

## Theoretical Studies on the Reaction of Solvated Methylithium Open Dimer with Aldehyde

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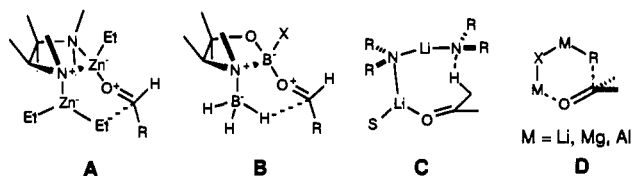
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The importance of open dimers in organometallic reactions is rapidly gaining recognition among chemists.<sup>2</sup> The unique reactivity of the open dimers **A**<sup>3</sup> and **B**<sup>4</sup> is considered to be the key for the spectacular success of catalytic asymmetric additions of organozinc<sup>5</sup> and boron<sup>6</sup> reagents. A very recent crystal



structural determination of an open dimer of lithium amide<sup>7</sup> led to a proposal that the coordinatively unsaturated open dimer **C** is a crucial intermediate in the carbonyl deprotonation.<sup>8</sup> The kinetic importance of a dimeric species in the carbonyl addition of BuLi has been experimentally demonstrated,<sup>9</sup> and there has been made frequent allusion to a six-centered transition state such as **D**,<sup>10</sup> in which an open dimer can be readily recognized. These experimental implications notwithstanding, there has been little theoretical information on the structure and energy of open dimers.<sup>11</sup> We report here the ab initio theoretical studies on the reaction of a solvated MeLi open dimer with aldehydes, which provides several important chemical implications on the reactivities of open dimeric species.

The reaction of (MeLi)<sub>2</sub> with formaldehyde and acetaldehyde with and without solvation (one water molecule) was studied with optimization at the HF/6-31+G\* level,<sup>12</sup> and structures were characterized by frequency analysis. Electron correlation at the MP2 level was found not to affect grossly the structures of intermediates. The overall reaction pathway and the structural

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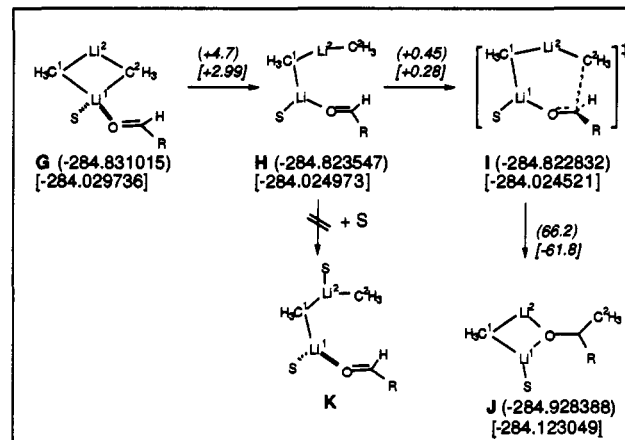
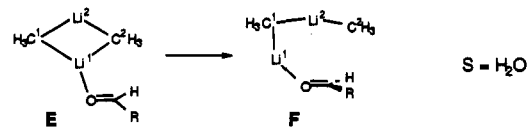
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(11) Cf.: Kaufmann, E.; Schleyer, P. v. R.; Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 5560. This pioneering study on the unsolvated (MeLi)<sub>2</sub> failed to recognize an open dimer as an intermediate. In addition, the reported C<sub>s</sub> TSs possess several imaginary frequencies and therefore are not true TSs.

## Scheme I. Intermediates in the Reaction of (MeLi)<sub>2</sub> with an Aldehyde<sup>a</sup>



<sup>a</sup> The energies (hartree; kcal/mol in italic) are for R = H, S = H<sub>2</sub>O. The MP2/6-31+G\*//HF/6-31+G\* energies are in parentheses, and the HF/6-31+G\*//HF/6-31+G\* in brackets.

features of intermediates were qualitatively the same for the solvated and unsolvated species, and, hence, those for the solvated dimers are described below.

