5844 J. Am. Chem. Soc. **1998,** *120,* 5844−5845

Theoretical Studies on Lewis Acid Acceleration in Simmons−Smith Reaction

Eiichi Nakamura,* Atsushi Hirai, and Masaharu Nakamura

Department of Chemistry, The University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

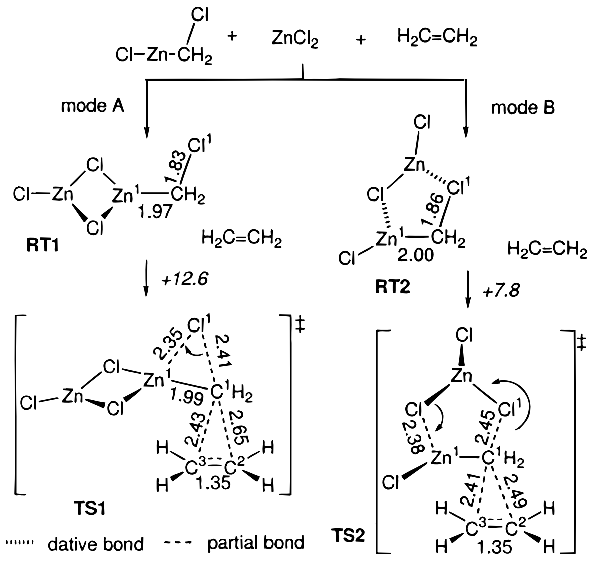
Received March 3, 1998
Revised Manuscript Received April 24, 1998

The mechanistic understanding of the Simmons−Smith (SS) reaction[1] entered a new phase since the recent discoveries that an added Lewis acid dramatically accelerates the SS reaction[2−4] and a chiral Lewis acid effects enantioface selective cyclopropanation of allylic alcohol.[5] Various models of Lewis acid effects have been suggested, but neither detailed experimental nor theoretical analysis on the Lewis acid participation has been reported so far.[6] With the aid of density functional theory (B3LYP/631A),[7] we have investigated the $ZnCl_2$ acceleration of the SS reaction of ethylene and allyl alcohol through comparison among mono- to pentametallic organozinc clusters and found two different modes of Lewis acid acceleration (paths A and B, Scheme 1). Path B, which involves direct Lewis acid activation of the leaving halogen atom[3] (**TS2**), was found to be a more facile process than more popular path A involving 1,2-chlorine migration (**TS1**).

The Lewis acid effects were examined first for ethylene and two isomeric aggregates of $ClZnCH_2Cl{\cdot}ZnCl_2$, **RT1** and **RT2** (Scheme 1). The di-μ-chlorodizinc(II) structure in **RT1** is a ubiquitous structure and is found for $CF_3CCl_2ZnCl{\cdot}ZnCl_2{\cdot}Et_2O)_2$,[8] which can be viewed as an inactivated SS reagent. **RT2** is a less stable isomer of **RT1** (by 3.5 kcal/mol). In **RT2**, the Cl^1 leaving group is directly activated by $ZnCl_2$, and the $C^1{-}Cl^1$ bond is elongated.

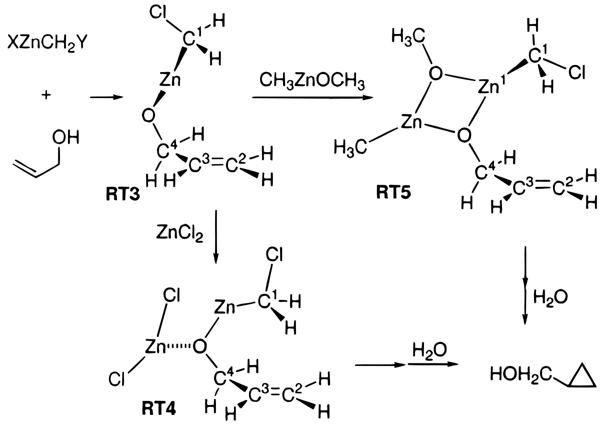
In path A, **RT1** (C_s) reacts with ethylene in a single step reaction with retention of C_s symmetry throughout the reaction course along intrinsic reaction coordinate (IRC), going directly to a product (cyclopropane + $2ZnCl_2$) with 57.5 kcal/mol exothermicity through **TS1**. The 1,2-migration of Cl^1 from C^1 to Zn^1 is taking place in **TS1**. When compared with the prototypal reaction ($ClZnCH_2Cl$ + ethylene, $\Delta E^{\ddagger} = 17.3$ kcal/mol, B3LYP/631A),[5c,9] $\Delta E^{\ddagger}$ in path A is 4.7 kcal/mol lower (12.6 kcal/mol).[10] In **TS1**, the activation is caused by Lewis acid activation of Zn^1 through $ZnCl_2$ complexation. The $C^1{-}Cl^1$ bond is elongated (32% than in **RT1**), but $C^1{-}Zn$ bond is not cleaved yet (0.9% elongated). This geometrical feature as well as the charge change[11] indicates that the reaction is essentially an S_N2 displacement of Cl^1 with ethylene. Such a picture is consistent with experimental data.[12]

