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^{15}N, ^{13}C, and ^{6}Li NMR Spectroscopic Studies and Colligative Measurements of Lithiated Cyclohexanone Phenylimine Solvated by Tetrahydrofuran

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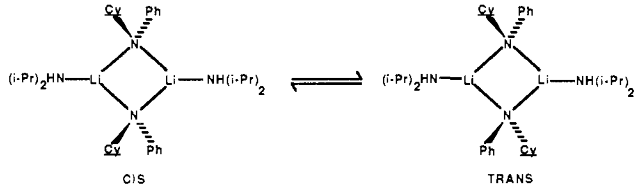
Abstract: ^{15}N, ^{6}Li, and ^{13}C NMR spectroscopic studies of lithiated cyclohexanone phenylimine (**1**) in tetrahydrofuran/hydrocarbon solutions detected three different species. ^{6}Li and ^{15}N NMR spectroscopic studies of [^{6}Li,^{15}N]-**1** showed the two species observed at low THF concentrations to be a pair of stereoisomeric dimers and the single species appearing at high THF concentrations to be a contact ion paired monomer. Colligative measurements demonstrated the dimers to be bis-solvated at 0 °C. Measurements of the dimer–monomer equilibrium at –94 °C provided best fit to an equilibrium between tris-solvated monomers and bis or higher solvated dimers.

We recently isolated a crystalline diisopropylamine solvate of lithiated cyclohexanone phenylimine that was shown to possess a bis-solved dimer structure in the solid state (Figure 1).[1] Spectroscopic analyses showed the existence of a 2:1 mixture of two rapidly interconverting species in hydrocarbon solution. Although previous studies of lithiated imines had uncovered similar resonance duplications,[2–4] explanations hinging upon various spatial orientations of the imine carbon skeleton (Figure 2) failed to account for the specific case in question. For example, discrete rotamers around the N–$C_{i\text{-}Pr}$ bond of lithiated isopropylimines described by Fraser[2] seemed highly unlikely for an *N*-phenyl-substituted imine anion. It seemed equally improbable that both syn and anti isomers would be observable since experimental[4d] and theoretical evidence[5] supported a very large (4–5 kcal/mol) stabilization of the syn orientation. *E*/*Z* isomer mixtures observed for acyclic lithiated *N*-alkyl- and *N*-phenylimines would be geometrically impossible for the corresponding endocyclic imine anions.[3]

To further understand the solution behavior of such a poorly precedented diisopropylamine solvate,[6] we turned to a strategy for determining both aggregation *and* solvation states that has been little used in organolithium chemistry since its introduction[7,8] over 20 years ago.[9] By titrating hydrocarbon suspensions of donor-solvent-free lithiated cyclohexanone phenylimine and monitoring the colligative and spectroscopic properties of the resulting solutions, we established that the two forms of diisopropylamine solvate observed in solution were stereoisomeric bis-solvated dimers (eq 1; Ph = phenyl, Cy = 1-cyclohexenyl).[1]



(1)

We have now extended our studies of lithiated cyclohexanone phenylimine to the corresponding tetrahydrofuran-solvated derivatives. The method of titrating solvent-free lithiated imine in conjunction with ^{6}Li–^{15}N double-labeling studies for determining N–Li connectivities[10,11] allows the detection of monomeric and dimeric forms of lithiated cyclohexanone phenylimine and provides insight into their solvation states. These results will be discussed in the context of recent structural studies of lithiated imines and lithium amides emanating from several laboratories.

Results

In the forthcoming discussion, lithiated cyclohexanone phenylimine in its natural isotopic form (^{7}Li, ^{12}C, ^{14}N) and solvated by tetrahydrofuran will be referred to simply as compound **1**. Lithiated imine **1** bearing no coordinating solvents has been designated $\mathbf{1}_{SF}$ (SF = solvent free). Isotopically labeled derivatives are designated with the appropriate prefix (e.g. [^{6}Li,^{15}N]-**1**), and monomeric, dimeric, and trimeric **1** will simply be referred to as such.

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(8) For leading references to other approaches for determining organolithium solvation state see: Geurink, P. J. A.; Klumpp, G. W. *J. Am. Chem. Soc.* **1986**, *108*, 538, and ref 11.

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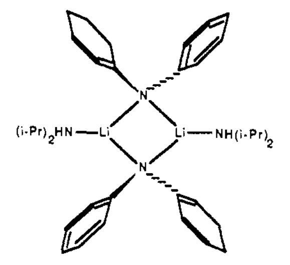


Figure 1.

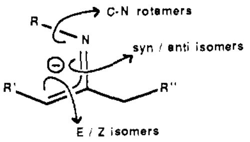


Figure 2.

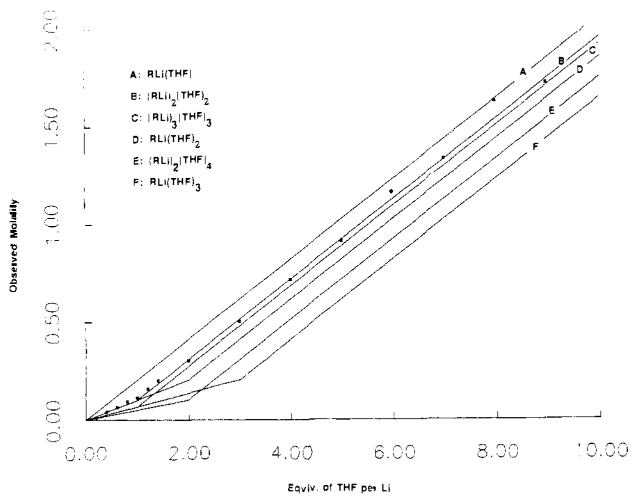
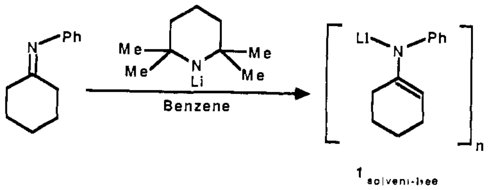


Figure 3. Observed molality measured as a function of added tetrahydrofuran for suspensions of 1_{SF} in benzene. The lines represent calculated plots for models based on various monomers, dimers, and trimers as labeled.

