Alcoholysis of *N*-Methyl-1,2-Thiazetidine-1,1-Dioxide: DFT Study of Water and Alcohol Effects

Maoxia He, Dacheng Feng,* Feng Zhu, and Zhengting Cai

Institute of Theoretical Chemistry, Shandong University, Jinan 250100, People's Republic of China

Received: April 13, 2004; In Final Form: June 29, 2004

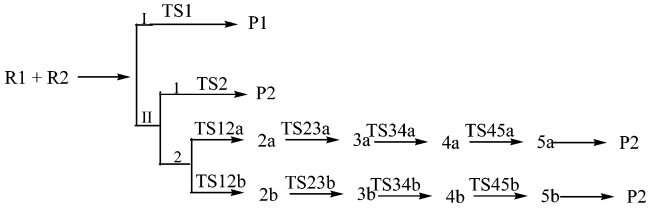
The effects of water and alcohol on the alcoholysis mechanisms of *N*-methyl-1,2-thiazetidine-1,1-dioxide and the differences of these effects have been studied using the Density Functional Theory (DFT) method at the B3LYP/6-31G* level. The results have been compared with a nonassisted study carried out previously. The results show that the water- and alcohol-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide reduces the active energy greatly compared to the nonassisted reaction. The most favored pathway for alcoholysis of 1,2-thiazetidine-1,1-dioxides is pathway a of the stepwise reaction. The orientation of attack of CH_3OH on S1 is from the more hindered side of the S1. The energy barrier of the cleavage of the C−S bond and producing *N*-methyl-*N*-ethyl-amino-methyl sulfonate (P1) is the highest among all of reaction pathways, and this may be the possible reason of having no experimental evidence on the formation of product P1. The results also show that reactions that are alcohol-assisted have a little higher energy barrier than one under water-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide.

1. Introduction

It is known that the 1,2-thiazetidine-1,1-dioxides (β-sultams) ring is much more reactive than the β-lactam ring.[1] β-Sultams are the sulfonyl analogues of β-lactam antibiotics or the cyclized compounds of taurine. It is appropriate to readily study sulfonyl transfer reactions,[1] which are of interest because of the potential use of sulfonyl compounds as sulfonating agents of serine proteases[2] and the use of sulfonamides as peptide mimics.[3] They are also of mechanistic interest for comparison with the analogous acyl transfer processes.[4] All these make it interesting to study the reactivity and mechanisms of reactions of β-sultams with nucleophiles. Page and co-workers have done many studies from experiments on the reactivity and reaction mechanism for β-sultams.[5−9] Within this scope, we have presented in previous works theoretical studies of nonassisted alcoholysis of 1,2-thiazetidine-1,1-dioxides as models of biological hydrolysis of β-sultams.[10, 11]

The nonassisted alcoholysis mechanism of *N*-methyl-1,2-thiazetidine-1,1-dioxide (R1) can be shown in Scheme 1.[11] There are two reaction channels in this reaction. Channel I is the cleavage of bond C−S and produces the product *N*-methyl-*N*-ethyl-amino-methyl sulfonate (P1) in which the attack of CH_3-OH and the breaking of bond C−S are concerted. Channel II is the cleavage of bond S−N, which leads to the product 2-(*N*-methyl) taurine methyl ester (P2) in which there are two reaction modes with two different mechanisms: concerted and stepwise. In the first one, the reactant complex directly leads to the product P2 through a single transition structure. In this transition structure, the methoxy OCH_3 and the atom H in CH_3OH attack the S1 atom and the N2 atom on the ring of β-sultam, respectively, while the bond between S1 and N2 breaks. The nucleophilic attack and the cleavage of S1−N2 occur simultaneously. In the second one, the reaction takes place via two steps. The first step is the proton transfer from CH_3OH toward the sulfonyl oxygen to form an intermediate, and the second step is proton transfer from sulfonyl oxygen to N and the ring opening. According to the orientation of nucleophilic attacking of CH_3OH on S1, there are two pathways: pathway a and pathway b. The most favored pathway for alcoholysis of 1,2-thiazetidine 1,1-dioxides was the reaction pathway a of the stepwise mechanism.

SCHEME 1



In our previous study, solvent effects were also considered by means of a polarizable continuum model, giving rise to only small changes in the reaction mechanisms.[10] However, one may expect specific solvent effects to play a role in the proton-transfer steps through a bifunctional catalysis mechanism and lead to an obvious diminution of the energy barriers. The water molecule acts as both proton donor and proton acceptor and serves as a bridge for proton relay, participating in the reaction processes. In the case of β-lactam hydrolysis, such an assisted mechanism has been also considered,[12−14] and the results show again an important catalytic effect.

In this paper, we report a theoretical chemical study of water and alcohol assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide. Water and alcohol act as both proton donor and proton acceptor participating in the reaction processes.

