Solution Structures of Lithium Dialkylamides and Related N-Lithiated Species: Results from $^6$Li–$^{15}$N Double Labeling Experiments

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Received August 18, 1992 (Resubmitted Manuscript Received January 12, 1993)

The chemistry of lithium is pervasive within organic chemistry. It would appear, for example, that well over 95% of natural products syntheses rely upon lithium-based reagents in one form or another. At the same time, however, the coordination chemistry of organolithium reagents and the mechanisms of organolithium-based reactions are extraordinarily complex and poorly understood. This complexity stems from a high propensity of organolithium compounds to self-associate into higher aggregates, a phenomenon that is markedly dependent on the choice of solvent and precise conditions. The problem is intensified by the rapid subunit and solvent exchanges within the various aggregates as well as the extreme oxygen and moisture sensitivity of most organolithium derivatives. As a result, a vast number of organolithium reagents are routinely generated and used without direct evidence of their solution structures, dynamic behavior, or even existence.

Lithium dialkylamides and related N-lithiated species constitute a very important class of organolithium reagents. They are the preferred bases for formation of ketone enolates and other stabilized carbanions as well as for generating low steady-state concentrations of some relatively unstable carbanions. The lithioamines and related lithiated Schiff's bases have played prominently as ketone enolate equivalents in cases where the enolates have proven less than adequate. In fact, the progress in synthetic organic chemistry over the last three decades would certainly have been less impressive without the contributions from lithium amid chemistry to the refinement of carbon–carbon bond forming technology.

This Account describes the solution structures of lithium dialkylamides and closely related N-lithiated species that have been determined by $^6$Li and $^{15}$N NMR spectroscopic analyses of isotopically enriched substrates. Strategies are described for extracting structural details from both inordinately simple and inordinately complex NMR spectra. Since a logical, stepwise presentation and a chronological narrative are mutually exclusive, the former will be attempted under pretense of the latter.

David Collum received a bachelor's degree in biology from the Cornell University College of Agriculture and Life Sciences in 1977. After receiving a Ph.D in 1980 from Columbia University working with Clark Still, he returned to the Department of Chemistry at Cornell, where he is now a Professor of Chemistry. His work at Cornell has addressed topics in natural products synthesis, organotransition metal chemistry, and organolithium structure and mechanism.
The Problem of Symmetry. Several excellent reviews offer details of lithium amide structure studies that will not be repeated here. The problem of symmetry and consequent numbing spectral simplicity is well worth emphasizing, however. One typically finds that NMR spectra of lithium amides contain a single \( ^{6}\text{Li} \) or \( ^{7}\text{Li} \) resonance and single sets of \( ^{13}\text{C} \) and \( ^{1}\text{H} \) resonances consistent with many plausible structures including free ions, solvent-separated ion pairs, monomers, dimers, cyclic oligomers, and polymers. The reliance on colligative measurements for determining aggregation is not without its problems; structural details are available only through considerable inference, colligative data are vulnerable to unseen impurities, and conclusions are often difficult to verify by independent methods. Nevertheless, substantial progress has been made in a few instances as best exemplified by the seminal studies of lithium hexamethyldisilazide (LiHMDS) reported by Kimura and Brown in 1971. They found that LiHMDS features solvent- and concentration-dependent spectroscopic and colligative properties consistent with a monomer-dimer mixture in ethereal solvents (eq 1) and a dimer-tetramer mixture in hydrocarbons (eq 2). In many respects, their progress can be attributed to the disruption of the spectral simplicity due to the coexistence of multiple aggregation states. The success of the \( ^{6}\text{Li}^{-15}\text{N} \) double labeling methods described in this Account arises from the disruption of spectral simplicity as well.

\[
\begin{align*}
\text{[Me,Si]}_2\text{NLiS}_2 & = \text{[Me,Si]}_2\text{NLiS}_2, \\
\text{[Me,Si]}_2\text{NLiI}_4 & = \text{[Me,Si]}_2\text{NLiI}_2
\end{align*}
\]

