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Structure and Reactivity of Lithium Amides. ^{6}Li, ^{13}C, and ^{15}N NMR Spectroscopic Studies and Colligative Measurements of Lithium Diphenylamide and Lithium Diphenylamide–Lithium Bromide Complex Solvated by Tetrahydrofuran

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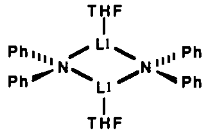
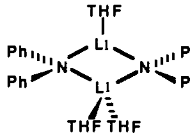
Abstract: ^{6}Li, ^{13}C, and ^{15}N NMR spectroscopic studies of lithium diphenylamide in THF/hydrocarbon solutions (THF = tetrahydrofuran) detected two different species. ^{6}Li and ^{15}N NMR spectroscopic studies of [^{6}Li,^{15}N]lithium diphenylamide showed the species observed at low THF concentrations to be a cyclic oligomer. Structural analogies provided strong support for a dimer while colligative measurements at 0 °C indicated the dimer to be di- or trisolvated. On the basis of the observed mass action effects, the species appearing at intermediate THF concentrations is assigned as a contact or solvent-separated ion-paired monomer. Lithium diphenylamide forms a 1:1 adduct with lithium bromide at low THF concentrations. A combination of ^{6}Li–^{15}N double labeling studies and colligative measurements supports a trisolvated cyclic mixed dimer structure. Although detailed spectroscopic studies at elevated THF concentrations were precluded by high fluctionality, the similarity of the ^{13}C chemical shifts of lithium diphenylamide in the presence and absence of lithium bromide provide indirect evidence that the mixed dimer undergoes a THF concentration dependent dissociation to the monomeric amide and free lithium bromide.

The importance of organolithium reagents in organic chemistry has monotonically increased since the turn of the century.[1,2] We suspect, for example, that well over 95% of the contemporary natural product syntheses use one or more lithium-containing reagents. Within this very broad class of synthetic reagents, the reactive lithium amide bases and related N-lithiated species have played pivotal roles in the development and refinement of carbon–carbon bond forming reactions.

We will describe in two parts studies of lithium diphenylamide. The first part details ^{6}Li, ^{13}C, and ^{15}N NMR spectroscopic studies and colligative measurements that provide aggregation state and solvation state data. We will provide evidence that (1) at reduced THF concentrations lithium diphenylamide exists as a di- or trisolvated dimer (**1a** or **1b**) in the absence of LiBr and a trisolvated mixed dimer (**2a**) in the presence of LiBr and (2) aggregates **1** and **2a** dissociate to a common monomeric or ion-paired amide **3** of ill-defined solvation state at elevated THF concentrations.[3,4]



1a



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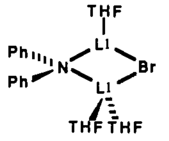

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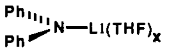

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The second part outlines kinetic studies of the N-alkylation of lithium diphenylamide that highlight the importance of mixed aggregation effects, deaggregations, and solvation as determinants of amide reactivity.

Results and Discussion

In the following discussion, the variants of lithium diphenylamide will be referred to as follows. Lithium diphenylamide in its natural isotopic form (^{7}Li, ^{12}C, ^{14}N) solvated by tetrahydrofuran (THF) will be referred to as Ph_2NLi. Lithium diphenylamide bearing no coordinating solvent will be designated $Ph_2NLi_{solvent\text{-}free}$. Isotopically labeled derivatives will include the appropriate prefix (e.g. [^{6}Li, ^{15}N]Ph_2NLi), and monomeric, dimeric, and other oligomeric forms will be referred to by using the appropriate descriptors and visual aids. We will refer to Ph_2NLi in the presence of equimolar concentrations of lithium bromide as Ph_2NLi/LiBr and the mixed aggregate with lithium bromide as $Ph_2NLi{\cdot}LiBr$. The latter designation will be restricted to specific reference to a discrete 1:1 complex. Whereas LiBr was always added in a

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solvent-free form, references to LiBr in solution are not intended to implicate either a specific structural form or solvation state. A summary of the results unadorned with experimental details follows the Results and Discussion Section.

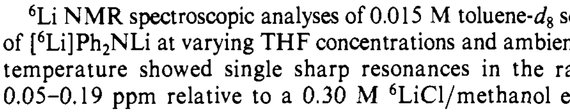
Ph_2NLi: ^6Li–^{15}N Double Labeling Studies. ^6Li-labeled, solvent-free Ph_2NLi ($[^6Li]Ph_2NLi_{solvent\text{-}free}$) was prepared from halide-free $[^6Li]$ethyllithium[5] (95.5% enriched) and isolated as an analytically pure, hydrocarbon-insoluble white solid (eq 1).

$$Ph_2NH \xrightarrow[Et_2O\,/\,0^{\circ}C]{EtLi} (Ph_2NLi)_x(Et_2O)_y \xrightarrow[80^{\circ}C\,/\,20\ hr]{0.01\ torr} (Ph_2NLi)_{solvent\text{-}free} \quad (1)$$

^6Li NMR spectroscopic analyses of 0.015 M toluene-d_8 solutions of $[^6Li]Ph_2NLi$ at varying THF concentrations and ambient probe temperature showed single sharp resonances in the range of 0.05–0.19 ppm relative to a 0.30 M ^6LiCl/methanol external standard. Cooling the probe to −90 °C caused upfield shifts without an increase in spectral complexity.[6] Overall, the spectral simplicity is consistent with virtually any structural form exhibiting either maximum possible symmetry or undergoing rapid chemical exchange on NMR timescales. To distinguish these two possibilities, we turned to ^6Li–^{15}N double labeling techniques.

Recent studies by Jackman and co-workers[7] and Collum and Kallman[8] demonstrated the potential of ^6Li–^{15}N doubly labeled compounds in conjunction with ^6Li and ^{15}N NMR spectroscopy for determining nitrogen–lithium connectivities of lithium amides and lithiated imines. By observing the spin −1/2 ^{15}N coupling to lithium by ^6Li NMR spectroscopy, the number of nitrogens connected to each lithium can be readily determined. Conversely, monitoring the spin 1 ^6Li coupling to nitrogen by ^{15}N NMR spectroscopy[9] provides the number of lithium atoms connected to each nitrogen. The combined results can distinguish monomeric, cyclic oligomeric, and ion triplet forms of lithium amides.

