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Solution Studies of Sulfur-Stabilized Lithiated Allylic Carbanions: HOESY (^{6}Li–^{1}H) NMR Spectroscopy of Lithiated (*E*)-1-(*t*-Butylthio)but-2-ene and (*E*)-1-(Phenylthio)but-2-ene

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The nature of the lithium counter cations association with sulfur-stabilized allylic carbanions is investigated by 2-D HOESY (^{6}Li–^{1}H) spectroscopy. The association is best described as either an unsymmetrical dihapto(η^2)-bonded lithium to the C1 and C2 carbons or a monohapto(η^1)-bonded lithium to C1 in a position close to C2. The lithium is spatially closer to C1 than C2 and there is no indication of interaction with the C3 carbon. These structural traits for lithiated (*E*)-1-(*t*-butylthio)but-2-ene in THF and in the presence of TMEDA at 220 K differ markedly to those obtained from the low temperature X-ray crystal structure of this anionic system.

The nature of the lithium counter cations association with sulfur-stabilized allylic carbanions has been the subject of much conjecture.[1] Crystallographic evidence indicates a trihapto(η^3)-bonding of lithium with the allylic carbons (C1 to C3) for the TMEDA complexed (*E*)-1-(*t*-butylthio)but-2-ene anion[2] and ab initio SCF MO calculations on a model lithiopropene-1-thiol system also suggest trihapto bonding with the allylic carbons.[2] X-Ray crystallography demonstrates a lithium-oxygen contact ion pair (CIP) association in lithiated allyl phenyl sulfone[3] and NMR spectroscopy suggests that there is a chelated four centered Li–O–S–C1 structure for lithiated methyl phenyl sulfoxide.[4]

A ^{1}H and ^{13}C NMR study of lithiated (*E*)-1-(*t*-butylthio)-but-2-ene (**1**) and lithiated (*E*)-1-(phenylthio)but-2-ene (**2**) has already been conducted.[5] Lithiated (*E*)-1-(*t*-butylthio)-but-2-ene (**1**) was shown to be a transoid carbanion, both in the presence of a metal-complexing agent such as TMEDA and in neat THF solutions with the lithium cation appearing to reside near either C1 or C3. In comparison, lithiated (*E*)-1-(phenylthio)but-2-ene (**2**) showed *cis* geometry about the C1–C2 bond. From this preliminary 1-D NMR study there was clearly no indication of trihapto bonding of the lithium to the allylic backbone (C1 to C3), as determined previous by X-ray crystallography.[2] It is therefore the purpose of this paper to accurately determine the position of the lithium cation in sulfur-stabilized allylic carbanions (**1**) and (**2**) (Chart 1) in solution by means of 2-D HOESY (^{6}Li–^{1}H) spectroscopy with ^{6}Li-labeled anions. The results obtained from these investigations provide additional insight into the ground state solution structure of these anions and analogous sulfur-stabilized allylic anions which allow further understanding of the possible role the structural characteristics of these anions play in their reactions with electrophiles.[6—8]

1 **2**

Chart 1.

Results and Discussion

Following an initial ^{1}H and ^{13}C NMR study of the solution structure of sulfur-stabilized allylic carbanions,[5] which qualitatively analyzed and described the allylic carbanion carbon framework, further understanding of the role and positioning of the lithium atom in these anions was desired. Therefore, attention was turned to the use of two-dimensional HOESY NMR techniques in order to gain an appreciation of the relative position the lithium atom may attain with respect to the allylic anion backbone (C1 to C3).

Investigation of the lithium's association with the allylic anion backbone focused on the nature of the bonding involved, which is of central importance when describing the structure and reactivity of these allylic anions. With the introduction of multidimensional pulsed NMR spectroscopy in conjunction with the nuclear Overhauser effect (nOe) it has been possible to determine the position of lithium in a number of organolithium compounds.[10—14] This method of structural elucidation, termed HOESY spectroscopy[9—11,13—15] relies on the judicious choice of the lithium isotope to be employed in the experiment, such that the nOe effect shows significant signal enhancement during the course of the experiment.[16]

