On the Mechanism of Internal *ortho*-Lithiation in a Mixed Complex Between BuLi and a Chiral Lithium Amide

by **Per I. Arvidsson***

Department of Organic Chemistry, Institute of Chemistry, Uppsala University, Box 531, SE-751 21 Uppsala

and

Göran Hilmersson* and **Öjvind Davidsson**[1])

Organic Chemistry, Department of Chemistry, Göteborg University, SE-412 96 Göteborg

Dedicated to Professor Dr. *Dieter Seebach*, a pioneer in the field of lithium organic chemistry and our role model as scientist, on the occasion of his 65th birthday

The chiral lithium amide Li-**1**, prepared from (*S*)-*N*-[(*R*)-2-methoxy-1-phenylethyl]-α-methylbenzylamine **1**, is known to form a mixed complex with BuLi, *i.e.*, Li-**1**/BuLi. When this complex is kept at room temperature for 3–5 h, a regioselective lithiation of one of the *ortho*-C-atoms in the amide occurs. Kinetic studies indicate that this reaction proceeds within the mixed aggregate with a first-order rate constant for the rate-limiting step $k_2 = 9.4 \times 10^{-4}$ s^{-1} ($\Delta G^{\ddagger}_{273\text{K}} = 21$ kcal mol^{-1}). Molecular modeling (semi-empirical PM3) suggests that the observed selectivity and reactivity are a consequence of the solvation and structure of the mixed complex, *i.e.*, an example of a complex induced proximity effect (CIPE).

Introduction. – *D. Seebach* wrote the following in this journal in 1983 [1]: '*Die noch immer steigende Bedeutung von Lithiumorganylen in der organischen Synthese – man denke z. B. an die 'neue' Aromatenchemie – weckt den Wunsch nach mehr Wissen über die Zusammenhänge zwischen Struktur und Reaktivität, das heisst nach einem weniger empirischen Vorgehen bei der Suche nach weiteren Anwendungen dieser Verbindungsklasse*'[2]). Detailed structural and mechanistic studies, too many to be properly cited here, have increased our knowledge about the structure and reactivity of organolithiums tremendously over these twenty years (for selected reviews, see [2]). Nonetheless, the unprecedented structural complexity of the aggregates formed by organolithiums makes the reactivity of these substances highly intricate. Thus, it is not uncommon that we still find new, and unforeseen, reactivity where these substances are involved. As this contribution illustrates, unexpected reactions may still be encountered in the, by now, quite '*alten Aromatenchemie*'[3]).

Among the many reactions involving lithium organic species, few have attracted the attention of organic chemists more than this '*Aromatenchemie*', *i.e.*, the *ortho*-directed lithiation of (especially) heteroatom-containing aromatic rings [3] *Scheme 1*.

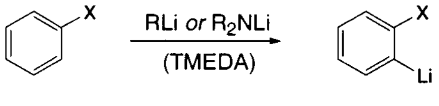
---

[1]) Present address: Medicinal Chemistry, *AstraZeneca R&D Mölndal*, SE-431 83 Mölndal.

[2]) Freely translated: '*The constantly growing importance of organolithiums in – one thinks especially on the 'new' aromatic substitution chemistry – encourage further knowledge about the connection between structure and reactivity, that means a less empirical approach for finding further use of this class of molecules*'.

[3]) '*Old*' aromatic substitution chemistry.

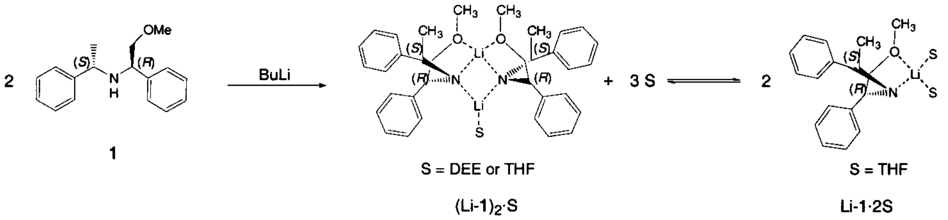
Scheme 1. ortho-*Lithiation of an Aromatic Ring by an Alkyllithium or Lithium Amide Reagent.* X = Heteroatom, TMEDA = *N,N,N′,N′*-tetramethylethylenediamine.



