Amine-Chelated Aryllithium Reagents—Structure and Dynamics

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Abstract: Multinuclear NMR studies of five-membered-ring amine chelated aryllithium reagents 2-lithio-\(N,N\)-dimethylbenzylamine (1), the diethylamine and diisopropylamine analogues (2, 3), and the \(o\)-methoxy analogue (4), isotopically enriched in \(^{6}\)Li and \(^{15}\)N, have provided a detailed picture of the solution structures in ethereal solvents (usually in mixtures of THF and dimethyl ether, ether, and 2,5-dimethyltetrahydrofuran). The effect of cosolvents such as TMEDA, PMDTA, and HMPA has also been determined. All compounds are strongly chelated, and the chelation is not disrupted by these cosolvents. Reagents 1, 2, and 3 are dimeric in solvents containing a large fraction of THF. Below \(-120^\circ\)C, three chelation isomers of the dimers are detectable by NMR spectroscopy: one (A) with both nitrogens coordinated to one lithium of the dimer, and two (B and C), in which each lithium bears one chelating group. Dynamic NMR studies have provided rates and activation energies for the interconversion of the 1-A, 1-B, and 1-C isomers. They interconvert either by simple ring rotation, which interconverts B and C, or by amine decoordination (probably associative, \(\Delta G^\circ_{\text{assoc}} = 8.5\) kcal/mol), which can interconvert all of the isomers. The dimers of 1 are thermodynamically more stable than those of model systems such as phenyllithium, \(o\)-tolyllithium, or 2-isoamylphenyllithium (5, \(\Delta G^\circ \geq 3.3\) kcal/mol). They are not detectably deaggregated by TMEDA or PMDTA, although HMPA causes partial deaggregation. The dimers are also more robust kinetically with rates of interaggregate exchange, measured by DNMR line shape analysis of the C−Li signal, orders of magnitude smaller than those of models (\(\Delta G^\circ \geq 4.4\) kcal/mol). Similarly, the mixed dimer of 1 and phenyllithium, 13, is kinetically more stable than the phenyllithium dimer by \(>2.2\) kcal/mol. X-ray crystal structures of the TMEDA solvate of 1-A and the THF solvate of 3-B showed them to be dimeric and chelated in the solid state as well. Compound 4, which has a methoxy group ortho to the C−Li group, differs from the others in being only partially dimeric in THF, presumably for steric reasons. This compound is fully deaggregated by 1 equiv of HMPA. Excess HMPA leads to the formation of ca. 15% of a triple ion (4-T) in which both nitrogens appear to be chelated to the central lithium.

Introduction

The recognition by Hauser in 1963\(^1\) that the dimethylaminoethyl group could facilitate the metalation of otherwise unreactive ortho aryl hydrogens (e.g., to form 1 from \(N,N\)-dimethylbenzylamine) provided the impetus for a large body of work aimed at exploiting the synthetic utility of chelating effects and understanding the role chelation plays in the formation, structures, and reactions of such lithium reagents. Aryl, vinyl, and even unactivated alkyl hydrogens can be metalated when suitable chelation is provided.\(^{2a,3a,4a,5}\)

\(\text{̂}\) Inquiries about the X-ray crystallographic studies should be directed to this author.


little detailed mechanistic and structural information on the hundreds of organolithium reagents for which chelated structures have been proposed.12a–d,47b,13a,14,15a–e

This paper deals with the solution structure and dynamics of chelated lithium reagents 1–4, as well as model system 5. Previous workers have reported solution NMR studies14a,16 as well as solid-state X-ray studies14ab of compound 1 and the more soluble p-methyl analogue 6. Analogues with many other metals including B,17a Mg,1a Al,17b Sn,18 and Zn19 have also been investigated. The X-ray structure of crystals of 1 grown from ether–hexane showed it to be tetrmeric,14e resembling the structure of PhLi,18,19 except that the amino group replaces the coordinated ether molecule on each Li atom. Solution studies were performed on the methyl analogue 6.14a In toluene or diethyl ether, the tetrmeric structure and N-chelation of 6 remain intact, as evident from the ipso carbon signal at 176.0 ppm with a line width corresponding to about a 12 Hz 13C–Li(13C–Li) coupling and diastereotopic methyl signals of the NM22 groups. Upon addition of a small amount of THF (1 equiv per Li) to a toluene or ether solution of tetrmeric 6, a new species was formed with an ipso carbon signal (septet at 189.2 ppm, 1/J(13C–Li) = 20 Hz) which suggested a dimeric structure.19,20 Since the NM22 13C signals were not diastereotopic and had a chemical shift much like those of N,N-dimethylbenzylamine, van Koten and co-workers suggested that in THF the intramolecular N–Li coordination has been broken.14a They drew similar conclusions about the effect of TMEDA. We report here


(20) (a) The U(13C–Li) coupling is typically on the order of 10–14 Hz in tetramers, 20 Hz in dimers, and 40 Hz in monomers.15a

Our investigation was aimed at probing the existence and strength of chelation effects, as well as effects on reactivity patterns. Impetus was provided by several observations. First was the discovery that a propargyllithium reagent 8 with a well-placed 2-pyridyl group was only partially chelated in THF,15c analogous to the report that 6 easily lost chelation when a strong donor solvent such as THF or TMEDA was added.14 Similarly, the lithium reagent 9 had an allenyl structure in THF solution,15c even though the propargyl structure (10) could enjoy the benefits of bidentate chelation of a type frequently proposed in the literature.10,13a,21 These observations cast doubt on the common assumption that lithium reagents with suitably placed pendant basic groups were normally chelated.

Results and Discussion

In addition to reexamining the previously studied Hauser compound 1, we also studied the diethylamino (2) and isopropylmethylmamino (3) analogues. We were unable to address the question of chelation in the triple ion of 1 (1-T) because not enough was formed. Since 2-methoxophenyllithium and 2,6-dimethoxophenyllithium give unusually large amounts of triple ions in THF–HMPA solution,15d we examined the o-methoxy analogue 4 to address the question of chelation in the triple ion 4-T. We will report separately on the pyrroldine analogue of 1, compound 7, as well as the higher homologues with longer side chains and the analogous ether-chelated systems.15b

Syntheses. Crystalline samples of 1 were prepared as reported1b by metalating N,N-dimethylbenzylamine with n-BuLi in ether at room temperature. Compound 4 was available by metalation of 3-methoxy-N,N-dimethylbenzylamine,1b allowing

studies of 1 and several analogues at much lower temperatures and using isotopically enriched materials which show that chelation remains intact under all conditions.15a,b

![Image](https://example.com/image1)

![Image](https://example.com/image2)

![Image](https://example.com/image3)
the mixture to equilibrate with HMPA and quenching with trimethylbromostannane. The pure lithium reagent was then formed by Sn-Li exchange with n-BuLi. Compounds 2\(^a\) and 3 could not be cleanly prepared by ortho metalation, and thus were prepared from the \(\alpha\)-trimethylstannylbenzenes. These were available by reaction of 2-bromobenzyl bromide with the appropriate secondary amine, conversion to the lithium reagents by Li/Br exchange, followed by stannylation. The bromo compounds were not used directly to prepare lithium reagents for spectroscopic studies because of interference from LiBr (if \(\epsilon\)-BuLi was used) or 1-bromobutane (if \(\alpha\)-or \(\rho\)-BuLi was used). To facilitate NMR studies, the \(^6\)Li-enriched isotopomers of all compounds were prepared from the \(^{1}\)Li-enriched isotopomers of 1, 2, and 4 were prepared from the \(\alpha\)-halobenzoic acids as exemplified in Scheme 1 for the precursor of 2.