$[^{15}N]$diphenylamine was prepared by trapping benzyne with $[^{15}N]$aniline. After exploring a number of procedures, we ultimately settled upon the preparation based on benzene diazonium carboxylate depicted in eq 2.[10] (*Caution: benzene diazonium carboxylate is highly explosive when fully dry.*)



(2)

$[^6Li,^{15}N]Ph_2NLi_{solvent\text{-}free}$ was prepared and submitted to ^6Li NMR spectroscopic analysis as 0.015 M toluene-d_8/THF solutions (Figure 1). The singlet of Ph_2NLi at 0.16 ppm (0.15 M THF, 1.2%) appears as a 1:2:1 triplet ($J_{N\text{-}Li}$ = 3.12 Hz) showing equivalent coupling of lithium to two neighboring ^{15}N nuclei (Figure 1a). As the THF concentrations were increased, coupling was lost, presumably due to rapid intermolecular exchange processes (Figure 1b). The complementary ^{15}N NMR spectroscopic analysis of $[^6Li,^{15}N]Ph_2NLi$ was also informative (Figure 1c). The lower sensitivity of the ^{15}N nucleus required elevated Ph_2NLi concentrations (0.05 M, 0.15 M THF). The spectrum recorded at −90 °C displays a 1:2;3:2;1 pentuplet ($J_{Li\text{-}N}$ = 3.34 Hz) centered at 128.84 ppm. The multiplicity and the magnitude of the coupling constant are fully consistent with Li–N–Li connectivity.

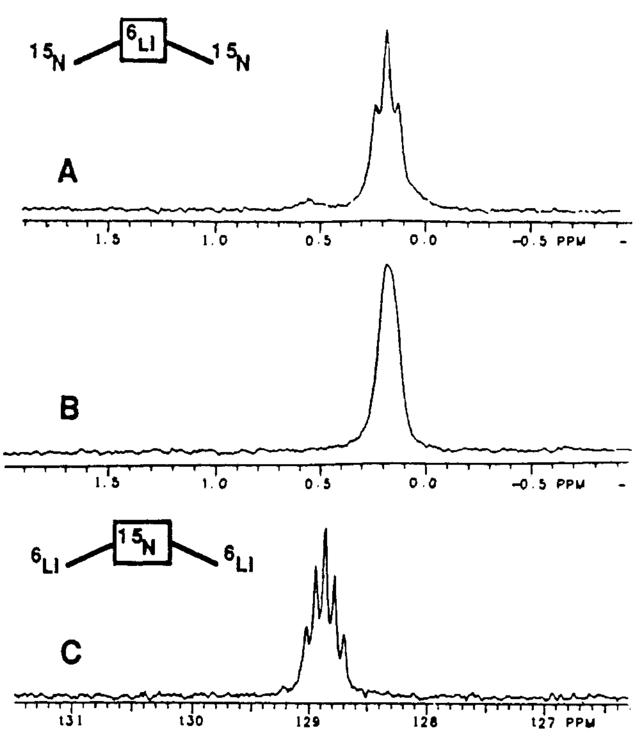


Figure 1. ^6Li and ^{15}N NMR spectra recorded at −90 °C of toluene-d_8 solutions of $[^6Li,^{15}N]Ph_2NLi$: (A) ^6Li NMR spectrum: 0.015 M, 0.15 M THF; (B) ^6Li NMR spectrum: 0.015 M, 2.25 M THF; (C) ^{15}N NMR spectrum: 0.05 M, 0.15 M THF. The chemical shifts are referenced to identical samples containing external standards.

Ph_2NLi: Structure at Low THF Concentrations. On the basis of the double labeling spectroscopic studies showing Li–N–Li and N–Li–N connectivities, lithium diphenylamide can be assigned as a cyclic oligomer with alternating nitrogen and lithium nuclei. Although the connectivity does not distinguish cyclic dimers from the higher order cyclic oligomers, strong arguments can be made in favor of the dimer structure. The crystallographic literature of lithium amides is dominated by dimeric structures of widely varying substituent and coordinating solvent structure.[11] Higher cyclic oligomers, predicted by MNDO calculations[12] to be close in stability to the corresponding cyclic dimers, have been observed for lithium dibenzylamide (trimer),[13] lithium hexamethyldisilazide (trimer),[14] and lithium tetramethylpiperidide (tetramer),[15] but only *in the absence of coordinating solvents*. In the presence of ethereal solvents, lithium dibenzylamide and lithium hexamethyldisilazide form crystalline dimeric etherates, while lithium tetramethylpiperidide forms an etherate of unknown structure. In addition, we recently described studies of the lithiated phenylimine of cyclohexanone (**4**), which is structurally quite similar

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Table I. ^{13}C (^{1}H) NMR Spectral Data of 0.015 M Toluene-d_8 Solutions of Ph$_2$NLi[a]

entry	[THF], mol/L	temp, °C	ipso	meta	ortho	para
1	0.23	-90	159.89	[c]	121.88	115.31
2	0.26	23	[b]	129.91	120.71	116.24
3	0.26	-90	159.90	[c]	121.90	115.31
4	0.60 (5%)	-90	159.88, 158.92	[c]	121.87, 119.21	115.25, 112.89
5	1.20	-90	158.89	[c]	119.24	112.84
6	4.43 (36%)	23	[b]	129.00	119.59	113.07
7	4.43	-90	158.72	[c]	118.95	112.44
8	12.28 (99%)	23	[b]	128.15	118.81	111.74
9	12.28[d]	-90	159.04	128.93	119.06	112.30

[a] The reported chemical shifts are in ppm relative to TMS. [b] The ipso carbon resonances were poorly resolved from base-line noise at ambient temperature at convenient scan times. [c] The resonance was obscured by the toluene-d_8. [d] THF-d_8 was used as the solvent.

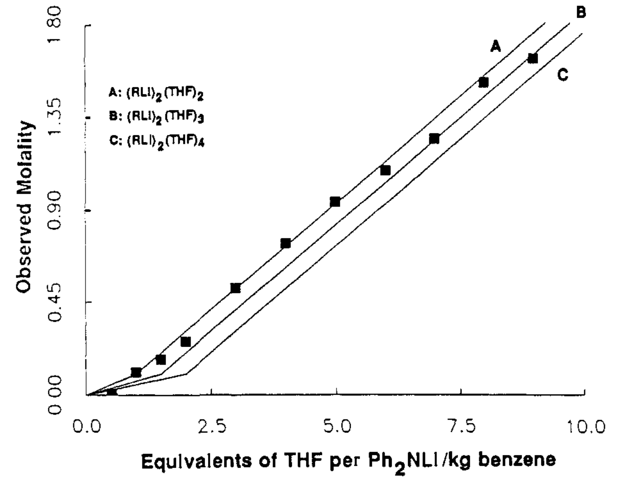


Figure 2. Observed molality of Ph$_2$NLi (0.21 M in monomer subunits) measured as a function of added THF. The solid lines represent calculated plots for models based on various solvated dimers as labeled.

