Lithium Ion Solvation: Amine and Unsaturated Hydrocarbon Solvates of Lithium Hexamethyldisilazide (LiHMDS)

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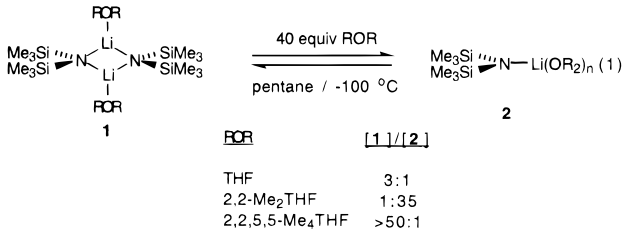
Abstract: ^{6}Li, ^{15}N, and ^{13}C NMR spectroscopic studies of ^{6}Li−^{15}N labeled lithium hexamethyldisilazide ([^{6}Li,^{15}N]-LiHMDS) solvated by more than 20 different mono-, di-, and trialkylamines (and ammonia) are described. LiHMDS dimers solvated by the least hindered trialkylamines and most dialkylamines exchange ligands by a dissociative mechanism that is sufficiently slow to observe discrete mono-, di-, and mixed-solvated dimers. Dimers solvated by the hindered trialkylamines and unhindered monoalkylamines undergo rapid ligand substitutions by relatively rapid dissociative and associative mechanisms (respectively). Mono- and disolvated dimers can be observed for the monoalkylamines at <1.0 equiv of ligand (per Li). The monomers that form at elevated trialkylamine concentrations are suggested to be di- and trisolvated. The relationship between ligand structure and lithium amide aggregation state is a complex and sensitive function of amine alkyl substituents. The dialkylamines prove to be remarkably similar to dialkyl ethers as ligands for the LiHMDS dimer despite pronounced differences expected for nitrogen- and oxygen-based coordination. A greater relative promotion of monomer formation by the dialkylamines than the dialkyl ethers can be traced to disproportionate monomer stabilization by the amines. Hydrocarbon-dependent aggregation effects are discussed in terms of primary and secondary shell solvation.

Introduction

We recently described NMR spectroscopic studies of lithium hexamethyldisilazide (LiHMDS; $(Me_3Si)_2NLi$) solvated by a variety of monodentate ethereal ligands.[1−5] The relationship of solvation and aggregation is quite complex as exemplified by eq 1. While the dimers are disolvated as expected, the monomers are trisolvated rather than disolvated even for relatively hindered ethers. Moreover, THF and oxetane cause a marked stabilization of the monomer due to putative five-coordinate tetrasolvates. The hypersensitivity of LiHMDS aggregation to the steric requirements of the solvent is *not* due to solvent-dependent aggregation enthalpies, but rather to highly variable internal entropies associated with ordering solvents



within the lithium coordination spheres. Overall, the complex relationship between the solvation energy and the tendency to aggregate could be adequately explained only by considering (1) solvent−amide and solvent−solvent interactions on both the monomer and the dimer, (2) the combined contributions of solvation enthalpy and entropy, and (3) variable monomer solvation numbers.

We now report investigations of LiHMDS solvation by monodentate amines. We predicted that the high steric demands of the splaying alkyl groups on the trialkylamines[6−8] would stabilize the disolvated monomers relative to the trisolvated monomers and that the monomer−dimer proportions might

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(12) Concentration dependencies suggest the higher oligomer to be tetrameric (ref 11).

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Table 1. ^{6}Li, ^{15}N, and ^{13}C NMR Spectral Data of LiHMDS Amine Solvates[a]

compd	^{6}Li, δ (mult, J_{LiN})	^{15}N δ (mult, J_{LiN})	^{13}C{^{1}H} (ligand)	^{13}C{^{1}H} (Me_3Si)	compd	^{6}Li, δ (mult, J_{LiN})	^{15}N δ (mult, J_{LiN})	^{13}C{^{1}H} (ligand)	^{13}C{^{1}H} (Me_3Si)
3a[k]	1.47 (t, 3.5)	41.7 (q, 3.7)	48.8	6.0	**4k**[e]	1.41 (t, 3.4)	41.1 (q, 3.4)	*d*	*d*
	1.68 (t, 4.1)				**4l**[e]	1.52 (t, 3.3)	38.9 (q, 3.3)	*d*	*d*
3b[k]	1.52 (t, 4.7)	*c*	53.5, 45.7, 11.5	5.9	**4m**[e]	1.10 (t, 3.2)	*c*	*d*	*d*
	1.60 (t, 4.9)				**4n**[e]	1.11 (t, 3.5)	*c*	*d*	*d*
3c,d[d]					**4o**[b]	1.44 (t, 3.3)	38.0 (q, 3.3)	40.3, 14.0	6.4
3e[b]	0.56 (t, 3.3)	41.6 (q, 3.5)	47.9, 24.8	6.0	**4p**[b]	0.72 (t, 3.3)	39.9 (q, 3.3)	49.8, 29.1	7.1
	0.79 (t, 3.6)				**4q**[b]	0.91 (t, 3.2)	37.9 (q, 3.3)	51.2, 35.3, 30.3, 14.5	6.4
3f−n[d]					**4r**[b]	1.56 (t, 3.3)	42.3 (q, 3.3)	*d*	*d*
3o[b]	0.59 (t, 3.7)	41.2 (q, 3.4)	41.9, 14.5	5.5	**4s**[b]	1.10 (t, 3.2)	38.3 (q, 3.2)	47.0, 27.0, 23.8	6.4
	1.25 (t, 3.1)				**4t**[b]	1.27 (t, 3.3)	38.5 (q, 3.3)	47.4, 25.1	6.6
3p[k]	1.33 (t, 3.3)	42.2 (q, 3.5)	51.7, 29.4	5.4	**4u**[b]	1.26 (t, 3.3)	39.3 (q, 3.3)	46.7	6.4
	1.80 (t, 3.6)			5.6	**4v**[b]	1.09 (t, 3.2)	39.0 (q, 3.3)	41.8, 34.5, 14.3	6.3
3q[b]	0.65 (t, 3.2)	41.1 (q, 3.5)	52.1, 36.5, 31.5, 14.5	5.4	**4w**[b]	1.13 (t, 3.9)	39.2 (q, 3.2)	43.0, 25.1	6.4
	0.81 (t, 3.7)			5.6	**4x**[b]	1.23 (t, 3.3)	39.0 (q, 3.3)	48.8, 31.6	6.8
3s[b]	0.62 (t, 3.7)	40.7 (q, 3.4)	46.8, 26.8, 23.7	5.7	**4y**[b]	1.51 (t, 3.3)	39.4 (q, 3.2)	53.9, 31.5, 25.6	6.4
	0.92 (t, 3.2)				**4z**[f]	1.19 (t, 3.0)	37.9 (q, 3.0)		
3t[b]	0.67 (t, 3.8)	40.6 (q, 3.3)	24.8, 24.4	5.7	**5a**[g]	0.49 (d, 5.7)	45.3 (t, 5.8)	47.4	6.5
	1.07 (t, 3.0)				**5b**[g]	0.39 (d, 6.2)	46.1 (t, 6.0)	53.5, 44.8, 11.5	6.7
3u[b]	0.56 (t, 3.9)	41.5 (m, −)	46.7	5.6	**5c**[e]	1.24 (d, 6.0)	46.8 (t, 6.0)	*d*	*d*
	1.09 (t, 3.2)				**4d**[e]	0.69 (d, 5.8)	*c*	*d*	*d*
3v[b]	0.50 (t, 3.8)	41.4 (m, −)	41.8, 34.7, 14.3	5.6	**5e**[g]	0.22 (d, 6.2)	45.6 (t, 6.2)	47.1, 25.0	6.8
	0.89 (t, 3.2)				**5f**[e]	1.31 (d, 6.0)	45.8 (t, 6.0)	*d*	*d*
3w[b]	0.53 (t, 3.9)	41.4 (m, −)	43.0, 25.1	5.6	**5g−j**[h]				
	0.92 (t, 3.2)				**5k**[e]	1.21 (d, 5.9)	*c*	*d*	*d*
3x[b]	0.62 (t, 3.3)	41.0 (q, 3.5)	48.7, 31.5	5.8	**5l**[e]	1.31 (d, 5.6)	47.9 (t, 5.7)	*d*	*d*
	0.98 (t, 3.7)				**5m**[e]	0.88 (d, 5.7)	*c*	*d*	*d*
3y[b]	0.64 (t, 3.8)	41.2 (q, 3.4)	53.7, 31.4, 25.5	5.7	**5n**[e]	0.87 (d, 5.8)	*c*	*d*	*d*
	1.27 (t, 3.2)				**5o**[i]	1.64 (d, 5.5)	47.6 (t, 5.6)	*d*	*d*
3z[f]	0.65 (t, 4.0)	39.9 (q, 3.5)			**5p**[i]	1.48 (d, 5.6)	47.9 (t, 5.7)	*d*	*d*
	1.08 (t, 3.0)				**5q**[i]	1.50 (d, 5.0)	48.2 (t, 5.0)	*d*	*d*
4a[b]	0.71 (t, 3.3)	39.2 (q, 3.3)	48.8	7.4	**5r**[h]				
4b[b]	0.64 (t, 3.1)	40.0 (q, 3.3)	53.5, 45.7, 11.5	7.4	**5s**[i]	1.45 (d, 5.2)	49.6 (t, 5.2)	*d*	*d*
4c[e]	1.37 (t, 3.5)	40.9 (q, 3.3)	*d*	*d*	**5t**[i]	1.85 (d, 4.9)	43.5 (t, 4.9)	*d*	*d*
4d[e]	1.33 (t, 3.3)	42.0 (q, 3.3)	*d*	*d*	**5u**[i]	1.20 (d, 4.0)	48.0 (t, 4.0)	*d*	*d*
4e[b]	0.72 (t, 3.5)	39.0 (q, 3.5)	47.9, 24.8	7.7	**5v**[i]	1.13 (d, 3.8)	45.9 (t, 4.0)	*d*	*d*
4f[e]	1.27 (t, 3.3)	38.9 (q, 3.3)	*d*	*d*	**5w**[i]	1.17 (d, 5.0)	48.5 (t, 5.1)	*d*	*d*
4g[e]	1.25 (t, 3.4)	41.3 (q, 3.4)	*d*	*d*	**5x**[i]	1.97 (d, 5.0)	48.9 (t, 5.0)	*d*	*d*
4h[e]	1.46 (t, 3.5)	42.1 (q, 3.5)	*d*	*d*	**5y**[i]	1.36 (d, 4.0)	45.0 (t, 4.1)	*d*	*d*
4i[e]	1.18 (t, 3.3)	39.9 (q, 3.2)	*d*	*d*	**5z**[j]	0.76 (s)	47.6 (s)		
4j[e]	1.41 (t, 3.4)	43.0 (q, 3.4)	*d*	*d*					

