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Theoretical Study of the Reaction Mechanism and Migratory Aptitude of the Pinacol Rearrangement

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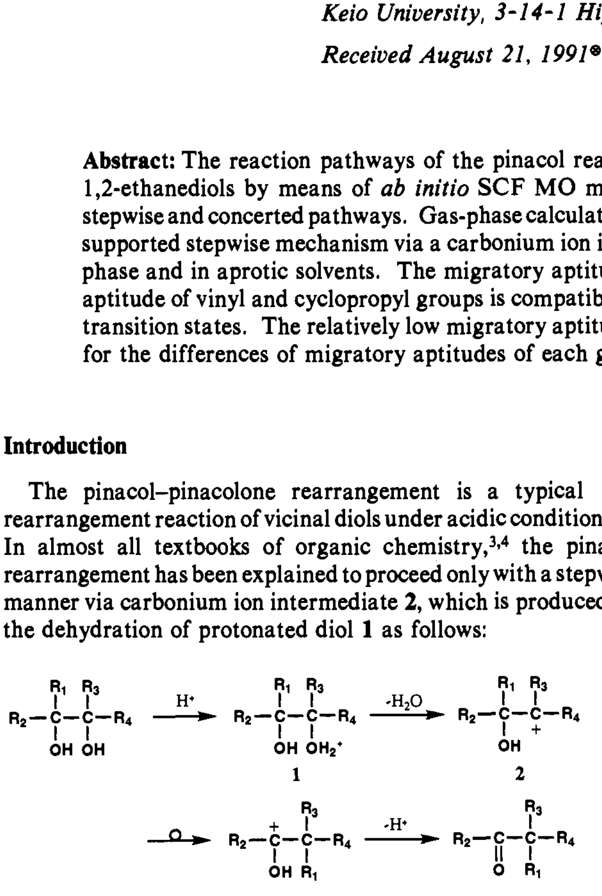
Abstract: The reaction pathways of the pinacol rearrangement are examined for some monosubstituted protonated 1,2-ethanediols by means of *ab initio* SCF MO methods. The relative activation energies are evaluated for both stepwise and concerted pathways. Gas-phase calculations show the concerted mechanism dominates over the traditionally supported stepwise mechanism via a carbonium ion intermediate. These results agree well with experiments in the gas phase and in aprotic solvents. The migratory aptitude is also calculated for some substituents. The high migratory aptitude of vinyl and cyclopropyl groups is compatible with the participation of π- or pseudo-π-orbitals to stabilize the transition states. The relatively low migratory aptitudes of alkyl and alkynyl groups are also reproduced. The reasons for the differences of migratory aptitudes of each group are discussed.

Introduction

The pinacol–pinacolone rearrangement is a typical 1,2-rearrangement reaction of vicinal diols under acidic conditions.[1,2] In almost all textbooks of organic chemistry,[3,4] the pinacol rearrangement has been explained to proceed only with a stepwise manner via carbonium ion intermediate **2**, which is produced by the dehydration of protonated diol **1** as follows:

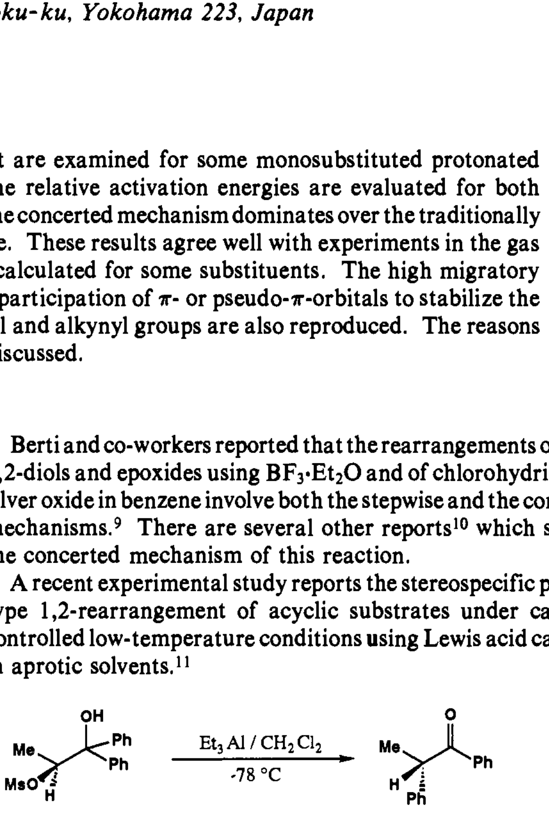


(1)

Similar reactions, including different leaving groups and substituents, are generally called pinacol-type rearrangements. There are not many examples of the pinacol-type rearrangement applied in organic synthetic strategies, due mainly to the difficulty in controlling product stereochemistry. Once a carbonium ion intermediate is formed, C–C bond rotation of intermediate **2** would result in mixing of the product stereochemistry after migration occurs.[3-5] However, there are experiments using cyclic systems where the rearrangement proceeds stereoselectively.[6-8] In these cases, the conformation of the reaction center is fixed by the ring structure, even if the carbonium ion intermediate is formed.

Berti and co-workers reported that the rearrangements of cyclic 1,2-diols and epoxides using $BF_3{\cdot}Et_2O$ and of chlorohydrins with silver oxide in benzene involve both the stepwise and the concerted mechanisms.[9] There are several other reports[10] which support the concerted mechanism of this reaction.

A recent experimental study reports the stereospecific pinacol-type 1,2-rearrangement of acyclic substrates under carefully controlled low-temperature conditions using Lewis acid catalysts in aprotic solvents.[11]



(2)

Presumably the rearrangement proceeds through a concerted mechanism without a carbonium ion intermediate, since elimination of the leaving group in concert with the 1,2-shift (S_N2-type mechanism) would lead to stereospecific inversion of the configuration.

In previous papers[12,13] we have proposed that, with some substrates, the pinacol rearrangement does not proceed by the stepwise mechanism via a carbonium ion intermediate, because our gas-phase calculations using *ab initio* methods have shown that the β-hydroxy carbonium ion cannot exist as a stable intermediate for the systems studied. Although the experimental and theoretical results seem to agree well, they do not eliminate the possibility that the stepwise mechanism may still occur when the reactions are conducted in ionizing solvents.

In addition to the difficulty in controlling stereoselectivity, problems also arise in the control of group migration. Various studies on the relative migratory aptitudes in the pinacol rearrangement were conducted during the period 1920–1960.[14,15] In general, the relative migratory tendency of aryl > alkenyl >

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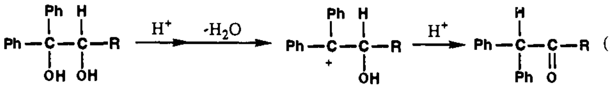
hydride > alkyl is observed. Reaction rates for various alkyl groups[1,15,16] and substituted aryl groups have been studied thoroughly.[17,18]

It is, however, difficult to define a general migratory aptitude of a specific group, because the stability of the transition state depends not only on the activity of the migrating group but also on the electronic and/or steric effects of the nonmigrating substituents. For example, the phenyl group possesses a high migratory aptitude, but also has the ability to stabilize a neighboring cation center. In the case of 1,1-diphenylethanediol, hydride migration from unsubstituted carbon predominates over the phenyl migration because formation of a highly stabilized cation from dehydration of the diphenyl-substituted carbon is accelerated.[19]



(3)

There have been some theoretical studies of nucleophilic rearrangements of carbonium ions using semiempirical or *ab initio* molecular orbital calculations with minimal basis sets.[20] These provided good information on the migratory aptitude.