NMR studies were performed in mixtures of THF, diethyl ether, 2,5-dimethyltetrahydrofuran, and/or dimethyl ether to allow NMR studies at temperatures as low as \(-155^\circ\)C. Dimethyl ether is slightly less strongly solvating than THF; ether is much less so.

**Model Compounds.** Before discussing the results with the chelated compounds 1–4, we briefly discuss some model systems. Phenyllithium has been extensively studied, both in solution\(^{26,27}\) and in the solid state.\(^{18,25–27}\) It exists as a mixture of monomer and dimer, with a \(K_{eq}\) for association of 30–40 M\(^{-1}\) in THF at \(-110^\circ\)C,\(^{26,23}\) and 50 M\(^{-1}\) in 4:1 THF/ether at \(-130^\circ\)C. \(\alpha\)-Tolylithium is slightly less associated, with \(K_{eq} = 1.7\) M\(^{-1}\) in 4:1 THF/ether at \(-125^\circ\)C (Figure 1). A system which better models the steric effect of an ortho-alkyl substituent, 2-isomethyl-3-lithio-1,5-dimethoxypentane (5), is monomeric within the limits of detection. The small signal at \(\delta 1.9\) in the \(^6\)Li NMR spectrum of 5 is the only signal which could conceivably be assigned to the dimer. It is 5% of the area of the monomer peak, so the compound is >95% monomeric, and the dimer association constant is \(<0.23\) M\(^{-1}\). Like PhLi, 5 complexes relatively weakly with TMEDA but quantitatively with PDMTDA (>99% complex at 1 equiv in 3:2 THF/ether),\(^{28}\) so the failure of some of the chelated compounds to complex effectively cannot be ascribed to steric effects of an ortho substituent. In fact, qualitatively the association equilibrium for PDMTDA and 5 is even higher than that for PhLi, probably the result of the presence of more dimer in solutions of PhLi.\(^{15c}\)

**Solution Structures of the Chelated Organolithium Reagents.** Figure 2 shows \(^7\)Li, \(^6\)Li, and \(^15\)N NMR spectra of a sample of 1. At low temperatures, four signals (which coalesced to one peak above \(-100^\circ\)C. Figure 2c–e) were observed in the \(^6\)Li NMR spectra. The ratio of the signals was concentration independent, so they do not correspond to different aggregates. The signals marked A and A’ were always present in a 1:1 ratio. One of them became a triplet in the \(^{15}\)N and \(^6\)Li doubly labeled compound (Figure 2c) and was thus coupled to two \(^{15}\)N nuclei.\(^{28,29,30}\) The other remained a singlet with no coupling to \(^{15}\)N. For the isomeric B and C, each Li was coupled to one nitrogen. The \(^{15}\)N signals in the \(^6\)Li–\(^{15}\)N double-labeled isotopomer were not resolved. Rather, the spectrum showed a prominent 1:1:1 triplet (presumably isomers A and B superimposed) as well as a slightly offset smaller triplet (isomer C) from coupling of each nitrogen to a single \(^6\)Li. These data strongly support the assignment to A and the B/C pair, as shown in Scheme 2, but do not allow the B and C isomers to be distinguished.\(^{31}\) We will refer to these as shown in Scheme 2.

**Figure 1.** \(^6\)Li NMR spectra of PhLi (0.2 M, 4:1 THF/CH\(_2\)Cl\(_2\), \(-130^\circ\)C), \(\alpha\)-TolLi (0.16 M, 4:1 THF/CH\(_2\)Cl\(_2\), \(-125^\circ\)C), and 5 (0.11 M, 3:2 THF/CH\(_2\)Cl\(_2\), \(-126^\circ\)C). The \(K_{eq}\) values are not strictly comparable because of small differences in the solvent composition and temperature.

**Scheme 1.** Synthesis of \(^{15}\)N-Enriched 2-Trimethylstannyl-N,N-diethylbenzylamine

![Proposed Structures of the Dimers of 1](image)

![Figure 2.](image)
The 13 C Chemical Shifts of ArLi

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<th>Compound</th>
<th>solvent</th>
<th>temp (°C)</th>
<th>δ C-1 (J_{CLi})</th>
<th>δ C-2</th>
<th>δ C-3</th>
<th>δ C-4</th>
<th>δ C-5</th>
<th>δ C-6</th>
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<td>a</td>
<td>-126</td>
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<td>54.1</td>
<td>32</td>
<td>54.1</td>
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* 45:25:30 THF/Me₂O/ether. ⁺ 3:2:1 THF/Me₂O/ether. ⁺⁺ Signal not found. ⁺⁺⁺ 3:2 THF/ether. ⁺⁺⁺⁺ Splitting not resolved; coupling estimated from simulated spectra. / Signal is broad at -127° C, probably due to intramolecular exchange. ⁺⁺⁺⁺⁺ Assignments were not made for chemical shifts marked with asterisks.

Figure 3. Li NMR spectra of ~0.16 M ArLi: 1 (Li, -136° C, 3:2:1 THF/Me₂O/ether); 2 and 7 (Li, -120° C, 3:2 THF/ether); 3 (Li, -120° C, 3:2 THF/ether) 4 (Li, -130° C, 3:2 THF/ether).

with the NMR signal assignments as in Figures 2 and 3, but we will defer discussion of the B/C distinction until after we have considered the spectroscopic properties of all the compounds in more detail.

Other spectroscopic data supported the assignments for 1 made above. The 13 C NMR spectra showed three sets of signals in the same ratio as the Li signals for A, B, and C (Table 1; the minor isomer C was not resolved for all of the carbons). The NMe₂ 13 C signals were diastereotopic, with a Δδ of ca. 4 ppm. Two distinct C–Li signals were observed at -135° C, each a 1:2:3:2:1 quintet with J_{C-Li} = 7.0 Hz from 13 C coupled to two 6 Li nuclei, consistent with a four-center dimer structure. The signals coalesced to a single quintet by -60° C.

The 6 Li NMR spectra of all of the ortho metalated aryllithiums are shown in Figure 3. The assignments for 2 were confirmed by NMR studies of the 15 N–6 Li doubly labeled compound (Figure 4). For 3, the chemical shifts showed sufficient consistency that we have assigned those similarly. The relative amounts of the A, B, and C isomers differed substantially as the N-substituents were changed, with A as the major isomer for 1, B as the major isomer for 2 and 7, and C as the major isomer for 3.

Compound 4 is qualitatively different from the others. The α-methoxy substituent has destabilized the dimer, so that now there are approximately equal amounts of monomer and dimer. This assignment was confirmed by a plot of log [monomer] vs log [dimer], which had a slope of 2.1.28 The 15 N isotopomer showed Li–N coupling to a single nitrogen for both signals, so the monomer and dimer are both chelated, and the dimer is of the B/C type (Figure 5).