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The 2-D HOESY experiment used in the study of organolithium compounds makes use of the nuclear properties of the proton nuclei and one of either of the two lithium isotopes ^{6}Li (I = 1) or ^{7}Li (I = 3/2). While ^{7}Li (92.5%) is significantly more abundant than ^{6}Li (7.5%), the ^{7}Li nuclei has a considerably larger quadrupole moment (^{7}Li -4.5×10^{-30} m^{2} cf. ^{6}Li -8.0×10^{-32} m^{2}) and hence the principle mechanism of relaxation of the ^{7}Li nuclei is via quadrupolar, and not dipolar, relaxation. The ^{7}Li T_1 relaxation for lithiated (*E*)-1-(*t*-butylthio)but-2-ene (**1**) were measured to be 81±1 ms at 220 K and 146±5 ms at 300 K generated with natural abundance lithium metal in the presence of TMEDA (2.2 equivalents). For comparison the values for ^{6}Li T_1 relaxation in isotopically enriched (95.5% ^{6}Li metal) lithiated (*E*)-1-(*t*-butylthio)but-2-ene (**1**) were measured to be 9.0±0.5 s in the presence of TMEDA (2.2 equivalents) at 220 K and 8.0±0.5 s in neat THF at 220 K. Clearly this larger value for T_1 relaxation in the ^{6}Li-labeled allylic carbanions would allow the nOe effect to be most effective.

Due to the inherent nuclear properties of natural abundance lithium metal (92.5% ^{7}Li) used in the production of commercially available alkyllithium compounds, a ^{6}Li-labeled (95.5% enriched) butyllithium base was synthesized and used to introduce the ^{6}Li-label into the anions studied here. Introduction of the ^{6}Li isotope resulted in a 50 to 100 fold increase in the T_1 relaxation of lithium. If the ^{6}Li cation and a proton nuclei on the anion are within approximately 350 pm of each other the larger T_1 found for ^{6}Li compared to ^{7}Li would allow effective nuclear Overhauser enhancements to be "built-up" and observed. A mixing time of between 2.0 and 2.5 seconds was used routinely in HOESY experiments on these anions as it allowed good spectra to be acquired over a 6 to 8 h time period and satisfied the necessary conditions for relaxation of both ^{1}H (T_1 typically 3.0 s) and ^{6}Li (T_1 between 6.0 to 9.0 s).

The carbanion of (*E*)-1-(*t*-butylthio)but-2-ene in THF-d_8 was generated at −70 °C with butyllithium (^{6}Li 95.5%) and a low-temperature (220 K) (^{6}Li–^{1}H) 2-D HOESY experiment was conducted on the yellow anionic solution. The resulting HOESY spectrum (Fig. 1) clearly shows correlations between lithium and two protons of the allylic anion. A very intense correlation peak is seen for H1 and indicates a short interatomic distance between the Li and H1. A peak of weaker intensity for H2 indicates a larger interatomic distance between the Li and H2. There is no correlation between the lithium counter cation and H3 of the allylic system nor any other proton of the anion.

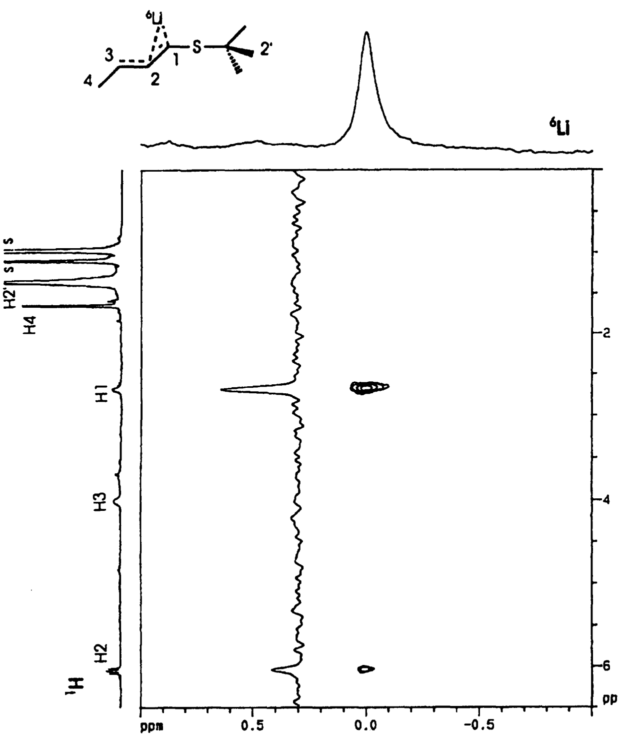
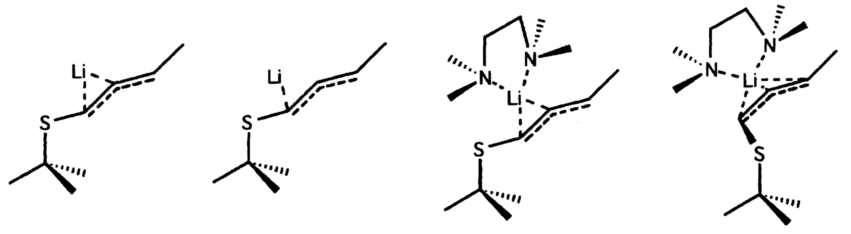


