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Crystal Structures of the Chiral Diamine (*R,R*)-TMCDA with the Commonly Used Alkyllithium Bases Methyllithium, *iso*-Propyllithium, and *sec*-Butyllithium

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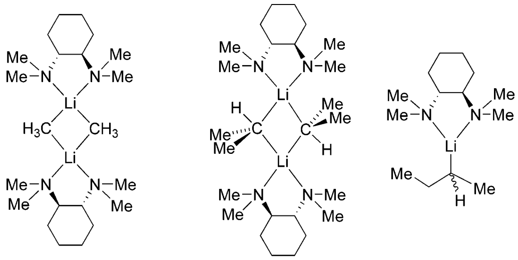
Combinations of organolithium compounds and chiral diamines, like (−)-sparteine and its derivatives as well as (*R*,*R*)-*N*,*N*,*N*′,*N*′-tetramethyl-1,2-diaminocyclohexane [(*R*,*R*)-TMCDA], are widely utilized in asymmetric synthesis.[1,2] Whereas *sec*-butyllithium and (−)-sparteine have proven to be a powerful reagent for asymmetric deprotonation, (*R*,*R*)-TMCDA and its (*S*,*S*)-enantiomer turns out to be more reactive but with modest enantioselectivity.[3] For determination of the structure/reactivity relationships of chiral alkyllithium bases the characterization of the solid-state structures is of great importance. Although the first (−)-sparteine coordinated alkyllithium structures have been uncovered, no structures with *sec*-butyllithium, the most frequently used lithium base in asymmetric synthesis, have been determined so far.[4] Although NMR studies conducted by Collum et al. have determined that *n*-BuLi and (*R*,*R*)-TMCDA form a dimer in solution, solid-state structures of this C_2-symmetric diamine complexed with alkyllithium bases are not known so far.[5] Here, we present the first molecular structures of (*R*,*R*)-TMCDA with the alkyllithium bases MeLi (**1**), *i*-PrLi (**2**) and *s*-BuLi (**3**) (Figure 1). Monomer **3** is the first Lewis base-coordinated adduct of *s*-BuLi, which is highly reactive owing to its monomeric structure.



1 (MeLi) **2** (*i*-PrLi) **3** (*s*-BuLi)

Figure 1. Structures of lithium alkyls with coordinating (*R*,*R*)-TMCDA.

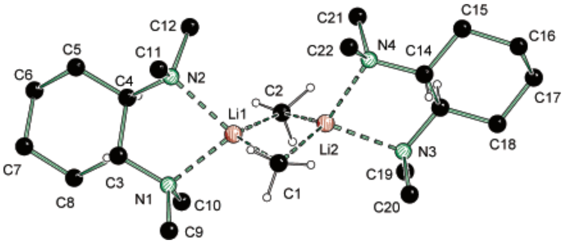


Figure 2. Molecular structure of [MeLi·(*R*,*R*)-TMCDA]$_2$ (**1**) in the crystal. Selected bond lengths (Å) and angles (deg) (some hydrogens omitted): C1−Li1, 2.252(7); C1−Li2, 2.277(7); C2−Li1, 2.214(7); C2−Li2, 2.219(7); Li1−N1, 2.168(7); Li1−N2, 2.184(7); Li2−N3, 2.176(6); Li2−N4, 2.179(7); Li1−C1−Li2, 64.4(2); Li1−C2−Li2, 65.9(2); C2−Li1−C1, 114.0(3); C2−Li2−C1, 112.8(3).