[a] Spectra were recorded on 0.1 M solutions of LiHMDS. Coupling constants were measured after resolution enhancement. Multiplicities are denoted as follows: d = doublet, t = triplet, q = quintet, m = multiplet. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −100 °C (0.0 ppm) and neat Me_2NEt at −100 °C (25.7 ppm). Chemical shifts are dependent upon temperature, donor solvent concentration, and hydrocarbon cosolvent. All *J* values are reported in hertz. [b] Recorded in toluene-d_8 at −100 °C with 0.7 equiv of donor solvent. [c] Spectra were not acquired due to solubility problems during long acqusition times. [d] Rapid solvent exchange obscured bound solvent resonances. [e] Recorded in pentane at −80 °C with 20 equiv of donor solvent. [f] Recorded in 2:1 toluene:pentane at −100 °C with 0.5 equiv of donor solvent. [g] Recorded at −100 °C with 2−5 equiv of donor solvent in toluene-d_8. [h] No observable monomer. [i] Recorded in pentane at −80 °C with 5−10 equiv of donor solvent. [j] Recorded in 2:1 toluene:pentane at −100 °C with 4.0 equiv of donor solvent. [k] The ^{6}Li and ^{15}N spectra were recorded in pentane solutions at −115 °C. ^{13}C NMR spectra were recorded at −110 °C in toluene-d_8.

show dependencies on amine steric requirements akin to those found for the ethers.[1] We were generally correct; however, some surprises emerged. The LiHMDS monomer is markedly stabilized relative to the dimer by toluene (vs pentane) co-solvent despite the substantial concentrations of ligand. The similarity of this effect to the hydrocarbon dependence on the LiHMDS dimer−higher oligomer distribution noted by Kimura and Brown and[2,11,12] the importance of lithium ion precomplexation[9,10] in metalations and polymerizations of unsaturated hydrocarbons prompted further investigations. We will show that the two hydrocarbon dependencies have very little in common. The low basicity of LiHMDS[13] also offers an opportunity to investigate lithium ion solvation by the sterically unhindered (and protic) dialkylamines, monoalkylamines, and ammonia. LiHMDS dimer solvation by dialkylamines correlates remarkably with their isostructural dialkyl ether counterparts.

Results

Structure Assignments of Amine-Solvated LiHMDS Dimers. The protocols for characterizing the various amine solvates of LiHMDS parallel those delineated previously.[1] ^{6}Li and ^{15}N NMR spectra recorded on 0.1 M solutions of [^{6}Li,^{15}N]-LiHMDS[14] in pentane exhibit ^{6}Li and ^{15}N multiplets (spin 1 and $^1/_2$, respectively) indicative of monomer and cyclic oligomer topologies.[3,12] The distinction of C_{2h} symmetric cyclic dimers and C_{nh} symmetric higher cyclic oligomers is achieved with inverse-detected ^{15}N zero-quantum NMR spectroscopy.[15] Resonance correlations necessary for the characterization of mixtures are available from either single-frequency decoupling experiments or ^{6}Li−^{15}N heteronuclear multiple quantum correlation (HMQC) spectroscopy.[16] The spectral data are summarized in Table 1. Selected spectra are shown in Figure 1. Additional spectra are included as supporting information. Slow solvent

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(14) Romesberg, F. E.; Bernstein, M. P.; Fuller, D. J.; Harrison, A. T.; Collum, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 3475.
(15) Gilchrist, J. H.; Collum, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 794.
(16) Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *Magn. Reson. Chem.* **1992**, *30*, 855.

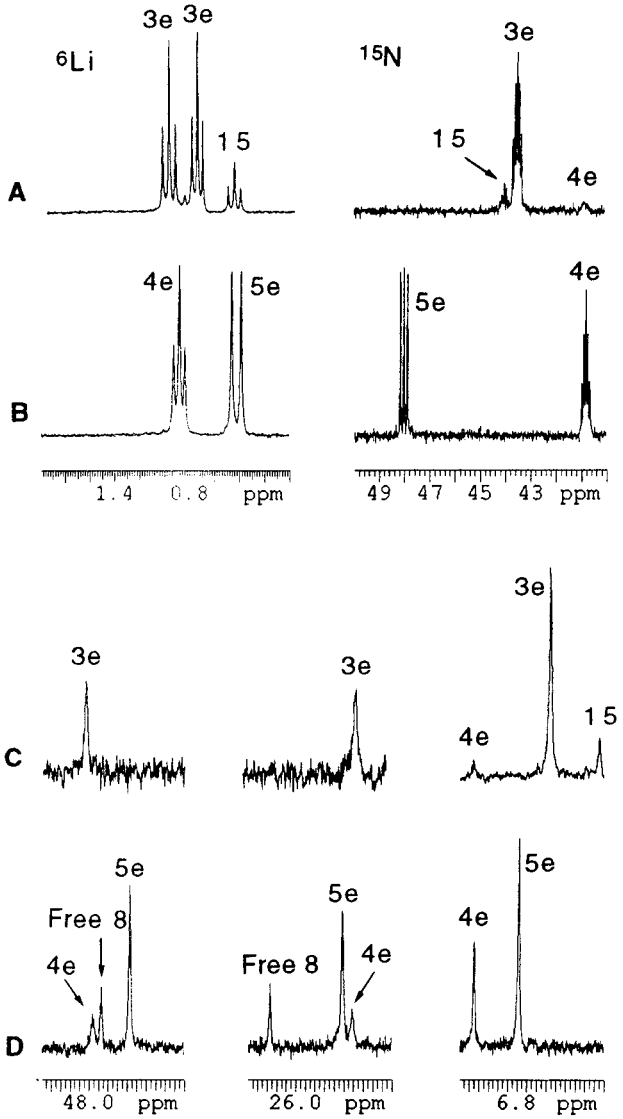
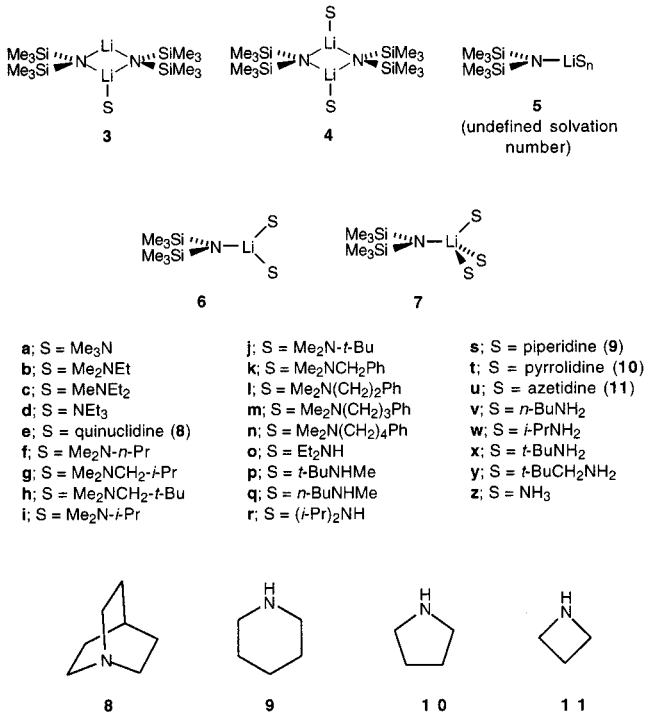