Molecular Weight Studies. Solvent-free lithiated cyclohexanone phenylimine (1_{SF}) was prepared as an analytically pure, hydrocarbon-insoluble white solid as described previously (eq 2).[1] Data on the solvation and aggregation state of lithiated imine **1** when solvated by THF were obtained by titrating benzene suspensions of 1_{SF} with varying quantities of THF. The incremental changes in added THF were monitored by cryoscopic solution molality measurements.[12] Figure 3 is a plot of observed molalities of 1_{SF} as a function of added THF. The measurements between 0.0 and 0.70 were made on visibly heterogeneous suspensions. We have included in Figure 3 the calculated plots if 1_{SF} dissolved to form (A) monosolvated monomers or monosolvated dimers (the plots superimpose), (B) bis-solvated dimers, (C) tris-solvated trimers, (D) bis-solvated monomers, (E) tetrakis-solvated dimers, and (F) tris-solvated monomers. The discontinuities in the theoretical plots represent the points at which saturation of the lithium coordination sphere would occur and additional solvent would remain uncoordinated in solution.[13,14]



$1_{\text{solvent-free}}$

(2)

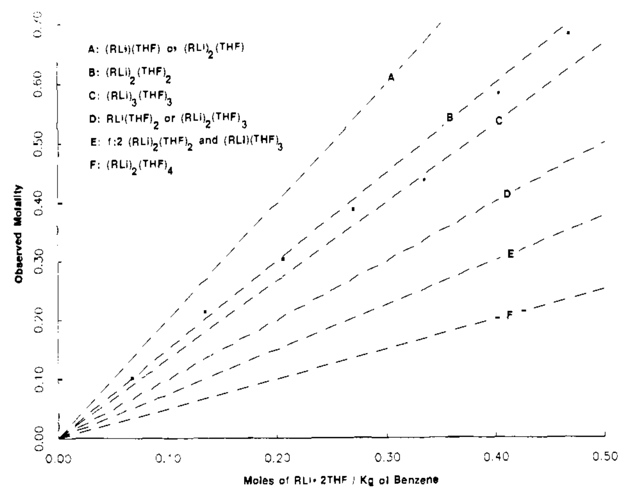


Figure 4. Observed molality measured as a function of added 1_{SF}. Each sample contained 2.0 equiv of tetrahydrofuran/lithium. The dashed lines (- - -) represent calculated plots for models based on various monomers, dimers, and trimers as labeled.

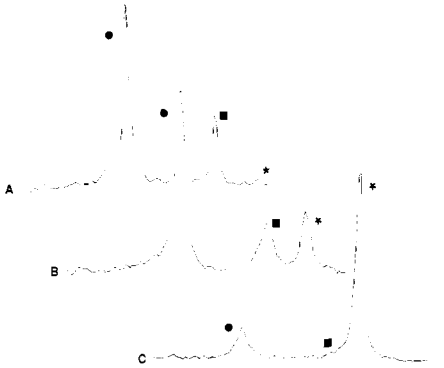


Figure 5. ^{6}Li NMR spectra recorded at −94 °C of 0.04 M toluene-d_8 solutions of [^{6}Li]-1_{SF} containing (A) 6 equiv of THF/lithium, (B) 24 equiv of THF/lithium, and (C) 53 equiv of THF/lithium. General chemical shift data are listed in Table II.

Figure 4 is a plot of measured molality as a function of the absolute concentration of 1_{SF}. For each data point, 1_{SF} was dissolved by adding 2.0 equiv of THF/lithium ion. The lines represent the calculated plots for (A) monosolvated monomers or monosolvated dimers (the plots superimpose), (B) bis-solvated dimers, (C) tris-solvated trimers, (D) bis-solvated monomers or tris-solvated dimers, (E) a 1:2 mixture of bis-solvated dimers and tris-solvated monomers (vide infra), and (F) tetrakis-solvated dimers.

The measured solution molalities correlated reasonably well with the theoretical line for the model based on bis-solvated dimers. Although the theoretical lines for tris-solvated trimers fit the empirical data to a lesser extent, the experimental data are sensistive to subtle systematic errors arising from trace impurities.[15] Thus, rejection of the trimer model awaited further spectroscopic data (vide infra).

Structural details of **1** at high THF concentrations were not available via this specific form of colligative measurement with mixed-solvent systems. Nonetheless, preliminary data were obtained from a commercial[16] osmometric molecular weight determination that showed 1_{SF} to exist as a monomer in neat THF at 25 °C (calcd for monomer, 179; found, 175). Spectral studies described below confirmed the assignment as a monomer.

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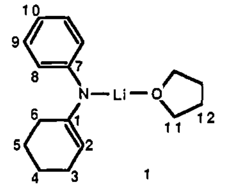
(13) Control experiments showed solutions of free THF in benzene measured within 3% of the correct molalities.

(14) Suspensions of 1_{SF} in benzene appeared to become homogeneous upon addition of only 0.7 equiv of THF/lithium. The ^{6}Li NMR spectrum recorded at −89 °C displayed complex envelopes of resonances.

(15) We had previously noted[1] preliminary studies indicating that **1** formed tris-solvated trimers in benzene–THF mixtures. We have now found these results to arise from small amounts of lithium halide in the sample. The sensitivity of the conclusions to trace impurities must be noted.

