Formation of Organolithium Hetero-Aggregates [Li4Ar2(nBu)2] (Ar=C6H4CH(Me)NMe2-2) during the Directedortho-Lithiation of [1-(Dimethylamino)ethyl]benzene

ARTICLE *in* CHEMISTRY · JANUARY 2005

Impact Factor: 5.73 · DOI: 10.1002/chem.200400828 · Source: PubMed

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Formation of Organolithium Hetero-Aggregates $[Li_4Ar_2(nBu)_2]$ ($Ar = C_6H_4CH(Me)NMe_2$-2) during the Directed *ortho*-Lithiation of [1-(Dimethylamino)ethyl]benzene

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Abstract: (*R*)-[1-(Dimethylamino)-ethyl]benzene reacts with *n*BuLi in a 1:1 molar ratio in pentane to quantitatively yield a unique hetero-aggregate (**2a**) containing the lithiated arene, unreacted *n*BuLi, and the complexed parent arene in a 1:1:1 ratio. As a model compound, $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_2(nBu)_2]$ (**2b**) was prepared from the quantitative redistribution reaction of the parent lithiated arene $Li(C_6H_4CH(Me)NMe_2\text{-}2)$ with *n*BuLi in a 1:1 molar ratio. The mono-Et_2O adduct $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_2(nBu)_2(OEt_2)]$ (**2c**) and the bis-Et_2O adduct $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_2(nBu)_2(OEt_2)_2]$ (**2d**) were obtained by re-crystallization of **2b** from pentane/Et_2O and pure Et_2O, respectively. The single-crystal X-ray structure determinations of **2b–d** show that the overall structural motifs of all three derivatives are closely related. They are all tetranuclear Li aggregates in which the four Li atoms are arranged in an almost regular tetrahedron. These structures can be described as consisting of two linked dimeric units: one Li_2Ar_2 dimer and a hypothetical Li_2nBu_2 dimer. The stereochemical aspects of the chiral Li_2Ar_2 fragment are discussed. The structures as observed in the solid state are apparently retained in solution as revealed by a combination of cryoscopy and ^1H, ^{13}C, and ^6Li NMR spectroscopy.

Keywords: directed orthometalation · lithium · N ligands · organolithium complexes · structure elucidation

Introduction

Organolithium compounds are valuable reagents in synthesis and have found widespread application in organic and organometallic chemistry.[1–5] In general, there are three primary synthetic routes to organolithium compounds: 1) direct metalation of an organic halide with Li metal, 2) halogen–Li exchange of an organic halide with a simple organolithium compound (typically *n*BuLi or *t*BuLi), and 3) deprotonation of a CH group from a suitable substrate with an alkyllithium compound.[1–3] This latter synthetic route is especially attractive because it is generally a very clean reaction, as the only products formed are the anticipated organolithium compound and an alkane. In this way, heteroatom-functionalized aromatic compounds can be easily lithiated selectively at the ortho position (i.e., "Directed *ortho* Metalation": DoM).[5] The actual mechanism of the *ortho*-lithiation reaction, specifically that involving Li–H exchange, has attracted considerable interest.[5–7] Two main reaction pathways for this lithiation have been put forward. According to one proposal, lithiation commences with complexation of the alkyllithium through a lone pair of electrons on the heteroatom-containing *ortho* substituent (the so-called "Directing Metalating Group": DMG). This interaction brings the metal center in close proximity to the "acidic" *ortho*-hydrogen atom. Thus, the reaction with the basic (formal) carban-

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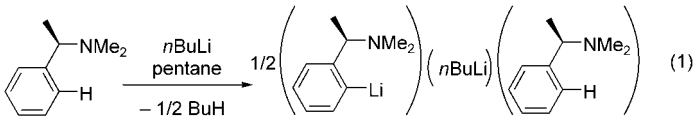
 DOI: 10.1002/chem.200400828

ion fragment is facilitated.[6] The second mechanistic proposal, put forward by von Eikema Hommes and von Ragué Schleyer, supports the concept of "kinetically enhanced metalation".[7] According to this hypothesis, the presence of a Li atom with more than one accessible coordination site is essential for DoM. In the initial step, complexation between the DMG and an alkyllithium takes place to give an intermediate aggregate in which the formation of a four-coordinate Li nucleus includes an agostic interaction of an *ortho*-H of the aryl ring. A strong (thermodynamic) complexation between the lithium atom and the lone-pair of the DMG can result in an *unreactive* intermediate and consequently no *ortho*-lithiation will take place.[7] The proponents of this mechanism stress the importance of the stabilization of the transition state for successful protolysis to occur. The addition of one equivalent of a base such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) presumably results in a solvated aggregate (i.e., complex) of the *n*BuLi, TMEDA, and the arene and this is thought to promote DoM.[5,8] For both reaction pathways, hydrogen abstraction is considered to be the rate-limiting step, which is supported by results from theoretical calculations.[9]

Sometime ago, we embarked on a study of the synthesis and applications of chiral organocopper and organotin compounds that involved the use of ortholithiated aromatic compounds containing a DMG.[10] A particularly puzzling result involved the DoM of [1-(dimethylamino)ethyl]benzene (**1**). The use of *n*BuLi to facilitate the formation of the DoM product invariably did not yield the desired *ortho*-lithiated precursor in greater than 50% yield, even in the presence of excess *n*BuLi. The use of *t*BuLi however, gave the expected product quantitatively.[10] Although the increased nucleophilicity of the formal $t\mathrm{Bu}^-$ ion is a reasonable explanation for the latter result, it does not explain why *some* of the aromatic compound *is ortho*-lithiated by *n*BuLi, whereas the remainder is unaffected. This evidence led us to propose the formation of an aryl-butyllithium hetero-aggregate formed by the replacement of *some* of the butyl groups of $[n\mathrm{BuLi}]_6$ by a combination of unreacted aminoarene groups *and* orthometalated [1-(dimethylamino)ethyl]benzene [Eq. (1)].[10] Thus, a stable hetero-aggregate **2a** is



(1)

2a

formed. This hypothesis helps to explain the observed 50% yield of *ortho*-metalated product. Such an aggregate with *t*BuLi was assumed to be thermodynamically unstable but led to a lower energy transition state (vide supra) giving rise to complete DoM. There were no crystallographically characterized examples of such hetero-aggregates at the time of this proposal, although it has been known for many years that, for example, mixtures of different alkyl lithium compounds readily exchange alkyl groups to form statistical mixtures of mixed aggregated species.[12] In addition, *t*BuLi is well known to be kinetically *more* reactive in the presence of *i*PrLi.[13] Hence, the structural nature of organolithium compounds can be changed by the presence of other organolithium species. In addition, solution NMR and cryoscopy measurements have shown that the presence of donor solvents (e.g., THF) and/or the addition of donor molecules (e.g., TMEDA) can modify the solution structure of organolithium compounds.[8] A molecule of unreacted [1-(dimethylamino)ethyl]benzene can be viewed as such a latter donating participant. Perhaps more importantly, it is known that such mixed species (hetero-aggregates) have *modified reactivity profiles* versus the isolated (single entity, homo-aggregates) organolithium compounds. For this reason, there has been considerable recent interest in these hetero-aggregates and it is now well established that alkyl and aryl lithium compounds also form hetero-aggregates with lithium halides (hence the "LiX effect"), lithium alkoxides, lithium amides, and even lithium oxide.[8,14] This topic has been recently reviewed.[11a] Examples of the application of such hetero-aggregates include the selective polymerization of styrene to isotactic polystyrene initiated by mixed alkyl alkoxy lithium aggregates.[16] Also, the recent synthesis and characterization of a hetero-aggregate containing six Li atoms, two 2,2′-ethylidenebis(4,6-di-*tert*-butylphenoxy) dianions, and two *n*-butyl groups has been reported. This species is an excellent catalyst for the ring-opening polymerization of L-lactide.[17] Lithium halides and amides, especially chiral ones, have found widespread application as additives in the (enantio)selective additions of alkyl lithium compounds to electrophiles. The formation of hetero-aggregates during such reactions as been identified in situ; hence, these materials appear to be key (stable) intermediates in a number of enantioselective processes, as suggested in related DoM chemistry.[7,8,11]

