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^{6}Li Diffusion-Ordered NMR Spectroscopy (DOSY) and Applications to Organometallic Complexes

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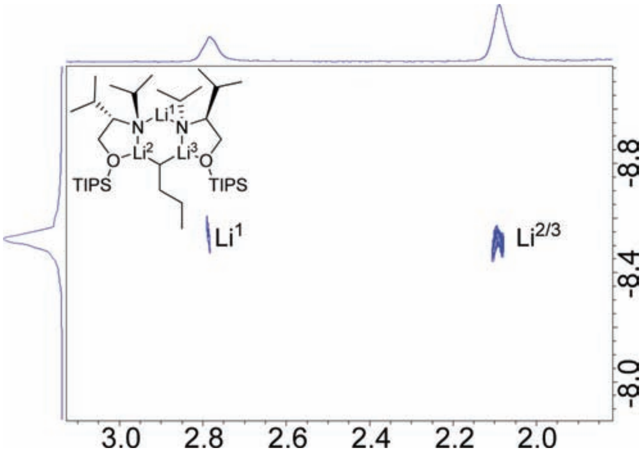
ABSTRACT



The development of ^{6}Li diffusion-ordered NMR spectroscopy (DOSY) is reported. This technique is applied to ^{6}Li organometallic complexes. ^{6}Li DOSY provides a facile means of identification of peaks in the ^{6}Li spectrum, as well as evidence of mixed aggregates based on relative diffusion coefficients. ^{6}Li data is correlated to ^{1}H diffusion experiments through ^{6}Li{^{1}H} HOESY and/or ^{1}H{^{6}Li} HMBC experiments to obtain formula weight information of Li aggregates.

Diffusion-ordered NMR spectroscopy (DOSY) has been established as an efficient method for identification of formula weights and particle size of compounds in solution based on their diffusion coefficients. Recently, our group has successfully applied diffusion coefficient-formula weight (D-FW) correlation analysis to generate formula weights of organometallic compounds using appropriate internal references in ^{1}H, ^{13}C, and ^{31}P DOSY, including boron enolates, an LDA-THF complex, chiral lithium amide bases with *n*-BuLi, chiral lithium amide bases with enolates, and a LiHMDS-HMPA complex.[1] Although ^{6}Li NMR and ^{7}Li diffusion NMR experiments have been known for some time, ^{6}Li DOSY experiments have not been reported.[2] ^{6}Li DOSY would provide valuable information about the relative diffusion coefficients of complexes in solution as well as rapid and unambiguous assignment of peaks in the ^{6}Li spectrum. Inferences can be made about complexes in solution

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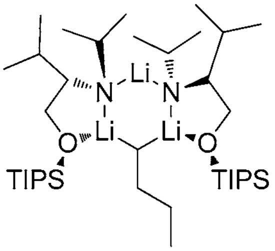

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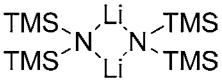

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Figure 1. Structures of organolithium complexes **1** and **2** in toluene-d_8.

based on their relative diffusion characteristics. Here we report the development and application of ^{6}Li DOSY methods to organolithium compounds.

We focused on ^{6}Li rather than ^{7}Li, because of its low quadrupolar moment yielding much narrower peaks. Therefore, we synthesized ^{6}Li *n*-butyllithium from ^{6}Li metal and 1-chlorobutane.[3] This formed the central building block for our ^{6}Li NMR studies, as a large number of organolithium complexes are formed from *n*-BuLi.