Scheme 1[a]



[a] Bond lengths and energy changes in italic at B3LYP/631A level are shown in angstroms and in kcal/mol, respectively. Total energies of **RT1**, **RT2**, **TS1**, and **TS2** are −5438.64437, −5438.63714, −5517.20711, and −5517.20918 hartrees, respectively.

Scheme 2



The five-centered complex **RT2** (C_s) is very reactive, reacting with ethylene via **TS2** only with 7.8 kcal/mol activation energy (Scheme 1, path B). **TS1** is C_1 symmetric to minimize electrostatic interaction between Cl^1 and Cl^2 atoms. **RT2**, **TS2**, and a cyclopropane product (not shown) are smoothly connected along IRC. The $C^1{-}Cl^1$ bond fission takes place in a five-centered manner, and Cl^1 becomes attached to Zn^2 later along IRC. Path B is kinetically favored over path A by 1.3 kcal/mol (**TS2** − **TS1**).

Next, the allylic alcohol reaction was examined in four stages (Scheme 2 and Figure 1): a monometallic species **RT3**, its $ZnCl_2$ complex (**RT4**), a dimer model **RT5**, and its two isomeric $ZnCl_2$ complexes (**RT6** and **7**). Very rapid SS cyclopropanation of a

---

[1] (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1−103. (b) Denmark, S. E.; O'Connor S. P. *J. Org. Chem.* **1997**, *62*, 3390−3401.

[2] Friedrich, E. C.; Lunetta, S. E.; Lewis, E. J. *J. Org. Chem.* **1989,** *54*, 2388−2390.

[3] Wittig, G.; Wingler, F. *Chem. Ber.* **1964**, *97*, 2146−2164.

[4] Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651−2652.

[5] Ukaji, Y.; Nishimura, M.; Fujisawa, T. *Chem. Lett.* **1992**, 61−64. Takahashi, H.; Yoshioka, M.; Ohno, M.; Kobayashi, S. *Tetrahedron Lett.* **1992**, *33*, 2575−2578. Takahashi, H.; Yoshioka, M.; Kobayashi, S. *J. Synth. Chem. Soc. Jpn.* **1997**, *55*, 714−724. Kitajima, H.; Aoki, Y.; Ito, K.; Katsuki, T. *Chem. Lett.* **1995**, 1113−1114. Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215−2218.

[6] (a) Hida, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2497−2501. (b) Bernardi, F.; Bottini, A.; Miscione, G. P. *J. Am. Chem. Soc.* **1997**, *119*, 12300−12305. (c) Hirai, A.; Nakamura, M.; Nakamura, E. Manuscript in preparation.

[7] GAUSSIAN 94 program was used for all calculations. See the Supporting Information for computational details.

[8] Behm, J.; Lotz, S. D.; Herrmann, W. A. *Z. Anorg. Allg. Chem.* **1993**, *619*, 849−852.

[9] The activation energy is 19.5 kcal/mol at the CCSD(T)/ 631A//B3LYP/631A level. $\Delta E^{\ddagger}$ for $IZnCH_2I$ is 13.1 kcal/mol (B3LYP/631A).

[10] $\Delta H^{\ddagger} = 17.3$ kcal/mol at 0 K, $\Delta S^{\ddagger} = -32.5$ cal/mol K, and $\Delta G^{\ddagger} = 26.2$ kcal/mol at 0 °C, 1 atm. These values are reasonable for a concerted cycloaddition. Cf.: Grimme, W.; Wiechers, G. *Tetrahedron Lett.* **1987**, *28*, 6035−6038.

[11] Natural population charges of atoms and groups in **RT1** and **TS1**. **RT1**: C^1H_2, −0.52; C^2H_2, C^3H_2, 0.00; Zn^1, +1.34; Cl^1, −0.09. **TS1**: C^1H_2, −0.33; C^2H_2, +0.06; C^3H_2, +0.08; Zn^1, +1.46; Cl^1, −0.57.