Although NMR spectroscopy (specifically $^6\mathrm{Li}$ and $^{13}\mathrm{C}$) and cryoscopy has characterized the presence of many of these hetero-aggregate species,[7,8] there is to date only a few well-characterized, isolated, and crystallographically elucidated structures of alkyl or aryl lithium hetero-aggregates. The few known examples include the synthesis and structure of $[\mathrm{Li}_4(\mathrm{Mes}^*)_2(n\mathrm{Bu})_2]$ ($\mathrm{Mes}^* = 2,4,6\text{-}t\mathrm{Bu}_3\mathrm{C}_6\mathrm{H}_2$),[18] $\{\mathrm{Li}_4[\mathrm{C}_6\mathrm{H}_3\text{-}(\mathrm{CH(Et)NMe}_2)_2\text{-}2,6]_2(n\mathrm{Bu})_2\}$,[19] $\{\mathrm{Li}_4[\mathrm{CH}_2\mathrm{C}_6\mathrm{H}(\mathrm{CH}_2\mathrm{NMe}_2)_2\text{-}2,6\text{-}\mathrm{Me}_2\text{-}3,5]_2(n\mathrm{Bu})_2\}$,[20] $\{\mathrm{Li}_4[\mathrm{CH}(\mathrm{SiMe}_3)\mathrm{C}_6\mathrm{H}(\mathrm{CH}_2\mathrm{NMe}_2)_2\text{-}2,6\text{-}\mathrm{Me}_2\text{-}3,5]_2(n\mathrm{Bu})_2\}$,[21] and $\{\mathrm{Li}_4[\mathrm{CH}_2\mathrm{Si(Ph)}_2\mathrm{CH}_2\mathrm{N}(\mathrm{CH}_2\mathrm{CH}_2\text{-}\mathrm{OMe})_2]_2(n\mathrm{Bu})_2\}$[22] and others.[23]

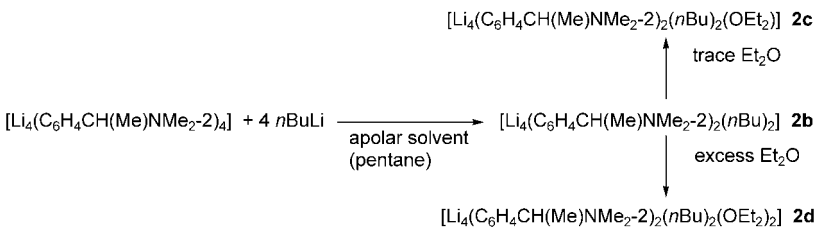
In this report, we reveal the formation of *n*-butyl aryl lithium hetero-aggregates during the DoM of [1-(dimethylamino)ethyl]benzene with *n*BuLi and detail the independent synthesis and structural characterization of these hetero-aggregates. With this information, we present unambiguous and compelling evidence for the intermediacy of aggregates of the type $\{[\mathrm{Li}_4\mathrm{Ar}_2\mathrm{Bu}_2](\mathrm{Ar\text{-}H})_2\}$ as resting states in *ortho*-lithiation reactions of DMG-containing arenes.[7]

Results and Discussion

Synthesis: The treatment of a pentane solution of (*R*)-[1-(dimethylamino)ethyl]benzene with *n*BuLi in a 1:1 molar ratio afforded, after evaporation of the solvent, a pale yellow solid, (**2a**: [Eq. (1)]). According to its ^{1}H and ^{13}C NMR spectrum this material contained the lithiated arene, "unreacted" *n*BuLi, and the complexed parent amino arene in a 1:1:1 ratio.

Changing the solvent of this process (Et_2O or toluene) and/or increasing the reaction temperature to 80 °C (toluene) did not influence the stoichiometry of the resulting product. Moreover, as reported earlier,[10] when the product was quenched with D_2O this always resulted in the formation of the parent arene and the mono-deuterated arene in a 1:1 ratio. Based on this "chemical evidence", we earlier proposed the formation of a species (**2a**) containing the lithiated arene, *n*BuLi, and the parent aminoarene in one hetero-aggregated species (vide supra).[10]

The availability of pure $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_4]$, (i.e., (*R*)-**1**) and the corresponding racemic compound (*rac*)-**1**, for which the synthesis and structural characterization has been reported,[24] opens an elegant route for the synthesis and examination of such aryl-butyllithium hetero-aggregates. The reaction of pure, isolated (*R*)-**1** with *n*BuLi (1:1 molar ratio: Scheme 1) in pentane, affords (after workup) a white solid.



Scheme 1. Synthetic routes to ether-free (**2b**), the mono- (**2c**), and dietherate (**2d**) hetero-aggregates.

This material contains, according to its ^{1}H NMR spectrum, aryl and butyl groups in a 1:1 molar ratio. Molecular weight determinations by cryoscopy indicated that this compound (**2b**), has a $[Li_4(aryl)_2(nBu)_2]$ stoichiometry. In a similar way, the racemic compound was prepared starting from (*rac*)-**1**. Crystalline **2b** was obtained by crystallizing the crude material from pentane. Surprisingly, depending on the amount of Et_2O in the solvent of crystallization, the diethyl ether adducts $[Li_4(aryl)_2(nBu)_2(OEt_2)]$ (**2c**) and $[Li_4(aryl)_2(nBu)_2(OEt_2)_2]$ (**2d**) can also be obtained (see Scheme 1 and Experimental Section). Compound **2c** was obtained by the crystallization of crude **2b** from pentane that (serendipitously) contained traces of Et_2O. Adduct **2d** was obtained by crystallization of **2b** from pure diethyl ether solution (Scheme 1).

In a similar manner, pure **2a** was obtained by mixing **2b** and two equivalents of (*R*)-[1-(dimethylamino)ethyl]benzene in pentane followed by evaporation of the solvent (see Experimental Section). The new aryl-butyllithium hetero-aggregates **2a–d** were fully characterized by ^{1}H and ^{13}C NMR spectroscopy, cryoscopy and elemental analysis, while the structures in the solid state of **2c** and **2d** were further established by X-ray crystallography (vide infra).

Structural aspects of (*R*)- and (*rac*)-$[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_2(nBu)_2(OEt_2)_n]$ in the solid state: It appeared that the acentric unit cell of **2b** contains two geometrically different molecules, A and B for which the differences will be discussed in detail below. The overall structural motifs of **2b** (molecule A), **2c**, and **2d** are closely related. They are all tetranuclear aggregates in which the four Li atoms are arranged in an almost regular tetrahedron. Both of the aryl groups are presumably bonded through an electron-deficient two-electron four-center bond to one of the faces of the Li_4 tetrahedron. Each of the nitrogen atoms of the amine substituents is coordinated to the apical position of a Li atom, rendering two of the Li atoms four-coordinate. The two butyl groups are likewise two-electron four-center bonded to the other two faces of the Li_4 tetrahedron. Owing to the lack of further coordinating ligands, either intra- or intermolecular, two of the lithium atoms are three-coordinate. In **2c**, an Et_2O molecule is coordinated to one of these lithium atoms, whereas in **2d** both lithium atoms are four-coordinate through the additional Li–Et_2O interactions. The overall structural geometries of **2b**, **2c**, and **2d** are depicted in Figure 1 and relevant bond lengths and angles are given in Table 1.

