Theoretical Study of Mechanism of 2,3-Dihydro-1,5-benzodiazepin-2-ones Hydrazinolysis

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Density functional theory approach was used for the 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one compound to determine the mechanism of hydrazinolysis of 4-substituted 2,3-dihydro-1,5-benzodiazepin-2-ones. Single point computations at the MP2/6-311+G(d,p)//B3LYP/6-31G(d) level were performed for the more precise energy prediction. The solvent effect was taken into account by carrying out single point calculations using the PCM methodology. The obtained results show that in the investigating mechanism the first step consists of the hydrazine molecule addition to the azomethine bond of the 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one. Further cyclization occurs with pyrazole ring formation, and then the diazepine ring opening is revealed. Finally, removal of *o*-phenylendiamine leads to 3-methylpyrazolone-5 as a main product that is in agreement with the experimental observation. The final step is a rate-determining step of this reaction.

Introduction

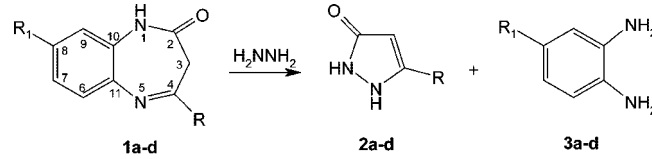
The increasing interest in the chemistry of 1,5-benzodiazepin-2-ones (**1**) is caused by their well-established biological activity.[1−5] Among the representatives of this class, there are compounds with anticonvulsant, tranquilizer, and antihypoxic actions. During investigations of the 1,5-benzodiazepin-2-ones transformations, many interesting aspects of their reactivity related to different rearrangements and isomerizations were revealed.[6−9] The clarification of mechanism of these reactions is important for theoretical studies and also for possible applications of these species.

It is known that interaction of 2,3-dihydro-1,5-benzodiazepin-2-ones with bifunctional nucleophilic reagents (hydrazine hydrate, phenylhydrazine, hydroxylamine, benzoyl hydrazine) leads to rearrangement with opening of the seven-membered diazepinone ring.[6−9] An application of these reactions facilitates synthesis of new heterocyclic systems. Mechanisms of these rearrangements have been proposed in some articles on the basis of experimental studies,[6−9] but theoretical investigation for suggested mechanisms has not been carried out yet.

As we have shown previously, hydrazinolysis of 2,3-dihydro-1,5-benzodiazepin-2-ones (**1**) results in recyclization of the seven-membered ring with formation of 3-*R*-substituted pyrazolones-5 (**2**) and 4-R_1-substituted *o*-phenylendiamines (**3**) (see Scheme 1).[10,11] It was proposed[11] that the hydrazinolysis of 2,3-dihydro-1,5-benzodiazepin-2-ones would take place through the addition of hydrazine to C_4═N_5 bond, cyclization (by attack of the amine group to the carbonyl), and cleavage of the amide bond with formation of pyrazolone ring and the removal of *o*-phenylendiamine (see Scheme 2).

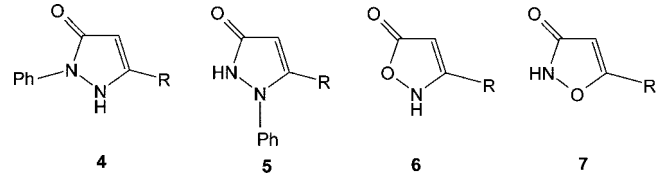
The formation of 1-phenyl-3-*R*-pyrazolones-5 (**4**) (instead of 2-phenyl-3-*R*-pyrazolones-5 (**5**)) by interaction of 2,3-dihydro-1,5-benzodiazepin-2-ones with phenylhydrazine, and 3-*R*-isoxazol-5-ones (**6**) (instead of the compounds **7**) by interaction with hydroxylamine leads the authors[8,11] to suppose that the initial nucleophile attack should be on the C_4 atom of the diazepinone ring. Thus, the recyclization of 2,3-dihydro-1,5-benzodiazepin-2-ones in reactions with phenylhydrazine and hydroxylamine may process by a mechanism similar to that of hydrazinolysis.