The sequence of structures in the box in Scheme I (details shown in Figure 1) represents important events in the carbonyl addition. This scheme shares its salient feature with the mechanism recently proposed for the deprotonation of a carbonyl group with a dimeric lithium amide (**C**)<sup>7</sup> and is similar to those proposed for the reactions of **A** and **B**. Four-centered structures of solvated RLi dimers have recently been determined for BuLi.<sup>13</sup>

The solvated dimer **G** is a direct precursor to the open dimer **H**. Li<sup>1</sup> is coordinated to the oxygen lone pair of formaldehyde in the carbonyl plane (Figure 1). For **G** to expose a methyl group for addition to the carbonyl group, the C<sup>2</sup>-Li<sup>1</sup> bond must be cleaved. The cleavage (**G** to **H**) takes place with a small energy loss of 4.7 kcal/mol, accompanying rotation in the C<sup>1</sup>-Li<sup>1</sup> axis.<sup>14</sup> As is commonly seen in the crystal structures of ligand-free ate complexes,<sup>15</sup> the **C**<sub>2</sub> open dimer **H** is characterized by its nearly linear arrangement of C<sup>1</sup>-Li<sup>2</sup>-C<sup>2</sup>, by which electrostatic interaction is minimized.<sup>16</sup> The structure **H** (in particular, the coordination environment of lithium atoms) shows striking resemblance to the crystal structure of a lithium amide open dimer.<sup>7</sup>

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(14) Without solvation, such cleavage (**E** to **F**) takes place with significant energy loss (8.9 kcal/mol, MP2/6-31+G\*//HF/3-21G). This difference is likely due to solvative stabilization of the developing positive charge on Li<sup>1</sup> upon conversion of **E** to **F** (natural orbital population of +0.783 in **E**s vs +0.843 in **F**; HF/3-21G).

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(16) Further solvation of the open dimer **H** on Li<sup>2</sup> (examined with S = Me<sub>2</sub>O, HF/3-21G) closes back the ring instead of giving **K**, probably because solvation bends the C<sup>1</sup>-Li-C<sup>2</sup> bond as well as polarizes the Li<sup>2</sup>-C<sup>2</sup> bond. This suggests in turn, that desolvation of Li<sup>2</sup> is a necessary step for the open dimer formation. Parenthetically, the use of H<sub>2</sub>O in this calculation resulted in the formation of CH<sub>4</sub> due to deprotonation of H<sub>2</sub>O.

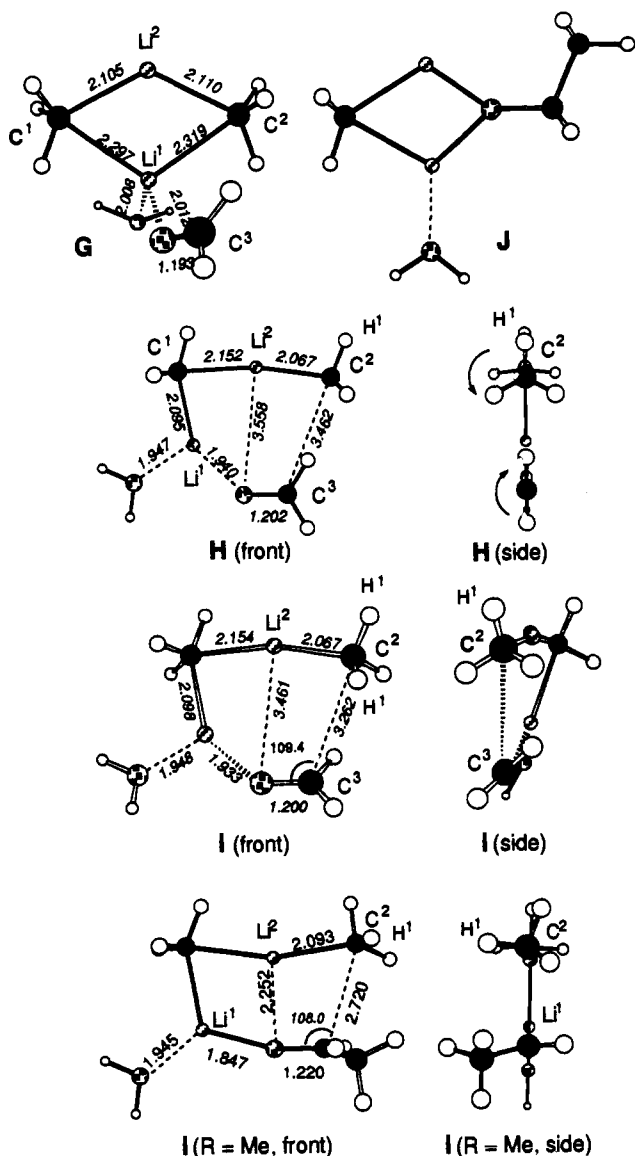


Figure 1. HF/6-31+G\*-optimized structures of G, H, I, and J. Bond lengths are in Å, and angles are in degrees.

