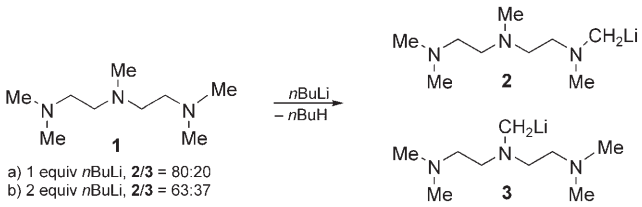
Alkyllithium Compounds

DOI: 10.1002/anie.200605105

From the Alkyllithium Aggregate [{(*n*BuLi)$_2$·PMDTA}$_2$] to Lithiated PMDTA**

Carsten Strohmann and Viktoria H. Gessner*

Organolithium compounds and their aggregates are reactive reagents in organic and inorganic chemistry; simple alkyllithium compounds such as *n*BuLi are generally used in deprotonation reactions.[1] These deprotonation reactions are usually assumed to occur in two steps, in the first of which precoordination forms a reactive intermediate that brings the reacting groups into close contact. This reaction mechanism involving precoordination is referred to as a complex-induced proximity effect (CIPE).[2] Because of their reactivity, such intermediates cannot usually be isolated and structurally characterized. To obtain organolithium species that can form such intermediates through precoordination, organolithium aggregates (e.g. hexameric *n*BuLi[3]) are broken up by coordinating additives such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) or *N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (PMDTA, **1**). Whereas the bidentate ligand TMEDA usually forms dimers (e.g. with *n*BuLi[4]) or bridged tetramers (e.g. with MeLi,[5] or *n*BuLi[4,6]), the tridentate ligand PMDTA (**1**), also gives monomers (e.g. with PhLi[7,8]).[1] Compound **1** also distinguishes itself through slow metallation of its central methyl group or one of its terminal methyl groups; the regioselectivity of this metallation reaction is influenced by the concentration of the alkyllithium compound.[9] NMR spectroscopy studies by Klumpp and co-workers indicate the presence of a monomeric species of *N*-lithiomethyl-*N*,*N*′,*N*′′,*N*′′-tetramethyldiethylenetriamine (**2**) in solution (Scheme 1).[9] With a tridentate ligand, such as PMDTA, it is easy to believe that monomeric systems exist in which the lithium center interacts with the three ligand nitrogen centers and with one negative charge. We thus wanted to try to characterize any such monomeric alkyllithium reagents in their crystalline form to gain an insight into the deprotonation reaction of PMDTA.[10] In the course of this pursuit, we were able to isolate the unusual aggregate [{(*n*BuLi)$_2$·PMDTA}$_2$] (**4**$_2$)—a potential intermediate in the deprotonation of PMDTA—as well as product **2**.



Scheme 1. Lithiation of the central and terminal methyl groups of PMDTA with *n*-butyllithium.[9]

Compound **4**$_2$ crystallizes out of a solution of two equivalents of *n*BuLi and one equivalent of PMDTA in *n*-pentane/*n*-hexane at −45 °C in the form of colorless needles in the triclinic crystal system in the space group $P\bar{1}$.[11] The molecular structure consists of a centrosymmetric dimer with a central Li-C-Li-C ring comprising two *n*BuLi molecules (Figure 1). The complete molecular structure can be formally understood as the coordination of two monomeric *n*BuLi·PMDTA units to the lithium centers of this central four-membered ring through short Li–C contacts. This arrangement is illustrated by the different Li–C distances within the crystal. Whereas the Li–C distances in the Li_2C_2 ring (2.207(5) and 2.225(6) Å) are within the range of typical bond lengths in dimeric organolithium aggregates with a central four-membered ring (2.20–2.32 Å), the Li–C distances within the outer *n*BuLi·PMDTA units and between them and the central ring are much smaller (2.121(6) and 2.146(5) Å), resembling the Li–C distance of 2.114(4) Å in monomeric *t*BuLi·(−)-sparteine.[1,10d] These are the shortest *n*BuLi Li–C distances

