Organometallics **1997,** *16,* 6021−6023

Origin of Solvent Acceleration in Organolithium Metal−Halogen Exchange Reactions

Brigitte Jedlicka and Robert H. Crabtree*

Yale Chemistry Department, 225 Prospect Street, New Haven, Connecticut 06520-8107

Per E. M. Siegbahn*

Department of Physics, University of Stockholm, Box 6730, S-113 85 Stockholm, Sweden

Received July 7, 1997[⊗]

Summary: Quantum chemical studies (B3LYP) of metal−halogen exchange in the model system $LiCH{=}CH_2/MeI$ are consistent with a T-shaped hypervalent iodine species of the type I(vinyl)(Me)(Li) being the transition state. In support of prior proposals by Collum and others that solvent acceleration of organolithium reactions does not result primarily from solvent-induced changes in the aggregation state of the lithium reagent, we find the solvent substantially accelerates the reaction even for a monomeric nonaggregated transition state. Introduction of a model solvent molecule suggests that solvent acceleration is the result of transition state stabilization by tighter binding of the solvent to lithium in the transition state as well as a destabilization of the reactant adduct, (vinylI)·(LiMe), relative to the separated reagents.

Introduction

Solvent acceleration of organolithium reactions by THF or TMEDA is very common,[1] but different possibilities have been discussed to account for the effect. It was once commonly ascribed to the formation of lower organolithium aggregates, but as noted in a recent review by Collum,[2a] this idea is not confirmed by careful scrutiny.[2] Here, we study the problem by quantum chemical methods[3] using the empirically parameterized DFT theory, B3LYP,[3b] implemented via the GAUSSIAN94 program,[3c] as previously used for organometallic problems[3d] with good reliability.[3e] We show that tighter binding of a donor solvent to the transition state is indeed sufficient to substantially accelerate a model reaction, metal−halogen exchange, without change in aggregation.

The metal−halogen exchange reaction[4] to synthesize organolithium compounds (eq 1), discovered by Wittig and by Gilman,[5] is of prime importance in organic synthesis. It is rightly considered[1] one of the most

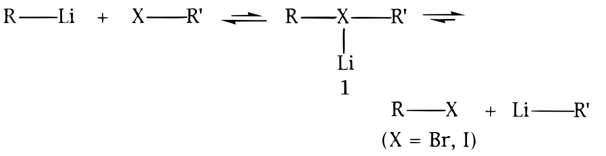
$$\mathrm{R{-}Li + R'{-}Br \rightarrow R'{-}Li + R{-}Br} \qquad (1)$$

remarkable reactions in organic chemistry because it often proceeds in seconds even at −90 °C and the formation of the thermodynamically strongly preferred coupling products of eq 2 is completely avoided. The

$$\mathrm{R{-}Li + R'{-}Br \rightarrow R'{-}R + LiBr} \qquad (2)$$

mechanism was the subject of prolonged debate. CIDNP studies[6] have shown evidence for radical intermediates, but if the whole reaction passed through such intermediates, it is difficult to see how the cross coupling products of eq 2 could be completely avoided, as observed. Early observations by Wakefield[7] suggested nucleophilic attack on halogen might be involved, but radical anion intermediates were later proposed by the same author.[1] Iodine ate complexes were proposed by Wittig et al.,[8] are consistent with kinetic data,[9] and in some cases have been observed in the reaction mixtures.[10] Finally, much important theoretical work has been carried out on other aspects of organolithium chemistry,[11] and detailed studies of solvation effects in organolithium compounds have been published.[2b]

This paper provides quantum chemical support for significant solvent acceleration of organolithium reactions in one model reaction, metal−halogen exchange. The mechanism of the exchange, confirmed by the present study, involves a T-shaped hypervalent iodine species, as illustrated in eq 3.



$$\mathrm{R{-}Li + X{-}R' \rightleftharpoons \underset{\underset{\textstyle 1}{Li}}{R{-}X{-}R'} \rightleftharpoons R{-}X + Li{-}R'} \qquad (3)$$

(X = Br, I)

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1997.

[1] Wakefield, B. J. In *Lithium*; Bach, R. O., Ed.; Wiley: New York, 1985.