The complementary of this method for aromatic substitution, as compared to traditional methods based on electrophilic substitution, has triggered an enormous collective effort of both academic and industrial chemists to exploit *ortho*-lithiations for the regiocontrolled synthesis of polysubstituted arenes (for a few recent examples, see [4]). The origin of the *ortho*-selectivity observed and rate enhancements found for heteroatom-substituted aromatics has also been under intense evaluation [5–7]. The most generally accepted explanation relies on the suggestion that an initial coordination of the metal to the lone pair on the substituent increases the inductive effect of the substituent as well as positions the metallating reagent in the vicinity of the *ortho*-H-atom and, thus, facilitates its removal of the carbanion. Although the details and relative importance of these factors are under discussion, the importance of complexation for controlling reactivity, stereo-, and regioselectivity, have been recognized and designated the 'complex induced proximity effect' (CIPE) [8].

Background. – Previous investigations by our group have outlined the solution-state structure of the chiral lithium amide Li-**1**, prepared from (*S*)-*N*-[(*R*)-2-methoxy-1-phenylethyl]-α-methylbenzylamine **1**. Detailed studies by NMR spectroscopy, X-ray diffraction, and computational methods have shown that Li-**1** forms a C_2-symmetric dimer, *i.e.*, (Li-**1**)$_2$ · S (S = DEE) in *Scheme 2*, in diethyl ether ((D$_{10}$)DEE) solution [9]. The dimer is solvated by one solvent molecule, exhibiting slow exchange on the NMR time-scale, and is capable of stereoselective solvation, when a racemic solvent mixture, *i.e.*, 2,3,4,5-tetrahydro-2-methylfuran, is added [10]. Application of the chiral lithium amide in the enantioselective rearrangement of *meso*-epoxides to chiral allylic alcohols has also been demonstrated [9a].

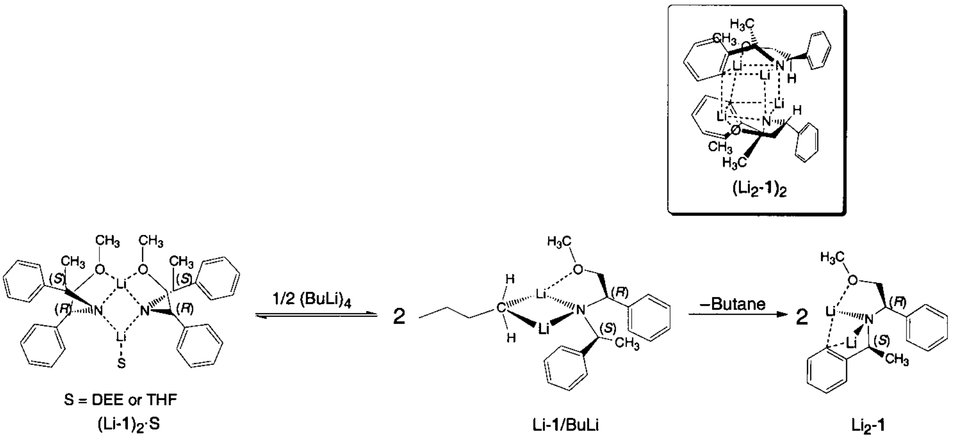
Scheme 2. *Preparation and Solution-Phase Aggregation of Li-*1. NMR-Spectroscopic studies have shown that the chiral lithium amide Li-**1** is present as a dimer (Li-**1**)$_2$ in DEE solution. In THF, both dimers and monomers are present.



Addition of small amounts of THF to a (D$_{10}$)DEE solution of (Li-**1**)$_2$ · S (S = DEE), results in replacement of the solvating DEE molecule by one molecule of THF. In pure (D$_8$)THF, Li-**1** persists as an equilibrium between the dimer (Li-**1**)$_2$ · S (S = THF) and the monomer Li-**1** · 2 S (S = THF). The disolvated monomer is the major aggregate in THF.

Addition of BuLi to the dimer (Li-**1**)$_2$ in DEE leads to formation of a mixed complex between the chiral lithium amide and BuLi, *i.e.*, Li-**1**/BuLi [11] (*Scheme 3*). The equilibrium between homo dimeric lithium amide, tetrameric BuLi, and the mixed lithium amide/BuLi complex depends on the reagents involved as well as on the solvent. Detailed knowledge about the factors influencing this equilibrium is pivotal, since mixed complexes of this kind are efficient reagents for the enantioselective addition of alkyllithiums to aldehydes, providing selectivities up to 99% enantiomeric excess (ee) [12].

Scheme 3. *Mixed Complex Formation between Li-*$\mathbf{1}$ *and BuLi.* The dimer (Li-**1**)$_2$ is in equilibrium with a mixed dimer Li-**1**/BuLi when excess BuLi is present. The mixed dimer undergoes a regioselective *ortho*-lithiation upon standing at room temperature for 3–5 h. The dilithiated species thus formed dimerizes to the structure shown in the insert.



