Triple Ion Formation in Localized Organolithium Reagents

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A variety of aggregation motifs dominate the structural chemistry of organolithium compounds. At least four distinct modes of dimerization exist: the common 4-center dimers,[1] 6-center dimers as in 2-lithio-2-methyldithiane,[2] solvent-bridged dimers as in $(LiBr)_2\cdot(HMPA)_3$,[3,4a] and triple ions (lithium ate complexes) of type R−Li−R$^-$//Li$^+$.[5,6a,7] The reactivity of these various dimers compared to monomers or higher aggregates is usually unknown. Triple ions possess an intriguing combination of features of both a dimer and a solvent-separated ion pair. Several lithium amides,[8,9a] β-keto[10] and β-imino[9b] enolates, and a few other lithium reagents[7b] have been rigorously shown through crystal structures or NMR data to form triple ions. Delocalized, lithiocene-type sandwich structures are also known;[6a,7a] however, there is only a single report of a *localized carbanion* triple ion: a crystal structure was obtained of the triple ion of tris-(trimethylsilyl)methyllithium.[5] Here, we present NMR evidence that triple ions form in THF/HMPA solution[4b] for a variety of localized lithiated carbanions, such as aryllithiums and sulfur- and silicon-substituted alkyllithiums.

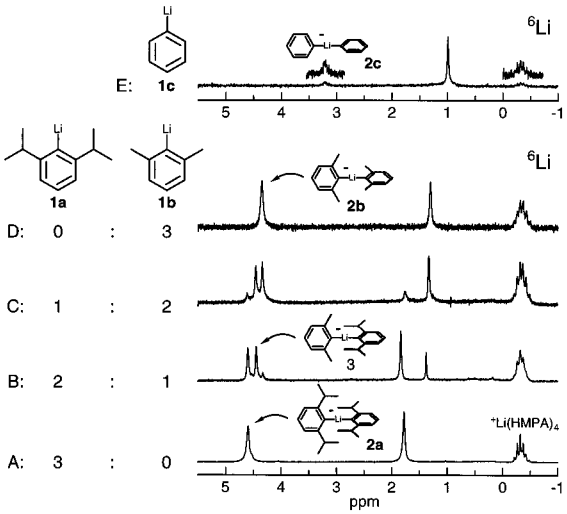
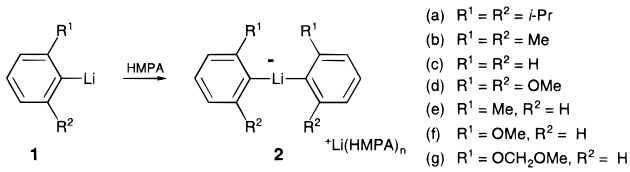


Figure 1. ^{6}Li NMR (52.98 MHz) spectra[15] of ^{6}Li isotopically enriched aryllithiums (0.16 M in 4:1 THF/ether at −125 °C with 2 equiv of HMPA): (A) **1a**; (B and C) 2:1 and 1:2 ratio of **1a** and **2a**; (D) **2a**; (E) phenyllithium with 5 equiv of HMPA.



2,6-Diisopropylphenyllithium (**1a**) is monomeric: the ^{13}C NMR spectrum of ^{6}Li-enriched **1a** at −125 °C in 4:1 THF/ether shows a 1:1:1 triplet (J_{C-Li} = 14.6 Hz) at 193.3 ppm for the *ipso* carbon, demonstrating connectivity to a single ^{6}Li (spin = 1) nucleus.[6b,11] Figure 1A shows the ^{6}Li spectrum of **1a** in the presence of 2 equiv of HMPA. A singlet at 1.8 ppm is seen for the monomer,[12] but there are two additional signals present in a 1:1 ratio, consistent with a triple ion of structure **2a**: a singlet at 4.6 ppm for the internal lithium and a quintet at −0.4 ppm for the external lithium (coupled to four coordinated HMPA molecules).[4b] The carbon NMR shows discrete 1:1:1 triplets for the carbanionic carbon of the putative triple ion (δ 197.7, J = 13.7 Hz). Compound **1b** is also monomeric,[13] and the addition of HMPA has a similar effect. Figure 1-D shows that with 2 equiv of HMPA, 73% of the monomer was converted to triple ion (internal lithium at δ 4.3).[14]