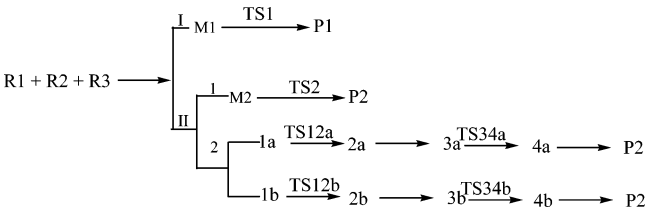
2. Computational Methods

The geometries of reactants, products, and transition states were fully optimized by using density functional theory (DFT) with Becke's three-parameter hybrid exchange functional and the Lee−Yang−Parr correlation functional (B3LYP)[15] with the

* Corresponding author. Fax: +86 531 8564464. E-mail: fdc@sdu.edu.cn.

10.1021/jp048374s CCC: $27.50
Published on Web 08/21/2004

SCHEME 2



6-31G* basis set. Every conformer was further characterized by the harmonic vibrational frequencies at the B3LYP/6-31G* level to determine the nature of these stationary points and to calculate the zero-point vibrational energy (ZPVE). The number of imaginary frequencies (0 or 1) confirms whether a bound minimum or a transition state has been located. Single-point energy calculations with the B3LYP/ 6-311+G* basis set are made at the 6-31G* optimized geometry. The basis set superposition error (BSSE) correction[16] has been used with B3LYP/6-311+G* to estimate the error levels for all the energies. DFT/B3LYP calculations on these selected structures are performed thoroughly because the hybrid methods of DFT can give very similar structural parameters, as compared to those from MP2.[10,11]

Partial IRC calculations were performed, and it was found that the trends are correct, which ensures that the minima correspond to the transition states found.

The energies emerging in this paper include the ZPVE or are otherwise specified specially. Calculations have been carried out with the Gaussian 98 package of programs.[17]

3. Results and Discussion

R1 (*N*-methyl-1,2-thiazetidine-1,1-dioxide), R2 (CH_3OH), and R3 (H_2O or CH_3OH) were selected as the reactants, and it was the zero point of all the reactions. The exploration of water- and alcohol-assisted alcoholysis of R1 renders two possible channels for both processes (see Scheme 2). The first channel corresponds to the concerted nucleophilic attack of the CH_3OH to the S1 atom, and H in CH_3OH is removed by the solvent (H_2O or CH_3OH), from which in turn a proton is transferred to the C4 atom with the simultaneous rupture of the ring R1 that produces the P1. Channel II is the cleavage of bond S−N and produces the product P2 in which there are two reaction modes with two different mechanisms. The first one is similar to channel I; the differences are that the proton is transferred to the N4 atom and producs the P2. In the second one, the reaction takes place via two steps. The first step is the nucleophilic attack of CH_3OH toward the sulfonyl and sulfonyl oxygen to form an intermediate, and the second step is proton transfer from the sulfonyl oxygen to N, and the ring opening is facilitated by the catalytic H_2O or CH_3OH. According to the orientation of nucleophilic attack of CH_3O on S1, there are two pathways: pathway a and b.

In this paper, the prefix Hy- means the structure of water-assisted system, and Al- means the structure of the alcohol-assisted system.

3.1. Water-Assisted Alcoholysis. Figure 1 shows the optimized structures for the water-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide, together with the atomic numbering used in the calculations and some selected geometric parameters. The total energies, relative energies, zero-point vibrational energies (ZPVE), and the decreased values between nonassisted and assisted reactions are summarized in Table 1. The energy profiles are shown in Figure 2.

HyM1, HyM2, Hy1a, and Hy1b in Figure 1 are the prereactive complexes in which the methanol and water interact with one of the oxygen atoms of R1 through a strong H-bond. They are stabilized by 78.6, 69.7, 79.1, and 77.5 kJ/mol with respect to the separate reactants, respectively.

3.1.1. Cleavage of S−N Bond and Producing HyP2. Channel II in Scheme 1 represents the cleavage of N−S bond and producing HyP2. There are two reaction modes in this channel: mode 1 and mode 2. Mode 1 proceeds via a concerted mechanism, and mode 2 proceeds via stepwise a mechanism. There is only one pathway in mode 1, while there are two pathways (pathway a and b) in mode 2.

3.1.1.1. Reaction Mode 1—Concerted Reaction. HyTS2 is the transition state structure connecting with HyM2 and HyP2. In this structure, the methoxy groups OCH_3 in CH_3OH attack the S1 atom on the ring of R1, and the atom H14 approaches the O13 atom. At the same time, the H15 atom approaches the N2 atom. These processes occur simultaneously and lead to the bond between S1 and N2 breaking, which produces the end structure HyP2. In HyP2, H15 has been transferred to the N2 completely, the bond S1−N2 has opened, and the catalytic water links with the taurine ester. The relative energy of HyTS2 and HyP2 are 68.1 and −125.9 kJ/mol, respectively, about 85.3 and 24.0 kJ/mol lower than the nonwater-assisted system.

3.1.1.2. Reaction Mode 2—Stepwise Reaction. In this mode, the reaction proceeds via a stepwise mechanism, that is to say, the reaction takes place via two steps. The first step is the OCH_3, and H15 attacks S1 and O6, respectively, to form an intermediate, and the second step is the transferring of H13, and the bond S1−N2 breaks are mediated by one water molecule. There are two pathways according to the orientation of nucleophilicity of CH_3O on S1—pathway a and b.