In both **2b** and **2c**, the β-carbon atoms of the butyl groups are in very close proximity to the three-coordinate lithium atoms (2.371(3) and 2.512(3) Å in **2b** [molecule A]; 2.468(3) and 2.250(3) Å in **2b** [molecule B]; 2.396(8) and 2.451(8) Å in **2c**). This provides compensation for the coordinative unsaturation of these Li centers, most probably by Li···H–C interactions.[18,23a–d] In this respect it is interesting to note that both β-carbon atoms of the two butyl groups are in close proximity to the same Li atom, that is, Li3. The observed overall structural geometry with a tetrahedral Li_4 core is similar to that observed in the hetero-aggregate $\{Li_4[C_6H_3(CH(Et)NMe_2)_2\text{-}2,6]_2(nBu)_2\}$,[19] but contrasts with the structures found for other $[Li_4(Aryl)_2Bu_2]$ and $[Li_4(Benz)_2Bu_2]$ hetero-aggregates,[11,20,23] for which structures have been found in which the Li and bridging carbon atoms are present in a "ladder-type" arrangement.

The tetranuclear aggregate can be described as consisting of two aggregated dimers: 1) a hypothetical Li_2Bu_2 dimer, having a similar structural motif as observed in the solid state structure of $[Li_2nBu_2(TMEDA)_2]$,[25] and 2) a $Li_2[C_6H_4(CH(Me)NMe_2)\text{-}2]_2$ dimer, which are linked together through four-center two-electron bonded bridging carbon atoms, in a similar way as is observed in the solid-state

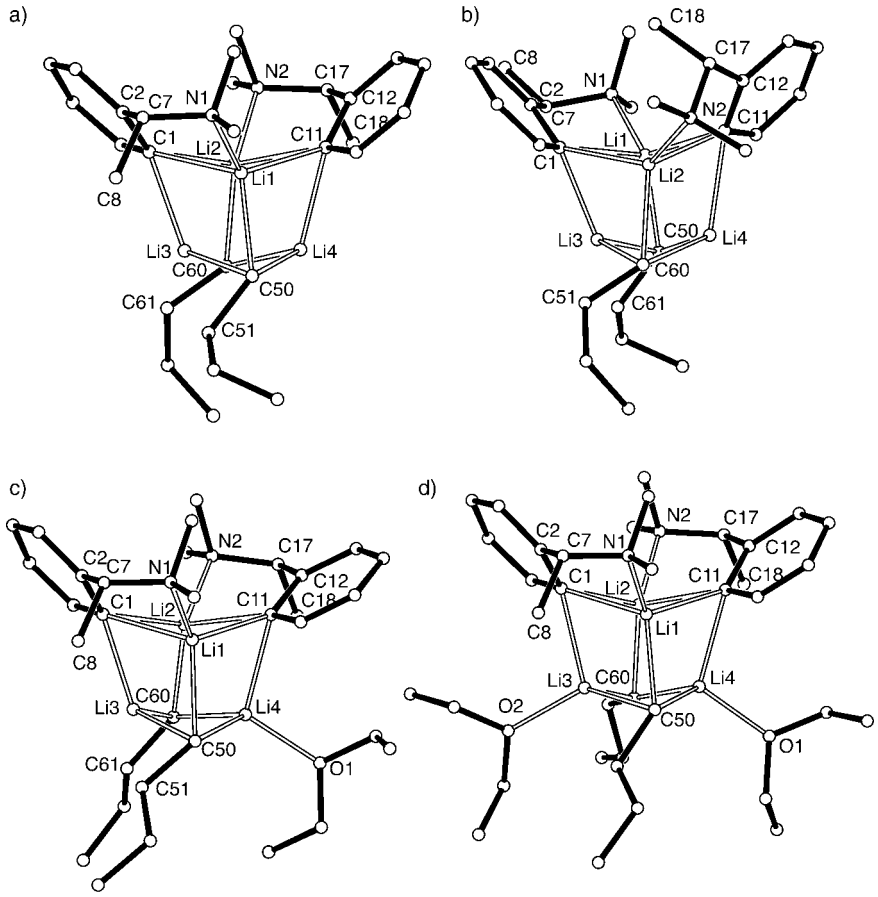


Figure 1. Ball-and-stick drawings of **2b** molecule A (a), **2b** molecule B (b), **2c** (c), and **2d** (d) all drawn with the same orientation of the Li_4 tetrahedron to show the similarity of the $(Aryl)_2Li_2$ dimeric unit. Note: To facilitate the comparison the applied numbering scheme is different from that in the Supporting Information deposited at the CCDC database.

structure of $Li_4[C_6H_4(CH(Me)NMe_2)\text{-}2]_4$ (**1**).[24] In this respect, it should be noted that such Li_2Aryl_2 dimers in which the remaining coordination sites at the Li atoms are occupied by coordinating THF molecules have also been observed.[8c–d] Owing to the chiral center (labeled C(b) in Figure 2) in the $C_6H_4CH(Me)NMe_2$ ligand, and taking into account the chirality of the bridging C_{ipso} atom, (labeled C(i) in Figure 2),[26] three different diastereoisomeric dimeric structures are possible for this complex, namely $\mathbf{C^1}$, $\mathbf{C^2}$, and $\mathbf{C^3}$, as schematically shown in Figure 2.

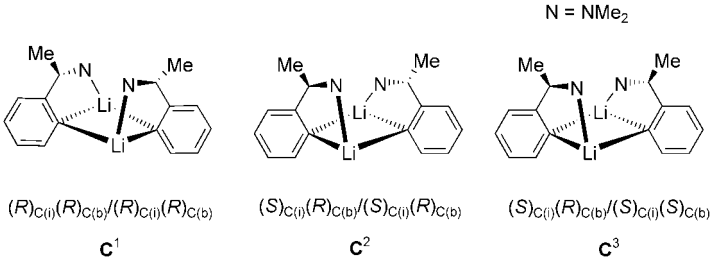


Figure 2. Possible diastereoisomers for the aryllithium dimer part in hetero-aggregate **2**: $\mathbf{C^1}$ and $\mathbf{C^2}$ for enantiopure and $\mathbf{C^3}$ for racemic dimers.

Note that other alternative dimeric structures, in which the coordinating N atoms approach the Li atoms from opposite sites of the central C_{ipso}-Li-C_{ipso}-Li plane have been observed as THF solvates in THF solution,[8c,d,27] but these forms are not considered here because aggregation to tetranuclear species is not possible from such dimers. Furthermore, it should be noted that the dimer $\mathbf{C^3}$ can only arise from *racemic* material because the two chiral benzylic carbon atoms have an opposite stereochemical configuration. In the configurations $\mathbf{C^1}$ and $\mathbf{C^2}$, the stereochemistry of the two (chiral) benzylic carbon atoms is identical (in Figure 2, only the enantiomers having (*R*)-benzylic carbon centers are shown, but it is obvious that the other enantiomers having (*S*)-benzylic carbon centers can also exist). Consequently, combination of an enantiomerically pure dimer, as present in (*R*)-**2b** and (*R*)-**2c** with a hypothetical Li_2Bu_2 dimer to form a "mixed" Li_4 hetero-aggregate can in principle give rise to the formation of two different diastereiosomeric Li_4 aggregates, one containing a $\mathbf{C^1}$-type and one containing a $\mathbf{C^2}$-type dimer (Figure 2). However, it appears that the one based on the $\mathbf{C^2}$ type dimer would be the most favored one from a steric point of view (in $\mathbf{C^1}$, the two benzylic methyl substituents are pointing towards each other, whereas in $\mathbf{C^2}$ these substituents will point away from each other). This view is in concert with the actual structures found for **2b** (molecule A), **2c**, and **2d** in the solid state, as all three contain a $\mathbf{C^2}$-type dimeric unit (Figure 1). At this point, it is interesting to compare the structures of **2b–d** with the structure of $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_4]$, (*R*)-**1**, that was reported recently.[24] The structure of (*R*)-**1** can likewise be described as consisting of two linked dimeric units, one of a $\mathbf{C^2}$ type and one of a $\mathbf{C^1}$ type. The structure of the $\mathbf{C^2}$ part is identical to those of **2b–d**. In the $\mathbf{C^1}$ fragment, a rather sterically congested situation arises, but to release its steric strain, the five-membered *C,N*-chelate rings in this section of the molecule are puckered in such a way that it places the α-Me substituents in an energetically less favorable in-plane orientation with respect to the aryl ring.