Interestingly, when a DEE solution of the mixed complex Li-**1**/BuLi is kept at room temperature for 3–5 h, one of the *ortho*-H-atoms on the methylbenzylamine moiety of the molecule is regiospecifically abstracted. Remarkably, this *ortho*-lithiation proceeds *without* addition of any specific Li-coordinating ligand, such as, for example, *N,N,N′,N′*-tetramethylethylenediamine (TMEDA). Based on multinuclear and multidimensional NMR experiments, including ^{6}Li,^{1}H heteronuclear *Overhauser* effect spectroscopy, we proposed that the resulting dilithiated product form a homo dimer, *i.e.*, (Li$_2$-**1**)$_2$ in the insert of *Scheme 3.*

The objective of the present study is to shed some light on this intriguing *ortho*-lithiation reaction with a combination of kinetic and computational methods.

Kinetic Study. – Our previous studies have established a fast exchange between homo complexed BuLi (in the form of (BuLi)$_4$), the dimer (Li-**1**)$_2$, and the mixed Li-**1**/BuLi complex. This exchange is fast also at low temperatures (– 90°). Thus, the *ortho*-lithiation reaction must consist of at least two consecutive reaction steps. The first step involves a pre-equilibrium between (Li-**1**)$_2$, BuLi, and the mixed complex Li-**1**/BuLi. This pre-equilibrium is then followed by the rate-determining *ortho*-lithiation reaction, suggested to proceed within the aggregate (*Scheme 4*). Subsequently, the *ortho*-

Scheme 4. *Schematic Representation of the* ortho-*Lithiation Reaction.* The reaction is proposed to proceed through a pre-equilibrium between the lithium amide and BuLi, followed by an intra-aggregate rate-limiting proton transfer.

$$2(\mathrm{Li}\text{-}\mathbf{1})_2 + (\mathrm{BuLi})_4 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 4\,\mathrm{Li}\text{-}\mathbf{1}/\mathrm{BuLi}$$

$$\mathrm{Li}\text{-}\mathbf{1}/\mathrm{BuLi} \xrightarrow{k_2} \mathrm{Li}_2\text{-}\mathbf{1} + \mathrm{C_4H_{10}}$$

lithiated lithium amide (Li_2-**1**) undergoes a rapid dimerization to yield the dimer (Li_2-**1**)$_2$ (*Scheme 3*), previously studied by NMR.

Knowing that the pre-equilibrium is much faster than the lithiation reaction, *i.e.*, $k_{-1} \gg k_2$, and by keeping [BuLi] $\gg$ [Li_2-**1**] we may formulate the pseudo-first-order rate law in *Eqn. 1.*

$$\frac{d[\mathrm{Li}_2\text{-}\mathbf{1}]}{dt} = k_{\mathrm{obs}}\left([\mathrm{Li}_2\text{-}\mathbf{1}]_\infty - [\mathrm{Li}_2 - \mathbf{1}]\right) \qquad (1)$$

Where k_{obs} is given by *Eqn. 2:*

$$k_{\mathrm{obs}} = \frac{k_2 K[\mathrm{BuLi}]}{(1 + K[\mathrm{BuLi}])} \qquad (2)$$

Kinetic data were obtained by monitoring the *ortho*-lithiation reaction of the amine ([Li-**1**] = 50 mM) with BuLi (1200 mM) in (D_{10})DEE at 20° directly in the NMR tube, as described in the *Exper. Part.* A straight line is obtained by plotting ln([Li_2**1**]$_\infty$ – [Li_2**1**]) *vs.* time (*Fig. 1*). Thus, apparently the reaction may be described as a pseudo-first-order process with $k_{\mathrm{obs}} = 5.6 \times 10^{-4}\ \mathrm{s}^{-1}$.

The pre-equilibrium constant for this reaction has previously been determined as 1.22M [12a]. Thus, the first-order rate constant for the rate-determining step k_2 may be derived from *Eqn. 2*, $k_2 = 9.4 \times 10^{-4}\ \mathrm{s}^{-1}$. This, in turn, corresponds to a free energy of activation of $\Delta G^{\ddagger}_{273\mathrm{K}} = 21$ kcal mol^{-1}.

The *ortho*-lithiation was also performed with different amounts of BuLi, while the concentration of lithium amide was kept constant at 50 mM. The pseudo-first-order rate constants k_{obs} thus obtained was plotted against [BuLi] (80, 700, and 1200 mM, *Fig. 2*). The plot shows only a weak dependence on k_{obs} *vs.* [BuLi], indicating that the reaction may follow saturation kinetics; otherwise, we would expect a linear dependence of k_{obs} *vs.* [BuLi] with the intercept close to zero, and not around 2.4 as observed. At even higher BuLi concentrations, we expect the observed rate constant to reach a maximum value for the situation, when all lithium amide is complexed with BuLi.