3.1.1.2.a. Pathway a. HyTS12a is the transition state connecting with Hy1a and Hy2a. In this structure, the methoxy group OCH_3 in CH_3OH attacks the S1 atom on the ring of *N*-methyl-1,2-thiazetidine-1,1-dioxide, and the atom H14 approaches the O13 atom. At the same time, the H15 atom approaches the O6 atom. The H14 atom is located between O12 and O13 atom, and H15 is located between O13 and O6. The relative energy of HyTS12a is 58.7 kJ/mol, and the potential barrier is about 59.4 kJ/mol lower than that of the nonwater-assisted.

Hy2a is the direct structure of nucleophilic attack of the $HOCH_3$ on the ring, which can be transformed to Hy3a that is 5.5 kJ/mol more stable than Hy2a. In Hy3a, the hydrogen H15 is oriented toward the O13 atom, which can ease the transfer of H15 from O6 to O13 and complete the hydrogen transfer. The pathway, not detailed here, would be feasible for connecting the Hy2a with Hy3a passing through low barrier energies because they only involve internal rotations, pyramidal inversion of the N atom, relocation of the water molecule, etc.

The structure of Hy3a involves ring opening and hydrogen transfer from hydroxyl oxygen to β-sultam N. These two processes occur simultaneously. The transition state HyTS34a connects the intermediate Hy3a and the product Hy4a. In the transition state HyTS34a, the atom H15 is located between atom O6 and atom O13, and atom H14 is located between atom O13 and atom N2. The relative energies of HyTS34a are 52.9 kJ/mol, and the energy barrier is about 69.5 kJ/mol lower than the nonwater-assisted reaction.

The result of ring opening gives a product complex Hy4a, which can be transformed to HyP2 by conformation changes because of the rotatable bond S1−C4 and C3−N2. In the

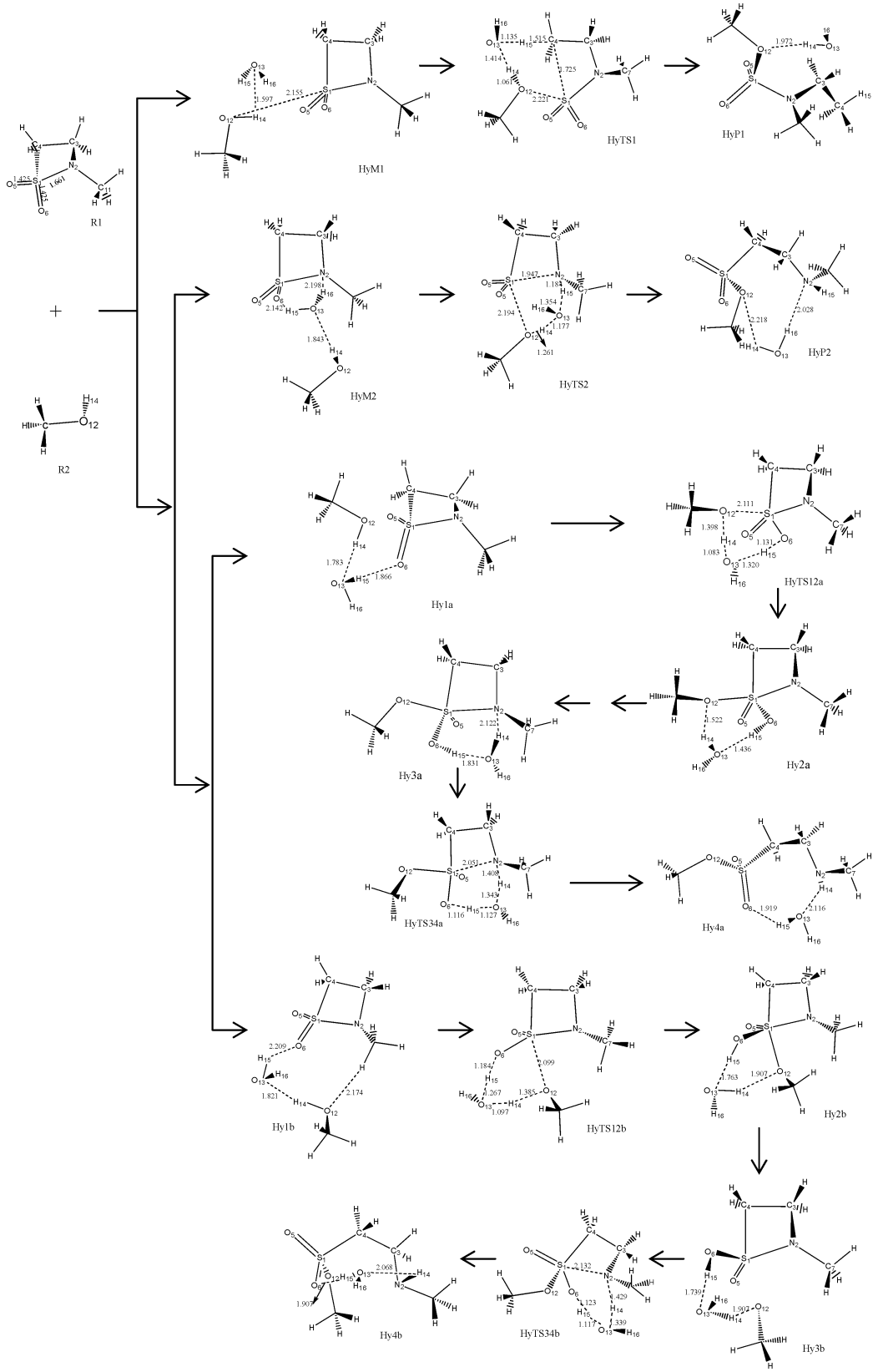


Figure 1. B3LYP/6-31G* optimized structures for the water-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide. Distances in angstroms.