[12] Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256−4264.

S0002-7863(98)00698-2 CCC: $15.00

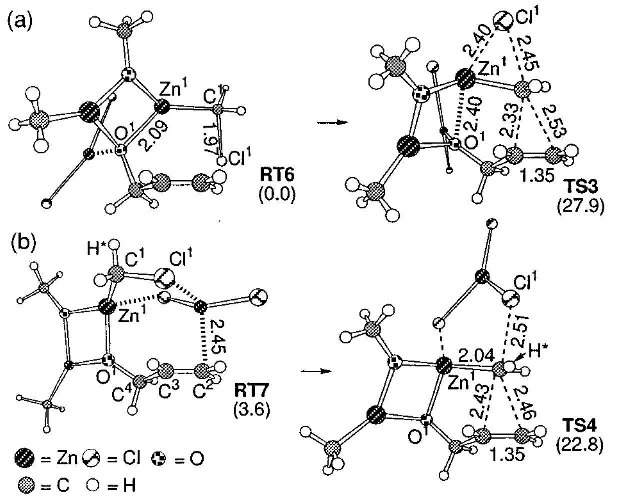


Figure 1. Cyclopropanation of allyl oxide dimer with $ClZnCH_2Cl$ (B3LYP/631A level): (a) mode A, $ZnCl_2$ coordination to O^1 and (b) mode B, to Cl^1. Bond lengths are given in angstroms. Energies relative to **RT6** are given in parentheses. Total energies of **RT6**, **RT7**, **TS3,** and **TS4** are −7105.23548, −7105.22976, −7105.19103, and −7105.19935 hartrees, respectively.

free allylic alcohol[13] takes place through formation of a ternary complex involving at least one molecule each of an allylic alkoxide, SS reagent, and a Lewis acid. Structures such as **RT4** have been suggested as reactive species.[4,14]

The monomer **RT3** (Scheme 2) cyclopropanates with $\Delta E^{\ddagger} = 35.7$ kcal/mol.[15] The energy cost of bending the linear O−Zn−C^1 bond (172.2°) in **RT3**, characteristic to coordination-free monomeric Zn(II) species,[16] to the 124.6° geometry in the TS of cyclopropanation (not shown) is a major contributor to the higher activation energy (ca. 10 kcal/mol). Deactivating effect of the alkoxy group also contributes to the activation energy (CH_3OZnCH_2Cl is deactivated by 3.5 kcal/mol than $ClZnCH_2Cl$ toward ethylene). The activation of **RT3** in mode A (i.e., **RT4**) lowers $\Delta E^{\ddagger}$ to 29.4 kcal/mol. When the dipole moment of CH_2Cl_2 (a frequently used solvent, 0 °C; $\epsilon = 9.814$) is considered with the self-consistent reaction field method[17] (applied without structure optimization), the energy becomes 26.4 kcal/mol. Because of the high Lewis basicity of the O^1 atom in **RT3**, a five-centered complex corresponding to **RT2** is overwhelmingly (by 23 kcal/mol) less stable than **RT4**, and hence, mode B activation is unimportant on a monometallic species. The energy barrier starting from the $ZnCl_2$ complex **RT4** (29.4 kcal/mol) is still too high to account for the experiments.

Experimentally, a zinc alkoxide monomer such as **RT3** may not exist in solution, and will form higher aggregates.[18] The model dimer **RT5** (Scheme 2) is a tight di-μ-oxo-bridged species and undergoes intramolecular cyclopropanation with 27.9 kcal/mol activation energy (structure not shown), which is quite high. The effect of mode A activation with $ZnCl_2$ (**RT6** to **TS3**) was found to be negligible ($\Delta E^{\ddagger} = 27.8$ kcal/mol; Figure 1a).[19]

We then examined mode B activation on **RT5** (Figure 1b). Coordination of $ZnCl_2$ to Zn^1 of **RT5** on the vacant coordination site forms a stable complex **RT7**, where the added zinc chloride is held among Zn^1, Cl^1, and the olefin. Moving C^1 toward the olefin led smoothly (along IRC) to the cyclopropane forming TS (**TS4**) notably with only 19.1 kcal/mol activation energy ($\Delta H^{\ddagger}$ 17.9 kcal/mol, $\Delta S^{\ddagger}$ −2.6 e.u., $\Delta G^{\ddagger}$ 18.7 kcal/mol at 25 °C, 1 atm). Even by taking the 3.6-kcal/mol energy difference between **RT6** and **RT7**, mode B activation is kinetically favored over mode A activation by 5.1 kcal/mol (**TS4** − **TS3**). This is due to the loss of Lewis basicity of O^1 in **RT5** (cf. **RT3** vide supra), which will also be the case in a tetramer.[20]