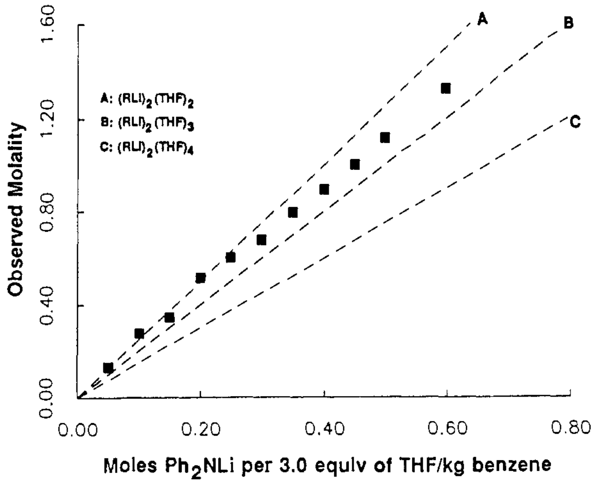
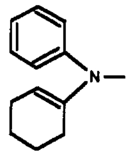


Figure 3. Observed molality measured as a function of Ph$_2$NLi concentration. Each sample contained 3.0 equiv of THF per lithium. The dashed lines represent calculated plots for models based on various solvated dimers as labeled.

to Ph$_2$NLi.[8] The asymmetry of **4** in conjunction with its spectral properties strongly supported cyclic dimers rather than higher oligomers as the observable aggregated form.



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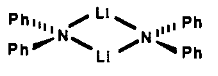

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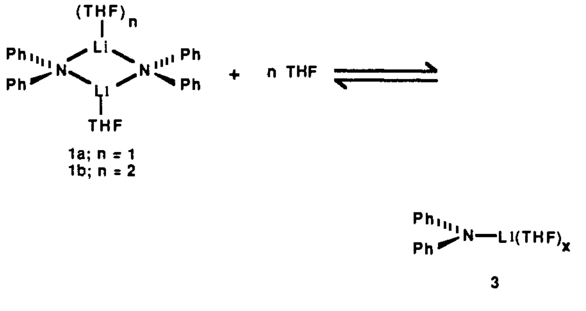
Thus, we concur with Snaith and co-workers[16] that the higher order cyclic oligomers might be restricted to ligand-free amides and assign the aggregated form of Ph$_2$NLi as a cyclic dimer of general structure **1**. To assign the solvation state of **1**, we turned to colligative studies of Ph$_2$NLi in benzene/THF mixtures.

Ph$_2$NLi$_{\text{solvent-free}}$ was prepared from halide-free ethyllithium[5] as shown in eq 1. Data on the solvation state of Ph$_2$NLi dimer solvated by THF were obtained by freezing point depression measurements.[17,18] Figure 2 is a plot of measured molality as a function of added THF at a fixed concentration of Ph$_2$NLi$_{\text{solvent-free}}$. The solid lines represent the calculated plots for di-, tri-, and tetrasolvated dimers. 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.[19] Figure 3 is a plot of measured molality as a function of the absolute concentration of Ph$_2$NLi$_{\text{solvent-free}}$. For each data point Ph$_2$NLi$_{\text{solvent-free}}$ was dissolved by adding 3.0 equiv of tetrahydrofuran per lithium. The dashed lines A–C represent the calculated plots for di-, tri-, and tetrasolvated dimers, respectively. The measured solution molalities correlated equally well with the theoretical lines for di- or trisolvated dimers **1a** or **1b**.

Ph$_2$NLi: ^{13}C NMR Spectroscopic Studies. We suspected that the high fluctionality of Ph$_2$NLi, evidenced by loss of ^{6}Li–^{15}N coupling at high THF concentration, obscured important THF concentration-dependent deaggregations. Indeed, the higher frequency of ^{13}C NMR spectroscopy allowed direct detection of what we believe to be a dimer-monomer equilibrium (eq 3).



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(19) Control experiments showed solutions of free THF in benzene measured within 3% of the correct molalities. Because of both the phase behavior of benzene solutions of naphthalene and the nonlinearity of the electronics within the temperature probe, the standard curve shows gentle curvature over the range of solute concentration. Apparently, the benzene/THF solutions show similar (cancelling) curvature. In contrast, other solutes such as pyridine can result in a distinct error in the measured molality.

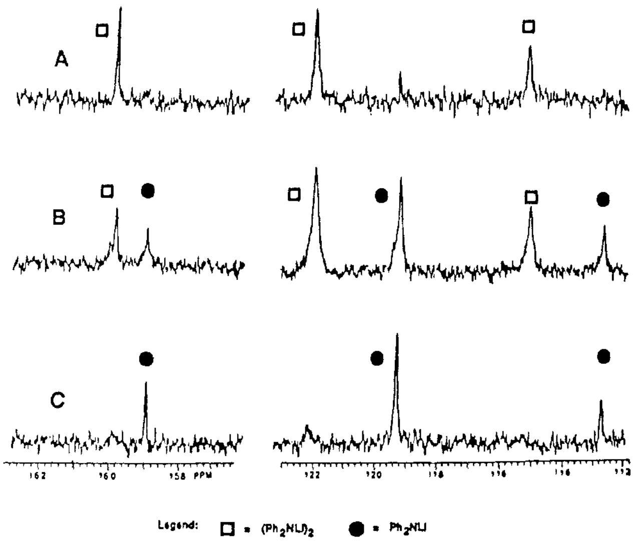
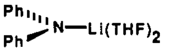


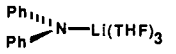
Figure 4. ^{13}C (^{1}H) NMR spectra recorded at −90 °C of 0.015 M toluene-d_8 solutions of Ph_2NLi: (A) 0.26 M in THF, (B) 0.60 M in THF, and (C) 1.2 M in THF. Chemical shift data are listed in Table I.