Additionally, we are able to bridge the results of ^{6}Li DOSY experiments to more definitive ^{1}H DOSY experiments through either ^{6}Li{^{1}H} heteronuclear Overhauser effect NMR spectroscopy (HOESY) or ^{1}H{^{6}Li} heteronuclear multiple bond correlation NMR spectroscopy (HMBC). Correlation of ^{6}Li DOSY data to ^{1}H NMR data allows indirect assignment of formula weights to peaks in the ^{6}Li DOSY by D-FW correlation analysis of the ^{1}H DOSY data with well established DOSY internal references. D-FW correlation analysis was performed on ^{1}H DOSY data by inclusion of internal references in the NMR samples. Plotting the logarithm of the diffusion coefficients versus the logarithm of the formula weights of the references results in a line, the equation of which was used to extrapolate formula weights of analytes based on their diffusion coefficients. These references were chosen based on their solubility, distinct resonance frequencies, and lack of reactivity toward the analytes. They are benzene (BEN, 78.1 g mol^{-1}), cyclooctene (COE, 110.2 g mol^{-1}), 1-tetradecene (TDE, 196.4 g mol^{-1}) and sometimes squalene (SQU, 410.7 g mol^{-1}).

Experiments were carried out on a previously reported chiral lithium mixed aggregate trimer **1**.[4] This trimer is a 1:2 mixed aggregate according to ^{6}Li NMR. Upon titration of *n*-Bu^{6}Li into a solution of the chiral ligand precursor derived from valinol in toluene-d_8, two peaks formed with a relative integration of 1:2. Though not in itself definitive, ^{6}Li DOSY confirmed that the 1:2 complex aggregate diffuses at a single diffusion coefficient, indicating that the resonances in the ^{6}Li spectrum are within the same complex (Figure 2). If the resonances diffused at different rates, we would expect that they could not belong to the same complex.

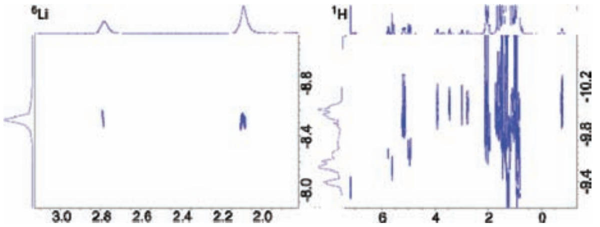

Figure 2. DOSY spectra for **1** in toluene-d_8: ^{6}Li (left), and ^{1}H with internal references (right).

Experiments at −60 °C showed no appreciable difference to those at room temperature. Curves of signal attenuation from which diffusion data was generated were smooth and showed complete attenuation (Figure 3).[5]

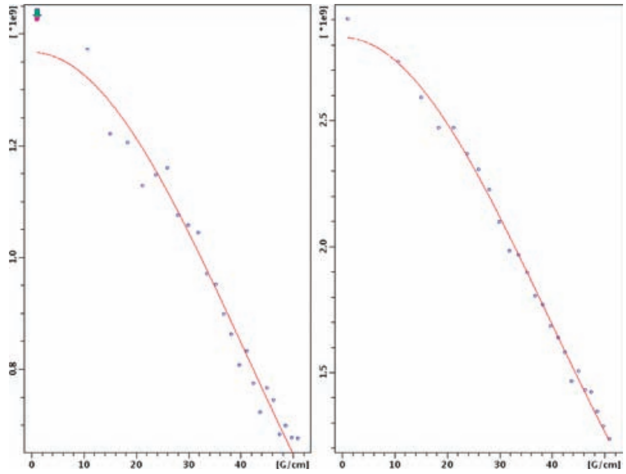

Figure 3. Signal attenuation curves from ^{6}Li DOSY of **1** in toluene-d_8.

The peaks of the 1:2 complex in the ^{6}Li DOSY were correlated to the peaks of the ligand in the ^{1}H spectrum by ^{6}Li{^{1}H} HOESY NMR (Figure 4, left). This spectrum clearly identifies the *n*-Bu^{6}Li peak furthest upfield as having an NOE to the two degenerate Li in the trimer complex and the single Li only having an NOE to protons through the nitrogens. Because both lithium peaks show NOEs to peaks of the ligand, it is clear that they belong to the same complex. Proton DOSY shows the expected diffusion order, with BEN having the largest diffusion coefficient and diffusing the most quickly, followed by COE, TDE, SQU, and finally the heavy trimer complex having the smallest diffusion coefficient and moving slowest.