In this paper, we would like to analyze the reaction mechanism of the pinacol rearrangement theoretically from the viewpoints of (a) intermediacy of the carbonium ion and (b) migratory aptitude. In the gas phase, some carbonium ion intermediates were found to be unstable in our previous report,[12] but some conjugative substituents, such as aryl and alkenyl, may stabilize cationic intermediates and enhance the stepwise mechanism. In such cases, our studies will determine whether the concerted mechanism still predominates, and provide essential information on the mechanism of the reaction. Although solvent is not included in this study, careful analysis of our results should help interpret experiments in the gas phase and nonpolar solvents, and form a foundation for a theoretical study of solvated system. Our study will also provide clear information of the migratory aptitudes of various substituents, such as aryl, vinyl, or cyclopropyl, which are known to have high migratory aptitudes. We will also discuss the origin of such high migratory tendencies on the basis of *ab initio* molecular orbital theory.

Computational Procedure

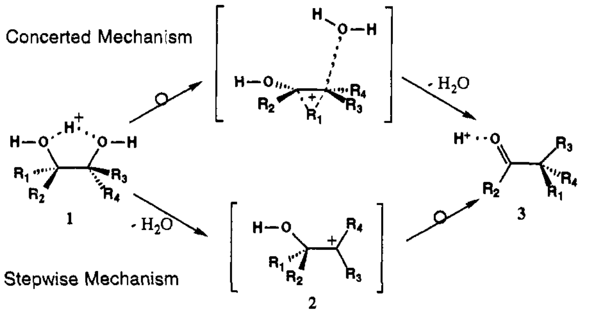
The geometries of reactants, monosubstituted protonated 1,2-ethanediols, products, and transition states were optimized with the restricted Hartree–Fock method using the analytical gradient procedure of the GAUSSIAN 82 program.[21] All geometrical parameters shown in the present paper were optimized by using the 6-31G basis set. The geometries of some possible stereoisomers and/or conformers for some species were optimized with the STO-3G basis set in order to confirm the structures are global minima. Each stationary point was characterized by harmonic frequency calculations with analytical second derivatives. All the relative energies cited in the text were obtained by the MP2/6-31G* single-point energy calculations at the RHF/6-31G geometries. We have shown in the previous papers[12,13] that geometries obtained at the RHF/6-31G level are close enough to those obtained at higher levels.

In order to confirm that the nondynamic electron correlation effect is not important in the system we have studied, MCSCF methods were employed for the parent and the mono-methyl-substituted systems. The CAS SCF calculation has been carried out for the transition state of methyl migration. The active space (five-orbital six-electron) consisted of the lone pair of the hydroxy oxygen and bonding and antibonding orbitals associated with the breaking and forming bonds. The MCSCF wave function is calculated to consist 95% of the main electron configuration. The energy barrier for methyl migration was calculated to be 26.6 kcal/mol using the CI method involving all single and double excitations with the 6-31G* basis set, while a value of 26.3 kcal/mol was obtained with the MP2 method. In this respect, we may safely conclude that the nondynamic electron correlation is not very important in the present systems.

Since dynamic correlation depends on geometrical crowding,[22] we have evaluated the relative energies by using the MP2 method with the 6-31G* basis set. The difference in energy barriers between RHF/6-31G and MP2/6-31G* methods has been found to be less than 3 kcal/mol. For the parent system, activation energies of concerted hydride shift were calculated to be 23.6 and 26.3 kcal/mol, at RHF/6-31G and MP2/6-31G*//RHF/6-31G, respectively.

Results and Discussion

There are two possible pathways for the pinacol rearrangement. One is the stepwise mechanism via a carbonium ion intermediate, and the other is the concerted mechanism where migration and elimination occur simultaneously.



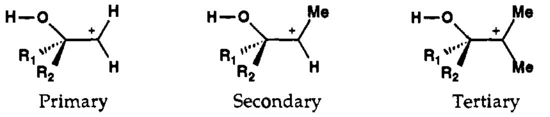
(4)

In the stepwise mechanism, β-hydroxy carbonium ion **2** has a finite lifetime as an intermediate formed by dehydration of the protonated diol.

The preference for one of these two possible mechanisms would be determined by the feasibility of carbonium ion formation. In this study, we will compare the relative energies between the carbonium ion intermediates in the stepwise mechanism and the transition states of the concerted mechanism in order to examine which mechanism is favored. In addition, we will calculate the differences of activation energies with various substituents and migrating groups, which will allow us to determine the migratory aptitude of each group.

Although our calculations involve H_2O as a leaving group, the protonated diols are considered to be a model system which represents the reactants with various active leaving groups such as OMs and OTs with Lewis acid catalysis or N_2^+ under deamination conditions (NH_2 with nitrous acid).

I. Stepwise Mechanism. In our previous paper,[13] we found that primary and secondary alkyl-substituted β-hydroxy carbonium ions are unstable and spontaneously rearrange to products in the gas phase. In such cases, the stepwise mechanism cannot occur unless solvation stabilizes the β-hydroxy carbonium ion intermediate.



Primary Secondary Tertiary (5)

Although the tertiary β-hydroxy carbonium ion was found to be stable, a survey of the potential energy surfaces for both the stepwise and the concerted mechanisms shows that the latter is still energetically favored.[13] In determining the proper mechanism of rearrangement, substituent effects are important, since β-hy-

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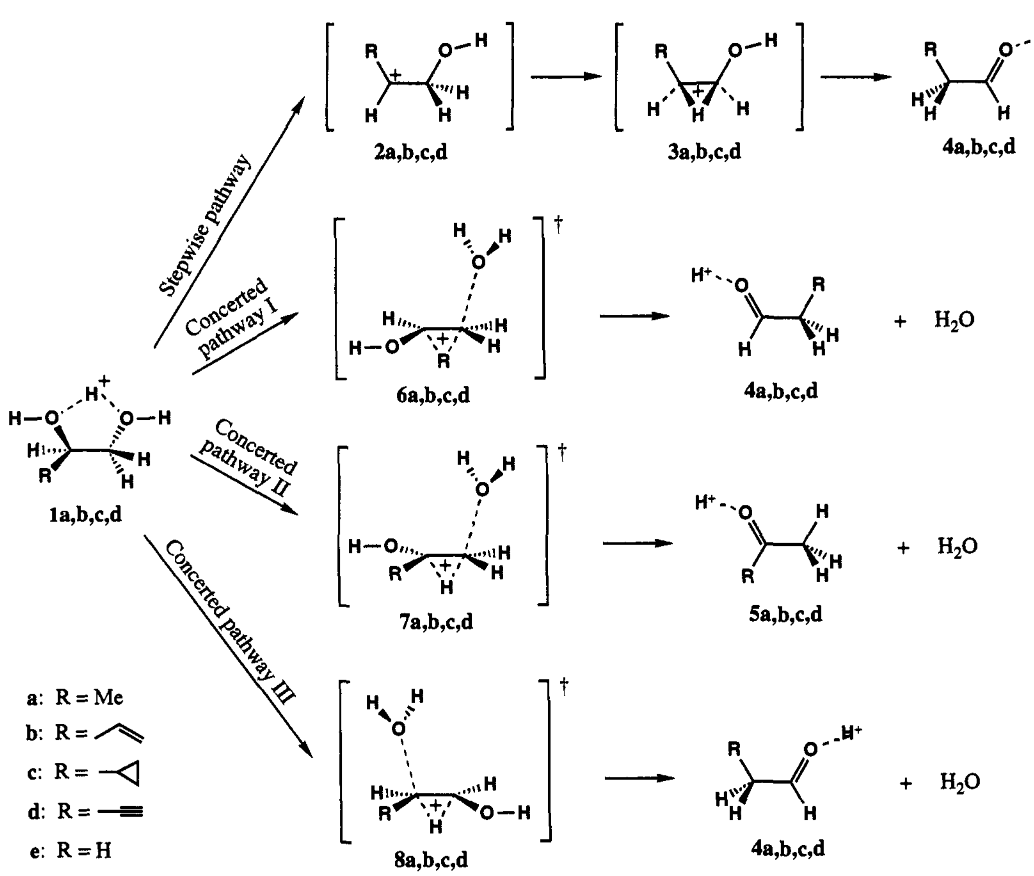
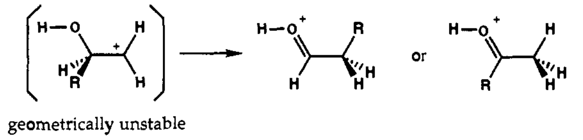