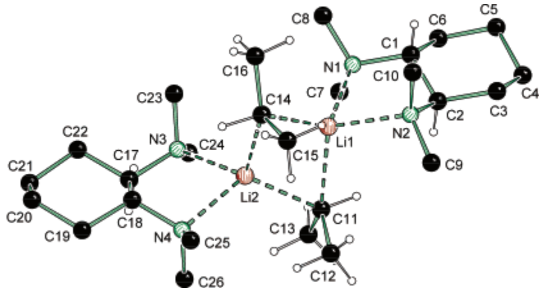


Figure 3. Molecular structure of [*i*-PrLi·(*R*,*R*)-TMCDA]$_2$ (**2**) in the crystal. Selected bond lengths (Å) and angles (deg) (some hydrogens omitted): C11−Li2, 2.234(11), C11−Li1, 2.332(6); C14−Li1, 2.206(6); C14−Li2, 2.321(6); Li1−N1, 2.240(6); Li1−N2, 2.219(5); Li2−N3, 2.256(6); Li2−N4, 2.229(6); Li2−C11−Li1, 66.0(2); Li1−C14−Li, 2 66.7(2); C14−Li1−C11, 109.2(2); C11−Li2−C14, 108.6(2)

The dimeric adduct [MeLi·(*R*,*R*)-TMCDA]$_2$ (**1**) crystallizes from pentane/diethylether in the orthorhombic crystal system, space group $P2_12_12_1$ (Figure 2).[6] The central structural motif of this aggregate is a central four-membered Li−C−Li−C ring, as is typical for dimeric alkyllithium compounds.[7] The sum of angles of 357.1° in this ring shows that there is a slight deformation toward an envelope conformation. The Li−C distances in the central four-membered ring range from 2.214(7) to 2.277(7) Å, and the Li−N distances range from 2.168(7) to 2.184(7) Å, which are comparable with the two other known dimeric MeLi adducts.[4c,d] Altogether, the lithium centers have four contacts each: two to the nitrogen centers of the (*R*,*R*)-TMCDA ligands and two to the methyl units. Besides the (−)-sparteine and one of its (±)-surrogate coordinated MeLi, **1** is the only known dimeric aggregate of methyllithium.[4c,d] Other commonly used amines, diamines, or ethers are not able to break the tetrameric aggregate of methyllithium.[7−9]

The structure of [*i*-PrLi·(*R*,*R*)-TMCDA]$_2$ (**2**), which crystallizes from pentane in the monoclinic crystal system, space group $P2_1$, is analogous to that of compound **1** (two dimeric molecules were detected in the asymmetric unit; one of them is shown in Figure 3). The central four-membered Li−C−Li−C ring also shows a slight deformation toward an envelope conformation (sum of ring angles 357.1° and 357.1°) but with a remarkable increase in the Li−C and Li−N distances. The distances between the lithium centers and the carbon centers range from 2.206(6) to 2.332(6) Å and the Li−N distances range from 2.219(5) to 2.256(6) Å. Compound **2** is the first dimeric adduct of *i*-PrLi.[4b,10]

The significantly lengthened Li−C and Li−N distances in **2** compared with similar compounds are due to steric interactions between the methyl groups of the *i*-Pr chain and the ligand and indicate a destabilization of the dimeric structure.[7] This tendency is confirmed by computational studies: at the B3LYP/6-31+G(d) level we find a decrease in the energy required for breaking the dimer into two monomers. Whereas cleavage of [MeLi·(*R*,*R*)-TMCDA]$_2$ needs 78.5 kJ·mol^{-1}, [*i*-PrLi·(*R*,*R*)-TMCDA]$_2$ requires 28.5 kJ·mol^{-1}, and the fictitious [*s*-BuLi·(*R*,*R*)-TMCDA]$_2$ requires merely 17.8 kJ·mol^{-1}. Because of entropic effects the monomeric *s*-BuLi·(*R*,*R*)-TMCDA (**3**) can be isolated from pentane/cyclohexane. Considered together, the compounds presented in Figure 1

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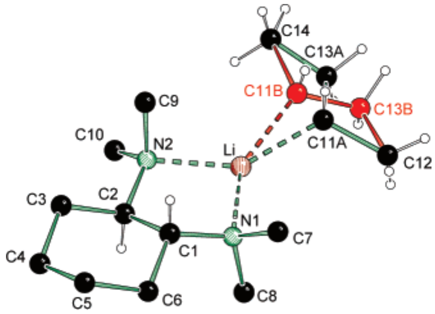

