

C–C couplings,^[7] they were allowed to react with the ketene silyl acetal **10** in the presence of titanium tetrachloride ("Mukaiyama–aldol reaction"^[8]). The *syn*-configured adducts **11a–c** (72–76% yield based on **7**) are formed with a remarkable stereoselectivity (*de* > 98%), which can be interpreted as arising from a chelate-controlled reaction.^[9] The relative configuration of the β -hydroxy esters **11a–c** is determined by its conversion into the oxazolidinones **12a–c** (COCl₂, pyridine, toluene). In the ¹H NMR spectra of **12a–c** the coupling constant (4.5 Hz) of the protons H4 and H5 allows an unambiguous assignment of the *trans* configuration (Table 2).^[11, 12] Furthermore, ¹H NMR shift experiments with [Eu(hfc)₃]^[12] indicate an enantiomeric excess of the heterocycles **12a–c** of 93–96%.^[13] The optical purity of **12a–c** lies only slightly below the diastereomeric excess of the corresponding purified adducts **4a, e, f**, which shows that the *N*-sulfonylated amino aldehydes **8** retain their configurations under the conditions of their formation, isolation, and conversion in the Mukaiyama reaction. However, as expected, heating the aldehydes **8** leads to racemization. The addition of the chiral vinyl anions (*S*)- and (*R*)-**2** to sulfonylimines **3** allows, in particular, an easy access to arylglycines^[14] and *N*-protected arylglycine aldehydes with high enantioselectivity. In the latter case the mesityl sulfonyl protecting group proves to be an efficient stereoregulating element for nucleophilic additions to the aldehyde group.

Received: November 28, 1992 [Z 57101E]
German version: *Angew. Chem.* **1993**, *105*, 595

Structures of Classical Reagents in Chemical Synthesis: (*n*BuLi)₆, (*t*BuLi)₄, and the Metastable (*t*BuLi · Et₂O)₂**

By Thomas Kottke and Dietmar Stalke*

Alkyl lithium compounds are particularly important in synthetic chemistry as deprotonating and substituting reagents and as catalysts in polymerization.^[1, 2] As long ago as 1917, Schlenk and Holtz reported the first synthesis of alkyl lithium compounds;^[3] in 1963 the first solid-state structural analysis of a substance of this class, namely tetrameric ethyllithium, was achieved by Dietrich.^[4] Subsequently, numerous RLi compounds have been characterized by X-ray structure investigations.^[5–12] The degree of oligomerization of the compounds of this class most commonly used in synthesis, *n*BuLi and *t*BuLi, have long been established by cryoscopic and spectroscopic measurements. In hydrocarbons *n*BuLi is hexameric^[13–16] and *t*BuLi is tetrameric;^[17–20] in donor solvents a lower degree of aggregation is preferred.^[21–23] Until now, however, no information about the crystal structures of *t*BuLi and of donor-free *n*BuLi have been available. This is probably due to the fact that these compounds (especially *t*BuLi) are pyrophoric and that *n*BuLi is an oil at room temperature. Herein we describe the crystallization and the X-ray single-crystal structures^[24] of donor-free *n*BuLi and *t*BuLi and also of the metastable adduct of *t*BuLi with one equivalent of diethyl ether.

For the crystallization, a temperature was chosen at which the nearly saturated solutions could be prepared; this should be as low as possible to avoid phase transitions during low temperature data collection (here: –90 °C). The limiting values taken into account were the melting point of *n*BuLi (–76 °C according to reference [1]; the melting point of the crystals investigated here, however, was –34(2) °C) and the temperature at which decomposition of *t*BuLi · Et₂O might occur (–40 °C^[25] and –35 °C^[26] for *t*BuLi · Et₂O). To achieve a gradual and controlled crystallization, all solutions were prepared at –80 °C. The crystallization period was extended to one week by redissolving crystals formed initially, thus leaving a small number of nucleation sites in the solution. This technique appears to increase the probability of forming single crystals suitable for X-ray crystallography.^[27] During the preparation of crystals for data collection (selecting and mounting a crystal and transporting it to the diffractometer) the temperature of a sample never exceeded –45 °C. This was facilitated by using apparatus developed for mounting crystals at low temperatures.^[28] Thus the crystals could be kept at –60 °C on the polarization microscope slide, and then transferred to the diffractometer with a portable liquid nitrogen evaporator (see also ref. [29]). The use of inert gas Schlenk techniques and sealing with inert oil^[28] were necessary to prevent the extremely oxygen and moisture-sensitive crystals from reacting with air.

