Isopropyllithium diamine adducts: from a non symmetric aggregate to monomeric *i*-PrLi·(1*R*,2*R*)-*N*,*N*,*N*′,*N*′-tetraethylcyclohexane-1,2-diamine†

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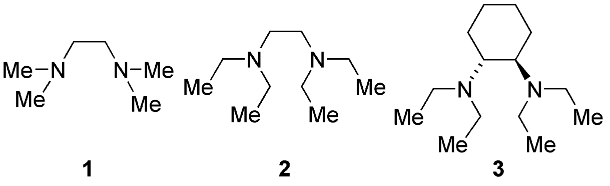
By means of isopropyllithium crystal structures, the transition from dimeric (*i*-PrLi·TMEDA)$_2$ (4) to monomeric *i*-PrLi·(*R*,*R*)-TECDA (6) *via* the non-symmetric aggregate [(*i*-PrLi)$_3$·(TEEDA)$_2$] (5) is shown, depending on the steric demand of the ligand.

Organolithium compounds are amongst the most often used reagents in synthetic chemistry. Therefore, the addition of Lewis bases, such as nitrogen ligands, plays an important role in controlling and increasing the reactivity of these compounds.[1] Especially chiral ligands mainly in combination with *sec*-butyllithium have become of great interest because of their application in asymmetric synthesis.[2,3] Due to the structure–reactivity relationship of lithium organics the understanding of the process of these reactions is strongly connected to the understanding of the structure formation patterns. However, to date there is only little structural information known about Lewis-base coordinated *s*-BuLi adducts.[4] In the case of chiral ligands, this lack of knowledge is probably due to the formation of diastereomers between the ligand and the lithium alkyl. These diastereomers lead to a hindered crystallisation of the adduct. Nevertheless, the elucidation of these compounds is still endeavoured for a better understanding of the reaction mechanism. An approach to this problem is the use of isopropyllithium instead of *s*-BuLi as organolithium compound. Both lithium bases possess almost the same steric demand and basicity. However, *i*-PrLi is more suitable for crystallisation due to the absence of diastereomeric mixtures.

We present herein the structure elucidation of three isopropyllithium adducts with the commonly used diamine ligands, *N*,*N*,*N*′,*N*′-tetramethylethylenediame (TMEDA, **1**), *N*,*N*,*N*′,*N*′-tetraethylethylenediamine (TEEDA, **2**) and the chiral (1*R*,2*R*)-tetraethylcyclohexane-1,2-diamine [(*R*,*R*)-TECDA, **3**] (Fig. 1). These structures show a transition from the dimeric compound (*i*-PrLi·TMEDA)$_2$ (**4**) to the monomer, *i*-PrLi·(*R*,*R*)-TECDA (**6**), *via* the non-symmetrical structure [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**), depending on the steric demand of the ligand. Therefore, the presented molecules impressively demonstrate the influence of the ligand on structure formation patterns.



1 **2** **3**

Fig. 1 Diamine ligands for alkyllithium compounds.

Out of a mixture of isopropyllithium and an equivalent amount of TMEDA in *n*-pentane, (*i*-PrLi·TMEDA)$_2$ (**4**) crystallises as colorless needles in the orthorhombic crystal system, space group *Fdd*2 (one molecule was detected in the asymmetric unit, Fig. 2). The central motif of the C_2 symmetric molecule is the central Li–C–Li–C four-membered ring, which shows a slight deformation from planarity (sum of angles 346.6°). The Li–C distances of the ring amount to 2.255(8) and 2.236(8) Å, the Li–N 2.234(8) and 2.258(8) Å and are thus comparable with other known dimeric lithium alkyl structures.[1,5] **4** is the second known dimeric structure of *i*-PrLi, which has also been detected with the chiral diamine (1*R*,2*R*)-*N*,*N*,*N*′,*N*′-tetramethylcyclohexane-1,2-diamine [(*R*,*R*)-TMCDA].[4] However, in this adduct the Li–C bond lengths [2.206(6)–2.332(6) Å] are considerably longer than in (*i*-PrLi·TMEDA)$_2$ (**4**) and other known dimeric alkyllithium compounds.[4,5]