Figure 1. NMR spectra of 0.1 M [^{6}Li,^{15}N]LiHMDS at −100 °C: (A) ^{6}Li and ^{15}N NMR spectra with 0.5 equiv of quinuclidine per Li in 2:1 toluene/pentane; (B) ^{6}Li and ^{15}N NMR spectra with 2.0 equiv of quinuclidine per Li in 2:1 toluene/pentane; (C) partial ^{13}C NMR spectra in toluene-d_8 at −100 °C with 0.5 equiv of quinuclidine per Li; (D) partial ^{13}C NMR spectra in toluene-d_8 at −100 °C with 2.0 equiv quinuclidine per Li.

exchange on ^{6}Li, ^{15}N, and ^{13}C NMR time scales[17a] allows characterization of monosolvated[17b] and disolvated dimers (**3** and **4**, respectively) bearing coordinated trimethylamine (Me_3N), dimethylethylamine (Me_2NEt, DMEA), and quinuclidine (**8**). The appearance of free (uncoordinated) amine in the ^{13}C spectra at >1.0 equiv per Li demonstrates that the dimers are disolvated rather than tri- or tetrasolvated. More hindered amines undergo rapid ligand exchange as low as −125 °C, but likely furnish disolvated dimers as well. Most dialkylamines bearing an N−H functionality afford LiHMDS mono- and disolvated dimers in the limit of slow solvent exchange. The exchange of $(i\text{-Pr})_2NH$ is rapid on NMR time scales. Azetidine solvates **3u** and **4u** can be observed in the slow exchange limit at <1.0 equiv of azetidine. For the majority of monoalkylamines, mono- and disolvated dimers are observable in the slow exchange limit below 1.0 equiv per Li. The ^{13}C resonances for the amine bound

(17) (a) Slow ethereal solvent exchange has been observed in other laboratories: Hilmersson, G.; Davidsson, O. *J. Org. Chem.* **1995**, *60*, 7660. Reich, H. J.; Kulicke, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 273. (b) For crystallographically characterized monosolvated LiHMDS dimers, see: Williard, P. G.; Liu, Q.-Y. *J. Org. Chem.* **1994**, *59*, 1596.

Chart 1



to the disolvated dimer and free amine are time averaged above 1.0 equiv of amine per Li. *t*-$BuNH_2$ is the only monoalkylamine that gives discrete resonances for disolvated dimer and free ligand.

LiHMDS seemed particularly promising as a probe of lithium ion solvation by ammonia.[18] The monosolvated and disolvated dimers **3z** and **4z** (respectively) can be observed in the limit of slow exchange of free and bound NH_3 at <1.0 equiv of NH_3 per Li. However, even a slight excess of NH_3 causes the onset of rapid exchange. [^{15}N]NH_3 affords one-bond ^{6}Li−^{15}N coupling constants of 3.9 and 3.8 Hz (respectively). These values are comparable to the $^1J_{Li-N}$ values of 2.4−3.7 Hz reported for chelated trialkylamines by Williard[19] and Koga.[20]

Mechanism of Solvent Exchange on LiHMDS Dimers. The exchange rates of free and bound quinuclidine, Me_2NEt (DMEA), NMe_3, and the majority of dialkylamines are independent of free amine concentration. For example, samples containing 0.2 equiv of free amine (5:1 integration ratio of bound and free ligand resonances) and samples containing 5.0 equiv of free amine per Li (1:5 integration ratio of bound and free ligand resonances) coalesce at the same temperature. This indicates that solvent substitution proceeds by a rate limiting solvent dissociation (Scheme 1).[21,22] The one exception is azetidine (**11**) for which an amine-concentration-dependent solvent exchange indicates contribution from (although not necessarily exclusively) an associative substitution. Within the

(18) Kaufmann, E.; Gose, J.; Schleyer, P. v. R. *Organometallics* **1989**, *8*, 2577. Somsen, G.; Weeda, L. *J. Electroanal. Chem. Interfacial Electrochem.* **1971**, *29*, 375. For additional leading references see ref 41.

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(20) Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1992**, *114*, 761.

(21) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; Wiley: New York, 1970; pp 1185−88.

(22) Under conditions where the two coalescing resonances are in 1:1 proportions, the relationship of the rate constant and coalescence temperature can be approximated as $\Delta G^\circ_{act} = -RT \ln(k_{obs}h/kT_{coalesc})$ such that $k_{obs} = 2.22\Delta\nu$. The coalescence temperatures measured on samples containing 1.0 equiv of free amine (1:1 ratio of bound and free ligand resonances) and affiliated activation energies (±0.3 kcal/mol) are as follows: S = quinuclidine, ΔG°_{act} = 9.6 kcal/mol; S = Me_3N, 8.4 kcal/mol; S = Me_2NEt, 8.0 kcal/mol.

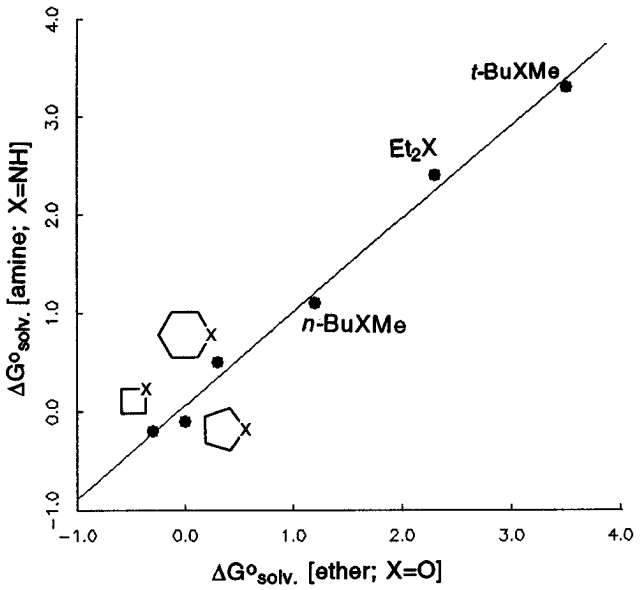
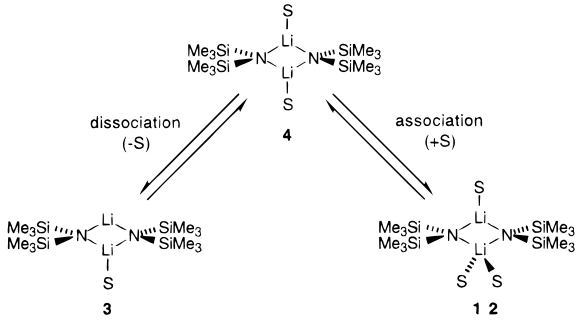


Figure 2. Plot of LiHMDS dimer solvation energies (ΔG°_{solv}) for ethers vs amines (eqs 2 and 3). All solvents are referenced to THF at 0.0 kcal/mol. The ether solvation free energies are taken from ref 1.