The ^{13}C NMR spectrum of a 0.015 M toluene-d_8 solution of Ph_2NLi containing 15 equiv of THF (0.26 M; 2.1%) at −90 °C displays four aromatic resonances and two resonances corresponding to the α and β carbons of THF (Figure 4a, Table I). Exchange of bound and free THF molecules is rapid on the NMR timescales, and the high spectral symmetry is consistent with facile rotation about the C–N bonds. Increasing the THF concentration to 0.6 M (4.8%) affords a second species (Figure 4b), which becomes the sole observable species as the THF concentration exceeds 1.2 M (9.8%; Figure 4c). The equilibrium is also amide concentration dependent; decreasing the Ph_2NLi concentration 10-fold results in a significant decrease in the proportion of the dimer. The THF and Ph_2NLi concentration dependencies are fully consistent with a dimer-to-monomer deaggregation (eq 3).

Jackman and Scarmoutzos reported that a variety of lithiated aniline derivatives display temperature- and solvent-dependent ^{13}C chemical shifts.[7] Para carbon upfield shifts in the range of 4–5 ppm were attributed to increasing solvation with concomitant deaggregation to the monomeric state. Within any given aggregation state, upfield para carbon shifts of 1–2 ppm were ascribed to the electronic changes resulting from increased solvation. We do not know whether the Ph_2NLi monomer exists as di- or trisolvated contact ion pairs **3a** and **3b** or tetrasolvated solvent-separated ion pair **3c**. It is noted, however, that as the THF concentration is increased from 1.2 to 12.28 M (neat), the para carbon resonance of the monomeric Ph_2NLi shifts an additional 0.54 ppm upfield, indicative of either increasing monomer solvation or medium effects.



3a



3b

3c

$Ph_2NLi\cdot LiBr$: ^{6}Li NMR Spectroscopic Studies. In the accompanying paper we will describe kinetic studies that uncovered autocatalysis by LiBr generated during the reaction of Ph_2NLi with *n*-butyl bromide. The role of the lithium bromide was traced to the intervention of a $Ph_2NLi\cdot LiBr$ mixed aggregate, which was characterized as follows.

Toluene-d_8 solutions of $[^{6}Li]Ph_2NLi$ and $^{6}LiBr$ in varying ratios were submitted to ^{6}Li NMR analysis at −90 °C (Figure 5). THF concentrations below 0.09 M were required to observe the limiting, slow exchange spectra. When the Ph_2NLi:LiBr ratio is <1.0, the resonance corresponding to the homonuclear Ph_2NLi dimer is observed at 0.16 ppm along with a resonance at 0.58 ppm corresponding to a $Ph_2NLi\cdot LiBr$ mixed aggregate (Figure 5a). At equimolar concentrations, the mixed aggregate is the only observable species (Figure 5b). In the presence of >1.0 equiv of LiBr, the resonance of the mixed aggregate is observed along with a resonance at 0.87 (Figure 5c) corresponding to free LiBr. At even moderately increased THF concentrations, the resonances corresponding to the mixed aggregate, the dimer, and LiBr become time averaged.

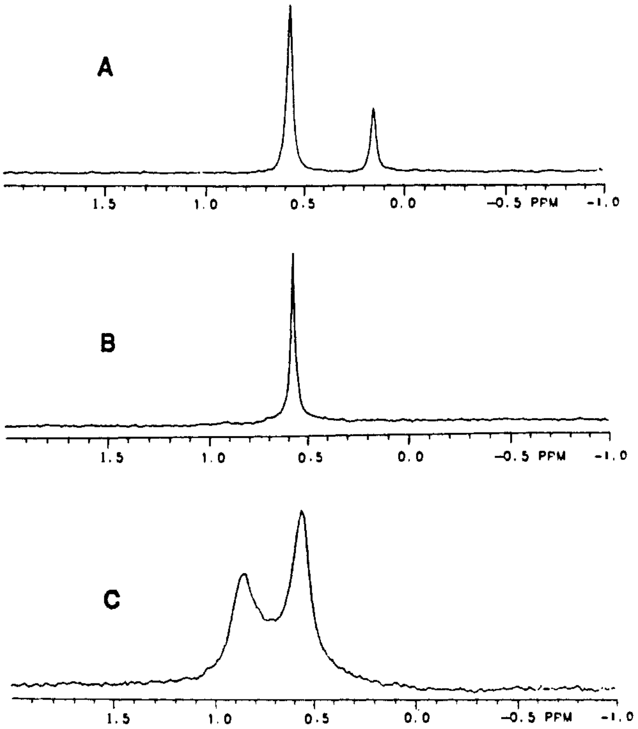


Figure 5. ^{6}Li NMR spectra recorded at −90 °C of 0.015 M toluene-d_8 solutions of $[^{6}Li]Ph_2NLi$ and $^{6}LiBr$, 0.09 M THF: (A) 2:1 ratio of $[^{6}Li]Ph_2NLi$ to $^{6}LiBr$, (B) 1:1 ratio of $[^{6}Li]Ph_2NLi$ to $^{6}LiBr$, and (C) 1:2 ratio of $[^{6}Li]Ph_2NLi$ to $^{6}LiBr$. The ^{6}Li chemical shifts are referenced to analogous samples containing 0.30 M $^{6}LiCl$/MeOH external standards.

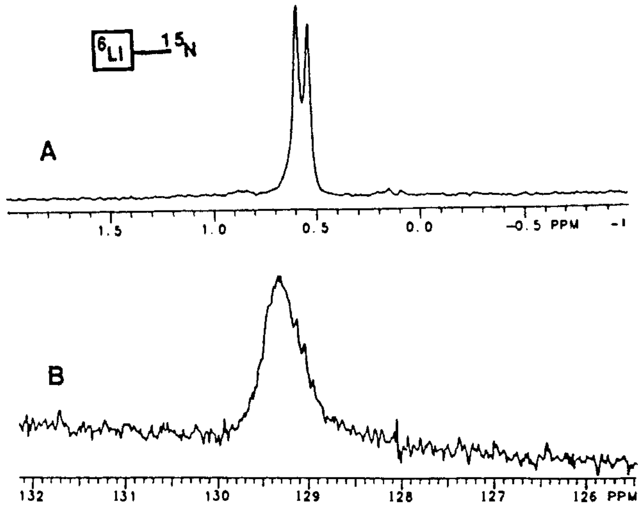


Figure 6. ^{6}Li and ^{15}N NMR spectra recorded at −90 °C of toluene-d_8 solutions of $[^{6}Li,^{15}N]Ph_2NLi\cdot LiBr$. (A) ^{6}Li NMR spectrum: 0.015 M in amide, 0.038 M THF. (B) ^{15}N NMR spectrum: 0.05 M in amide, 0.10 M THF.