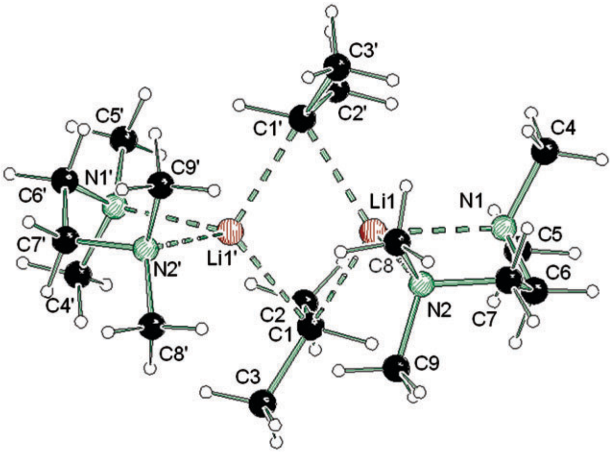


Fig. 2 Molecular structure of (*i*-PrLi·TMEDA)$_2$ (**4**) in the crystal. Selected bond lengths (Å) and angles (°) [symmetry operation for (′): 1/2 − *x*, 1/2 − *y*, *z*]: C(1)–Li(1) 2.255(8), C(1)–Li(1′) 2.236(8), Li–N(1) 2.234(8), Li–N(2) 2.258(8); N(1)–Li(1)–N(2) 81.9(3), C(1)–Li1–C(1′) 108.2(3), Li(1)–C(1)–Li(1′) 65.1(3).

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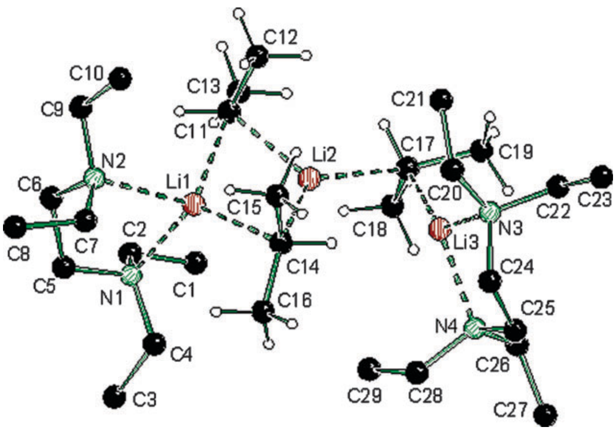
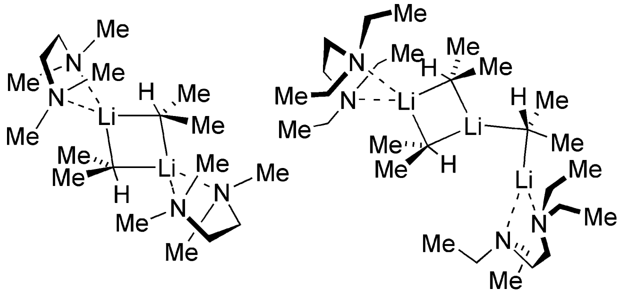


Fig. 3 Molecular structure of [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**) in the crystal. Selected bond lengths (Å) and angles (°) (hydrogens of the ligand are omitted for clarity): C(11)–Li(2) 2.175(5), C(11)–Li(1) 2.264(5), C(14)–Li(2) 2.231(5), C(14)–Li(1) 2.282(5), C(14)–Li(3) 3.402(5), C(17)–Li(3) 2.095(4), C(17)–Li(2) 2.229(4), Li(1)–N(1) 2.227(5), Li(1)–N(2) 2.279(4), Li(3)–N(3) 2.078(4), Li(3)–N(4) 2.111(4); Li(2)–C(11)–Li(1) 66.04(16), Li(2)–C(14)–Li(1) 64.85(14), C(11)–Li(1)–C(14) 107.25(18), C(11)–Li(2)–C(14) 112.35(19), Li(3)–C(17)–Li(2) 82.20(16), Li(3)–C(14)–Li(2) 83.24(15), C(14)–Li(2)–C(17) 129.85(19), C(11)–Li(2)–C(17) 117.56(19).