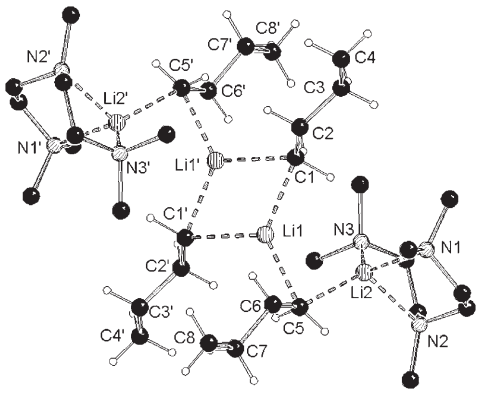


Figure 1. Molecular structure of **4**$_2$ (Schakal representation).[14a] Selected interatomic distances [Å] and angles [°]: C1-Li1 2.207(5), C1-Li1′ 2.225(6), C5-Li1 2.121(6), C5-Li2 2.146(5), C1-C2 1.492(5), C2-C3 1.500(4), C5-C6 1.536(4), C6-C7 1.539(4), Li1-Li1′ 2.371(10), Li1-Li2 2.848(7); C2-C1-Li1 129.8(3), Li1-C5-Li2 83.7(2), C1-Li1-C1′ 115.3(2).

[*] 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

[**] We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support of this work. PMDTA = *N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine.

Supporting information for this article is available on the WWW under http://www.angewandte.de or from the author.

known to us, and such short contacts would be expected on the basis of an electrostatic bonding model of the *n*BuLi·PMDTA units.[1,12,13] The Li–C_β distance of the outer *n*BuLi units is short (2.498(6) Å), while the corresponding C–C distances are slightly lengthened.[1]

The α-lithiated PMDTA **2** crystallizes in the monoclinic crystal system in the space group $P2_1/c$ as the centrosymmetric dimer $\mathbf{2}_2$. The central unit consists of a six-membered N-C-Li-N-C-Li ring in the chair conformation (Figure 2). The metallated C centers only interact with one Li center each, while the Li centers enter into three Li–N bonds and one Li–C bond. The short C–Li distance of 2.122(6) Å is at the low end of the range for comparable crystal structures of α-lithiated amines (2.101–2.375 Å) and stems from the highly directional electrostatic C–Li interactions.[15]

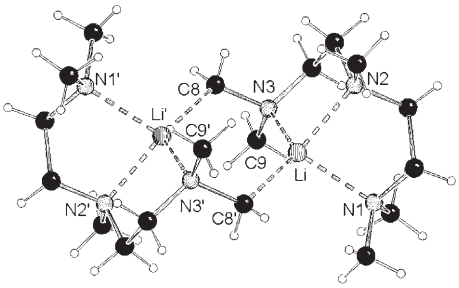


Figure 2. Molecular structure of $\mathbf{2}_2$ (Schakal representation).[14a] Selected interatomic distances [Å] and angles [°]: Li-C8′ 2.122(6), Li-N1 2.243(6), Li-N2 2.170(5), Li-N3 2.078(6); N3-C8-Li′ 119.3(3), N3-Li-C8′ 121.3(3).

In earlier experiments, Klumpp and co-workers observed only one C–Li coupling in the ^{13}C NMR spectrum and thus postulated a monomer in solution, which was shown to have two isomers when the dynamic processes were frozen. However, a dimeric molecular structure analogous to $\mathbf{2}_2$ should also show only one C–Li coupling in its ^{13}C NMR spectrum, meaning that this coupling cannot be relied on to differentiate between the monomer and dimer. The dynamic processes in solution can also be explained by the presence of C_i- ($\mathbf{2}_2$, see molecular structure) and C_2-symmetric dimers that can interconvert at higher temperatures.[9] An energy minimization carried out at the B3LYP/6-31+G(d) level calculates energetic preferences of 103.9 kJ mol^{-1} for the C_2-symmetric dimer and 101.5 kJ mol^{-1} for the C_i-symmetric dimer relative to two monomers in the gas phase, which supports the preferred formation of the two dimers.[16]

Experimentally, metallation of PMDTA at 25 °C with formation of **2** and **3** in an 80:20 ratio with one equivalent of *n*BuLi and 63:37 with two equivalents of *n*BuLi was observed.[9a,c] This result raises the following questions: which transition states does the deprotonation of PMDTA with *n*BuLi pass through (central and terminal), and how big are the corresponding barriers?

Monomer: Assuming that the metallations are intramolecular and start from monomeric *n*BuLi·PMDTA, a reasonable transition state for the metallation could be localized on either the terminal methyl group (**TS-1**; Figure 3) or the central methyl group (**TS-2**; Figure 4). **TS-1** is favored over **TS-2** by 23.2 kJ mol^{-1}. Together with the energy difference of 93.0 kJ mol^{-1} between the minimum **Min-1** and the transition state **TS-1**, this result would lead us to expect selective metallation of the terminal methyl group (Figure 3).