The stoichiometries clearly indicate that Ph_2NLi and LiBr form a 1:1 mixed aggregate quantitatively at low THF concentrations, with the equilibrium shifted substantially toward the mixed aggregate form. The atomic connectivity within the mixed aggregate was probed by using the ^{6}Li–^{15}N double labeling techniques as described below.

$Ph_2NLi\cdot LiBr$: ^{6}Li and ^{15}N Double Labeling Studies. The ^{6}Li NMR spectrum of a 0.015 M toluene-d_8 solution of a 1:1 $[^{6}Li,^{15}N]Ph_2NLi/^{6}LiBr$ mixture (−90 °C, 0.038 M THF) displays a doublet centered at 0.56 ppm (Figure 6a). The coupling pattern

Table II. ^{13}C (^{1}H) NMR Spectral Data for $Ph_2NLi/LiBr$ Mixtures[a,b]

entry	[THF], mol/L	amide/LiBr	temp, °C	ipso	meta	ortho	para
1	0.26	2/1	-90	159.90, 158.17	*a*	121.91, 120.02	115.31, 114.97
2	0.59	2/1	-90	159.90, 158.17	*a*	121.87, 119.90	115.24, 114.56
3	1.20	2/1	-90	158.24	*a*	119.78	114.82
4	0.26 (2%)	1/1	23	*b*	129.56	120.15	115.63
5	0.26	1/1	-90	157.90	*a*	120.00	114.94
6	0.26	1/2	23	*b*	129.62	120.19	115.82
7	0.26	1/2	-90	157.96	*a*	120.05	114.98
8	4.43 (36%)	1/1	23	*b*	128.87	119.81	113.67
9	4.43	1/1	-90	158.53	*a*	119.18	112.97
10	4.43	1/2	23	*b*	128.83	119.87	113.84
11	4.43	1/2	-90	158.46	*a*	119.30	113.24
12	12.28 (99%)	1/1	23	*b*	128.13	118.89	111.93
13	12.28	1/2	23	*b*	128.12	118.95	112.06

[a] The resonance was obscured by the toluene-d_8. [b] The ipso carbon resonances were poorly resolved from base-line noise in the ambient temperature spectra recorded at convenient scan times.

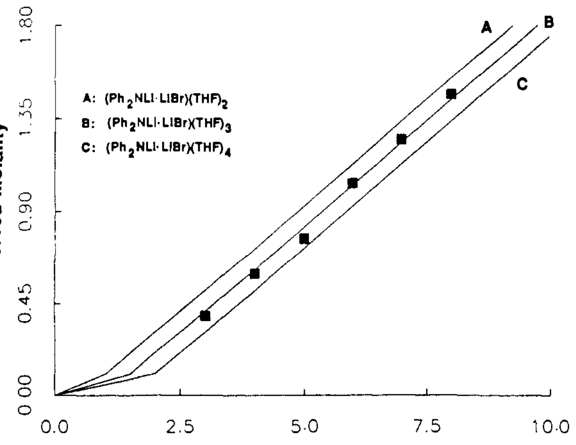


Figure 7. Observed molality measured as a function of added THF for suspensions of $Ph_2NLi/LiBr$ (0.21 M) in benzene. The lines represent calculated plots for models based on dimers of varying solvation state as labeled.

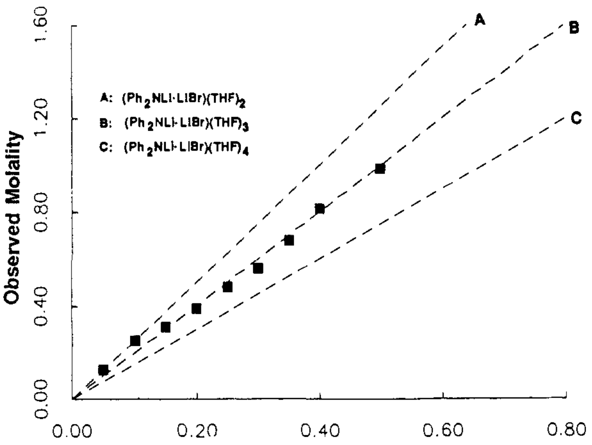


Figure 8. Observed molality measured as a function of $Ph_2NLi/LiBr$ concentration. Each sample contained 3.0 equiv of THF per lithium. The dashed lines represent calculated plots for models based on dimers of varying solvation states as labeled.

demonstrates that each lithium is connected to only one ^{15}N nucleus. Although this would be consistent with either a mixed dimer (cf. **2**) or some variant of a monomeric amide, the 3.24-Hz coupling constant is well within the 3–4-Hz range previously observed for lithium amide dimers rather than the 6–7-Hz range observed for monomeric amides.[7,8]

The high fluctionality of $Ph_2NLi·LiBr$ is apparent from the loss of coupling as the THF concentration exceeds 0.06 M. Unfortunately, at the elevated $Ph_2NLi/LiBr$ and THF concentrations required for ^{15}N NMR spectroscopic analysis, only poorly resolved coupling can be observed (Figure 6b). Nonetheless, on the basis of the observed 1:1 $Ph_2NLi/LiBr$ stoichiometry, the ^{6}Li NMR coupling pattern, and the magnitude of the observed coupling constant, the $Ph_2NLi·LiBr$ mixed aggregate is assigned general structure **2** with reasonable confidence. The solvation state was determined cryoscopically as follows.

$Ph_2NLi·LiBr$: Colligative Studies. Figure 7 is a plot of observed molalities of benzene solutions of $Ph_2NLi/LiBr$ as a function of added THF.[20] Measurements recorded on heterogeneous mixtures from 0.0 to 3.0 equiv of THF were highly variable and are not displayed. Included in Figure 7 are calculated plots for the various solvation states of $Ph_2NLi·LiBr$ as labeled. Figure 8 is a plot of measured molality as a function of the absolute concentration of $Ph_2NLi·LiBr$. For each data point solvent-free $Ph_2NLi/LiBr$ was dissolved by adding 3.0 equiv of THF per lithium atom.