Table 1. Selected bond lengths [Å] and torsion angles [°] for **2a**, **2b**, and **2c**.[a]

	2a molecule A	**2a** molecule B	**2b**	**2c**
C1–Li	2.315(3)	2.273(3)	2.296(7)	2.250(8)
C1–Li2	2.319(3)	2.416(3)	2.341(6)	2.326(8)
C1–Li3	2.262(3)	2.218(3)	2.240(8)	2.325(7)
C11–Li1	2.344(3)	2.229(3)	2.256(6)	2.318(8)
C11–Li2	2.292(3)	2.280(3)	2.260(7)	2.228(8)
C11–Li4	2.245(3)	2.343(3)	2.329(7)	2.287(7)
N1–Li1	2.024(3)	2.028(3)	2.042(6)	2.035(7)
N2–Li2	2.028(3)	2.036(3)	2.000(6)	2.038(7)
C50–Li1	2.274(3)	2.269(3)	2.265(7)	2.209(8)
C50–Li3	2.290(3)	2.192(3)	2.157(8)	2.293(8)
C50–Li4	2.179(3)	2.243(3)	2.280(7)	2.256(8)
C60–Li2	2.242(2)	2.247(3)	2.239(7)	2.214(9)
C60–Li3	2.239(3)	2.179(3)	2.212(7)	2.206(8)
C60–Li4	2.195(3)	2.300(3)	2.278(8)	2.132(9)
C51 ··· Li3	2.371(3)	2.468(3)	2.396(8)	
C61 ··· Li3	2.512(3)	2.250(3)	2.451(8)	
O1–Li4			2.004(7)	1.970(7)
O2–Li3				1.999(7)
Li1–Li2	2.557(4)	2.589(4)	2.491(8)	2.486(10)
Li1–Li3	2.504(4)	2.392(4)	2.406(8)	2.490(9)
Li1–Li4	2.518(4)	2.604(4)	2.647(9)	2.572(9)
Li2–Li3	2.591(4)	2.542(4)	2.494(8)	2.590(9)
Li2–Li4	2.387(4)	2.466(4)	2.539(8)	2.477(10)
Li3–Li4	2.498(4)	2.511(4)	2.525(9)	2.630(9)
C1-C2-C7-C8	71.9(2)	169.14(19)	70.1(4)	69.0(5)
C11-C12-C17-C18	71.8(2)	84.6(2)	80.4(4)	76.0(4)

[a] To facilitate the comparison the applied numbering scheme is different from that in the Supporting Information deposited at the CCDC database.

In all three structures of **2b–d**, the two five-membered *C,N*-chelate rings are puckered in such a way that the benzylic methyl substituents are placed in the energetically favored *anti*-periplanar orientation. Interestingly, the solid-state structure of **2b** (molecule B) contains a Li_4 aggregate based on a $\mathbf{C^1}$-type dimer together with a nBu$_2$Li$_2$ dimer (see Figure 1). The molecular geometry of **2b** (molecule B) clearly shows the steric congestion between the two benzylic methyl substituents. To release this repulsive interaction, the five-membered chelate rings have opposite puckering conformations that results in methyl groups of which one has *anti*- and one has periplanar orientation; hence, a less congested situation results. It is remarkable to find two geometrically different situations for one molecule (an apparently sterically favored one and a sterically less favored one) in a single crystal lattice, which is most likely a result of packing effects. In solution, only one isomer could be observed (vide infra) which is most likely sterically the most favored one (see Figure 1a) although the occurrence of a fluxional process (with low activation barriers) involving ring puckering inversion can not be excluded.

It should be noted that the crystals of **2d** were obtained from a reaction starting from (*rac*)-**1**. Indeed, the centrosymmetric unit cell contains two enantiomeric Li_4 aggregates: one with (*R,R*)- and the other with (*S,S*)-stereochemistry. Obviously, the alternative "racemic" Li_4 aggregate containing a $\mathbf{C^3}$-type dimer (see Figure 2), is not formed (i.e. is not thermodynamically favorable), which is therefore an illustration of diastereoselective self-aggregation.

Unfortunately we were unable to obtain single crystals suitable for an X-ray structure determination of **2a**, to establish its structure in the solid state. However, based on the similarity of the ^{1}H and ^{13}C NMR spectra of **2a** with those of **2c** and **2d** (see Experimental Section), it is most likely that **2a** has a structure comparable to that of **2d**, but with the two coordinating diethyl ether ligands present in **2d** replaced by two monodentate, N-coordinating $C_6H_5CH(Me)NMe_2$ ligands (see also [Eq. (1)]).

Structural aspects of (*R*)- and (*rac*)-[Li$_4$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$(*n*Bu)$_2$(OEt$_2$)$_n$] in apolar solvents: To gather information about the structures in solution of **2a–d**, NMR studies (^{1}H, ^{13}C, and ^{6}Li: [D$_8$]toluene solution) were carried out at various temperatures. Relevant data are given in Table 2 and in the Experimental Section.

Table 2. Relevant variable temperature ^{1}H and ^{13}C NMR data for **2b**, **2c**, and **2d**.[a]

Compound	T[K]	δ(^{1}H) [ppm]				
		NMe_2	α-Me	α-CH	*o*-H$_{aryl}$	α-CH$_2$ (Bu)
2b	373	1.96	1.17	3.01	8.00	−0.58
	298	1.22 and 2.11	1.22	2.79	8.03	−0.57
	273	1.12 and 2.08	1.26	2.70	7.97	−0.60
2c	298	1.27 and 2.16	1.27	2.82	8.13	−0.40
2d	298	1.29 and 2.19	1.29	2.83	8.15	−0.37

Compound	T [K]	δ(^{13}C) [ppm]					
		NMe_2	α-Me	α-C	C1	C2	α-C (Bu)
2b	373	41.5 and 45.1	23.5	71.8	171.0	158.7	10.9
	298	41.8 and 44.8	23.4	72.4	170.5	159.5	11.2
	273	42.1 and 45.1	23.6	72.7	170.5	159.6	10.7
2c	298	42.2 and 45.3	23.6	72.9	171.8	159.6	11.0
2d	298	42.3 and 45.3	23.8	72.9	171.5	159.5	10.4

[a] All values are in δ [ppm] relative to $SiMe_4$ as an external standard in [D$_8$]toluene as solvent.

It appears that the ^{1}H and ^{13}C NMR data of independently prepared **2a** (see Experimental Section) are identical with the data observed for the product formed from the reaction of (*R*)-[1-(dimethylamino)ethyl]benzene with *n*BuLi in a 1:1 molar ratio. This observation indicates that it is indeed **2a** that is formed during this reaction.

A molecular weight determination of **2b** (cryoscopy: C_6H_6) showed that a Li_4 aggregate, as observed in the solid state, is retained in solution. The observation of one resonance pattern in the ^{1}H and ^{13}C NMR spectrum ([D$_8$]toluene: Table 2) for the *ortho*-amine chelated aryl group indicates that in toluene solution only one of the two possible diastereoisomeric forms is present. The diastereotopicity of the coordinated NMe_2 methyl groups is reflected in the observation of two resonances in both the ^{1}H ($\delta = 1.22$ and 2.11 ppm) and ^{13}C NMR spectra ($\delta = 41.8$ and 44.8 ppm). This indicates that Li–N coordination is inert on the NMR time scale. The α-protons of the butyl groups are observed at $\delta = -0.57$ ppm as a complicated multiplet that was not analyzed in detail, but is in agreement with the expected ABCD pattern as a result of the various chiral centers in