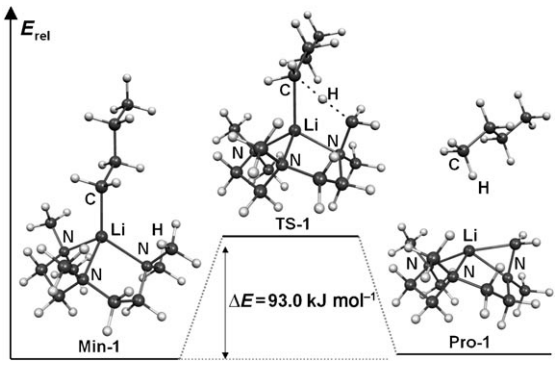


Figure 3. Relative energies of the stationary points for the deprotonation of the terminal methyl group of PMDTA with *n*BuLi (monomer) with formation of **2**; B3LYP/6-31+G(d) (Molekel representation[14b]).

Dimer: When excess *n*BuLi is present, the formation of $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$ is favored over two *n*BuLi·PMDTA and $^1/_3$ $(n\text{BuLi})_6$ by 46.5 kJ mol^{-1}. Assuming an intramolecular metallation starting from the C_i-symmetric aggregate $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$, a C_i-symmetric transition state **TS-3** for metallation of the terminal methyl group can be found (two simultaneous metallations).[17] Metallation of the terminal methyl group has a barrier of 124.8 kJ mol^{-1} (half the value of the two simultaneously occurring metallations, see the Supplementary Information). This barrier is higher than that of 93.0 kJ mol^{-1} for the reaction mechanism involving a monomer (Figure 3); however, formation of the monomer from $^1/_2$ $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$ requires an additional energy contribution of 23.2 kJ mol^{-1}. We thus expect both reaction mechanisms (via the monomer and the aggregate) to compete with each other.

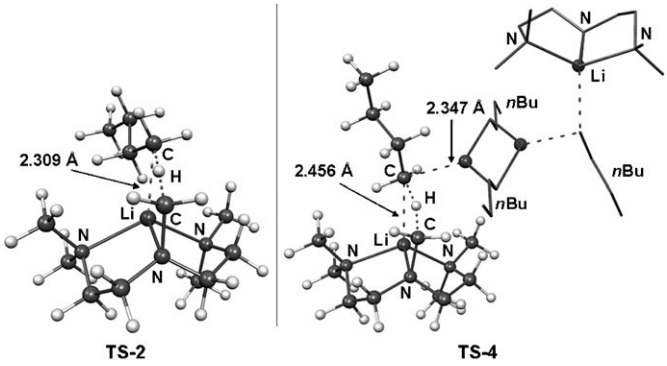


Figure 4. Transition states **TS-2** and **TS-4** and their relevant C–Li distances for the deprotonation of the central methyl group of PMDTA with *n*BuLi; B3LYP/6-31+G (Molekel-representation[14b]).

But why does formation of the aggregate make the metallation to form regioisomers **2** and **3** less selective? In the transition states of the aggregate (**TS-3**: terminal methyl group and **TS-4**: central methyl group), the anionic center of

the reacting *n*BuLi group is stabilized relative to those of the transition states of the monomer (**TS-1** and **TS-2**) by a second C–Li contact (Figure 4). This contact results in an increase of the Li–C distance relative to the corresponding distance in the monomer and thus to a more energetically favorable, less deformed geometry, especially for the deprotonation of the central methyl group (**TS-4**). This situation reduces the energy difference between the two relevant transition states for metallation starting with $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$ from 23.2 kJ mol^{-1} (monomer; **TS-1, TS-2**) to 15.6 kJ mol^{-1} (aggregate; **TS-3, TS-4**). The experimentally observed tendency to form an increasing proportion of regioisomer **3** when the proportion of *n*BuLi is increased is thus supported by these calculations.[18]

$[\{(n\text{BuLi})\cdot\text{PMDTA}\}_2]$ can be regarded as a transition to an *n*BuLi·PMDTA monomer (only one Li–C contact for Li2). The regioselectivity of the metallation of PMDTA is critically influenced by the formation of $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$, because steric interactions in the corresponding transition states are decreased by these additional Li contacts. We are now working to determine the molecular structures of other simple alkyllithium compounds (coordinated by multidentate and, in part, chiral ligands) to gain insights into the relationships between structure and reactivity in these widely used alkyllithium reagents.