A totally different type of structure is formed with the higher homologous of TMEDA, TEEDA (**2**). [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**) crystallises out of *n*-pentane in the monoclinic crystal system, space group $P2_1/n$ (one molecule was detected in the asymmetric unit, Fig. 3). Compound **5** consists of three isopropyllithium units coordinated by two TEEDA molecules.[6] The central structural motif is formed by a Li–C–Li–C four-membered ring which is linked with another isopropyllithium unit. However, the contact between C14 and Li3 is considerably elongated in comparison to other known Li–C distances. While the lithium atoms, Li1 and Li2, show Li–C distances typical for dimeric compounds [2.175(5) to 2.282(5) Å], Li3 possesses a very short contact in the range of monomeric organolithiums [Li3–C17: 2.095(4) Å] and an uncommonly long one [Li3–C14: 3.402(5) Å], indicating no bond. Thus, the lithium atoms Li2 and Li3 possess three contacts each, whereas Li1 shows four contacts, two to the nitrogen atoms of the ligand and two to the carbanionic centers. Interestingly, between C19 and Li3 a very short Li–C$_\beta$ contact of only 2.377(5) Å is found, which is in the range of the elongated Li–C distances of the dimeric [*i*-PrLi·(*R*,*R*)-TMCDA]$_2$. This short non-bonding contact is due to steric reasons forcing the isopropyl group into this specific arrangement. The Li–N distances show analogous tendencies as the Li–C distances, with those to Li1 in range of dimers and those of Li3 in the range of monomers. Altogether, [(*i*-PrLi)$_3$·(TEEDA)$_2$] can formally be considered as an isopropyllithium dimer, into which an additional *i*-PrLi molecule is inserted. Consequently, compound **5** represents a transition from the dimeric adduct to the monomer.

[(*i*-PrLi)$_3$·(TEEDA)$_2$] is a remarkable type of alkyllithium structure. While these compounds generally tend to form symmetric structures as dimers, tetramers or hexamers, compound **5** possesses an uneven number of lithium units. Furthermore, contrary to other known structures with such an uneven number, the isopropyllithium molecules are asymmetrically arranged and coordinated in the molecule (Fig. 4).[6]



(*i*-PrLi·TMEDA)$_2$ (**4**) [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**)

Fig. 4 Drawing of the molecular structures of (*i*-PrLi·TMEDA)$_2$ (**4**) and [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**).

The formation of [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**) can be understood by computational studies at the B3LYP/6-31 + G(d) level.[7] These calculations show an energetic preference by 19 kJ mol^{-1} of compound **5** over 1/2 (*i*-PrLi)$_6$ and two molecules TEEDA and an preference of 17 kJ mol^{-1} over 1/6 (*i*-PrLi)$_6$ and a hypothetic dimeric (*i*-PrLi·TEEDA)$_2$. The formation of monomeric *i*-PrLi·TEEDA is even more disfavoured by 26 kJ mol^{-1} in comparison to [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**) and 1/6 (*i*-PrLi)$_6$. The disfavoured formation of the dimer can be explained by the steric demand of the isopropyllithium molecules. Most recently, we isolated dimeric [*i*-PrLi·(*R*,*R*)-TMCDA]$_2$ with the chiral ligand (*R*,*R*)-TMCDA, showing strongly elongated Li–C distances.[4] The more demanding TEEDA finally prevents such an expanded dimer, so that only the formation of the non-symmetrical adduct **5** is possible.

Replacing the ethylene bridge of TEEDA with a cyclohexyl ring results in the diamine (*R*,*R*)-TECDA (**3**). Structure elucidation with this ligand yields again a change in the degree of aggregation. Monomeric *i*-PrLi·(*R*,*R*)-TECDA crystallises from an equivalent amount of the amine in *n*-pentane in the orthorhombic crystal system, space group $P2_12_12_1$ (one molecule was detected in the asymmetric unit, Fig. 5). The lithium center possesses three contacts, two to the nitrogen atoms of the ligand and one to the carbanionic center of the isopropyl group. In comparison to oligomeric alkyllithium compounds, **6** shows shortened Li–N [2.073(5) and 2.115(5) Å] and Li–C distances [2.099(5) Å], which are typical for monomeric alkyllithiums.[4,8–10] Contrary to *t*-BuLi·(−)-sparteine, the *i*-PrLi molecule is almost vertically coordinated to the ligand (sum of angles: 359.5°). However, both sides of the molecule are unequally free due to the isopropyl group. This is depicted by the Connolly surface and the electrostatic potential, indicating a free, positively charged side for coordination or an electrophilic attack (Fig. 5).[11] Besides *t*-BuLi·(−)-sparteine[8] and the adducts of *t*-BuLi and *s*-BuLi with (*R*,*R*)-TMCDA,[4,9] *i*-PrLi·(*R*,*R*)-TECDA (**6**) is one of the rare monomeric saturated alkyllithium compounds.[4,8–10] Additionally it is the first monomeric isopropyllithium adduct isolated so far.