the molecule. In the temperature range of −80 to +100 °C, with the exception of some slight chemical shift differences, the ^{1}H and ^{13}C NMR spectra are unaffected, indicating that fluxional processes are still absent or slow within this temperature range. Above +100 °C, coalescence of these resonances begins, indicating that either a process becomes operative involving Li–N dissociation/association or that intra- or interaggregate exchange becomes fast on the NMR time scale. The presence of two distinctly different dimeric fragments in the Li_4 hetero-aggregate (one Li_2Aryl_2 and one Li_2Bu_2 dimer) is nicely illustrated by the observation of two ^{6}Li chemical shift values at $\delta = -0.35$ and -1.05 ppm in the ^{6}Li NMR spectrum of **2b**. A remarkable observation is the fact that the ^{1}H, ^{13}C, and ^{6}Li NMR spectra of the "racemic" material that is obtained from reaction of (*rac*)-**1** and BuLi are identical to that of **2b**. Obviously, in solution diastereoselective aggregation occurs resulting in Li_4 aggregates that contain an enantiopure $\mathbf{C}^2$-type dimer (i.e., there is no *meso* form present). It is obvious that starting from (*rac*)-**1**, both enantiomers must be present in solution. It must be noted that for a Li_4 aggregate containing the racemic dimer $\mathbf{C}^3$ (see Figure 2), an NMR spectrum is expected that is different from that of **2b**. The exclusive formation of dimers in which both ligands have the same stereochemistry is most likely driven by thermodynamics and points to a considerable difference in stability between species that contain either a $\mathbf{C}^1$-, $\mathbf{C}^2$-, or $\mathbf{C}^3$-type dimeric unit.

For **2c** and **2d**, essentially the same ^{1}H and ^{13}C NMR spectra are observed as for **2b** (Table 2), indicating that in solution **2b**, **2c**, and **2d** have structures that are closely related. The only difference is that for **2c** and **2d** the α-protons of the butyl groups are slightly shifted downfield to $\delta = -0.40$ ppm, compared to $\delta = -0.57$ ppm for **2b**. The resonances for the CH_2 groups of the diethyl ether CH_2 protons in **2c** and **2d** are observed at $\delta = 3.08$ and 3.15 ppm, respectively. This upfield shift, compared to free diethyl ether, is as expected for coordinated diethyl ether molecules. The diastereotopicity of the CH_2 protons as a consequence of the lack of a molecular symmetry plane containing the benzylic carbon atom is reflected in the observation of a complicated multiplet (ABX_3 pattern) for these protons. Moreover, these data indicate that under these conditions the diethyl ether molecule is not exchanging. It should be noted that in the presence of more than two equivalents of diethyl ether, the proton resonances of the CH_2 group are shifted in the direction of those in free diethyl ether ($\delta = 3.40$ ppm). Under these conditions even spectra recorded at −80 °C did not show separate signals for free and coordinated diethyl ether. This strongly suggests that exchange of free and coordinated diethyl ether is already fast on the NMR time scale at this temperature.

Concluding Remarks

The present study shows that the reaction of *n*BuLi with *ortho*-amine substituted arenes in apolar solvents is sensitive to the nature and size of the benzylic substituent. Whereas *N,N*-[(dimethylamino)methyl]benzene reacts with *n*BuLi quantitatively to form $[Li_4(C_6H_4CH_2NMe_2\text{-}2)_4]$,[27] the analogous reaction of the α-methyl-substituted arene proceeds under the same reaction conditions to yield only 50% DoM. Isolation and characterization of the resulting compound shows it to be a unique aryl-butyllithium hetero-aggregate to which two equivalents of "unreacted" aminoarene remains, likely acting as coordinated "solvent" molecules to the aggregate (see **2a** in Equation (1)). Obviously, the remaining butyl groups that are incorporated into the aggregate are deactivated for further DoM chemistry. In other words, formation of this type of structural aggregate leads to suppression of further DoM, possibly due to a kinetic barrier which does not allow *ortho*-arene hydrogen atoms in close proximity (i.e., to become agostic) to the formal butyl anionic C nuclei. Model compounds that are representative for this stable (inactive) intermediate can be obtained by direct and selective interaggregate exchange reactions of pure $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_4]$ with a 2/3 equivalent of $[nBu_6Li_6]$ in pentane solution.

These results point to the formation and existence of unique intermediates by self-assembly processes during the heteroatom-assisted lithiation (DoM) of arenes. The fact that these intermediates can be isolated indicates that they are formed under thermodynamic control. Using *t*BuLi instead of *n*BuLi, the formation of aryl-, *tert*-butyllithium hetero-aggregates such as **2a** has not been observed. Instead this reaction results in the quantitative formation of the aryl lithium homo-aggregate $[Li_4(C_6H_4CH(Me)NMe_2\text{-}2)_4]$ as the thermodynamic end product.[24]

As perhaps a final caveat to those involved in DoM chemistry, a final important consequence of this chemistry is as follows. If, during a lithiation reaction, a particular combination of substrate (functionalized arene) and lithiating agent (alkyllithium) results in a large enhancement of the thermodynamic stability of the hetero-aggregated species compared to that of the anticipated end-product (the lithiated arene), then the hetero-aggregated species will invariably be the end-product (cf. Equation (1)). The observation of the existence of mixed intermediates of type **2a** also has important implications for the understanding and design of synthetic routes to pure aryl lithium species. The presence of hetero-aggregates in synthetic lithiation reactions could be problematic when these in situ prepared aryl lithium compounds are thereafter used in subsequent (organic) reactions.[28–30] Hence, reduced product yields will be a direct consequence. This may be particularly distressing in multistep synthesis, in which the self-assembly of such aggregates leads to poor product optimization.

Experimental Section

General data: All experiments were carried out under a dry, oxygen-free, nitrogen atmosphere, using standard Schlenk techniques. Solvents were dried and distilled from Na/benzophenone prior to use. [Li((*R*)-

$C_6H_4CH(Me)NMe_2$-2)]$_4$ ((*R*)-**1**) and the corresponding racemic compound ((*rac*)-**1**) were prepared according to a published procedure.[10] ^{1}H, ^{13}C, and ^{6}Li NMR spectra were recorded on a Varian 300 MHz spectrometer at ambient temperature or stated otherwise. Chemical shifts (δ) are given in ppm relative to $SiMe_4$ as an external standard. The ^{6}Li NMR spectra are referenced to LiCl (1.0 M) in D_2O as an external standard. Elemental analyses were obtained from Dornis und Kolbe Mikroanalytisches Laboratorium, Mülheim a.d. Ruhr, Germany. Cryoscopic measurements are carried out using a S2541 thermolyzer and a metal-mantled Pt-100 sensor. For the calibration naphthalene was used to give the cryoscopic constant $K_f = 5.46\ K\,kg\,mol^{-1}$.

Preparation of [Li$_4$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$(*n*Bu)$_2$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$] (2a): (*R*)-$C_6H_5CH(Me)NMe_2$ (1.66 mL, 10.07 mmol) was added at room temperature to a stirred solution of **2b** (2.21 g, 5.04 mmol) in pentane (25 mL). After 10 min, the solvent was removed in vacuo to afford a yellow powder. Yield 3.56 g (4.83 mmol; 96%). ^{1}H NMR ([D$_6$]benzene, 300.105 MHz, 298 K): $\delta = -0.40$ (bm, 2H; CH_2Li), 1.13 (t, $^3J = 6.9$ Hz; $LiCH_2(CH_2)_2CH_3$), 1.23 (d, 3H; (*R*)-$C_6H_5CH(Me)NMe_2$), 1.27 (bs, 6H; NMe_2, ArCH(*Me*)), 1.45, 1.71 (m, 2×2H; $LiCH_2(CH_2)_2CH_3$), 1.95 (s, 6H; (*R*)-$C_6H_5CH(Me)NMe_2$), 2.16 (bs, 3H; NMe_2), 2.83 (bs, 1H; ArC*H*(Me)), 3.21 (q, $^3J = 6.9$ Hz, 1H; (*R*)-$C_6H_5CH(Me)NMe_2$), 6.95 (d, 1H; ArH(*3*)), 7.07 (m, 5H; (*R*)-$C_6H_5CH(Me)NMe_2$), 7.12 (m, 2H; ArH(*4,5*)), 8.11 ppm (bd, $^3J = 5.40$ Hz, 1H; ArH(*6*)); ^{13}C NMR ([D$_6$]benzene, 75.469 MHz, 298 K): $\delta = 11.1$ (bs; $LiCH_2$), 13.9 ($LiCH_2(CH_2)_2CH_3$), 20.2 ((*R*)-$C_6H_5CH(Me)NMe_2$) 32.5, 45.3 ($LiCH_2(CH_2)_2CH_3$), 32.8 (CH(*Me*)), 23.7, 45.1 (NMe_2) 72.8 (ArCH), 125.4, 126.3, 126.9, 139.4 (Ar(*3,4,5,6*), 127.1–128.2 (((*R*)-$C_6H_5CH(Me)NMe_2$), 159.7, 170.5 ppm (Ar(*1,2*) quaternary).