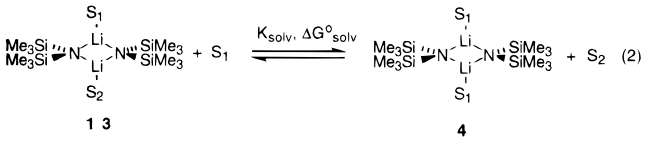
Scheme 1



monoalkylamine series, only *t*-$BuNH_2$ exchanges by a predominantly dissociative mechanism; amine-concentration-dependent coalescence shows that *n*-$BuNH_2$, *i*-$PrNH_2$, *t*-$BuCH_2NH_2$, and NH_3 substitute, at least partially, by associative mechanisms via trisolvated dimers **12**.[23] Associative substitution may predominate for all amines at high amine concentrations.

Relative LiHMDS Dimer Solvation Energies. Rapid exchange of dimer-bound and free trialkylamine ligands precludes determination of relative dimer solvation energies for all amines except quinuclidine (**8**), NMe_3, and Me_2NEt. Competitions of these latter three solvents against Et_2O or THF to determine the relative dimer binding affinities afford ether-solvated dimers[1] and amine-solvated dimers (as well as amine-solvated monomers; *vide infra*) to the exclusion (<10%) of mixed solvated dimers. This cooperativity of amine and ether solvation contrasts with non-cooperative ether/ether mixed solvation.[1] By adjusting the amine:ether proportions, we measured the concentrations of the bis(ether)-solvated dimers and bis(amine)-solvated dimers and determined qualitatively that the capacity for solvating LiHMDS dimer follows the order THF > quinuclidine > Et_2O > Me_3N > Me_2NEt.[24]

The sterically less hindered dialkylamines undergo substantially slower ligand exchange and display non-cooperative mixed solvation. The concentrations of mixed and homosolvated dimers as well as free ligands (eq 2) were obtained by integrating the well-resolved resonances corresponding to either the Me_3Si fragments or the coordinated solvents in the ^{13}C NMR spectra.[25] Relative solvation energies (ΔG°_{solv}) were determined according to eq 3. A plot of ΔG°_{solv} for the dialkylamines vs ΔG°_{solv} for the isostructural dialkyl ethers determined previously[1] reveals a 1:1 correlation (Figure 2).[24b]



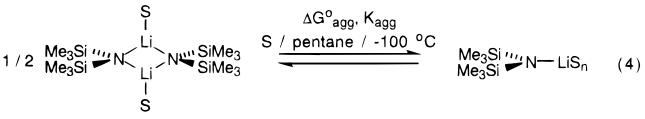
(2)

a; S_1 = Et_2O, S_2 = Et_2NH
b; S_1 = THF, S_2 = pyrrolidine (**10**)
c; S_1 = *t*-BuOMe, S_2 = *t*-BuNHMe
d; S_1 = *n*-BuOMe, S_2 = *n*-BuNHMe
e; S_1 = THP, S_2 = piperidine (**9**)
f; S_1 = oxetane, S_2 = azetidine (**11**)

$$K_{solv} = [\mathbf{4}][S_2]/[\mathbf{13}][S_1] = \exp(-\Delta G^\circ_{solv}/RT) \quad (3)$$

Competition of the least hindered monoalkylamines with THF reveals broad resonances with unresolved coupling in the ^6Li NMR spectra (with the exception of *t*-$BuNH_2$). The broadening stems from high ligand exchange rates. Nonetheless, we could tentatively assign the resonances to the THF and amine solvates from the chemical shifts. With the absolute ligand concentrations (confirmed by ^{13}C resonance integration), we obtained the following relative binding affinities: *n*-$BuNH_2$ > *i*-$PrNH_2$ ≈ THF ≈ *t*-$BuCH_2NH_2$ > *t*-$BuNH_2$ > Et_2O.

Amine- and Hydrocarbon-Dependent LiHMDS Deaggregation. At increased amine concentrations, we observe LiHMDS monomers showing characteristic $^6Li-^{15}N$ coupling (Table 1). Elevated concentrations of azetidine, *n*-$BuNH_2$, and NH_3 cause the relatively unusual loss of the $^6Li-^{15}N$ coupling.[26] Spectroscopic analyses on 0.1 M solutions of [^6Li,^{15}N]LiHMDS in pentane containing different amines (eqs 4 and 5, Table 3)



(4)

$$K_{agg} = [\mathbf{5}]/\{[\mathbf{4}]^{1/2}[S]^{(n-1)}\} = \exp(-\Delta G^\circ_{agg}/RT) \quad (5)$$

reveal that formation of the monomer crudely correlates with ligand bulk following the order NR_3 < HNR_2 < RNH_2. Monomer:dimer ratios observed for 0.1 M LiHMDS in pentane in the presence of 8 out of 10 di- and trialkylamines are invariant over wide (≥40 °C) temperature ranges, indicating that the monomer−dimer equilibrium (eq 4) is thermoneutral (ΔH°_{agg} ≈ 0; Table 3).

Toluene promotes monomer formation by ≈0.5 kcal/mol (per Li) relative to pentane for a number of hindered trialkylamines. The monomer stabilization by toluene is a sterically insensitive (non-primary shell) solvent effect unique to aromatic hydrocarbons. For example, 1,3-dimethylbenzene (*m*-xylene) and 1,3,5-trimethylbenzene (mesitylene) afford monomer stabilizations that are indistinguishable from those observed for toluene. In contrast, the monomer−dimer equilibria in 1-pentene, 2-bu-

(23) Evidence of trisolvated organolithium dimers: Seebach, D.; Bauer, W.; Hansen, J.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. *J. Chem. Soc., Chem. Commun.* **1984**, 853. Williard, P. G.; Liu, Q.-Y. Unpublished. See also ref 26a.

(24) (a) Competition studies revealed that pyridine binds more strongly than THF to LiHMDS dimer (ΔG° = −0.4 kcal/mol per Li). (b) 2,2,6,6-Tetramethylpiperidine appears to coordinate to LiHMDS despite the high steric demands as evidenced by the shift of the LiHMDS equilibrium to exclusively dimer by 5 equiv of amine. In contrast, $(Me_3Si)_2NH$ shows no tendency whatsoever to coordinate to LiHMDS.

(25) The integrations were cross-checked and confirmed by ^6Li NMR spectroscopy.

(26) (a) Depue, J. S.; Collum, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 5518. (b) Kallman, N.; Collum, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 7466.

Table 2. ^{6}Li, ^{15}N, and ^{13}C NMR Spectra Data of [^{6}Li,^{15}N]LiHMDS Mixed Solvated Dimers[a]

compd	^{6}Li	^{15}N{^{1}H} (m, J_{LiN})	^{13}C (amine)	^{13}C (ether)	^{13}C(Me_3Si)
13a	0.84 (t, 3.0) 0.65 (t, 3.6)	38.3 (q, 3.6)	40.4, 14.1	60.3, 12.4	6.1
13b	0.93 (t, 3.4) 1.30 (t, 3.4)	38.7 (q, 3.5)	47.4, 24.8	68.2, 25.0	6.2
13c[b]	0.57 (t, 3.3) 1.21 (t, 3.4)	38.4 (q, 3.4)	49.7, 29.4	75.8, 50.2, 26.7	6.2
13d	0.85 (t, 3.3) 0.71 (t, 3.4)	38.3 (q, 3.3)	51.3, 35.6, 30.5, 14.7	71.8, 56.2, 28.8, 18.5, 14.5	6.0 6.2
13e	0.76 (t, 3.4) 1.07 (t, 3.4)	38.4 (q, 3.6)	47.0, 26.9, 25.2	68.7, 25.2, 22.0	6.2

[a] Spectra were recorded on 0.1 M solutions of LiHMDS at −100 °C in toluene-d_8. Coupling constants were measured after resolution enhancement. Multiplicities are reported as follows: t = triplet, q = quintet. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −100 °C (0.0 ppm) and dimethylethylamine (25.7 ppm). All *J* values are reported in hertz. Resonances of **13f** were broad with poor coupling due to rapid solvent exchange. [b] The ^{6}Li and ^{15}N spectra were recorded in 2:1 pentane/toluene at −120 °C.