The trimetallic **TS4** involves a rigid polycyclic framework. The dihedral angle $C^2{-}C^3{-}C^4{-}O$ in **TS4** was found to be 132°, and agrees with the ca. 150° value experimentally suggested in the Denmark asymmetric SS reaction.[14,21]

The present studies revealed several pieces of new mechanistic information. First, $ZnCl_2$ lowers the energy barrier of methylene transfer through two potentially competing modes of Lewis acid activation. It is thus probable that the SS reaction under conventional conditions benefits from Lewis acid assistance,[3] since zinc halide is generated in situ in the reaction. Theory favors five-centered migration of the halide leaving group (path B) rather than the 1,2-halide migration mechanism, which has been described in the literature for many years.[1]

Second, mode B is particularly favorable for the SS reaction of oligomeric allyl oxide SS reagent (**TS4**) and provides a new working model of asymmetric SS reaction. It is also likely that the reactive precursor **RT7** and functionally related species[20] will form in various other ways. Such possibilities may account for the experimental diversity of optimum conditions of asymmetric SS reactions. Finally, the present research provides one of the growing numbers of examples of metal cluster participation in synthetically important organometallic reactions.[22]

Acknowledgment. We thank Profs. S. E. Denmark and D. A. Evans for helpful comments. This work was supported by Grant-in-Aid for Scientific Research on Priority Areas (no. 283, "Innovative Synthetic Reactions") from Monbusho, Japan. Generous allotment of computational time from the Institute for Molecular Science is gratefully acknowledged.

Supporting Information Available: Computational details and Cartesian coordinates of stationary points **RT1-7** and **TS1-4** at B3LYP/631A level (7 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA9806985

---

(13) Winstein, S.; Sonnenberg, J.; de Vries, L. *J. Am. Chem. Soc.* **1959**, *81*, 6523−6524. Chan, J. H.-H.; Rickborn, B. *J. Am. Chem. Soc.* **1968**, *90*, 6406−6411.

(14) Denmark, S. E.; O'Conner, S. P. *J. Org. Chem.* **1997**, *62*, 584−594.

(15) In contrast, $ClCH_2ZnCl$ forms a dimetallic 1:1 zinc/oxygen complex with neutral $HOCH_2CH{=}CH_2$ and transfers the methylene group with $\Delta E^{\ddagger} = 29.9$ kcal/mol, indicating that the neutral hydroxy group (model of an alkoxy group) is not a serious deactivator.

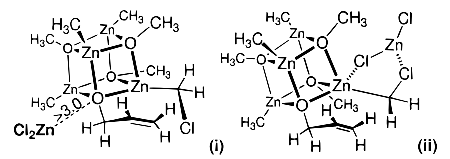
(16) Ernst, R. D.; Freeman, J. W.; Swepston, P. N.; Wilson, D. R. *J. Organomet. Chem.* **1991**, *402*, 17−25.

(17) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486−1493. Wiberg, K. B.; Frisch, M. J. *J. Comput. Chem.* **1995**, *16*, 385−394.

(18) Shearer, H. M. M.; Spencer, C. B. *Acta Crystallogr., Sect. B* **1980**, *36*, 2046−2050.

(19) Since O^1 is already tri-coordinated in **RT3**, further coordination of $ZnCl_2$ loosens the $O^1{-}Zn^1$ bond as seen in **TS3**.

(20) We also examined a $ZnCl_2$ complex of a cubic tetramer (see below, HF/321A). The O^1 alkoxide oxygen in the tetramer has three zinc atoms and does not accept the added $ZnCl_2$ any more **(i),** Zn−O = >3.0 Å, and therefore mode B activation is more likely **(ii)**.



(21) Replacement of the less hindered asterisked hydrogen atom in **TS4** with a methyl group accounts for the diastereoselectivity of ethylidene transfer (Charette, A. B.; Lemay, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1090−1092.).

(22) (a) Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887−4899. Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4900−4910. (b) Mori, S.; Kim, B. H.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1997**, 1079−1080.