I. Simple Equilibria

Lithioimines and Lithium Anilides. Our interest in the structures of N-lithiated species originated from investigations of lithiated hydrazine alkylates and intensified during studies of lithioimine \(^{1}\). The \(^{13}\text{C} \) and \(^{6}\text{Li} \) spectra of 1 in the presence of low THF concentrations revealed two discrete sets of resonances that could be attributed to a pair of isomeric species in a 2:1 ratio. Colligative techniques described in the literature for determining both aggregation and solvation state provided some assistance. Titration of solvent-free lithiated imine with limited quantities of THF revealed average solution molalities consistent with a monomer-dimer mixture. In several instances they observed resonances consistent with aggregate stereoisomers analogous to 2 and 3. Their method for determining solvation states is especially noteworthy. They found that \(^{7}\text{Li} \) quadrupolar splitting constants (QSCs) determined from \(^{7}\text{Li} \) and \(^{13}\text{C} \) spin–lattice relaxation times correlate with the degree of solvation and the reasonable sensitivity of both \(^{6}\text{Li} \) (spin 1) and \(^{15}\text{N} \) (spin 1/2) suggested that \(^{6}\text{Li}^{-15}\text{N} \) scalar coupling observed by \(^{6}\text{Li} \) and \(^{15}\text{N} \) NMR spectroscopy could afford insight into N–Li connectivities (Table I). Although previous NMR spectroscopic studies of \(^{15}\text{N} \)-labeled lithium amides did not uncover coupling at ambient temperatures, we suspected that coupling would be observable at low temperatures where aggregate subunit exchanges typically become slow on the NMR timescales. As we initiated our investigations Professor Lloyd Jackman and co-workers at Penn State were already making substantial progress in their studies of \('[\text{Li}^{-15}\text{N}]\text{liithium anilides (vide infra)},^{13-15}\)

\(^{6}\text{Li} \) and \(^{15}\text{N} \) NMR spectra of \('[\text{Li}^{-15}\text{N}]\) display resonance multiplicities in full accord with a 2:1 mixture of two isomeric dimers at low THF concentrations and a monomer in neat THF. Supplemented with additional information on the quantitative concentration dependencies of the monomer–dimer ratio, we completed the aggregation-state and solvation-state assignments summarized in Scheme I. Unfortunately, the resonances ascribed to the 2:1 mixture of dimers 2 and 3 are equally consistent with a single stereoisomeric trimer 5. Three years later single-frequency decouplings provided the explicit resonance correlations necessary to rigorously exclude trimer 5. Single-frequency decoupling became an important component of our studies by allowing us to systematically unravel the \(^{6}\text{Li}^{-15}\text{N} \) resonance correlations of complex equilibria.

Jackman’s early studies of \('[\text{Li}^{-15}\text{N}]\) lithium anilides revealed predominantly monomer–dimer mixtures in analogy to lithiated imines. The monomer–dimer ratios depend on the precise substitution pattern of the aniline and solvent chosen. Generally, increasing the steric demands of the N-alkyl moieties promotes formation of monomer. In several instances they observed resonances consistent with aggregate stereoisomers analogous to 2 and 3. Their method for determining solvation states is especially noteworthy. They found that \(^{7}\text{Li} \) quadrupolar splitting constants (QSCs) determined from \(^{7}\text{Li} \) and \(^{13}\text{C} \) spin–lattice relaxation times correlate with the degree of solvation and the reasonable sensitivity of both \(^{6}\text{Li} \) (spin 1) and \(^{15}\text{N} \) (spin 1/2) suggested that \(^{6}\text{Li}^{-15}\text{N} \) scalar coupling observed by \(^{6}\text{Li} \) and \(^{15}\text{N} \) NMR spectroscopy could afford insight into N–Li connectivities (Table I). Although previous NMR spectroscopic studies of \(^{15}\text{N} \)-labeled lithium amides did not uncover coupling at ambient temperatures, we suspected that coupling would be observable at low temperatures where aggregate subunit exchanges typically become slow on the NMR timescales. As we initiated our investigations Professor Lloyd Jackman and co-workers at Penn State were already making substantial progress in their studies of \('[\text{Li}^{-15}\text{N}]\text{liithium anilides (vide infra)},^{13-15}\)

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within each class of aggregation state. Trisolvated monomers and tetrasonvated dimers having tetrahedral coordination about lithium show substantially smaller QSCs than do their trigonal planar disolvated monomer and disolvated dimer counterparts. As one might expect, higher solvation numbers correlate with strong donor solvents and sterically unhindered substrates. Although their method for solvation number determination has so far been limited to ArXLi (X = NR, O) derivatives, it constitutes one of the most incisive solutions to the extremely difficult and persistent problem of lithium ion solvation state determination.18