The kinetic data presented indicate that the stoichiometry of the TS is composed of only the mixed aggregate BuLi/(Li-**1**); this suggests an intra-aggregate mechanism for the *ortho*-lithiation. To gain further insight into the details of this mechanism, we turned to a computational approach.

Computational Study. – Several high-level computational studies have addressed the mechanism and origin of selectivity in the *ortho*-lithiation of heteroatom-containing aromatic rings [7]. Despite these efforts, a detailed understanding of the different factors, *e.g.*, precomplexation and inductive effects, and their relative importance for

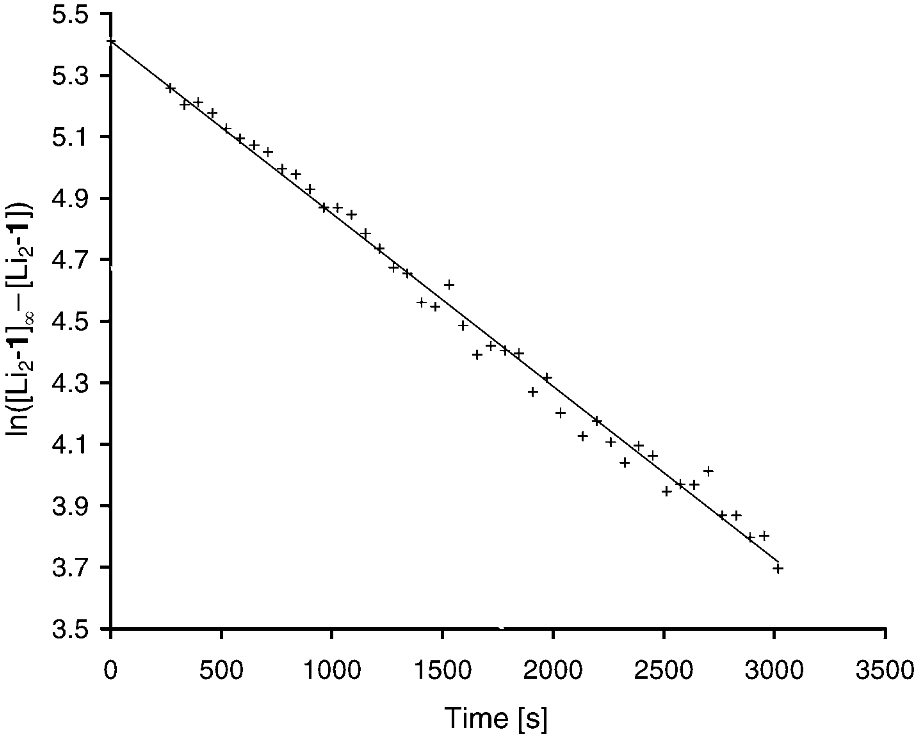


Fig. 1. *Plot of ln([Li$_2$-**1**]$_\infty$-[Li$_2$-**1**]) vs. time.* The straight line in this plot shows that the *ortho*-lithiation follows a pseudo-first-order process with $k_{obs} = 5.6 \times 10^{-4}$ s^{-1}.

reactivity and selectivity remains undisclosed. Thus, instead of adding to this debate with our quite special system, we chose to settle for a simpler theoretical model, *i.e.*, the semi-empirical PM3 method. This method is known to give reliable structural data for lithium-organyl complexes [9b]; however, the energies obtained with this method should be treated with care.

The result of our calculations is shown in *Fig. 3.* The initial complex between the lithium amide Li-**1** and EtLi (used as a model for BuLi) has a dimeric core where the two Li-atoms are coordinated to the amide N-atom and to the carbanionic C-atom. One of the Li-atoms is internally coordinated to the MeO group of the amide. In the initial state, the distance between the carbanionic C-atom and the *ortho*-H-atom of the top Ph ring (hypothetical reaction) is somewhat shorter than the distance to the H-atom being abstracted experimentally (bottom Ph ring). Two transition states (TS), corresponding to lithiation of the top and the bottom Ph rings, respectively, could be located^4). The

---

^{4}) Although the alkyllithium is the thermodynamically strongest base, another TS, involving initial proton transfer to the N-atom, was also investigated. Proton transfers to more-electronegative atoms, *e.g.*, N and O, are known to be kinetically preferred to those involving less-electronegative atoms, *i.e.*, C; thus a fast intermediate 'shuffling' of the abstracted proton *via* the N-atom could not be excluded from the kinetic data. However, this TS was found to be significantly higher in energy (> 20 kcal mol^{-1} above the observed TS); consequently, this possible pathway was excluded.

