Lithium Alkyl compounds

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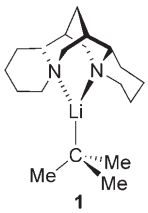
# From Monomeric *t*BuLi·(*R*,*R*)-TMCDA to α-Lithiated (*R*,*R*)-TMCDA**

*Carsten Strohmann* and Viktoria H. Gessner*

Lithiated hydrocarbons are known for their distinctive tendency to form oligomeric aggregates.[1] Nevertheless, in reactions like deprotonations, monomeric structures are usually assumed to be the reactive species in commercially available saturated alkyl lithium compounds. To date, only a single such monomer, *t*BuLi·(−)-sparteine (**1**), could be isolated and characterized by single crystal X-ray structure analysis.[2] The sterically demanding ligand (−)-sparteine prevents the formation of higher aggregates. Like sparteine, the $C_2$-symmetric (1*R*,2*R*)-*N*,*N*,*N*′,*N*′-tetramethylcyclohexane-1,2-diamine [(*R*,*R*)-TMCDA, (*R*,*R*)-**2**], a less demanding ligand, is used in asymmetric deprotonation.[3] In light of these properties, we wondered what structure is formed by (*R*,*R*)-TMCDA and *t*BuLi. In the course of the ensuing investigations, we observed the unexpected α-lithiation of (*R*,*R*)-TMCDA, which can be explained by assuming a monomeric *t*BuLi·(*R*,*R*)-TMCDA precursor. Recently, we suggested a different reaction pathway for the α-lithiation of *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylentriamine (PMDTA) on the basis of the molecular structure of $[(n\text{BuLi})_2\cdot\text{PMDTA}]_2$.[4]




**1**

α-Lithiated amines are usually only accessible by transmetalation or through the more readily deprotonated aminoboranes.[5] The synthesis of α-lithiated amines by direct deprotonation usually requires intramolecular activation, which can take place through a second nitrogen center. Examples of such α-lithiated di- and triamines are PMDTA, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), and *N*,*N*,*N*′,*N*′-tetramethylmethylenediamine (TMMDA).[6] The repulsive interaction between the carbanion and the free electron pair on the nitrogen atom is often offered as explanation for the hindered metalation. These interactions can, however, only be employed as an argument for transition states close to the products. In contrast, a two-stage process is usually assumed for deprotonation in the presence of donor centers; in the first step, a reactive intermediate in which the reacting groups approach one another spatially is formed by pre-coordination. This reaction pathway (or this pre-coordination) is called the complex-induced proximity effect (CIPE).[7] Assuming such a thermodynamically favorable pre-coordination of *t*BuLi to (*R*,*R*)-TMCDA, as we propose herein, deprotonation of a methyl group should be possible.

Monomeric *t*BuLi·(*R*,*R*)-TMCDA (**3**) crystallizes from an equimolar solution of *tert*-butyllithium and (*R*,*R*)-TMCDA in *n*-pentane at −78 °C as colorless needles in the monoclinic crystal system in the space group $P2_1$.[8] Apart from *t*BuLi·(−)-sparteine (**1**), **3** is the only structurally characterized monomeric alkyl lithium compound bearing a saturated hydrocarbon.[2] Similar to **1**, *t*BuLi·(*R*,*R*)-TMCDA has shorter Li–C bonds [2.064(15) Å] than dimeric compounds.[9,10] However, as the space-filling model of **3** shows (Figure 1) the sterically less demanding nature of the ligand (*R*,*R*)-TMCDA leaves a positively polarized coordination site at the lithium center quite exposed. This site of attack explains the high reactivity of *t*BuLi·(*R*,*R*)-TMCDA. During preparation of the crystals, **3** proved to be significantly more reactive than **1** or $(t\text{BuLi})_4$, and in toluene solution it deprotonated the methyl group of toluene at −30 °C.