Figure 1. Four possible pathways for the pinacol rearrangement of monosubstituted protonated diols **1**.

droxy carbonium ions are expected to be substantially stabilized by substituents such as vinyl and aryl groups.

Figure 1 shows the rearrangement pathways of monosubstituted 1,2-ethanediols considered in the present study. In this case, dehydration is favored on the substituted carbon because the carbonium ion produced is stabilized by electron delocalization from the substituent. Even if a β-hydroxy carbonium ion was formed by the dehydration from the unsubstituted carbon, the cation formed is unstable and would spontaneously give the rearranged product.



(6)

Due to this result, we have considered only one stepwise rearrangement pathway, i.e., hydride shift from the unsubstituted carbon, as illustrated in Figure 1.

Figure 2 shows the optimized geometries of the methyl-, vinyl-, cyclopropyl-, and ethynyl-substituted β-hydroxy carbonium ions **2a–d**. The structures of the transition states of the hydride 1,2-shift from these (**3a–d**) and the rearrangement products (**4a–d**) are also depicted in Figure 2.

The energies of the cation intermediates **2** formed from the protonated diols **1** shown in Figure 2 indicate the large stabilization of the cation center by vinyl and cyclopropyl groups. The formation energy of vinyl-substituted carbonium ion **2b** was calculated to be 19.5 kcal/mol, a much smaller value compared to that of the methyl-substituted cation (44.1 kcal/mol). The two C–C bond lengths of the vinyl moiety have identical (1.365 Å) values expected for an allyl cation C–C bond length, indicating the cation center is well delocalized. The cyclopropyl group also stabilizes the cation **2c**, evident in the small formation energy (17.4 kcal/mol). Cation stabilization by the electron delocalization is also reflected in the geometry. The cyclopropyl group in this cation species (**2c**) has relatively long C–C bonds (1.631 Å), while the distance between the cation center and the cyclopropyl group is short (1.364 Å). The alkynyl group is less effective (35.3 kcal/mol) in stabilizing the carbonium ion **2d** than either the vinyl or cyclopropyl group, despite the fact that π-electron delocalization is possible with this group. The two C–C bond lengths of the ethynyl moiety of **2d** are 1.214 and 1.351 Å, which indicate a magnitude of electron delocalization similar to those of the vinyl and cyclopropyl cations.

The activation energies of the transition states **3** of the 1,2-hydride shift correlate with the energies of formation of the carbonium ions **2**. However, the relative energies of these transition states from the carbonium ion intermediates (shown with italic characters) are in reverse order. This is due to the fact that conjugative stabilization has more effect on carbonium ions than on transition states. This keeps the overall activation energy of the stepwise mechanism high, even when the cation center is substituted by a conjugative group.

II. Concerted Mechanisms. Concerted reaction mechanisms considered in this paper are also illustrated in Figure 1. There are three possible pathways (I–III) for the concerted 1,2-shift reactions of monosubstituted 1,2-ethanediol **1**, in addition to the stepwise mechanism discussed in the previous section. These are the migration of the substituent R (concerted path I), migration of the hydride from the substituted carbon (concerted path II), and migration of the hydride from the unsubstituted carbon (concerted path III). We optimized the geometries of the transition states of the rearrangement in concert with the dehydration, and of the products of each pathway. As is discussed in the previous section, for paths I and II, a corresponding stepwise mechanism is not possible in the gas phase, since the primary and secondary β-hydroxy carbonium ions do not exist as stable intermediates.[12,13] The pathway of the stepwise mechanism discussed in the previous section corresponds to path III of the concerted mechanism.