The 13 C chemical shifts of the lithium reagents are presented in Table 1, together with the shifts of the tetramer, dimer, and monomer of phenyllithium15e and 2-methoxyphenyllithium (11).32 Particularly the C–Li carbon (C-1) chemical shift of 186–189 ppm is strongly supportive of dimeric structures for 1–3 in solution, since in related monomers and tetramers this carbon appears at ca. 195 and 175 ppm, respectively.15e,33 This assignment is supported by the C–Li coupling observed (1:2:2:1:20:20:20) at -135° C, with a C–Li coupling of 7.1 Hz.

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Dimers of the trimer, and/or dimer-isomers) and interaggregate exchange (dimer-loss of Li coupling to \( ^{13} \)C or \( ^{15} \)N).

changes:4c,d molecular processes which might be responsible for these meric PMDTA complex.32 Like PhLi, toluene solvate, the dimeric TMEDA complex, and the mono-

11

involving the chelating groups (e.g., interconversion of NMR spectra. These are of two types: intraaggregate processes reagents show dynamic effects in their variable-temperature

\[ \text{Figure 5.} \text{ HMPA titration of 0.21 M} \ ^{6}\text{Li}^{15}\text{N-labeled 4 in 3:2 THF/ether at } -127 \ ^{\circ}\text{C}. \]

\[ \text{Scheme 3.} \text{ Key Structural Features of the A, B, and C Dimers of 1 (S = solvent)} \]

3:2:1 quintet in the \( ^{6}\)Li compounds). The \( ^{13}\)C chemical shifts of the methoxy analogue of 1, compound 4, are more properly compared to those of 11. The available data are for the tetrameric toluene solvate, the dimeric TMEDA complex, and the monomeric PMDTA complex.32 Like PhLi, 11 shows a progression of downfield shifts for the C—Li carbon between tetramer, dimer, and monomer. Compound 4 is anomalous, with the dimer shift downfield of the monomer by 6.6 ppm. Perhaps the \( \omega \)-methoxy substituent is hindering solvation of the dimer (see structures A and C in Scheme 3), resulting in an abnormally strongly polarized C—Li bond in the dimer, and consequently a larger paramagnetic shift.13c,25

Variable-Temperature NMR Studies. All of the lithium reagents show dynamic effects in their variable-temperature NMR spectra. These are of two types: intraaggregate processes involving the chelating groups (e.g., interconversion of A/B/C isomers) and interaggregate exchange (dimer—tetramer, dimer—trimer, and/or dimer—monomer exchange, detected mainly by loss of Li coupling to \( ^{13}\)C or \( ^{15}\)N).

(i) Intraaggregate Exchange. Above \(-135 \ ^{\circ}\text{C}, the A, B, and C isomers of 1 undergo a dynamic process detectable by \( ^{6}\)Li, \( ^{7}\)Li, \( ^{13}\)C, and \( ^{15}\)N NMR spectroscopy. Figure 6 shows that the four signals in the \( ^{6}\)Li NMR spectrum coalesce to a single peak between \(-122 \) and \(-88 \ ^{\circ}\text{C}. There are several discrete molecular processes which might be responsible for these changes:4c,d

1. Dissociation of the B and C isomers to monomers and recombination. This would interconvert isomers B and C and cause loss of C—Li coupling. Isomer A cannot directly fragment to two chelated monomers but would have to isomerize to B first.
2. Decoordination of both amino groups and ring rotation. This would interconvert all signals.
3. Decoordination of one of the dimethylamino groups.
4. Ring rotation around the C\(^{1}\)—C\(^{1}\) axis faster than recoordination. This would interconvert any isomer to any of the others but would not directly interconvert the A and A’ signals.

3-b) Ring rotation slower than recoordination. This would allow interconversion of A with B, but neither A nor B could be interconverted with C by this process alone.

4) Rotation of one phenyl group about the C\(^{1}\)—C’ axis without Li—N decoordination. This mode of isomerization, which requires little more than dissociation of a solvent molecule, would allow only interconversion of isomers B and C.

Mechanism (1) can be ruled out on the basis of several kinds of NMR data. The C—Li coupling for C\(^{1}\) is not lost until temperatures above \(-35 \ ^{\circ}\text{C} \) (vide infra), an observation also made by van Koten and co-workers for a THF/toluene solution of 6.34 In the \( ^{15}\)N NMR study shown in Figure 2d,e, the \( ^{6}\)Li signals of I-A, I-B, and I-C have coalesced to a broad singlet at \(-55 \ ^{\circ}\text{C}, but the \( ^{15}\)N signal, which was a 1:1:1 triplet at low temperature, is now a 1:2:3:2:1 quintet, characteristic of a nitrogen equally coupled to two \(^{6}\)Li nuclei. The dimethylamino groups are rapidly exchanging between all sites, but dissociation to monomers or association to tetramers is slow on the NMR time scale. At \(-29 \ ^{\circ}\text{C}, \ ^{6}\text{Li}—^{15}\text{N} coupling is lost, so intermolecular exchange has now become fast, and process (1) is occurring.

Mechanism (2) would allow all four signals to interconvert with each other. The direct exchange between the A and A’ signals of I-A was ruled out by a \(^{6}\)Li EXSY experiment.34 At a mixing time of 0.05 s at \(-131 \ ^{\circ}\text{C}, cross-peaks were detected between the A/A’ signals and B signals of I, as well as between signals B and C. No cross-peaks were detected between the A and A’ signals, thus ruling out mechanism (2). Cross-peaks were also not detected between A and C, either because of the small size of the C signal or because of the slow rate of exchange between A/A’ and C.


The exclusive operation of either (3-b) or (4) can be ruled out for 1 because each would require selective coalescences: for (3-b) only between B and C without involving A, and for (4) only between A and B without involving C. Thus, if one of these processes is occurring, it cannot be the only one. We are thus left with (3-a) or both (3-b) and (4) operating at comparable rates.

A four-spin DNMR simulation of the variable-temperature NMR spectra in Figure 6 was performed using the exchange matrix in Figure 7.15,35 Three independent rate constants were optimized, \( k_{AB}, k_{BC}, \) and \( k_{AC} \). A satisfactory line fit could be achieved only when no exchange between the A and A’ signals was permitted, confirming that random exchanges are not involved (mechanisms 1 and 2).

The changes in line shape are dominated by the A/B exchange, which is reasonable since these are the major isomers and this process requires only minimal rearrangement of the structure (movement of a dimethylamino group from one lithium to another). The B/C exchange appears to be slower than the A/B exchange but cannot be defined very accurately because of the small intensity of the C signal, its nearness to the signal for B, and the presence of a small impurity on top of the signal for C. This is in contrast to 2, which shows \( k_{BC} \) larger than \( k_{AB} \) or \( k_{AC} \) (vide infra). The spectra can be adequately simulated with a small or no A/C exchange.

The temperature dependence of \( k_{AB} \) is presented in Figure 8. The substantial negative entropy of activation for the process (−18 eu) suggests an associative process for the isomerization, e.g., a mechanism in which a solvent molecule coordinates to one of the lithiums, followed by expulsion of the chelating group.