SCHEME 1



1a-d **2a-d** **3a-d**

R=CH_3, R_1=H (**1a**); R=Ph, R_1=H (**1b**); R=Ph, R_1=Cl (**1c**); R=CH_3, R_1=Cl (**1d**)



4 **5** **6** **7**

Because the literature provides no data concerning quantum chemical evaluation of 2,3-dihydro-1,5-benzodiazepin-2-ones reactivity in the present study, the recyclization mechanism of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one during hydrazinolysis was theoretically investigated using DFT and MP2 levels of theory. Some experimental studies of hydrazinolysis indicate a catalytic role of ethanol molecule.[12,13] Moreover, many examples exist on reducing the activation energy of reaction by assistance of solvent molecule in proton-transfer process.[14−16] Therefore, the ethanol-assisted mechanism modeled by explicit consideration of one ethanol molecule in the reaction is discussed in this study. Activation barriers for reaction pathways were used for comparative purposes and to identify the most probable hydrazinolysis mechanism.

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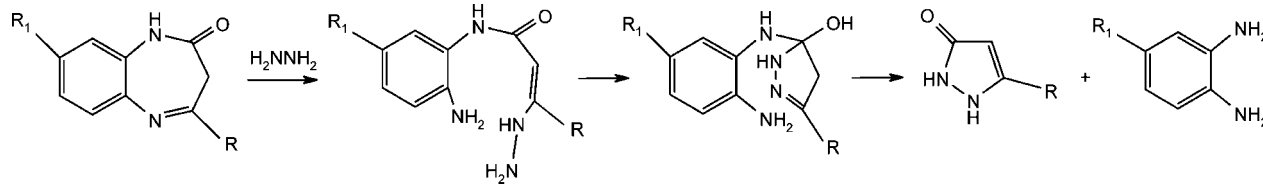
SCHEME 2



Computational Methodology

Molecular geometries of the minima and transition state structures along the reaction pathways were optimized using Density Functional Theory with Becke's three-parameter hybrid functional[17] and Lee, Yang, and Parr's (LYP)[18] correlation functional. The structures of the most favorable reactive channel were reoptimized using MP2 method. The 6-31G(d) and 6-311+G(d,p)[19] basis sets were used in this study. All geometries were optimized without any symmetry restrictions and characterized as minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency) by calculations of harmonic vibrational frequencies. Gibbs free energies of activation ($\Delta G^{\ddagger}$) were calculated as the difference of free energies between transition states and prereactive complexes. Single point computations at the MP2/6-311+G(d,p)//B3LYP/6-31G(d) and MP2/6-311+G(d,p)//MP2/6-31G(d) levels were performed for the more precise energy prediction. The zero-point energies were scaled by factors of 0.9806 and 0.9670[20] for B3LYP/6-31G(d) and MP2/6-31G(d) levels, respectively. Long-range effects of ethanol medium solvent were taken into account by means of a polarized continuum model (PCM).[21] Single point PCM/MP2/6-311+G(d,p)//B3LYP/6-31G(d) and PCM/MP2/6-311+G(d,p)//MP2/6-31G(d) computations for gas-phase optimized geometries were performed for estimation of the change in energy profile of the reaction in the presence of ethanol. All calculations have been carried out using the Gaussian 03 program package.[22]

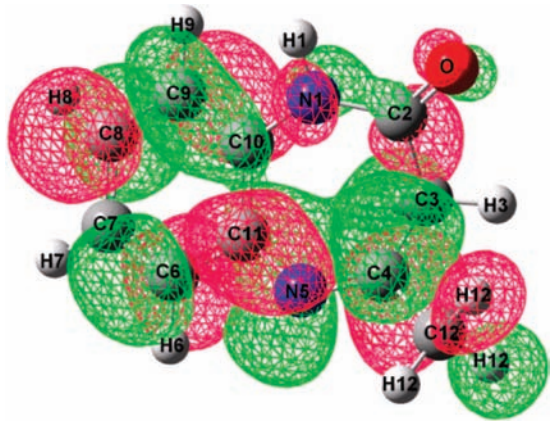


Figure 1. LUMO orbital for the 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one calculated at the B3LYP/6-31G(d) level.

TABLE 1: PCM/MP2/6-311+G(d,p)//B3LYP/6-31G(d) Relative Gibbs Free Energies (at 298 K) for Transition States, Intermediates, and Products for Ethanol-Assisted Hydrazinolysis of 2,3-Dihydro-1,5-benzodiazepin-2-one (kcal/mol) (Relative to Corresponding Prereactive Complexes)