structure of Hy4a, the bond S1−N2 has opened completely, and the catalytic water interacts with sulfonic ester through O6···H15O13 and O13···H14N2 with distances of 1.831 Å and 2.116 Å. The relative energy of Hy4a is −119.3 kJ/ mol.

3.1.1.2.b. Pathway b. Pathway b and pathway a have similar reaction mechanisms, but the orientation of the attack of CH_3-OH is different. In this way, the CH_3OH attacks S1 from the α-side of the *β*-sultam ring. HyTS12b is the transition state connecting with Hy1b and Hy2b. The relative energy of HyTS12b is 81.6 kJ/ mol, which is 21.9 kJ/mol greater than the HyTS12a and 38.2 kJ/mol lower than the nonwater-assisted reaction.

The attack of the $HOCH_3$ on the ring formed the intermediate Hy2b, which can be transformed to the structure of Hy3b that

TABLE 1: Energies, Relative Energies, and ZPVE for the H_2O-Assisted and Non-H_2O-Assisted Alcoholysis of *N*-Methyl-1,2-thiazetidine-1,1-dioxide (R1)

	ZPE	E^b	E^c	ΔE^d	E^e
R1 + R2 + R3[a]	0.18225	−3.94895(0/0)	−7.54233(0)		−4.13858(0.0)
HyM1	0.18919	−3.98551(−78.6/−96.1)			−4.16553(-52.5)
HyTS1	0.18036	−3.86985(202.8/207.5)	−7.44834(230.8)	−28.1	−4.05046(226.4)
HyP1	0.18901	−4.00067(−118.9/−135.9)	−7.58144(−94.9)		−4.06777(203.6)
HyM2	0.18935	−3.98228(−69.7/−87.6)			−4.16206(−42.9)
HyTS2	0.18439	−3.92501(68.1/62.7)	−7.48104(153.8)	−85.3	−4.10226(100.9)
HyP2	0.19027	−4.00453(−125.1/−146.1)	−7.57957(−88.4)		−4.18037(−84.9)
Hy1a	0.18876	−3.98525(−79.1/−95.4)			−4.16792(−59.9)
HyTS12a	0.18439	−3.92858(58.7/53.4)	−7.49530(118.5)	−59.4	−4.10569(91.9)
Hy2a	0.18897	−3.93259(59.7/42.8)	−7.50257(108.9)		−4.10962(93.7)
Hy3a	0.18964	−3.93534(54.2/35.6)	−7.50504(103.1)		−4.11067(92.7)
HyTS34a	0.18459	−3.93097(52.9/47.1)	−7.49356(122.9)	−69.5	−4.10519(93.8)
Hy4a	0.19167	−4.00337(−119.3/−143.1)	−7.57713(−82.6)		−4.18277(−94.9)
Hy1b	0.18911	−3.985(−77.5/−94.8)			−4.16394(−48.6)
HyTS12b	0.18503	−3.92048(81.6/74.6)	−7.49487(120.3)	−38.2	−4.09291(127.2)
Hy2b	0.18985	−3.93227(62.8/43.7)	−7.49915(118.7)		−4.10589(105.8)
Hy3b	0.18975	−3.93221(62.7/43.8)	−7.48003(166.8)		−4.10772(100.7)
HyTS34b	0.18379	−3.90802(111.2/107.3)	−7.47483(170.9)	−59.4	−4.08269(150.8)
Hy4b	0.19076	−4.00364(−122.3/−143.7)	−7.57582(−78.3)		−4.18213(−91.9)

[a] R3 is H_2O. [b] Values calculated by B3LYP/6-31G*: energy in Hatree, and the values of total energies should equal −910.0 au. Relative energies including ZPVE before slash and the relative energies after are without ZPVE in kJ/mol. [c] Values calculated by B3LYP/6-31G*: energy in Hatree, and the values of total energies should equal −830.0 au. Relative energies in parentheses in kJ/mol, which include ZPVE for the non-H_2O-assisted of the R1 (see ref 11). [d] The energy differences in kJ/mol between H_2O-assisted and non-H_2O-assisted alcoholysis of the R1. [e] Values calculated by B3LYP/6-311+G*: energy in Hatree, and the values of total energies should equal −910.0 au. Relative energies including ZPVE before slash and the relative energies after are without ZPVE in kJ/mol.