Synthesis of [Li$_4$((*R*)-C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$(*n*Bu)$_2$] (2b): *n*BuLi (22.0 mL of a 1.6 M solution in hexane, 35.20 mmol) was added at room temperature to a stirred solution of (*R*)-**1** (5.36 g, 34.54 mmol) in C_6H_6 (40 mL). After 1 h, the solvents were removed in vacuo to afford a yellow oil. The addition of pentane (40 mL) to this oil, followed by subsequent evaporation in vacuo, gave **2b** in the form of a white powder (7.64 g, 34.52 mmol; 99%). Crystallization from hexane at room temperature gave colorless crystals of **2b**, which were suitable for X-ray crystallographic studies.

^{1}H NMR ([D$_6$]benzene, 300.105 MHz, 298 K): $\delta = -0.57$ (bm, 2H; CH_2Li), 1.09 (t, $^3J = 7.33$ Hz; $LiCH_2(CH_2)_2CH_3$), 1.22 (bs, 6H; NMe_2, ArCH(*Me*)), 1.44, 1.70 (m, 2×2H; $LiCH_2(CH_2)_2CH_3$), 2.11 (bs, 3H; NMe_2), 2.72 (bs, 1H; ArC*H*(Me)), 6.93 (d, $^3J = 5.5$ Hz, 1H; ArH(*3*)), 7.17 (m, 2H; ArH(*4,5*)), 8.03 ppm (bd, $^3J = 5.27$ Hz, 1H; ArH(*6*)); ^{13}C NMR ([D$_6$]benzene, 75.469 MHz, 298 K): $\delta = 10.5$ (bs; $LiCH_2$), 13.5 ($LiCH_2(CH_2)_2CH_3$), 23.3 (NMe_2), 31.7, 44.8 ($LiCH_2(CH_2)_2CH_3$), 32.1 (CH(*Me*)), 41.8 (NMe_2), 72.4 (ArCH), 125.2, 126.1, 126.9, 139.0 (Ar(*3,4,5,6*), 159.6, 170.5 ppm (Ar(*1,2*) quaternary); ^{6}Li NMR ([D$_8$]toluene, 44.165 MHz, 258 K): $\delta = -0.34$ and -1.03 ppm; elemental analysis calcd (%) for $C_{28}H_{46}N_2Li_4$: C 76.70, H 10.58, N 6.39; found: C 76.60, H 10.65, N 6.34. M.p. 120 °C (decomp). Molecular weight determination by cryoscopy (1.46 g in 29.31 g C_6H_6): analysis calcd for $C_{28}H_{46}N_2Li_4$ 438.45; found: 460.98.

Synthesis of [Li$_4$((*R*)-C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$(*n*Bu)$_2$(OEt$_2$)] (2c): Crystallization of **2b** from a mixture of toluene/Et_2O (10:1 v/v) at -30 °C afforded pale yellow crystals of **2c**.

^{1}H NMR ([D$_6$]benzene, 300.105 MHz, 298 K): $\delta = -0.36$ (bm, 4H; CH_2Li), 0.82 (dt, 6H; Et_2O), 1.13 (t, $^3J = 6.73$ Hz, 6H; $LiCH_2(CH_2)_2CH_3$), 1.27 (bs, 12H; NMe_2 and ArCH(*Me*)), 1.60, 1.71 (m, 2×4H; $LiCH_2(CH_2)_2CH_3$), 2.16 (bs, 6H; NMe_2), 2.82 (bs, 2H; ArC*H*(Me)), 3.06

Table 3. Crystallographic data for crystal structure determinations **2b**, **2c**, and **2d**.

Compound	**2b**	**2c**	**2d**
formula	$C_{28}H_{46}Li_4N_2$	$C_{32}H_{56}Li_4N_2O$	$C_{36}H_{66}Li_4N_2O_2$
mol. weight	438.4	512.57	586.70
crystal system	monoclinic	orthorhombic	triclinic
space group	$P2_1$ (no. 4)	$P2_12_12_1$ (no. 19)	$P\bar{1}$ (no. 2)
a [Å]	9.5228(1)	9.4149(13)	9.448(5)
b [Å]	13.7804(2)	13.251(3)	10.187(2)
c [Å]	21.6040(3)	26.908(3)	20.915(12)
α [°]	–	–	100.87(3)
β [°]	94.2080(10)	–	101.51(4)
γ [°]	–	–	96.21(3)
V [Å^3]	2827.41(6)	3357.0(10)	1914.8(15)
ρ_{calcd} [g cm^{-3}]	1.030	1.014	1.018
Z	4	4	2
F(000)	960	1128	648
μ [mm^{-1}] $Mo_{K\alpha}$	0.056	0.058	0.059
crystal color	colorless	yellow	pale yellow
crystal size [mm]	0.2×0.3×0.5	0.3×0.3×0.5	0.1×0.3×0.4
θ_{min}, θ_{max} [°]	2.4, 27.5	0.8, 25.0	1.0, 25
θ, θ [°]		11.52, 13.70	10.04, 13.99
diffractometer	KappaCCD	CAD4	CAD4
scan type	area detector	ω .	ω .
$\Delta\omega$ [°]		0.90 + 0.35 tan θ	1.60 + 0.35 tan θ
mosaicity	0.443(1)		
X-ray exposure [h]	3	40	48
data set	−10:12,−13:17, −28:21	−10:12,−17:17, −34:0	−11:0,−12:12, −24:24
total data	18624	9264	7195
total unique data	10158 [$R_{int} = 0.049$]	5906 [$R_{int} = 0.067$]	6746 [$R_{int} = 0.072$]
no. of params	629	400	417
final *R*1[a]	0.0481 [9454; $I > 2\sigma(I)$]	0.0696 [4215; $I > 2\sigma(I)$]	0.0853 [3713; $I > 2\sigma(I)$]
final w*R*2[b]	0.1322	0.1868	0.2383
goodness of fit	1.023	1.053	1.181
w^{-1} [c]	$\sigma^2(F^2) + (0.0851P)^2 + 0.34P$	$\sigma^2(F^2) + (0.10P)^2$	$\sigma^2(F^2) + (0.10P)^2$
$\Delta/\sigma)_{max}$, (Δ/σ_{av})	< 0.014, < 0.002	< 0.025, < 0.001	< 0.007, < 0.001
$\Delta\rho_{min}$, $\Delta\rho_{max}$ [e A^{-3}]	−0.20, 0.31	−0.27, 0.23	−0.29, 0.44

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = |\Sigma[w(F_o^2 - F_c^2)^2/\Sigma[w(F_o^2)^2]]^{1/2}$. [c] $P = (Max(F_o^2, 0) + 2F)/3$.

(m, 4H; Et_2O), 6.92 (d, $^3J = 5.9$ Hz, 2H; ArH(*3*)), 7.15 (m, 4H; ArH(*4,5*)), 8.13 ppm (bd, $^3J = 5.9$ Hz, 2H; ArH(*6*)); ^{13}C NMR ([D_6]benzene, 75.469 MHz, 298 K): $\delta = 11.0$ (bs; Li*C*H_2), 13.9 (Li$CH_2(CH_2)_2C$$H_3$), 14.4 ($Et_2O$), 32.7, 45.3 (Li$CH_2$(*C*$H_2$)$_2$$CH_3$), 32.9 (CH(*Me*)), 23.6, 42.2 (NMe_2), 64.6 (Et_2O), 72.9 (Ar*C*H), 125.3, 126.1, 139.3 (Ar(*4,5,6*), 159.6, 171.8 ppm (Ar(*1,2*) quaternary); elemental analysis calcd (%) for $C_{32}H_{56}N_2Li_4O$: C 74.99, H 11.01, N 5.47; found: C 75.10, H 10.95, N 5.46.