On warming from −78 °C to room temperature, a suspension of *t*BuLi and (*R*,*R*)-TMCDA in *n*-pentane becomes clear at about −30 °C. From this temperature on, slow lithiation of the ligand can be observed. The reaction of the solution formed at room temperature with $MePh_2SiCl$ yields compound **5**, the silylated reaction product of α-lithiated (*R*,*R*)-TMCDA. No carbenoid behavior of the lithiated nitrogen compound was evident. From an analogously prepared reaction solution of *t*BuLi and (*R*,*R*)-TMCDA in pentane at −78 °C, α-lithiated (*R*,*R*)-TMCDA **4**

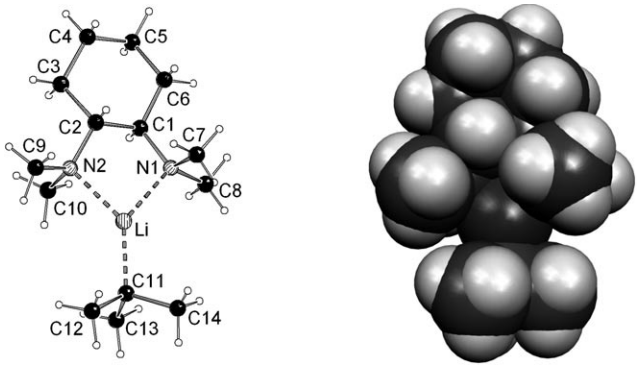



***Figure 1.*** Left: molecular structure and numbering scheme for *t*BuLi·(*R*,*R*)-TMCDA (**3**).[11] Selected bond lengths [Å] and angles [°] (for one of the two molecules in the asymmetric unit): C11-Li 2.064(15), Li-N1 2.086(15), Li-N2 2.055(11); C11-Li-N2 134.1(6), C11-Li-N1 135.6(7), N2-Li-N1 87.4(5). Right: space-filling model.

[*] Dr. C. Strohmann, V. H. Gessner
Institut für Anorganische Chemie, Universität Würzburg
Am Hubland, 97074 Würzburg (Germany)
Fax: (+49) 931-888-4605
E-mail: mail@carsten-strohmann.de

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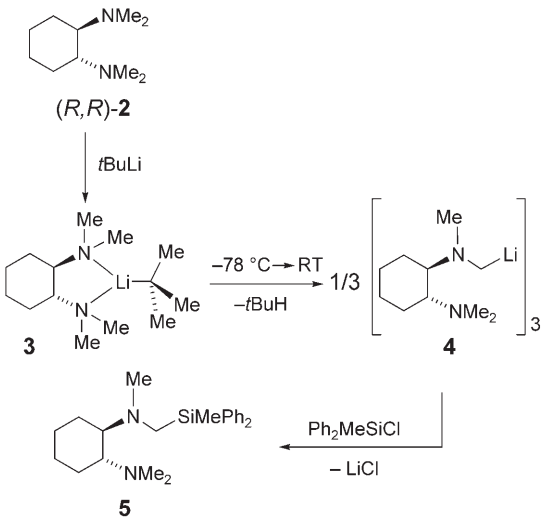
(Scheme 1) crystallizes as a trimer in the orthorhombic crystal system in the space group $P2_12_12_1$ (Figure 2). The Li–C distances of compound **4** vary between 2.140(11) and 2.265(11) Å and thus lie in the region of monomeric and dimeric compounds.[2,9,10] The same is true for the Li–N distances; each lithium center is closer to the nitrogen center attached to the lithiated carbon atom [1.942(9)–1.992(10) Å] and further away from the second nitrogen center [2.085(10)–2.182(10) Å]. [(*R*,*R*)-TMCDA-Li]$_3$ is one of only few trimeric alkyl lithium compounds.[12] Without addition of Lewis bases, alkyl lithium compounds preferentially exist as hexameric or tetrameric aggregates. Variable-temperature NMR spectroscopy studies with a solution of **4** in [D$_8$]toluene showed highly broadened signals between −80 and 20 °C in both the $^1$H NMR and the $^{13}$C NMR spectra. Both dynamic processes and freezing of the unsymmetric trimeric structure with three




***Scheme 1.*** Formation of monomeric *t*BuLi·(*R*,*R*)-TMCDA (**3**) and its reaction to α-lithiated (*R*,*R*)-TMCDA (**4**).

