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Ab initio studies of the allylic hydroxylation: DFT calculation on the reaction of 2-methyl-2-butene with selenium dioxide

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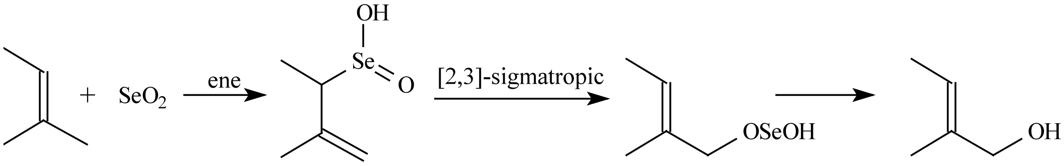
Abstract—The mechanism of the allylic oxidation of 2-methyl-2-butene with selenium dioxide has been investigated by ab initio quantum mechanics. Transition states for two major steps (an ene reaction and a [2,3]-sigmatropic rearrangement) of this reaction have been optimized by the B3LYP/6-311+G(d,p) method. A comparison of the energies of the transition states shows that the *anti-endo* and *syn-endo* approaches are the efficient routes in the ene reaction and the methyl (C4) group is sited in a *pseudo-equatorial* environment in cyclic transition states during the [2,3]-rearrangement. Calculations also show the kind of the terminal alkyl (C4) substituents may control (*E*)-selectivity in the formation of the allylic alcohols. © 2003 Elsevier Science Ltd. All rights reserved.

Treatment of alkenes with selenium dioxide introduces an hydroxyl group into the allylic position.[1] The reaction reveals a very useful regio- and stereoselectivity when applied to trisubstituted olefins, producing (*E*)-allylic alcohol predominantly.[2] The mechanism of this highly selective process was a subject of keen interest for many years until Sharpless proposed a mechanism, a generally accepted, consisting of two consecutive pericyclic reactions (an electrophilic ene reaction followed by the 2,3-sigmatropic rearrangement).[3]



While a recent mechanistic study[4] of the selenium dioxide-mediated allylic oxidation of 2-methyl-2-butene clarifies the stereochemical aspect of this reaction successfully and is limited on the ene reaction step, the overall profile of the stereocontrol observed in the whole transformation still needs to be accounted for. Here we report the results of ab initio studies on the allylic oxidation of 2-methyl-2-butene. All calculations were performed with Gaussian-98 package.[5] The structures of the intermediates and transition states were then fully optimized using the density functional theory B3LYP/6-311+G(d,p).[6,7] Frequency calculations were subsequently carried out for the transition state structures and in each case one imaginary frequency was found, confirming that the structures obtained were indeed transition states.

For the initial ene reaction step, six different approaches (**1**–**6**) are possible; *anti*-addition (C_1-H and C_3), *syn*-addition (C_5-H and C_3) and *terminal*-addition (C_4-H and C_2) of Se–O, as well as an *endo* and an *exo* arrangement of the other oxygen at Se in the ring geometry of **TS**s. For the following [2,3]-sigmatropic rearrangement, access of oxygen has two possibilities (**a**, **b**) via both faces of the double bond of the initial product (Fig. 1).

We successfully found the energies of **TS1**s and **TS2**s at B3LYP/6-311+G(d,p)//B3LYP/6-311+G(d,p).[8] In the ene reaction, *endo* approaches are more favorable than *exo* approaches. The activation energy for **TS1-1**, for example, appears lower than **TS1-2** by 2.88 kcal/mol. The *endo* orientation of the other Se=O group facilitates the geometry required for a maximum overlap of π-electrons with the C=C double bond. For the ene reaction, the *anti*-*endo* approach (**1**) and *syn*-*endo* approach (**3**) are predicted as energetically favorable;