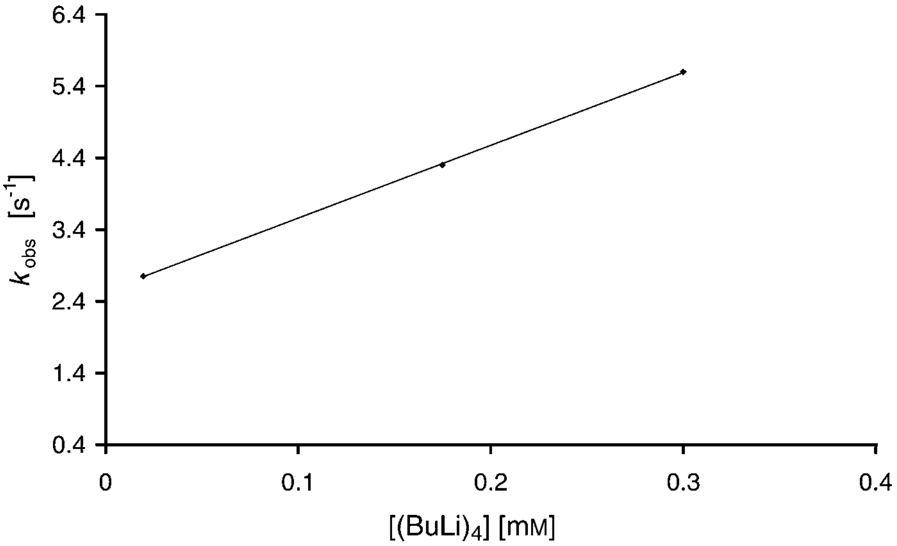


Fig. 2. *Plot of* k_{obs} *vs. [BuLi]*. The weak dependence of k_{obs} on [BuLi] suggests that the reaction follows saturation kinetics. ([Li-**1**] = 50 mM and [BuLi] = 80, 700, and 1200 mM).

energy for the TS leading to the experimentally observed product is somewhat lower than that for the hypothetical reaction. The H-atom is transferred to the same extent, somewhat more than halfway (C_α–H 1.46 Å and C_o–H 1.53 Å), in both transition states. The stabilization of the negative charge developing on the *ortho*-C-atoms are also similarly compensated for in the two TS as seen from the similar Li–C_o distances (2.21 and 2.19 Å, resp.). The two *ortho*-lithiated products obtained from the two routes are also shown in *Fig. 3*. Here, it can be seen that both Li-atoms stabilize the newly formed carbanion in the experimentally observed product, while only one Li-atom is coordinating to the carbanion in the product that would result from *ortho*-lithiation of the top Ph ring. These structures are of minor importance, since the dilithiated amide is known to undergo rapid dimerization.

Discussion. –The small energy differences found between the two transition states, and the similarities observed in their structures, do not account for the complete regioselectivity observed. An alternative explanation for the high selectivity must be invoked.

When solvation of the Li-atoms is included in the analysis, one initially expects two DEE molecules to coordinate to the Li-atom lacking internal coordination (Li(2)), and one DEE molecule to coordinate to the internally (MeO) coordinated lithium (Li(1)). A simple inspection of the models suggest that the gain in enthalphy by coordination of a DEE molecule to Li(1), will probably be low due to congestion; when also taking the negative contribution from the entropy into account, it is highly likely that this process will be unfavorable. This notion is supported by our previous NMR spectroscopic studies, which suggested the presence of one tricoordinated- and one tetracoordinated