(16) Alfred Bernhardt Analytisches Laboratorien, Elbach, West Germany.

Table I. $^{13}C\{^1H\}$ NMR Spectroscopic Data on Lithiated Imine $[^6Li]$-**1**



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nucleus^a	29.1 °C^b	−94 °C aggregate: major^c	aggregate: minor^c	monomer^b
C7	158.24	159.08	158.48	159.10
C1	151.00	150.28	150.50	150.81
C9	128.77	*e*	*e*	*e*
C8	115.80	109.1, 105.6, 103.8,		114.2^d
C2	109.51	102.1, 100.9, 95.1		114.2^d
C10	106.00	br envelope		105.7
C3, C4, C5, C6	28.63	br envelope		22–27
	24.77	22–27		br envelope
	24.09	br envelope		br envelope
	e	br envelope		br envelope
C11 (THF$_\alpha$)	67.89	br envelope		67.9
C12 (THF$_\beta$)	26.05	67.9		26.0
		26.9		

[a] Assignments were made through a variety of techniques as described previously.[1,10,48] [b] Spectrum recorded as a 0.30 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 20 equiv of THF. [c] Spectrum recorded as a 0.30 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 3.0 equiv of THF. [d] Coincidental overlap of C8 and C2 was shown by raising the probe temperature. [e] Obscured by solvent resonances.

^6Li and ^{13}C NMR Spectroscopic Analyses. ^6Li-labeled, solvent-free lithiated cyclohexanone phenylimine ($[^6Li]$-$\mathbf{1}_{SF}$) was prepared from 95.5% $[^6Li]$ethyllithium via $[^6Li]$tetramethylpiperidide as described previously (eq 2).[1] The 0.04 M toluene-d_8 solutions of $[^6Li]$-$\mathbf{1}_{SF}$ at varying THF concentrations were submitted to ^6Li NMR spectroscopic analysis (Figure 5).[17,18] At ambient probe temperature, a single sharp resonance at 0.65 ppm (relative to 0.30 M ^6LiCl in methanol internal standard) was observed. Cooling the probe caused an upfield shift[19] and a coalescence between −50 and −60 °C. The spectrum at −94 °C displayed resonances at 0.34 and 0.08 ppm in a 3:1 ratio. The peak ratio was found to be independent of both the organolithium and THF concentrations over a limited range, indicating the two species to be equivalently aggregated and equivalently solvated (isomeric). At high THF concentrations a new singlet appeared at 0.01 ppm at the expense of the two original resonances. Only the single new resonance could be observed as the concentration of THF exceeded 47% by volume (144 equiv/Li). Additional details of the ^6Li NMR spectral properties and the concentration-dependent equilibria will be discussed subsequently.

We observed similar behaviors in the low-temperature (−94 °C) ^{13}C NMR spectra of **1** (Figure 6; Table I). At low THF concentrations, the quaternary carbons of the cyclohexenyl and phenyl groups each appeared as pairs of resonances in approximate 3:1 ratios. As the concentration of THF was increased, the pairs of peaks corresponding to the cyclohexenyl quaternary carbon (150.50 and 150.28 ppm; 1:2.3 ratio) and the phenyl quaternary carbon (159.08 and 158.48 ppm; 3.3:1 ratio) were gradually replaced by single resonances at 151.81 and 159.10 ppm, respectively.

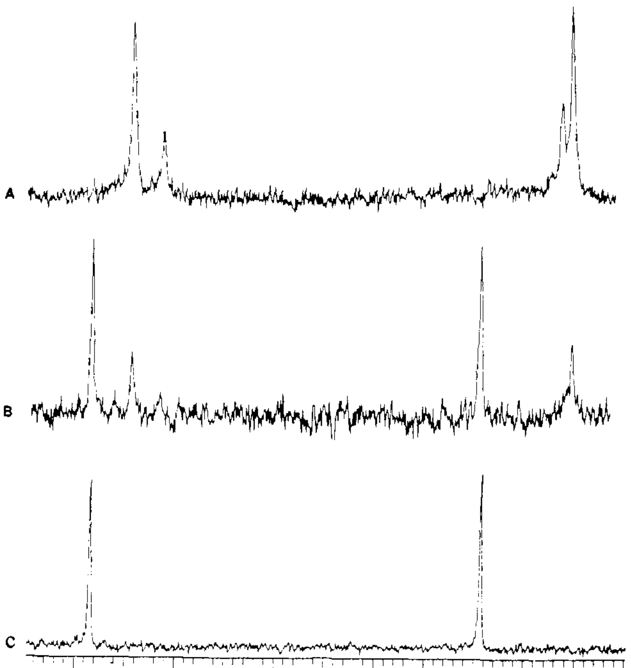

Figure 6. $^{13}C\{^1H\}$ NMR spectra recorded at −94 °C of 0.30 M toluene-d_8 solutions of $[^6Li]$-$\mathbf{1}_{SF}$ containing (A) 3 equiv of THF/lithium, (B) 7 equiv of THF/lithium, and (C) 20 equiv of THF/lithium. General chemical shift data are listed in Table I.

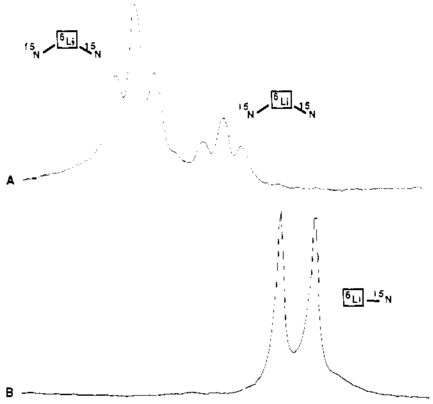

Figure 7. ^6Li NMR spectra recorded at −94 °C of 0.30 M toluene-d_8 solutions of $[^6Li,^{15}N]$-$\mathbf{1}_{SF}$ containing (A) 2 equiv of THF/lithium and (B) 20 equiv of THF/lithium. Chemical shifts and coupling constants are listed in Table II. Related uncoupled spectra appear in Figure 5.