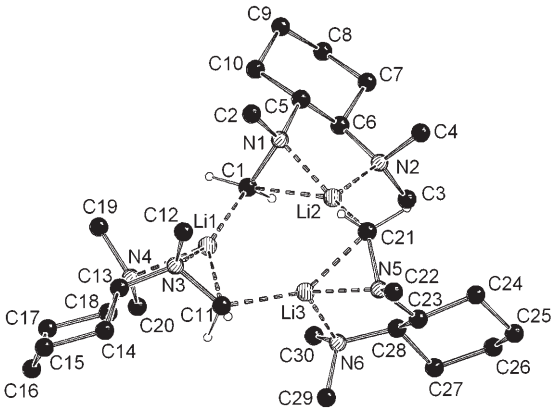



***Figure 2.*** Molecular structure and numbering scheme for [(*R*,*R*)-TMCDA-Li]$_3$ (**4**).[11] Selected bond lengths [Å] and angles [°]: C1-Li1 2.171(11), C1-Li2 2.265(11), C21-Li2 2.140(11), C21-Li3 2.148(10), C11-Li3 2.159(11), C11-Li1 2.187(11), Li1-N3 1.973(12), Li1-N4 2.182(10), Li2-N1 1.942(9), Li2-N2 2.153(11), Li3-N5 1.992(10), Li3-N6 2.085(10); Li1-C1-Li2 96.7(4), Li3-C11-Li1 81.7(4), Li2-C21-Li3 81.7(4), C1-Li1-C11 143.4(5), C21-Li2-C1 136.6(5), C11-Li3-C21 137.7(5).

differently arranged molecular groups should result in such broadened or overlapping signals.[1]

Why is (*R*,*R*)-TMCDA lithiated? The otherwise difficult α-lithiation is facilitated in monomeric *t*BuLi·(*R*,*R*)-TMCDA (**3**) by the spatial proximity of the reacting groups, in agreement with the CIPE concept.[7] Quantum-chemical studies at the B3LYP/6-31 + G(d) level (Figure 3) confirm this interpretation with a calculated reaction barrier of only 98 kJ mol$^{-1}$ for the intramolecular metalation of TMCDA starting from monomeric *t*BuLi·(*R*,*R*)-TMCDA. Slow metalation below room temperature would be anticipated from these energy barriers.

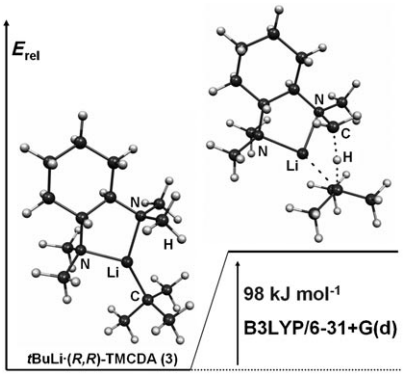



***Figure 3.*** Transition state of the metalation of (*R*,*R*)-TMCDA in the monomeric aggregate with *t*BuLi; B3LYP/6-31 + G(d).[13]

α-Deprotonation of a methyl group has also been described for TMEDA, which raises the question as to whether other structurally related diamines also undergo deprotonation of their methyl group.[5a–c] For achiral *N*,*N*′-dimethylpiperazine, we were also able to elucidate a molecular structure with *t*BuLi in the solid sate, but no deprotonation was observed in solution. The coordination polymer [(*t*BuLi)$_2$·(*N*,*N*′-dimethylpiperazine)]$_\infty$ (**6**) crystallizes with an additional half molecule *N*,*N*′-dimethylpiperazine from an equimolar solution of *t*BuLi and the ligand in *n*-pentane at −30 °C in the form of colorless needles in the triclinic crystal system in the space group $P\bar{1}$ (Figure 4). The coordination polymer consists of central *tert*-butyllithium dimers, which are coupled to further dimers through two ligand molecules to form a coordination polymer. In this structure, the *N*,*N*′-dimethylpiperazine molecules are orientated at right angles to one another, thus creating a zigzag arrangement of the chains. Compound **6** is the first coordination polymer of *t*BuLi, which on account of its spatial demand otherwise forms smaller aggregates.[2,9b]