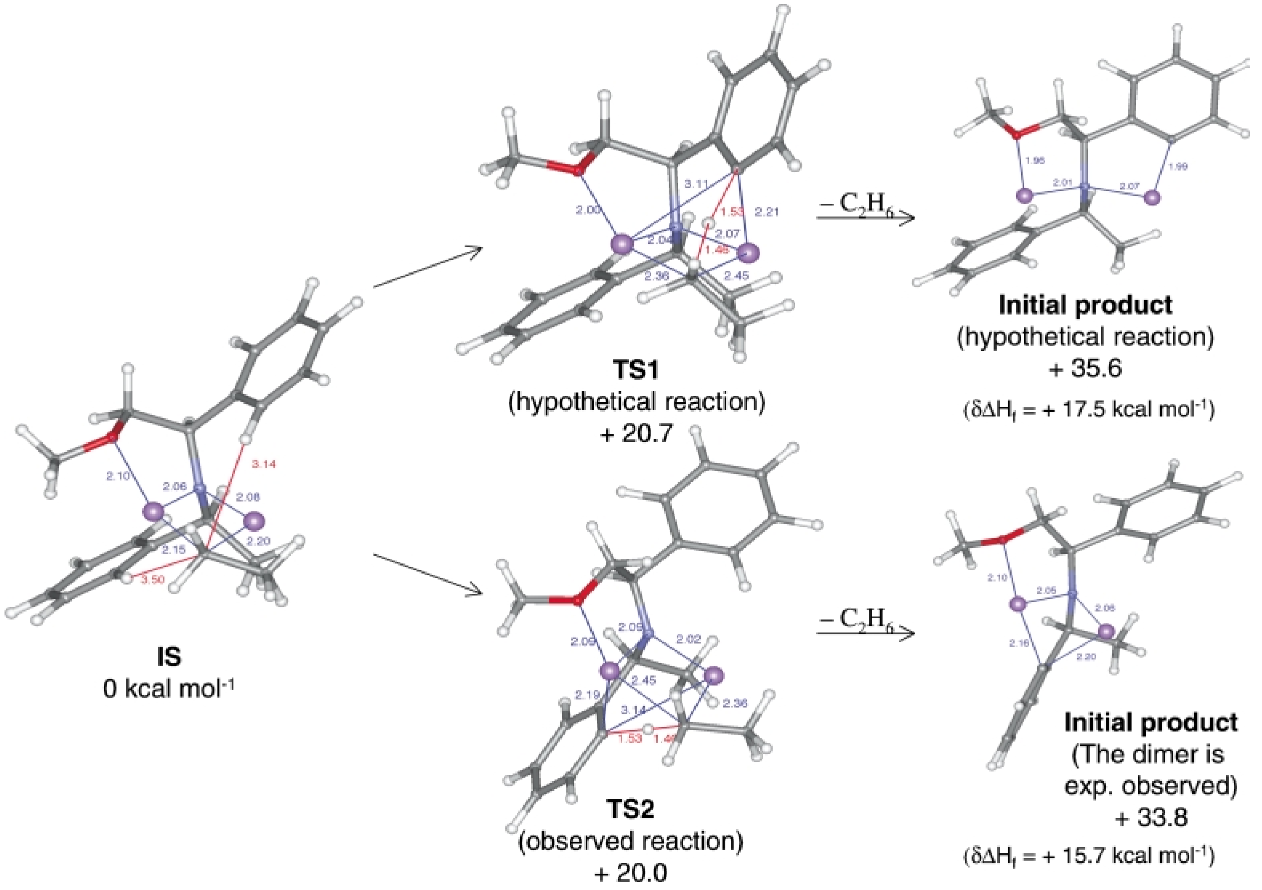


Fig. 3. *PM3-Optimized Geometries.* The structure of the initial mixed complex is shown to the left, the TS leading to the experimentally observed product is shown in the center (*bottom*), while the TS for the hypothetical reaction that would lead to the alternative regioisomer is shown in the center (*top*). The optimized geometries of the final states of the two paths are also shown; *however*, these complexes are known to rapidly form heterodimers. Selected distances [Å] are shown in blue, and key distances in the TS are shown in red. Also shown are the relative energies [kcal mol^{-1}] for the different species, and the calculated reaction enthalphies.

Li-atom in the Li-**1**/BuLi complex in DEE [12a][5]). Thus, Li(1) is expected to be tricoordinated in the mixed complex.

Consequently, the TS leading to observed product is probably reasonably well described in this calculation. On the other hand, the energy for TS involving lithiation of the top Ph ring is expected to increase dramatically, if solvating ligands were included in the calculation – since the two DEE molecules at this Li-atom would make Li(2) less capable of stabilizing the developing negative charge. This explanation is supported by the good (almost too good) agreement between the experimentally observed activation energy ($\Delta G^{\ddagger}_{273\mathrm{K}} = 21$ kcal mol^{-1}) and the calculated activation barrier (20 kcal mol^{-1}). The important role of the solvent in this reaction is further evidenced by the lack of observable *ortho*-lithiation in THF, where both Li-atoms are known to be tetracoordinated.

Conclusions. – Kinetic investigations of the *ortho*-lithiation reaction in the mixed Li-**1**/BuLi complex in DEE solution showed that the reaction proceeds within the mixed complex. The rate constant for the lithiation step at 20° was found to be $k_2 = 9.4 \times 10^{-4}$ s^{-1}, corresponding to $\Delta G_{273K}{}^{\ddagger} = 21$ kcal mol^{-1}. With knowledge about the transition-state composition, we investigated the reaction computationally with the semi-empirical PM3 method. Calculations in the absence of solvent molecules did not give a completely satisfactory explanation for the regioselectivity observed. However, when the solvation around the Li-atoms is included in the analysis, a more adequate explanation emerges. Thus, in conclusion, it seems likely that the observed reactivity is a direct consequence of the complex formation (no mixed complex formation – no observable *ortho*-lithiation); further, the presence of one coordinatively unsaturated Li-atom in DEE solution appears to be a prerequisite for the observed reactivity and selectivity.