Lithium Dialkylamides. Lithium isopropylcyclohexylamide (LiCA) is a commonly used base in organic synthesis. We turned to LiCA rather than more symmetrical lithium dialkylamides to capitalize upon the stereochemical consequences of aggregation.19 A single 13C NMR spectrum of LiCA evidenced aggregation by displaying twice the number of resonances anticipated for a simple monomer. [6Li,15N]LiCA in THF exhibited spectroscopic properties fully consistent with a 1:1 mixture of dimer stereoisomers at all LiCA/THF concentrations (eq 3). The depiction of LiCA dimers as disolvates is based upon indirect kinetic,20 theoretical,21 and spectroscopic20,22 evidence (vide infra). Failure to observe any monomer was surprising in light of colligative measurements suggesting that a 0.05 M solution of lithium diisopropylamide (LDA) in neat THF contains primarily monomer.23 However, follow-up spectroscopic studies of [6Li,15N]LDA revealed only cyclic oligomer (presumed to be a dimer by analogy to LiCA) under all conditions and highlighted the limitation of structure determinations based solely on molality measurements that can be highly sensitive to impurities.

The [6Li–15N] double labeling method readily confirmed previous suggestions7 that unsolvated lithium amides can exist in a variety of cyclic oligomers. Hexane solutions of solvent-free [6Li,15N]LDA, for example, contain 3–5 discrete cyclic oligomers.24 In contrast, suggestions that lithium dialkylamides in donor solvents exist only as cyclic dimers to the exclusion of higher cyclic oligomers were difficult to confirm for highly symmetric cases.25 Moreover, the ambiguities stemming from the seemingly innocuous distinction of D2h dimers from D4h higher oligomers (see Table I) haunted rate and mechanism studies.20,26,27

Inverse-detected 15N homonuclear zero-quantum NMR spectroscopy provided a rigorous distinction of D2h cyclic dimers from D4h higher oligomers. In the 15N zero-quantum experiment, homonuclear 15N two-spin coherence is prepared from the two 15N spins neighboring a 6Li atom in a 6Li–15N doubly labeled lithium dialkylamide cyclic oligomer.28 During the evolution period, the zero-quantum coherence will evolve under scalar coupling only to 6Li spins that couple to one, but not both, 15N spins. For a lithium amide dimer, all 6Li spins coupled to 15N spins involved in the two-spin coherence couple to both 15N spins. Consequently, the coupling pattern will be a singlet along the f1 dimension of the two-dimensional spectrum. In higher cyclic oligomers, there exist two 6Li spins that couple to one, but not both, 15N spins. The zero-quantum coherence will develop scalar coupling to the two nonshared 6Li spins, resulting in a 1:2:3:2:1 pattern along the f1 dimension. As a result of a refocusing delay employed prior to detection, all oligomers will be a 1:2:1 pattern along the f2 dimension.

The 14N zero-quantum NMR spectrum of [6Li,14N]LDA in THF (Figure 1A) shows no coupling in f1, consistent with a cyclic dimer.29 For comparison, the zero-quantum spectrum of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) in benzene shows splitting in f1 consistent with a cyclic trimer or tetramer (Figure 1B).29 Other solvated lithium amide cyclic oligomers found to be cyclic dimers include LDA in TEMED,27 LiTMP in

Table I. Predicted NMR Resonance Multiplicities for 6Li–15N Doubly Labeled N-Lithiated Species

<table>
<thead>
<tr>
<th>structural form</th>
<th>6Li NMR spectrum</th>
<th>15N NMR spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>R3N (+LiS₂)</td>
<td>singlet</td>
<td>singlet</td>
</tr>
<tr>
<td>R₃N–Li₂</td>
<td>doublet</td>
<td>1:1:1 triplet</td>
</tr>
<tr>
<td>R₃N–Li₂</td>
<td>1:2:1 triplet</td>
<td>1:2:3:2:1 quintet</td>
</tr>
<tr>
<td>R₃N–Li₂</td>
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<td>1:2:3:1 quintet</td>
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</tbody>
</table>

Scheme I

![Scheme I](image)

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(25) For a summary of the indirect evidence supporting the dimer assignments, see ref 22.
Figure 1. $^6\text{Li}$-detected $^{15}\text{N}$ zero-quantum NMR spectra of (A) 0.15 M $^{[6\text{Li},^{15}\text{N}]}\text{LiDA}$ in THF at -90 °C and (B) 0.25 M $^{[6\text{Li},^{15}\text{N}]}\text{LiTMP}$ in 3:1 benzene at 30 °C.

THF,$^{26}$ LiHMDS in toluene,$^{36}$ and LiHMDS in THF.$^{36}$ These results support the contention that solvated lithium amides in the presence of donor solvents are cyclic dimers rather than higher oligomers, whereas solvent-free lithium amides can exist as any of several $D_3h$ cyclic oligomers.