Received: December 18, 2006
Revised: February 15, 2007
Published online: May 7, 2007

Keywords: aggregation · alkyllithium compounds · butyllithium · lithiation · N ligands

[1] T. Stey, D. Stalke in *The Chemistry of Organolithium Compounds* (Eds.: Z. Rappoport, I. Marek), Wiley, Chichester, **2004**, S. 47–120.
[2] M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem.* **2004**, *116*, 2256; *Angew. Chem. Int. Ed.* **2004**, *43*, 2206.
[3] T. Kottke, D. Stalke, *Angew. Chem.* **1993**, *105*, 619; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 580.
[4] M. A. Nichols, P. G. Williard, *J. Am. Chem. Soc.* **1993**, *115*, 1568.
[5] H. Köster, D. Thoennes, E. Weiss, *J. Organomet. Chem.* **1978**, *160*, 1.
[6] N. D. R. Barnett, R. E. Mulvey, W. Clegg, P. A. O'Neil, *J. Am. Chem. Soc.* **1993**, *115*, 1573.
[7] Examples of monomeric PMDTA structures of hydrocarbons: a) U. Schümann, J. Kopf, E. Weiss, *Angew. Chem.* **1985**, *97*, 222; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 215; b) L. M. Engelhardt, W.-P. Leung, C. L. Raston, G. Salem, P. Twiss, A. H. White, *J. Chem. Soc. Dalton Trans.* **1988**, 2403 Examples of monomeric PMDTA structures with an additional heteroatom: c) H. H. Karsch, K. Zellner, P. Mikulcik, J. Lachmann, G. Muller, *Organometallics* **1990**, *9*, 190; d) M. F. Lappert, L. M. Engelhardt, C. L. Raston, A. H. White, *J. Chem. Soc. Chem. Commun.* **1982**, 1323.
[8] Benzyllithium and the cyclic, PMDTA-analogous ligand *N,N′,N″*-trimethyl-1,4,7-triazacyclononane also form a monomeric structure. This structure results when a dimer composed of *t*BuLi and the lithiated ligand are treated with toluene. The lithiated ligand crystallizes as a C_2-symmetric dimer: J. Arnold, V. Knapp, J. A. R. Schmidt, A. Shafir, *J. Chem. Soc. Dalton Trans.* **2002**, 3273.
[9] a) M. Schakel, M. P. Aarnts, G. W. Klumpp, *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 305; b) G. W. Klumpp, H. Luitjes, M. Schakel, E. J. J. de Kanter, R. F. Schmitz, N. J. R. van Eikema Hommes, *Angew. Chem.* **1992**, *104*, 624; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 633; c) H. Luitjes, M. Schakel, M. P. Aarnts, R. F. Schmitz, F. J. J. de Kanter, G. W. Klumpp, *Tetrahedron* **1997**, *53*, 9977.
[10] a) B. Walfort, L. Lameyer, W. Weiss, R. Herbst-Irmer, R. Bertermann, J. Rocha, D. Stalke, *Chem. Eur. J.* **2001**, *7*, 1417; b) C. Strohmann, K. Lehmen, K. Wild, D. Schildbach, *Organometallics* **2002**, *21*, 3079; c) C. Strohmann, D. H. M. Buchold, T. Seibel, K. Wild, D. Schildbach, *Eur. J. Inorg. Chem.* **2003**, 3453; d) C. Strohmann, T. Seibel, K. Strohfeldt, *Angew. Chem.* **2003**, *115*, 4669; *Angew. Chem. Int. Ed.* **2003**, *42*, 4531; e) C. Strohmann, K. Strohfeldt, D. Schildbach, *J. Am. Chem. Soc.* **2003**, *125*, 13672; f) C. Strohmann, T. Seibel, D. Schildbach, *J. Am. Chem. Soc.* **2004**, *126*, 9876; g) C. Strohmann, K. Strohfeldt, D. Schildbach, M. J. McGrath, P. O'Brien, *Organometallics* **2004**, *23*, 5389; h) C. Strohmann, B. C. Abele, K. Lehmen, D. Schildbach, *Angew. Chem.* **2005**, *117*, 3196; *Angew. Chem. Int. Ed.* **2005**, *44*, 3136; i) C. Strohmann, S. Dilsky, K. Strohfeldt, *Organometallics* **2006**, *25*, 41; j) C. Strohmann, K. Lehmen, S. Dilsky, *J. Am. Chem. Soc.* **2006**, *128*, 8102.