Financial support from *Vetenskapsrådet – The Swedish Research Council*, is gratefully acknowledged.

Experimental Part

General. All glassware were dried overnight in an oven at 120° (syringes were dried at 50° in a vacuum oven) before transfer into a glove box (*Mecaplex GB 80* equipped with a gas-purification system that removes O_2 and moisture) containing a N_2 atmosphere. Typical moisture content was less than 2 ppm. All manipulations of the Li compounds were carried out in the glove box with gas-tight syringes. Ethereal solvents were distilled and stored over *Deporex* (*Fluka*) prior to use. All NMR spectra were recorded with a *Varian Unity 400* spectrometer equipped with an inverse detection probe. Measuring frequency was 400 MHz (^{1}H). The ^{1}H-NMR spectra were referenced to the solvent (D_{10})DEE signal at δ 1.06 (^{1}H–Me). Probe temp. were measured after more than 30 min of temp. equilibrium with the standard MeOH thermometer supplied by *Varian* instruments.

Computational Methods. Geometry and transition-state optimizations were done on a *Silicon Graphics Indy* workstation by the semi-empirical PM3 method as implemented in the Spartan 5.0 program package [13]. Several initial geometries for the optimizations were tried in order to find the global minimum. The vibrational frequencies were also calculated to verify that all optimized structures were either minima (no imaginary frequency) or transition states (one imaginary frequency) on the potential energy-surface.

---

[5]) Addition of THF to a DEE solution of Li-**1**/BuLi initially leads to an increased solvation of one of the Li-atoms (before all DEE molecules were replaced by THF). At that point, it was not clear which Li-atom was tri- or tetracoordinated.

(S)-N-[(R)-2-Methoxy-1-phenylethyl]-α-methylbenzylamine (**1**) *and the [^{6}Li]-Salt* (Li-**1**). The preparation and characterization of this amine, and the *in situ* generation of the corresponding [^{6}Li]-containing lithium amide have been reported in [11].

Kinetic Studies of the ortho-*Lithiation.* Amine **1** (10 mg, *ca.* 0.035 mmol) was transferred into a dry 5-mm NMR tube. The NMR tube was fitted with a *Wilmad/Omnifit Teflon* valve assembly *OFV* with *Teflon*/silicon septum. The solvent (D$_{10}$)DEE (750 µl) was added *via* syringe. To the resulting 52 mM soln. of **1** at $-20°$ was added 10M [^{6}Li]BuLi (*ca.* 30 µl, 0.37 mmol) with a syringe. The mixture containing Li-**1** (96% in 6Li atom) was then put into the temp.-equilibrated NMR probe. The progress of the reaction was followed by obtaining ^{1}H-NMR spectra every 4 min. The disappearing ^{1}H-NMR signals for the α-H-atom of BuLi and the appearing signals from the MeO group of the *ortho*-lithiated amide were integrated and used in the kinetic analysis. Typically, rate measurements were obtained by following the reactions up to *ca.* 25% completion.

REFERENCES

[1] D. Seebach, R. Hässig, J. Gabriel, *Helv. Chim. Acta* **1983**, *66*, 308.

[2] a) G. W. Klumpp, *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 1; b) D. Seebach, *Angew. Chem., Int. Ed.* **1988**, *27*, 1624; c) K. Gregory, P. v. R. Schleyer, R. Snaith, *Adv. Inorg. Chem.* **1991**, *37*, 47; d) P. G. Williard, in 'Comprehensive Organic Synthesis', Vol. 1, Eds. B. M. Trost, I. Fleming, Pergamon Press, Oxford, 1991, p. 1; e) D. B. Collum, *Acc. Chem. Res.* **1993**, *26*, 227; f) C. Lambert, P. v. R. Schleyer, *Angew. Chem., Int. Ed.* **1994**, *33*, 1129; g) A. Streitwieser, S. M. Bachrach, A. Dorigo, P. v. R. Schleyer, in 'Lithium Chemistry A Theoretical and Experimental Overview', Eds. A.-M. Sapse, P. v. R. Schleyer, John Wiley & Sons, New York, 1995, p. 1; h) B. L. Lucht, D. B. Collum, *Acc. Chem. Res.* **1999**, *32*, 1035; i) A. R. Katritzky, M. Piffl, H. Y. Lang, E. Anders, *Chem. Rev.* **1999**, *99*, 665; j) G. Boche, J. C. W. Lohrenz, *Chem. Rev.* **2001**, *101*, 697; k) C. Gaul, P. I. Arvidsson, W. Bauer, R. E. Gawley, D. Seebach, *Chem.–Eur. J.* **2001**, *7*, 4117.