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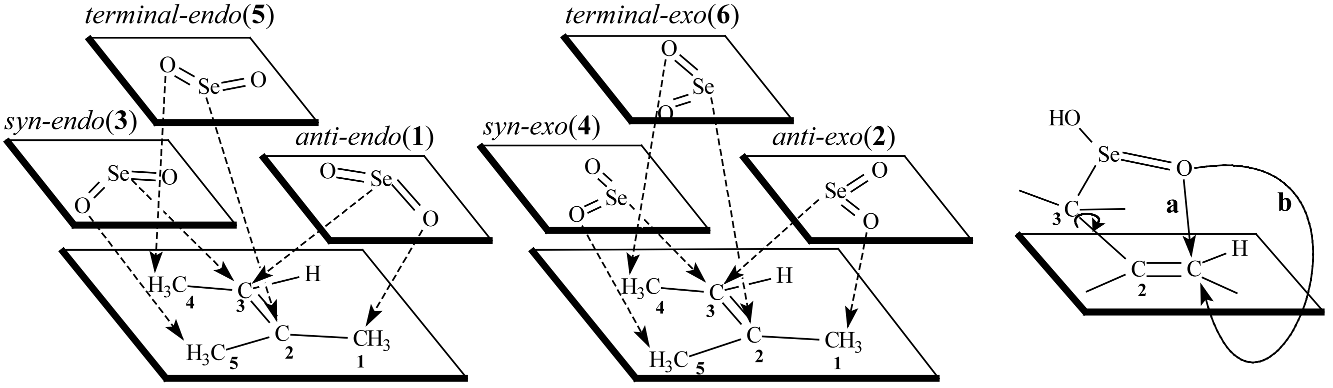
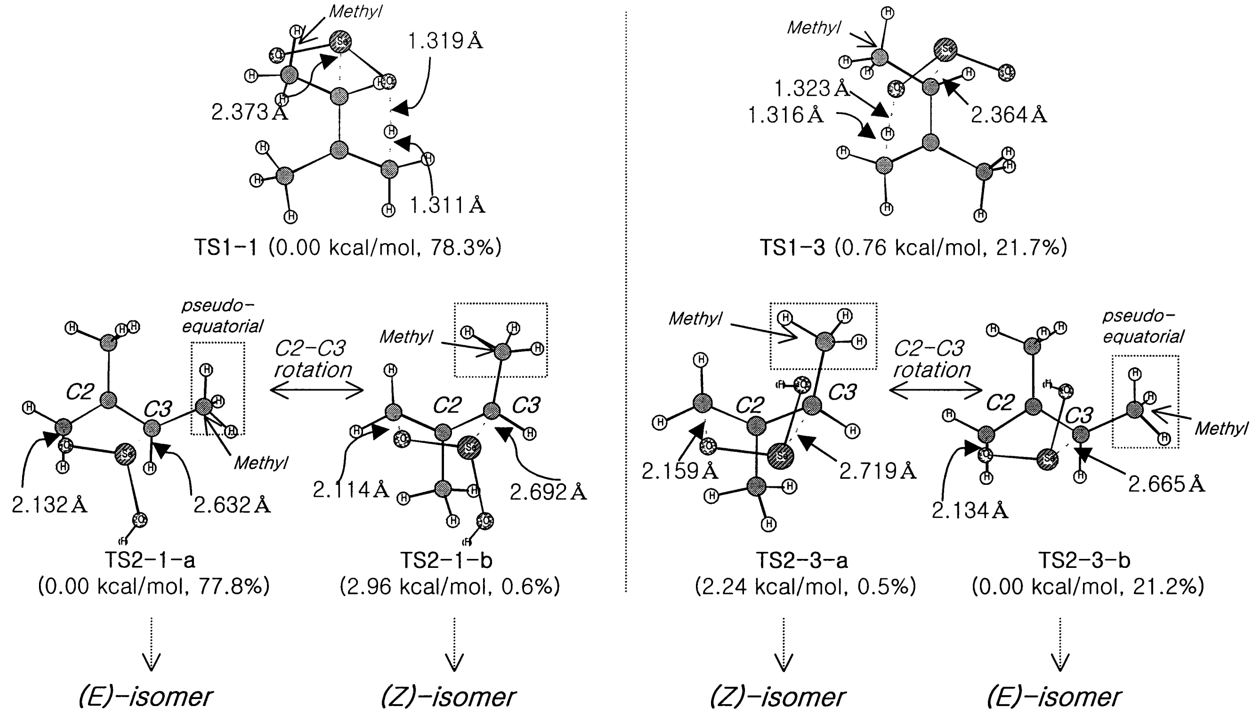