Fig. 1. (^{6}Li–^{1}H) HOESY spectrum of lithiated (*E*)-1-(*t*-butylthio)but-2-ene (^{6}Li-labelled), in THF-d_8 at 220 K (uncorrected), mixing time $\tau_m = 2.0$ s, 256 increments in t_1 (^{6}Li axis is uncalibrated), Insert = F_1 trace of column through ^{6}Li signals, s = solvent peaks.

The nOe decreases at a rate which is inversely proportional to the sixth power of the distance[17] between the two nuclei in question and the magnitude of the nOe is also affected by any rapid interatomic exchange which may be occurring. It was therefore not possible to quantitate the position of the lithium with respect to the enhanced nuclei. However, it is possible to deduce the position of the lithium counter cation with respect to the anionic protons by appreciating the relative intensity of the enhanced peaks.

Based on the result of this HOESY experiment and the results of the 1-D NMR investigation described in a previous paper,[5] the solution structure of lithiated (*E*)-1-(*t*-butylthio)-but-2-ene in THF at 220 K can be described as a transoid or "W" shaped carbanion in which the lithium counter cation is located closer to C1 and unsymmetrically between C1 and C2 in a dihapto (**3a**) or monohapto (with C1) arrangement



3a **3b** **4** **5**

Chart 2.

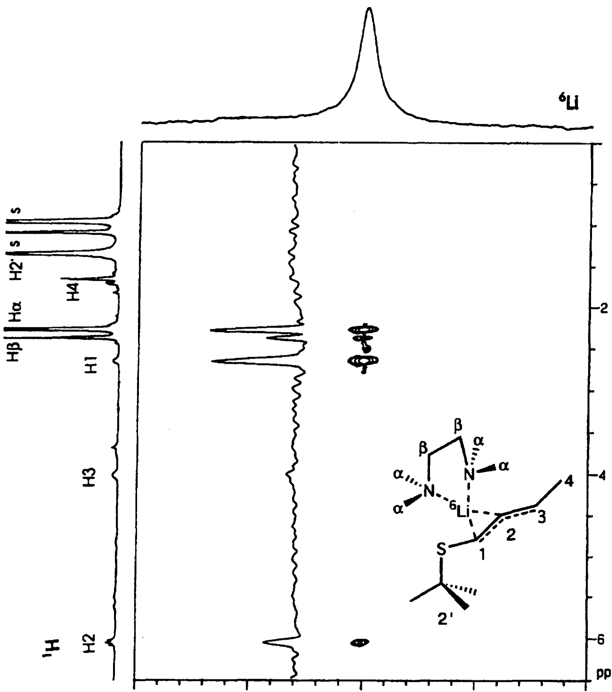


Fig. 2. Phase sensitive ^{6}Li–^{1}H HOESY of TMEDA (2.2 equivalents) complexed lithiated (*E*)-1-(*t*-butylthio)but-2-ene in THF-d_8 at 220 K (uncorrected), mixing time $\tau_m = 2.0$ s, 256 increments in t_1 (^{6}Li axis is uncalibrated). Insert = F_1 trace of column through ^{6}Li signals, s = solvent peaks.

