Interconversion of Contact and Separated Ion Pairs in Silyl- and Arylthio-Substituted Alkyllithium Reagents
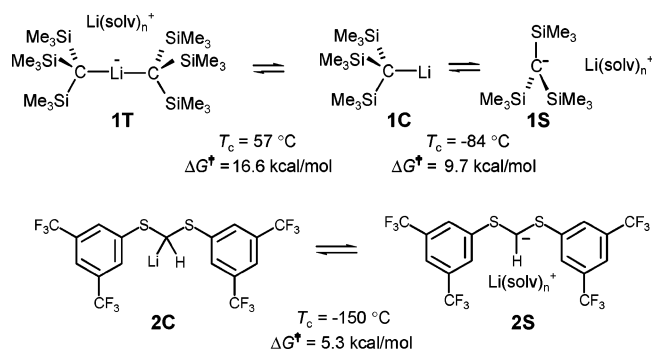
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ABSTRACT

Ether-solvated contact and separated ion pairs (CIP and SIP) for two lithium reagents, tris(trimethylsilyl)methyllithium (1) and bis(3,5-bistrifluoromethylphenylthio)methyllithium (2), have been characterized and observed for the first time under conditions of slow exchange by NMR spectroscopy, and barriers to interconversion have been measured. A Saunders isotope perturbation experiment was used to support identification of the CIP and SIP species for 2.

Organolithium reagents in solution exist as a variety of structures, depending in a complex way on solvent donicity, the presence of Lewis basic additives, and the structure of the carbanion.[1a,2,3,4a,5a] In nonpolar media, they tend to be aggregated, but most are converted progressively to lower aggregates as solvent donicity increases. This is a consequence of the fact that lithium is normally tetracoordinate: only one basic group can coordinate to each lithium in a cubic tetramer, two can coordinate to each lithium in a four-center dimer, and three can coordinate to the lithium in a monomer. If the carbanion has sufficient charge delocalization, ion separation can occur (conversion of a contact ion pair (CIP) to a separated ion pair (SIP)) driven by tetra (or even higher) coordination of the lithium by basic solvents or additives.[4a,6a] The conversion of CIP to SIP can lead to enormous increases,[6b,7,8] as well as decreases,[4b,6b] in reactivity. Selectivity changes have also been detected.[6c,6d,9] We report on NMR spectroscopic studies of two systems which address the barrier to interconversion of CIP and SIP structures.

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The lithium reagent **1**, formed by deprotonation of tris(trimethylsilyl)methane,[10a] Li/Hg exchange of [(Me$_3$Si)$_3$C]$_2$Hg,[11] or Li/Se exchange[12a] of (Me$_3$Si)$_3$CSePh, has unusual structural properties: in the solid state, it forms a four-center dimer when no solvent is present[11] and a triple ion when solvated by THF (**1T**).[10a] An NMR study[10b] suggested that the triple ion is also present in solution, in addition to a second species, which was tentatively assigned the structure **1C**, the monomeric contact ion pair. We have reinvestigated the solution structure of **1** by multinuclear NMR spectroscopy of natural abundance as well as of ^{13}C- and ^{6}Li-enriched material in ether−THF solvent mixtures and found that below −80 °C there are actually three species present *in slow exchange on the NMR time scale*: the triple ion **1T**, the contact ion pair **1C**, and the separated ion pair **1S**.
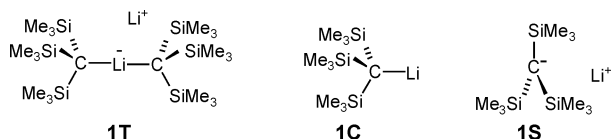
Evidence for this assignment was provided by the ^{13}C, ^{7}Li, ^{6}Li, ^{29}Si, and ^{1}H NMR spectra at various temperatures and in several solvents. Two of the species, **1C** and **1T**, can be readily identified from the NMR spectra of the ^{13}C-enriched sample (Figure 1). For **1T**, the ^{13}C NMR signal of the C−Li carbon at δ 1.8 with lithium at natural abundance is a broad doublet, a consequence of unusually fast quadrupolar relaxation of ^{7}Li which partially averages the peaks of
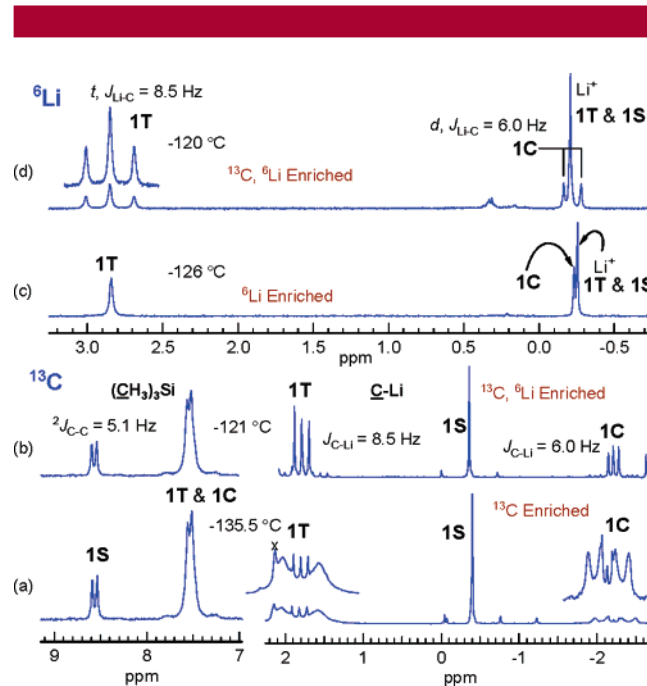