Support of our assignment comes from NMR studies of mixtures of these two aryllithiums. Thus, **1a** and **1b** were mixed in a 2:1 and a 1:2 ratio in the presence of 2 equiv of HMPA (Figure 1B,C). The mixed experiments show three distinct signals for the internal lithium, the middle one belonging to the mixed triple ion **3**. The mirror-like appearance of the two spectra is

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(14) Quenching a sample of **1b** with 3 equiv of HMPA (80% conversion to **2b**) with Me_2S_2 produced 87% of 2,6-dimethylthioanisole; therefore, the signal assigned to the triple ion is a structural form of the aryllithium and not a decomposition product. Similarly, **1a** with 2 equiv of HMPA (75% of **2a**) gave 75% of the sulfide.

(15) Lithium NMR spectra were referenced to external 0.3 M LiCl in methanol.

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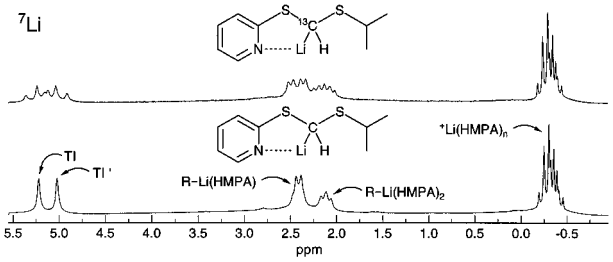


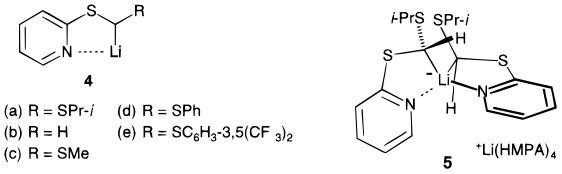
Figure 2. ^{7}Li NMR (139.96 MHz) spectra[15] of natural abundance and ^{13}C-enriched **4a** (0.16 M in 3:2 THF/ether at −125 °C) with 1.5 equiv of HMPA.

strong evidence that triple ions are responsible for the spectral data observed.

Figure 1E shows the parent phenyllithium **1c** in the presence of 5 equiv of HMPA. A small signal is observed at δ 3.2 ppm, which is equal in intensity to the small signal at −0.4 ppm, and we assign these signals to a triple ion, by analogy to the above results.[4c] Wittig, when considering possible structures of a PhLi dimer, proposed a triple ion structure.[16] The species that he was referring to is known today to be a 4-centered dimer, but we now have evidence that a small amount of the triple ion he proposed does form in THF/HMPA solutions of PhLi.

In addition, we have observed that small amounts of triple ion also form in THF/HMPA solutions of **1e**, **1g**, and 2-lithio-5-methylthiophene, while significant amounts form with **1f** and **1d**. The relative amount of triple ion is sensitive to *o*-substitution on the aryllithium: monomeric **1a** and **1b** form 65 to 80% triple ion in the presence of 1−3 equiv of HMPA, whereas **1c** and **1e** (which are a mixture of monomer and dimer in THF[4d]) formed less than 20% at 5 equiv of HMPA.

Pyridylthio-substituted carbanions **4** show a propensity to form triple ions in THF/HMPA solutions. Figure 2 compares the ^{7}Li spectra of unlabeled and ^{13}C-labeled **4a** in the presence of 1.5 equiv of HMPA. Singlets at 5.0 and 5.2 ppm have been assigned to diastereomeric triple ions **5** since each becomes a triplet (J_{C-Li} = 16.9 and 16.7 Hz) in the ^{13}C-labeled compound. The chemical



shifts of the triple ions indicate that they are bis-chelated, as each successive pyridyl coordination causes a 2−2.5 ppm downfield shift (ascribed to lithium's location coordinated to the edge of an aromatic ring, as amine coordination does not cause such large chemical shift changes[4e]). The chemical shifts of the HMPA-coordinated monomers demonstrate that chelation is intact for them as well.