LiTMP is one of the most reactive and most hindered lithium amide bases commonly used to generate carbanions. In 1988, Renaud and Fox reported that the $^7\text{Li}$ NMR spectra of LiTMP contain two resonances consistent with a monomer–dimer mixture.$^{31}$ Follow-up studies of $^{[6\text{Li},^{15}\text{N}]}\text{LiTMP}$ confirmed the existence of a monomer–dimer mixture in THF and revealed added subtleties due to conformational isomerism.$^{29,32}$ Although the single dimer resonance implicated the $C_{2v}$ conformer 6b rather than the $C_{3v}$ conformer 7a, we could not exclude the possibility that the facile (7.0 kcal/mol) chair–chair ring flip was causing time averaging of the two signals. In contrast, conformationally locked dimers 6b and 7b of lithium 2,2,4,6,6-pentamethylpiperidide (LiPMP)$^{33}$ are forced to exchange by a less facile ring scission process. Indeed, $^{[6\text{Li},^{15}\text{N}]}\text{LiPMP}$ displays a single $^6\text{Li}$ dimer resonance in analogy to $^{[6\text{Li},^{15}\text{N}]}\text{LiTMP}$. By slowing the site exchanges, differential N–Li$_{axial}$ and N–Li$_{equatorial}$ coupling becomes readily discernible as a $^6\text{Li}$ doublet of doublets. The observed coupling excludes any possibility of time averaging of the two different resonances anticipated for 7b. Thus, the high inherent symmetry typical of lithium amides is diminished in lithium piperidides by conformational isomerism. Differential N–Li$_{axial}$ and chemical shifts for axially and equatorially bound lithium nuclei are readily observable in LiTMP mixed aggregates as well (vide infra).

With the key techniques in hand, we reinvestigated the structure of LiHMDS.$^{30}$ Spectroscopic studies of $^{[6\text{Li},^{12}\text{N}]}\text{LiHMDS}$ confirmed the existence of a cyclic dimer in toluene, a mixture of oligomers in pentane (eq 2), and a monomer–dimer mixture in THF (eq 1). Thus, despite limited spectroscopic tools available at the time, Kimura and Brown’s assignments$^8$ are correct in every respect. Differentiation of the unsolvated cyclic trimers and tetraromers must await further developments in multiple-quantum NMR spectroscopy.

We began studying the solvation of lithium amides with $N,N,N',N'$-tetramethylhydrazinediamine (TMEDA) during the course of kinetic analyses of $N,N'$-dimethylhydrazone metalations by LDA. The spectroscopy clearly shows that LDA exists as a cyclic dimer in neat TMEDA. Moreover, a combination of spectroscopic, computational, and kinetic data support dimer 8 being labile (relative to THF) $^7\text{Li}$ linkages rather than the anticipated doubly chelated dimer 9.

This result, taken in conjunction with an extensive survey of the literature of TMEDA,$^{33}$ led to the suggestion that TMEDA-mediated deaggregations may be more a consequence of the instability of the solvated oligomers than the stability of the monomers. A preliminary test of this idea using $^{[6\text{Li},^{15}\text{N}]}\text{LiHMDS}$ proved provocative (Scheme II). Treatment of lithium hexamethyldisilazide (LiHMDS) with 5.0 equiv of THF affords exclusively dimer 10. LiHMDS in the presence of 5.0 equiv of TMEDA affords exclusively monomer 11. Contrary to a preponderance of conventional wisdom, a competition with equimolar quantities of THF and TMEDA affords exclusively (THF-solvated) dimer rather than monomer. Thus, TMEDA competes poorly with THF for coordination sites on LiHMDS. Moreover, the observable deaggregation in TMEDA/pentane does not necessarily result from a strong metal–ligand interaction.$^{34}$ We shall describe further evidence below that the highly revealing NMR spectroscopy of lithium dialkylamides promises to shed light on issues of organolithium aggregation and solvation in a general sense.

The discussion of simple equilibria is concluded aptly with some exciting new results from the laboratory of Kenji Koga pertaining to the structures of chiral lithium amides.$^{35}$ $^6\text{Li}$ and $^{15}\text{N}$ NMR spectroscopic analyses of $^{[6\text{Li},^{12}\text{N}]}_{12}$ reveal solvent-dependent structure changes that appear to correlate with deprotonation enantioselectivities. Dimer 13 is the only observable form in toluene or ether/toluene, while monomer 14 predominates.