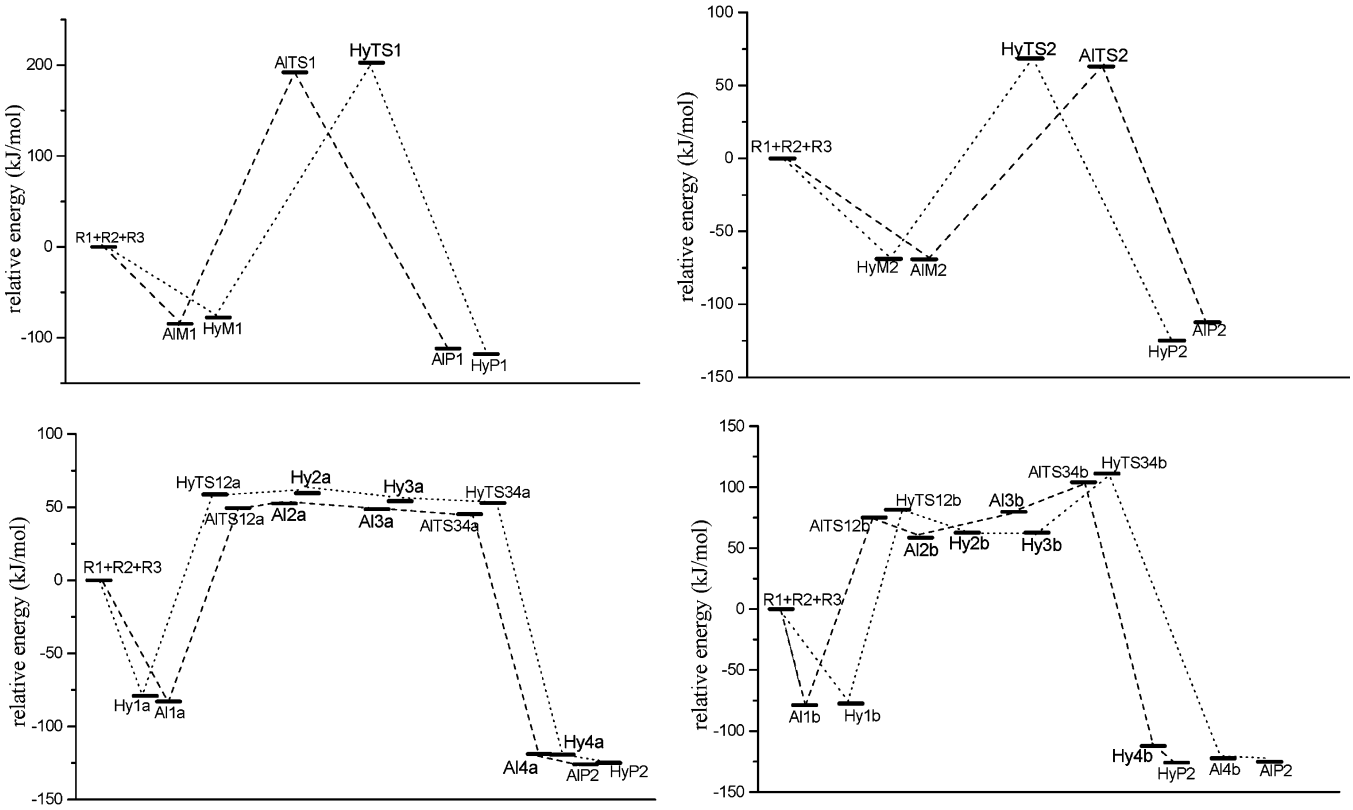


Figure 2. Energy profiles for the water and alcohol-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide.

is 0.1 kJ/mol lower than Hy2b. The most important idea is that the hydrogen H15 in Hy3b is oriented toward the O13 atom, which can ease the transfer of H15 from O6 to O13 and complete the hydrogen transfer. As well as Hy2a and Hy3a, the transformation of Hy2b and Hy3b would also be feasible.

The HyTS34b connects the intermediate Hy3b and the product Hy4b. HyTS34b involves ring opening and hydrogen transfer from the hydroxyl oxygen to the N atom N2. These two processes occur simultaneously. In this structure, the atom H15 is located between atom O6 and atom O13, and atom H14 is located between atom O13 and atom N2. The relative energies of HyTS34b are 111.2 kJ/mol, which is 58.3 kJ/mol greater than HyTS34a and about 59.4 kJ/mol lower than the nonwater-assisted.

The reaction product is Hy4b, which can be transformed to HyP2 by conformational change. In Hy4b, the bond S1−N2 has opened completely, and the catalytic water molecule interacts with sulfonic ester through O6···H15O13 and O13···