Table II. $^{15}N\{^1H\}$ and $^6Li\{^1H\}$ NMR Spectroscopic Data on Lithiated Imine $[^6Li,^{15}N]$-**1** at −94 °C

nucleus	aggregate: major	aggregate: minor	monomer
Li	0.34^a	0.08^a	0.01^b
	(t, J_{NLi} = 3.3)	(t, J_{NLi} = 3.3)	(d, J_{NLi} = 6.3)
N	134.58^c	136.53^c	155.01^d
	(p, J_{LiN} = 3.4)	(p, J_{LiN} = 3.4)	(t, J_{LiN} = 6.1)

[a] Spectrum recorded as a 0.04 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 2.0 equiv of THF. [b] Spectrum recorded as a 0.04 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 20 equiv of THF. [c] Spectrum recorded as a 0.30 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 2.0 equiv of THF. [d] Spectrum recorded as a 0.30 M toluene-d_8 solution of $\mathbf{1}_{SF}$ containing 8.0 equiv of THF.

Double-Labeling Studies: ^6Li and ^{15}N NMR Spectroscopic Analyses. Recent studies of Jackman and co-workers have dem-

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(17) For the first report of ^6Li NMR spectroscopic studies of alkyllithiums, see: Wehrli, F. *J. Magn. Reson.* **1978**, *30*, 193.

(18) For additional leading references to ^6Li NMR spectroscopy, see: (a) Seebach, D.; Hässig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, *66*, 308. (b) Fraenkel, G.; Fraenkel, A. M.; Geckle, M. J.; Schloss, F. *J. Am. Chem. Soc.* **1979**, *101*, 4745. (c) Najera, C.; Yus, M.; Hässig, R.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1100. (d) Seebach, D.; Gabriel, J.; Hässig, R. *Helv. Chim. Acta* **1984**, *67*, 1083. (e) Rajca, A.; Tolbert, L. M. *J. Am. Chem. Soc.* **1985**, *107*, 2969. (f) Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345. (g) Thomas, R. D.; Clarke, M. T.; Jensen, R. M.; Young, T. C. *Organometallics* **1986**, *5*, 1851. Hoell, D.; Lex, J.; Müllen *J. Am. Chem. Soc.* **1986**, *108*, 5983.

(19) Although the effects of temperature and THF concentration on the ^6Li chemical shift were not investigated in detail, they could be indicative of increased solvation number per lithium.

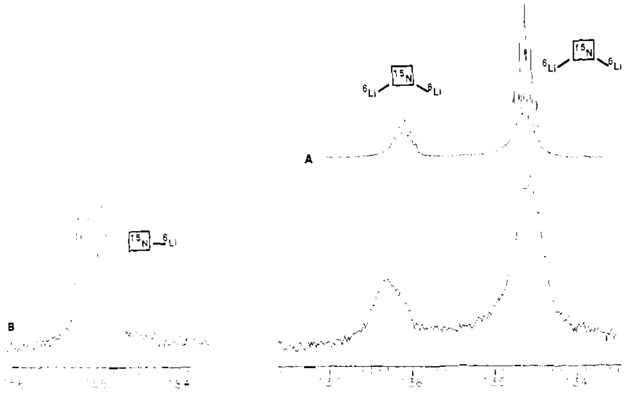


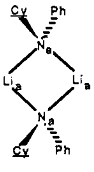
Figure 8. ^{15}N NMR spectra recorded at −94 °C of 0.30 M toluene-d_8 solutions of [^{6}Li,^{15}N]-$\mathbf{1}_{SF}$ containing (A) 2 equiv of THF/lithium and (B) 7 equiv of THF/lithium. Chemical shifts and coupling constants are listed in Table **II**.

onstrated the potential of ^{15}N–^{6}Li double-labeled compounds in conjunction with ^{15}N and ^{6}Li NMR spectroscopy for determining N–Li connectivities.[10] When the spin $^1/_2$ ^{15}N coupling to lithium by ^{6}Li NMR spectroscopy is observed, the number of nitrogens neighboring each lithium can be readily determined. Conversely, monitoring the spin 1 ^{6}Li coupling to nitrogen by ^{15}N NMR spectroscopy[20] provides the number of neighboring lithiums to each nitrogen. The combined results can distinguish monomeric, cyclic oligomeric, and ion triplet forms of lithium amide derivatives (see Discussion).

Doubly labeled lithiated imine [^{6}Li^{15}N]-$\mathbf{1}_{SF}$ was prepared from 99% [^{15}N]aniline and submitted to ^{6}Li NMR spectroscopic analysis (Figure 7; Table II). The resonances previously at 0.34 and 0.08 ppm at low THF concentrations (Figure 5) appeared as triplets ($^1J_{\mathrm{N-Li}}$ = 3.3 Hz for both), showing coupling of each lithium to two seemingly equivalent neighboring ^{15}N atoms. The resonance centered at 0.01 ppm that appeared at elevated THF concentrations was displayed as a doublet ($^1J_{\mathrm{N-Li}}$ = 6.3 Hz) consistent with a single Li–N contact of a monomeric amide.