[3] a) H. W. Gschwend, H. R. Rodriguez, *Org. React.* **1979**, *26*, 1; b) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; c) F. Mongin, R. Maggi, M. Schlosser, *Chimia* **1996**, *50*, 650; d) P. Beak, A. Basu, D. J. Gallagher, Y. S. Park, S. Thayumanavan, *Acc. Chem. Res.* **1996**, *29*, 552; e) C. S. Salteris, I. D. Kostas, M. Micha-Screttas, G. A. Heropoulos, C. A. Screttas, A. Terzis, *J. Org. Chem.* **1999**, *64*, 5589.

[4] a) E. Marzi, A. Bigi, M. Schlosser, *Eur. J. Org. Chem.* **2001**, *7*, 1371; b) M. Kauch, D. Hoppe, *Can. J. Chem.* **2001**, *79*, 1736; c) P. Garibay, P. Vedso, M. Begtrup, T. Hoeg-Jensen, *J. Comb. Chem.* **2001**, *3*, 332; d) G. Amiet, H. M. Hugel, F. Nurlawis, *Synlett* **2002**, 495; e) G. Karig, N. Thasana, T. Gallagher, *Synlett* **2002**, 808; f) P. Gros, S. Choppin, J. Mathieu, Y. Fort, *J. Org. Chem.* **2002**, *67*, 234.

[5] a) H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109; b) G. Wittig, G. Fuhrmann, *Chem. Ber.* **1940**, *73*, 1197; c) J. D. Roberts, D. Y. Curtin, *J. Am. Chem. Soc.* **1946**, *68*, 1658.

[6] a) C. G. Screttas, J. F. Eastham, *J. Am. Chem. Soc.* **1965**, *87*, 3276; b) C. D. Broaddus, *J. Org. Chem.* **1970**, *35*, 10; c) C. G. W. Bauer, P. v. R. Schleyer, *J. Am. Chem. Soc.* **1989**, *111*, 7191; d) J. M. Saá, G. Martorell, A. Frontera, *J. Org. Chem.* **1996**, *61*, 5194; e) M. Stratakis, *J. Org. Chem.* **1997**, *62*, 3024; f) R. A. Rennels, A. J. Maliakal, D. B. Collum, *J. Am. Chem. Soc.* **1998**, *120*, 421; g) M. Schlosser, F. Mongin, J. Porwisiak, W. Dmowski, H. H. Büker, N. M. M. Nibbering, *Chem.–Eur. J.* **1998**, *4*, 1281; h) R. Maggi, M. Schlosser, *Tetrahedron Lett.* **1999**, *40*, 8797; i) D. W. Slocum, P. Dietzel, *Tetrahedron Lett.* **1999**, *40*, 1823; j) D. R. Anderson, N. C. Faibish, P. Beak, *J. Am. Chem. Soc.* **1999**, *121*, 7553.

[7] a) N. J. R. van Eikema Hommes, P. v. R. Schleyer, *Tetrahedron* **1994**, *50*, 5903; b) S. T. Chadwick, R. A. Rennels, J. L. Rutherford, D. B. Collum, *J. Am. Chem. Soc.* **2000**, *122*, 8640; c) J. M. Saá, *Helv. Chim. Acta* **2002**, *85*, 814.

[8] P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356.

[9] a) G. Hilmersson, P. I. Arvidsson, Ö. Davidsson, M. Håkansson, *Organometallics* **1997**, *15*, 3352; b) G. Hilmersson, P. I. Arvidsson, Ö. Davidsson, M. Håkansson, *J. Am. Chem. Soc.* **1998**, *120*, 8143.

[10] G. Hilmersson, P. Ahlberg, Ö. Davidsson, *J. Am. Chem. Soc.* **1996**, *118*, 3539.

[11] a) G. Hilmersson, Ö. Davidsson, *J. Org. Chem.* **1995**, *60*, 7660; b) G. Hilmersson, Ö. Davidsson, *J. Organomet. Chem.* **1995**, *489*, 175; c) G. Hilmersson, Ö. Davidsson, *Organometallics* **1995**, *14*, 912.

[12] a) P. I. Arvidsson, G. Hilmersson, Ö. Davidsson, *Chem.–Eur. J.* **1999**, *5*, 2348; b) P. I. Arvidsson, Ö. Davidsson, G. Hilmersson, *Tetrahedron: Asymmetry* **1999**, *10*, 527; and refs. cit. therein.

[13] SPARTAN, Version 5.0.1, *Wavefunction, Inc.*, Irvine, CA, USA, 1995.

Received June 7, 2002