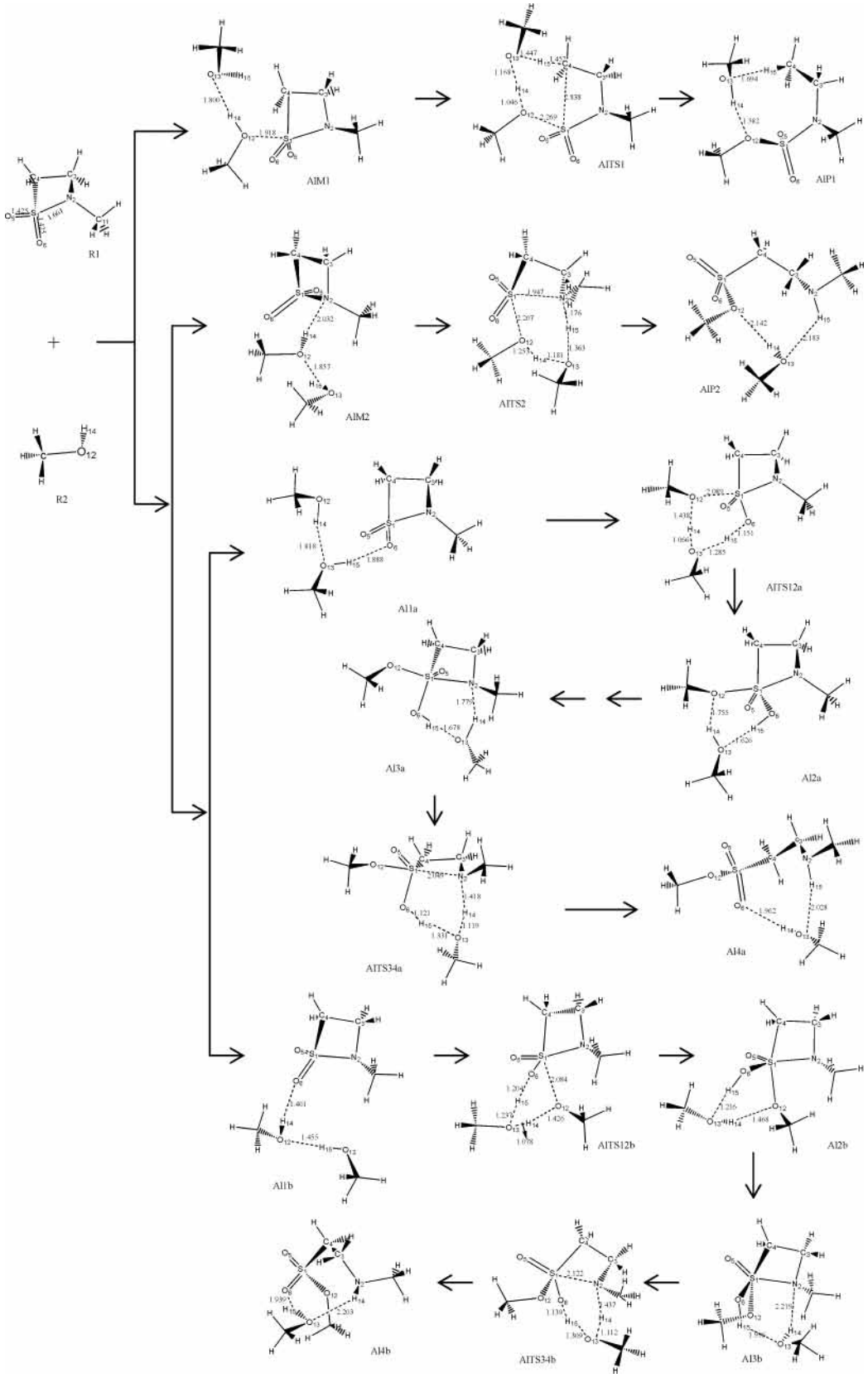


Figure 3. B3LYP/6-31G* optimized structures for the alcohol-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide. Distances in angstroms.

H14N2 with distances of 1.907 and 2.068 Å. The relative energy of Hy4b is −122.3 kJ/mol.

3.1.2. Cleavage of C−S Bond and Producing HyP1. HyTS1 is the transition state structure connecting with HyM1 and HyP1. In this structure, the methoxy group OCH_3 in CH_3OH attacks the S1 atom on the ring of β-sultam, and the atom H14 approaches the O13 atom. At the same time, the H15 atom approaches the C4 atom. These processes occur simultaneously and lead to the breaking of bond S1−C4, which produces the end structure HyP1. In this structure, H15 has been transferred to the C4 completely, and the bond S1−C4 has opened. The relative energy of HyTS1 and HyP1 are 202.8 and −118.9 kJ/

TABLE 2: Energies, Relative Energies. and ZPVE for the Alcohol-Assisted and Non-Alcohol-Assisted Alcoholysis of the *N*-Methyl-1,2-thiazetidine-1,1-dioxide (R1)