Synthesis of [Li$_4$(C$_6$H$_4$CH(Me)NMe$_2$-2)$_2$(*n*Bu)$_2$(OEt$_2$)$_2$] (2d): *n*BuLi (7.8 mL of a 1.6 M solution in hexane; 12.09 mmol) was added at room temperature to a stirred solution of (*rac*)-**1** (1.86 g; 11.99 mmol) in Et_2O (30 mL). After 15 min, the solvents were removed in vacuo to afford an off-white powder: yield 2.74 g (9.34 mmol, 78%). Crystallization of the crude product from pure Et_2O at −30 °C gave pale yellow crystals of **2d**. ^1H NMR ([D_6]benzene, 300.105 MHz, 298 K): $\delta = -0.37$ (bm, 2H; CH_2Li), 0.91 (dt, 6H; Et_2O), 1.14 (t, $^3J = 6.60$ Hz, 3H; Li$CH_2(CH_2)_2C$$H_3$), 1.29 (bs, 6H; NMe_2 and ArCH(*Me*)), 1.72 (bm, 2×2H; LiCH_2(*C*H_2)$_2$$CH_3$), 2.19 (bs, 3H; NMe_2), 2.83 (bs, 1H; Ar*C*H(Me)), 3.10 (m, 4H; Et_2O), 6.94 (d, $^3J = 5.7$ Hz, 1H; ArH(*3*)), 7.13 (m, 2H; ArH(*4,5*)), 8.15 ppm (bd, $^3J = 5.4$ Hz, 1H; ArH(*6*)); ^{13}C NMR ([D_6]benzene, 75.469 MHz, 298 K): $\delta = 10.4$ (bs, Li*C*H_2), 13.9 (Li$CH_2(CH_2)_2C$$H_3$), 14.7 ($Et_2O$), 32.9, 45.4 (Li$CH_2$(*C*$H_2$)$_2$$CH_3$), 33.0 (CH(Me)), 23.5, 42.3 (NMe_2), 64.9 (Et_2O), 72.9 (Ar*C*H), 125.2, 125.9, 139.5 (Ar(*4,5,6*), 159.5, 171.5 ppm (Ar(*1,2*) quaternary); elemental analysis calcd (%) for $C_{36}H_{66}N_2Li_4O_2$: C 73.70, H 11.34, N 4.77; found: C 73.58, H 11.31, N 4.83.

X-ray crystal structure analyses of 2b, 2c, and 2d: Pertinent data for the structure determinations are collected in Table 3. X-ray data for crystal structure **2b** were collected on a Nonius KappaCCD diffractometer; data for the other structure determinations were collected on a Nonius CAD-4T diffractometer. All sets were measured at 150 K, using graphite monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) from a rotating anode source. Accurate unit cell parameters and an orientation matrix were determined by least-squares fitting of the setting angles of 25 well-centered reflections[31] for structures **2c** and **2d**. The unit cell parameters for structure **2b** were refined against the setting angles of all reflections. All structures were solved with direct methods by using SHELXS97.[32] Refinement on F^2 was performed with SHELXL-97.[32] One of the Bu moieties of **2d** displays disorder. A two-site disorder model in which atoms 1 (the C involved in Li coordination) and 3 of major and minor components coincide, satisfactorily described the observed electron density. Hydrogen atoms were included in the refinement on calculated positions riding on their carrier atoms. The non-hydrogen atoms of all structures were refined with anisotropic displacement parameters, except those belonging to the minor disorder component of **2d**. The hydrogen atoms were refined with a fixed isotropic displacement parameter related to the value of the equivalent isotropic displacement parameter of their carrier atoms by a constant factor. Owing to the absence of strong anomalous scatters, the absolute configuration could not be experimentally determined. The absolute configuration for all compounds was therefore assigned in accordance with the known configuration of the asymmetric carbon atoms of the starting compounds. Geometrical calculations and illustrations were performed with PLATON;[33] all calculations were performed on a DEC Alpha 255 station. CCDC-247120 (**2b**), CCDC-247121 (**2c**), and CCDC-247122 (**2d**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgement

This work was supported in part (A.L.S.) by The Netherlands Foundation for Chemical Sciences (CW) with financial aid from the Netherlands Organization for Scientific Research (NWO). Dr. J. Boersma is thanked for critical reading of this manuscript.

[1] B. J. Wakefield, *The Chemistry of Organolithium Compounds*, Pergamon Press, New York, **1974**.
[2] J. L. Wardell, *Comprehensive Organometallic Chemistry*, *Vol. 1*, Pergamon Press, New York, **1982**, Chapter 2.
[3] H. W. Gschwend, H. R. Roderiguez, *Org. React.* **1979**, *26*, 1–360.
[4] a) *Topics in Organometallic Chemistry Volume 05: Organolithiums in Enantioselective Synthesis*, (Ed.: D. M. Hodgson), Springer, Berlin, **2003**; b) T. Stey, D. Stalke in *The Chemistry of Organolithium Compounds*, (Eds.: Z. Rappoport, I. Marek), Wiley, London, **2004**.
[5] a) N. Sotomayor, E. Lete, *Curr. Org. Chem.* **2003**, *7*, 275–300; b) E. J.-G. Anctil, V. Snieckus, *J. Organomet. Chem.* **2002**, *653*, 150–160; c) L. Green, B. Chauder, V. Snieckus, *J. Heterocycl. Chem.* **1999**, *36*, 1453–1468; d) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879–933; e) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306–312; f) I. Omae, *Chem. Rev.* **1979**, *79*, 287–321; g) H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109–112.
[6] a) M. Stratakis, *J. Org. Chem.* **1997**, *62*, 3024–3025; b) J. D. Roberts, D. Y. Curtin, *J. Am. Chem. Soc.* **1946**, *68*, 1658–1660.
[7] a) N. J. R. von Eikema-Hommes, P. von Ragué Schleyer, *Angew. Chem.* **1992**, *104,* 768–771; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 755–758; b) P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356–363; c) P. Beak, S. T. Kerrick, D. J. Gallagher, *J. Am. Chem. Soc.* **1993**, *115*, 10628–10636; d) J. M. Saá, G. Martorell, A. Frontera, *J. Org. Chem.* **1996**, *61*, 5194–5195.
[8] a) X. Fu, R. A. Reamer, R. Tillyer, J. M. Cummins, E. J. J. Grabowski, P. J. Teider, D. B. Collum, J. C. Huffman, *J. Am. Chem. Soc.* **2000**, *122*, 11212–11218; b) L. M. Pratt, A. W. Streitweiser, *J. Org. Chem.* **2003**, *68*, 2830–2838; c) H. J. Reich, W. S. Goldenberg, B. Ö. Gudmundsson, A. W. Sanders, K. J. Kulicke, K. Simon, I. A. Guzei, *J. Am. Chem. Soc.* **2001**, *123*, 8067–8079; d) H. J. Reich, W. S. Goldenberg, A. W. Sanders, K. L. Jantzi, C. C. Tzschucke, *J. Am. Chem. Soc.* **2003**, *125*, 3509–3521; e) H. J. Reich, W. H. Sikorski, B. Ö. Gudmundsson, R. R. Dykstra, *J. Am. Chem. Soc.* **1998**, *120*, 4035–4036; f) P. I. Arvidsson, P. Ahlberg, G. Hilmersson, *Chem. Eur. J.* **1999**, *5*, 1348–1354; g) C. H. Galka, D. J. M. Trösch, M. Schubart, L. H. Gade, S. Radojevic, I. J. Scowen, M. McPartlin, *Eur. J. Inorg. Chem.* **2000**, 2577–2583; h) G. Hilmersson, B. Malmros, *Chem. Eur. J.* **2001**, *7*, 337–341; i) P. I. Arvidsson, G. Hilmersson, Ö Davidsson, *Helv. Chim. Acta* **2002**, *85*, 3814–3822; j) J. S. DePue, D. A. Collum, *J. Am. Chem. Soc.* **1988**, *110*, 5524–5533; k) A. Ramírez, E. Lobkovsky, D. B. Collum, *J. Am. Chem. Soc.*, **2003**, *125*, 15376–15387; l) R. E. Mulvey, *Chem. Soc. Rev.* **1998**, *27*, 339–346; m) A. E. H. Wheatley, *New J. Chem.* **2004**, *28*, 435–443; n) J. E. Davis, P. R. Raithby, R. Snaith, A. E. H. Wheatley, *Chem. Commun.* **1997**, 1721–1722; o) R. P. Davies, P. R. Raithby, G. P. Shields, R. Snaith, A. E. H. Wheatley, *Organometallics* **1997**, *16*, 2223–2225; p) T. F. Briggs, M. D. Winemiller, D. B. Collum, R. L. Parsons, A. H. Davulcu, G. D. Harris, J. M. Fortunak, P. N. Confalone, *J. Am. Chem. Soc.* **2004**, *126*, 5427–5435, and references therein.
[9] a) T. Kremer, M. Junge, P. von Ragué Schleyer, *Organometallics* **1996**, *15*, 3345–3359; b) J. R. von Eikema-Hommes, P. von Ragué Schleyer, *Tetrahedron* **1994**, *50*, 5903–5916; c) W. Bauer, P. von Ragué Schleyer, *J. Am. Chem. Soc.* **1989**, *111*, 7191–7198.
[10] G. van Koten, J. T. B. H. Jastrebski, *Tetrahedron* **1989**, *45*, 569–578.
[11] a) L. M. Pratt, *Mini-Rev.Org.. Chem.* **2004**, *1*, 209–217; b) X. Fu, R. A. Reamer, R. Tillyer, J. M. Cummins, E. J. J. Grabowski, P. J. Teider, D. B. Collum, J. C. Huffman, *J. Am. Chem. Soc.* **2000**, *122*, 11212–11218.
[12] R. F. Schmitz, F. J. J. de Kanter, M. Schakel, G. W. Klupp, *Tetrahedron* **1994**, *50*, 5933–5944.
[13] W. Peascoe, D. E. Applequist, *J. Org. Chem.* **1973**, *38*, 1510–1512.
[14] a) S. K. Varshney, J. P. Hautekeer, R. Fayt, R. Jérôme, Ph. Teyssié, *Macromolecules* **1990**, *23*, 2618–2622; b) L. M. Jackman, F. Rakiewicz, *J. Am. Chem. Soc.* **1991**, *113*, 1202–1210; c) D. B. Collum, *Acc. Chem. Res.* **1993**, *26*, 227–234; d) J. S. Wang, R. Warin, R. Jérôme, Ph. Teyssié, *Macromolecules* **1993**, *26*, 6776–6781; e) R. E. Ewin,