structure	ΔG_{rel}	structure	ΔG_{rel}
TS(R→1)·et	16.75	**INT7[a]·et**	−11.02
INT1·et	−7.85	**TS(8→11)·et**	36.65
TS(R→2)·et	15.09	**(INT11+H_2O)·et**	18.05
INT2·et	−5.93	**TS(8→12)·et**	34.17
TS(R→3)·et	21.90	**(INT12+H_2O)·et**	3.88
INT3·et	8.43	**TS(8→13)·et**	53.76
TS(R→4)·et	21.46	**(INT13+H_2O)·et**	36.14
INT4·et	10.36	**TS(8→14)·et**	34.57
TS(R→5)·et	27.96	**INT14·et**	−9.28
INT5·et	1.55	**TS(8→15)·et**	43.29
TS(R→6)·et	25.98	**INT15·et**	8.06
INT6·et	−5.45	**TS(8→16)·et**	30.36
TS(1→7)·et	34.59	**INT16·et**	−4.64
INT7·et	3.32	**TS(8→17)·et**	42.09
TS(1→8)·et	20.55	**INT17·et**	10.47
INT8·et	14.45	**TS(7[a]→Pr)·et**	26.99
TS(1→9)·et	30.17	**(Pr+*o*-phenylendiamine)·et**	−8.13
INT9·et	−2.29	**TS(7[a]→Pr[a])·et**	38.51
TS(1→10)·et	33.65	**(Pr[a]+*o*-phenylendiamine)·et**	−4.47
INT10·et	30.84	**TS(Pr→Pr[a])·et**	34.20
TS(2→9)·et	35.07	**Pr[a]·et**	4.64
TS(2→10)·et	32.91	**TS(Pr→Pr[a])·et$_2$**	19.82
TS(8→7[a]) ·et	20.47	**Pr[a]·et$_2$**	3.61