Figure 1. Six possible topologies (**1**–**6**) for the 'ene' reaction and two pathways (**a**, **b**) for the [2,3]-sigmatropic rearrangement.

the *anti*-*endo* approach (**TS1-1**) is the most favorable one, while the *syn*-*endo* approach (**TS1-3**) is with a higher energy of 0.76 kcal/mol. The other routes as the terminal additions (**TS1-5** and **TS1-6**) are ruled out, for the activation energies for them are much higher (4 kcal/mol) than that for **TS1-1**. Calculation results reproduce the regioselective addition of Se atom onto the C-3 position and the following transformation into the corresponding (*E*)- and (*Z*)-selenous esters (Fig. 2).

In the [2,3]-sigmatropic rearrangement, the methyl (C4) group may adopt a *pseudo*-*equatorial* or *axial* position in the cyclic transition states geometries (**TS2**). The activation energies for the transition states with the *axial* methyl group appear higher than for those of the *pseudo*-*equatorial* conformations. **TS2-1-a** (the transition state of the [2,3]-sigmatropic rearrangement of the intermediate obtained from **TS1-1**) has the *pseudo*-*equatorial* methyl (C4) group and the energy for **TS2-1-a** is lower than that for **TS2-1-b** by 2.96 kcal/mol. **TS2-3-b** is energetically favored by 2.24 kcal/mol than its *axial* isomer, **TS2-3-a**. Presumably the reactions should occur by two routes: either **TS2-1-a** via **TS1-1** or **TS2-3-b** via **TS1-3**. Both pathways would give the same (*E*)-allylic alcohol via mixtures of (*E*)- and (*Z*)-selenous esters. It seems likely that a selective formation of (*E*)-allylic alcohol is determined at the **TS2** step. A higher (*E*)-selectivity expected in the formation of the allylic alcohol by tuning the energy gap between **TS2-a** and **TS2-b**, for example, by introducing a bulky C4 substituent can be explained on the same grounds.

Figure 2 shows the optimized geometries of the transition structures (**TS1-1**, **TS1-3**, **TS2-1-a**, **TS2-1-b**, **TS2-3-a** and **TS2-3-b**) and their representative parameters.



TS1-1 (0.00 kcal/mol, 78.3%)

TS1-3 (0.76 kcal/mol, 21.7%)

TS2-1-a (0.00 kcal/mol, 77.8%)

TS2-1-b (2.96 kcal/mol, 0.6%)

TS2-3-a (2.24 kcal/mol, 0.5%)

TS2-3-b (0.00 kcal/mol, 21.2%)

Figure 2. The optimized geometries and their representative parameters of transition states at B3LYP/6-311+G(d,p).

