Solution Structure of 2-[(Dimethylamino)methyl]phenyllithium[1]

Hans J. Reich* and Birgir Ö. Gudmundsson

Department of Chemistry, University of Wisconsin Madison, Wisconsin 53706

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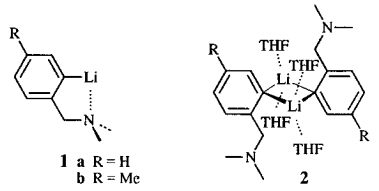
The solution structure, reactivity, and selectivity of organolithium reagents are dominated by coordination to Lewis bases, both intermolecular (solvation, substrate coordination[2]) and intramolecular (chelation[3a]). Information about the competition between solvation and chelation is essential to provide a structural and mechanistic basis for the effects of chelation on lithium reagent reactivity.[1a,1b] We make a distinction between chelation within lithium reagents,[4−6] which we are concerned with here, and complex induced proximity effects (CIPE),[2] which usually involve transition state chelation effects originating in the substrate.

There is abundant evidence from X-ray studies[3b−d,7−9] and solution properties that intramolecular coordination by nitrogen and oxygen bases is strong in the absence of donor solvents.[3,7b] The situation is less clear in donor solvents like THF. The metalation of *N*,*N*-dimethylbenzylamine, the classical example of a chelation-controlled process,[10] produces 2-[(dimethylamino)methyl]phenyllithium (**1a**). Crystalline **1a** is a fully chelated tetramer (X-ray structure), and **1b** is tetrameric in toluene



solution.[7] However, small amounts of THF cleave the tetramer to a dimer, and NMR spectra suggest that THF displaces the dimethylamino groups coordinated to lithium (**2b**).[7] Other studies also imply that amine and ether chelation is easily disrupted by THF.[11]

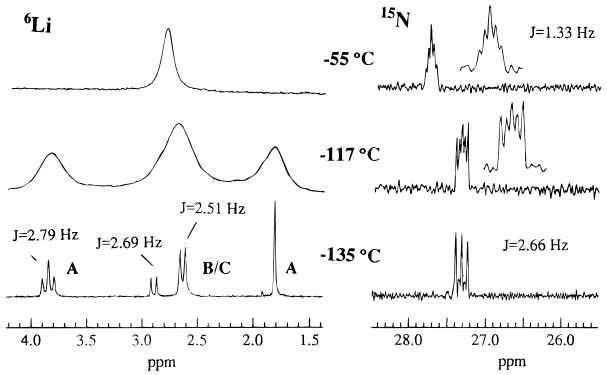
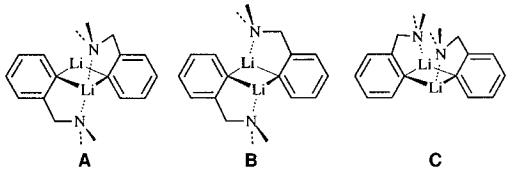


Figure 1. ^{6}Li NMR and ^{15}N NMR spectra of ^{6}Li/^{15}N isotopically labeled **1a**, 0.15 M in 50/33/17 THF/Me_2O/Et_2O at −135, −117, and −55 °C.[13]

We report a reexamination of the solution structure of **1a** which shows that not only is chelation intact in THF but **1a** is fully chelated even when excess *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), *N*,*N*,*N*′,*N*″,*N*′-pentamethyldiethylenetriamine (PMDTA), or HMPA is present. We also show that the chelating groups have the unexpected effect of substantially stabilizing dimeric **1a** compared to its monomer when compared with phenyllithium dimer and monomer.

Crystalline ^{6}Li-labeled **1a** dissolved in a mixture of THF, dimethyl ether, and diethyl ether (50:33:17)[12] at −135 °C showed a mixture of three species in the ^{13}C NMR spectra. The



two major species showed resolved ipso-carbon signals at δ 188.9 and 188.4 (each a 1:2:3:2:1 quintet from coupling to two ^{6}Li nuclei, $J_{C-Li} = 7.0$ Hz) and resolved diastereotopic NMe_2 signals ($\Delta\delta \approx 4$ ppm).

