Transition Structures of [2,3]-Wittig Rearrangement of 2-Oxa-5-methylhexene-1-carboxylic Acid

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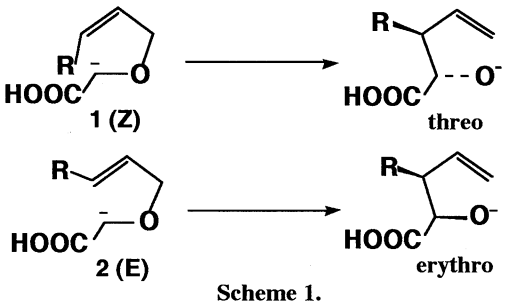
(Received October 3, 1996)

Transition structures for [2,3]-Wittig rearrangement of dilithium salts of 2-oxa-4-(Z and E)-methylhexene-1-carboxylic acid (**1** and **2**, respectively) have been located with *ab initio* molecular orbital calculation at the level of 6-31G* basis set. The origin of the observed stereoselectivity of [2,3]-Wittig rearrangement of **1** and **2** was clarified.

[2,3]-Wittig rearrangement is one of the powerful tools for carbon-carbon bond forming reaction.[1] Generally, threo products were obtained predominantly from (E)-olefins. On the other hand, (Z)-olefins give erythro isomers as the major products.[2,3] However, the opposite stereoselection is observed in the reaction of compounds (**1** and **2**) having carboxylic group at C_1 position. (Scheme 1)[4] It is thus desirable to understand the substitution effect on the stereochemistry of this reaction.



Scheme 1.

We now wish to report on the transition structures in [2,3]-Wittig rearrangement of **1** and **2** to clarify the origin of the opposite stereoselectivities observed in **1** and **2**. Three transition structure models in [2,3]-Wittig rearrangement have been proposed by Trost,[5] Rautenstrach,[6] and Nakai.[7] We[8] and Houk[9] have located 3-21G transition structures corresponding to Trost's (**I**) and Rautenstrach's model (**II**), respectively.

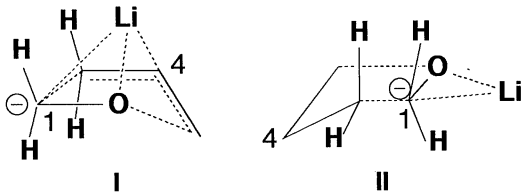


Figure 1. Trost's(**I**) and Rautenstrach's envelop(**II**) for the transition structures of [2,3]-Wittig rearrangement.

From the results of IRC calculations,[10] it is clear that while TS(**II**) corresponds to concerted process, TS(**I**) does not give directly the final product but leads to five-membered intermediate (two-step mechanism). The activation enthalpy ($\Delta H^{\ddagger}$) for Trost's type TS(**I**), however, is considerably smaller (MP2/6-31(+)G*//3-21G) than that of Rautenstrach's type TS(**II**) by 2 kcal/mol. Nakai's type transition structure has much larger activation enthalpy (by > 10 kcal/mol) than those of TS(**I**) and TS(**II**). Recently, Houk applied the technique of MM2 transition state modeling to interpret the origin of observed stereoselectivity by using Rautenstrach's envelop (**II**).[9] They attributed the observed stereoselection in compound **1** partially to the secondary orbital interaction (SOI) between carbonyl group of the formyl substituent at C_1-carbon and allyl anion moiety, which is known to be the main factor of the endo approach of the diene to the dienophile in Diels-Alder cycloadditon reaction. According to 6-31G* geometry optimization[11] of transition structure and energetic consideration at MP2/6-31G* level[12] for the reactions of dilithium salts of **1** and **2**, SOI seems to be rather unimportant and the coulomb interaction between C_1-substituent and the reaction core seems to play an important role.

TS(**I**) and TS(**II**) are both envelop shaped, but different with each other by the positions of the top of the envelop lid. In addition, the two structures have other prominent difference of the location of a cation (Li^+). TS(**II**) has the lithium ion anti to an incipient C-C bond and the adjacent oxygen atom (O_2) coordinates to it roughly in the plane defined by four atoms of the envelop. TS(**I**), on the other hand, has lithium ion syn to the forming bond and it coordinates to both O_2 atom and a newly developed partial anion center at C_4. When two substituents on the both termini of the reaction core are introduced, there should be four transition structures, making E and Z on the olefin terminus and two configurations on lithiated sp^3 carbon terminus, which lead to threo and erythro products. They are noted as **A** (Z, threo), **B** (Z, erythro), **C** (E, erythro), and **D** (E,threo), respectively.

Thorough search for the transition structures[13] was carried out with *ab initio* molecular orbital calculation at the level of 6-31G* basis set. Among eight reaction modes for [2,3]-Wittig rearrangement of **1** and **2**, three transition structures for each reaction of **1** and **2** could be located. Figures 2 and 3 show the energetically favorable 6-31G* transition structures, TS(**I**)-**A** and TS(**II**)-**B** for the reaction of **1**, and TS(**I**)-**C** and TS(**II**)-**D** for **2**, respectively. TS(**I**)-**A** and TS(**I**)-**C** lead to major stereoisomers and TS(**II**)-**B** and TS(**II**)-**D** to minor ones. Two types of reaction modes (TS(**II**)-**A** and TS(**II**)-**C**) gave the same geometries with TS(**I**)-**A** and TS(**I**)-**C**, respectively, during the geometry optimization. The transition structures, TS(**I**)-**B** and TS(**I**)-**D**, have much larger activation energies (by > 30 kcal/mol) than the most stable TS(**I**)-**A** and TS(**I**)-**C**, respectively.