	ZPE	E^b	E^c	ΔE^d	E^e
R1+R2+R3[a]	0.2119	−3.25210(0/0)	−7.54233(0)		−3.44877(0.0)
AlM1	0.21794	−3.29010(−84.5/−99.8)			−3.47698(−58.8)
AlTS1	0.20834	−3.17556(191.9/200.9)	−7.44834(230.8)	-39.2	−3.36036(223.2)
AlP1	0.21854	−3.30112(−111.9/−128.7)	−7.58144(-94.9)		−3.44476(27.3)
AlM2	0.21816	−3.28445(−69.1/−84.9)			−3.4703(−40.8)
AlTS2	0.21227	−3.22844(63.1/62.1)	−7.48104(153.8)	−90.7	−3.41115(99.7)
AlP2	0.21954	−3.30739(−125.9/−145.2)	−7.57957(−88.4)		−3.48548(−78.5)
Al1a	0.21801	−3.28955(−82.9/−98.3)			−3.47487(−53.1)
AlTS12a	0.21329	−3.23464(49.4/45.8)	−7.49530(118.5)	−68.9	−3.41573(90.3)
Al2a	0.21821	−3.23813(52.6/36.7)	−7.50257(108.9)		−3.41903(93.9)
Al3a	0.21839	−3.23975(48.8/32.4)	−7.50504(103.1)		−3.41915(94.1)
AlTS34a	0.21293	−3.23588(45.2/42.6)	−7.49356(122.9)	−77.6	−3.41443(92.7)
Al4a	0.21919	−3.30438(−118.9/−137.3)	−7.57713(−82.6)		−3.48657(−80.9)
Al1b	0.21801	−3.28793(−78.7/−94.1)			−3.47471(−52.7)
AlTS12b	0.21342	−3.22492(75.2/71.4)	−7.49487(120.3)	−44.9	−3.40332(123.2)
Al2b	0.21897	−3.23659(58.6/40.7)	−7.49915(118.7)		−3.41603(103.8)
Al3b	0.21691	−3.22651(79.8/67.2)	−7.48003(166.8)		−3.40810(119.4)
AlTS34b	0.21174	−3.21228(104.1/104.5)	−7.47483(170.9)	−66.7	−3.39159(149.7)
Al4b	0.21901	−3.30168(−112.2/−130.2)	−7.57582(−78.3)		−3.49056(−90.5)

[a] R3 is CH_3OH. [b] Values calculated by B3LYP/6-31G*: energy in Hatree, and the values of total energies should equal −950.0 au. Relative energies including ZPVE before slash and the relative energies after are without ZPVE in kJ/mol, for the CH_3OH-assisted of R1. [c] Values calculated by B3LYP/6-31G*:energy in Hatree, and the values of total energies should equal −830.0 au. Relative energies in parentheses in kJ/mol, which include ZPVE for the non-CH_3OH-assisted of R1 (see ref 11). [d] Energy differences in kJ/mol between CH_3OH-assisted and non-CH_3OH-assisted reaction of R1. [e] Values calculated by B3LYP/6-311+g*: energy in Hatree, and the values of total energies should equal −950.0 au. Relative energies including ZPVE before slash and the relative energies after are without ZPVE in kJ/mol.

mol, respectively. The decrease value of HyTS1 is 28.1 kJ/mol as compared to the nonwater-assisted system.

From the previous results we can see that the most favored pathway for water-assisted alcoholysis reaction is pathway a in mode 2 of channel II. The energy barrier of the cleavage of C−S bond and producing HyP1 is the highest among them. We think that this may be the possible reason of having no experimental evidence on the formation of product HyP1.

Compared to the systems of nonwater-assisted, the preliminary bonds and bond angles have little differences. However, the energy barriers reduce obviously (Table 1), from which we can see that the participation of water can diminish the energy barrier of the reactions for alcoholysis of *N*-methyl β-sultam obviously.

3.2. Alcohol-Assisted Alcoholysis. The exploration of the alcohol-assisted reaction between R1 and alcohol gave comparability to the previously mentioned water-assisted reaction.

Figure 3 shows the optimized geometries of structures along with the reaction paths, together with the atomic numbering used in the calculations and some selected geometric parameters. The total energies, relative energies, zero-point vibrational energies (ZPVE), and the decreased values between nonassisted and assisted reactions are summarized in Table 2. The energy profiles of the whole reaction are shown in Figure 2.

As already mentioned, the analogous reaction mechanism has been found for the alcohol-assisted reaction. Corresponding to the system of water-assisted reaction, in this reaction, all the structures are similar besides the H_2O having been replaced by CH_3OH.

As in the water-assisted reaction, AlM1, AlM2, Al1a, and Al1b in Figure 3 are the prereactive complexes in which the methanol interacts with one of the oxygen atoms of R1 through a strong H-bond. They are stabilized by 84.5, 69.1, 82.9, and 78.7 kJ/mol with respect to the separate reactants, respectively.

AlTS2 in Figure 3 is the transition state for mode 1 of channel II. The relative energy of AlTS2 is 63.1 kJ/mol. This energy barrier is 90.7 kJ/mol lower than the corresponding values for the nonassisted reaction. The corresponding product of this reaction is the structure of AlP2 in Figure 3, which is 37.5 kJ/mol more stable than that for the nonassisted reaction.

AlTS12a is the transition state connecting with prereactive complex Al1a and the intermediates Al2a. As in the water-assisted reaction, Al2a can be transformed to be Al3a through the conformation. Finally, Al3a gives the product 4a through AlTS34a. The relative energies of AlTS12a and AlTS34a are 49.4 and 45.2 kJ/mol, respectively, which are about 68.9 and 77.6 kJ/mol lower than those for the nonassisted system.

Pathway b and pathway a have similar reaction mechanisms, but the orientation of the attack of CH_3OH on S1 is different. AlTS12b connects Al1b and Al2b, which can be transformed to Al3b. The relative energy of AlTS12b is 75.2 kJ/mol, which is about 44.9 kJ/mol lower than that of the nonassisted reaction.