[11] Diffractometer: Stoe-IPDS; Mo-K_α radiation: $\lambda = 0.71073$ Å, $T = 173$ K; all structures were refined anisotropically against F^2 (G. M. Sheldrick: SHELXS90 and SHELXL-97, Universität Göttingen, **1990** and **1997**). a) Structure refinement of $[\{(n\text{BuLi})_2\cdot\text{PMDTA}\}_2]$ (**4**$_2$, colorless needles from *n*-pentane/*n*-hexane, $0.5\times0.3\times0.2$ mm^3): $C_{34}H_{82}Li_4N_6$, $M_r = 602.82$, triclinic, space group $P\bar{1}$, $a = 9.173(5)$, $b = 10.931(3)$, $c = 11.847(4)$ Å, $\alpha = 84.29(4)$, $\beta = 68.51(5)$, $\gamma = 76.03(5)°$, $V = 1072.6(8)$ Å^3, $Z = 1$, $\rho = 0.933$ Mg m^{-3}, 2θ range: 4.9–48.0°; 6056 reflections, 3188 independent reflections ($R_{int} = 0.0452$); $R_1 = 0.0570$, $wR_2 = 0.2170$ (all data); b) Structure refinement of **2**$_2$ (colorless rhombuses from *n*-pentane, $0.3\times0.3\times0.2$ mm^3): $C_{18}H_{44}Li_2N_6$, $M_r = 358.47$, monoclinic, space group $P2_1/c$, $a = 8.7146(17)$, $b = 8.9731(18)$, $c = 15.402(3)$ Å, $\beta = 97.43(3)°$, $V = 1194.3(4)$ Å^3, $Z = 2$, $\rho = 0.997$ Mg m^{-3}, 2θ range: 4.8–52.0°; 10156 reflections, 2328 independent reflections ($R_{int} = 0.0608$), $R_1 = 0.0697$, $wR_2 = 0.2035$ (all data). CCDC-628590 (**4**$_2$) and CCDC-628589 (**2**$_2$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[12] Selected examples of mixed *n*BuLi structures: a) C. Strohmann, B. C. Abele, *Organometallics* **2000**, *19*, 4223; b) B.-T. Ko, C.-C. Lin, *J. Am. Chem. Soc.* **2001**, *123*, 7973; c) G. Müller, A. Feustel, *Organometallics* **2003**, *22*, 3049; d) C. M. P. Kronenburg, E. Rijnberg, J. T. B. H. Jastrzebski, H. Kooijman, M. Lutz, A. L. Spek, R. A. Gossage, G. van Koten, *Chem. Eur. J.* **2005**, *11*, 253; e) R. Gossage, J. T. B. H. Jastrzebski, G. van Koten, *Angew. Chem.* **2005**, *117*, 1472; *Angew. Chem. Int. Ed.* **2005**, *44*, 1448; f) B. Goldfuss, M. Steigelmann, T. Löschmann, G. Schilling, F. Rominger, *Chem. Eur. J.* **2005**, *11*, 4019.
[13] The next-largest Li–C distances in an *n*BuLi unit are found in the *n*BuLi hexamer.
[14] a) Schakal99, E. Keller, Universität Freiburg, **1999**; b) Molekel, S. Portmann, ETH Zürich (Switzerland), Zürich, **2001**.
[15] a) S. Harder, M. Lutz, *Organometallics* **1994**, *13*, 5173; b) F. Becke, F. W. Heinemann, T. Rüffer, P. Wiegeleben, R. Boese, D. Bläser, D. Steinborn, *J. Organomet. Chem.* **1997**, *548*, 205; c) C. Bruhn, F. Becke, D. Steinborn, *Organometallics* **1998**, *17*, 2124; d) G. Müller, T. Schätzle, *Z. Naturforsch. B* **2004**, *59*, 1400; e) X. Tian, M. Woski, C. Lustig, T. Pape, R. Fröhlich, D. Le Van, K. Bergander, N. W. Mitzel, *Organometallics* **2005**, *24*, 82; f) A. Hildebrand, P. Lönnecke, L. Silaghi-Dumitrescu, I. Silaghi-Dumitrescu, E. Hey-Hawkins, *Dalton Trans.* **2006**, 967.

[16] Gaussian 03 (Revision B.04), M. J. Frisch et al., see the Supporting Information
[17] In addition to both of the C_i-symmetric transition states **TS-3** and **TS-4** (two simultaneous deprotonations), we also calculated the energies (SCF) of the corresponding C_1-symmetric transition states **TS-3-C_1** and **TS-4-C_1** (one deprotonation), which differ only slightly from the half barriers for **TS-3** and **TS-4** (see the Supporting Information). Because the size of the molecule only allowed a frequency calculation for the C_i-symmetric transition states, these values are given and discussed.
[18] The energies and energy differences determined by gas-phase calculations are about 10 kJ mol^{-1} too high for the description of the experimental observations in solution, but this deviation is within the expected error of a calculation of the energies of stationary points of polar alkyl metal compounds by the B3LYP/6-31 + G method.