$Ph_2NLi·LiBr$: Structure at Low THF Concentrations. Corroborative evidence from the two colligative experiments taken in conjunction with the spectroscopic evidence supports trisolvated mixed dimer **2a** as the most likely solution structural form of $Ph_2NLi·LiBr$.[21] One of the more curious features of **2a** is the unsymmetrical tris solvation state. Jackman has discussed in some detail the possibility of equilibria between di-, tri-, and tetrasolvated amide dimers in the context of condition-dependent ^{13}C chemical shifts.[7] However, to the best of our knowledge a lithiated diketopiperazine represents the only fully characterized trisolvated dimeric lithium amide derivative reported to date.[22,23]

$Ph_2NLi/LiBr$: ^{13}C NMR Spectroscopic Studies. We were interested in whether $Ph_2NLi·LiBr$ dissociated to a monomer at elevated THF concentrations (eq 4) in analogy to the Ph_2NLi dimer (eq 3). Although the high fluctionality of $Ph_2NLi·LiBr$ precluded ^{6}Li NMR spectroscopic studies, the higher frequency of ^{13}C NMR spectroscopy once again proved advantageous.

2:1 mixtures of Ph_2NLi and LiBr were monitored over a large portion of the THF concentration range (Figure 9, Table II). The Ph_2NLi dimer and $Ph_2NLi·LiBr$ are fully resolved at 0.26 M THF (Figure 9a). As the THF concentration increases, the resonances

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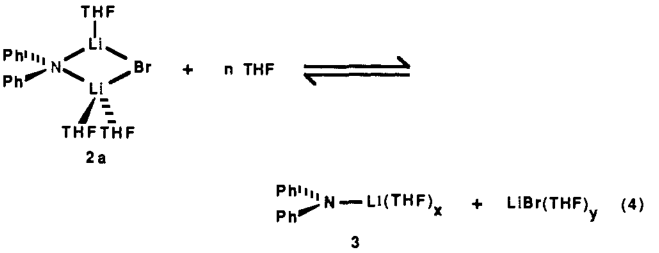
(20) A sample of a 1:1 mixture of Ph_2NLi and LiBr used for the cryoscopic measurements analyzed correctly. Anal. Calcd for $C_{12}H_{10}NLi_2Br$: C, 55.01; H, 3.85; N, 5.35. Found: C, 54.73; H, 3.76; N, 5.19.

(21) Stable lithium halide adducts of lithium amides have been isolated. Huisgen, R.; Mack, W. *Chem. Ber.* **1960**, *93*, 412. Huisgen, R. In *Organometallic Chemistry*; American Chemical Society: Washington, DC, **1960**; Monograph Series # 147, pp 36–87. Goralski, P.; Chabanel, M. *Inorg. Chem.* **1987**, *26*, 2169. For a structurally characterized enolate/amide mixed aggregate, see: Williard, P. G.; Hintze, M. J. *J. Am. Chem. Soc.* **1987**, *109*, 5539.

(22) Seebach, D.; Bauer, W.; Hansen, J.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. *J. Chem. Soc., Chem. Commun.* **1984**, 853.

(23) As drawn, the asymmetry of such tris solvates would not be expected to be observable by NMR spectroscopy due to high solvent exchange rates. Sharp, H. J.; Symons, M. C. R. In *Ions and Ion Pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley: New York, 1972; Vol. 1, Chapter 5. Jackman, L. M.; DeBrosse, C. W. *J. Am. Chem. Soc.* **1983**, *105*, 4177. As noted by one referee, a single η^3-azaallyllithium interaction could cause the preference for tris solvation.



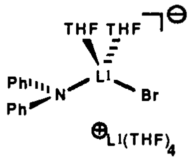
2a

3

(4)

corresponding to the Ph_2NLi dimer decrease without the concomitant appearance of the Ph_2NLi monomer (Figure 9b,c). The resonances corresponding to the Ph_2NLi monomer and $Ph_2NLi{\cdot}LiBr$ appear to be time averaged, creating the illusion of an increase in the concentration of the mixed aggregate. The ^{13}C chemical shifts of the 2:1 $Ph_2NLi/LiBr$ samples are approximate averages of the values for monomeric Ph_2NLi and 1:1 mixtures of $Ph_2NLi/LiBr$.

We presumed that if Ph_2NLi exists as distinctly different structural forms in the presence and absence of LiBr, then one should see significant chemical shift differences. On the other hand, if Ph_2NLi exists as a monomer in the presence of LiBr, then the ^{13}C chemical shifts of Ph_2NLi should be unaffected by added LiBr. Comparison of the ^{13}C chemical shifts of Ph_2NLi (Table I; entries 3, 7, and 8) with those of samples containing LiBr (Table II, entries 5, 9, and 12) shows that the perturbations caused by the LiBr become progressively less pronounced at increasing THF concentrations. Thus, with some caution, we infer that $Ph_2NLi{\cdot}LiBr$ dissociates to monomer **3** and free LiBr as depicted in eq 4. We cannot, however, rigorously exclude the existence of such species as ion triplet **5** at high THF concentrations.[24] This ambiguity will be further highlighted in the accompanying paper.



5

Summary and Conclusions

The conclusions from the spectroscopic and colligative studies are summarized in Scheme I.

At low THF concentrations ^6Li and ^{15}N NMR spectroscopic analyses revealed that Ph_2NLi exists in a cyclic aggregate form. Although cyclic dimers, trimers, and tetramers cannot be distinguished from the ^6Li–^{15}N coupling patterns alone, strong arguments and structural analogies support a dimer structure. Within the constraints imposed by the assignment of Ph_2NLi as a cyclic dimer, the colligative measurements are consistent with either a di- or trisolvate (**1a** or **1b**).

As the THF concentrations were increased, rapid fluctional processes rendered the powerful ^{15}N and ^6Li NMR spectroscopic probes completely ineffective. Nonetheless, dissociation of dimer **1** to monomer **3** was observed directly by ^{13}C NMR spectroscopy, although details of the monomer structure and solvation state remain obscure.

^6Li and ^{15}N NMR spectroscopic studies and colligative measurements of $Ph_2NLi/LiBr$ mixtures at low THF concentrations demonstrated the presence of mixed aggregate **2a** in a rarely observed, unsymmetrical tris solvation state. ^{13}C NMR spectral studies of $Ph_2NLi/LiBr$ mixtures showed the $Ph_2NLi{\cdot}LiBr$ mixed aggregate to be involved in slow exchange with dimeric Ph_2NLi and rapid exchange with monomeric Ph_2NLi. Despite substantial losses in structural information arising from the high fluctionality, effects of LiBr on the time-averaged ^{13}C chemical shifts of Ph_2NLi provide indirect evidence that $Ph_2NLi{\cdot}LiBr$ dissociates to a monomer and free LiBr at intermediate and high THF concentrations. However, ion triplet **5** cannot be rigorously excluded as a plausible solution structural form.

