in LiTMP: Hall, P. L.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 9575.

(31) Intraaggregate exchange in Et$_2$NLi is observed in both the slow and fast exchange limits: Rutherford, J. L.; Collum, D. B. Unpublished data.

(32) For ab initio calculations of ^{6}Li−^{15}N coupling constants see: Koizumi, T.; Morihashi, K.; Kikuchi, O. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 305.

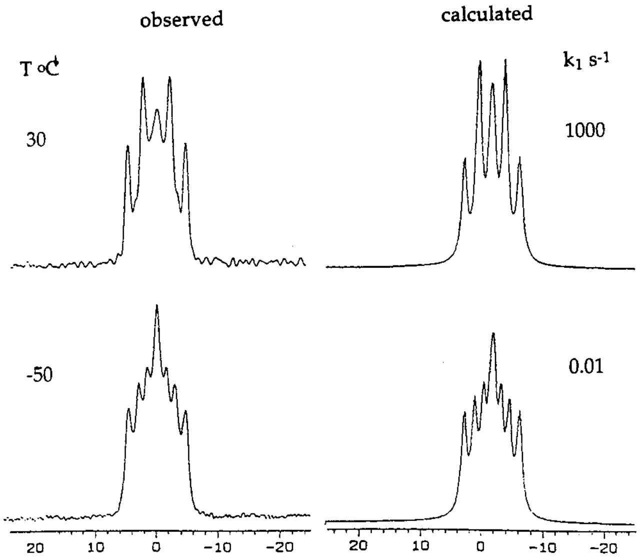
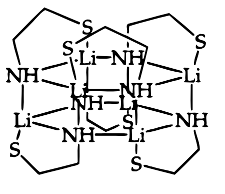


Figure 2. (Left) ^{6}Li NMR spectra of 0.1 M [^{6}Li,^{15}N]-LiDMEDA in 2:1 pentane/toluene at 30 and −50 °C. (Right) Calculated line shapes with first-order rate constants.

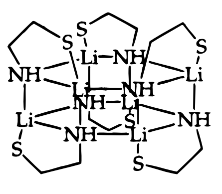
a range of Et_2O−toluene combinations or in toluene solutions containing 0.5−2.0 equiv of THF, the higher aggregate characterized by the ^{6}Li quartet remains intact. (The ^{15}N resonance appears as a poorly resolved signal.) Addition of >10 equiv of THF causes the ^{6}Li resonance to broaden into a structureless mound.

LiDMEDA. The solution structure of LiDMEDA (**4**)[12] is determined to be a hexagonal or octagonal prism (**2** or **3**) by ^{6}Li NMR spectroscopy. The ^{6}Li{^{1}H} NMR spectrum of [^{6}Li,^{15}N]LiDMEDA in 2:1 pentane/toluene recorded at −50 °C displays a seven-line multiplet (Figure 2). We originally inferred that the multiplet results from rapid *intraaggregate* exchange within a hexamer. However, it deviates substantially from the anticipated 1:6:15:20:15:6:1 intensity ratios and regular peak intervals. Furthermore, warming the sample reveals a coalescence ($T_{\text{coalescence}} = -10$ °C) to give a doublet of triplets ($J_{\text{Li-N}} = 4.3$ and 2.5 Hz, respectively). At 25 °C each ^{6}Li nucleus displays coupling to one magnetically distinct and two magnetically equivalent ^{15}N nuclei. Accordingly, we assign the 7-line multiplet observed at low temperature as a ddd arising from coupling to three magnetically inequivalent ^{15}N nuclei ($J_{\text{Li-N}} = 1.7$, 3.1, and 4.3 Hz). Spectral simulations with DNMR (Figure 2) show consistency of the model and afford an activation energy ($\Delta G°_{\text{act}}$) for the exchange of 15 ± 2 kcal/mol. Not surprisingly, the corresponding ^{15}N{^{1}H} NMR spectra each display a single poorly resolved multiplet at low and ambient temperatures, where 27- and 15-line multiplets would be expected, respectively.