As shown in Figures 2 and 3, the coordination of Li cation located in the reaction core to the lone pair of the carbonyl oxygen was found, when the CO_2Li group is syn to the Li cation with respect to the five-membered envelop. Interestingly, the most stable TS(**I**)-**A** and TS(**I**)-**C** hold Trost's envelop (**I**) and TS(**II**)-**B** and TS(**II**)-**D** hold Rautenstrach's one (**II**). The

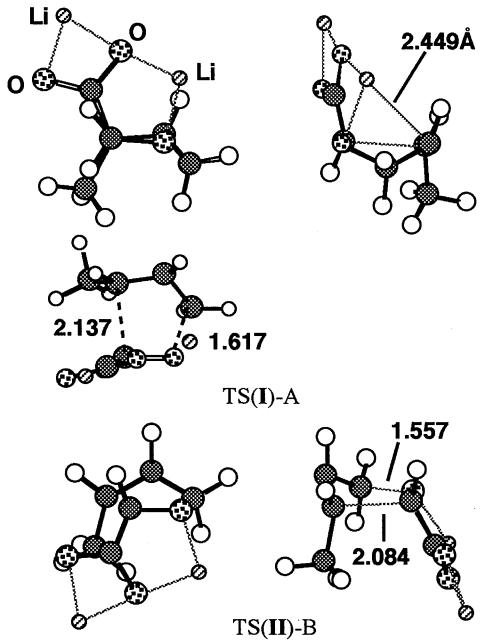


Figure 2. 6-31G* transition structures for [2,3]-Wittig rearrangement of Z-olefin (**1**).

distances between Li and C_4 atom, which interact at the parent transition structures (**I**) (2.114Å),[8] are 2.449 Å for TS(**I**)-**A** and 2.425 Å for TS(**I**)-**C**, respectively. The positive charge on Li atom still stabilizes the developed negative charge at C_4 carbon at transition state. Judging from the distances (2.0~2.2 Å) of the newly forming C-C bonds, those (1.5-1.7 Å) of the breaking C-O bonds, and the large heat of reactions (40~50 kcal/mol) at MP2/6-31G*//6-31G*, all the transition states are in the early stage of the reaction.

Although the unsubstituted TS(**I**) leads to the five-membered ring intermediate, the transition structures (TS(**I**)-**A** and TS(**I**)-**C**), having Trost's envelop, lead to their final products in a concerted one-step manner. IRC analysis shows that both of the forming bonds and the breaking bonds changed their length monotonously from the transition structures to the direction of the products. There is no energy hill nor even plateau in between the transition states and their products. These results suggest that the coordination of Li cation to two oxygen atoms (O_2 and carbonyl oxygen)[14] and C_4-carbon atom plays a significant role in stabilizing the transition structures (TS(**I**)-**A** and TS(**I**)-**C**) and in making O_2-C_3 bond breaking easier.

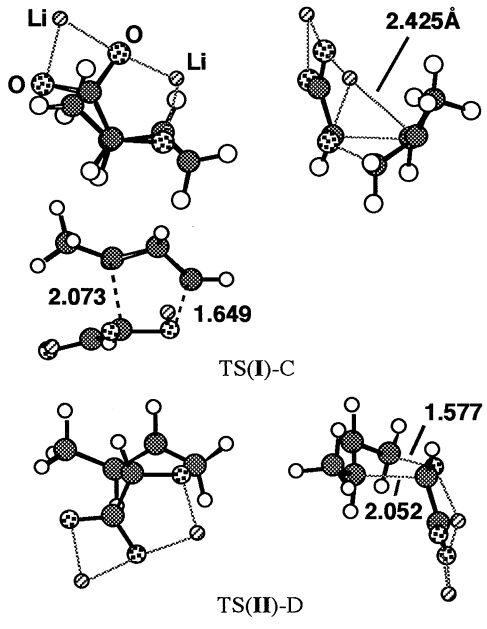


Figure 3. 6-31G* transition structures for [2,3]-Wittig rearrangement of E-olefin (**2**).

The energy differences between the two transition structures, TS(**I**)-**A** and TS(**II**)-**B** for **1** and TS(**I**)-**C** and TS(**II**)-**D** for **2**, estimated at MP2/6-31G*//6-31G* level are 6.72 and 5.62 kcal/mol, respectively. Although these energy differences are too large, as compared with the observed threo/erythro ratios (80/20 for **1** and 8/92 for **2**),[2] the major stereoisomers were nicely reproduced by this calculation.

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13 Transition Structure optimization was started from the initial geometries of Trost's (**I**) and Rautenstrach's (**II**) envelops simply substituted at C_1 and C_5 hydrogen into CO_2Li and methyl group, respectively. This operation generated eight initial geometries. For example, the term "TS(**I**)-**A**" is used to indicate the transition structure having Trost's envelop (**I**) and leading to (Z, threo) stereoisomeric product.

14 The transition structures for 1-formyl derivatives were located at minimal basis set. See: K. Mikami, T. Uchida, T. Hirano, Y-D. Wu, and K. N. Houk, *Tetrahedron*, **50**, 5917 (1994).