The identification of the three species as the chelation isomers **A**, **B**, and **C** (54:38:8 ratio)[14] was made possible by examination of the ^{6}Li NMR spectra of the ^{6}Li−^{15}N doubly labeled isotopomer of **1a** (Figure 1). The most upfield and downfield lithium signals at δ 1.80 and 3.85 (which integrate 1:1)[13] can be assigned to **A**, on the basis of the triplet splitting of the downfield signal ($J_{Li-N} = 2.8$ Hz) and the absence of Li−N coupling in the upfield one. The two middle lithium resonances can be assigned to **B** and **C** in which each lithium is coordinated by one amino group, resulting in a doublet.[14] The use of ^{15}N−^{6}Li coupling to establish solution structures of lithium amides and metalloenamines has been elegantly demonstrated,[15,16ab] but there is only one previous example of a coupling between nitrogen and lithium that does not involve formal bonding between the two atoms.[4]

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(12) This solvent mixture is close in donor strength to THF and allows measurement of spectra to below −150 °C.

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(14) We have not been able to assign **B** and **C** individually, since their predicted NMR properties are indentical. Attempts to make this distinction based on the effect of chelating solvents (in principle, **C** can chelate, **B** cannot) have not been successful. Evidence for across-ring chelation of this type in a tetramer has been reported: Bartlett, P. D.; Goebel, C. V.; Weber, W. P. *J. Am. Chem. Soc.* **1969**, *91*, 7425.

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Above −111 °C the four lithium resonances broaden and coalesce to a single peak. Since the Li−C coupling was maintained up to −55 °C (Figure 1), the exchange process between **A**, **B**, and **C** was intra-aggregate, involving neither dissociation to monomers nor association to higher aggregates. Furthermore, the 1:1:1 triplet in the ^{15}N NMR spectrum at −135 °C (J_{N-Li} = 2.6 Hz, the three ^{15}N signals for **A**, **B**, and **C** are nearly coincident) became a 1:2:3:2:1 quintet (J_{N-Li} = 1.3 Hz) at −55 °C. The nitrogens are now equally coupled to both lithiums, so Li−N coordination is intact with **A**, **B**, and **C** in dynamic equilibrium; compound **2a** is not detectably formed.[7] Qualitatively all four lithium signals broaden comparably, so ring rotation through a planar carbon transition state[17] (required to interconvert **B** and **C**) must have rates comparable to, or greater than, N-decoordination.

A second dynamic process above −55 °C results in loss of C−Li and N−Li coupling, probably caused by reversible cleavage to monomers. From the broadening of the ^{15}N quintet lines at −56 °C we estimate that $\Delta G^{\ddagger}_{-55}$ for dimer−monomer interconversion is >11.9 kcal/mol. The dimers **A**, **B**, and **C** dissociate to monomers more slowly than does phenyllithium dimer, for which the monomer−dimer equilibration has $\Delta G^{\ddagger}_{-75}$ = 8.8 kcal/mol,[18] and which is detectably dissociated to monomer under comparable conditions. The higher relative stability of the chelated dimers cannot be a direct consequence of chelation (only for **A** does chelation tie the two ArLi together) but must be an indirect consequence of replacing THF by an amino group.

We have examined the behavior of **1a** in the presence of three cosolvents used to suppress chelation and reduce aggregation effects: TMEDA,[16c,19] PMDTA[20] and HMPA.[21] The addition of TMEDA gave a new species with the same spectral characteristics as dimer **A**, a downfield triplet and an upfield singlet (Figure 2). The isomers **B** and **C** did not detectably complex TMEDA, and at 3 equiv of TMEDA per lithium the **A**−TMEDA complex **3** represents over 75% of the species present (the structure shown is supported by an X-ray crystal structure,[22] see supporting information). Thus TMEDA displaced any coordinated THF and Me_2O molecules from one of the dimers (the X-ray structure shows no coordinated solvents) but did not cause detectable deaggregation or disruption of the chelation.[22] PMDTA behaved like TMEDA, it coordinated in a bidentate fashion; no monomers could be detected.[20b]

The effects of HMPA on **1a** are more substantial. At low equivalents the mono-HMPA complexes of **A**, **B**, and **C** were formed, and monomeric **4** was detected. At 1 equiv of HMPA per lithium the bis-HMPA complexes of **B** and **C** were the main species present. At high equivalents the monomeric bis-HMPA complex **5** was observed, characterized by a triplet in the ^{6}Li NMR spectrum resulting from coupling to two ^{31}P nuclei (Figure 3). In the ^{15}N-labeled material, this signal was a quartet, resulting from near identity of $^{1}J_{N-Li}$ and $^{2}J_{P-Li}$. Thus, the chelation between the dimethylamino groups and the lithium is intact even with excess HMPA present. In addition, there were still detectable amounts of chelated HMPA complexed dimers (**B**/**C**·$(HMPA)_2$), testifying to the tenatious nature of dimerization of **1a** (PhLi is fully dissociated to monomers at 1 equiv of HMPA[1c,18]).