A. M. MacLeod, D. A. Price, N. S. Simpkins, A. P. Watt, *J. Chem. Soc. Perkin Trans. 1* **1997**, 401–415.
[15] H. Dietrich, D. Rewicki, *J. Organomet. Chem.* **1981**, *205*, 281–289.
[16] L. Cazzangia, R. E. Cohen, *Macromolecules* **1989**, *22*, 4125–4128.
[17] B.-T. Ko, C.-C. Lin, *J. Am. Chem. Soc.* **2001**, *123*, 7973–7977.
[18] K. Ruhlandt-Senge, J. J. Ellison, R. J. Wehmschulte, F. Pauer, P. P. Power, *J. Am. Chem. Soc.* **1993**, *115*, 11353–11357.
[19] P. Wijkens, E. M. van Koten, M. D. Janssen, J. T. B. H. Jastrzebski, A. L. Spek, G. van Koten, *Angew. Chem.* **1995**, *107*, 239–242, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 219–222.
[20] P. Wijkens, J. T. B. H. Jastrzebski, N. Veldman, A. L. Spek, G. van Koten, *Chem. Commun.* **1997**, 2143–2144.
[21] J. G. Donkervoort, J. L. Vicario, E. Rijnberg, J. T. B. H. Jastrzebski, H. Kooijman, A. L. Spek, G. van Koten, *J. Organomet. Chem.* **1998**, *550*, 463–467.
[22] C. Strohmann, B. C. Abele, *Organometallics* **2000**, *19*, 4173–4175.
[23] a) N. J. Hardman, B. Twamley, M. Stender, R. Baldwin, S. Hino, B. Schiemenz, S. M. Kauzlarich, P. P. Power, *J. Organomet. Chem.* **2002**, *643–644*, 461–467; b) J. Arnold, V. Knapp, J. A. R. Schmidt, A. Shafir, *J. Chem. Soc. Dalton Trans.* **2002**, 3273–3274; c) W. Scherer, P. Sirsch, M. Grosche, M. Spiegler, S. A. Mason, M. G. Gardiner, *Chem. Commun.* **2001**, 2072–2073; d) W. Scherer, P. Sirsch, D. Shorokhov, G. S. McGrady, S. A. Mason, M. G. Gardiner, *Chem. Eur. J.* **2002**, *8*, 2324–2334.
[24] C. M. P. Kronenburg, E. Rijnberg, J. T. B. H. Jastrzebski, H. Kooijman, A. L. Spek, G. van Koten, *Eur. J. Org. Chem.* **2004**, 153–159.
[25] M. A. Nichols, P. G. Williard, *J. Am. Chem. Soc.* **1993**, *115*, 1568–1572.
[26] a) The configuration of the bridging C_{ipso} center in the rotamer having the aryl plane perpendicular to the Li–Li vector is determined by the priority of the atoms connected to C_{ipso} in the *C,N*-chelate ring, viewing in the direction of the second Li atom; b) G. van Koten, J. G. Noltes, *J. Am. Chem. Soc.* **1979**, *101*, 6593–6599.
[27] J. T. B. H. Jastrzebski, G. van Koten, M. Konijn, C. H. Stam, *J. Am. Chem. Soc.* **1982**, *104*, 5490–5492.
[28] This is nicely illustrated by the observation of the formation in low yield (< 50 %) of the corresponding organocopper or tin compounds starting from in situ prepared "Li(C_6H_4CH(Me)NMe_2-2)" using *n*BuLi as the lithiating agent. The formation of hetero-aggregated species such as **2** were not considered at that time.[29] Later we established that selective removal (by reaction with Me_3SiCl) of the *n*Bu groups in such hetero-aggregates affords the pure organolithium compound (although hetero-aggregation with the formed LiCl may not be excluded, but this obviously did not interfere with a further transmetalation reaction) suitable for the for example, high yield synthesis of the corresponding organoplatinum compounds.[21,30]
[29] G. van Koten, J. T. B. H. Jastrzebski, J. G. Noltes, W. M. G. F. Pontenagel, J. Kroon. A. L. Spek, *J. Am. Chem. Soc.* **1978**, *100*, 5021–5028.
[30] J. G. Donkervoort, J. L. Vicario, J. T. B. H. Jastrzebski, W. J. J. Smeets, A. L. Spek, G. van Koten, *J. Organomet. Chem.* **1998**, *551*, 1–7.
[31] J. L de Boer, A. J. M. Duisenberg, *Acta Crystallogr. Sect. A* **1984**, *40*, C-410.
[32] G. M. Sheldrick, SHELXL-97, SHELXS-97, Programs for crystal structure refinement. University of Göttingen, Germany, **1997**.
[33] A. L. Spek, *J. Appl. Cryst.* **2003**, *36*, 7–13.

Received: August 11, 2004
Published online: November 17, 2004