Table 3. Thermochemical Data for LiHMDS Dimer−Monomer Equilibria (Eq 4) in Amine/Hydrocarbon Mixtures[a]

R_3N	equiv of R_3N (per Li)	monomer:dimer ([**5**]:[**4**]) pentane	monomer:dimer ([**5**]:[**4**]) toluene	$\Delta H°_{agg}$[b]	$\Delta G°_{agg}$[c]
Me_3N	20	1.3:1	9.4:1	0.0	0.6
Me_2NEt	20	1.2:1	10:1	0.0	0.6
Me_2N*n*-Pr	20	1:3.8	1.3:1	−0.1	1.1
Me_2N*i*-Pr	20	1:2.2	4.3:1	−0.5	1.0
Me_2N*t*-Bu	20	1:>99	1:49		>2.3
Me_2NCH_2*i*-Pr	20	1:>99	1:>99		>2.3
Me_2NCH_2*t*-Bu	20	1:>99	1:>99		>2.3
Me_2NCH_2Ph	20	1:50	1:13		2.0
$Me_2N(CH_2)_2Ph$	20	1:1.2	1:1.4		0.8
$Me_2N(CH_2)_3Ph$	20	1:2.2	1.3:1		1.0
$Me_2N(CH_2)_4Ph$	20	1.2:1	3.0:1		0.6
$MeNEt_2$	20	1:7.3	1.3:1	−0.1	1.4
NEt_3	20	1:>99	1:13		>2.3
quinuclidine (**8**)	20		>99:1		<−0.3[e]
quinuclidine (**8**)	5		19:1		−0.7[e]
pyridine	5		1:>99		>1.7[e]
pyrrolidine (**10**)	8	70:1		−2.4	−0.8
piperidine (**9**)	8	5.7:1		−2.9	−0.3
Et_2NH	8	1:15	1:1.8	0.0	1.1
t-BuN(H)Me	8	1:6.1		+0.4	0.8
n-BuN(H)Me	8	1:4.3		−0.5	0.6
(*i*-Pr)$_2$NH	8	1:>99			>1.9
azetidine (**11**)	8	>99:1			<−0.5
n-$BuNH_2$	10	>99:1			<−0.5
i-$PrNH_2$	10	5.6:1		−2.2	−0.1
t-$BuCH_2NH_2$	10	>99:1			<−0.5
t-$BuNH_2$	10	7.3:1		−0.3	−0.1
NH_3	4[d]	5:1		−2.3	−0.6

[a] Spectra recorded at −80 °C on 0.1 M solutions of LiHMDS in pentane or toluene with added amine. Ratios were determined by ^{6}Li NMR spectroscopy. Values should be viewed as only approximate. [b] Enthalpies were determined from variable-temperature ^{6}Li NMR spectroscopy over at least a 40 °C range for each solvent with errors of <10%. [c] Free energies were determined from monomer:dimer ratios in pentane assuming the monomer is disolvated and have errors of <10%. [d] Recorded in 2:1 toluene/pentane. [e] Free energies were determined in toluene.

tyne, and a pentane−ethylene mixture (≈50% by volume of ethylene) are indistinguishable from that in pure pentane. As we shall see in the following section, the influence of toluene causes substantial deviations from normal solvent-dependent mass action behavior.

The influence of toluene on the LiHMDS aggregation state prompted investigations of the trialkylamine ligands containing aromatic rings (e.g. $Me_2N(CH_2)_nPh$). The monomer might receive additional stabilization by the proximate aromatic ring, whether the result of a discrete lithium−arene π complex[27] or a more long-range effect. The results are inconclusive, yet somewhat interesting. $Me_2NCH_2CH_2Ph$ promotes monomer formation (relative to Me_2N-*n*-Pr) in pentane. Moreover, the monomer stabilization is accompanied by complete loss of the hydrocarbon co-solvent dependence. $Me_2N(CH_2)_3Ph$ and $Me_2N(CH_2)_4Ph$ show only a slight monomer stabilization that is due, at least in part, to adding 20 equiv of a toluene equivalent.[28]

LiHMDS Monomer Solvation Numbers. Quinuclidine, Me_2NEt, and NMe_3 in toluene undergo slow exchange of *monomer*-bound and uncoordinated solvent on NMR time scales. Careful integration of the ^{13}C resonances of the bound ligands and the Me_3Si moieties reveals that the monomers are disolvated (**6**). Notably (see below), the existence of disolvated monomers in *pentane* cannot be documented by direct spectroscopic methods because relatively high amine concentrations are required to observe monomers.

The monomer solvation number in pentane solutions was determined by measuring the monomer−dimer ratio as a function of amine concentration (eq 4).[1,29] To properly monitor the monomer and dimer concentrations requires their coexistence in excess amine (>10 equiv per Li) over a broad (>5-fold) range of amine concentrations as well as sufficient ^{6}Li resonance resolution. These stringent requirements were met by $MeNEt_2$, Me_2N-*i*-Pr, and Et_2NH. Figure 3 shows a plot of [monomer]/[dimer]$^{1/2}$ vs [$MeNEt_2$] measured at −80 °C using pentane as the co-solvent. Rearranging eq 5 to give eq 6 and subsequent nonlinear least-squares fit afford a monomer solvation number, "*n*", of 2.8 ± 0.1 consistent with formation of at least predominantly trisolvate **7c**.[30] Analogous studies of Me_2N-*i*-Pr at −80 °C afford $n = 2.7 \pm 0.1$. Substantial concentrations of trisolvated monomers are surprising in light of the steric requirements of Me_2N-*i*-Pr as well as the direct observation of disolvates **6a**,**b**,**e** in toluene (but *not* pentane).

The analogous plot of [monomer]/[dimer]$^{1/2}$ vs [$MeNEt_2$] using toluene rather than pentane as the co-solvent (Figure 3)

(27) Leading references to $^{+}$Li−arene solvates: Siemeling, U.; Redecker, T.; Neumann, B.; Stammler, H.-G. *J. Am. Chem. Soc.* **1994**, *116*, 5507.

(28) The monomer−dimer ratio in solutions of LiHMDS containing 20 equiv of Me_2N-*i*-Pr in toluene/pentane mixtures is a linear function of the toluene concentration.

(29) (a) Waack, R.; Doran, M. A.; Stevenson, P. E. *J. Am. Chem. Soc.* **1966**, *88*, 2109. (b) Chan, L. L.; Smid, J. *J. Am. Chem. Soc.* **1967**, *89*, 4547. (c) Chan, L. L.; Wong, K. H.; Smid, J. *J. Am. Chem. Soc.* **1970**, *92*, 1955. (d) See also ref 26b.

(30) The simple expression in eq 6 reveals a mixture of solvation states; the overall scenario is more accurately described by the equations below (ref 1), where $[AS_n]_{total}$ is the total monomer concentration.

$$2S + {}^{1}/_{2}A_2S_2 \overset{K_{eq(1)}}{\rightleftharpoons} AS_2 + S \overset{K_{eq(2)}}{\rightleftharpoons} AS_3$$

$$[AS_n]_{total}/[A_2S_2]^{1/2} = K_{eq(1)}[S](K_{eq(2)}[S] + 1)$$

While the improved fit is not statistically significant, it offers predicted concentrations of the three species as a function of donor solvent concentration.

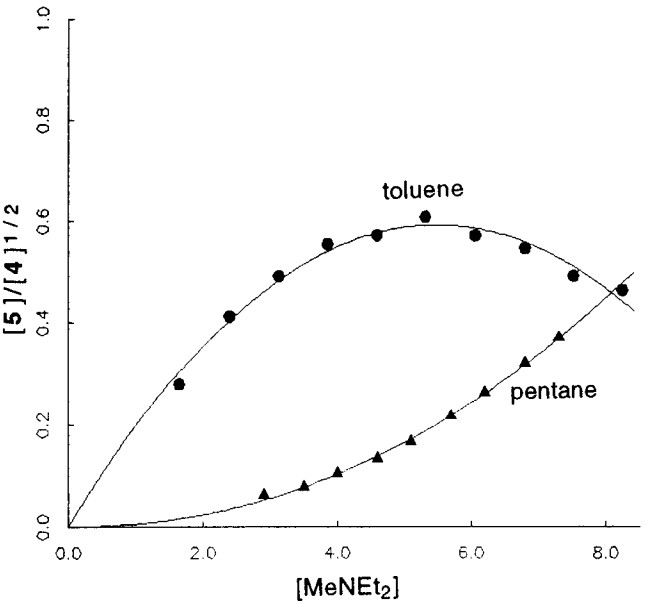


Figure 3. Plot of $[\mathbf{5}]/[\mathbf{4}]^{1/2}$ vs $[MeNEt_2]$ for 0.1 M LiHMDS at −80 °C in pentane (▲) and in toluene (●). The data are fit by nonlinear least-squares methods to the function in eq 5 ($K_{eq} = 1.4 \times 10^{-2}$, $n = 2.8$). The data in toluene are fit to the function in eq 8 ($K_{eq(1)} = 2.3 \times 10^{-2}$ $M^{-3/2}$, $K_{eq(2)} = 4.8 \times 10^{-1}$).