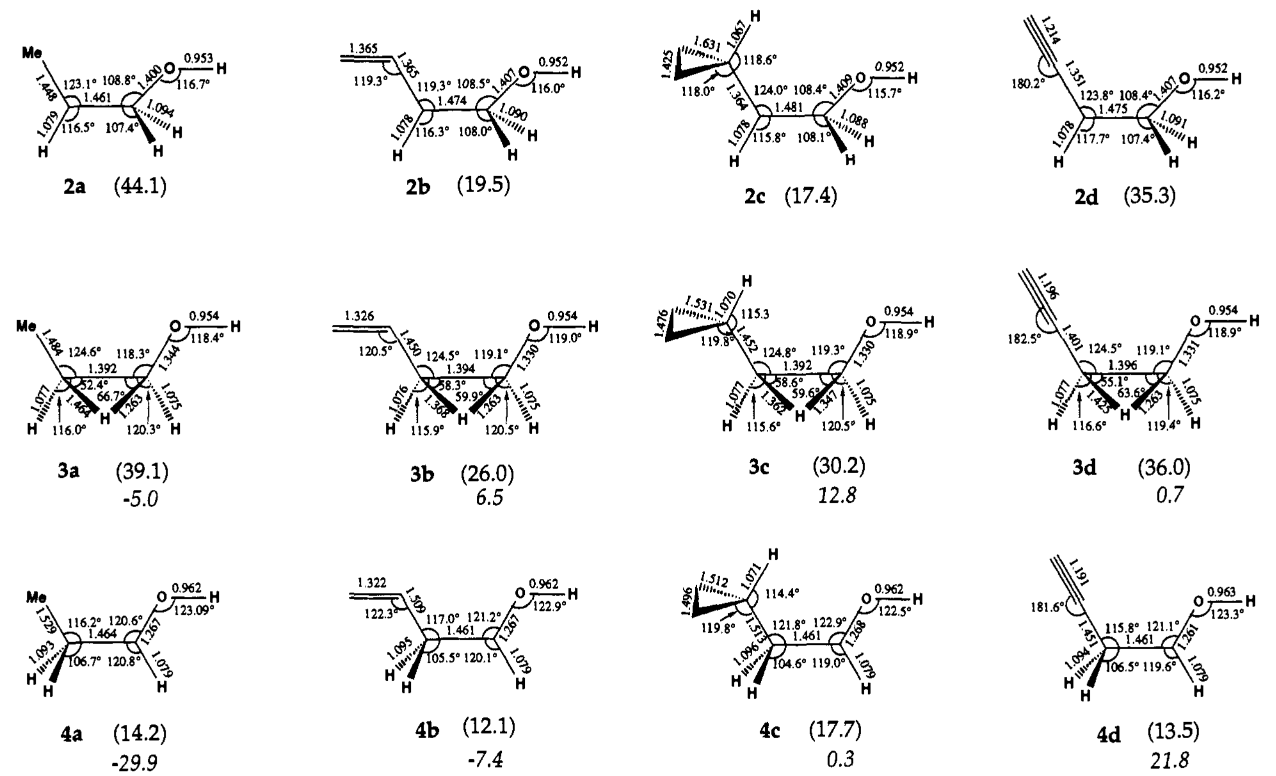

2a (44.1)
2b (19.5)
2c (17.4)
2d (35.3)
3a (39.1) *-5.0*
3b (26.0) *6.5*
3c (30.2) *12.8*
3d (36.0) *0.7*
4a (14.2) *-29.9*
4b (12.1) *-7.4*
4c (17.7) *0.3*
4d (13.5) *21.8*

Figure 2. Optimized structures of the cation intermediates **2**, the transition states for 1,2-hydride shifts **3**, and the protonated aldehydes **4** as products. The values in parentheses are the sums of energies with a water molecule relative to the reactants **1**, and italic values are relative energies compared to the cation intermediate **2** in kcal/mol (MP2/6-31G*//RHF/6-31G).

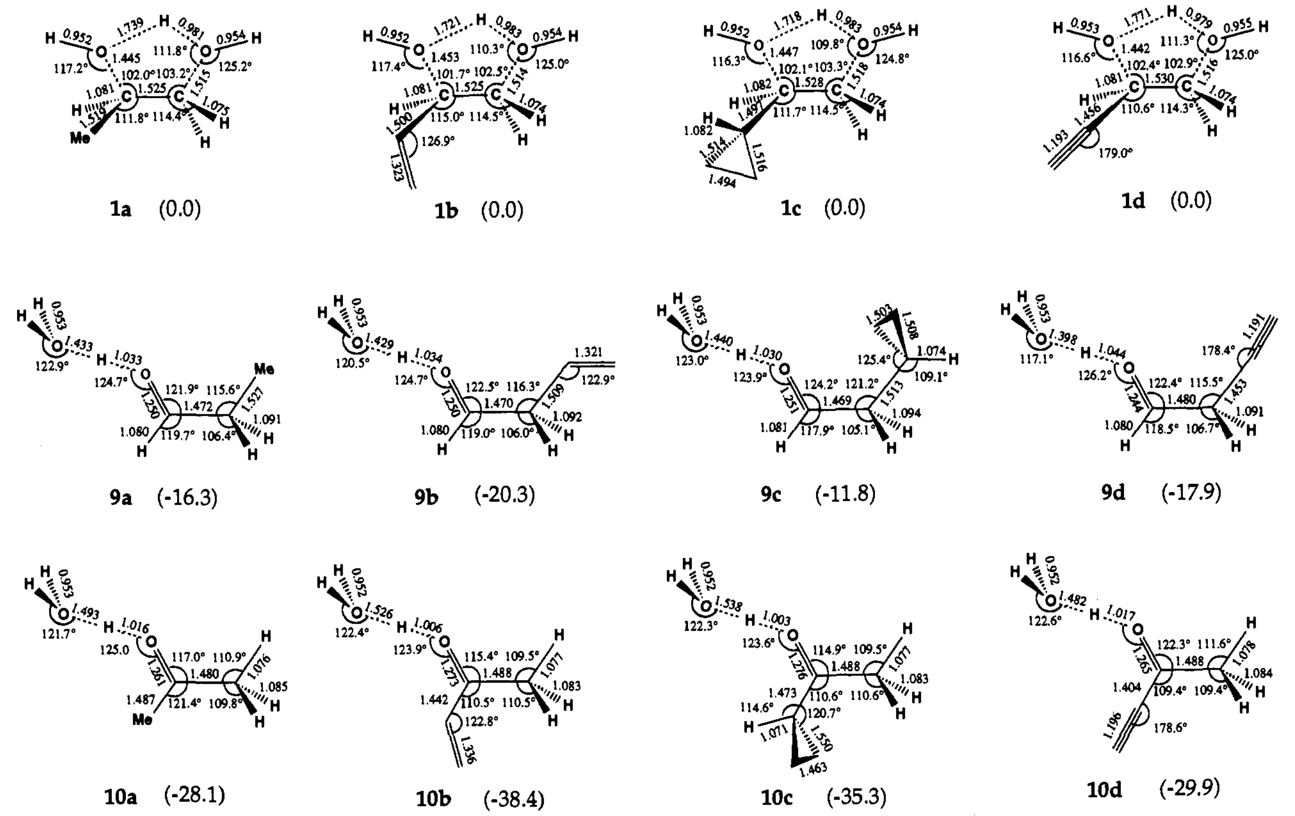
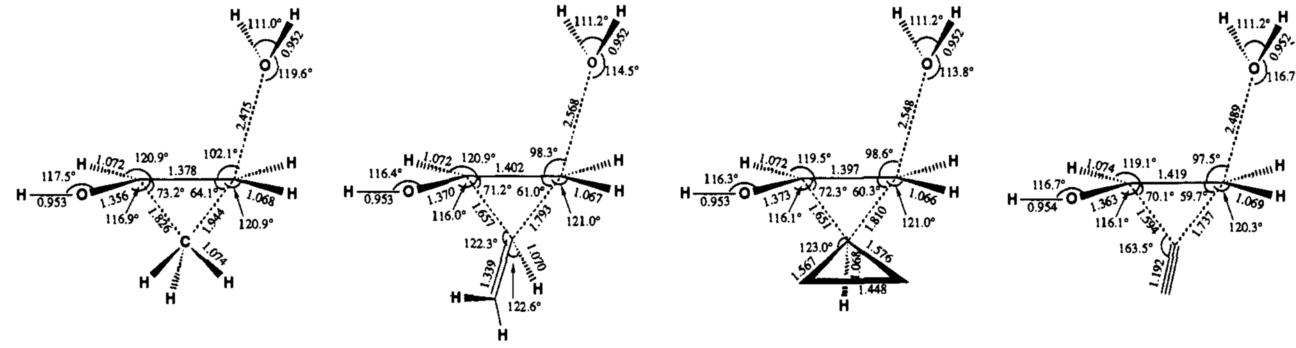

1a (0.0)
1b (0.0)
1c (0.0)
1d (0.0)
9a (-16.3)
9b (-20.3)
9c (-11.8)
9d (-17.9)
10a (-28.1)
10b (-38.4)
10c (-35.3)
10d (-29.9)