Figure 1. NMR spectra of **1** in 3:2 THF/ether. ^{13}C NMR spectra of (a) ^{13}C-enriched and (b) ^{13}C−^{6}Li doubly enriched **1**. ^{6}Li NMR spectra of (c) ^{6}Li-enriched and (d) ^{13}C−^{6}Li doubly enriched **1**.

the expected 1:1:1:1 quartet, superimposed on which is the natural abundance (7.4%) 1:1:1 triplet of the ^{6}Li isotopomer (Figure 1a).[13] The ^{6}Li-enriched sample shows a 1:2:1 triplet at δ 2.8 in the ^{6}Li (Figure 1d) and a 1:1:1 triplet in the ^{13}C NMR spectra (Figure 1b), defining a carbon bonded to one lithium and a lithium bonded to two carbons. Compound **1C** shows the expected doublet at δ −0.2 in the ^{6}Li and a 1:1:1:1 quartet (natural abundance) or a 1:1:1 triplet (^{6}Li enriched) at δ −2.2 in the ^{13}C NMR spectra ($J_{Li−C}$ = 8.5 Hz).

The third species was eventually assigned the separated ion pair structure **1S**, although not without some trepidation because the observation of distinct NMR signals for CIP/SIP pairs in ethereal solvents is unprecedented.[14] The evidence for this assignment can be summarized as follows. The signals for **1S** were present in all samples prepared by several different methods (metalation, Li/Se exchange, Li/I exchange) provided that the solvent contained a significant fraction of THF. The appropriate signals of all of the nuclei (^{6}Li, ^{1}H, ^{13}C, ^{29}Si) of **1S** and **1C** coalesced at around −70 °C, showing that the signals assigned to **1S** were not a structurally different impurity. The species shows no C−Li coupling or signal broadening, even at −135 °C, and only one signal for the separated lithium cation of **1T** and **1S** was

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(13) Similar signals have been observed for the C−Li carbons of phenyllithium[12b] and 2,4,6-tri-*tert*-butylphenyllithium.[5b] For an explanation, see: Bacon, J.; Gillespie, R. J.; Quail, J. W. *Can. J. Chem.* **1963**, *41*, 3063−3069.

(14) Separate NMR signals for SIP and CIP have been observed for crypt[15] and HMPA[6a] solvated species, where the SIP and CIP have different levels of crypt/HMPA solvation. Such strong ligands for lithium have relatively slow ligand exchange rates, so distinct solvates can be readily observed on the NMR time scale.

observed in the lithium NMR spectra. In dimethyl and diethyl ether, the signals for **1S** disappear due to poorer solvation, whereas the addition of HMPA led to complete conversion to **1S**, as is seen for many related reagents.[6c,6e] The C–Si coupling for **1S** ($^1J_{Si–C}$ = 64.9 Hz) was significantly larger than that for **1C** ($^1J_{Si–C}$ = 42.0 Hz, which was close to the value of 37.5 Hz in tris(trimethylsilyl)methane[6h]) and **1T** ($^1J_{Si–C}$ = 42.6 Hz), suggesting increased s character in the C–Si bond on ion separation.[6e,16] Removal of the lithium cation should favor a more planar carbon to relieve strain and allow better π delocalization of charge into the C–Si σ^* bonds. Finally, dilution studies at room temperature showed that the concentrations of **1T** and the averaged **1C**/**1S** signal changed in a way consistent with a dimeric structure for **1T** (a plot of log[**1C–S**] vs log[**1T**] had a slope of 1.91). However, at −105 °C, where **1S** and **1C** can be measured independently, comparison of **1T** with **1C** gave a molecularity of 2.2, whereas comparison with **1S** gave a value of 1.6. We do not understand the origin of these deviations from the expected value of 2, but they suggest a small degree of aggregation for **1S**.