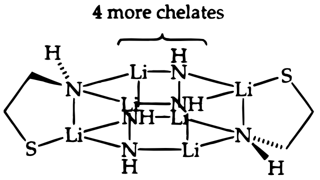
The ^{6}Li{^{1}H} NMR spectral data and additional spectroscopic properties of LiDMEDA are consistent with the symmetry properties of hexagonal or octagonal prisms containing chemically equivalent yet *magnetically inequivalent* nuclei. Taking the hexagonal prism for illustration, we see that the simplest hexagonal prism **2** contains six chemically equivalent ^{6}Li nuclei and six chemically equivalent ^{15}N nuclei. However, viewed from a given locus, the two neighboring nuclei common to one of the hexagonal rings are magnetically equivalent, while the third neighboring nucleus of the adjoining hexagonal ring connected via a “strut” is magnetically distinct. Consequently, a ^{6}Li resonance would appear as a dt (as observed at high temperatures). Additional symmetry constraints imposed by chelation affords three possible stereoisomeric hexagonal prisms bearing chemically equivalent ^{6}Li and ^{15}N nuclei (**11**−**13**). (The stereogenic center at the NH moiety causes the S_6 symmetry of **13**.) In each case, a given ^{6}Li or ^{15}N nucleus bears three adjoining neighbors that are chemically equivalent, yet magnetically distinct. Thus, a ^{6}Li resonance with three neighboring ^{15}N nuclei would appear as a ddd (as observed at low temperatures).



11; NMe$_2$
S_6 symmetry

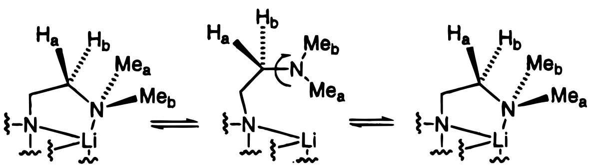


12; S = NMe$_2$
D_3 symmetry



13; S = NMe$_2$
S_6 symmetry

Variable-temperature ^{1}H and ^{13}C NMR spectroscopy provides insight into the dynamics of the chelates. The ^{13}C NMR spectrum recorded at ambient temperature displays two methylene resonances and a single methyl resonance. Cooling the sample reveals a coalescence at −13 ± 3 °C due to chemically inequivalent methyls in the low-temperature limit ($\Delta G°_{\text{act}} = 11.5 \pm 0.3$ kcal/mol). This is consistent with the exchange process depicted in eq 1. The ^{1}H NMR spectrum provided evidence of two distinctly different exchange processes. Spectra recorded at −60 °C display diastereotopic methyl and methylene protons along with a dramatically upfield shifted N−H proton (δ −2.35 ppm). A coalescence of the chemically distinct methyl resonances at −29 ± 3 °C ($\Delta G°_{\text{act}} = 11.7 \pm 0.3$ kcal/mol) coincides with the methyl−methyl exchange detected by ^{13}C NMR spectroscopy (eq 1). However, if the chelate is regenerated by coordination to the original Li nucleus, the protons on the methylene chain will remain diastereotopic. Indeed, the coalescence of one pair of diastereotopic methylene protons occurs at 53 ± 3 °C with a substantially larger activation energy ($\Delta G°_{\text{act}} = 15.2 \pm 0.3$ kcal/mol).[33] The $\Delta G°_{\text{act}}$ value



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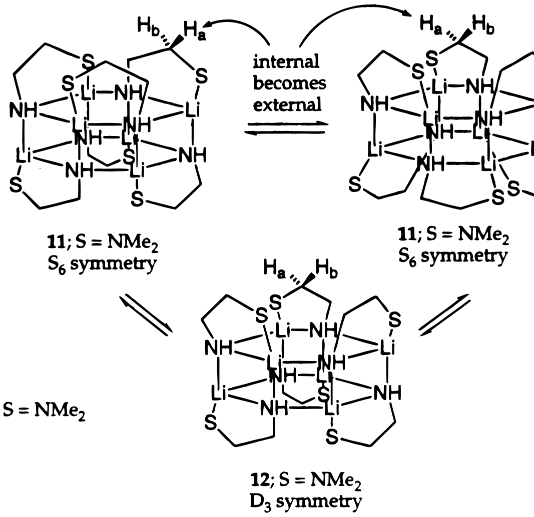
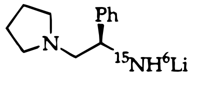
[33] The other methylene resonance is obscured.

Scheme 1

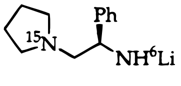


of this latter process coincides with the ΔG°_{act} value for the exchange of the two magnetically inequivalent ^{15}N nuclei within the hexagonal ring (vide supra).