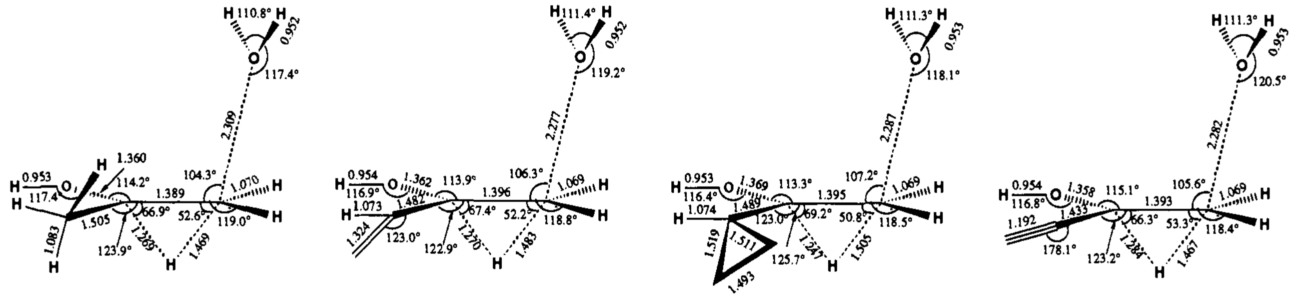
Figure 3. Optimized structures of methyl-, vinyl-, cyclopropyl-, and ethynyl-substituted protonated 1,2-ethanediols (**1**) and their rearranged products **9** and **10**. The values in parentheses are the energies relative to the reactants **1** in kcal/mol (MP2/6-31G*//RHF/6-31G).

All of these reaction pathways are considered for methyl- (**a**), vinyl- (**b**), cyclopropyl- (**c**), and ethynyl- (**d**) substituted protonated 1,2-ethanediols **1**. The optimized geometries of the reactants **1a–d** are illustrated in Figure 3. Products of the unimolecular rearrangements are the protonated aldehydes **4** and the protonated ketones **5** shown in Figure 2. The combined energies of these products with a water molecule are higher than those of the reactants, protonated 1,2-ethanediols **1**. This endothermicity might be due to the fact that the proton has two hydrogen bonds with hydroxy groups in the reactant, while the protonated carbonyl



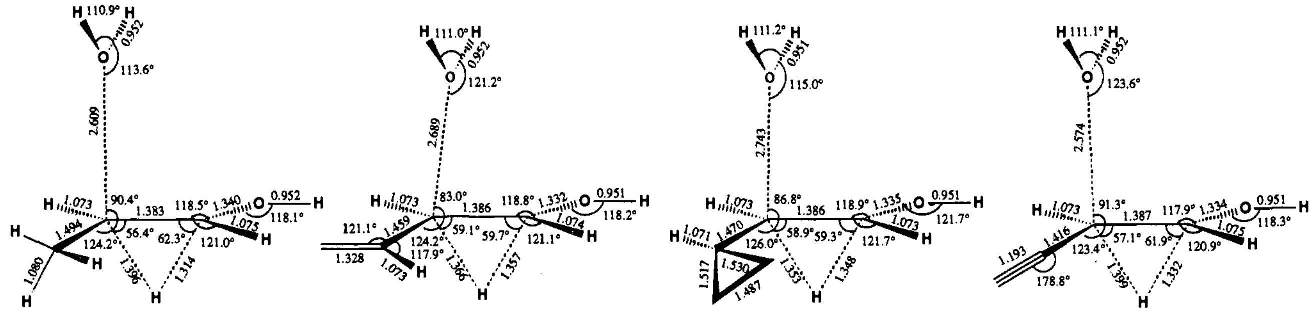
6a (26.3) **6b** (10.2) **6c** (17.0) **6d** (20.7)

Figure 4. Calculated geometries of the transition states **6** of the concerted pinacol rearrangement through path I. The values in parentheses are the energies relative to the reactants **1** in kcal/mol (MP2/6-31G*//RHF/6-31G).



7a (25.6) **7b** (21.4) **7c** (25.9) **7d** (26.8)

Figure 5. Calculated geometries of the transition states **7** for the concerted pinacol rearrangement through path II. The values in parentheses are the energies relative to the reactants **1** in kcal/mol (MP2/6-31G*//RHF/6-31G).



8a (23.2) **8b** (15.5) **8c** (21.3) **8d** (22.8)

Figure 6. Calculated geometries of the transition states **8** for the concerted pinacol rearrangement through path III. The values in parentheses are the energies relative to the reactants **1** in kcal/mol (MP2/6-31G*//RHF/6-31G).

products have only one hydrogen bond. In considering this unimolecular reaction mechanism, the elimination of H_2O destabilizes the entire system. In this respect, the product might be more stabilized by solvation after the dehydration. We have also optimized the most stable geometries of the protonated aldehyde or ketone **9** or **10** as products solvated by a water molecule in order to estimate the overall reaction energies. These structures are also given in Figure 3.

The structures of the transition states for each concerted reaction pathway are shown in Figures 4–6. We will discuss each case in more detail in the following sections.

1. Alkyl Group. First, we considered a methyl substituent as an example of an alkyl group.[13] In this case, the reactant is protonated 1,2-propanediol (**1a**). As shown in Figure 3, the product **9a** via path I or III is less stable than **10a** through path II, because aldehyde species are generally less stable than the corresponding ketone isomers. This suggests that path II would be thermodynamically predominant over paths I and III. The activation energies, however, cannot be predicted from the stability of the products, and most of the reaction pathways at low temperature are determined kinetically by the stability of the transition state.

Figure 7 summarizes the energy diagrams of the alkyl-substituted systems for all possible concerted pathways I–III along with the stepwise pathway. The lowest activation energy (23.2 kcal/mol) is found for path III, which involves a hydride shift from the unsubstituted carbon. The reason for this comes from stabilization of the cationic carbon through hyperconjugation from the methyl group. Path II is 2.4 kcal/mol higher in energy (25.6 kcal/mol), while methyl migration (path I) is found to be most energetically unfavorable (26.3 kcal/mol). These results are in agreement with experimental findings in which reactions of mono-alkyl-substituted diols usually give the products by hydride shifts.

It is possible to estimate the relative migratory aptitude between hydride and a methyl group by comparing the activation energy between the 1,2-hydride shift of the parent protonated ethylene glycol (**1e**) and methyl migration of this methyl-substituted diol. The activation energy of the 1,2-hydride shift of the parent system was calculated to be 26.3 kcal/mol (MP2/6-31G*//RHF/6-

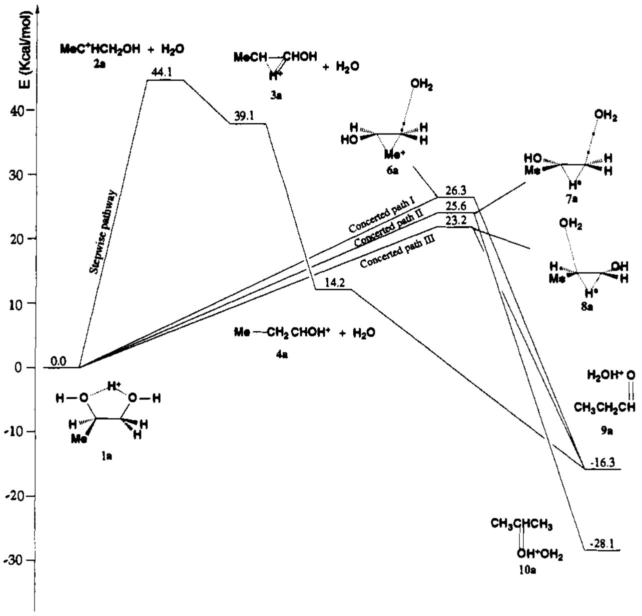


Figure 7. Schematic energy diagram of the pinacol rearrangement of the protonated 1,2-propanediol (**1a**) (MP2/6-31G*//RHF/6-31G).