[2] (a) Collum, D. B. *Acc. Chem. Res.* **1992**, *25*, 448. (b) Streitwieser, A.; Reuben, D. M. E. *J. Am. Chem. Soc.* **1971**, *93*, 1794. Chang, C. J.; Hogan-Esch, T. E. *Tetrahedron Lett.* **1976**, 323. Hogan-Esch, T. E. *Adv. Phys. Org. Chem.* **1977**, *15*, 153. Mc Ewen, I.; Ronnqvist, R.; Ahlberg, P. *J. Am. Chem. Soc.* **1993**, *115*, 3989.

[3] (a) The methods used have been described in detail in the literature.[3b] (b) Becke, A. D. *Phys. Rev.* **1988**, *A38*, 3098. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. R.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzales C.; Pople, J. A. *GAUSSIAN 94, Revision A.1*; Gaussian, Inc.: Pittsburgh, PA, 1995. (d) For example: Siegbahn, P. E. M.; Crabtree, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 4442. (e) The reliability of the method may be somewhat lower for transition states, however.

[4] Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300.

[5] Wittig, G.; Pockels, U. *Chem. Ber.* **1938**, *71*, 1903. Gilman, H.; Jacoby, A. L. *J. Org. Chem.* **1938**, *3*, 108.

[6] Ward, H. R.; Lawler, R. G. *J. Am. Chem. Soc.* **1967**, *89*, 5518. Ward, H. R.; Lawler, R. G.; Cooper, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 746. Lepley, A. R.; Landau, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 748.

[7] Wakefield, B. J. *J. Organomet. Chem.* **1975**, *99*, 191.

[8] Wittig, G.; Schöllkopf, U. *Tetrahedron* **1958**, *3*, 91.

[9] Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101.

[10] (a) Farnham, W. B.; Calabrese, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 2449. (b) Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1989**, *111*, 3444. Reich, H. J. *Phosphorus, Sulfur and Silicon* **1992**, 6783.

[11] Streitweiser, A.; Bachrach, S. M.; Dorigo, A.; Schleyer, P. v. R. In *Lithium Chemistry—A Theoretical and Experimental Overview*; Sapse, A.-M., Schleyer, P. v. R., Eds.; Wiley: New York, 1995.

S0276-7333(97)00572-4 CCC: $14.00

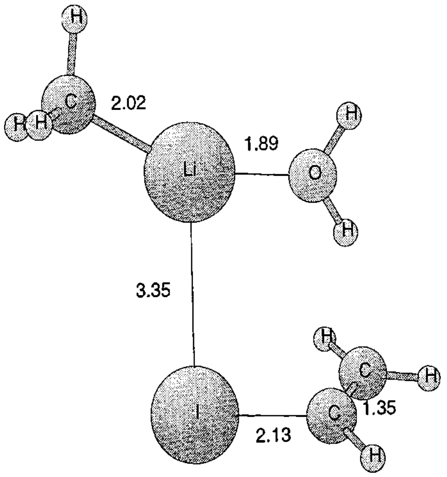
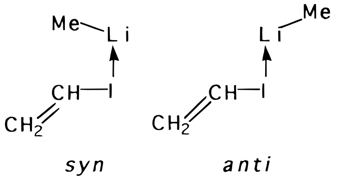


Figure 1. The *anti* monosolvated adduct between $CH_2{=}CHI$ and MeLi which is considered to be the reactive conformer.

Results and Discussion

To investigate this pathway, we have performed B3LYP theoretical studies (see Computational Details section). A model system was chosen involving monomeric LiMe and $CH_2{=}CHI$. LiMe is in reality aggregated in solution, but we wished to simplify the system by taking the monomer in this initial work in order to test the idea[2a] that solvent acceleration might occur independent of the state of aggregation. Another reason for choosing the monomeric model is the finding by Streitweiser and co-workers[12] that the monomer is indeed the true reactive species in a number of reactions of lithium enolates where the oligomer is the main form in solution. Because we needed to locate a transition state, a very difficult procedure, we needed to simplify the quantum model system as much as possible, hence our use of a single H_2O rather than one or more Me_2O ligands.

