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Notes

Isolation and Structure Analysis of Neohexyllithium Generated by Ether Cleavage: Primary and Secondary Coordination in Alkyllithium Aggregates

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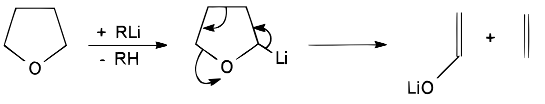
Summary: Ether cleavage of THF at low temperature affords halide-free neohexyllithium in a two-step reaction via insertion of in situ formed ethylene into the C-Li bond of tert-butyllithium. The crystal structure analysis reveals the formation of tetrameric THF-solvated aggregates in the solid state. The neohexyl ligands adopt a staggered arrangement with respect to the tetrahedral lithium core, in contrast to the eclipsed conformation generally observed in unsolvated species. The different conformations in these oligomers can be rationalized readily by distinguishing between primary and secondary cation coordination.

Introduction

The use of ethers as solvents for organolithium reagents is known to significantly enhance the reactivity of these compounds in metalation and displacement reactions.[1] Very often, however, the solvent itself is the target of attack by the organometallic reagent, yielding "undesirable" side products as the result of ether cleavage.[2] To date, several articles reporting the mechanisms[2c,3] and kinetics[4] of ether cleavage reactions have been published, and the stability of a variety of organolithium/ether systems have been investigated.[4a,5] Possible reaction pathways are the nucleophilic cleavage and the deprotonation followed by α-,[2b] β-,[6] or α,β'-elimination[3a,7] or Wittig rearrangement.[7,8]

Nucleophilic cleavage of THF, the most commonly used cyclic ether, is observed only when soft organolithium compounds with resonance stabilized anions (e.g trityllithium[9] and 1,1-diphenylmethyllithium[10]) are used. Hard organolithium bases (e.g. alkyllithium compounds) deprotonate at the α-position forming as a first intermediate α-lithiated THF **1**.[11] A $[\pi 4s + \pi 2s]$ cycloreversion follows affording the corresponding enolate **2** and ethylene (eq 1).[3b,11,12]



1 **2**

(1)

In a secondary reaction, the ethylene can (multiply) insert into the C-Li bond of the unreacted organolithium reagent, forming homologous organolithium derivatives.[3c,13] When secondary or tertiary alkyllithium compounds are employed this reaction stops after a single insertion.[14] Bartlett et al. attributed these results to the difference in reactivity between the secondary (tertiary) organolithium compound and the primary lithium base, which forms by a single insertion

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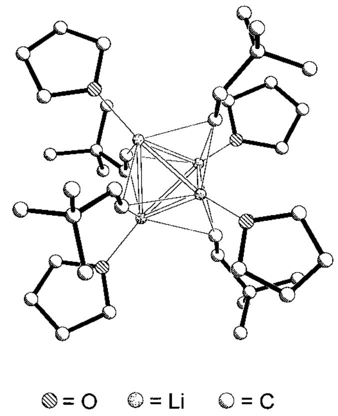
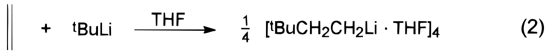


Figure 1. Molecular structure of **3**. The tetrahedral aggregate is generated from the monomeric unit (t-BuCH$_2$CH$_2$Li·THF) via the crystallographic inversion axis $\bar{4}$. The hydrogen atoms have been omitted for clarity.

of ethylene.[14a] Thus, the liberated ethylene is instantly consumed by the secondary (tertiary) lithium base before a reaction with the higher homologue arises. While the existence of the ethylene insertion products have been indirectly confirmed by trapping experiments, direct characterization has not been achieved to date. In this paper we describe the isolation and the solid-state structure of tetrameric THF-solvated neohexyllithium **3**, which was formed upon single insertion of ethylene into the C-Li bond of t-BuLi (eq 2) following the deprotonation and cleavage of THF.



$$+\ {}^{t}\mathrm{BuLi} \xrightarrow{\mathrm{THF}} \tfrac{1}{4}\ [{}^{t}\mathrm{BuCH_2CH_2Li}\cdot\mathrm{THF}]_4 \qquad (2)$$