The diethylamino analogue 2 also showed the A, B, and C isomers (Figure 3), but the dynamic processes were more complex than for 1. Relevant \(^{6}\)Li NMR spectra are shown in Figure 4 for the \(^{6}\)Li/\(^{11}\)B-labeled isotope. The −128 °C spectrum was very similar to the −135 °C spectrum for 1 in Figure 2, except that the signal assigned to 2-B was quite broad. Lowering the temperature to −159 °C caused decoalescence of this signal into three doublets (labeled B’, B”, and B”). No similar changes were seen for 1. A plausible assignment for this dynamic process, which has an activation energy of around 6.5 kcal/mol, is a restricted rotation around the N-ethyl groups.36 If this is correct, it supports the isomer assignment we have made to B, which features a close approach of the diethylamino group to the ortho proton of the other aryl ring (Scheme 3). The A and A’ signals also broaden substantially below −145 °C, and there may be an incipient decoalescence for these signals as well.

As the temperature was raised above −128 °C, another interesting phenomenon was observed. The signals of 2-B and 2-C coalesced and at −103 °C formed an \(^{13}\)N coupled doublet. In contrast to the behavior of 1, the 2-B and 2-C isomers are substantially more labile than the 2-A isomer. Process (4), rotation around the C1−C2 axis to interconvert B and C without involving A, is faster than the others. At −103 °C and higher, 2-A begins to exchange with the coalesced 2-B/C signals, as for 1.

(ii) Interggregate Exchange. Aggregate exchange can be addressed using the \(^{13}\)C NMR signal of the C−Li carbon.13d This carbon appears as one or more 1:2:3:2:1 quintets at low temperature, which coalesces first to a single quintet (A/B/C exchange), and then to a singlet at higher temperatures, signaling the onset of interaggregate exchange.

The loss of C–Li coupling can occur by a number of mechanisms. For example:

(1) An associative process in which two dimers form a tetramer.

(2) An associative process in which a low steady-state concentration of monomers (or an adventitious Li−X salt) reacts with dimers to form transient trimers (or mixed trimers).

(3) A dissociation of dimers to monomers.

(4) A process in which a four-center dimer isomerizes to a triple ion (Ar−Li−Ar Li+) followed by rapid intermolecular exchange of the free lithium cation. Associative mechanisms (1) and (2) would show concentration-dependent rates, first-order increase for the tetramer mechanism, and half-order for the trimer mechanism. Mechanisms (3) and probably also (4) would give concentration-independent rates. We have determined the concentration dependence of the exchange rate for 1. Experiments were performed on two samples differing in concentration by a factor of 4 (0.7 and 0.18 M) in 3:2 THF/ether solvent.

Simulations were performed using the exchange matrix of Figure 9,15 which corresponds to a random exchange mechanism. The exchange matrix was identical to one developed for a tetramer exchange mechanism57 and differs only by a scaling factor of 1.5 for a trimer exchange mechanism. In the random and tetramer mechanism, 2/3 of encounters lead to exchange,

\[ k_{AB} = k_{BC} = k_{AC} = k_{AB} = k_{BC} = k_{AC} \]


(37) We thank Prof. Gideon Fraenkel for developing the exchange matrix for the exchange via tetraters.
while in the trimer mechanism only 4/9 of the encounters result in exchange of spins. The line shape of the coalescing 1:2:3:2:1 quintet of the dimer cannot be used to distinguish the exchange mechanisms. Rates are summarized in the graph of Figure 8. Activation energies (AG°) for loss of C—Li coupling were in the range of 12–13 kcal/mol (Figure 10).

The rate data obtained are shown as an Arrhenius plot in Figure 10. The sample with a factor of 4 higher concentration has rate constants a factor of 2.3 higher at −23 °C, and a factor of 2.4 higher at −38 °C. We conclude, therefore, that the process is associative; the numbers obtained fit best for the trimer mechanism (2), which predicts a factor of 2 rate increase for a factor 4 increase in concentration. Of course, a mixture of mechanisms (1) and (3) or (1) and (2) could also lead to the fractional order observed.

Effect of Cosolvents. (i) Effect of TMEDA and PMDTA.
We have examined the effect of TMEDA on the solution structures of 1 and 5. A 6Li NMR study of the addition of TMEDA to doubly labeled 1 is shown in Figure 11. The characteristic signals of the AB/C isomers were replaced by a single major pair of signals in a 1:1 ratio, one a singlet and the other a triplet from coupling to two 15N nuclei. These changes can be unambiguously interpreted in terms of conversion to a 1:1 complex 1-A-TMEDA. The dependence on concentration of TMEDA is first order (a plot of 1/[TMEDA]/1[A] vs [TMEDA] has a slope of 1.1), ruling out the alternative monodentate structure for the TMEDA complex of dimeric 6 in toluene proposed by van Koten and co-workers.14a

An equilibrium constant for the TMEDA association with 1 of Keq = 7.9 M−1 was measured. Thus, TMEDA effectively displaces THF and/or dimethyl ether in this system.38a One comparison is as follows. When the molar ratio of TMEDA to THF is 1:36 (1 equiv of TMEDA), the ratio of the TMEDA and THF complexes is 4:6. The actual effect is a factor of 2 higher since only about 50% of the material is the isomer 1-A capable of complexing TMEDA in a bidentate fashion. These conclusions are supported by the single-crystal X-ray structure (Figure 12) of the complex.39 The structure shares many of the features found in other aryllithium dimers.19 The central four-membered ring has the typical small Li–C–Li angles (67.3 and 67.8°) and large C–Li–C angles (110 and 115°). The Li bond lengths are shorter for the chelated amines (2.06 and 2.06 Å) than for the TMEDA (2.36 and 2.35 Å) and the constraint of intramolecular chelation also rotates the benzene rings from their normal orientation perpendicular to the central C2Li2 ring (as in the crystal structure of PhLi dimer39b) to an angle 24° off perpendicular (the angle between the planes of the two benzene rings is 48.9°).

The effect of PMDTA on 1 was almost identical to that of TMEDA (conversion to a complex 1-A-PMDTA) in which the
PMDTA coordinates in a bidentate fashion to the free lithium of 1-CH2. The two Li peaks in the NMR spectrum of 1-PMDTA were doubled due to stereoisomerism at the central nitrogen atom of the PMDTA. The association was significantly weaker, with a $K_{eq}$ of 2.2 for the PMDTA complex vs 7.9 for TMEDA. There was one small signal at $\delta$ = 2.2 in the 6Li NMR spectra at 4 equiv of PMDTA (ca. 7% of total RLi equivalents) which could be the mononeric PMDTA complex, but a secure identification was not made (5-PMDTA has a Li signal at $\delta$ 2.1 in 3:2 THF/ether, and PhLi-PMDTA has a Li signal at $\delta$ 2).

(ii) Effect of HMPA. We have studied the changes in solution structure of 1-4 after addition of HMPA. We hoped this would provide qualitative information about the electrophilic nature of the different lithium environments in the various structures, as well as about the curiously strong dimerization of these chelated organolithium reagents. Figure 13 shows four spectra from an HMPA titration of 1. The assignments we have made. At 0.5 equiv of HMPA, mono complexes of each of the chelation isomers 1-A, 1-B, and 1-C were identified. The A and C isomers have about twice the HMPA affinity of the B isomer. Some mono-HMPA complex of 1 monomer (1-M) is also present (doublet at $\delta$ 1.7). At 1 equiv of HMPA, bis-solvates of the B and C isomers of 1 can be detected (one HMPA on each lithium), whereas no bis-HMPA complex of A was detected for this or the other compounds. This is reasonable, since the presence of one coordinated HMPA must greatly reduce the electrophilicity of the lithium.