All three compounds are discrete aggregates and no interactions between oligomers were found such as have been observed, for example, in the solid-state structure of MeLi (the shortest Li–C distance between two oligomeric units is 382 pm found in *n*BuLi; in MeLi it is 252 pm^[5]). The framework of *n*BuLi consists of six Li atoms in a trigonal anti-prismatic (distorted octahedral) conformation (approximately *D*_{3d} symmetry) with six short (241.3(3)–243.7(3), average

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[10] The diastereomeric (at C3) product is formed in addition to **11a** from the aldol reaction with the lithium enolate of methyl isobutyrate in the ratio 8:1 in favor of the chelate-controlled compound. The coupling constant $J(^4\text{H}, ^5\text{H})$ for *cis*-configured **12a** is 6.8 Hz.

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[12] [Eu(hfc)₃] = tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]-europium (purchased from Aldrich).

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

242.9 pm), and six long (289.8(3)–297.0(3), average 293.9 pm) Li–Li distances (Fig. 1). Analogous to cyclohexyllithium,^[8] isotopic cyclopentyllithium,^[12] and a lithio-methylcyclopropane derivative,^[10] six faces of the octahedron are each capped by a single *n*Bu unit; two almost equilateral (and opposite) triangular faces with the longest edges remain unoccupied. Each α -carbon atom is coordinat-

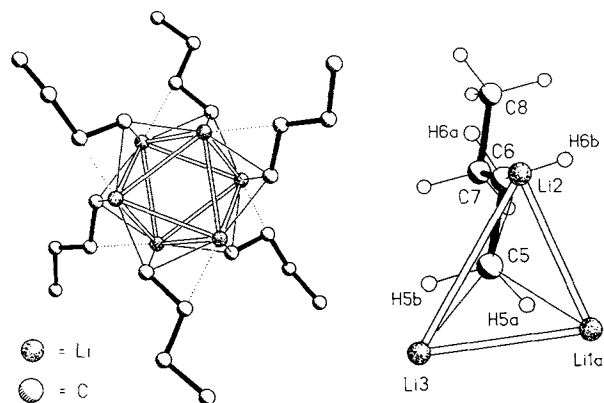


Fig. 1. Left: Crystal structure of *n*BuLi. Right: The projection perpendicular to one of the Li triangles of the distorted octahedron with a coordinated *n*Bu group. Selected bond lengths [pm] and angles [°] (average values): C₇–C₆ 153.3(2), C₆–C₇ 152.1(5), C₇–C₈ 150.5(6); C₇–C₆–C₇ 117.4(5), C₆–C₇–C₈ 113.7(1).

ed to two Li atoms positioned at the corners of one of these (noncapped) triangles through short bonds (213.7(3)–217.5(3), average 215.9 pm), whereas the bond to the Li atom at the corner of the opposite triangle is significantly longer (226.2(3)–227.7(3), average 227.0 pm). Hence, the *n*Bu moieties do not lie centrally over the isosceles Li triangles but are shifted to one edge (Fig. 1 right). As a result of this, short distances occur between the β -C atoms and the Li atoms, which may be interpreted as electrostatic interactions (Li–C distance: 228.0(3)–229.5(3), average 228.7 pm; though they are in the range of the longer Li–C _{α} bonds). At the same time this conformation has short Li–H _{α} and Li–H _{β} distances (Fig. 1 right: 204(2) pm for Li3–H5b and 203(2) pm for Li2–H6a). The hydrogen atoms at the α -C and β -C atoms are arranged staggered with respect to the nearest Li atom. In conclusion, *n*BuLi shows similar structural characteristics to the cyclic alkyl lithium compounds mentioned above. Even in the complex (*n*BuLi · LiO*t*Bu)₄ remarkably short Li–C _{β} distances are observed (234(1) pm^[30]). Apparently a fourfold coordination of the Li atoms by including β -C atoms is preferred in spite of the elongation of a Li–C _{α} bond.