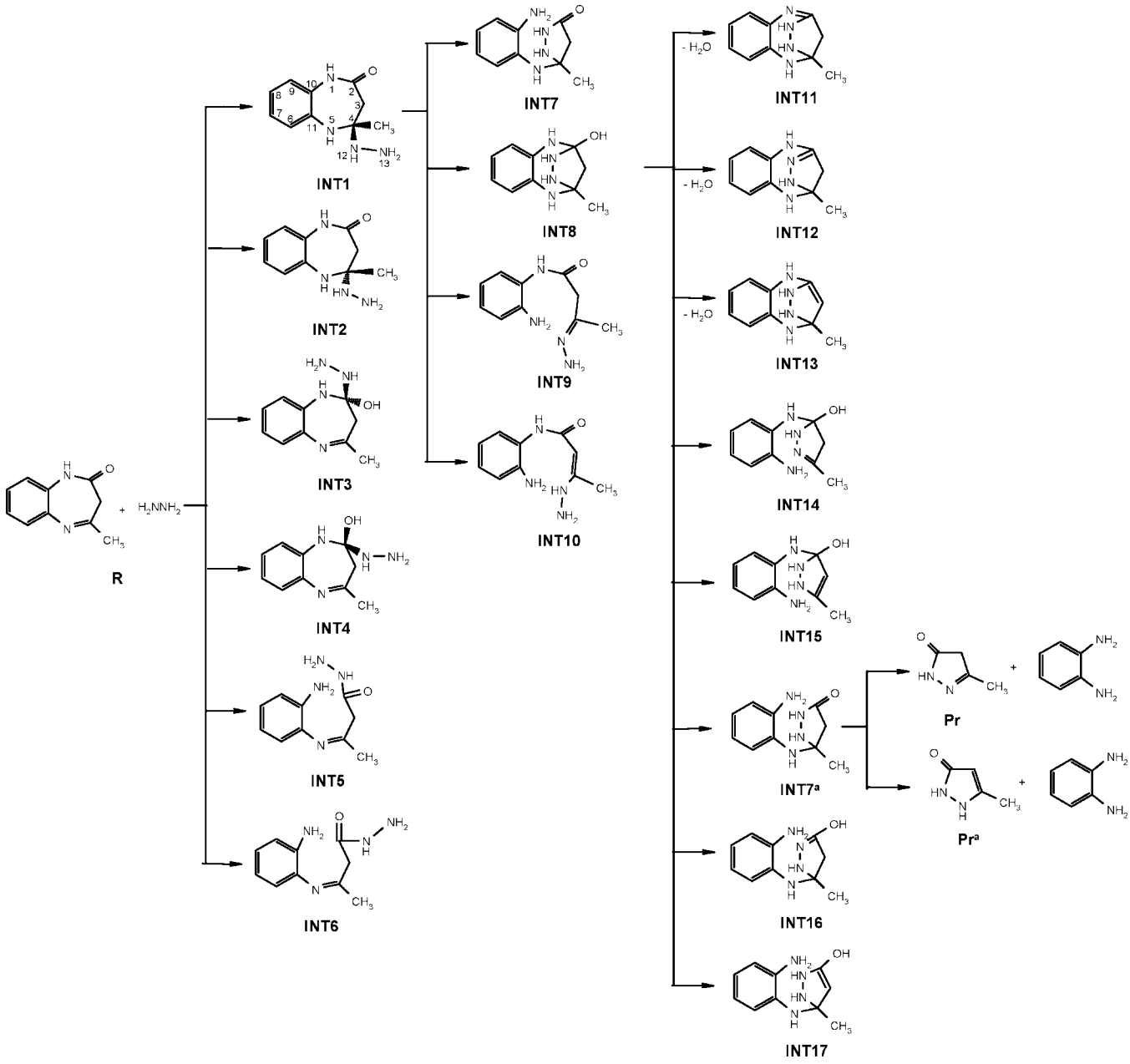
Results and Discussion

Evaluation of Reactivity of Carbon Atoms of 4-Methyl-2,3-dihydro-1,5-benzodiazepin-2-one. There are two potential reaction centers in 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one where the added hydrazine molecule could attack: the C_2 carbonyl carbon atom and C_4 azomethine carbon of the benzodiazepine system. To elucidate the most reactive electrophilic site of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one, we first analyzed the LUMO isodensity surface (examining the nodal structure of the wave function). Figure 1 shows the LUMO nodal structure. The carbon atom at position 4 of the diazepine ring contributes stronger to the LUMO than does the carbon atom at position 2. This can be readily rationalized by inspecting the corresponding LUMO orbital densities, which reveal a large coefficient on C_4 but a small coefficient (node) on C_2. As a consequence, the C_4 carbon atom of the benzodiazepine system is the most favorable position for nucleophilic attack of hydrazine.

As the local reactivity index we also used the Fukui function (f_{unoc}) on the basis of the reactive hybrid orbital method.[23] The B3LYP/6-31G(d) level calculated magnitudes of the f_{unoc} values are equal to 0.0157 and 0.2978 for C_2 and C_4 atoms, respectively. The f_{unoc} value for the C_4 position is larger than that for the C_2 position, predicting the initial attack of hydrazine molecule to azomethine bond of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one.

Mechanism of 4-Methyl-2,3-dihydro-1,5-benzodiazepin-2-one Hydrazinolysis. Scheme 3 displays the reaction mechanism considered for the hydrazinolysis of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one. For simplicity, the ethanol molecules are not shown in Scheme 3. The numbering of systems used throughout the discussion is also shown in Scheme 3. Figure 2 displays the B3LYP/6-31G(d) level-optimized geometries of the transition states located along the reaction coordinate. The prereactive complexes and transition states are denoted as **PRC(n_1→n_2)** and **TS(n_1→n_2)**, respectively, where

SCHEME 3: Calculated Reaction Pathways for the Hydrazinolysis Mechanism of 4-Methyl-2,3-dihydro-1,5-benzodiazepin-2-one



n_1 is the reactant and **n_2** is the product of the considered step. The letters "et" in bold after structure numbers refer to the presence of one molecule of ethanol. The relative Gibbs energies for transition states, intermediates, and products in ethanol solution are presented in the Table 1. The relative PCM/MP2/6-311+G(d,p)//B3LYP/6-31G(d) single point energies of all structures are discussed through the text. The B3LYP/6-31G(d) and MP2/6-31G(d) calculated total energies and Gibbs free energies are listed in Tables S1 and S2, and the relative Gibbs energies for transition states, intermediates, and products in the gas phase are presented in Table S3 as Supporting Information.

Hydrazine molecule may approach the electrophilic centers of ketone from the same side (bottom attack) or from the opposite side (top attack) of the methylene group (see Figure 3). Therefore, for the first step of the reaction, we examined six pathways: the addition of hydrazine molecule to C_2═O, C_4═N_5, and N_1−C_2 bonds from both sides of the diazepinone ring. These addition reactions are concerted, so the formation of C−N bond and proton transfer between benzodiazepinone and hydrazine occurs in one step. As could be seen from the Figure 2, the formed and broken C−N and C−O bonds are predicted earlier than the proton transfers between heteroatoms.