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inates in THF, DME, or solvent mixtures containing HMPA. Of special note, the internal ligation by the pendant piperidine is retained in both 13 and 14 as evidenced by a small (2 Hz) coupling to the isotopically labeled piperidine moiety. The use of labeled amines to study internal ligation will certainly find applications in other areas of organolithium chemistry. The contrasting insights into chelation provided by lithium amide–TMEDA solvates and these chiral amides are also curious. The chelate effect continues to present interesting challenges to the mechanistically inclined.4

II. Complex Equilibria

HMPA-Solvated Lithium Amides. Despite its extreme carcinogenicity, hexamethylphosphoramide (HMPA; 15) remains the solvent of choice for enhancing organolithium reactivities; lithium amides are no exception.66 Recent investigations of the influence of HMPA on the structures of lithium amides have been especially illuminating. For example, Jackman and co-workers found that treatment of doubly labeled lithium anilides with HMPA affords mixtures of the anticipated monomers as well as triple ions of general structure 16.15 They made the astute observation that the factors often said to promote deaggregation also promote triple ion formation. Although triple ions are mentioned infrequently in the organolithium literature,39 analogies

with other main group “ate” complexes38 suggest that their relative obscurity is temporary.

In 1989, the groups of Reich39 and Snaith40 reported the first examples of two-bond Li–31P coupling by 6Li, 7Li, and 31P NMR spectroscopy, providing a view of lithium ion solvation of unparalleled clarity and importance. As applied to lithium amides, the 6Li–16N–31P combination constitutes a highly effective triple-labeling method. For example, [6Li,16N]LDA in THF with added HMPA is shown to undergo a serial solvation of the dimer (Scheme III) to give mixed solvate 17 and disolvate 18.22 Neither further solvation nor deaggregation occurs with excess HMPA. The asymmetry of 17 provided a means to exclude a cyclic trimer prior to the development of the 15N zero-quantum NMR method.29 The absence of a tetrasolvated dimer suggests that hinderedamide dimers do not readily attain tetrahedral coordination at lithium.

Surprised by the failure of HMPA to deaggregate LDA, we studied the influence of HMPA on the LiTMP

monomer–dimer equilibrium. We surmised that addition of HMPA would shift the equilibrium completely to monomer. In fact, addition of HMPA to [^6Li,^15N]LiTMP in THF/pentane affords the bewildering distribution of species shown in Scheme IV. Tetrasolvated dimer 23, disolvated monomer 22, and tetrascovatal triple ion 26 are the observable forms in the limit of excess HMPA. Such oddities as open dimer 24, triple ions 25 and 26, and tetrasolvated dimer 23 are especially noteworthy. (Recall that the analogous tetrascovate of dimeric LDA is not observable.) Most importantly, contrary to our original supposition, HMPA does not substantially deaggregate LiTMP.

The failure of HMPA to deaggregate LDA or LiTMP prompted us to investigate its influence on the monomer–dimer mixture of LiHMDS in THF solution. The overall structure assignments are illustrated in Scheme V. The parallels of LiHMDS and LiTMP in THF/HMPA mixtures are striking. The primary difference is that triple ion 33a is observed in place of a LiHMDS open dimer analogous to 24. Once again, we find that HMPA does not appreciably deaggregate LiHMDS.

Although the assignments in Scheme V were discerned from one-dimensional NMR spectroscopic methods with the aid to single frequency decouplings, the need for a more efficient two-dimensional analog was evident. ^6Li–^15N heteronuclear multiple quantum correlation (HMOC) spectroscopy affords the ^6Li–^15N resonance correlations in a single experiment (Figure 2). The pulse sequence is the same as that used by Günther and co-workers for ^6Li–^13C correlation spectroscopy. Improved resolution and decreased overall spectrometer time provided substantial advantages relative to the one-dimensional methods. The analogous ^6Li–^31P HMOC spectroscopy was used to determine ^6Li–^31P resonance correlations.

**Lithium Amide–LiX Mixed Aggregates.** It is now fully established that lithium salts generated during the course of an organolithium reaction can profoundly

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(41) ^6Li–^15N heteronuclear multiple quantum correlation spectroscopy was first evaluated using LiTMP–LiX mixed aggregates that had been characterized previously: Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. Magn. Reson. Chem. 1992, 30, 855.


influence structure and reactivity by virtue of mixed aggregate formation. However, mixed aggregates have been well characterized on only a few occasions. The 6Li-15N double labeling methods offer opportunities to investigate mixed aggregation in detail.