3

Results and Discussion

At low temperature, the ether cleavage of THF with t-BuLi proceeds stepwise, which may explain the changes of color of the reaction solution as well as the initial formation of a precipitate. It is very likely that the formation of a t-BuLi/THF solvate precedes the actual ether cleavage reaction. According to low-temperature NMR investigations, t-BuLi forms a monomeric solvate in THF.[15] Since the monomeric form is even more reactive than the unsolvated tetramer, multiple insertion of in situ generated ethylene is suppressed completely. The different solubilities of both lithium compounds in nonpolar solvents were used to almost quantitatively separate the lithium enolate **2** and the insertion product **3** (the ^{1}H integrated NMR spectrum of precipitated **2**[16] revealed a 7% molar impurity of **3**). Pure **3** was obtained by low-temperature crystallization and was identified by NMR spectroscopy and crystal structure analysis.

Table 1. Selected Atomic Distances (Å) and Angles (deg) of 3[a]

Li1−O1	1.946(5)	C1−Li1c	2.304(6)
Li1−Li1a	2.419(9)	C1−C2	1.522(4)
Li1−Li1c	2.539(9)	C2−C3	1.542(4)
Li1a−Li1c	2.539(9)	C3−C4	1.519(5)
C1−Li1	2.239(6)	C3−C5	1.526(5)
C1−Li1a	2.242(6)	C3−C6	1.516(5)
Li1a−Li1−Li1c	61.55(11)	C1−C2−C3	120.7(3)
Li1−Li1c−Li1a	56.9(2)	C2−C3−C4	110.1(3)
Li1c−Li1a−Li1	61.55(11)	C2−C3−C5	109.8(3)
Li1a−C1−Li1	65.4(2)	C2−C3−C6	110.6(3)
Li1−C1−Li1c	67.9(2)	H1a−C1−H1b	98(2)
Li1c−C1−Li1a	67.9(2)		

[a] Symmetry transformations used to generate equivalent atoms: (a) $-x + 1$, $-y + 0.5$, z; (b) $y + 0.25$, $-x + 0.75$, $-z - 0.25$; (c) $-y + 0.75$, $x - 0.25$, $-z - 0.25$.

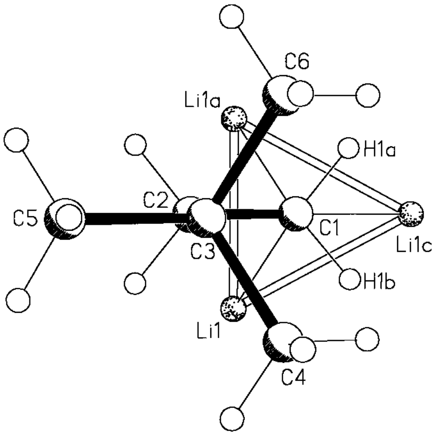


Figure 2. Projection of the molecular structure of **3** perpendicular to one of the Li triangles of the Li$_4$ tetrahedron. The picture illustrates the staggered arrangement of the coordinated neohexyl group with respect to the lithium framework.

The solid-state structure of **3** is depicted in Figure 1; selected bond lengths and angles are listed in Table 1. Within the tetrameric aggregates the monomeric units of **3** are connected via a crystallographic inversion axis $\bar{4}$, generating S_4 symmetry in the tetramers. Each face of the Li$_4$ tetrahedron is capped by a neohexyl group, while the coordination sites at the corners are occupied by THF molecules. Within the standard deviation, each deprotonated C$_\alpha$ carbon atom coordinates to two Li atoms of the isosceles triangles through equidistant bonds (C1−Li1 = 2.239(6) Å, C1−Li1a = 2.242(6) Å). The third Li atom exhibits the longest Li-C$_\alpha$ bond (C1-Li1c = 2.304(6) Å) as well as the longest Li−Li distances within the triangle (Li1c−Li1 = Li1c−Li1a = 2.539(8) Å, Li1−Li1a = 2.419(9) Å). The distance to the coordinating THF molecule is 1.946(5) Å (Li1−O1). Thus, the structural parameters observed for **3** are similar to those determined in related structures (for comparison, average distances for Li−Li, Li−C$_\alpha$, and Li−O$_{\mathrm{solvent}}$ in [MeLi·THF]$_4$[17] are 2.51, 2.24, 1.96 Å, in [^{n}BuLi·THF]$_4$[18] are 2.54, 2.24, and 1.97 Å, and in [^{t}BuC≡CLi·THF]$_4$[19] are 2.69, 2.19, 1.96 Å). However, the arrangement of the alkyl groups in **3** differs significantly from the conformation observed in solvent-free aggregates. The C$_\beta$ atoms of the neohexyl groups adopt a staggered arrangement with respect to the Li skeleton (Figure 2), whereas an eclipsed orientation is preferred in unsolvated alkyllithium aggregates.[20] The latter has been