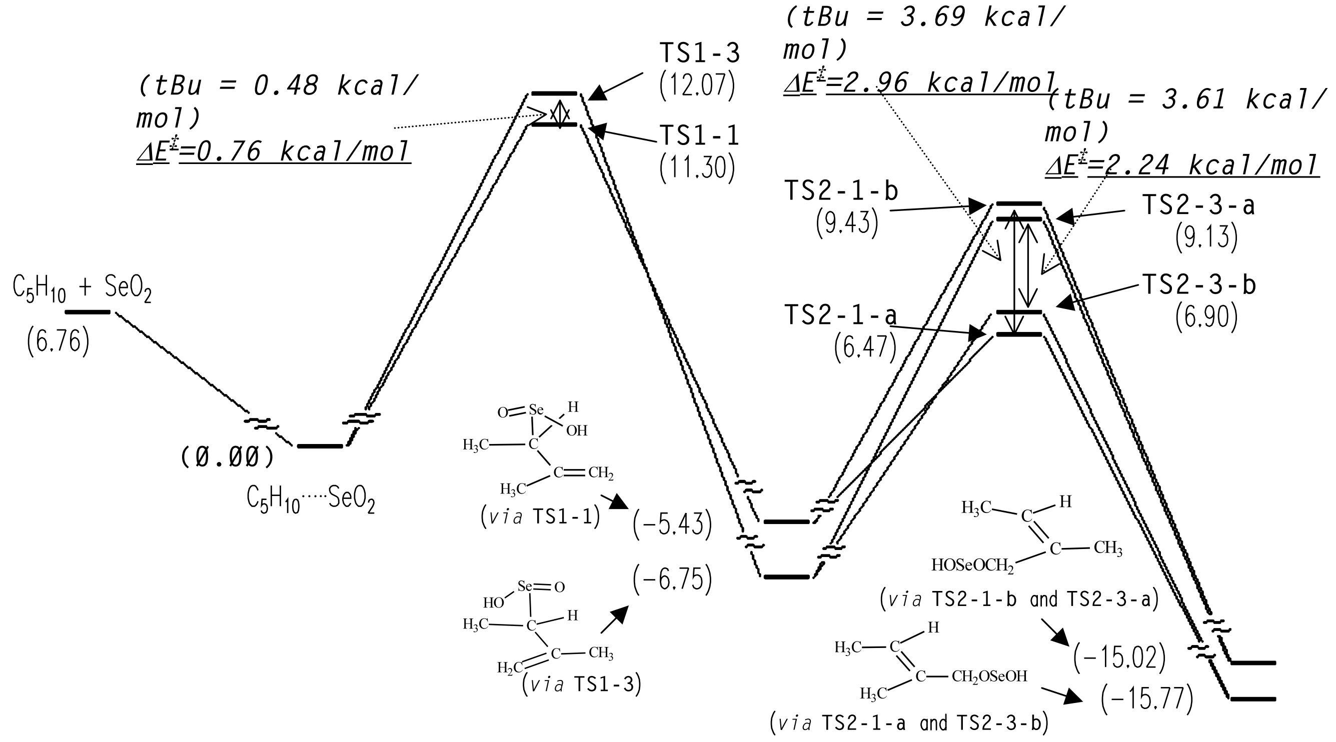


Figure 3. Reaction profile for the allylic oxidation of 2-methyl-2-butene using SeO_2.

Assuming the compound ratio, A/B depends on the relative energies of the transition states, $E_A^{\ddagger}$ and $E_B^{\ddagger}$, then A/B = exp[($E_B^{\ddagger}$–$E_A^{\ddagger}$)/rt]. The ratios of (*E*)-/(*Z*)-products will be determined by the distribution ratios of **TS1-1**/**TS1-3** and **TS2-1-a**/**TS2-1-b**/**TS2-3-a**/**TS2-3-b**: 78.3/21.7 and 77.8/0.6/0.5/21.2 (at 298.15 K), respectively. Thus, these highly selective processes providing (*E*)-allylic alcohol (up to 99%) may occur by two routes: **TS2-1-a** via **TS1-1** and/or **TS2-3-b** via **TS1-3** (Fig. 3). The above results are in excellent agreement with the experimental observations of the allylic hydroxylation of 2-methyl-2-butene using selenium dioxide.

In conclusion, we have investigated the allylic oxidation of 2-methyl-2-butene using selenium dioxide by the B3LYP/6-311+G(d,p) method. According to the transition state energies in the ene reaction step, the approaches of selenium dioxide are predicted to occur by the *anti-endo* and/or *syn-endo* modes, where the *anti-endo* approach is energetically favored than the *syn-endo* one by 0.76 kcal/mol. In the transition state geometries of the [2,3]-sigmatropic rearrangement, the terminal methyl (C4) group may locate at a *pseudo-equatorial* and/or an *axial* position. The *pseudo-equatorial* conformation is calculated energetically more favored than the *axial* conformation by 2.96 kcal/mol, which also contributes to high stereo-control observed in the overall reaction. Two viable routes for the allylic hydroxylation of 2-methyl-2-butene into the (*E*)-allylic alcohol are then **TS2-1-a** via **TS1-1** and **TS2-3-b** via **TS1-3**. Substitution of the methyl group (C4) of 2-methyl-2-butene by the bulkier one like a *tert*-butyl group may be expected to increase the (*E*)/(*Z*)-ratio of the allylic alcohols (see Fig. 3). Application of these theoretical implications to synthesis of (*E*)-allylic alcohols is being pursued by us.

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