*t*BuLi consists of tetrameric units of almost T_d symmetry (Fig. 2) in the crystal. The asymmetric unit is made up of 4.5 tetramers; one tetramer is crystallographically generated through a twofold axis. Each face of the Li₄ tetrahedron is capped by a *t*Bu group such that the (terminal) Me groups are eclipsed with respect to the corresponding Li atoms of the (within the standard deviation) equilateral triangles (Fig. 2 right). This conformation again involves comparatively short Li–C _{β} distances (227.5(8)–256.6(9), average 237.4 pm). Thus, the structure of *t*BuLi is essentially different from that of MeLi in which the hydrogen atoms of the Me groups (in contrast to the conformation of C _{β} atoms in *t*BuLi) are staggered relative to the Li atoms.^[6] As in *n*BuLi Li–C _{β} interactions may participate in determining the conformation of *t*BuLi, especially since the β -C atoms would

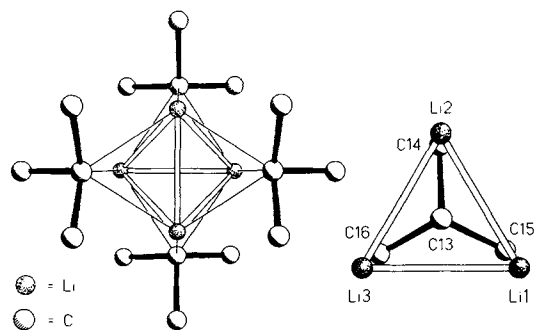


Fig. 2. Left: Crystal structure of *t*BuLi. Right: The projection perpendicular to one of the Li triangles of the tetrahedron with coordinated *t*Bu group. Selected bond lengths [pm] and angles [°] (minimum/maximum/average): C₁₆–C₁₃ 150.9(5)/157.9(9)/153.4; C₁₆–C₁₃–C₁₄ 104.1(4)/108.5(5)/105.9; Li₁–C₁₃–Li₃ 62.1(4)/66.7(4)/64.9.

preferentially be staggered for steric reasons. The Li–C _{α} bond lengths (214.7(17)–237.0(14), average 224.6 pm) are in the range of the values observed in similar compounds, while the Li–Li distances in *t*BuLi (238.3(9)–243.1(8), average 241.2 pm) are significantly shorter (Li–Li and Li–C [pm] in EtLi:^[4] 255 and 225, respectively, in MeLi:^[6] 256 and 227, respectively). The relatively large variation of the C–C and Li–C distances in *t*BuLi is caused by disorders of the *t*Bu groups.

*t*BuLi · Et₂O is a dimer which is generated crystallographically from the monomeric unit through a twofold axis (Fig. 3). The central four-membered ring consisting of two

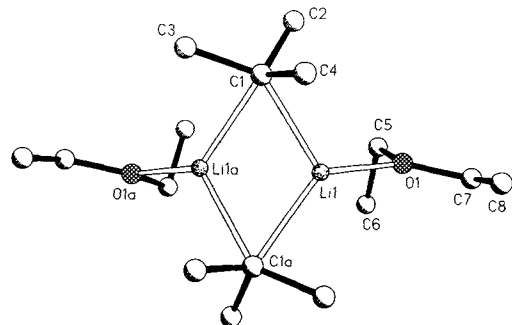


Fig. 3. Crystal structure of (*t*BuLi · Et₂O)₂. Selected bond lengths [pm] and angles [°]: Li1–C1 217.4(6), Li1–C1a 219.4(6), Li1–O1 194.0(5); Li1–C1–Li1a 63.6(2), C1–Li1–C1a 110.7(2).

Li and two bridging α -C atoms of the *t*Bu groups is strongly distorted about the Li–Li axis (the angle between the planes Li1–C1–Li1a and Li1–C1a–Li1a is 29.1(4)°, which is consistent with the steric demand of the Et₂O molecules and the *t*Bu groups. This steric hindrance provides a possible explanation for the absence of a second donating Et₂O molecule per Li atom as postulated for *t*BuLi in ether.^[26] In connection with this it should be noted that solutions of *t*BuLi in ether are stable even with a large excess of ether (Et₂O:*t*BuLi \approx 6:1) over a wider temperature range (up to about –40 °C), as observed in NMR studies.^[26]

Experimental Procedure

All three compounds were prepared starting with commercially available solutions (in hexane or pentane); solvent was removed from these solutions under vacuum.