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(16) NMR data for **2** ([^{2}H$_8$]THF, 25 °C): ^{1}H, δ 6.88 [dd, 1H, LiOCH, ^3J(HH$_t$) = 13.3, ^3J(HH$_c$) = 4.9Hz], 3.12 [d, 1H, H_cH$_t$C, ^3J(H$_c$H) = 4.9 Hz] (the THF signal overlaps the H$_c$$H_t$C signal at 3.6 ppm); ^{13}C, δ 159.08 [s, LiOCH], 81.76 [s, CH$_2$]. ^{1}H chemical shifts and coupling constants are consistent with the data published in ref 11.

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explained in terms of favorable electrostatic Li−C_β interactions which complete the coordination shell of lithium.[20c] In **3**, as well as in other solvated alkyllithium clusters, these additional coordination sites at the Li-centers are occupied by polar ligands.

Apparently, the cation coordination in alkyllithium aggregates follows a general pattern. Theoretical analyses have already established the predominantly ionic nature of the Li−C bond in organolithium compounds.[21] This explains the formation of oligomeric species as well as the position of the deprotonated carbon atoms C_α above a triangular Li_3 face, providing the maximum number of interactions with the lithium core. In addition, a "secondary" cation coordination which involves the corners of the respective Li skeleton is achieved by the association of solvent molecules or by the formation of *intra*aggregate Li−C_β interactions. If neither of these are possible *inter*aggregate Li−C'_α interactions (e.g. in MeLi[22]) are formed, resulting in a network structure. Hence, the formation of distinct alkyllithium aggregates in nonpolar solvents requires the presence of C_β atoms accessible for Li−C_β interaction. This may explain why MeLi is only soluble in polar solvents, whereas EtLi also dissolves in nonpolar solvents, despite the fact that *both* form networks via *inter*aggregate interactions in the solid state. The oligomeric structures of the THF solvates of *t*-BuC≡CLi[19] may serve as another example for this situation. Here, the C_β atoms are unavailable for lithium coordination due to the linear conformation of the anion. In the presence of more than equimolar amounts of THF the compound crystallizes as a tetrameric aggregate [(*t*-BuC≡CLi)·THF]$_4$, similar to **3**. Upon addition of substoichiometric amounts of THF the dodecamer [(*t*-BuC≡CLi)$_{12}$·4THF] is isolated. The aggregate may be interpreted as an array of three tetrameric subunits connected via *inter*aggregate Li−C'_α interactions and end-capped by THF molecules. A similar situation may determine the structure of PhLi; the C_β atoms are blocked at least to a certain extent by the aromatic hydrogen atoms. To achieve a soluble form of this reagent, polar solvent molecules are necessary to contribute to the formation of distinct aggregates, as exemplified by the solid-state structure of tetrameric [PhLi·Et_2O]$_4$.[23] In contrast, cyclohexyllithium is soluble in nonpolar solvents. The solid-state structure of solvent-free cyclohexyllithium reveals the formation of distinct hexameric aggregates featuring short Li−C_β distances and an eclipsed arrangement of the cyclohexyl groups with respect to the lithium triangles.[20b]

As mentioned above, insertion reactions of in situ generated ethylene have been reported for various alkyllithium[3c,14] and aryllithium[2c] compounds. Furthermore, as is the case with EtLi,[3b] several other alkyllithium species are capable of cleaving ethers with formation of alkenes, even at low temperature. It is therefore reasonable to assume that—starting with the corresponding halide free precursors—a variety of homologous halide-free organolithium species are accessible via this reaction sequence. Multiple ethylene insertion into the C−Li bond of primary organolithium compounds could be suppressed by keeping the reaction temperature low. Further studies with the aim of achieving stoichiometric conversion in the ether cleavage reaction discussed are under way, and other organolithium/ether systems are to be examined in terms of their suitability and efficiency with respect to the synthesis of pure organolithium derivatives.