Above 1 equiv of HMPA, there is a progressive increase in the fraction 1-M(HMPA)$_2$ complex (which shows an apparent quartet at $\delta$ 1.5 in the 15N-labeled material due to approximately equal Li-P and Li-N coupling). Even at 3 equiv of HMPA, there are still significant amounts of the dimeric B and C bis-HMPA complexes. Thus, it is possible to break the dimers of 1, although not quantitatively. At all equivalents of HMPA (and throughout this study for all compounds investigated which could form a five-membered-ring nitrogen chelate), we saw no indication of any species where the nitrogen was not fully chelated. At higher equivalents of HMPA, there are small signals for a separated Li(HMPA)$_2$ species at $\delta$ = 0.4, which we believe are due to the triple ion 1-T. The carbon-bound lithium of the triple ion can barely be detected at $\delta$ 3.35, so no clear identification of 6Li--15N coupling could be made in the double-labeled compound.

The behavior on treatment of 2 with HMPA was similar to that observed for 1, which showed an increase in the fraction of 1-C of the mono-HMPA complexes (from 3:1 to 1:1 B:C), but then the bis-HMPA complexes favored 1-B again by about a 2:1 margin. The ratio of isomers for 2, which was 1:4:1 A:B:C in THF/ether, went to about 1:1:1 A:B:C for the mono-HMPA complexes and 0:3:1 A:B:C for the bis HMPA complexes.

Compound 3 showed another variation, with the 3-C mono- and bis-HMPA adds forming predominantly and lesser amount of the 3-A mono-HMPA complex. An interesting feature is that the 31P signals of the monomeric bis-HMPA complexes are diastereotopic (Figure 14), confirming that at $\angle$ 120 ° coordination and configurational inversion at both lithium and nitrogen are slow on the NMR time scale. The mono-HMPA complex of the monomer showed only a single HMPA signal, so the Li center is probably configurationally unstable as a result of fast dissociation of THF.

Compound 4 showed several interesting effects in its HMPA titration (Figure 5). In the early parts of the titration of the 15N--1Li-labeled compound, only the HMPA complex of the monomer was seen ($\delta$ 1.9, dd, J$_{LP}$ = 3.8, J$_{LN}$ = 2.2 Hz). Past 1 equiv of HMPA, free HMPA was observed, and bis-HMPA monomer signals appeared ($\delta$ 1.7, td, J$_{LP}$ = 2.9, J$_{LN}$ = 2.1 Hz). At no point was any dimer HMPA complex detected, in contrast to 1, 2, and 3, in which both dimer and monomer mono- and bis-HMPA complexes are formed prominently. Exceptionally well resolved 11C NMR spectra were obtained, and these allowed an examination of the effect of HMPA on C--Li $\delta$ and J values. The J$_{C--Li}$ decreased in magnitude from 12.6 Hz for the THF-complexed monomer to 11.5 Hz for the mono-HMPA complex and 9.7 Hz for the bis-HMPA complex. The chemical shift moved progressively downfield from $\delta$ 165.4 to 167.9 and 171.5 ppm as HMPA was added. Both effects are consistent with C--Li bond-weakening as HMPA coordinates to Li. The most interesting signal, however, was the internal lithium of the triple ion at $\delta$ 3.6, a well-defined triplet, with J$_{LP}$=15N = 1.6 Hz. Thus, the triple ion adopts the predicted chelated structure 4-T. Not even the presence of two strongly electron-donating Ph--ligands on Li breaks the chelation.

X-ray Crystal Structure of 3. Figure 15 shows the single crystal X-ray structure of the THF solvate of 3. According to the assignment we have made, 3 is mostly isomer C in solution (the ratio A:B:C is 3:1:6, but the X-ray structure is that of the B isomer. Presumably the minor isomer crystallized, but we cannot rule out that the assignments of the signals in the Li NMR spectrum (Figure 3) are incorrect. The NMR spectra of 3 are potentially more complicated than those of 1, 2, and 4 because of the possibility of multiple isomers due to the asymmetric center at nitrogen (see Figure 14).
The molecule occupies a crystallographic inversion center, and only one-half of the dimer is symmetry independent. The structure shows no unusual features compared to other aryllithiums, with normal N–Li (2.139(3) Å) and THF O–Li (1.939(3) Å) bond lengths. The two C–Li bonds are slightly different (2.186(3), 2.252(3) Å), with the shorter bond within the chelate ring (distortion in the direction of separating into two chelated monomers). The chelate bite angle C–Li–N is 98.62(11)°. The central C$_2$Li$_2$ ring has a C–Li–C angle of 113.05(11)° and a Li–C–Li angle of 66.95(11)°. The structure has several features of interest in the context of the B/C assignment. As found for the solid-state structure of 1-A•TMEDA (Figure 12), chelation causes the phenyl rings to be rotated from their normal orientation perpendicular to the central TMEDA plane, whereas 3-B and 7-B have the rings essentially coplanar by symmetry, but with this plane well off perpendicular to the C$_2$Li$_2$ plane (the angle is 32° in 3-B(THF)$_2$ and 38° in 7-B(THF)$_2$) [43]. Consequently, in A and C there are steric repulsions between the aryl ortho hydrogen and one of the solvent molecules on Li, whereas in B the solvent location is very open (Scheme 3). On the other hand, B suffers from steric interactions between this same hydrogen and one of the N-alkyl groups of the other aryl ring. This provides a rationale for the curious observation that, which is a 2:6:2 ratio of A:B:C in THF/ether, in 2,5-dimethyltetrahydrofuran/ether shows only a single isomer, with a chemical shift close to that of the peak assigned to the 2-B isomer in THF/ether. The larger solvent molecule can best be accommodated in the 2-B structure. (An alternative explanation could be that B is favored in the less polar solvent because it is the only isomer with no dipole moment.) On the other hand, the molecule with the largest N-alkyl groups, 3, is the only one in which isomer C is more populated than isomer B (Figure 3), because here B is maximally destabilized by the o-HN–R interaction. Along the same lines, the compound with the smallest N-alkyl groups, 7, shows only isomer B [42].

**Mixed Dimer of Phenyllithium and 1.** One of the most puzzling aspects of the chemistry of these chelated aryllithium reagents is the strong propensity to form dimers under conditions where nonchelated analogues are significantly or entirely monomeric (Figure 1). We therefore examined mixtures of 1 with PhLi to see whether mixed dimers formed, and how they behaved in solution. The spectra in Figure 16 show that a mixed dimer 13 is prominently formed. The 11C NMR signals of the phenyl portion are very close to those of PhLi dimer, and the remaining signals are very close to those of 1 [28]. The two lithiuns of the dimer are nonequivalent, with Li chemical shifts nearly identical to PhLi dimer and 1-B. As seen for the homodimer, amine decoordination is slow on the NMR time scale below −110 °C. The equilibrium constant for mixed dimer formation was $K_{eq} = 27$ at −131 °C. The statistical value would be $K_{eq} = 4$.