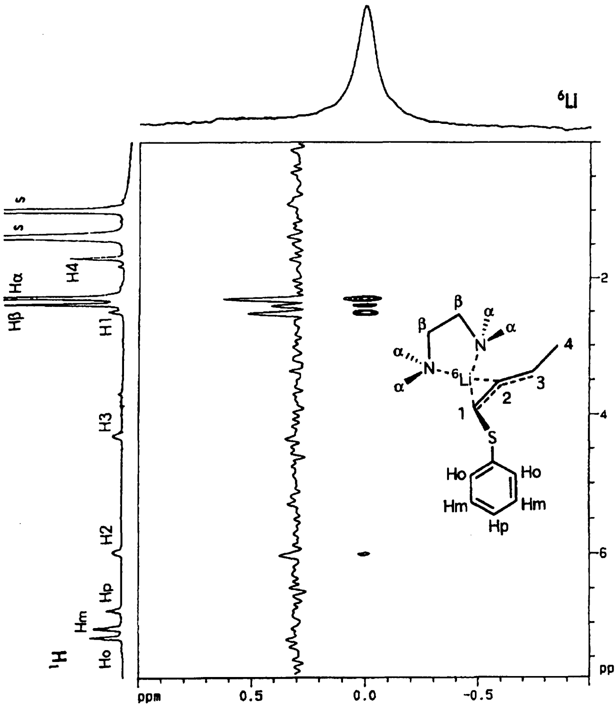


Fig. 3. Phase sensitive ^{6}Li–^{1}H HOESY of TMEDA (2.2 equivalents) complexed lithiated (*E*)-1-(phenylthio)but-2-ene in THF-d_8 at 220 K (uncorrected), mixing time $\tau_m = 2.0$ s, 256 increments in t_1 (^{6}Li axis is uncalibrated). Insert = F_1 trace of column through ^{6}Li signals, s = solvent peaks.

(**3b**) (Chart. 2).

A low-temperature X-ray crystal structure of lithiated (*E*)-1-(*t*-butylthio)but-2-ene complexed with TMEDA indicated that the lithium cation was associated in a symmetrical trihapto bonding arrangement with the three carbons of the allylic backbone (**5**).[2] It was therefore of interest to see if the addition of TMEDA had any effect on the association of the lithium in the solution case. The resultant HOESY spectrum for the TMEDA (2.2 equivalents) complexed carbanion of (*E*)-1-(*t*-butylthio)but-2-ene is shown in Fig. 2. It can be seen that in the TMEDA complexed anion there is a strong correlation to H1 and a medium correlation to H2 which are similar in relative intensity to the enhancements seen for the uncomplexed (*E*)-1-(*t*-butylthio)but-2-ene carbanion (Fig. 1). It has been well-documented that TMEDA functions as a metal-coordinating agent by displacing the solvent molecules from around the metal and in doing so functionally coordinates to the metal via the lone pair of electrons on the nitrogen atom.[18] This is visualized in the HOESY spectrum (Fig. 2) with two cross-peaks corresponding to the methylene protons (×4) on TMEDA (downfield signal) and the methyl protons (×12) on TMEDA (upfield signal) correlating with the lithium signal. Thus, the solution structure of lithiated (*E*)-1-(*t*-butylthio)but-2-ene complexed with TMEDA (**4**), bears little resemblance to its solid state counter part and is best described as a transoid or "W" shaped carbanion with lithium located much closer to C1 than C2 in a unsymmetrical, dihapto or monohapto (with C1) bonding arrangement.

Examination of the position of lithium in lithiated (*E*)-1-(phenylthio)but-2-ene complexed with TMEDA, a carbanion shown to be cisoid about C1–C2,[5] was also conducted. It was thought that the 'sickle' shape of the carbanionic backbone might have some effect on the position of the lithium in allylic sulfide carbanions. As can be seen in the plot of the HOESY experiment (Fig. 3) the lithium cation in (*E*)-1-(phenylthio)but-2-ene complexed with TMEDA is adopting a position relative to the allylic carbon backbone which is akin to that seen for the uncomplexed (*E*)-1-(*t*-butylthio)but-2-ene and TMEDA complexed (*E*)-1-(*t*-butylthio)but-2-ene in THF at 220 K (Figs. 1 and 2). Therefore the shape of the underlying allylic backbone (C1 to C3) has no bearing on the association of the lithium in these anions.