reveals a substantial deviation from a simple exponential dependence. The maximum in the monomer concentration at intermediate $MeNEt_2$ concentrations underscores the marked stabilization by toluene. If we include provisions for stabilization of the bis(amine)-solvated monomer by toluene ("AS_2T"; eq 7) the resulting algebraic description (eq 8) readily accom-

$$[\mathbf{5}]/[\mathbf{4}]^{1/2} = K_{agg}[S]^{(n-1)} \quad (6)$$

$$1/2\ A_2S_2 + 2S + T \underset{}{\overset{K_{eq(1)}}{\rightleftharpoons}} AS_2T + S \overset{K_{eq(2)}}{\rightleftharpoons} AS_3 + T \quad (7)$$

such that A = $[Me_3Si]_2NLi$, S = donor solvent, T = toluene

$$[A_{Total}]/[A_2S_2]^{1/2} = K_{eq(1)}[S]\{K_{eq(2)}[S] + [T]\} \quad (8)$$

such that $[A_{Total}] = [AS_2T] + [AS_3]$

modates the odd amine concentration dependencies (Figure 3);[31] the adjustable parameters provide predicted proportions of disolvated dimer **4c**, disolvated monomer **6c**, and trisolvated monomer **7c** shown in Figure 4. Moreover, other mathematical models such as that based upon toluene-stabilized trisolvated monomers (e.g. AS_3T) do not adequately describe the behavior.[31] However, the success of the model delineated in eqs 7 and 8 does not necessarily implicate a discrete (primary-shell) coordination by toluene. Quite to the contrary, investigations of other aromatic and olefinic hydrocarbons described above implicate a sterically insensitive (long-range) effect.[32] "AS_2T" only serves to mathematically describe the stabilization of disolvated monomers by toluene.[33]

(31) Models based upon exclusively trisolvated monomers AS_3 or AS_3T do not afford satisfactory fits. If the toluene dependence is floated as an adjustable parameter (AS_2T_n), we obtain a toluene order, n, of 1.3.

(32) For comparison, the LiHMDS dimer−monomer equilibria in hydrocarbons containing THF or Et_2O show no such hydrocarbon dependencies.

(33) Quinuclidine *in toluene* provides solutions of LiHMDS that remain homogeneous for weeks at −70 °C and contain unusually high proportions of monomer. In contrast, pentane solutions of LiHMDS instantly deposit an insoluble powder.

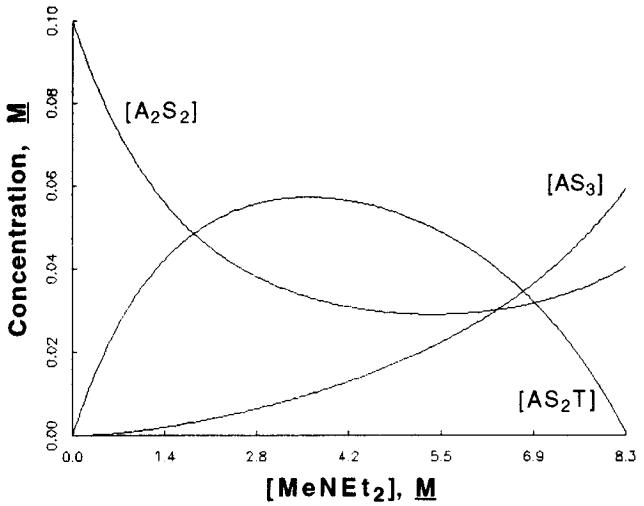


Figure 4. Predicted concentrations of disolvated dimer $\mathbf{A_2S_2}$, toluene-stabilized disolvated monomer $\mathbf{AS_2T}$, and trisolvated monomer $\mathbf{AS_3}$ (S = $MeNEt_2$). The functions are calculated using adjustable parameters $K_{eq(1)} = 2.3 \times 10^{-2}$ $M^{-3/2}$ and $K_{eq(2)} = 4.8 \times 10^{-1}$ derived from a nonlinear least-squares fit to eq 8. (See supporting information for derivations.)

Table 4. ^{6}Li and ^{15}N NMR Spectral Data of LiHMDS Hydrocarbon Solvates[a]

solvent	^{6}Li, δ (mult, J_{LiN})	^{15}N δ (mult, J_{LiN})
butyne[b]	1.78 (t, 3.6)	39.0 (q, 3.6)
ethylene[c]	1.72 (t, 3.5)	41.3 (q, 3.5)
1-pentene[d]	1.54 (t, 3.4)	
	1.88 (t, 3.6)	
m-xylene[e]	0.33 (t, 3.5)	42.8 (q, 3.5)
	1.21 (t, 4.3)	45.6 (q, 4.3)
mesitylene[e]	0.70 (t, 3.5)	45.9 (q, 3.5)
	1.21 (t, 4.2)	46.2 (q, 4.2)
toluene[e]	0.26 (t, 3.7)	42.8 (q, 3.7)
	1.05 (t, 4.1)	45.2 (q, 4.1)

[a] Spectra were recorded on 0.1 M solutions of LiHMDS. Coupling constants were measured after resolution enhancement. Multiplicities are denoted as follows: t = triplet, q = quintet. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −100 °C (0.0 ppm) and neat Me_2NEt at −100 °C (25.7 ppm). All J values are reported in hertz. [b] Spectra were recorded at −80 °C with 15 equiv of butyne. [c] Spectra were recorded at −80 °C with ≈40 equiv of ethylene. [d] Spectra were recorded at −80 °C with 60 equiv of 1-pentene. [e] Spectra were recorded in neat solvent at −60 °C.

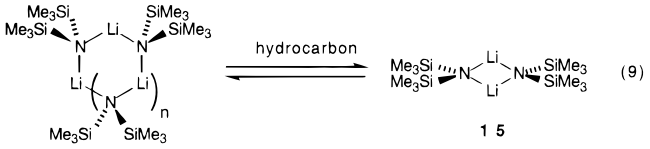
Table 5. LiHMDS Higher Oligomer−Dimer Proportions ([**14**]/[**15**]) in Hydrocarbons (Eq 9)[a]

solvent	oligomer:dimer	solvent	oligomer:dimer
n-pentane	1:1	ethylene	1:>99[c]
toluene	1:11	1-pentene	1:10
m-xylene	1:12	*cis*-2-pentene	1:1
mesitylene	1:1	*trans*-2-pentene	1:1
2-butyne	1:>99[b]		

[a] Spectra were recorded at −80 °C on 0.1 M solutions of LiHMDS in neat hydrocarbon. [b] Recorded on pentane solutions containing 5 equiv (4% by volume) of added butyne. [c] Recorded on pentane solutions with 40 equiv (25% by volume) of added ethylene.

The solvation numbers of dialkylamines were not easily determined because the monomer emerges at low amine concentrations. We obtained reasonable data for Et_2NH showing a monomer solvation number of (2.6 ± 0.2 at −40 °C) consistent with a mixture of di- and trisolvated monomers (over the amine concentration range of 1.0−4.5 M). The competitive stability of disolvated dimers relative to trisolvated monomers receives additional support from a hydrocarbon dependence analogous to that described above.

