On the Configurational Stability of α-Bromo-alkyllithium Compounds

Reinhard W. Hoffmann,* Thomas Ruhland and Martin Bewersdorf

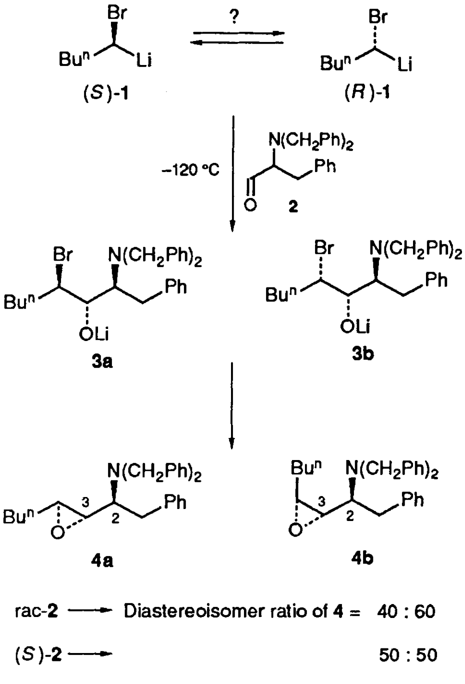
Fachbereich Chemie der Philipps-Universität, Hans-Meerwein-Strasse, D-3550 Marburg, Germany

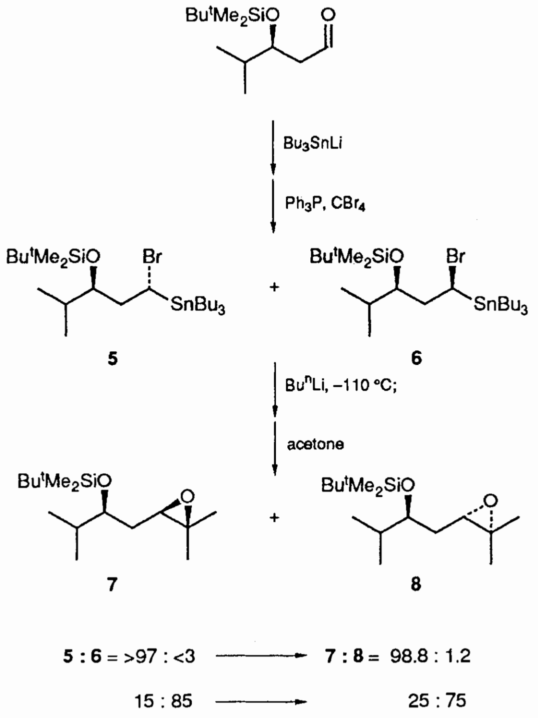
1-Bromopentyllithium **1**, a typical 'bromocarbenoid,' has been established to be chiral and configurationally stable at −120 °C by a test based on kinetic resolution; likewise, diastereoisomeric 1-bromoalkyllithium compounds were generated from the bromo-tin compounds **5** and **6** and found to be configurationally stable at −110 °C.

We have recently developed a test[1] by which the rate of configurational equilibration of a chiral organolithium compound such as **1** can be compared to the rate of trapping by an electrophile. The test is based on kinetic resolution and can be applied to racemic organolithium compounds. By reaction of racemic **1** with the racemic aldehyde **2**[2] it was shown that there is a sufficient level of kinetic resolution in the addition of **1** to **2**. After warming to room temperature the intermediary β-bromo-alkyllithium compounds **3** cyclized to the *cis/trans* isomeric epoxides **4**. The diastereoisomer ratio determined from the crude reaction mixture was 60 : 40; the isolated yield after purification was 71%. Substantial precedent[2] suggests that the relative configuration at C-2 and C-3 is as shown.

In the actual test racemic **1** was trapped by enantiomerically pure (*S*)-**2**. This time the diastereoisomeric products **4** were formed in a different ratio of 50 : 50 (80%). This product ratio reflects the enantiomer ratio of (racemic) **1**. If the carbenoids **1** were prochiral instead of chiral, or if the enantiomers of **1** had equilibrated more rapidly than they are trapped by **2**, the 60 : 40 product ratio defined by kinetic resolution should have resulted. Thus, these experiments established the chirality of the carbenoids **1** as well as their configurational stability on a timescale defined by their rate of addition to the aldehyde **2**. We therefore wanted to learn whether such species are also stable on a macroscopic time scale. To this end, a 2 : 1 mixture of the diastereoisomeric bromo-tin compounds **5** and **6** was synthesized (53%)[3] and separated by HPLC.

After treatment of the diastereoisomerically pure (>97%) **5** with n-butyllithium in a Trapp-solvent-mixture[4] at −110 °C acetone was added after 10 min and the mixture was processed[5] to give the epoxides **7** and **8** of established[6] relative configuration in a 98.8 : 1.2 ratio (80%). Identical treatment of an 85 : 15 mixture of **6** and **5** led to the epoxides **8** and **7**, now with **8** predominating (75 : 25). In **5** the tin is in the stereochemically significant position, at which tin–lithium exchange is kinetically favoured by 1,3-asymmetric induction.[5] For the same reason tin–lithium exchange is expected to be slowed down in the reaction of the diastereoisomer **6**. This is apparently reflected in the change of the diastereoisomer composition (15 : 85 of **5**, **6** going to 25 : 75 for **7**, **8**). Moreover, in **6** (and not in **5**) bromine–lithium exchange should be favoured by 1,3-asymmetric induction. A competing bromine–lithium exchange on reaction of **6** with n-butyllithium may account for the low yield (30%) of **7**, **8** in the latter experiment.





The differences in the **7**:**8**-product ratios in the two experiments indicate that the intermediary α-bromo-organolithium compounds had not equilibrated prior to the addition of acetone. This demonstrates that chiral α-bromoalkyllithium compounds such as **1** can be added to electrophiles maintaining configurational integrity.

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