The favorable equilibrium constant for formation of the mixed dimer 13 allowed us to address the question of ring rotation about the C1–C1 axis, discussed above in connection with the 1-A/B/C interconversion. In a static structure, the two ortho and two meta carbons of the phenyl group in 13 should be diastereotopic. However, only a single set of signals could be detected for these carbons. Thus, either the ring rotation is still fast on the NMR time scale below −120 °C, or the signals are accidentally coincident.

A variable-temperature study of the mixed dimer (Figure 16) gave a remarkable series of spectra. A sequence of coalescences occurred on warming,

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(43) Even larger distortions toward coplanarity of the central C$_2$Li$_2$ and aryl rings in dimers have been observed for 8-(dimethylamino)-1-naphthyllithium, and 8-methoxy-1-naphthyllithium.
can be observed. Between −115 and −63 °C, the 1-A/B/C isomers coalesce into a single peak at 3.0 ppm. At a very similar rate, the two lithium signals of 13 coalesce to a signal at 2.5 ppm. Not easily observable in this sample is the coalescence of PhLi monomer and dimer which occurs at −100 to −75 °C. At −71 °C, the three signals correspond to the rapidly equilibrating 1-A/B/C isomers, the equilibrated 13 signal, and the average of PhLi monomer and dimer. Between −71 and −49 °C, PhLi begins to coalesce with the two signals of 13, suggesting that 13 is now undergoing dissociation to monomers. At −49 °C, the 1-A/B/C and 13/PhLi begin to average as 1 begins to exchange with the mixed dimer and the PhLi on the NMR time scale.

A complete line shape analysis of this system is not feasible because there are too many variables (>25) to establish them realistically from the data available: eight chemical shifts (four for 1, two for 13, two for PhLi), eight T1 values, and five independent populations for the lithium signals; and rate constants for interconversion of the 1-A/B/C isomers, equilibration of the lithium signals of 13, equilibration of PhLi with 13, equilibration of 1 with 13, and equilibration of PhLi dimer and monomer.

We have performed simulations with the following simplifying assumptions: (1) we have ignored 1-C (the peak is small, hidden under the downfield mixed dimer peak D, and quickly coalesces with 1-B) and used only one rate constant, kAB, for the intraaggregate exchange of 1; (2) the PhLi monomer signal and the exchange between PhLi dimer and monomer was ignored (since in this solvent mixture there is <20% monomer, this exchange causes only a small degree of broadening of (PhLi)2 around −80 to −100 °C); (3) only the D signal of the mixed dimer 13 was allowed to exchange with 1-B (direct dissociation of 1-A would require simultaneous breaking of both C−Li and N−Li bonds), and only the D’ signal of the mixed dimer was allowed to exchange with PhLi dimer (these assumptions would be true if the exchange was dissociative); (4) all peaks were assumed to have the same natural line width, 12 Hz (except for PhLi dimer at −80 and −95 °C, for which the line widths were 7 and 9 Hz). This is reasonable since all are ArLi dimers, with similar rates of molecular motion. The line shapes were simulated using the exchange matrix of Figure 17. This simulation used four rate constants, kAB (the exchange between 1-A and 1-B), kBB (exchange between the two peaks of the mixed dimer), kBD (the exchange between 1-B and the D peak of the mixed dimer 13), and kDP (the rate of exchange between PhLi and the D’ peak of the mixed dimer).

The high quality of the simulation (Figure 18) confirms that the rather complex changes in line shape have been correctly assigned and that the assumptions made are reasonable ones. The two rate constants for intra-aggregate exchange, kAB and kBB, are almost identical throughout the temperature range, and these rates are 100–500 times as fast as the exchange between 1-B and the mixed dimer 13 (kBD). The exchange between PhLi and 13 was marginally faster than exchange between 13 and 1-B. Both of the interaggregate exchanges were just beginning to cause significant broadening at the highest temperature studied, so the rate data are less accurate than for the intramolecular exchanges. Thus, the unusually large ΔS° of −28 eu for kBD is probably in error.

Chelation and Aggregation. The results obtained with the mixed dimer provide some quantitative information about, but no real understanding of, the strong tendency for these chelated compounds to aggregate (Scheme 4). Phenyllithium itself is
Scheme 4. Association Equilibria

\[
\begin{align*}
R = \text{H} & \quad (\text{THF}, -75 \, ^{\circ}C) & K_{eq} &= \frac{[\text{ArLi}]_2}{[\text{ArLi}]} = 40 \text{ M}^{-1} \quad \Delta G^{\circ} = -1.5 \text{ kcal/mol} \\
R = \text{CH}_3 & \quad (1:1 \text{ THF/ether, -135 \, ^{\circ}C}) & K_{eq} &= 1.7 \text{ M}^{-1} \quad \Delta G^{\circ} = -0.2 \text{ kcal/mol} \\
R = \text{CH}_3\text{CH}_3\text{CHMe}_2 & \quad (\text{THF}, -75 \, ^{\circ}C) & K_{eq} &= <0.23 \text{ M}^{-1} \quad \Delta G^{\circ} = 0.6 \text{ kcal/mol} \\
R = \text{CH}_3\text{NMe}_2 & \quad (2:3:1 \text{ THF}/\text{Me}_2\text{O/ether, -137 \, ^{\circ}C}) & K_{eq} &= 20,000 \text{ M}^{-1} \quad \Delta G^{\circ} = -2.7 \text{ kcal/mol}
\end{align*}
\]

partially monomeric in THF solutions, ca. 1:1 monomer/dimer at 0.08 M,\textsuperscript{15c,23a} and the model system 5 is entirely monomeric. Except for 4, in which there are some additional steric and electronic effects, the chelated organolithium reagents are dimeric within the limits of detection. We estimate that \(<1.2%\) of monomer signal could be present (area of a small peak at \(\delta\) 1.69 at \(-137 \, ^{\circ}C\)). Thus, assuming that the monomer signal is not hidden under one of the dimer signals, the dimer is at least 3 kcal/mol more stable when compared to the model dimer 5.

The mixed dimer 13 is both thermodynamically (since it is formed in higher than statistical amount) and kinetically more stable toward dissociation than PhLi. The activation energy for aggregate exchange for 13 (\(AG^{\circ} = 11.2 \, \text{kcal/mol}\)) is almost 3 kcal/mol higher than the barrier for dissociation of PhLi dimers (\(AG^{\circ} \approx 8.3 \, \text{kcal/mol}\)).\textsuperscript{15e} The homodimer 1 has a still higher barrier, with a \(AG^{\circ} = 12.9 \, \text{kcal/mol}\) measured from the rate of collapse of the \(^1\text{C}^-\)Li coupling in the \(^1\text{C}^-\)NMR spectra (Figure 10). This process is definitely bimolecular, so dissociation to monomer has a barrier higher than this. A second measure is provided by estimating the maximum broadening of the 1:2:3:2:1 quintet in the \(^7\text{Li}\) NMR spectrum of \(^1\text{N}^-\)Li doubly labelled 1 at \(-55 \, ^{\circ}C\) (Figure 2d), which corresponds to a rate constant of \(\leq 4.5 \, \text{s}^{-1}\) (DNMR simulation).\textsuperscript{24} Since dissociation of the dimers would cause loss of Li–N coupling, \(\Delta G^{\circ} \geq 12 \, \text{kcal/mol}\) for this process.