Cleaving a chelate ring does not render the methylene protons chemically equivalent. Interconversion of the diastereotopic methylene protons and the magnetically inequivalent pair of neighboring ^{15}N nuclei requires a rather intrusive rearrangement involving the degenerate exchange of S_6-symmetric hexamer **11** via D_3-symmetric hexamer **12** (Scheme 1). While it is not necessary for three chelate rings to be cleaved at one time (two is sufficient), the exchange requires a net cleavage and reorientation of all six chelates.[34] A similar process would also exchange the diastereotopic methylene protons in D$_3$-symmetric isomer **12** via its enantiomer (not drawn).



[^{6}Li,^{15}N]6a



[^{6}Li,^{15}N]6b

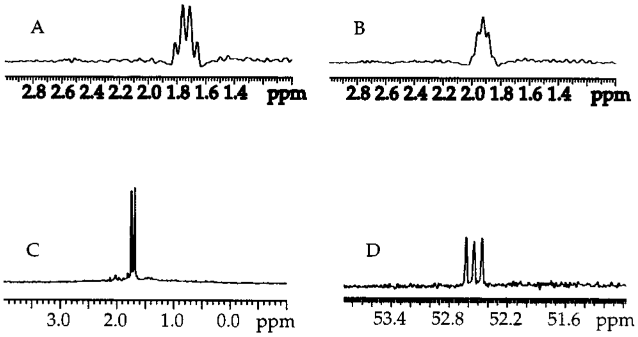
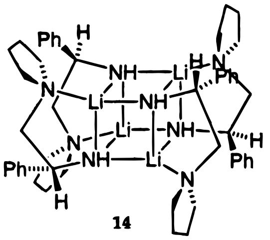


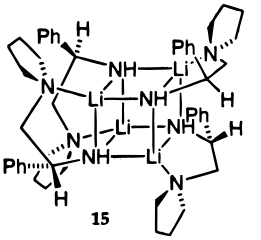
Figure 3. ^{6}Li and ^{15}N NMR spectra of 0.1 M solutions of **6** in toluene: (A) ^{6}Li spectrum of [^{6}Li,^{15}N]**6a** at −60 °C; (B) ^{6}Li NMR spectrum of [^{6}Li,^{15}N]**6a** at −30 °C; (C) ^{6}Li NMR spectrum of [^{6}Li,^{15}N]**6b** at −90 °C; (D) ^{15}N{^{1}H} NMR spectrum of [^{6}Li,^{15}N]**6b** at −80 °C.

(*R*)-PhCH(NHLi)CH$_2$N(CH$_2$)$_4$. Spectroscopic analysis of 0.1 M [^{6}Li,^{15}N]**6a** (i.e., R^{15}NHLi) in toluene at −95 °C reveals a ^{6}Li quartet and a poorly resolved ^{15}N multiplet (Table 1, Figure 3). The ^{6}Li resonance displays coupling to 3 magnetically equivalent (or nearly equivalent) ^{15}N nuclei. The broad ^{15}N multiplet is consistent with coupling to 3 neighboring ^{6}Li nuclei that could cause splitting into as few as 7 lines (assuming 3 magnetically equivalent ^{6}Li nuclei) or as many as 27 lines (assuming 3 magnetically inequivalent ^{6}Li nuclei). In contrast to the results obtained for *t*-BuNHLi, we find that warming the sample of [^{6}Li,^{15}N]**6a** to −30 °C causes the quartet to become a quintet with concomitant 25% reduction of the coupling constant, implicating rapid intraaggregate exchange within a cubic tetramer. Spectroscopic analysis of pyrrolidine-labeled [^{6}Li,^{15}N]**6b** in toluene at −80 °C reveals a ^{6}Li doublet ($^1J_{Li-N}$ = 3.4 Hz) and a 1:1:1 ^{15}N triplet, indicating static (nonexchanging) chelation of the pyrrolidino moieties. There are two possible stereoisomeric tetramers: D_2-symmetric **14** and C_2-symmetric **15**. Tetramer **14** would display one ^{6}Li resonance, one amide ^{15}N resonance, one pyrrolidino ^{15}N resonance, and four ^{13}C resonances corresponding to the *C*−N subunits (CH(Ph)N and CH$_2$N). Tetramer **15** would show twice as many resonances. All of the spectra display the number of resonances consistent with **14**.