The addition of the hydrazine to C_4═N_5 bond can yield two possible intermediates, **INT1·et** (top attack) and **INT2·et** (bottom attack). The activation barriers for these pathways are 16.75 and 15.09 kcal/mol, respectively. The hydrazine addition to C_2═O bond following the formation of intermediates **INT3·et** (top attack) or **INT4·et** (bottom attack) requires activation energies of 21.90 and 21.46 kcal/mol, respectively. The highest activation barriers for the first step are observed for hydrazine addition to N_1−C_2 bond with cleavage of diazepine ring and formation of intermediates **INT5·et** and **INT6·et**. The values of the barriers are equal to 27.96 and 25.98 kcal/mol for the top and bottom attacks, respectively. The most favorable pathway for the first step of hydrazinolysis is the addition of the hydrazine to C_4═N_5 bond. This result confirmed the

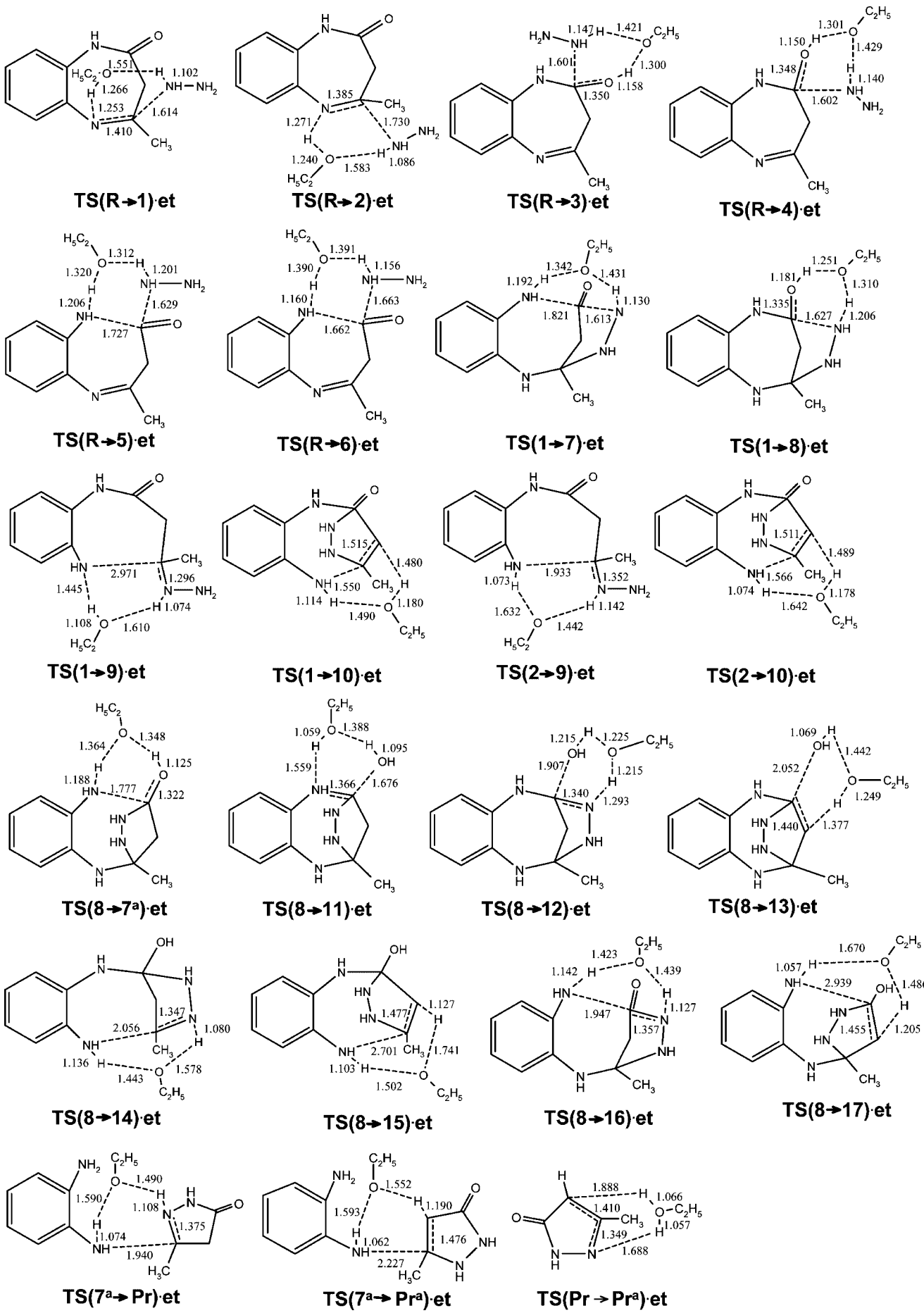


Figure 2. Structures and selected geometrical parameters (Å) of transition states for ethanol-assisted 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one hydrazinolysis calculated at the B3LYP/6-31G(d) level.