DNMR studies of the ^{13}C and ^{1}H NMR spectra (Me$_3$Si signals) provided barriers to the interconversion of the three species.[6h] The barrier between **1S** and **1C** was over 9 kcal/mol ($\Delta G^{\ddagger}_{-78}$ = 9.6 kcal/mol, $\Delta H^{\ddagger}$ = 8.1 ± 0.2 kcal/mol, $\Delta S^{\ddagger}$ = −8.0 ± 0.8 eu). The ratio of **1S** and **1C** is essentially temperature independent. Coalescence of **1T** with the averaged signals of **1C** and **1S** could barely be achieved in the 3:2 THF/ether medium because it occurred near the boiling point of the solution ($\Delta G^{\ddagger}_{41.3}$ = 16.4 kcal/mol, $\Delta H^{\ddagger}$ = 12.9 ± 0.4 kcal/mol, $\Delta S^{\ddagger}$ = −11.1 ± 1.1 eu for conversion of **1T** to **1C** and **1S**).

The extraordinary high barriers to interconversion of **1S** and **1C** encouraged us to look for other systems where this barrier could be measured. The requirements are stringent— the lithium reagent must be evenly balanced between CIP and SIP at low temperatures in THF–ether mixed solvent. We have previously reported on bis(3,5-bistrifluoromethylphenylthio)methyllithium (**2**) as an easily separable ion pair in connection with studies of the competition between 1,2- and 1,4-addition to enones.[6c]

A study of the effect of solvent donicity revealed that in pure diethyl or dimethyl ether only **2C** was present, but it was converted completely to **2S** if several equivalents of HMPA were added. This can be seen from the ^{13}C chemical shifts of the aryl C–S carbon, which, as observed for other lithium reagents of this type,[6e] moved over 10 ppm downfield on ion separation. Figure 2 shows ^{13}C NMR spectra of **2** in ether, where only **2C** is present, and various ether/THF and HMPA mixtures where the downfield progression of the C–S carbon signals indicates increasing fractions of **2S** (the spectra of Figure 2 were taken on a 60:40 mixture of D/H
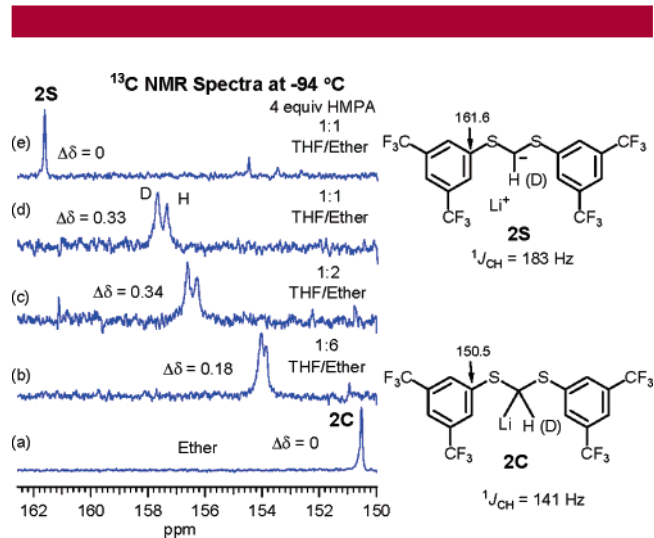

Figure 2. Saunders isotope perturbation experiment: ^{13}C NMR spectra of a THF titration of a 0.23 M solution of **2** (55% D-labeled) in 7:1 ether/pentane at −94 °C. Spectrum (e) contains 4 equiv of HMPA.

isotopomers, and the signals in Figure 2b–d are doubled as a consequence of isotope perturbation; see below).

Although we have assigned the chemical shift changes of Figure 2 and the decoalescence of two signals described below to a SIP/CIP interconversion, there are a number of other structural changes which can cause chemical shift changes and signal doubling in NMR spectra. These include conformational equilibrations, aggregate exchanges, or variable solvation. Only the SIP/CIP interconversion is likely to involve a significant change in hybridization, so we performed the Saunders isotope perturbation experiment[17] shown in Figure 2. In samples where significant fractions of both **2S** and **2C** were present, the signal of the deuterated compound was 0.30−0.34 ppm downfield of the protio isotopomer. These isotope shifts are far too large, and of the wrong sign, to be normal $^3\Delta$ shifts, where $\Delta\delta$ of <0.05 ppm upfield would be expected.[18] In fact, no isotope shift could be detected when only **2S** (in THF/ether/HMPA) or **2C** (in ether) was present. The observation of a large isotope shift signals a hybridization change of the C–H(D) bond, as expected for a SIP/CIP equilibration.[1b] The downfield shift of the D-isotopomer means that there is a larger fraction of **2S** in the deutero compound. This is as expected from the much larger $^1J_{CH}$ in **2S** vs **2C** (183 vs 141 Hz), indicating a change in hybridization of the carbanion toward sp^2 in **2S**, hence a stronger C–H(D) bond and an energetic preference for C–D in the SIP.[6e] We believe that this is the first time that a SIP/CIP dichotomy has been established using the Saunders isotope perturbation method, although carbanion properties, such as the localization of allyllithiums[5c,19,20] and

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propargyl/allenyllithiums,[6f] the cyclopropylcarbinyl−allyl interconversion,[21a,22] and the symmetry of carbanion−CH bonds,[21b] have been probed.