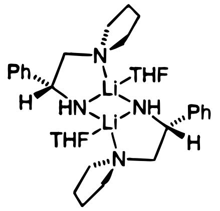
14

D$_2$ Symmetry (observed)



15

C$_2$ Symmetry (not observed)



16

Tetramer **14** is retained in toluene containing varying quantities of Et$_2$O at −95 °C. In contrast, incremental additions of THF reveal **14** at low THF concentrations with the doubly chelated dimer **16** becoming dominant at high THF concentrations.[35] Dimer **16** derived from NH-labeled [^{6}Li,^{15}N]**6a** displays a ^{6}Li triplet and an ^{15}N quintet. Spectroscopic analysis of pyrrolidine-labeled [^{6}Li,^{15}N]**6b** in 1:1 THF/pentane at −115 °C reveals a ^{6}Li doublet ($^1J_{Li-N}$ = 2.3 Hz) and a 1:1:1 ^{15}N triplet consistent with chelates in the slow exchange limit. The coupling, in conjunction with the THF concentration dependence, indicates that the lithiums of **16** are four-

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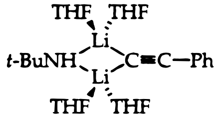
[34] Alternative exchange mechanisms involving N−Li bond scission are excluded because they would entail intraaggregate exchange, which is not observed.

[35] Other doubly chelated lithium amide dimers have been observed: Reich, H. J.; Gudmundsson, B. Ö. *J. Am. Chem. Soc.* **1996**, *118*, 6074. Hilmersson, G.; Davidsson, Ö. *J. Org. Chem.* **1995**, *60*, 7660. Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1992**, *114*, 761.

coordinate. Neither the stereochemistries at lithium nor those at nitrogen can be assigned at this time.

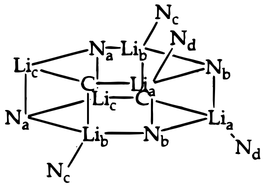
RNHLi−Lithium Phenylacetylide Mixed Aggregates. We carried out limited investigations of RNHLi/LiX mixed aggregates. Our choice of lithium phenylacetylide[36] ([^{6}Li]PhCCLi and [^{6}Li,^{13}C]PhCCLi) stems, in part, from related investigations of mixed aggregates of lithium acetylides with potentially isostructural lithium aminoalkoxides.[37,38]

Mixtures of [^{6}Li,^{15}N]*t*-BuNHLi (**5**) and [^{6}Li]PhCCLi form the 1:1 mixed dimer **17**, displaying a characteristic ^{6}Li doublet and ^{15}N quintet, along with the homoaggregates of [^{6}Li,^{15}N]*t*-BuNHLi and [^{6}Li]PhCCLi.[39] The spectra recorded on mixtures of [^{6}Li]*t*-BuNHLi and [^{6}Li,^{13}C]PhCCLi display a ^{6}Li doublet and a ^{13}C quintet. Samples containing only 5.0 equiv of THF in pentane/toluene show substantially higher proportions of the homoaggregates, indicating that high THF concentrations promote mixed aggregation.



17

Mixtures of [^{6}Li]PhCCLi and [^{6}Li]LiDMEDA (**4**) over a range of proportions and conditions afford ^{6}Li and ^{15}N{^{1}H} NMR spectra displaying broad signals that offer no structural insights. Mixtures of [^{6}Li]**6** and [^{6}Li]PhCCLi also afford very complex NMR spectra when the lithium acetylide is in excess. However, a single, albeit structurally complex, mixed aggregate is observed at ≤1:2 proportions of PhCCLi to **6**. The partial structure of the 4:2 mixed aggregate **18** was assigned on the basis of a series of labeling studies with the aid of detailed single-frequency decoupling experiments (Tables 2 and 4).[40] However, there are four possible stereoisomers that could not be distinguished.



18

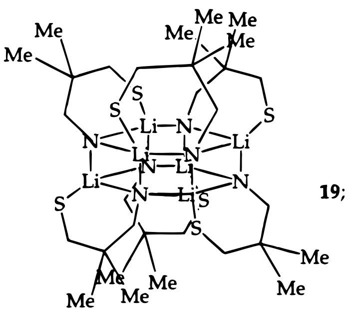
Discussion

A growing crystallographic record suggests that the solution structures of lithium monoalkylamides[16,17] bear a greater resemblance to lithium alkoxides and alkyllithiums[18] than to the more sterically demanding lithium dialkylamides.[13] In particular, prismatic structures that are only rarely observed for the dialkylamides[14] seem to be common for lithium monoalkylamides. Overall, the NMR spectroscopic studies described herein confirm the prevalence of prismatic structures.