The complementary ^{15}N NMR spectroscopic analyses of [^{6}Li^{15}N]-**1** were equally informative (Figure 8). At low THF concentrations, the −94 °C spectrum displayed a pair of ^{15}N resonances at 136.53 and 134.58 ppm (relative to 0.15 M [^{15}N]aniline/THF external standard at 50 ppm[20]) in an approximate 3:1 ratio. Both were 1:2:3:2:1 pentuplets ($^1J_{\mathrm{Li-N}}$ = 3.37 and 3.70 Hz, respectively), consistent with Li–N–Li subunits containing equivalently coupled lithiums. The combined results from ^{6}Li and ^{15}N NMR spectroscopies showing Li–N–Li and N–Li–N subunits confirm the solution structures as cyclic oligomers. At high THF concentrations, a new ^{15}N resonance appeared at 155.01 ppm as a 1:1:1 triplet ($^1J_{\mathrm{Li-N}}$ = 6.10 Hz), consistent with a single Li–N subunit (Figure 8), while the two pentuplets began to lose definition. Overall, the combined ^{15}N and ^{6}Li spectroscopic data show unambiguously that **1** exists as a monomer at high THF concentrations.

Aggregation and Solvation State of 1. To briefly summarize, molecular weight studies were consistent with **1** existing as bis-solvated dimers at 0 °C. The ^{6}Li–^{15}N coupling patterns clearly demonstrated that the basic cyclic oligomer connectivity was maintained below −60 °C. Furthermore, the organolithium and THF concentration-independent resonance doublings implicated a pair of dimers i and ii differing only in their stereochemistry. We could not, however, rigorously exclude a single stereoisomeric cyclic trimer iii containing two discrete forms of lithium in a 2:1 stoichiometry.[21] Indeed, it has been shown experimentally (in



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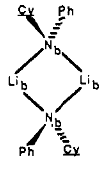

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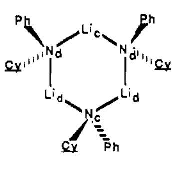

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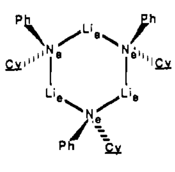

iv

the absence of donor solvents)[22] and theoretically[23] that cyclic trimeric and tetrameric lithium amides are close in stability to the more frequently observed dimers.[24,25] Delicately balanced equilibria between stereoisomeric pairs of dimeric and trimeric amides have also been documented in group 13.[26]

When the molecular symmetry of the dimers and trimers is noted, additional arguments can be made against the existence of cyclic trimers.

(1) The ^{15}N–^{6}Li coupling patterns of cyclic trimer iii should, at least in principle, be more complex than those of the stereoisomeric dimers. Li$_c$ would appear as a symmetric 1:2:1 triplet as observed. However, Li$_d$, bearing two chemically inequivalent neighboring ^{15}N atoms, should be a doublet of doublets. Analogously, N$_c$ and N$_d$ should appear as a 1:2:3:2:1 pentuplet and a triplet of triplets, respectively. To contrast this, the pair of dimers i and ii would display a total of two lithium resonances (Li$_a$ and Li$_b$) and two nitrogen resonances (N$_a$ and N$_b$), with each showing coupling to two chemically equivalent neighboring nuclei. Thus, the ^{15}N and ^{6}Li NMR spectra of the dimer mixture should display pairs of 1:2:3:2:1 pentuplets and 1:2:1 triplets, respectively. The increased resonance complexities expected for the trimer were not detected.

(2) It seems highly unlikely that trimerization would afford isomeric trimer iii to the exclusion of isomer iv given the comparable steric demands of cyclohexenyl and phenyl substituents.[27] (Trimers iii and iv would exist in a 3:1 statistical ratio.) Similar stereoisomeric mixtures of group 13 amide trimers support such a contention.[26] If trimer iv did exist, then the anticipated third set of resonances eluded detection in three quite different forms of NMR spectroscopy.

Thus, the spectroscopic and colligative data are consistent with an equlibrium between a monomer and two stereoisomeric dimers. In addition, the molecular weight studies *at ambient temperatures and low THF concentrations* implicated a predominance of bis-solvated dimers. However, since negative entropies of solvation typically favor increased solvation at reduced temperatures,[28] the

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Table III. Concentration-Dependent Dimer–Monomer Equilibrium Ratios

[**1**$_{SF}$]	[THF]	[dimer]	[monomer]	[monomer]^2/[dimer] × 10^{-3}
0.080	1.28	0.025	0.031	40.0
0.160	0.49	0.077	0.006	0.508
0.040	0.61	0.018	0.005	1.35
0.040	1.21	0.012	0.016	20.7
0.040	1.53	0.011	0.019	33.8
0.040	1.92	0.007	0.026	96.6
0.040	0.89	0.016	0.007	3.34
0.040	1.29	0.012	0.017	25.2
0.040	1.66	0.008	0.025	78.9
0.040	2.06	0.005	0.031	199
0.160	1.08	0.067	0.025	9.40
0.160	1.64	0.041	0.078	149

colligative measurements provide little information pertaining to the solvation state of either the monomers or the dimers at the reduced temperatures of the spectroscopic analyses. We attempted to resolve these structural issues as follows.

The THF concentration dependence of the equilibrium had been fully established. We also reasoned that the dimer must contain at least one solvent per lithium at low temperatures and that the contact ion paired monomer could attain a maximum of three solvating THF molecules without exceeding the preferred four-coordinate, tetrahedral geometry at lithium.[29] Within these constraints, there are five equilibria consistent with the spectroscopic behavior of **1**.