Two diastereomeric triple ions are observed due to the stereogenic carbon centers. In principle, there should be a third diastereomer due to the stereochemical arrangement about lithium. The fact that only two are observed indicates one of the following: (1) isomerization about lithium is fast on the NMR time scale (even down to −150 °C), (2) the structure is not chelated, (3) two of the signals are coincident, or (4) one isomer does not form. We doubt the third explanation, since in **4c**−**e**, which have appreciably different chemical shifts for their triple ion signals, we still see only two (**4b**, lacking a stereocenter, forms only one). A β-ketohydrazone anion possessing stereogenic centers also showed only two triple ion diastereomers.[9b]

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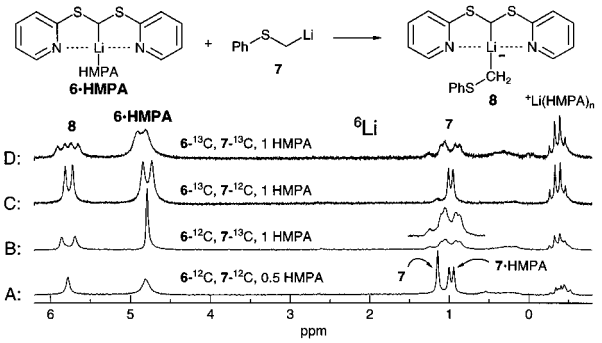

Figure 3. ^{6}Li NMR (52.98 MHz) spectra[15] of ^{6}Li isotopically enriched 1:1 mixtures of bis(2-pyridylthio)methyllithium (**6**) and phenylthiomethyllithium (**7**), 0.16 M in total lithium reagent in 3:2 THF/ether at −125 °C, with and without ^{13}C labeling at the carbanion carbons. The signal for **6**·HMPA at 4.8 ppm splits into a doublet (J_{Li-P}) at lower temperatures.

An electronic effect was observed by comparing **4a**−**e**. The better stabilized carbanions formed triple ions with less HMPA and to a greater extent, consistent with the greater ease of ion pair separation.

To probe the significance of chelation in promoting triple ion formation, bis(2-pyridylthio)methyllithium (**6**) was investigated, and it was found to form mixed triple ions with a variety of nonchelated organolithium reagents. For instance, phenylthiomethyllithium (**7**) formed a mixed triple ion **8** almost quantitatively when 2 equiv of HMPA (relative to total lithium reagent) were added. The connectivity was proved by ^{13}C labeling of the carbanionic carbon in both components (Figure 3). The coupling across the lithium ($^{2}J_{C-Li-C}$) in the doubly ^{13}C-labeled material was not observed. The coupling to HMPA of the monomer signal at δ 4.7 ppm could be resolved at −145 °C ($^{2}J_{Li-P}$ = 9.2 Hz).[4f]

Lithium halide salts are often present in organolithium reactions. A significant result is that LiCl also quantitatively formed triple ions with **6** and, therefore, could affect its chemistry if the triple ion is a reactive species. Lithium phenolate, intended as a model for enolates and alkoxides which are also present in many organolithium reactions, showed no evidence of mixed aggregation with **6**.

Triple ion formation is not unique to the chelated and aryl systems. Several nonchelated sulfur-, selenium-, and silicon-stabilized alkyllithiums also form significant fractions of triple ions in ether/THF/HMPA solution. This was shown by ^{13}C labeling of the carbanion carbons of phenylselenomethyllithium (**9**) and bis(trimethylsilyl)methyllithium (**10**), which converted the internal lithium signals into triplets, whereas the labeled carbons showed coupling to only one Li nucleus.

It is noteworthy that the addition of HMPA, which normally deaggregates lithium reagents,[17] converts a monomeric lithium reagent into a dimeric triple ion. The presence of triple ions in this range of systems suggests that even in cases where they are not detectable ground-state structures, they should be considered as possible reactive intermediates for all organolithium reactions run in relatively polar media. Triple ions might be expected to have reactivities competitive with contact ion pair monomers. For instance, the downfield shift of the carbanion carbon of **1a** from the monomer (193.3 ppm) to the triple ion (197.7 ppm) is indicative of increased electron density at the carbanion carbon. It remains to be shown whether triple ions are reactive species, but for lithium reagents such as **1**, **7**, **9**, and **10** that do not form classical separated ion pairs even with large excesses of HMPA, triple ion involvement in their chemistry seems especially likely.

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