On first glance, TEEDA (**2**) and (*R*,*R*)-TECDA (**3**) possess almost the same steric demand. However, both diamines form different *i*-PrLi structures in the crystal. Hence, the question

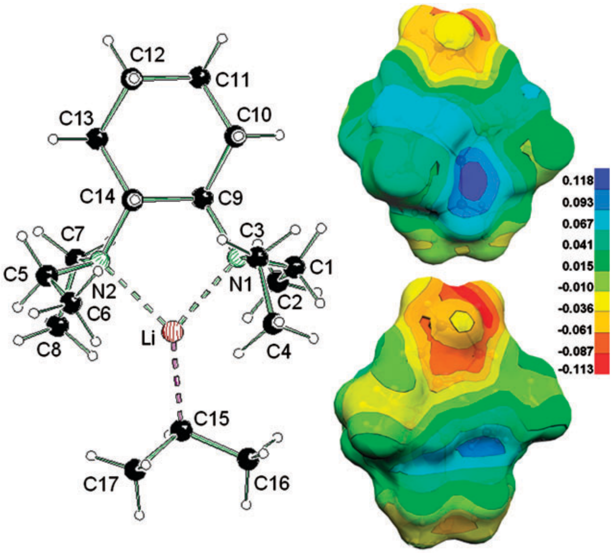


Fig. 5 (left) Molecular structure of *i*-PrLi·(*R*,*R*)-TECDA (**6**) in the crystal. Selected bond lengths (Å) and angles (°): C(15)–Li 2.099(5), Li–N(1) 2.073(5), Li–N(2) 2.115(5); N(1)–Li–C(15) 134.0(2), C(15)–Li–N(2) 138.7(2), N(1)–Li–N(2) 86.8(2); (right) Connolly surface mapped with the electrostatic potential [V_{max} = 0.131; V_{min} = −0.126] of both sides of compound **6** [B3LYP/6-31 + G(d) probe radius, 1.2 Å].

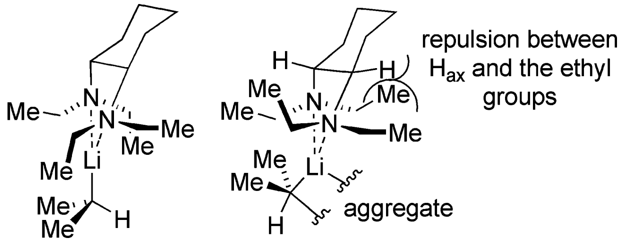


Fig. 6 Drawing of monomeric *i*-PrLi·(*R*,*R*)-TECDA and illustration of the repulsion between the cyclohexane ring and the ethyl groups in a hypothetical dimer or aggregate.

arises why (*R*,*R*)-TECDA forms a monomer and TEEDA an aggregate with *i*-PrLi. This can be explained by both crystal structures. In [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**), one ethyl group of each nitrogen atom is arranged in the direction of the isopropyllithium molecules and one towards the ligand. By contrast, in the monomeric *i*-PrLi·(*R*,*R*)-TECDA no ethyl group is directed towards the cyclohexane ring of (*R*,*R*)-TECDA. Such an arrangement would lead to strong repulsion between the ethyl groups and the axial hydrogen atoms of the ring. Therefore, all ethyl groups are arranged towards the *i*-PrLi molecule (Fig. 6), thus preventing the formation of a hypothetic dimer [*i*-PrLi·(*R*,*R*)-TECDA]$_2$ or an analogous structure to **5**. This is confirmed by DFT studies [B3LYP/6-31 + G(d)] showing no stationary point for the dimer and an opening of an analogous structure to **5**. Consequently, for steric reasons (*R*,*R*)-TECDA and *i*-PrLi can only form a monomeric structure.

In summary, we have presented molecular structures of isopropyllithium with three nitrogen ligands. The different steric demand of these Lewis bases leads to a change in the degree of aggregation from the dimeric TMEDA adduct (**4**) to the first monomeric isopropyllithium structure, *i*-PrLi·(*R*,*R*)-TECDA (**6**), *via* the interesting, non-symmetrical aggregate [(*i*-PrLi)$_3$·(TEEDA)$_2$] (**5**). These three adducts indicate the influence of the ligand on the structure formation patterns and thus of the reactivity of organolithium compounds.

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