The results show that unsolvated LiMe reacts with $CH_2{=}CHI$ to give a reactant adduct of the two species, $CH_2{=}CHLi(IMe)$, with the vinyl and methyl groups in a *syn* conformation and having a calculated exothermicity of 6.4 kcal/mol relative to the reagents. The *anti* adduct, only 0.3 kcal/mol less stable, is considered on least-motion grounds to be the one that leads on to reaction. A transition state of type **1** with one imaginary frequency was successfully located at an energy of +16.5 kcal/mol relative to the separated reagents and +22.9 kcal/mol relative to the *syn* reactant adduct. The geometry of the *anti* adduct and transition states closely resemble those shown in Figure 1 and 2, which are for the monosolvated species (see below). The energy relationships involved, measured relative to the separated reagents, are shown in Figure 3.



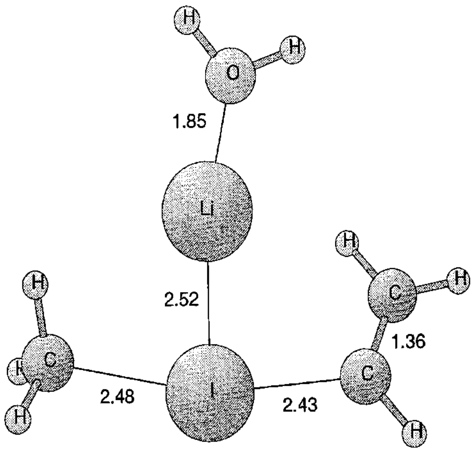


Figure 2. The monosolvated transition state with one model H_2O ligand found for the metal–halogen exchange reaction between $CH_2{=}CHI$ and MeLi. The unsolvated transition state has an almost indistinguishable structure except that the Li–I distance changes to 2.50 Å.

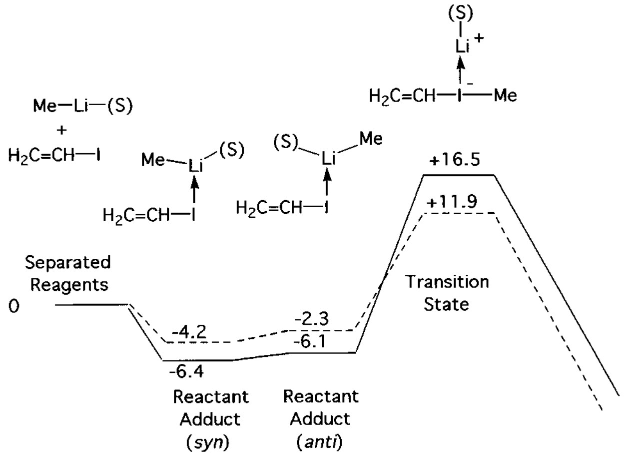


Figure 3. The energy profile of the reaction, showing the origin of the change in barrier heights. The unsolvated case is shown by a full line and the solvated by a dotted line. Energies are in kcal/mol relative to the separated reagents, LiMe + CH_2CHI for the unsolvated case or to $H_2O{\cdot}LiMe$ + CH_2CHI for the monosolvated case (S = solvent or vacancy).

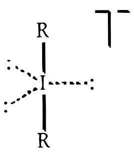
Nucleophilic attack on halide as the key step is consistent with the reaction going well for iodides and to some extent for bromides but poorly for chlorides, where hypervalency is much less common. The proposed T-shaped transition state **1** keeps R and R′ well apart, allowing the system to avoid the formation of cross coupling products, RR′. This species (**1**) can be thought of as an ion pair between a linear $[XR_2]^-$ anion and Li^+. The T-shaped structure of **1** can, therefore, be considered as resulting from the preference[13] for a linear geometry in IR_2^-, as also seen in such well-known hypervalent ions as I_3^- (or in general, $[XY_2]^-$ where X = Br or I, Y = Cl; X = Y = I). Indeed, stable perfluoroalkyl versions of this species (R = $(CF_3)_3C$, C_6F_5) were prepared by Farnham and Calabrese,[10a] and solvent-separated $Li[IPh_2]$ was directly observed by Reich[10b] by ^{13}C NMR in samples formed from PhLi and PhI in the presence of HMPA. As a hypervalent species, the ion is expected to have three lone pairs in the

---

[12] Abbotto, A.; Streitweiser, A. *J. Am. Chem. Soc.* **1995**, *117*, 6358.

[13] Shamir, J. In *Encyclopedia of Inorganic Chemistry*; King, R. B., Ed.; Wiley: New York, 1994; p 646.

equatorial plane (**2**), to one of which the lithium cation would naturally be expected to coordinate, hence producing an overall T-shape for **1**.