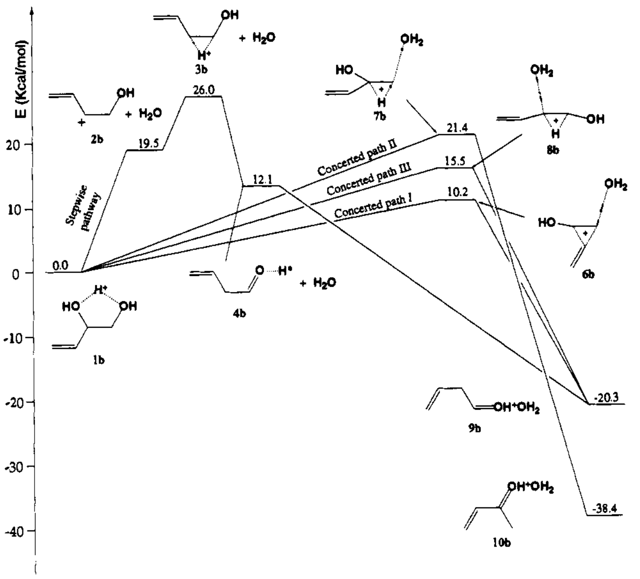
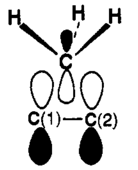


Figure 8. Schematic energy diagram of the pinacol rearrangement of the protonated 1-butene-3,4-diol (**1b**) (MP2/6-31G*//RHF/6-31G).

31G), an identical value to the activation energy of the methyl shift calculated at the same level. While this result may be a coincidence, it is possible that the intrinsic migratory aptitudes of a hydride and a methyl group are almost identical. The smaller activation energies of the hydride shift for paths II (25.6 kcal/mol) and III (23.2 kcal/mol) compared to that of the parent system (26.3 kcal/mol) show the stabilizing effects of the nonmigrating methyl group at the transition states **7a** and **8a**. Although alkyl groups stabilize the transition state of a 1,2-shift more effectively as nonmigrating substituents rather than as migrating groups, the migration of the alkyl group is experimentally observed with tetrasubstituted diols such as pinacol itself or in the case where the conformation of the reactant is constrained to allow only alkyl migration.

As shown in Figure 4, the geometry of the transition state of methyl migration **6a** suggests a two-electron three-centered structure where an sp^3 orbital of the migrating methyl group bridges over the π-orbital of the C(1)–C(2) bond, which is similar to the structure of the corner-protonated cyclopropane or nonclassical carbocations.



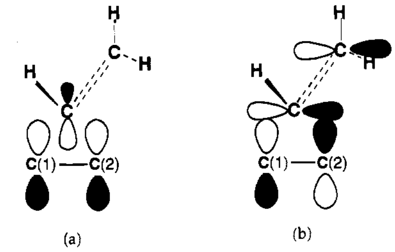
(7)

It should be noted that the C(1)–C(2) bond length in the transition state (1.378 Å) is much shorter than that in both the reactant (1.525 Å) and the product (1.464 Å), because of this three-center bond.

2. Alkenyl Group. Both the alkenyl and the aryl groups are known to possess high migratory aptitudes. The vinyl-substituted system was studied as a representative of alkenyl- and aryl-substituted systems, because the aryl group is too large to treat with *ab initio* MO calculations and the most important character of these groups is their π-orbital nature. It should be noted, however, that these groups also conjugatively stabilize the neighboring cation. This enhances the migration of other substituents.

Figure 8 summarizes the energy diagrams of the reaction pathways of the vinyl-substituted protonated 1,2-ethanediol **1b**. As shown in this figure, the activation energy for vinyl migration (path I) is found to be the lowest among all pathways. The activation energy of path I (10.2 kcal/mol) is significantly smaller than that of the concerted 1,2-shift of the methyl group and the 1,2-hydride shift of the parent protonated 1,2-ethanediol (26.3 kcal/mol). These differences show the high migratory aptitude of the vinyl group compared to that of a methyl group or a hydride.

The transition state of the vinyl migration also involves mainly the two-electron three-center structure as discussed for the methyl migration (8a). Electron delocalization to the π^*-orbital of the C(1)–C(2) bond from the π-orbital of the migrating vinyl group contributes to the extra stabilization in the transition state, as shown below (8b).

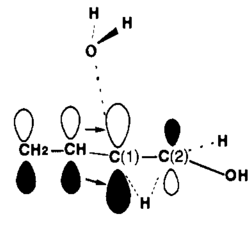


(a) (b)

(8)

This situation can be clearly seen in the transition-state geometry of vinyl migration. The longer C(1)–C(2) bond distance in the transition state of vinyl migration (**6b**, 1.402 Å) compared to that of the methyl migration (**6a**, 1.378 Å) indicates donation from the π-orbital of the vinyl group to the π^*-orbital of C(1)–C(2).

The activation energy of path III is also calculated to be lower (15.5 kcal/mol) than that of the 1,2-hydride shift in the parent system (26.3 kcal/mol). This can be rationalized by the fact that the cationic carbon (C(1)) center produced by dehydration is stabilized through conjugation with π-orbital of the neighboring vinyl group as follows:



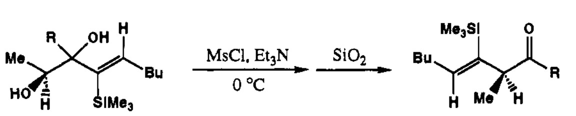
(9)

In this case, vinyl migration (path I) is preferred over the hydride shift (path III) by 5.3 kcal/mol. However, these values may reverse when one carbon atom is substituted with two alkenyl groups, since two geminal substituents can better stabilize the cationic center. An experimental example is found in the case of 1,1-diphenylethanediol, as was discussed in the introduction (see eq 3).[3,19]

The activation energy for path II (21.4 kcal/mol) is also lower than that of the 1,2-hydride shift of the parent system (26.3 kcal/mol), which indicates that the vinyl group at this position can also stabilize the transition state.

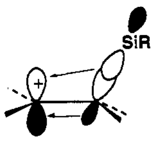
The course of rearrangement may be difficult to predict for multifunctional diols, but it is possible to control the direction of rearrangement in actual syntheses by replacing hydroxide with a more reactive leaving group, such as mesylate or tosylate. Collins et al.[5] used deamination in nitrous acid for this specific purpose. These methods simplify the situation such that the course of migration is determined only by the relative migratory aptitude of two groups on the hydroxy-substituted carbon atom. Steric repulsion is also an important factor in determining the selectivity of the migration.