The dimerization of organolithium reagents cancels the C–Li dipole, and this is presumably the major driving force promoting aggregation. Opposing effects are loss of solvation as well as steric repulsion between the carbonan and solvent ligands on lithium. Thus, either an increase in the C–Li dipole of the monomer or reduced steric effects might be responsible for the high tendency of these chelated compounds to aggregate. The smaller C–Li–N bite angle (90° in 1-A-TMEDA\textsuperscript{15b}) for a chelated group compared to the C–Li–(solv) angle of a nonchelated analogue could result in a larger dipole since there would be less cancellation of the C–Li and X–Li dipoles (where X is either the chelating N or the O of a solvent molecule). The smaller bite angle could also result in less steric resistance to dimerization. In addition, the N-chelating group may be a weaker donor than a molecule of THF which it replaces, which would also increase the C–Li dipole.

Some support for a more polar lithium environment in N-chelated compounds is provided by the observation that the mononemic amine-chelated organolithium reagents 14 and 16 showed a higher HMPA affinity than did nonchelated analogues 15 and 17 (Scheme 5). HMPA was added to a 1:1 mixture of 14 and 15, and the concentration of the THF- and HMPA-complexed lithium reagents was measured by \(^3\text{P}\) and \(^7\text{Li}\) NMR spectroscopy. There was a significant preference for coordination of HMPA to the chelated compound 14, corresponding to a free energy of 0.5 kcal/mol. The effect was larger for the analogue in which PhMe\(_2\)Si replaced the PhS group (comparison of 16 and 17), where \(K_{eq} = 10\) and \(\Delta AG = -0.7 \, \text{kcal/mol}\).\textsuperscript{28}

Scheme 5. HMPA Affinities

(44) This rate constant was estimated from a DNMR simulation using the exchange matrix of Figure 9, with a natural line width of 0.1 Hz.

same experiment on the methoxy-chelated analogue 18 gave a \(K_{eq} = 1\) (\(\Delta AG = 0\)). These experiments imply that the steric effect of a tertiary amine chelating group is not overwhelming and that the amino group of the chelated compound 14 is a weaker donor than a solvated THF in 15 or the chelated oxygen in 18. In other words, the lithium is more electrophilic and the C–Li bond is more strongly polarized in 14 and 16 than in the model systems.

If the same effect is present in the amine-chelated aryllithium reagents, it provides at least a partial explanation for their tendency to dimerize, since dimerization cancels the C–Li dipole. There are some weak indications that the chelated lithiunm in these aryllithium reagents are more electrophilic from examination of HMPA complexation to the 1/PhLi mixed dimer.\textsuperscript{28} HMPA showed a slightly higher affinity (3:2) for the N-chelated lithium (signal D, Figure 16) of the mixed dimer 13 than for the other one. On the other hand, the nonchelated lithium of 1-A showed a higher affinity than the chelated lithium of the 1-B and 1-C isomers, which would imply the opposite effect. Unfortunately, one knows very little about steric effects and the other solvation state of these compounds, so comparisons of this type provide little basis for understanding the aggregation state.

Summary. Three of the compounds with ortho dialkylaminomethyl groups investigated (1, 2, and 3) are strongly chelated and dimeric in solvents containing THF mixed with ether and/or dimethyl ether based on NMR spectroscopic studies of \(^6\text{Li}\) and \(^1\text{H}\)-enriched compounds. The dimers exist as mixtures of three chelation isomers, which are in dynamic equilibrium with activation energies of ca. 8 kcal/mol (analogous to several chelated aliphatic organolithium reagent aggregates). Both TMEDA and PMDTA complex to 1 in a bidentate fashion, but neither cosolvent causes loss of chelation or significant dissociation to monomers. Not even HMPA causes dechelation, although a large excess causes almost complete cleavage of dimers to monomers.

A fourth compound with a methoxy ortho substituent (4) is also strongly chelated but is only partially dimeric, presumably for steric reasons. Addition of HMPA first causes complete deaggregation to HMPA-complexed monomer, and then a partial redimerization to form the bis-chelated triple ion 4-T.

The most unusual aspect of the behavior of these compounds is the relatively high kinetic and thermodynamic stability of the dimers. It remains to be determined whether this is a general phenomenon, but oxygen-chelated analogues are also more dimeric than model systems.\textsuperscript{15b} Some support for a hypothesis in which this effect is a consequence of a higher C–Li bond polarity was obtained. Interaggregate exchange of 1 has been shown to proceed by a mechanism involving association through trimers or tetramers and not by dissociation to monomers, yet another reflection of the high stability of the dimers.
Compound I forms a mixed dimer with PhLi, which also shows the formation of high kinetic and thermodynamic stability in dissociation to monomers compared to nonchelated analogues. Thus, even a single chelating group stabilizes a dimeric structure.

**Experimental Section**

**General.** All reactions requiring a dry anoxic atmosphere were performed in glassware flame-dried or dried overnight in a 110 °C oven, sealed with septa, and flushed with N2. Tetrahydrofuran (THF) and diethyl ether (ether) were freshly distilled under N2 from sodium benzophenone ketyl. Dimethyl ether (Me2O, bp –24.8 °C) was condensed from a pressurized gas cylinder into a graduated conical tube connected to the reaction vessel. Me2O was added dropwise (slowly, 1 h). The dry Me2O was passed by cannula into the desired vessel cooled to –78 °C. N,N,N′,N″-Tetramethylethylenediamine (TMEDA), N,N,N′,N″-pentamethyldiethylenetriamine (PMDTA), and hexamethylphosphoramide (HMPA) were distilled from CaH2 under reduced pressure (if required) and stored under N2 over 4 Å molecular sieves. Common lithium reagents were prepared by literature methods. All reported reaction temperatures are those of the cooling baths.

**Routine NMR Spectroscopy.** Routine 1H and 13C nuclear magnetic resonance (NMR) spectra were obtained on Bruker AC-300, AVANCE or AM-360 and AM-500 spectrometers. All spectra were acquired in CDCl3 or CD2OD with tetramethylsilane (TMS, δ 0.00) as an internal reference for 1H NMR and CDCl3 (δ 77.0) or CD2OD (δ 128.0) for 13C NMR spectra. Routine 15N Sn NMR spectra were obtained on a Bruker AM-360 spectrometer (unlocked) and were acquired in proto-THF, with tetramethylstannane (δ 0.00) as an internal reference.

**Low-Temperature Multinuclear NMR Spectroscopy.** All low-temperature multinuclear NMR experiments were conducted on a Bruker AVANCE-360 or AM-360 spectrometer equipped with a 10-mm wide-bore broadband probe at the following frequencies: 360.148 MHz (1H), 90.556 MHz (13C), 45.2 MHz (15N), and 145.785 MHz (19F).

All spectra were taken in samples of a combination of the proto solvents THF, ether, and/or Me2O with the spectrometer unlock. 13C NMR spectra were referenced internally to the C-2 carbon of THF (δ 67.96), the C-2 carbon of ether (δ 66.57), or Me2O (δ 60.25). Lorentzian multiplication (LB) of 2–3 Hz was applied to 13C NMR spectra. Li and 1Li NMR spectra were referenced externally to 0.3 M LiCl or MeOH (δ 0.00) or internally to Li2(HMPA) (δ –0.40). 13C NMR spectra were referenced externally to 1.0 M PPh3/THF (δ –6.00) or internally to free HMPA (δ 26.40). Probe temperatures were measured externally by ejecting the sample and inserting a thermocouple into the probe or dissolved in THF to give a stock solution (typically 1.0 –1.5 M) used for subsequent reactions. Similar procedures were used with n-ButLi and/or 15N-enriched N,N-dimethylbenzylamine.