2

On including an ether solvent in the reaction, modeled here by a single H_2O ligand on lithium, we find new *syn* and *anti* (Figure 1) reactant adducts, exothermic relative to the reactants by 4.2 and 2.3 kcal/mol, respectively. The difference in the dipole moments between MeLi (5.6 D) and $MeLi(OH_2)$ (8.5 D) appears to be the major factor responsible for the larger energy difference between the *syn* and *anti* adducts in the solvated case versus the nonsolvated one, a result of dipole−dipole interactions with vinyl iodide. A new transition state (Figure 2) was found with an energy of +11.9 kcal/mol relative to the separated reagents and +16.1 kcal/mol relative to the *syn* reactant adduct. Since the dipole moment of the reactant complex is very similar to the one for the transition state, 9.56 D compared to 9.58 D, additional long-range polarization effects are not expected to have a differential effect on the activation barrier. The calculated barrier height for the solvated case (16.1 kcal/mol) is not very different from those found ($E_a = ca.$ 12 kcal/mol) experimentally[14] for related reactions, especially considering that polysolvation is likely in the real experimental system and this is expected to lead to an additional stabilization, resulting in a further reduction in the activation energy.[15] We cannot rigorously exclude the possibility that the real solvent, thf, might not be so tightly bound in a real transition state with more bulky R and R′ ligands, but this is unlikely since the iodine is only three coordinate and so not excessively crowded.

These results suggest that a ca. 6.8 kcal/mol decrease in the barrier height is possible from monosolvation in the absence of any change in the aggregation state of the organolithium reagent—a substantial value and well able to account for most of the observed accelerating effect of THF. Tighter binding of the solvent in the transition state is evident from the shorter Li−O distance in the transition state (Li−O 1.85 Å) versus the reactant adduct (1.89 Å). The stabilization of the transition state is most easily interpreted in terms of stronger solvation as a result of the greater positive charge expected for lithium in a relatively ionic $Li^+[IR_2]^-$ transition state structure. The energy profile of the reaction is summarized in Figure 3, where it is clear that the effect of solvation is not just to stabilize the transition state but to destabilize the reactant adduct between the solvated organolithium and the halide, relative to the separated reagents.

We confirm the generally accepted[1,8,10] mechanism involving a hypervalent iodine ate intermediate, as shown in eq 3 and Figure 2. The proposal of Collum[2] that solvent acceleration of the reaction can occur by solvent stabilization of the transition state independent of the state of aggregation of the organolithium reagent is also confirmed. This work also provides a detailed mechanism for the solvent effect: solvent stabilization of the transition state and destabilization of the reagent adduct relative to the separated reagents.

Computational Details

We used an empirically parameterized DFT theory, B3LYP,[3b] as implemented via the GAUSSIAN94 program,[3c] which has previously been successfully applied to organometallic problems.[3d] In the B3LYP calculations, large basis sets were used for the energies. For hydrogen, carbon, and oxygen, the 6-311+G(2d,2p) basis was used, which is a triple ζ basis containing two polarization functions and an additional set of diffuse functions on all atoms except hydrogen. For lithium the d95v(1d) basis was used, and iodine was treated with an effective core potential due to Hay and Wadt[16] to which two sets of diffuse p-functions and three sets of d-functions were added. All degrees of freedom were optimized, and Hessians were calculated at the B3LYP level using standard DZ basis sets (LANL2DZ). The transition states were found to have one imaginary frequency, and the equilibrium structures were found to have no imaginary frequencies.

Acknowledgment. R.H.C. thanks the DOE for funding. B.J. thanks the Österreichen Fonds zur Förderung der Wissenschaftlichen Forschung for support.

Supporting Information Available: Tables of the coordinates and energies for the structures studied are provided (1 page). Ordering information is given on any current masthead page.

OM9705721

---

[14] Rogers, H. R.; Houk, J. *J. Am. Chem. Soc.* **1982**, *104*, 522.

[15] The solvent polarity (thf, $\epsilon = 7.5$) is expected to favor the *anti* over the *syn* adduct as a result of dielectric effects. The transition state should be stabilized to a similar extent, and so it might be more realistic to count the barriers from the *anti* form in the monosolvated case, in which case, we would have unsolvated, 22.9 kcal/mol; monosolvated, 14.8 kcal/mol; barrier difference on monosolvation, 8.1 kcal/mol.

[16] Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.