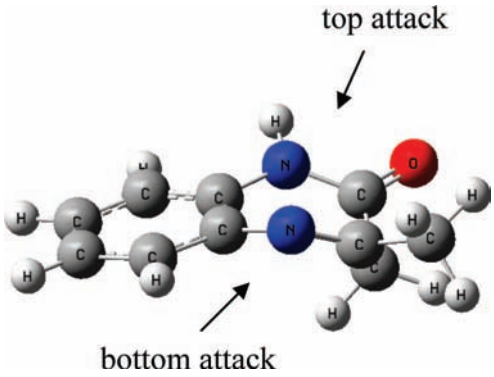


Figure 3. Structure of the 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one.

preliminary evaluation of reactivity of carbon atoms using MO analysis and Fukui index, which indicates that C_4 atom is the most reactive electrophilic site of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one. It has been noticed that the activation barriers for addition of the hydrazine to $C_4{=}N_5$ bond from the both sides of methylene bridge differ insignificantly (1.66 kcal/mol) and the relatively free energies of **INT1·et** and **INT2·et** are also closed; thus the following transformations of **INT1·et** and **INT2·et** intermediates are discussed.

The reaction continues from **INT1·et** intermediate either by cyclization, or by opening of the seven-membered ring, or these processes occur simultaneously. The nucleophilic attack of N_{13} to C_2 carbon causes cyclization with formation of five-membered ring and is accompanied by proton transfer from N_{13} either to N_1 (or O) atom, leading to intermediate **INT7·et** or intermediate **INT8·et**, respectively. These cyclizations require activation energies of 34.59 and 20.55 kcal/mol. The opening of the seven-membered ring at the $C_4{-}N_5$ bond is accompanied by proton transfer from N_{12} (or C_3) to N_5 forming intermediates **INT9·et** and **INT10·et**, respectively. The activation barriers for these pathways are high (30.17 and 33.65 kcal/mol). The transformation of intermediate **INT2·et** into intermediates **INT9·et** or **INT10·et** requires activation energies of 35.07 and 32.91 kcal/mol, respectively. The nucleophilic attack of N_{13} to C_2 carbon in intermediate **INT2·et** is not possible because of steric hindrance of methylene bridge. Comparing activation energies of different transformations pathways of intermediates **INT1·et** and **INT2·et**, one may conclude that the transformation **INT1·et→INT8·et** is the most energy favorable for the second step of hydrazinolysis.

The elimination of H_2O molecule or the opening of the seven-membered ring is possible as further transformations of the **INT8·et** intermediate. A proton transfer in intermediate **INT8·et** from the N_1, N_{13}, or C_3 to OH group causes consecutive departure of the water molecule, and, in addition, as proton is abstracted, a double $N_1{=}C_2$, $C_2{=}N_{13}$, or $C_2{=}C_3$ bond is formed on the ring leading to **INT11·et**, **INT12·et**, or **INT13·et** intermediates. The obtained results show that these pathways have high activation energies: 36.65, 34.17, and 53.76 kcal/mol, respectively (see Table 1). The cleavage of the seven-membered ring in intermediate **INT8·et** may occur by breaking the $N_1{-}C_2$ or $C_4{-}N_5$ bonds accompanied by proton transfer. The breaking of $C_4{-}N_5$ bond is followed by proton transfer from N_{12} (or C_3) to N_5 and requires the activation energy of 34.57 or 43.29 kcal/mol, respectively, leading to the **INT14·et** or **INT15·et** intermediates. The proton transfer from O, N_{13}, or C_3 to N_1 leads to the rupture of $N_1{-}C_2$ bond and formation of the **INT7^a·et**, **INT16·et**, or **INT17·et** intermediates, respectively. It has been noticed that intermediate **INT7^a·et** differs from **INT7·et** by ethanol molecule position toward pyrazole ring. As could be seen from Table 1, the transformation **INT8·et→INT7^a·et** has the lowest activation energy among the considered pathways. Comparing pathways with the breaking of C−N and C−O bonds, one may notice that the C−N bond breaks easier than the C−O bond, and the leaving NH_2Ar group is more stable than the water molecule.