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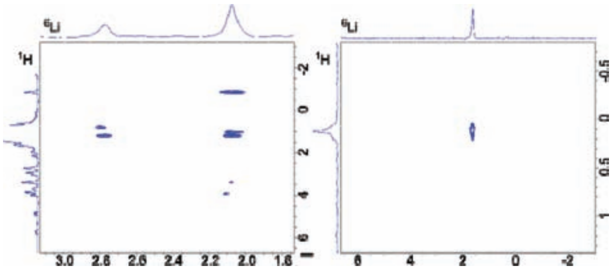

Figure 4. ^{6}Li{^{1}H} HOESY spectra for **1** (left) and **2** (right).

D-FW analysis of the specified peaks in the ^{1}H DOSY corroborates the existence of a mixed 1:2 trimer (Figure 5). Heavier internal references could alleviate the larger than normal errors.

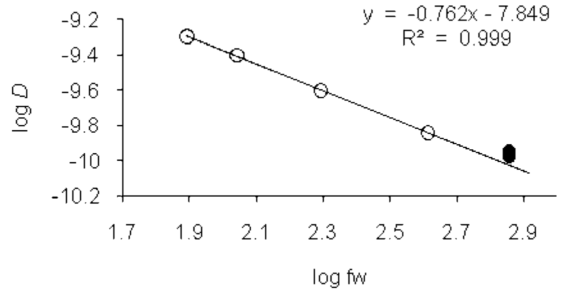

Figure 5. D-FW correlation ^{1}H DOSY data of complex **1** in toluene-d_8. Internal references are shown as open circles and are, from left to right, BEN, COE, TDE, and SQU. Diffusion coefficients of peaks of the ligand and complexed *n*-Bu^{6}Li are shown as solid circles.

Experiments were also carried out on a preparation of ^{6}Li hexamethyldisilazide (^{6}LiHMDS) in toluene-d_8, prepared from *n*-Bu^{6}Li and hexamethyldisilazane (HMDS). ^{6}LiHMDS and its structures have been extensively studied both in crystal and in solution, and its behavior is well understood. ^{6}Li DOSY shows a single peak with a single diffusion coefficient (Figure 6, left). This was confirmed to belong to ^{6}LiHMDS by ^{6}Li{^{1}H} HOESY correlation of the single lithium peak to the methyl protons on the TMS groups (Figure 4, right). ^{1}H DOSY confirmed the presence of an aggregate in agreement with the unsolvated ^{6}LiHMDS dimer **2** in toluene-d_8 (Figure 6, right). The ^{1}H DOSY spectrum shows the expected diffusion order from highest to lowest diffusion coefficient from BEN, followed by COE, TDE and then ^{6}LiHMDS. D-FW correlation analysis predicted the weight of the HMDS containing complex to be within 2% of the unsolvated ^{6}LiHMDS dimer (Figure 7).

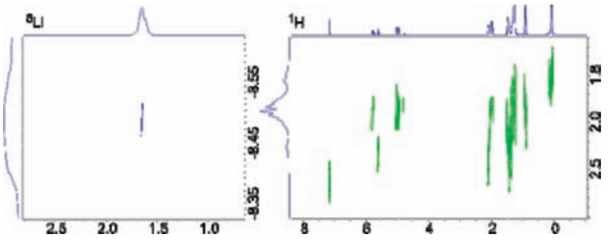

Figure 6. DOSY spectra for **2** in toluene-d_8: ^{6}Li (left), and ^{1}H with internal references (right).

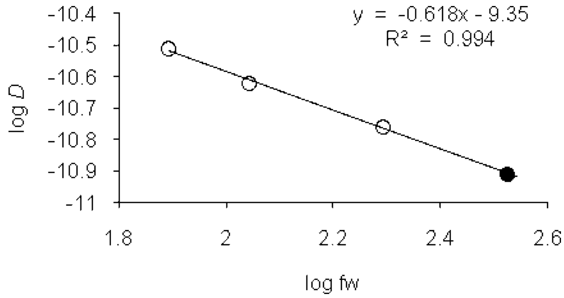

Figure 7. D-FW correlation of complex **2** in toluene-d_8. Internal references are shown as open circles and are, from left to right, BEN, COE, and TDE. The diffusion coefficient of the TMS peak of LiHMDS is shown as a solid circle.