Each system that we studied shows peculiarities that offer insights into the structures of lithiated monoalkylamides while leaving a number of structural issues unresolved. Investigations of LiDMEDA (**4**) in pentane revealed some form of higher prism. We cannot distinguish hexamers from octamers (**2** and **3**, respectively), nor can we distinguish symmetry-related isomers (e.g., **11**−**13**). Nonetheless, the prismatic structure offers unanticipated and potentially useful spectral properties. The six lithiums and six nitrogens of a hexagonal prism of LiDMEDA are chemically equivalent; however, from the vantage point of a given site, all three neighboring nuclei are *magnetically* inequivalent. At elevated probe temperatures, the onset of rapid chelate exchange causes the neighboring nuclei located around the perimeter of the "drum" of LiDMEDA to become magnetically equivalent, while coupling along the vertical "strut" of the drum remains distinct. Although we are unaware of distinctly different coupling constants being documented for prismatic alkyllithiums, they could provide a useful structural probe.

^{1}H NMR spectroscopy of LiDMEDA revealed, in addition to the deep-seated chelate exchanges shown in Scheme 1, a more facile process involving simple reversible cleavage of a single chelated ring (eq 1). The LiDMEDA prism is quite robust, displaying no tendency to deaggregate in THF solution and unusually slow interaggregate subunit exchanges.

[^{6}Li,^{15}N]*t*-BuNHLi (**5**) displayed a ^{6}Li quartet from −128 to +30 °C. The failure to attain slow and fast intraaggregate exchange limits leaves open the question of whether the quartet arises from cyclic trimer **7**[29−31] in rapid intraaggregate exchange or prismatic oligomers **8**−**10** in slow intraaggregate exchange. Any of the four structures are plausible: (1) the crystallographic characterization of octamer **10** by Mulvey and co-workers supports an analogous octameric solution structure; (2) tetramer **8** derives support by drawing analogy to the cubic structure assigned to lithium amide **6** (vide infra); (3) hexamer **9** is very similar to the crystal structure **19** obtained by Williard;[15] (4) the seemingly least plausible structure, trimer **7**, derives support from the crystallographically characterized trimer of *t*-Bu$_3$SiNHLi[41] as well as spectroscopic investigations of Et$_2$-



19; S = NMe$_2$

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[36] For extensive leading references to the structures of lithium acetylides, see ref 37.

[37] Thompson, A.; Corley, E. G.; Huntington, M. F.; Grabowski, E. J. J.; Remenar, J. F.; Collum, D. B. *J. Am. Chem. Soc.* **1998**, *120*, 2028.

[38] For solution structural studies of R$_2$NLi/RLi mixed aggregates see: Corruble, A.; Valnot, J.-Y.; Maddaluno, J.; Prigent, Y.; Davoust, D.; Duhamel, P. *J. Am. Chem. Soc.* **1997**, *119*, 10042. Hilmersson, G.; Davidsson, Ö. *J. Organomet. Chem.* **1995**, *489*, 175.

[39] We briefly reinvestigated[36] the structure of [^{6}Li,^{13}C]lithium phenylacetylide; all spectra are archived in the Supporting Information. In toluene containing <30 equiv of THF, we observe the previously characterized dimer as well as two prismatic structures displaying ^{6}Li quartets. The ^{13}C spectra were not resolved. In toluene solution with added TMEDA a [^{6}Li,^{13}C]lithium phenylacetylide dimer is observed, as evidenced by a ^{6}Li triplet (J = 8.7 Hz) and a ^{13}C quintet (J = 8.8 Hz). A single prismatic structure, displaying a ^{6}Li quartet (J = 5.7 Hz), is observed in toluene with Et$_3$N. Two species were observed in toluene with added Et$_2$O. The major species has a prismatic structure.

[40] Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1990**, *112*, 4069.

[41] Cummins, C. C.; Wolczanski, P. T. Unpublished data.

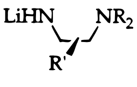
NLi showing that the intraaggregate subunit exchange within a cyclic trimer might be too fast to observe in the slow exchange limit.[31]

Of the three lithium amides, the dynamic properties of lithium amide **6** provides us with the most compelling and complete structural assignment. A clear view of intraaggregate subunit exchange offers convincing support for the cubic tetramer structure **1**. Thus, in the low-temperature limit each lithium is coupled to only the three neighboring ^{15}N nuclei, whereas at higher temperatures the ^{6}Li resonance displays coupling to four ^{15}N nuclei with a reduced coupling constant in proportion to the reduced residence times. The assignment of lithium amide **6** as stereoisomer **14** rather than **15** follows directly from the distinct symmetry properties.