Case I: $(R_2NLi)_2(THF)_2 + 2THF \rightleftharpoons 2R_2NLi(THF)_2$

Case II: $(R_2NLi)_2(THF)_2 + 4THF \rightleftharpoons 2R_2NLi(THF)_3$

Case III: $(R_2NLi)_2(THF)_3 + THF \rightleftharpoons 2R_2NLi(THF)_2$

Case IV: $(R_2NLi)_2(THF)_3 + 3THF \rightleftharpoons 2R_2NLi(THF)_3$

Case V: $(R_2NLi)_2(THF)_4 + 2THF \rightleftharpoons 2R_2NLi(THF)_3$

The general form of the dimer–monomer equilibrium and the corresponding expression for the equilibrium constant (K_{eq}) are depicted in eq 3 and 4. From the linearized expression in eq 5

$$\text{dimer} + n\text{THF} \rightleftharpoons 2\text{monomer} \qquad (3)$$

$$K_{eq} = [\text{monomer}]^2/[\text{dimer}][\text{THF}]^n \qquad (4)$$

$$\ln([\text{monomer}]^2/[\text{dimer}]) = n \ln[\text{THF}] + \ln K_{eq} \qquad (5)$$

it can be seen that a plot of ln ([monomer]^2/[dimer]) vs [THF] will afford a line whose slope, n, represents the number of THF molecules in the equilibrium equations and whose y intercept equals the value of ln K_{eq}.[30]

The absolute monomer and dimer concentrations were determined over a range of THF and lithiated imine concentrations by integrating the ^{6}Li NMR spectra (Table III). The free THF concentrations were estimated by assuming that the dimer retained 1 THF per lithium and the monomer retained 2.5 THF's per lithium. (The typically large excess of THF made the calculations relatively insensitive to estimates of coordinated THF molecules.) The nonweighted linear least-squares fit of eq 5 (Figure 9) afforded $n = 4.12 \pm 0.35$ and $K_{eq} = 9.0 \times 10^{-3}$ M^{-3}. A less visually retrievable, but more reliable,[31] *nonlinear* least-squares fit of eq 4 obtained $n = 3.59 \pm 0.81$ and $K_{eq} = (13.4 \pm 6.9) \times 10^{-3}$ M^{-3}.[32]

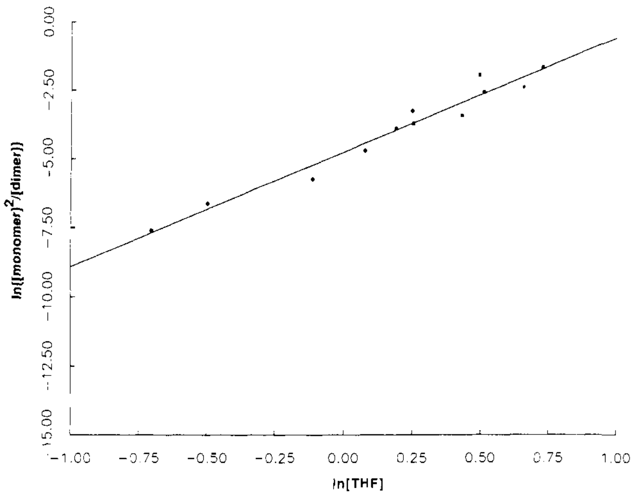
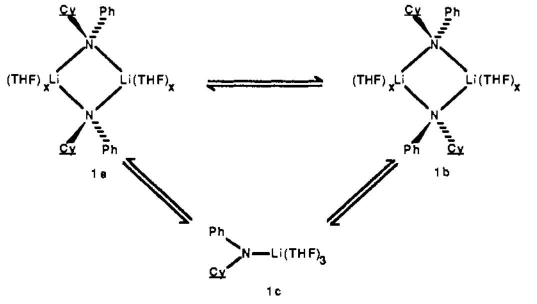


Figure 9. Observed dimer and monomer concentrations as a function of the concentrations of free THF and **1**. Raw data are listed in Table III.

Scheme I



The relatively large number of THF molecules in the empirically derived equilibrium expression (n = 3–4) is only consistent with the equilibria in cases II and IV, providing evidence that the monomer is tris-solvated.[33] It is not possible within the error of the measurements, however, to establish whether the dimer existed predominantly as the bis-solvate (case II; n = 4), tris-solvate (case IV; n = 3), or a mixture of bis- and either tris- or tetrakis-solvated dimers.[34]

Discussion

Scheme I summarizes our results. At low THF concentrations, lithiated cyclohexanone phenylimine exists in a cyclic oligomeric form that exhibits spectroscopic properties most consistent with a pair of stereoisomeric dimers **1a** and **1b**. Systematic increases in the THF concentration cause the appearance and eventual dominance of a species shown to be the corresponding monomer. Colligative measurements indicate the dimers **1a** and **1b** to be bis-solvated (x = 1) at ambient temperatures. The ^{6}Li NMR spectroscopic measurements of the concentration-dependent dimer–monomer equilibrium at −94 °C are consistent with an equilibrium between tris-solvated monomer **1c** and dimers **1a** and **1b** that are either bis-solvates (x = 1) or a mixture of bis and higher solvates (x_{obsd} = 1.2).[34,35]

The ambiguities that remain highlight many of the difficulties of pinpointing the often elusive details of organolithium aggregation and solvation states in solution. The importance of Jackman's ^{6}Li and ^{15}N double-labeling techniques for assigning

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[32] Reported errors represent 1 standard deviation.

[33] One ought to add that the calculation is insensitive to the model used for the aggregated form; similar calculations assuming a trimer–monomer equilibrium also support a tris-solvated monomer, albeit with a poorer fit.

[34] Only one tris-solvated dimeric N-lithiated species has been characterized: Seebach, D.; Bauer, W.; Hansen, J.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. *J. Chem. Soc., Chem. Commun.* **1984**, 853.