Lastly, we designed an experiment to probe the capability of ^{6}Li DOSY in separating resonances based on diffusion coefficients, similar to DOSY experiments with other nuclei. We chose a mixture of trimer **1** and ^{6}LiHMDS dimer **2**. These compounds are appropriate, as they have no interaction or exchange with one another, both being strong and bulky lithium bases.[1e]

Indeed, three peaks were evident in the ^{6}Li spectrum, those of the 1:2 complex **1**, and ^{6}LiHMDS **2**. ^{6}Li DOSY showed that the two peaks from complex **1** diffuse together, as expected, and **2** diffuses more quickly, in accordance with its lower fw (Figure 8, left). There was no significant chemical shift difference between the compounds' resonances in the mixture and the resonances of the pure compounds. These resonances were correlated to ^{1}H NMR resonances and ^{1}H DOSY data through both ^{6}Li{^{1}H} HOESY and ^{1}H{^{6}Li} HMBC (Figure 9). Resonances in the ^{1}H DOSY

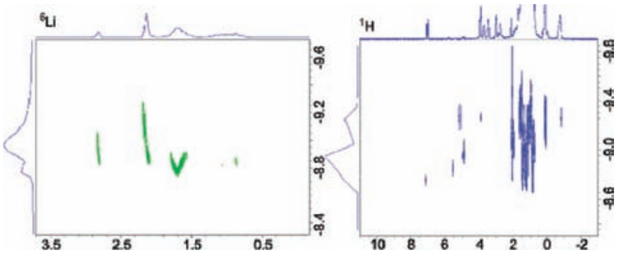

Figure 8. DOSY spectra for a mixture of **1** and **2** in toluene-d_8: ^{6}Li (left), and ^{1}H with internal references (right).

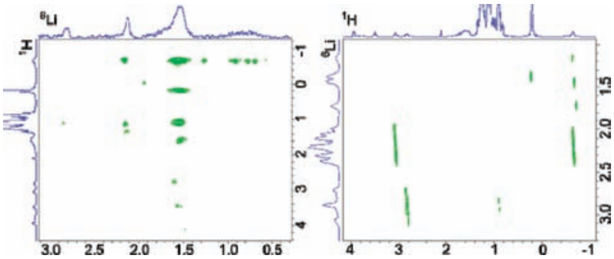

Figure 9. Spectra for a mixture of **1** and **2** in toluene-d_8: ^{6}Li{^{1}H} HOESY spectra (left) and ^{1}H{^{6}Li} HMBC (right).

diffused as expected for **1** and **2**, with BEN diffusing most quickly, followed by COE, TDE, **2**, then **1** (Figure 8, right).

These data illustrate the utility of ^{6}Li DOSY in the study of mixed aggregates and the applicability to organolithium compounds in general. The most important addition to this work will be the development of internal references to permit determination of formula weights of organolithium complexes in solution using D-FW correlation analysis directly from ^{6}Li DOSY data. This poses difficulties due to the inherent reactivity of organolithium species. However, facile correlation of ^{6}Li resonances to ^{1}H data through HOESY and HMBC techniques secure the utility of ^{6}Li DOSY in structure analysis by solidifying relationships between ^{6}Li DOSY data to ^{1}H DOSY D-FW analyses. We intend to fully develop internally referenced ^{6}Li DOSY D-FW correlation analysis. This development will foster related research on lithium aggregate studies, and may be applicable to aid lithium-ion battery designs.[7]

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Supporting Information Available: Full spectroscopic data for NMR experiments as well as diffusion data. This material is available free of charge via the Internet at http://pubs.acs.org.

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