The AlTS34b connects the intermediate Al3b and the product Al4b. The relative energy of AlTS34b is 104.1 kJ/mol, which is about 66.7 kJ/mol lower than that of the nonassisted system.

AlTS1 is the transition state for channel I. The relative energy of AlTS1 is 191.9 kJ/mol. This energy barrier is 39.2 kJ/mol lower than the corresponding values for the nonassisted reaction. The corresponding product of this reaction is the structure of AlP1 in Figure 3.

As was stated previously, compared with the systems of the nonassisted reaction, the preliminary bonds and bond angles have little differences. However, the energy barriers also have obvious decreases (Table 1), from which we also can see the phenomena that the participation of alcohol can diminish the energy barrier of the reactions for alcoholysis of *N*-methyl β-sultam.

3.3. Comparisons of Water and Alcohol Effects. The reaction mechanisms have no changes under both conditions. The most favored pathway for the reaction is still pathway a. The energy barrier of the cleavage of the C−S bond and producing P1 is the highest among them. The results also show that the reaction under the alcohol-assisted reaction has higher energy barriers than one under water-assisted alcoholysis of *N*-methyl β-sultam.

3.4. Effects of Basis Set. To evaluate the basis set effects on the reaction, the single-point energy calculations with the 6-311+G* are made at the 6−31G*-optimized geometry. The relative energies are shown in Tables 1 and 2. The results show that no BSSE corrections are included in the aforementioned calculations of the relative energies because they are minor and would not affect our conclusions qualitatively. The basis set has no effect on the reaction mechanism in both cases.

4. Conclusion

In this work, water- and alcohol-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide has been investigated at the B3LYP/6-31G* level of theory. The following conclusions can be drawn from this work:

(1) the water- and alcohol-assisted alcoholysis mechanisms are similar with the nonwater and alcohol-assisted ones.

(2) The water and alcohol-assisted alcoholysis of *N*-methyl 1,2-thiazetidine-1,1-dioxide reduces the activation energy greatly as compared with nonwater- or nonalcohol-assisted reaction; thus, the calculations in solution must include the reaction of the participation of water or alcohol.

(3) The most favored pathway of reaction is still pathway a of mode 2 in channel II. The energy barrier of the cleavage of C−S bond and producing P1 is the highest among them.

(4) The alcohol-assisted reaction has a little higher energy barrier than the water-assisted alcoholysis of *N*-methyl-1,2-thiazetidine-1,1-dioxide.

Acknowledgment. This work was supported financially by the National Nature Science Foundation of China (20173032, 20373034) and a Ph.D. Special Research Foundation of Chinese Education Department.

References and Notes

(1) Baxter, N. J.; Rigoreau, L. J. M.; Laws, A. P.; Page, M. I. *J. Am. Chem. Soc.* **2000**, *122*, 3375.

(2) Baxter, N. J.; Laws, A. P.; Rigoreau, L. J. M.; Page, M. I. *Chem. Commun.* **1999**, 2401.

(3) Beardsell, M.; Hinchliffe, P. S.; Page, M. I. *Chem. Commun.* **2001**, 497.

(4) Wood, J. M.; Hinchliff, P. S.; Laws, A. P.; Page, M. I. *J. Chem. Soc., Perkin Trans. 2* **2002**, 938.

(5) Page, M. I.; Laws, A. P. *Tetrahedron* **2000**, *56*, 5631.

(6) Hinchliff, P. S.; Wood, J. M.; Davis, A. M.; Austin, R. P.; Beckett, R. P.; Page, M. I. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2503.

(7) Hinchliff, P. S.; Wood, J. M.; Davis, A. M.; Austin, R. P.; Beckett, R. P.; Page, M. I. *Org. Biomol. Chem.* **2003**, *1*, 67.

(8) Wood, J. M.; Hinchliff, P. S.; Davis, A. M.; Austin, R. P.; Page, M. I. *Chem. Commun.* **2002**, 772.

(9) Baxter, N. J.; Laws, A. P.; Rigoueau, L.; Page, M. I. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2245.

(10) He, M. X.; Zhu, F.; Feng, D. C.; Cai, Z. T. *Chem. Phys. Lett.* **2003**, *377*, 13.

(11) He, M. X.; Zhu, F.; Feng, D. C.; Cai, Z. T. *J. Mol. Struct. (THEOCHEM)* **2004**, *674*, 199.

(12) Pitarch, J.; Ruiz-Lopez, M. F.; Silla, E.; Pascual-Ahuir, J. L.; Tunon, I. *J. Am. Chem. Soc.* **1998**, *120*, 2146.

(13) Diaz, N.; Suarez, D.; Sordo, T. L.; Tunon, I.; Silla, E. *Chem.—Eur. J.* **2002**, *8*, 859.

(14) Diaz, N.; Suarez, D.; Sordo, T. L.; Tunon, I. *J. Am. Chem. Soc.* **2000**, *122*, 6710.

(15) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (c) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(16) Boys, S. F.; Bermardi, F. *Mol. Phys.* **1970**, *19*, 53.

(17) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Z akrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Oritz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98W*; Gaussian, Inc.: Pittsburgh, PA, 1998.