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structures of N–Li-bonded species cannot be overstated.[10] By monitoring the coupling of spin 1 ^{6}Li and spin $^{1}/_{2}$ ^{15}N by both ^{6}Li and ^{15}N NMR spectroscopy, we could readily distinguish the aggregated and monomeric forms of lithiated imine **1**. In general, however, cyclic dimeric,[24] trimeric,[22] and tetrameric lithium amides[22]—all of which are precedented in the crystallographic literature—cannot be distinguished by Li–N connectivities alone. In the case of the aggregated form of **1**, we were able to enhance the confidence in the assignment as a mixture of stereoisomeric dimers by noting the absence of increased spectral complexity expected for the lower symmetry trimers and tetramers (cf. i–iv).

Colligative measurements are used routinely for determining organolithium aggregation states.[36] The technique of titrating solvent-free organolithiums with controlled concentrations of donor solvents appears to be a notably useful probe of both aggregation *and* solvation states.[1,7–9] Within the experimental error, colligative measurements in benzene–THF mixtures excluded many of the plausible solvation and aggregation states of **1**, which, in turn, placed a considerably lower reliance on the spectroscopic techniques. Limitations to colligative measurements in mixed-solvent systems include the following: (1) the restriction to relatively low donor–solvent concentrations ($\leq$10 equiv/per lithium) and, (2) in the case of freezing point depression measurements, the requirement that the molalities be monitored only at the freezing point of the hydrocarbon solvent. The quantitative spectroscopic measurements of the dimer–monomer equilibrium provided an excellent means of extrapolating to the high THF concentrations opaque to the mixed-solvent colligative measurements. Unfortunately, negative entropies of solvation favoring increased solvation at reduced temperatures[28] prevented assignment of the solvation state to the dimeric form of **1** at the temperatures monitored spectroscopically. Nonetheless, the monomer could be tentatively assigned as the tris-solvate.

Jackman and co-workers recently reported progress toward determining organolithium solvation states in *neat* donor solvents. They found that substantial differences in quadrupole splitting constants (QSC's) calculated from the ^{13}C relaxation times appear to coincide with planar 3-coordinate versus tetrahedral 4-coordinate lithium.[11] Using ^{15}N,^{6}Li doubly labeled lithium anilides in neat THF, they observed concentration- and structure-dependent monomer–dimer mixtures.[10] The large QSC's of the monomers were indicative of a tetrahedral coordination sphere (tris-solvation) about lithium, whereas the dimers appeared to be either 3-coordinate (one THF per Li) or 4-coordinate (two THF's per Li) depending on the structure of the amide substituents. All lithium amides and anilides in diethyl ether showed Li–N connectivities and QSC's consistent with dimers bearing monosolvated, 3-coordinate lithiums.

Overall, our structural assignments of the monomeric and dimeric forms of **1** show close parallels with Jackman's results on lithium anilides. Furthermore, as knowledge of the detailed solvation states of the various aggregated forms of lithium amides[37] and (azaallyl)lithiums accumulates, one can better use the crystallographic data base for clues to the solution structures.

We are especially interested in the coordination modes of (azaallyl)lithiums (including the lithium anilides). Several stereochemical models to account for (azaallyl)lithium alkylation stereoselectivities have placed importance on the presence of lithium π interactions with the azaallylic fragment.[38] Support comes from η^3-Li-π interactions observed in the solid-state structures of monomeric and dimeric (lithiomethyl)pyridines[39] and polymeric lithiated dimethyl hydrazones.[40] Of special note, the X-ray structure of dimeric pinacolone phenylimine reported by Knorr displayed a Li–phenyl rather than Li–cyclohexenyl π interaction.[41] Calculations by Streitweiser and Glaser detail η^3–π complexation for monomer lithiated oximes and oximino ethers.[42] On the other hand, lithium–carbon contacts are *not* apparent in other monomeric[43] and dimeric (azaallyl)lithiums,[25] including the dimeric lithiated imine **1** solvated by diisopropylamine (Figure 1).[1]

We have no compelling evidence supporting a Li π interaction in the dimeric THF solvates of **1**. Despite the relatively few monomeric (azaallyl)lithiums[39,43] and lithium amides,[44,45] of which none bear monodentate neutral donor ligands for direct comparison, we can begin to speculate on the structures of the tris-solvated monomeric form of **1**. When the solvation states of the corresponding η^1- and η^3-allylic or -benzylic organolithium structures[46] are noted, it can be argued that the tris-solvated monomeric form of **1** would not require a Li–π interaction to saturate the metal coordination sphere. In either case, whether alkylations of lithiated imines proceed via η^3–π complexed intermediates remains unresolved. It should be noted, however, that only the alkylation stereoselectivities of the *N*-alkyl—not the highly anion stabilizing *N*-phenyl—lithiated imines have been studied in detail.[4] Thus, an investigation of the solution aggregation and solvation states of lithiated *N*-alkylimines would be instructive.

Experimental Section

Instrumentation. ^{13}C NMR spectra were recorded on JEOL FX90Q and Varian XL 400 spectrometers operating at 22.49 and 100.55 MHz, respectively. The chemical shifts are reported (ppm) downfield of tetramethylsilane. ^{6}Li and ^{15}N NMR spectra were recorded on a Varian XL 400 spectrometer operating at 58.84 and 40.53 MHz, respectively. The ^{6}Li chemical shifts are reported (ppm) downfield of an external 0.30 M LiCl/methanol standard. The ^{15}N chemical shifts are reported (ppm) relative to an external 0.15 M [^{15}N]aniline/THF standard at 50 ppm.[20] Low-temperature ^{13}C, ^{15}N, and ^{6}Li NMR spectroscopic data are summarized in Tables I and II.