Addendum: LiHMDS Dimer-Higher Oligomer Equilibrium. Kimura and Brown noted that the LiHMDS dimer and higher oligomer coexist in nearly equimolar proportions in polymethylated aromatic hydrocarbons, whereas the dimer becomes the dominant form in toluene (eq 9; Tables 4 and 5).[12] Since the LiHMDS dimer-higher oligomer equilibrium is shifted to dimers by coordinating ligands,[14] one could infer the existence of a direct ligand−Li interaction. Using [^{6}Li,^{15}N]LiHMDS, we confirmed Kimura and Brown's observations and garnered further support by expanding the study to include non-aromatic unsaturated hydrocarbons. Ethylene−pentane (≈1:1 by volume), 1-pentene, and 2-butyne all stabilize the dimer relative to pentane. Only 5 equiv (4% by volume) of 2-butyne in pentane was required to displace the equilibrium entirely to dimer. While 1-pentene causes dimer stabilization commensurate with toluene, the more substituted olefins *cis*- and *trans*-2-pentene are indistinguishable from pentane. Related hydrocarbon dependencies on alkyllithium hexamer−tetramer equilibria have been reported.[34]

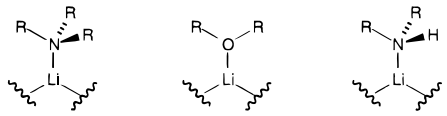


14 **15**

Discussion

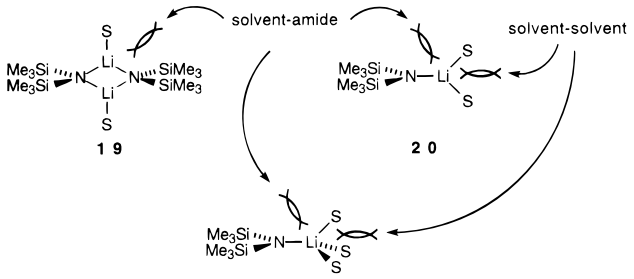
NMR spectroscopic studies of LiHMDS solvated by amines reveal many of the anticipated parallels with ether solvation described previously.[1] Me_3N, Me_2NEt, and quinuclidine can be observed in free and LiHMDS dimer-bound forms on NMR time scales. These three ligands are shown to exchange on disolvated dimers (**4**) by dissociative mechanisms (Scheme 1). The more hindered trialkylamines are too labile to resolve the resonances of free and dimer-bound forms. LiHMDS dimers solvated by the relatively unhindered dialkylamines are also found to be disolvated with excess ligand and undergo relatively slow ligand substitution by rate-limiting ligand dissociation (except for azetidine). Monoalkylamines and ammonia afford spectroscopically discrete mono- and disolvated dimers only at low (<1.0 equiv/Li) amine concentrations. Associative substitutions for sterically unhindered monoalkylamines are fast on NMR time scales at >1.0 equiv of ligand per Li.

Direct competitions of the selected amines with ethers for coordination to the LiHMDS dimer provided relative binding affinities. Although high exchange rates precluded a detailed study, a limited number of competitions afforded the following relative LiHMDS dimer affinities: THF > quinuclidine > Et_2O > Me_3N > Me_2NEt. The greater steric requirements of the three splaying alkyl groups when contrasted with the dialkyl ethers (cf. **16** and **17**)[7,8] were predicted from computational studies[8] and solvation studies of alkyllithiums.[7] We also noted an interesting cooperativity in which mixtures of ethers and trialkylamines afford homosolvated dimers to the exclusion of the mixed ether−trialkylamine solvates (**13**). The absence of such cooperative effects with dialkylamine−ether combinations suggests that the steric requirements of trialkylamines may be prerequisite for the cooperative effects.



16 **17** **18**

The tendency of trialkylamines to deaggregate LiHMDS follows the order $Me_3N \approx Me_2NEt > MeNEt_2 > NEt_3$. This is consistent with the conventional descriptions of solvation and aggregation relationships; however, studies with ethereal solvents[1] suggest that dominant solvent−solvent interactions in the monomer (see **19**−**21**) caused by amine bulk are responsible for the preference for dimers. A similar trend is observed within the Me_2NR series in which α-branching in the R group (R = *t*-Bu > *i*-Pr > Et > Me) and β branching in the R group (R = CH_2-*t*-Bu > *i*-Bu > *n*-Pr > Et) promote dimer formation. One might predict a more marked shift toward dimer with branching at the α rather than β position, but the opposite proves to be the case. A more pronounced dependence on branching at the β position of Me_2NR ligands suggests that moving the bulky substituent further from the amine nitrogen relieves steric interactions in the dimer more so than in the monomer.



19 **20** **21**

The low basicity of LiHMDS allowed us to assess the relative capacities of dialkyl ethers and dialkylamines to solvate the cyclic dimer. Although such a comparison could, at least in principle, offer an evaluation of the relative aza- and oxaphilicity of lithium ion, it is quite complicated because of the superposition of several competing factors including (1) an enormous (10^{10}) difference in Brønsted basicity of amines and ethers and even larger differential Lewis basicity toward non-lithium Lewis acids,[35,36] (2) the mandated tetrahedral coordination at lithium-bound amine nitrogens that contrasts sharply with the trigonal planar coordination at lithium-bound ethereal oxygens[37] (cf. **17** and **18**), and (3) the possibility of an albeit ill-defined amine−amide hydrogen-bonding interaction.[38] Consequently, the probability of a strong correlation of ether and amine binding energies seemed very low. Nevertheless, structurally diverse dialkylamines and their isostructural dialkyl ethers spanning a wide (4 kcal/mol) range of relative binding energies correlate quite well (Figure 2). In essence, dialkyl ethers and dialkylamines are interchangeable ligands for the LiHMDS dimer. The cancellation of so many opposing factors requires some rather extraordinary coincidences that we do not yet understand.[39]

(34) Lewis, H. L.; Brown, T. L. *J. Am. Chem. Soc.* **1970**, *92*, 4664.
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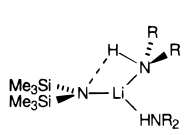
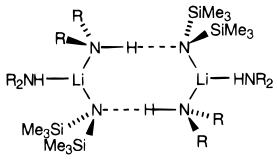
(36) Gutmann, V. *The Donor−Acceptor Approach to Molecular Interactions*; Plenum: New York, 1978. Marcus, Y. *J. Solution Chem.* **1984**, *13*, 599.
(37) Chakrabarti, P.; Dunitz, J. D. *Helv. Chim. Acta* **1982**, *64*, 1482.
(38) For an excellent discussion of and references to protic amine-solvated organolithium derivatives, see: Vedejs, E.; Lee, N. *J. Am. Chem. Soc.* **1995**, *117*, 891. For recent examples of organolithium reactions where protic amine functionalities have been left intact, see: Myers, A. G.; Yoon, T.; Gleason, J. L. *Tetrahedron Lett.* **1995**, *36*, 4555. Imai, M.; Hagihara, A.; Kawasaki, H.; Manabe, K.; Koga, K. *J. Am. Chem. Soc.* **1994**, *116*, 8829. Yasukata, T.; Koga, K. *Tetrahedron Asymmetry* **1993**, *4*, 35. Regan, A. C.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1983**, 764. Ando, A.; Shioiri, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1620.
(39) For studies of gas-phase ion solvation by oxygen-based and amine-based ligands, see: Davidson, W. R.; Kebarle, P. *J. Am. Chem. Soc.* **1976**, *98*, 6125. Guo, B. C.; Conklin, B. J.; Castleman, A. W., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 6506.

The dialkylamines display a substantially greater propensity to deaggregate LiHMDS than either the trialkylamines or the isostructural dialkyl ethers. Since the studies of dimer solvation reveal that dialkylamines and dialkyl ethers are virtually interchangeable, *the monomers must be disproportionately stabilized by the dialkylamines*. It is possible that the splay of the dialkyl moieties might relieve dominant solvent−solvent interactions in the monomer. It then seems odd, however, that solvation number determinations using Et_2NH indicate appreciable concentrations of the disolvated monomer while even relatively hindered ethers appear to form exclusively the trisolvated monomer.[1] N−H hydrogen bonding may stabilize the monomer[38] via either an intramolecular hydrogen bond (**22**) or an intermolecular hydrogen bond (**23**) akin to carboxylic acid and related derivatives.[40] We have no direct evidence to either support or refute such a hypothesis.