The breaking of the $C_4{-}N_5$ bond in the **INT7^a·et** intermediate is accompanied by proton transfer from N_{12} (or C_3) to N_5. It causes elimination of *o*-phenylendiamine with formation of **Pr·et** or **Pr^a·et**. As could be seen from Table 1, the first pathway is energetically favored by approximately 11 kcal/mol with an activation barrier that amounts to 26.99 kcal/mol.

Structures **Pr** and **Pr^a** represent two tautomers. The tautomerization of **Pr·et** into **Pr^a·et** requires the high activation energy (34.20 kcal/mol), which is reduced to 19.82 kcal/mol in the case of explicit consideration of two ethanol molecules in the process. It should be noticed that the intermediate **Pr·et** is slightly more stable than **Pr^a·et** in ethanol solution, and thus we assume that this tautomerization can also take place in other solvents, as was shown in the study on tautomerism of substituted pyrazolones.[24]

On the basis of the obtained results, one may conclude that the most energetically favorable reactive channel for the hydrazinolysis of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one is **R→INT1→INT8→INT7^a→Pr**. The final step is a rate-determining step for this reaction.

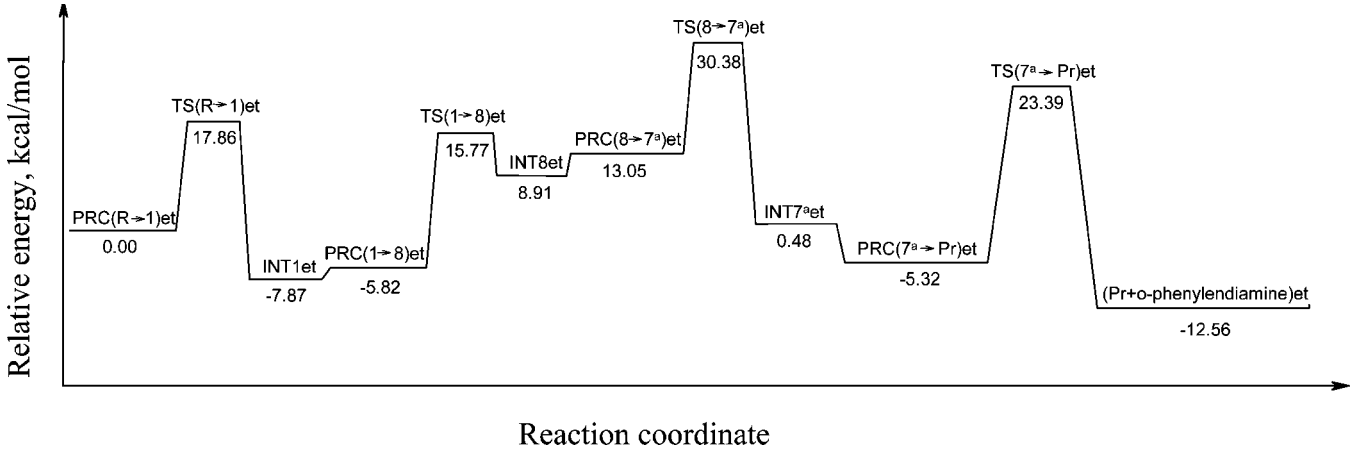
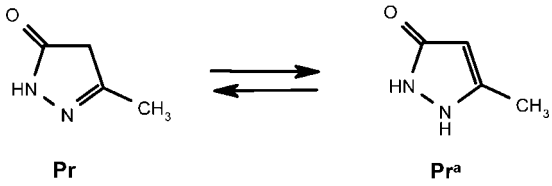


Figure 4. Relative energy profiles (kcal/mol) for ethanol-assisted hydrazinolysis of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one calculated at the PCM/MP2/6-311+G(d,p)//MP2/6-31G(d) level.



Pr **Pr^a**

We reexamine the reactive channel at the PCM/MP2/6-311+G(d,p)//MP2/6-31G(d) level for the more accurate energy evaluation. The obtained results (Figure 4) confirmed the final step as a rate-limiting step of this reaction with activation barrier of 28.71 kcal/mol.