For the TMEDA complexed lithiated (*E*)-1-(*t*-butylthio)-but-2-ene system, there is evidently a disparity in structures obtained from X-ray crystallography (**5**) to that found in solution (**4**) (Chart 2). A possible explanation for this incongruity may include an equilibrium between the two distinct cisoid/trihapto (X-ray) and transoid/dihapto or transoid/monohapto (NMR) forms in solution. This equilibrium, tending to the transoid/dihapto or transoid/monohapto isomer in solution, results in low concentrations of the cisoid/trihapto isomer which cannot be detected by NMR spectroscopy. On freezing of the carbanion solution this equilibrium may be reversed with the cisoid isomer preferentially precipitating. Alternatively an increase in energy (for example, crystal lattice energy) on going from solution to solid, with an associated decrease in entropy in the solid state may result in the cisoid/trihapto isomer being preferred in the solid phase.

Regardless of a possible explanation for these structural differences in the TMEDA complexed lithiated (*E*)-1-(*t*-butylthio)but-2-ene system, it can be stated from the results obtained in this study and a previous study[5] that clearly there exists dramatic differences in the solution and solid structures of these highly reactive nucleophilic species. The drawing of conclusions with regard to the structure of these and other analogous species from the results of X-ray crystallography to the possible solution structure may therefore be not valid.

Experimental

Preparation of [^{6}Li]-Butyllithium. [^{6}Li]-Butyllithium was prepared from ^{6}Li metal (Aldrich) immediately prior to allylic anion generation and NMR analysis according to the following method.

^{6}Li metal (0.5 g, 72.0 mg atoms) was prepared by flattening with pliers, cutting into small pieces and repeatedly washing with distilled pentane.[19] Dry pentane (20 ml) was added and the reaction mixture stirred under a steady stream of argon between -10 and 0 °C. A solution of freshly distilled 1-bromobutane (4.8 g, 35.0 mmol, 3.7 ml) in dry pentane (15 ml) was added slowly over 2.5 to 3 hours between -10 and 0 °C. The initially clear solution turned a cloudy grey to purple during the course of the addition as the ^{6}Li metal reacted. Upon completion of the addition the temperature of the reaction mixture was raised to room temperature and stirred for a further 48 h. The heterogeneous mixture was allowed to stand for a further 2 h, giving a clear supernatant. The mother liquor was carefully cannulated into a separate vessel under argon and the volume of solvent reduced by approximately one half in vacuo. The remaining clear liquid was titrated against a known amount of 2,5-dimethoxybenzyl alcohol according to the method of Winkle, Lansinger, and Ronald,[20] to give [^{6}Li]-butyllithum in pentane (8 to 10 ml, 3.78 Molar). Using variations of the above procedure, [^{6}Li]-butyllithium was obtained in varying concentrations from 2.2 to 6.1 Molar.[21]

Preparation of [^{6}Li]-Lithiated (*E*)-1-(*t*-Butylthio)but-2-ene (1) and [^{6}Li]-Lithiated (*E*)-1-(Phenylthio)but-2-ene (2). The preparation of the substrate precursors and the ^{6}Li-labeled anions (1) and (2) used in this study have been described previously.[5]

HOESY NMR Spectroscopy. NMR spectra were recorded with a Bruker AMX400 spectrometer fitted with a multinuclear probe in tetrahydrofuran-d_8 (Aldrich). ^{1}H spectra were acquired at 400.14 MHz and referenced to the low field THF-d_8 signal ($\delta = 3.70$) and ^{6}Li at 58.88 MHz and are unreferenced. The spectra acquisition temperatures stated have an error of ±5 K and were obtained from the uncalibrated spectrometer variable temperature unit. ^{6}Li T_1 values were measured with an inversion–recovery pulse sequence.[22] Phase sensitive HOESY spectra were acquired using a $t_D-(\pi/2)_H-t_1-(\pi/2)_H-\tau_m-(\pi/2)_{Li}-t_2$ pulse sequence as previously described.[9,10,15] Typically, 32 or 16 scans for each of 256 or 128 experiments were acquired, with relaxation delays of 2 s between scans. HOESY spectra were transformed with zero filling by a factor of two in both dimensions, and exponential weighting functions in both dimensions (line broadening value of 1.0 Hz in ω_2 and 2.0 Hz in ω_1).

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