Why is *N*,*N*′-dimethylpiperazine not lithiated by *t*BuLi? On the basis of the molecular structure of **6**, deprotonation starting from either a dimeric aggregate or a monomer should be open to discussion. Whereas monomeric *t*BuLi·(*R*,*R*)-TMCDA is 14 kJ mol$^{-1}$ more favorable than 0.25 (*t*BuLi)$_4$ and (*R*,*R*)-TMCDA, 36 kJ mol$^{-1}$ are required for the formation of monomeric *t*BuLi·*N*,*N*′-dimethylpiperazine starting from 0.25 (*t*BuLi)$_4$ and *N*,*N*′-dimethylpiperazine, which cannot be compensated by entropic effects. Nevertheless, if the formation of the monomeric model compound *t*BuLi·*N*,*N*′-dime-

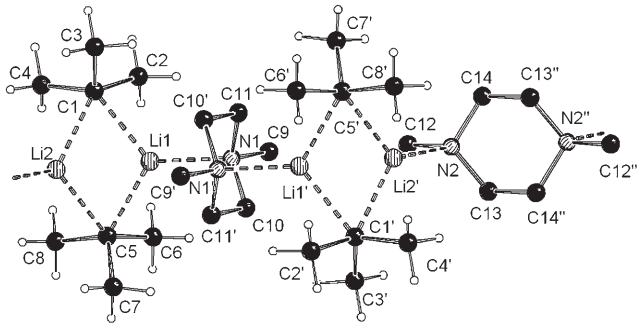



***Figure 4.*** Molecular structure and numbering scheme for $[(t\text{BuLi})_2\cdot(N,N'\text{-dimethylpiperazine})]_\infty$ (**6**).[11] Selected bond lengths [Å] and angles [°] (for clarity, the additional half molecule of *N*,*N*′-dimethylpiperazine was omitted): C1-Li1 2.244(5), C1-Li2 2.212(4), C5-Li1 2.224(4), C5-Li2 2.228(5), Li1-N1 2.191(5), Li2-N2′ 2.158(6), Li1-Li2 2.357(6); Li1-C1-Li2 63.86(16), Li2-C5-Li1 63.93(15), C1-Li1-C5 109.25(17), C5-Li2-C1 110.27(19), C1-Li2-Li1 58.74(16), C5-Li2-Li1 57.94(15).

thylpiperazine is assumed, α-lithiation involves overcoming a barrier of 131 kJ mol$^{-1}$. Deprotonation starting from the dimeric model compound ($t$BuLi·*N*,*N*′-dimethylpiperazine)$_2$ gives an energy barrier of 132 kJ mol$^{-1}$, which might be reduced by 10 kJ mol$^{-1}$ released by the formation of the dimer from 0.5 ($t$BuLi)$_4$ and two *N*,*N*′-dimethylpiperazine.[14,15] Thus, *N*,*N*′-dimethylpiperazine is not lithiated by $t$BuLi, because monomeric molecular structures or transition states are only poorly stabilized and a corresponding transition state in a dimer also lies too high energetically.

Whether or not α-lithiation of methylamines occurs can be explained on the basis of the molecular structures presented. In monomeric $t$BuLi·(*R*,*R*)-TMCDA (**3**), the carbanionic carbon atom and the H atom of the methyl group approach each other, which facilitates α-lithiation of (*R*,*R*)-TMCDA. Such a spatial proximity is not reached in $[(t\text{BuLi})_2\cdot(N,N'\text{-dimethylpiperazine})]_\infty$ (**6**). Since the breakdown into smaller aggregates requires too much energy and possible reaction barriers are too high, no lithiation of *N*,*N*′-dimethylpiperazine can take place. We are currently searching for further di- and triamines which, owing to their good coordination properties and the associated formation of reactive intermediates with spatially preorientated reacting groups, may be deprotonated.

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