We were intrigued by the prospects that the similar structures observed for lithium monoalkylamides and lithium alkoxides (cf. **20**−**23**) might eventually find important applications in asymmetric synthesis. Accordingly, we investigated mixed aggregation of lithium monoalkylamides with lithium acetylides. No mixed aggregation between lithium phenylacetylide and *t*-BuNHLi is observed in hydrocarbon solutions. With added THF, mixed dimer **17** forms to the exclusion of higher prismatic mixed aggregates. Lithium phenylacetylide/LiDMEDA mixtures are intractable. Significant progress was made toward the characterization of a 4:2 mixed aggregate of **6** and lithium phenylacetylide. The ^{6}Li, ^{13}C, and ^{15}N labeling studies afford the assignment as a drum with atomic connectivities shown by structure **18**. In this case, four isomers are consistent with the NMR spectral data.

$\text{RNHLi} \overset{???}{\equiv} \text{ROLi}$

20 **21**



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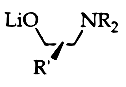
$\overset{???}{\equiv}$



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Conclusion

The investigations of RNHLi derivatives described herein confirm their tendency to form prismatic structures first detected by the crystallographic community. The symmetry properties of the prisms offer mixed results. On one hand, the high symmetry leaves ambiguities in a substantial number of the structural assignments. On the other hand, the differing symmetries resulting from cubic tetramers compared to higher prismatic oligomers, in conjunction with observable intraaggregate subunit exchanges, offer several unusually clear structural insights. Of particular note, the higher prismatic "drums" can, in some cases, display coupling of the nuclei around the perimeter that differs from the coupling along the vertical "struts". This may prove important in investigations of carbanions as well.

The tendency to form prismatic structures supports an analogy with lithium alkoxides and points to a possible niche in asymmetric synthesis. However, previous investigations by Vedejs[9] and co-workers on asymmetric protonations foreshadow an unusual underlying complexity when such reagents are involved. Protic lithium amides pose unique challenges stemming from their physical properties, their tendencies to liberate strongly coordinating neutral amine ligands upon protonation, and the underlying structural complexities of both the homoaggregates as well as mixed aggregates. While we are optimistic that the importance of such protic amides will continue to grow, the development of new synthetic methods as well as a detailed understanding of their chemistry will require some persistence.

Experimental Section

Reagents and Solvents. All solvents were distilled by vacuum transfer from blue or purple solutions containing sodium benzophenone ketyl. The hydrocarbon stills contained 1% tetraglyme to dissolve the ketyl. ^{6}Li metal (95.5% enriched) was obtained from Oak Ridge National Laboratory. The [^{6}Li]-*n*-BuLi used to prepare the ^{6}Li-labeled compounds was prepared and recrystallized by the standard literature procedure.[26] [^{6}Li,^{15}N]LiDMEDA was prepared and isolated as an analytically pure solid, as described previously.[12] [^{6}Li,^{15}N]*t*-BuNHLi[23] and [^{6}Li]**6**,[25] [^{6}Li,^{15}N]**6a**,[25] [^{6}Li,^{15}N]**6b**,[24] and [^{6}Li,^{13}C]-LiCCPh were prepared using modified literature methods. Detailed preparations are provided in the Supporting Information. The diphenylacetic acid used to check solution titers[42] was recrystallized from methanol and sublimed at 120 °C under full vacuum. Air- and moisture-sensitive materials were manipulated under argon or nitrogen using standard glovebox, vacuum line, and syringe techniques.

NMR Spectroscopic Analyses. Samples for spectroscopic analyses were prepared using a sample preparation protocol described in detail elsewhere.[27] Routine ^{1}H, ^{6}Li, ^{15}N, and ^{13}C NMR spectra were recorded on a Varian XL-400 spectrometer operating at 399.70, 58.84, 40.52, and 100.58 MHz, respectively, or on a Varian Unity 500 spectrometer operating at 499.93, 73.57, 58.84, and 125.76 MHz, respectively. The ^{1}H, ^{6}Li, ^{15}N, and ^{13}C resonances are referenced to tetramethylsilane (0.0 ppm), 0.3 M [^{6}Li]LiCl/MeOH at −90 °C (0.0 ppm), neat Me_2NEt at −90 °C (25.7 ppm), and the toluene methyl resonance at −90 °C (20.4 ppm), respectively.

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Supporting Information Available: Text giving details of the preparations and figures giving NMR spectra of the various compounds discussed in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

OM981051W

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(42) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.