22



23

The LiHMDS monomer−dimer equilibrium (eq 4) also displays some odd thermochemical characteristics. Specifically, the monomer−dimer equilibrium is thermoneutral ($\Delta H^\circ_{agg} \approx$ 0 kcal/mol) for 8 of 10 di- and trialkylamines. Similar solvent-independent aggregation enthalpies were previously observed during studies of LiHMDS−ether solvates.[1] The invariant aggregation enthalpies mandate that the substantial variations in the observed aggregation free energies (ΔG°_{agg}; eqs 4 and 5) must stem from the solvent dependence on the entropies. Discussions of the entropy of metal ion solvation[41] usually focus upon the translational entropy associated with conversion of a free ligand to a bound (more constrained) form. Highly solvent-dependent entropies are interpreted as evidence of variable solvation numbers. In contrast, the solvation numbers for LiHMDS dimers and monomers are insensitive to solvent structure. Therefore, the solvent dependence on ΔG°_{agg} stems from variable internal entropies associated with packing ligands into sterically congested coordination spheres.[39,42,43] The LiHMDS−ether solvates afforded a similar conclusion.[1]

The monoalkylamines and ammonia cause a striking promotion of monomer formation that appear to stem from shifting monomer solvation numbers. As the amine concentrations are increased, one observes (1) a substantial change of ΔH°_{agg} (favoring monomer), (2) a pronounced (≈0.4 ppm) upfield drift in the monomer ^{6}Li chemical shift, and (3) an unusual loss of Li−N coupling in the monomer.[26] We suspect that the sterically unhindered monoalkylamines may afford five-coordinate tetrasolvated LiHMDS monomers (as suggested for THF and oxetane)[1] as well as facilitate ion pair separation.

We complete the discussion by underscoring a surprising dependence of LiHMDS aggregation on hydrocarbon solvent. A switch from pentane to toluene as the co-solvent causes 5- to 10-fold increases in monomer:dimer proportions (Table 3) despite the presence of excess trialkylamine. Further investigation revealed that olefinic and acetylenic hydrocarbons are indistinguishable from pentane while aromatic hydrocarbons stabilize monomers with nearly identical proficiency irrespective of the degree of substitution (e.g. toluene vs mesitylene). Clearly, this sterically insensitive influence of aromatic hydrocarbons cannot be attributed to the incorporation of the arene within the primary coordination shell of the LiHMDS monomer. Monitoring the dimer−monomer proportions as a function of amine concentration revealed a marked deviation from ideal behavior with the monomer attaining a maximum concentration at *intermediate* amine concentrations (Figure 3). The unusual aromatic solvent effect was traced to the stabilization of the *disolvated* monomer. Amines containing aromatic moieties held proximate to the N−Li bond (e.g. $Me_2N(CH_2)_nPh$) show a curious chain-length-dependent monomer stabilization. However, these experiments do not clarify our understanding of secondary shell solvation by aromatic hydrocarbons. We surmise that the large quadrupole of aromatic hydrocarbons may be the source of the disolvated monomer stabilization and that a greater dipolar character of the N−Li bond in the disolvate may be important. Cation stabilization by aromatic hydrocarbons is a topic of considerable biological and chemical interest as reviewed by Dougherty.[44]

Kimura and Brown noted a hydrocarbon dependence on the oligomer−dimer equilibrium (eq 9) that, at least superficially, appeared to be similar to the hydrocarbon dependence on the LiHMDS monomer−dimer equilibrium.[11] While the two cyclic oligomers are equally populated in highly methylated aromatic hydrocarbons (e.g. mesitylene) and hexanes, toluene causes a 10-fold promotion of the dimer concentration. Further spectroscopic studies of LiHMDS in the presence of a variety of olefinic and acetylenic hydrocarbons supported a direct (primary shell) hydrocarbon solvation proffered by Kimura and Brown.[11,27] In particular, ethylene and 2-butyne cause a marked dimer stabilization characteristic of conventional donor solvents. Thus, the dimer stabilization is readily attributed to a direct (primary shell) hydrocarbon−lithium interaction.

Summary and Conclusions

We described studies of solvation and aggregation of lithium hexamethyldisilazide (LiHMDS) by amine ligands. The capacity to study dimeric LiHMDS in the limit of slow solvent exchange on NMR time scales allows direct observation and characterization of mono- and disolvated dimers. The emergence of monomers at elevated amine concentrations is a sensitive function of the amine structure. The monomers appear to be both di- and trisolvated, consistent with a high steric demand of trialkylamines relative to dialkyl ethers. Mixtures of ether and amine solvents offer relative dimer binding energies in some cases and provide evidence of cooperative solvation due to an absence of mixed solvates. The dialkylamines are remarkably similar to dialkyl ethers as ligands for the LiHMDS dimer despite pronounced differences expected for nitrogen- and oxygen-based coordination. Promotion of monomer formation

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(42) For entropically dominated solvent-dependent ion pairing that may be related, see: Strong, J.; Tuttle, T. R., Jr. *J. Phys. Chem.* **1973**, *77*, 533. See also ref 39.

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by the dialkylamines when compared to the dialkyl ethers results from a disproportionate monomer stabilization by the amines. During the course of these studies, we discovered that monomers—disolvated monomers in particular—are stabilized relative to the dimers by aromatic hydrocarbons in a putative secondary solvation shell.

The challenges associated with studying metal ion solvation leave some of the conclusions controvertible. However, the results point to conclusions of practical importance as follows:

(1) Trialkylamines have found applications as ligands for lithium primarily as components of chelating ligands including *N*,*N*,*N*′*N*′-tetramethylethylenediamine (TMEDA),[45] higher polyamines,[46] and various chiral ligands.[47] Practitioners of organolithium chemistry often reflexively remove all protic amine moieties from their reagents and ligands. However, for those cases where modification of less basic anions is desired (enolates for example), it may be productive to disregard the potential complications caused by the protic RNH_2 and R_2NH functionalities. Ligands bearing mono- and dialkylamine moieties will certainly coordinate lithium very strongly and are beginning to play important roles in synthetic organic chemistry.[38]

(2) Efforts to enhance organolithium reactivities typically focus upon strong donor ligands. Thus, early studies showing the trialkylamines to be weakly coordinating[7] may have discouraged further studies. However, there is increasing evidence that ligand lability can enhance organolithium reactivity.[37,40,41,48] This can be understood if one draws on analogy to the transition elements. Reconsideration of conventional notions of structure and reactivity may elicit renewed interest in the weakly coordinating trialkylamines. Their physical characteristics and low cost make solvents such as DMEA (Me_2NEt; bp = 36−38 °C, mp = −140 °C) especially promising (despite the odor).

(3) Monosolvated and mixed solvated dimers foreshadow possible advantages to executing reactions near or below 1.0 equiv of donor solvent per Li using hydrocarbon co-solvents.[49] There are a number of documented cases of rate maxima at very low ligand concentrations.[50] A greater attention to donor solvent concentration may offer improved yields, reaction rates, and selectivities. Will the choice of hydrocarbon co-solvent matter? It seems likely, given that primary shell coordination of unsaturated hydrocarbons to the otherwise naked LiHMDS dimer and the secondary shell solvation of the amine-coordinated LiHMDS can produce significant aggregation state changes. While one might question the mechanistic consequences of solvent effects on the order of 1.0 kcal/mol per Li, accompanying 10-fold changes in reaction rates or selectivities could have practical consequences.

Note Added in Proof. Beak and co-workers (Wu, S.; Lee, S.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 715) report a 5-fold increased enantioselectivity of *sec*-BuLi/sparteine-mediated metalations upon changing from pentane to toluene cosolvent.

Experimental Section

Reagents and Solvents. All amines and hydrocarbons 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]ethyllithium used to prepare the [^{6}Li]LiHMDS and [^{6}Li,^{15}N]LiHMDS were prepared and purified as described previously.[14,51] 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.[14,52] Standard ^{6}Li, ^{15}N, and ^{13}C NMR spectra were recorded on a Varian XL-400 spectrometer operating at 58.84, 40.52, and 100.58 MHz (respectively) or on a Varian Unity 500 spectrometer operating at 73.57, 58.84, and 125.76 MHz (respectively). The ^{6}Li, ^{15}N, and ^{13}C resonances are referenced to 0.3 M [^{6}Li]LiCl/MeOH at −100 °C (0.0 ppm), neat Me_2NEt at −100 °C (25.7 ppm), and the toluene methyl resonance at −100 °C (20.4 ppm), respectively. The ^{6}Li−^{15}N HMQC spectra were recorded on the Varian Unity 500 spectrometer equipped with a custom-built 3-channel probe designed to accommodate lithium and nitrogen pulses with concurrent proton decoupling. The HMQC pulse sequence[53] was obtained through Varian. The ^{6}Li-detected ^{15}N zero-quantum NMR spectra were recorded using the same spectrometer configuration as for the ^{6}Li−^{15}N HMQC experiments with a pulse sequence described previously.[54]

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Supporting Information Available: NMR spectra and selected derivations (31 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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