Samples of **2** (H only, no D) in mixtures of dimethyl ether and THF behaved similarly to those in ether and THF, with a large predominance of **2C** in pure dimethyl ether and an increasing fraction of **2S** as THF was added. Both the ^{7}Li and ^{13}C spectra of such samples developed significant broadening at temperatures below −130 °C. This effect could be assigned to slow interconversion between **2C** and **2S**. In a sample with an appropriate mixture of THF and Me$_2$O such that the averaged ^{13}C NMR signal indicated nearly equal amounts of **2C** and **2S**, it was possible to decoalesce the two signals at −151 °C (Figure 3), giving peaks with
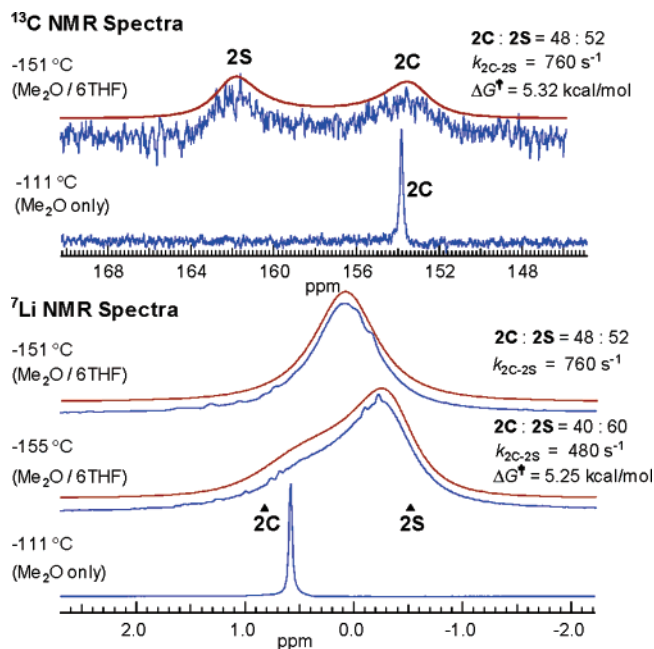

Figure 3. ^{13}C and ^{7}Li NMR spectra of a 0.16 M solution of **2** in Me$_2$O and a Me$_2$O/THF mixture. The upper lines are simulations (two-spin exchange).[6g,6h]

approximately the shifts of **2C** in ether (Figure 2a) and **2S** in THF/ether/HMPA (Figure 2e). Because of the smaller chemical shift difference (714 vs 1007 Hz), the ^{7}Li signals were not quite decoalesced even at −155 °C, the lowest temperature that could be achieved.

Line shape simulation of the spectra gave a free energy of activation of 5.3 kcal/mol for interconversion of the contact and separated ion pairs of **2**. Previous measurements of the barrier to interconversion of lithium reagent SIP and CIP species have come from ESR studies of aromatic radical anions, with values of 2−4 kcal/mol.[23] The slightly higher barrier in **2** seems reasonable, given the greater localization of charge and hence the stronger C−Li coordination expected for this system compared to aromatic radical anions. However, the much higher barrier for the SIP/CIP interconversion of tris(trimethylsilyl)methyllithium (**1**) must have its origin in the extraordinary steric hindrance at the carbanion center. It seems likely that solvent-induced ion pair separation occurs by an associative mechanism.[24] In **1**, such a process may be sterically prohibited, requiring an S$_E$1-type dissociation of a Li(THF)$_3^+$ or perhaps even a Li(THF)$_2^+$ cation with little or no solvent assistance. Similarly, the ion association process would then require predissociation of one or two solvent molecules from the Li(THF)$_4^+$ cation before the C−Li contact could be established.

The even higher barrier for dissociation/association of **1T** must have similar origins: if the triple ion simply fragments to a molecule of **1C** and **1S**, then the departing **1C** fragment may be unable to coordinate adequately with solvent to assist cleavage of the C−Li bond.[28] Conversely, if the triple ion fragments to two molecules of **1C** by electrophilic attack of Li$^+$ on **1T**, then the steric inaccessibility of the C−Li bond of **1T** will require a substantially desolvated cation electrophile, as well as a poorly solvated or unsolvated departing lithium. A zinc analogue of **1T**, bis[tris(trimethylsilyl)methyl]-zinc, shows legendary stability toward electrophiles[10c] attributed to this kind of steric shielding of the metal and carbanion reactive centers.

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