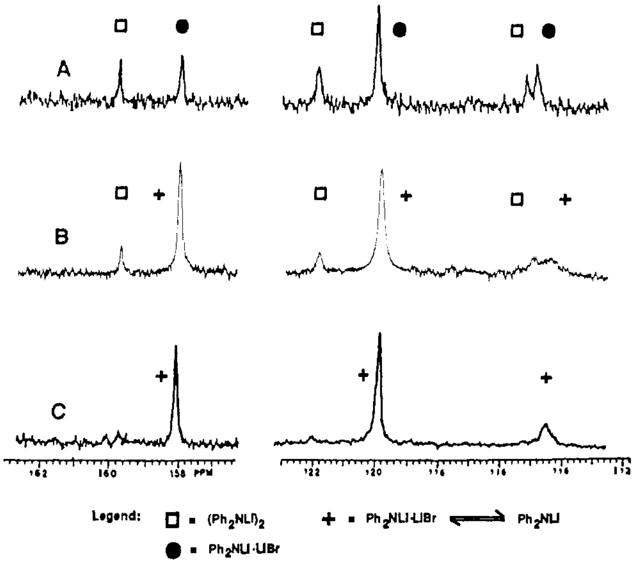
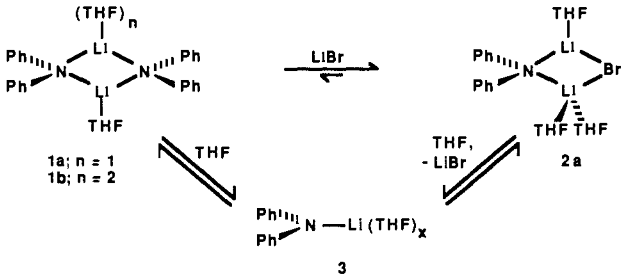


Figure 9. ^{13}C (^1H) NMR spectra recorded at −90 °C of toluene-d_8 solutions of 2:1 mixtures of Ph_2NLi and LiBr, 0.03 M Ph_2NLi. (A) 0.26 M THF, (B) 0.80 M THF, (C) 1.20 M THF.

Scheme I



In the following paper, we will describe kinetic studies of the N-alkylation of Ph_2NLi with n-BuBr. Although some of these structural issues remain unresolved, the kinetic data demonstrate the role of solvation and the importance of homo- and heteronuclear aggregates, monomers, and free ions as contributors to the reactivity of lithium amides.

Experimental Section

General Procedures. Benzene, tetrahydrofuran (THF), and all deuteriated solvents were distilled from blue or purple solutions containing sodium benzophenone ketyl under vacuum. The hydrocarbon stills contained 1% tetraglyme to dissolve the ketyl. The benzene used in the molecular weight determinations was distilled from $LiAlH_4$. ^6Li metal (95.5%) was obtained from Oak Ridge National Laboratory. Ethyllithium and [^6Li]ethyllithium were prepared by the standard literature procedures and were recrystallized from benzene and doubly sublimed to remove lithium halide impurities.[5] [^{15}N]aniline (99%) was obtained from Cambridge Isotope Laboratory and used without further purification. Diphenylamine was purified sequentially by (1) washing an ethereal solution with 10% NaOH, drying the ethereal layer over $NaSO_4$, and concentrating in vacuo; (2) recrystallizing the off-white solid from hexane; and (3) subliming the resulting white crystalline solid under full vacuum at 60 °C. Air- and moisture-sensitive materials were manipulated under argon or nitrogen with standard glovebox and vacuum-line techniques with the aid of gas-tight syringes. Microanalyses were performed by Alfred Bernhardt Analytisches Laboratorien (Elbach, West Germany).

NMR Spectroscopic Analyses. ^{13}C, ^6Li, and ^{15}N NMR spectra were recorded on a Varian XL-400 spectrometer operating at 100.56, 58.84,

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(24) Robinson, R. A.; Stokes, R. H. *Electrolyte Solutions*; Buttersworth: London, 1965; Chapter 14. Beronius, P.; Linbäck, T. *Acta Chem. Scand., Ser. A* **1978**, *A32*, 423. Beronius, P.; Linbäck, T. *Acta Chem. Scand., Ser. A* **1979**, *A33*, 397. Saar, D.; Petrucci, S. *J. Phys. Chem.* **1986**, *90*, 3326. Cachet, H.; Cyrot, A.; Fekir, M.; Lestrade, J.-C. *J. Phys. Chem.* **1979**, *83*, 2419. Fuoss, R. M.; Kraus, C. A. *J. Am. Chem. Soc.* **1933**, *55*, 2387. Fraenkel, G.; Hallden-Abberton, M. P. *J. Am. Chem. Soc.* **1981**, *103*, 5657. Cambillau, C.; Bram, G.; Corset, J.; Riche, C. *Nouv. J. Chem.* **1979**, *3*, 9. Cambillau, C.; Ourevitch, M. *J. Chem. Soc., Chem. Commun.* **1981**, 996. Raban, M.; Noe, E. A.; Yamamoto, G. *J. Am. Chem. Soc.* **1977**, *99*, 6527.

and 40.53 MHz, respectively. ^{1}H NMR spectra were recorded on a Varian XL-200 spectrometer. ^{1}H and ^{13}C NMR shifts are reported in ppm downfield of tetramethylsilane. The ^{6}Li chemical shifts are reported in ppm relative to an external 0.3 M ^{6}LiCl/methanol standard. The ^{15}N chemical shifts are reported in ppm relative to an external 0.15 M [^{15}N]aniline/THF standard set at 50 ppm.[9] NMR probe temperatures are accurate to ±2 °C.

The following is a representative procedure for preparing samples for spectroscopic analysis. A stock solution was prepared in a glovebox by sequentially mixing [^{6}Li,^{15}N]$Ph_2NLi_{solvent\text{-}free}$ (20 mg, 0.11 mmol), toluene-d_8 (472 μL), and THF (18 μL, 0.22 mmol). A 5-mm NMR tube was charged sequentially with the pale yellow stock solution (129 μL), toluene-d_8 (840 μL), and THF (31 μL). The tube was placed under septum, removed from the glovebox, and sealed with a flame under reduced pressure.