Solvents and Materials. Benzene and hexane were distilled from benzophenone ketyl containing 1% tetraglyme to dissolve the ketyl. The benzene used in molecular weight determinations was refluxed over CaH_2 for at least 7 days, distilled under argon, and degassed by three freeze–pump–thaw cycles. Toluene was distilled from neat *n*-BuLi. Toluene-d_8 and benzene-d_6 were distilled from sodium/benzophenone ketyl. ^{6}Li metal (95.5%) was obtained from Oak Ridge National Laboratory. Ethyllithium and [^{6}Li]ethyllithium prepared by the standard literature procedure were recrystallized from benzene and doubly sublimed to remove lithium halide impurities.[47] [^{15}N]Aniline (99%) was obtained from

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Cambridge Isotope Laboratory and used without further purification. Cyclohexanone phenylimine and ^{15}N-labeled cyclohexanone phenylimine were prepared as described previously.[1] Analytically pure solvent-free lithiated cyclohexanone phenylimines $\mathbf{1}_{SF}$, $[^6Li]$-$\mathbf{1}_{SF}$, and $[^6Li,^{15}N]$-$\mathbf{1}_{SF}$ were prepared from ethyllithium or $[^6Li]$ethyllithium via the lithium tetramethylpiperidides as described previously.[1] Air- and moisture-sensitive materials were manipulated by standard glovebox and vacuum-line techniques with the aid of gas-tight syringes.

Molecular Weight Determinations. Molecular weights were measured by the freezing point depression technique in a modification of an apparatus described by Seebach[12] interfaced to a Commodore 64 or VIC 20 minicomputer. Samples were prepared in a glovebox, and measurements were made under Ar with standard inert-atmosphere techniques. Calibrations were performed with known concentrations of naphthalene in benzene. The linear least-squares fit in Figure 4 was anchored with a high statistical weight to the origin.

Nuclear Magnetic Resonance Studies. The following is a representative procedure for preparing samples for spectroscopic analysis. A stock solution was prepared in a glovebox by sequentially mixing $[^6Li^{15}N]$-$\mathbf{1}_{SF}$ (110 mg, 0.62 mmol), toluene-d_8 (600 μL), and THF (100 μL, 1.23 mmol). A 5-mm NMR tube was charged sequentially with the pale yellow stock solution (205 μL) and toluene-d_8 (395 μL), placed under septum, removed from the glovebox, and sealed with a flame under reduced pressures.

Acknowledgment. We thank the National Institutes of Health for generous financial support of this work, Professor C. F. Wilcox for the nonlinear least-squares fitting program, and Professor L. M. Jackman for providing details of his results prior to publication. We also thank Sang-Mo Kang and Carol Lamberson for the refinements and computer interfacing of the cryoscopic molecular weight determination apparatus. Acknowledgment is made to the National Science Foundation Instrumentation Program (Grants CHE 7904825 and PCM 8018643) for support of the Cornell Nuclear Magnetic Resonance Facility.

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Nucleophilic Substitution Reaction of Phenylmethanesulfonyl Halides with Anilines[1]

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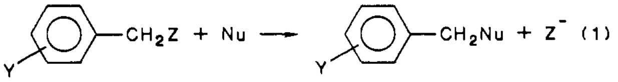
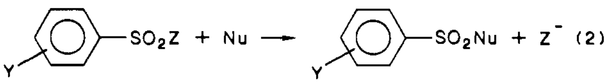
Abstract: Kinetic studies on the nucleophilic substitution reaction of Y-substituted phenylmethanesulfonyl halides with X-substituted anilines in methanol–acetonitrile have been carried out in order to elucidate the reaction mechanism. The phenylmethanesulfonyl fluorides (PSF) had markedly lower rates and smaller magnitudes of ρ_X and ρ_Y values compared with those for the chlorides (PSC). On the contrary, however, the magnitude of the cross-interaction constant $|\rho_{XY}|$ was greater for PSF than for PSC, so that the degree of bond making in the transition state is actually greater in the reaction of PSF as compared with that for PSC. We have thus demonstrated that extensive charge transfer from a nucleophile to a substrate does not necessarily mean a tight bond in the transition state. Moreover the nonzero ρ_{XY} values obtained for both PSC and PSF are taken as evidence in support of a common, associative S_N2 mechanism for the two halides.

Nucleophilic substitution reactions of substituted benzyl halides (eq 1) have been extensively studied.[2] In this reaction, halides



(Z) are displaced by a nucleophile (Nu) at the benzylic (C_α) carbon. On the other hand, nucleophilic substitution reactions of benzenesulfonyl halides (eq 2) have also attracted much in-



terest;[3] in this case the displacement of halides (Z) occurs at the sulfonyl sulfur (S). There are similarities and differences in the mechanisms of these two nucleophilic reactions. The two reactions are notable examples of the S_N2 reaction with a borderline mechanism exhibiting U-shaped nonlinear Hammett plots;[2b,3a,e] with an uncharged neutral nucleophile (Nu), the former reaction (1) proceeds by a dissociative S_N2 mechanism in which the bond breaking is relatively more advanced than the bond formation,[2c] while the latter reaction (2) proceeds by an associative S_N2 mechanism with bond formation being more extensive than bond breaking in the transition state (TS).[3b,4] The main objective in this work is to gain insight into the mechanistic changes involved

Table I. Pseudo-First-Order Rate Constants ($k_1 \times 10^4$ s^{-1}) and Activation Parameters for the Methanolysis of Phenylmethanesulfonyl Chloride in MeOH–MeCN

	temp, °C		activation parameters	
MeOH (v/v), %	45.0	55.0	$\Delta H^{\ddagger}$ [a]	$-\Delta S^{\ddagger}$ [b]
100	0.527	1.21	16.6	26.0
90	0.489	1.16	17.3	24.0
80	0.430	1.00	16.9	25.6
70	0.351	0.814	16.8	26.2
50	0.190	0.421	15.9	30.4

[a] Kilocalories/mole. [b] Entropy units.

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(1) Nucleophilic Displacement at Sulfur Center. 22.

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