The open dimer H is a highly reactive species, making the potential surface around H and TS I quite flat. Thus, rotation of the formaldehyde moiety in the C–O axis (arrows for H) transforms H to the six-centered TS I (Scheme I, Figure 1) with only 0.45 kcal/mol activation energy. Whereas the carbonyl rotation disrupts the favorable Li<sup>2</sup>-lone pair interaction in H, it causes, in turn, energy gain due to the developing C<sup>2</sup>–π\* interactions.<sup>17</sup> The open dimer H for acetaldehyde (R = Me, not shown) is virtually identical with the one for formaldehyde, but the TS (I, R + Me) is more advanced and ladderlike.<sup>3b,18</sup> The

oxygen lone pair in I (R = Me) is losing directionality and has started to interact with Li<sup>1</sup> and Li<sup>2</sup>. Conversion from I to the product J takes place exothermically (66.2 kcal/mol).

These calculations provided several general implications. (1) An open dimer complex such as H must be a very reactive species, and, once formed in solution,<sup>3,7,8</sup> it will readily engage in the intramolecular C–C bond formation. (2) The two lithium atoms in the dimer are nonequivalent and play different roles in the TS. Li<sup>1</sup> activates the carbonyl group, and Li<sup>2</sup> acts as an anchor of the methyl nucleophile. Realization of such a difference should be of great practical value in the analysis and design of new synthetic reactions, in particular, those employing bimetallic reagents.<sup>19</sup> (3) The exact geometrical shape for the TS I may change, depending on the carbonyl substrate and likely also on the organometallic reagent.

(4) It is notable from an organic view point that (i) the TSs I (R = H, Me) are chiral despite the absence of chirality in the starting materials and (ii) the nucleophilic C<sup>2</sup> atom does not travel through the stereotypical C<sub>S</sub> Bürgi–Dunitz trajectory<sup>20</sup> in the plane perpendicular to the plane of the carbonyl group.<sup>21</sup> These are the intrinsic consequence of the fact that the oxygen lone pair is perpendicular to the π\* orbital. With these results, two inferences may be made. First, the site of metal coordination to the carbonyl group is important in the diastereoselective carbonyl additions, since it must influence the trajectory of the nucleophile.<sup>22</sup> Second, the “face selection” in the carbonyl addition may be viewed theoretically as the result of the intramolecular rotation of the carbonyl group and the twisting of the entire TS. The seemingly related case of olefinic face differentiation operates in a different manner,<sup>23</sup> proceeding via a bimolecular association/dissociation process, while this difference has not so far been fully appreciated by experimentalists.

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**Supplementary Material Available:** Geometries of structures shown in Figure 1 and the intermediates on the IRC (5 pages). Ordering information is given on any current masthead page.

(17) Energy decomposition analysis for the acetaldehyde reaction (Kitaura, K.; Morokuma, K. *Int. J. Quantum Chem.* 1976, 10, 325) indicated that the small activation energy is due to cancellation for the gains for the electrostatic and orbital interactions with loss by the exchange repulsion. *sen*: Details will be discussed later in a full paper.

(18) This seemingly large structural difference is a matter of the position of the TSs as seen in the intrinsic reaction coordinates (IRC) analysis in the supplementary material. This potential around H and I is very flat again, and the activation energy from H to I is 1.83 kcal/mol at the HF/6-31+G\*\*//HF/6-31+G\* (–1.16 kcal/mol at the MP2/6-31+G\*\*//HF/6-31+G\*).

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(21) Clearly seen in the snapshots along the IRC in supplementary material.

(22) For a different view, see: Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* 1987, 109, 2819.

(23) Cf.: Kubota, K.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* 1993, 115, 5867.