Colligative Measurements. Solution molalities were measured by freezing-point depression by using a modification of an apparatus described by Seebach[17] interfaced to a Commodore 64 or VIC-20 minicomputer. Samples were prepared in a glovebox and measurements were made under N_2 with standard inert atmosphere techniques. Calibrations were performed with known concentrations of naphthalene in benzene.

[^{15}N]Diphenylamine. Benzenediazocarboxylate (2.9 g, 19.6 mmol) was generated via a literature method.[10] (*Caution: benzenediazocarboxylate is highly explosive when fully dry.*) The diazocarboxylate was suspended in 110 mL of 1,2-dichloroethane and [^{15}N]aniline (950 μL, 10.2 mmol) was added to the suspension. The mixture was heated to 70 °C for 30 min with noted gas evolution. The resultant red-brown solution was concentrated to a brown oil, dissolved in THF, passed through a 2 in. silica gel plug, and evaporated to a red oil. The red oil was multiply flash chromatographed on silica gel (5% ethyl acetate, hexane) to afford [^{15}N]diphenylamine (214 mg, 12.3%) as a white solid. ^{1}H NMR (C_6D_6): δ 7.12 (m, 5 H), 6.86 (m, 5 H), 5.06 (d, $J_{N\text{-}H}$ = 88 Hz, 1 H). ^{13}C (^{1}H) NMR (C_6D_6): δ 143.54 (d, $J_{N\text{-}C}$ = 14.9 Hz), 129.50, 121.20, 118.13 (d, $J_{N\text{-}C}$ = 2.7 Hz).

Solvent-Free Lithium Diphenylamide ($Ph_2NLi_{solvent\text{-}free}$). The various isotopomers of solvent-free lithium diphenylamide were prepared as follows. A 500-mL round-bottom flask fitted to a glass filter frit was charged with diphenylamine (5.27 g, 31.1 mmol) and ethyllithium (1.18 g, 32.8 mmol). To this was added 300 mL of a 2:1 hexane/diethyl ether mixture via vacuum transfer at −78 °C. The milky white solution was warmed to 0 °C and stirred for 1.5 h. The resultant clear solution was concentrated in vacuo to 80 mL and then cooled to −78 °C. Filtration afforded an off-white solid, which was recrystallized from hexane at −78 °C. The resulting white crystalline solid was heated to 80 °C for 24 h under dynamic vacuum to liberate diethyl ether. Sequential washing with 150 mL of near-boiling benzene and 100 mL of near-boiling hexane afforded $Ph_2NLi_{solvent\text{-}free}$ (5.21 g, 95.5%) as an amorphous white solid. ^{1}H NMR (C_6D_6) with 2.0 equiv of 4-picoline: δ 7.95 (picoline) (d, $J_{H\text{-}H}$ = 4.69 Hz), 7.56 (d, $J_{H\text{-}H}$ = 8.25 Hz), 7.32 (dd, $J_{H\text{-}H}$ = 8.19 Hz), 6.80 (dd, $J_{H\text{-}H}$ = 8.17 Hz), 6.34 (picoline) (d, $J_{H\text{-}H}$ = 5.46 Hz). Anal calcd for $C_{12}H_{10}NLi$: C, 82.29, H, 5.75; Li, 3.96; N, 8.00. Found: C, 82.02; H, 5.67; Li, 3.85; N, 7.82. Detailed ^{6}Li, ^{13}C, and ^{15}N NMR spectroscopic data are found in Tables I and II and Figures 1, 4–6, and 9.

Acknowledgment. We wish to thank the National Science Foundation Instrumentation Program (Grant CHE 7904825 and PCM 8018643) for support of the Cornell Nuclear Magnetic Resonance Facility and the A. P. Sloan Foundation for unrestricted support.

Structure and Reactivity of Lithium Diphenylamide. Role of Aggregates, Mixed Aggregates, Monomers, and Free Ions on the Rates and Selectivities of N-Alkylation and E2 Elimination

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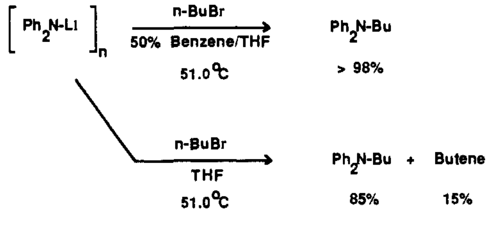
Contribution from the Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301. *Received January 11, 1988*

Abstract: Rate studies of the N-alkylation of lithium diphenylamide with *n*-butyl bromide in THF/hydrocarbon mixtures (THF = tetrahydrofuran) are described. Dramatic induction periods observed for the N-alkylation at low THF concentrations are ascribed to the intervention of reactive mixed dimers of lithium diphenylamide and lithium bromide. In the presence of 1.0 equiv of added lithium bromide, the alkylation rate exhibits a first-order dependence on both the mixed aggregate and *n*-butyl bromide concentrations, supporting a pathway involving direct mixed aggregate alkylation. Incremental changes in the THF concentration uncovered contributions from several additional species. Regions of first or higher order followed by zero-order dependence on the THF concentration are interpreted as an equilibrium shift to a more reactive, highly solvated species assigned as a monomer (or ion pair). At elevated THF concentrations, the alkylation rate increases sharply as a function of the THF concentration, indicating the contribution of an additional, highly solvent dependent alkylation pathway. This latter pathway exhibits fractional-order dependence on the amide concentration, approximate first order dependence on the *n*-butyl bromide concentration, and a seventh-order dependence on the THF concentration. Common ion rate inhibitions by lithium perchlorate and lithium tetraphenylborate, a significant dependence on dielectric effects, and the observed reaction orders implicate a mechanism involving predissociation of free lithium ions. The appearance of competitive eliminations of the *n*-alkyl bromides to form 1-alkenes coincides with the appearance of the free ion alkylation pathway.

Lithium dialkylamides are used routinely throughout organic chemistry as highly reactive and selective bases. Elegant quantitative studies of lithium amides include Streitwieser's[1] and Fraser's[2] ion pair acidity measurements, Newcomb's[3] investigations of amide-mediated hydride transfer, and Huisgen's[4] extensive studies of dehydrohalogenations of aryl halides. However, most

Scheme I



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