Suzuki and co-workers reported that silyl substitution enhances the migratory aptitude of the vinyl group.[11c]



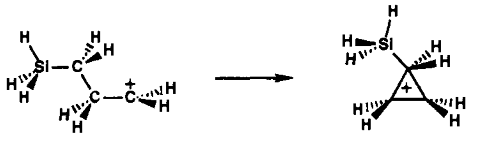
(10)

In this case, the silyl-substituted vinyl group migrates even without a Lewis acid catalyst, which has been required in other cases.[11] They proposed that migration is accelerated by the β-cation stabilization effect of the silyl group. It is known that the silyl group generally stabilizes the cationic center at the β-position.[23] This "β-effect" is due to the relatively strong character of electron donation from the C–Si σ-bonding orbital into the vacant π-orbital on the cationic center, as illustrated below:



(11)

In the case of the vinyl migration in eq 10, one should note that stabilization at the transition state is different from the normal β-effect, since no overlap exists between the cationic π^*-orbital and the C–Si bond (13). Davidson and co-workers have reported that the lowest energy structure of $H_3SiCH_2CH_2CH_2^+$ (eq 12)



(12)

is calculated to be a three-membered ring.[24] The similarity of this stable cyclic structure to the transition-state structure of the silyl group migration can rationalize the large enhancement of the pinacol rearrangement by silyl substitution on the migrating group.

Acceleration of migration by silyl substitution occurs as a result of electron delocalization from the C–Si bond into the two-electron three-centered cationic system to stabilize the positive center, as illustrated below:

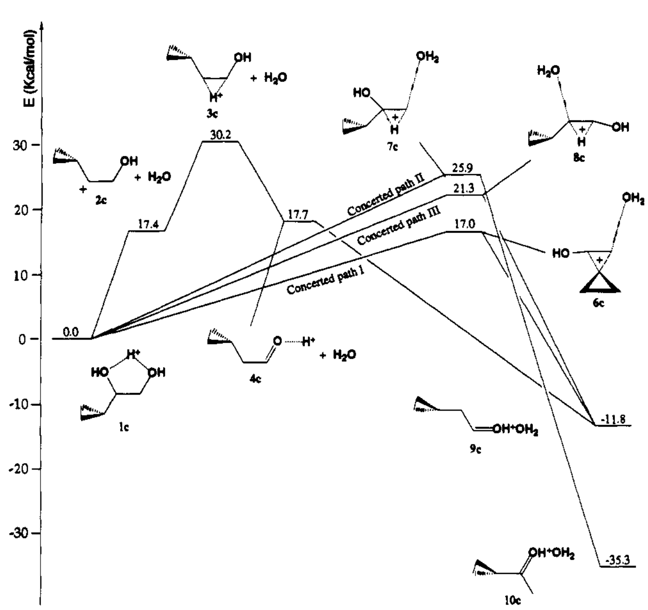
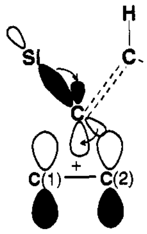


Figure 9. Schematic energy diagram of the pinacol rearrangement of the protonated 1-cyclopropyl-1,2-ethanediol (**1c**) (MP2/6-31G*//RHF/6-31G).



(13)

Since trimethylsilyl groups are used in experiments, steric interaction may also enhance the reactivity of substituted alkenyl groups. Elongation of the C(1)–C(2) bond at the transition state would relieve the steric repulsion greatly. Even though such a steric situation may be one of the reasons for the high migratory aptitude of the silyl-substituted vinyl group, the electronic effect of silyl substitution plays the most important role in accelerating the rearrangement.

3. Cyclopropyl Group. The cyclopropyl group possesses a high migratory aptitude.[25] Figure 9 shows the energy diagram for the rearrangement pathways of this group. The cyclopropyl migration (path I) was found to be the most favored among four possible pathways in Figure 9, an indication of its high migratory aptitude. The activation energy for migration of the cyclopropyl group (path I) from **1c** is 17.0 kcal/mol, considerably lower than that of methyl migration (26.3 kcal/mol). Path III was somewhat higher in energy at 21.3 kcal/mol, and path II was found to be highest in energy (25.9 kcal/mol) among the concerted pathways. This pattern is similar to that of the vinyl-substituted system.

Shono and co-workers explained the high migratory aptitude of the cyclopropyl group as delocalization of positive charge into the three-membered ring.[26] Theoretical calculations (Figure 4) clearly indicate the participation of a pseudo-π-orbital. The cyclopropyl group possesses highly strained C–C bonds whose σ-orbitals are projecting out of the three-membered-ring skeleton.

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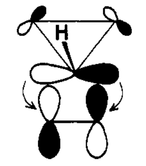
[23] (a) Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496. (b) Lambert, J. B.; Wang, G. T.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838. (c) White, J. C.; Cave, R. J.; Davidson, E. R. *J. Am. Chem. Soc.* **1988**, *110*, 6308.

[24] Davidson, E. R.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 3135.

[25] (a) Shimazaki, M.; Hara, H.; Suzuki, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1987**, *28*, 5891. (b) Shimazaki, M.; Hara, H.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 5443. (c) Shimazaki, M.; Hara, H.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 5447. (d) Shimazaki, M.; Morimoto, M.; Suzuki, K. *Tetrahedron Lett.* **1990**, *31*, 3335.

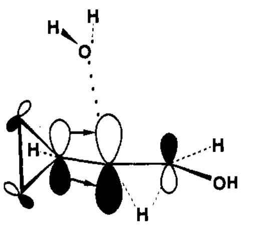
[26] Shono, T.; Fujita, K.; Kumai, S.; Watanabe, T.; Nishiguchi, I. *Tetrahedron Lett.* **1972**, 3249.

These pseudo-π-orbitals can take part in stabilizing the transition state as well as the π-orbital in the migration of alkenyl and aryl groups.[25]



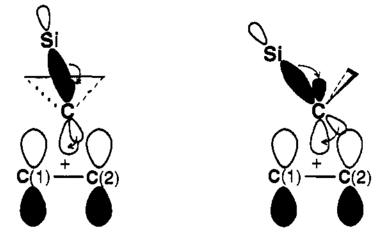
(14)

The relatively low activation energy of the hydride shift in path III (21.3 kcal/mol) compared to that of the parent system (26.3 kcal/mol) suggests electron donation from the pseudo-π-orbital of the cyclopropyl group to the cationic carbon.



(15)

It is known that the migratory aptitude of the cyclopropyl group can be enhanced by silyl substitution.[25b] As in the case of vinyl migration, electron donation from the Si–C σ-orbital into the two-electron three-center orbital results in stabilization of the transition state as shown below.



(16)

(a) perpendicular form (b) parallel form

Although the γ-effect of the silyl group works most effectively in the parallel form of the transition state shown in the structure above (16b), the pseudo-π-orbital of the cyclopropyl does not overlap with the π*-orbital of the C(1)–C(2) bond in this arrangement. In the perpendicular structure (16a), both the pseudo-π-orbital and the C–Si σ-bonding orbital have good overlap to stabilize the two-electron three-center structure. Consequently, the transition state is likely to be the perpendicular form. The relatively high migratory aptitude of the cyclopropyl group as compared to hydride and alkyl groups, which comes as a result of pseudo-π-orbital participation, is reproduced by our results.

4. Alkynyl Group. Speculating from the high migratory aptitude of the alkenyl, aryl, and cyclopropyl groups, the alkynyl group is expected to show a high migratory aptitude, since it also possesses π-orbitals. Experimentally, however, the alkynyl group is known to migrate less easily than the alkenyl group, after requiring conformational restriction for selective migration. The relatively low migratory aptitude of this group can be utilized to obtain the product in which the alkynyl group is the nonmigrating group.[27]

As shown in Figure 10, the activation energies of all pathways I–III are calculated to be larger than 20 kcal/mol. The activation energy of the ethynyl shift is larger than that of the vinyl migration by 10.5 kcal/mol. Since the level of π-orbital participation for alkynyl and alkenyl groups should be similar, the large difference in activation energies seems to derive from the stability of the two-electron three-centered systems. Compared to the alkenyl system, the alkynyl group requires more energy to form a two-electron three-centered structure due to its larger s character from sp hybridization.