Conclusions

This work presents the results of the first quantum chemical investigation of interaction mechanism between 1,5-diazepin-2-one systems and bifunctional nucleophiles. In the present Article, we describe a theoretical study on the mechanism of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one hydrazinolysis in ethanol solution. The investigated reaction pathways indicate that the 3-methylpyrazol-5-one is the main product for the above-mentioned reaction, which is in agreement with the experimental results for hydrazinolysis of 4-substituted 2,3-dihydro-1,5-benzodiazepin-2-ones.[10,11]

The most favorable pathway for the first step of hydrazinolysis of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one is the hydrazine addition to the C_4=N_5 bond with formation of the **INT1**. The attack of amine group on C_2 atom in **INT1** leads to pyrazole ring formation that yields **INT8**. The opening of the seven-membered ring in **INT8** follows through proton transfer from O to N_1 and leads to **INT7^a**. The cleavage of the C_4−N_5 bond in **INT7^a** is accompanied by the elimination of *o*-phenylendiamine and formation of **Pr**, which then can isomerize to the **Pr^a** by proton transfer from C_4 to N_1. The elimination of *o*-phenylendiamine from **INT7^a** is a rate-determining step for hydrazinolysis.

We believe that our study reveals a general mechanism that characterizes interactions of 1,5-diazepin-2-one systems with other bifunctional nucleophiles, such as phenylhydrazine and hydroxylamine.

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Supporting Information Available: Absolute energies tabulated for all related compounds at the B3LYP/6-31G(d) level (Table S1); absolute energies tabulated for structures of the reactive channel at the MP2/6-31G(d) level (Table S2); and MP2/6-311+G(d,p)//B3LYP/6-31G(d) calculated relative Gibbs free energies for transition states, intermediates, and product for ethanol-assisted hydrazinolysis of 4-methyl-2,3-dihydro-1,5-benzodiazepin-2-one (Table S3). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Solomko, Z. F.; Proshkina, V. N.; Boganova, N. Ya. USSR Inventor's Certificate # 1072433, 1982.
(2) Boganova, N. Ya.; Proshkina, V. N.; Solomko, Z. F. USSR Inventor's Certificate # 1198917, 1984.
(3) Solomko, Z. F.; Proshkina, V. N.; Hmel, M. P. USSR Inventor's Certificate # 1295700, 1985.
(4) Solomko, Z. F.; Zlenko, E. T.; Gaponov, A. A.; Demchenko, E. M. USSR Inventor's Certificate # 1586135, 1988.
(5) Solomko, Z. F.; Zlenko, E. T.; Gaponov, A. A. USSR Inventor's Certificate # 1633779, 1989.
(6) Pogarskiy, A. F. Theoretical bases of chemistry of heterocycles. Moscow: Chemistry; 1985; p 280.
(7) Dzvinchuk, I. B.; Lozinsky, M. O. *Russ. J. Org. Chem.* **1998**, *34*, 740.
(8) Essassi, E. M.; Salem, M.; Viallefont, Ph. *Bull. Soc. Chim. Fr.* **1987**, *5*, 890.
(9) Essassi, E. M.; Lavergne, J.-P.; Viallefont, Ph. *Tetrahedron* **1977**, *33*, 2807.
(10) Gaponov, A. A.; Solomko, Z. F.; Boganova, N. Ya.; Pantyuh, E. I. *Chem. Heterocycl. Compd.* **1989**, *7*, 997.
(11) Gaponov, A. A.; Solomko, Z. F.; Tarabara, I. N. *Quest. Chem. Chem. Technol.* **2007**, *1*, 24.
(12) Merrow, R. T. *J. Am. Chem. Soc.* **1956**, *78*, 1297.
(13) Ferren, R. A.; Miller, J. G.; Day, A. R. *J. Am. Chem. Soc.* **1957**, *79*, 70.
(14) Akdag, A.; McKee, M. L.; Worley, S. D. *J. Phys. Chem. A* **2006**, *110*, 7621.
(15) Bottoni, A.; Frenna, V.; Lanza, C. Z.; Macaluso, G.; Spinelli, D. *J. Phys. Chem. A* **2004**, *108*, 1731.
(16) Lundin, A.; Panas, I.; Ahlberg, E. *J. Phys. Chem. A* **2007**, *111*, 9087.
(17) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
(18) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
(19) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1972**, *66*, 217.
(20) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.
(21) (a) Miertus, S.; Scrocco, E.; Tomasi, J. *J. Chem. Phys.* **1981**, *55*, 117. (b) Barone, V.; Cossi, M.; Tomasi, J. *J. Comput. Chem.* **1998**, *19*, 404.
(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision B.05; Gaussian, Inc.: Wallingford, CT, 2004.
(23) Hirao, H.; Ohwada, T. *J. Phys. Chem. A* **2005**, *109*, 816.
(24) Freyer, W.; Koppel, H.; Radeglia, R.; Malewski, G. *J. Prakt. Chem.* **1983**, *325*, 238.

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