*n*BuLi: To *n*BuLi (2.9 g, 46 mmol), constantly stirred at -80°C , precooled pentane was added dropwise until a homogeneous solution was obtained (ca. 20 mL). After one week at -90°C colorless blocks crystallized with a melting point of $-34(2)^{\circ}\text{C}$.

*t*BuLi: *t*BuLi (2.2 g, 34 mmol) was treated as described for *n*BuLi (ca. 18 mL pentane added). Crystallization over one week yielded colorless elongated blocks.

(*t*BuLi · Et₂O)₂: From various pentane/Et₂O ratios the best results were obtained by first adding 5 mL pentane and then 12 mL Et₂O (each precooled to -60°C) dropwise to solid *t*BuLi (2.2 g, 34 mmol) at -80°C . At -90°C colorless blocks with a melting point of $-38(2)^{\circ}\text{C}$ were formed from the pale yellow solution.

Received: December 7, 1992 [Z 5732 1E]
German version: *Angew. Chem.* **1993**, 105, 619

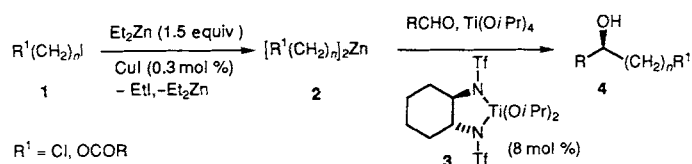
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Enantioselective Catalytic Addition of Functionalized Dialkylzinc Compounds to β-Stannylated Aldehydes: A Convenient Preparation of Chiral β- and γ-Functionalized Secondary Alcohols**

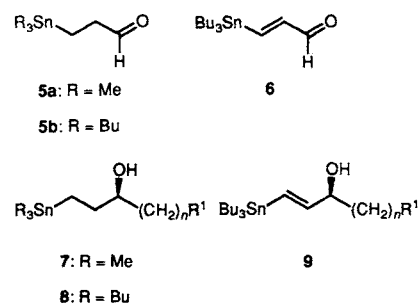
By Walter Brieden, Roswitha Ostwald, and Paul Knochel*

Recently we described a general method for the preparation of dialkylzinc compounds of the type **2** from the corresponding alkyl iodides **1**.^[1] These functionalized organozinc reagents proved to be extremely useful for the catalytic asymmetric addition to aldehydes in the presence of the chiral catalyst **3**.^[1, 2] The method allows an easy access to polyfunctional secondary alcohols **4** in both enantiomeric forms with excellent enantioselectivity.^[12m] Unfortunately, as we



tried to extend this reaction to functionalized aldehydes bearing, for example, an oxygen functionality in the γ-position, stoichiometric amounts of the catalyst **3** were necessary.^[1] In addition, acceptable chemical yields could only be obtained with *unfunctionalized* diorganozinc compounds **1**. We report now that this problem does not arise if β-stannylated aldehydes such as **5**^[3] or **6**,^[4] are used, and that with these aldehydes polyfunctionalized alcohols are readily accessible, which, in a second step, can be converted into polyoxygenated molecules.

The aldehydes **5** and **6** react readily under mild conditions (-35 to -25°C , 16 h for **5a, b** and -60 to -50°C , 2 h for **6**) with the functionalized diorganozinc compounds **2**, and afford good to excellent yields (67–89%) and enantioselectivities (90–97% ee)^[5] of the stannylated alcohols **7–9** (Table 1). All reactions have been performed with a catalytic amount of **3** (ca. 8 mol %). Remarkably, the presence of an ester or halide functionality does not interfere in these reactions, even if the ester group is relatively close to the metal center (γ position), as is the case in the formation of **9f**. This method allows a one-step enantioselective synthesis of the



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**] This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Fonds der Chemischen Industrie, and the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 260). We thank Dr. U. Klar and Dr. D. Ventur (Scheer AG) for a generous gift of Me₂SnCl₂ and Bu₃SnH.