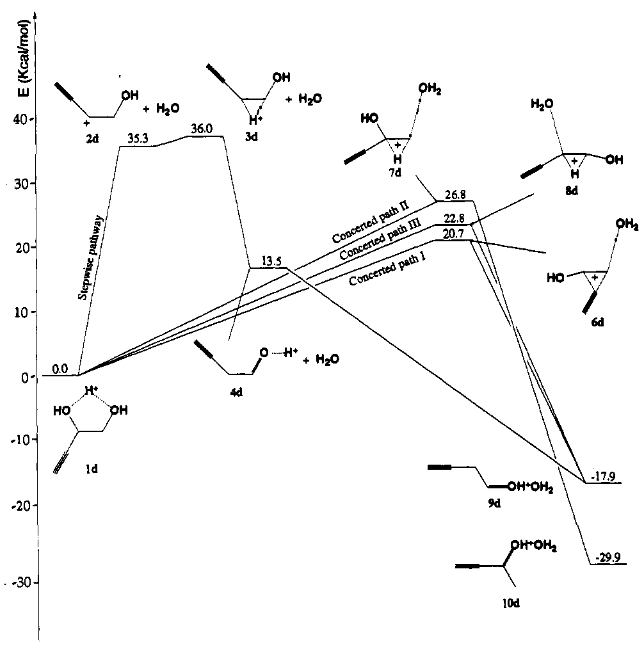


Figure 10. Schematic energy diagram of the pinacol rearrangement of the protonated 1-butyne-3,4-diol (**1d**) (MP2/6-31G*//RHF/6-31G).

The stability of such a two-electron three-centered system is related to the stability of the migrating group as a cation. Cation stability follows the order $H^+ > R^+ > H_2C{=}C^+H > HC{\equiv}C^+$; hence, the low migratory aptitude of alkynyl groups comes as a result of their instability in forming cations. The relatively high activation energies of hydride shifts (26.8 and 22.8 kcal/mol for paths II and III, respectively) for the alkynyl-substituted diol also reveals the poor ability of this group to stabilize adjacent cationic centers.

III. Comparison of the Stepwise Mechanism and the Concerted Mechanism. In our previous paper,[13] we had concluded that the concerted rearrangement mechanism is superior for the reactions of various methyl-substituted diols in the gas phase. As is shown in Figure 7, formation of the secondary cation intermediate **2a** in a stepwise pathway by the dehydration of protonated 1,2-propanediol requires 44.1 kcal/mol. Once the carbonium ion is formed, the intermediate easily isomerizes to the protonated aldehyde **4a** without activation energy. On the other hand, all energy barriers for the concerted mechanisms are calculated to be less than 30 kcal/mol. Note that the activation energy of concerted path III is 21 kcal/mol less than the energy to produce the cation intermediate **2a** in the corresponding stepwise pathway.

Stabilization of the cation intermediate occurs with vinyl, cyclopropyl, or ethynyl groups as substituents, while lowering the dehydration energy in the process. As shown in Figures 8–10, the energies required for the dehydration of the protonated diols by vinyl, cyclopropyl, and ethynyl substituents are calculated to be 19.5, 17.4, and 35.3 kcal/mol, respectively. Even though the β-hydroxy carbonium ions are produced as a stable intermediate, activation energies for the subsequent rearrangement via the stepwise pathway become large, since the stabilized intermediate requires extra activation energy for the 1,2-shift. Consequently, the total activation energy of the stepwise mechanism is calculated to be higher than those of any other concerted pathways (path I–III) for all substituents considered here.

While experimental evidence in the gas and solid phases has shown the stepwise mechanism to be less favored,[28,29] intermediacy of a substituted β-hydroxy carbonium ion in polar solutions remains controversial. Our computational efforts were successful

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[27] Suzuki, K.; Ohkuma, T.; Miyazawa, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1986**, *27*, 373.

in reproducing the experimental results carried out in an aprotic solvent (CH_2Cl_2), where stereospecific products are obtained. However there are experiments in polar protic solvents which support the possible existence of a β-hydroxy carbonium ion with a short lifetime. Our theoretical results do not exclude the possibility of the stepwise mechanism in ionizing solvents, but the mechanism should be reconsidered and reexamined both from experimental and theoretical points of view.

The report that deamination of a β-amino alcohol[5] gives partial racemization of the product has been considered as evidence for the stepwise mechanism of the pinacol rearrangement in water. We propose an alternative explanation for the observed racemization. As shown in Figure 3, the two hydroxy groups of the reactant adopt the cis form, since it allows internal hydrogen bonding. This conformation should predominate in the gas phase or in nonpolar solvents. However in polar solvents the reactant diol may also adopt a trans conformation so that each hydroxy group can interact with solvent molecules. This makes the racemization possible even with consideration of the concerted mechanism.

Pocker and Ronald have reported that the epoxide intermediate is also involved in the course of the pinacol rearrangement using multiaromatic functionalized glycols in polar solution.[30] This is one of the most clear cases, utilizing careful kinetic analysis, where the stepwise mechanism takes place.

Concluding Remarks

We have studied the reaction mechanism of pinacol rearrangement by developing a theoretical model involving the fundamental reaction system in the gas phase. The importance of a stepwise mechanism depends on the stability of the carbonium ion intermediates. When a methyl, vinyl, cyclopropyl, or ethynyl group is introduced into the diol as a substituent, dehydration of the protonated diol is facilitated through stabilization of the resulting carbonium ion. On the other hand, the activation energy for the subsequent 1,2-shift increases as the carbonium ion intermediate is stabilized. Consequently, the overall activation energy for the stepwise mechanism is found to be higher than that for the concerted mechanism in all cases examined here. The calculated values of the activation energies are 10–25 kcal/mol for concerted pathways and over 25 kcal/mol for stepwise mechanisms. The present findings are in good agreement with experimental results for pinacol-type reactions in nonpolar solution, as well as the reactions in the gas phase. It also provides a foundation for further theoretical investigations which may include solvation effects, an important factor when discussing the reaction mechanism of an ionic system.

Each potential energy surface for the pinacol rearrangement provides information about the migratory aptitude of the various substituents. The activation energy of the 1,2-shift of the vinyl group is shown to be the lowest among the substituents we have studied. The structure of the transition state **6b** clearly indicates the π-orbital participation, as shown in Figure 4. The cyclopropyl group also stabilizes the transition state **6c** by a pseudo-π-type participation, which is similar to the π-orbital participation of the vinyl group. The activation energies for the rearrangement of the hydride, methyl, vinyl, cyclopropyl, and ethynyl groups are calculated to be 26.3, 26.3, 10.2, 17.0, and 20.7 kcal/mol, respectively. These values represent the qualitative relative migratory aptitudes of these groups.

The results obtained in this study provide information not only on the intrinsic nature of the reaction mechanism but also on the relative migratory aptitudes of various substituents. Although it was not discussed in this paper, the migratory aptitudes of other alkyl groups (ethyl, *tert*-butyl, etc.) would also be of interest.

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