Table 2. Crystal Data of 3

formula	$C_{40}H_{84}Li_4O_4$
fw	656.83
cryst size (mm^3)	0.5 × 0.5 × 0.3
space group	$I4_1/a$
a (Å)	20.7006(14)
c (Å)	10.8304(13)
V (Å^3)	4641.0(7)
Z	4
temp (K)	173(2)
ρ_{calc} (Mg m^{-3})	0.940
μ (mm^{-1})	0.056
$F(000)$	1472
2θ range (deg)	7−45
no. of rflns collected	2925
no. of unique rflns (R_{int})	1499 (0.039)
no. of restraints	32
no. of refined params	135
R1^a ($I > 2\sigma(I)$)	0.058
wR2^b (all data)	0.177
largest diff peak/hole (e Å^{-3})	+0.176/−0.166

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

Experimental Section

All manipulations were carried out under an argon atmosphere using standard Schlenk techniques. Solvents were dried over Na/K alloy and freshly distilled prior to use. ^1H and ^{13}C NMR spectra were obtained with a General Electric QE-300 spectrometer at a frequency of 300 MHz (^1H) and 75 MHz (^{13}C), respectively. All spectra were recorded in THF-d_8 at room temperature from 5−10% solutions with $SiMe_4$ as external standard. Due to the high sensitivity of **3** toward oxygen and moisture an accurate elemental analysis could not be obtained.

[*t*-BuCH$_2$CH$_2$Li·THF]$_4$ (3). At −78 °C 20 mL of precooled THF (0.25 mol) is added to 100mL of a 1.5 M solution of *t*-BuLi in pentane (0.15 mol) over a period of 2 h. The initially formed yellow precipitate, probably α-lithiated THF, dissolves with stirring, yielding a pale yellow solution. Subsequently, a white precipitate of the lithium enolate of acetaldehyde forms, which dissolves when the reaction solution is warmed to 0 °C. After removal of the solvents under vacuum, a yellow oil is obtained. A 50 mL portion of pentane is added and the precipitate of lithium enolate is filtered off at 0 °C. At −85 °C colorless blocks of **3** crystallize from the remaining solution after 1−2 days. Yield: 3.8 g (31%). ^1H NMR (ppm): δ 1.33 [t, 2H, $LiCH_2CH_2$, ^3J(HH) 9.4 Hz], 0.73 [s, 9H, $C(CH_3)_3$], −1.22 [t, 2H, $LiCH_2$, ^3J(HH) 9.4Hz]. ^{13}C NMR (ppm): δ 47.27 [s, $LiCH_2CH_2$], 33.29 [s, $C(CH_3)_3$], 29.42 [s, $C(CH_3)_3$], 1.16 [s, $LiCH_2$].

X-ray Crystallography. The crystal data of **3** are presented in Table 2. At low temperature, an oil-coated crystal was mounted on the tip of a glass fiber and shock-cooled under a cold nitrogen gas stream.[24] The data were collected at −100

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°C on a Siemens P4 four-circle diffractometer equipped with a modified version[25] of the Siemens LTII low-temperature device (graphite-monochromated Mo Kα radiation, $\lambda = 0.710\ 73$ Å, $2\theta/\omega$ scans with variable scan speed, profile analysis using background intensities). The structure was solved by direct methods (SHELXS-90[26]) and refined by full-matrix least-squares methods (SHELXL-93[27]) against F^2 by employing all data, with a weighting scheme of $w = 1/[\sigma^2(F_o^2) + (0.0821P)^2 + 2.3454P]$ ($P = [\max(0,F_o^2) + 2F_c^2]/3$) and anisotropic refinement of all non-H atoms. H atoms of the THF molecule and the methyl groups were included on calculated positions with constrained isotropic displacement parameters and refined according to a riding model (methyl groups rotating); free isotropic refinement of the methylenic H atoms of the neohexyl group was carried out by applying geometric restraints. A disorder in the THF molecule was refined to 70%/30% occupation using geometric and ADP restraints.

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Supporting Information Available: Tables of crystal data, fractional coordinates, bond lengths and angles, anisotropic displacement parameters, and hydrogen atom coordinates and completely labeled figures of 50% anisotropic displacement parameters of the structure of **3** (9 pages). Ordering information is given on any current masthead page.

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