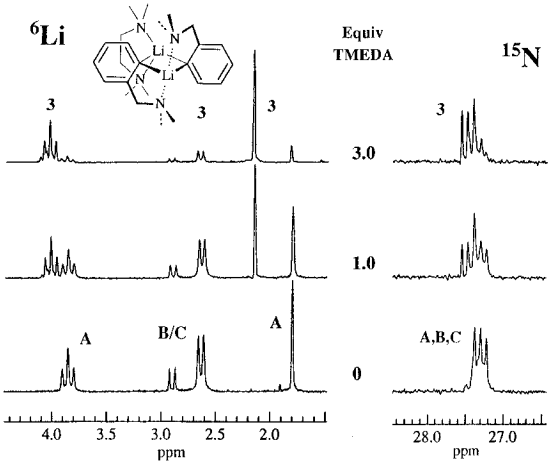

Figure 2. ^{6}Li and ^{15}N NMR spectra of isotopically double-labeled **1a** with increasing amounts of TMEDA.[13]

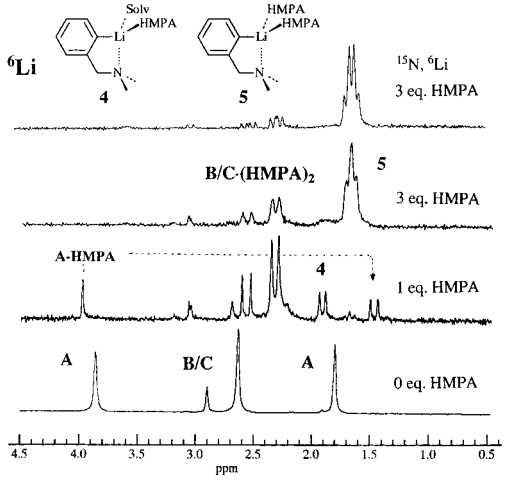

Figure 3. ^{6}Li NMR spectra of an HMPA titration of **1a** (0.15 M) in 50/33/17 THF/Me_2O/Et_2O.[13]

Summary

o-(Dimethylaminomethyl)phenyllithium (**1a**) forms three isomeric chelated dimers in THF−Me_2O solution. In contrast to earlier reports that chelation in toluene solution was disrupted by stoichiometric amounts of THF, we find that chelation between the dimethylamino groups and the lithium is fully maintained in solvents containing 50% by volume THF. Furthermore, neither TMEDA, PMDTA, nor HMPA breaks the chelation, although the latter does largely deaggregate the dimer, to form the bis-HMPA complex **5**. Both the thermodynamic stability (monomer−dimer equilibrium constant) and kinetic stability (rate of dissociation) of the dimer **1a** is higher than those of phenyllithium.

Acknowledgment. We thank the National Science Foundation for support of this research and D. R. Powell and T. K. Firman for the X-ray structure determination.

Supporting Information Available: Details of the preparation and X-ray crystal structure of **3** (16 pages). Ordering information is given on any current masthead page.

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(17) Neither the *o*-tolyllithium dimer nor the mixed dimer of **2a** and phenyllithium show any NMR signal doubling at low temperature from restricted rotation around the C−C axis. Slow interconversion of cis−trans isomers (rotation around N−N axis) has been reported for lithium amide (N−Li) dimers.[15,16a]

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(22) X-ray data for **3**: $C_{24}H_{40}Li_2N_4$, triclinic, *P*1, a = 9.113(3) Å, b = 9.226 Å, c = 16.011(3) Å, α = 91.81(2)°, β = 91.31(2)°, γ = 106.72(3)°, V = 1287.9(6) Å^3, Z = 2, D_{calc} = 1.028 mg/m^3, R = 0.0794 based on 3423 reflections, GOF = 1.027.

(23) The complexation is 1:1. The competition between THF and TMEDA can be judged from the observation that half of the dimers **A**/**B**/**C** were converted to **3** at a ratio of [THF]/[TMEDA] of 60.