Kinetic studies of lithium diphenylamide (Ph2NLi) N-alkylation revealed evidence of autocatalysis by LiBr, prompting us to investigate the structure of [6Li,15N]-Ph2NLi with added [6Li]LiBr. At low THF concentration, [6Li,15N]Ph2NLi exists as a disolvated dimer. Addition of 1.0 equiv of [6Li]LiBr affords mixed dimer 35 quantitatively. The N-Li-N connectivity of 35 can be gleaned from the 6Li-15N coupling patterns. Rapid THF exchange precludes direct spectroscopic detection of two discrete lithium resonances for 35; the unsymmetrical solvation is based on colligative titration data. The placement of the bromide ion is based on analogy with the homonuclear amide dimers. At elevated THF concentrations, both dimer 34 and mixed dimer 35 appear to be converted to THF-solvated monomer 36. Unfortunately, loss of 6Li-15N coupling renders the monomer assignment tentative.

Interestingly, all three structural forms were found to be kinetically reactive toward n-butyl bromide.

In 1984, Corey and Gross reported that remarkable improvements in E/Z enolization selectivities are obtained when an extremely hindered lithium di-tert-alkylamide base is used in the presence of chlorotrimethylsilane to trap the enolate as it forms. Although explanations for E/Z enolization selectivities are typically couched in terms of competing thermodynamic and kinetic control, we suspected that mixed aggregation effects might be important. We addressed the influence of lithium enolates and lithium halides on the structure and reactivity of lithium amides using a combination of methods. Stereochemical studies of 3-pentanone enolization by LDA uncovered little evidence of intervening LDA-lithium enolate mixed aggregates. In contrast, a substantial influence of lithium halides on the E/Z enolization selectivity was detected. Parallel spectroscopic studies of mixed aggregate revealed an apparent structure-reactivity correlation. [6Li,15N]LDA fails to form mixed aggregates with unhindered lithium enolates such as [6Li]cyclohexenolate and forms mixed aggregates with hindered enolates reluctantly. However, [6Li,15N]LDA readily forms both 2:1 and 1:1 mixed aggregates with [6Li]LiCl and [6Li]LiBr (eq 4).

\[
\begin{align*}
\text{EIZ} & \quad \text{LiX} \\
\text{X} & \quad \text{Cl, Br, but not OR} \\
\text{X} & \quad \text{Cl, Br, and OR}
\end{align*}
\]

Enolization stereochemical studies using LiTMP suggested that both LiTMP-lithium halide and LiTMP-lithium enolate mixed aggregates may strongly influence LiTMP reactivity. Spectroscopic studies of [6Li,15N]LiTMP in the presence of lithium halides and lithium enolates revealed mixed aggregates of varying stoichiometry and conformational preference (Scheme VI). Although both lithium enolates and lithium halides (LiBr and LiCl) afford the 2:1 and 1:1 mixed aggregates (e.g., 39-41 and 42, respectively), only lithium cyclohexenolate forms a detectable 2:2 mixed aggregate (e.g., 43). The hindered enolate derived from disopropyl ketone, on the other hand, affords a 1:1 mixture aggregate to the exclusion of all other forms.

Conclusions

Organolithium reagents display a rich structural chemistry that is proving to be as complex and interesting as that observed for any of the transition elements. The lithium amides offer an excellent combination of synthetic utility, high kinetic reactivity,
and thermal stability. The $^6$Li–$^{15}$N double labeling study offers a view of metal ion solvation and aggregation that is beginning to impact on areas beyond traditional organolithium chemistry. As organolithium chemistry emerges as a legitimate subdiscipline of coordination chemistry, longstanding empirically determined relationships of aggregation state and solvent donicity are beginning to be replaced by working models founded upon firmly established organolithium solution structures. One of the goals of ongoing rate and mechanism studies is to more precisely define the role of solvation and aggregation in determining organolithium reactivity. I hope to present a detailed Account of lithium dialkyamide structure–reactivity relationships in the not-so-distant future.

I am deeply indebted to my talented co-workers for their skill, enthusiasm, and dedication. I am also grateful to colleagues and to Aidan Harrison and David Fuller of our NMR facility for stimulating discussions and valuable contributions. The work was supported by the National Institutes of Health. I also acknowledge the National Science Foundation Instrumentation Program (CHE 7904825 and PCM 8018643), the National Institutes of Health (RR02002), and IBM for support of the Cornell Nuclear Magnetic Resonance Facility.