An alternate method was also used. Et2Li (0.304 g 8.67 mmol) was dissolved in 8.0 mL of ether. The solution was cooled to –78 °C, and N,N-dimethylbenzylamine (1.30 mL, 8.65 mmol) was added. The resulting clear yellow solution was warmed to room temperature and kept for 7 d. The supernatant was removed by cannula transfer, and the crystals were washed with ether (3 x 15 mL) and dried in vacuo. The crystals were stored in a glovebox until used.

After completion of the NMR experiment, some samples were quenched with Me3Si to give N,N-dimethyl-2-(methylthio)benzylamine.47 1H NMR (CDCl3, 300 MHz): δ 2.26 (s, 6H), 2.46 (s, 3H), 3.46 (s, 2H), 7.07–7.15 (m, 1H), 7.16–7.31 (m, 3H). 13C (1H) NMR (CDCl3, 75.45 MHz): δ 15.67 (CH3), 45.37 (CH3), 62.00 (CH2), 124.22 (CH), 124.89 (CH), 127.63 (CH), 129.72 (CH), 136.61 (C), 138.71 (C), 140.45 (C), 145.78 (C), 148.53 (C), 151.28 (C), 152.97 (C), 163.61 (C).
crystals were dissolved in THF (1.5 mL) and ether (0.5 mL) and transferred by cannula, and the crystals were washed with ether (3 × 1.5 - 2.0 mL). From the supernatant and washings, 0.044 g (28%) of 15 N-labeled N,N-dimethylbenzylamine was recovered. The washed crystals were dissolved in THF (1.5 mL) and ether (0.5 mL) and transferred by cannula to a dried and N2-flushed 10-mm NMR tube. The reaction flask was rinsed with 0.3 mL of THF, which was also transferred into the NMR tube. The addition of Me2O (1.0 mL) gave an aryllithium concentration of 0.28 M. The variable-temperature experiment was monitored by 6 Li, 15 N, and 13 C NMR spectroscopy. Spectra are shown in Figure 2. This sample was also used for a TMEDA titration (see below).

TMEDA and HMPA Titration of 1-[6 Li/15 N]. The sample from the variable-temperature study was titrated with TMEDA and monitored by 6 Li, 15 N, and 13 C NMR spectroscopy. An accurate molarity of the solution was unknown, but three portions of TMEDA were added: 80 μL, 0.54 mmol; 160 μL, 1.08 mmol; and 240 μL, 1.62 mmol (total 480 μL, 3.24 mmol). After the TMEDA titration, an excess of HMPA (480 μL, 2.76 mmol) was added, and 6 Li, 15 N, and 13 C spectra were acquired. A spectrum is shown in Figure 11. The probe temperature ranged from −125 to −135 °C during the experiment. The sample was quenched with MeOH/CH2OAc to give N,N-dimethylbenzylamine-[15 N] (0.05 g, 0.35 mmol).

(Chloromethyl)dimethylsilyl(phenylthio)methane. Thioanisole (3.52 mL, 30.0 mmol) and TMEDA (4.64 mL, 30.0 mmol) were dissolved in THF (20 mL). The solution was cooled to 0 °C, 1.6 M n-BuLi (18.8 mL, 30.7 mmol) in pentane was added, and the solution was stirred for 1 h. In a second flask, chloro(chloromethyl)dimethylsilylene (5.2 mL, 32.0 mmol) was dissolved in THF (35 mL). The solution was cooled to −78 °C, and the phenylthiomethylsilyl solution was added slowly via cannula and stirred for 5 min. Hexanes (200 mL) and water (500 mL) were added, and the water layer was extracted with hexanes (1 × 100 mL). The organic layer was washed with water (2 × 30 mL) and dried (Na2SO4), and the solvent was evaporated. Kugelrohr distillation (100–120 °C, 1–2 mm) gave 6.17 g (89%) of a colorless liquid. 1 H NMR (200.132 MHz, CDCl3): δ = 0.28 (s, 6H), 2.32 (s, 2H), 2.90 (s, 2H), 7.07–7.18 (m, 1H), 7.22–7.32 (m, 4H). 15 N NMR (90.556 MHz, CDCl3): δ = −4.7 (2C, SiMe2), 15.6 (SiCH2Cl), 125.0 (p), 126.5 (2C, m), 128.7 (2C, o), 139.3 (i). MS (EI): M+ = 230.0355 (calc for C10H15NS2, M+ = 230.0352).

Dimethyl(N-pyrrolidinomethyl)silyl(phenylthio)methane (Precursor for 14). (Chloromethyl)dimethylsilyl(phenylthio)methane (690 mg, 3.0 mmol) was refluxed in pyrididine (7 mL) for 3 h. Excess pyrididine was evaporated, and the emulsion was redissolved in CH2Cl2 (2 mL) and

hexanes (2 mL). The emulsion was purified by column chromatography (200 mL of 95:5 hexanes/ethyl acetate followed by 250 mL of 90:5:5 hexanes/ethyl acetate/triethylamine), yielding 703 mg (2.65 mmol, 88%) of a light yellow liquid. 1 H NMR (200.132 MHz, CDCl3): δ = 0.23 (s, 2J6Li−H = 6.7 Hz, 6H), 1.73–1.80 (m, 4H), 2.16 (s, 2J6Li−H = 5.5 Hz, 2H), 2.25 (s, 2J6Li−H = 6.4 Hz, 2H), 2.42–2.54 (m, 4H), 7.06–7.17 (m, 1H), 7.22–7.32 (m, 4H). 13 C NMR (90.556 MHz, CDCl3): δ = −3.1 (2C, 1J6Li−C = 39 Hz, SiMe2), 16.9 (1C, 1J6Li−C = 46 Hz, SCH2Si), 23.9 (2C, β-pyrrolidine), 45.8 (1C, 1J6Li−C = 59 Hz, SiCH2N), 58.0 (2C, α-pyrrolidine), 124.5 (p), 126.1 (2C, m), 128.5 (2C, o), 140.1 (i). MS (EI): M+ = 265.1381 (calc for C14H15N2Si = 265.1320).

**Table 2.** Competitive Titration of 14 and 15 with HMPA

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<th>equiv</th>
<th>HMPA %</th>
<th>% 14</th>
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<th>% 15</th>
<th>% 15-h1</th>
<th>(14-h1)/ (15-h1)</th>
<th>Kq</th>
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*a h = HMPA. \( K_{q} = [14][15-h]/[14-h][15].\)

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Supporting Information Available: Experimental procedures for the preparation of 2 (15 N labeled), 3, 4 (15 N labeled), 5, 16, 17, and 18; and data and spectra from variable-temperature NMR experiments and simulations on 1, 2, and 13; spectra and data from the variable-concentration NMR studies of 1 and 4; spectra from HMPA titrations of 2, 3, 4, and 13; spectra and data for competitive NMR titration of 16/17 and 18/15; NMR spectra and data for TMEDA and PMDTA titrations of 1 and 5; X-ray crystal structure data for 3 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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