Figure 4. Molecular structure of [*s*-BuLi·(*R*,*R*)-TMCDA]$_2$ (**3**) in the crystal (disordered *sec*-Butyl). Selected bond lengths (Å) and angles (deg) (some hydrogens omitted): C11B−Li, 2.118(12); C11A−Li, 2.104(11); Li−N1, 2.054(5); Li−N2, 2.076(6); N1−Li−N2, 86.71(17); N1−Li−C11A, 122.0-(4); N2−Li−C11A, 146.1(4); N1−Li−C11B, 144.0(5); N2−Li−C11B, 122.5(4).

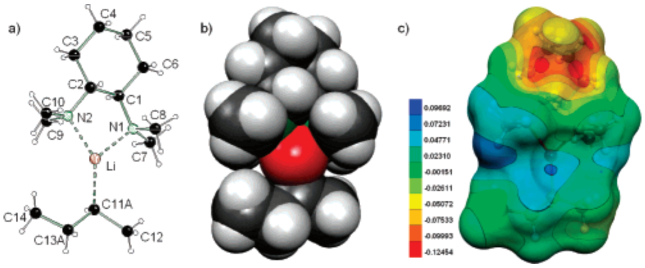

Figure 5. Molecular structure (crystal) (a), space-filling model (crystal) (b) and Connolly surface mapped with electrostatic potential [B3LYP/6-31+G(d) probe radius, 1.2 Å] of compound (*S*)-**3**.

clearly demonstrate the strong effect of the size of the alkyllithium compound on the type of aggregation.

The monomeric compound **3** crystallizes in the orthorhombic crystal system, space group $P2_12_12_1$. In the crystal disorder of both possible diastereomers, [(*R*)-*s*-BuLi·(*R*,*R*)-TMCDA] and [(*S*)-*s*-BuLi·(*R*,*R*)-TMCDA], in a 55:45 ratio was observed and refined using a split model (both diastereomers are shown in Figure 4). Calculations at the B3LYP/6-31+G(d) level showed a marginal energetic difference of 0.7 kJ·mol^{-1} between the two diastereomers, further confirming the coexistence of both in **3**. The Li−C distances [2.118(12) and 2.104(11) Å] and Li−N distances [2.054(5) to 2.076-(6) Å] are typically shorter than in comparable dimeric compounds.[7] Monomer **3** is the first Lewis base adduct of *sec*-butyllithium with a known crystal structure and a rare example of a monomeric saturated alkyllithium compound.[4a,11] As compounds **2** and **3** show, the oft-suggested structural analogy between *i*-PrLi and *s*-BuLi is not in any case appropriate.

The monomeric *s*-BuLi·(*R*,*R*)-TMCDA provides an impressive demonstration of the structure/reactivity relationship of organolithium compounds. As depicted by the space-filling model and the Connolly surface of compound **3** (Figure 5) the lithium center is barely shielded by the ligand and positively polarized. Thus it offers a free coordination site for the formation of intermediates via coordination of electrophiles in accordance to the CIPE mechanism.[12] The effects of the open lithium center are also seen in the strong reactivity of **3**, which is able to deprotonate non-coordinating benzene and toluene in substoichiometric amounts of (*R*,*R*)-TMCDA.

In summary, the first (*R*,*R*)-TMCDA-coordinated organolithium adducts show a clear influence of the size of the organolithium on the type of aggregation. In addition to the mechanism of aromatic deprotonation proposed by Collum et al. via triple ions or open dimers, the highly reactive monomeric *s*-BuLi·(*R*,*R*)-TMCDA may react by interactions involving the open lithium center of a monomeric species.[13] We are currently investigating structure/reactivity patterns based on the observed molecular structures.

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Supporting Information Available: Crystallographic (CIF), experimental, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) X-ray crystallography data for **1**, **2**, and **3** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication Nos. CCDC 644635 (**1**), CCDC 644636 (**2**), and CCDC 644637 (**3**).

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