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Possible intramolecular rearrangements of *O*-vinyloximes initiated by N—O bond dissociation: a quantum-chemical analysis

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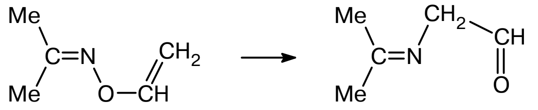
The potential surface of conformational transitions of *O*-vinylacetoxime was studied and the regions of "starting" states for possible isomeric transformations with the N—O bond dissociation as the limiting stage were recognized. The activation parameters and heat effects of intramolecular rearrangement *O*-vinylacetoxime → iminoacetaldehyde were evaluated. Transition-state structure of the rearrangement was identified.

Key words: *ab initio* quantum-chemical calculations, *O*-vinylacetoxime, iminoacetaldehyde, conformation, stationary state, dissociation, rearrangement, activation energy.

The ability of *O*-vinyloximes to exist in different isomeric forms and the search for isomers of their transformations into pyrroles have been the subject of our studies in the last two decades.[1—7] Of particular interest is the possibility of hypothetical intramolecular rearrangement of *O*-vinyloximes (*e.g.*, *O*-vinylacetoxime (**1**)), into iminoacetaldehyde (**2**), which has not been detected experimentally as yet.

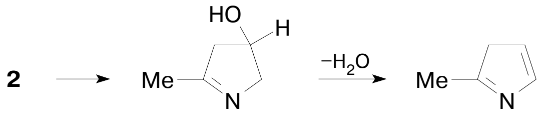


(1)

1 **2**

This isomeric transformation seems not to be improbable under appropriate thermodynamic and stereochemical conditions. It is favored by specific combination of stability of compound **1** (this makes possible the formation of an appropriate rotamer that produces no steric hindrances to the isomeric transformation), weakness of the N—O bond, and small energy difference between the activation parameters of reaction (1) and those of the alternative, experimentally observed, rearrangements. It cannot be ruled out that rearrangement (1) is an intermediate stage of certain chemical transformations of *O*-vinyloximes and has not been unambiguously detected so far owing to high reactivity of iminoacetaldehyde (**2**). Possibly, the formation of pyrroles can proceed involving this rearrangement as an alternative or concurrent channel.

An analogy between base-catalyzed intramolecular cyclization of iminoacetaldehyde (**2**) into 3-hydroxypyrroline and aldol condensation suggests that the former is likely.



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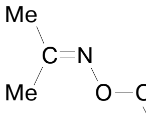
The aim of this work was to study intramolecular rearrangements of *O*-vinyloximes initiated by dissociation of the N—O bond.

Calculation Procedure

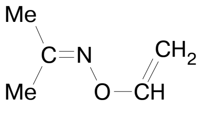
Ab initio calculations were carried out by the restricted Hartree—Fock (RHF) method[8,9] in the split-valence 6-31G** basis set using the GAUSSIAN-94 program package.[10] Full optimization of the geometry of the molecular systems corresponding to the transition structures ($\lambda = 1$, where λ is the number of negative eigenvalues of the Hesse matrix at a given stationary point[11]) and to the energy minima ($\lambda = 0$) on the potential energy surface (PES) was carried out up to the gradient magnitude of 10^{-5} au bohr^{-1}. The force constant matrix was calculated analytically using a subroutine incorporated into the GAUSSIAN-94 program package. The structures corresponding to the energy minima on the PES were identified by the method of steepest descent (movement along the gradient line) from the saddle point to the neighboring critical point. The initial direction of the gradient line was specified by minor displacement along the transition vector. This allowed a correct determination of the gradient reaction pathway.[11] Optimization of the geometry in the vicinity of stationary states was performed by the Newton—Raphson method according to the Berny scheme. The basis set superposition error (BSSE) was ignored since the intra-associate reaction pathways in different fragments of the same molecule were mostly studied. It is also known that BSSE is negligible for the 6-31G** basis set.[9,12]

Results and Discussion

According to calculations, stationary states of isolated molecule **2** are much more energetically favorable than those of its isomer **1** (Table 1). In studies of rotational isomerism it has been shown[6] that only two out of four theoretically possible rotamers of compound **1** ((*ap*, *ap*), (*ap*, *sp*), (*sp*, *ap*), and (*sp*, *sp*)) do exist. These are the (*ap*, *ap*) and (*ap*, *sp*) rotamers, the former being more stable.



1 (*ap*, *ap*)



1 (*ap*, *sp*)

Stereochemically, the best "starting point" of transformation (1) is the (*ap*, *sp*) conformer (~20% in the mixture of rotamers of **1** at 25 °C). Stereochemical hindrances to rearrangement (1) are mainly due to unfavorable orientation of the lone electron pair (LEP) of the N atom. Since the LEP lies in the plane passing through the heavy atoms, the interaction with the π-system of the vinyl fragment is weak. (The electron cloud of the LEP can play the role of a nucleophilic center only if the LEP is appropriately oriented.[13]) Note that the molecules of heterocyclic compounds containing the N—O—Vin fragment are free from this kind of steric hindrances and the rearrangements proceed with ease.[14]

Table 1. Total (E_{tot}) and relative (ΔE) energies and the number of negative eigenvalues of the Hesse matrix (λ) for the structures obtained from RHF/6-31G** calculations

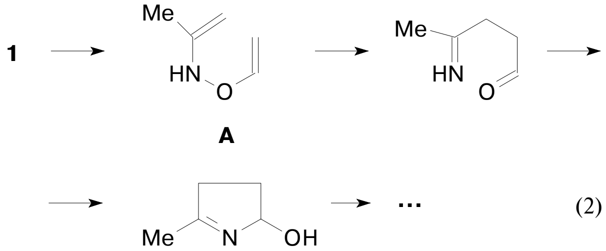
Structure	E_{tot}[a]/au.	ΔE/kcal mol^{-1}	λ
1 (*ap*, *ap*)	−323.81823	39.8	0
1 (*ap*, *sp*)	−323.81706	40.5	0
1a	−323.81053	44.59	1
1b	−323.80717	46.70	1
2 (*ap*, *ap*)	−323.88159	0	0
2 (*ap*, *sp*)	−323.87525	4.0	0
2 (*sp*, *sp*)	−323.86408	11.0	0
A (*ap*, *ap*)[b]	−323.79316	55.5	0
A (*ap*, *sp*)[b]	−323.79265	55.8	0
3	−323.69659	116.1	1
4	−323.86921	7.8	0
5	−323.75042	82.3	1
6	−323.69864	114.8	1
7	−998.37584	4.6[c]	0
8	−998.38323	0	0
9	−998.36116	13.8[c]	1
10	−323.84473	23.1	0
11	−323.65562	141.8	1
12	−323.69264	118.6	1
13	−323.80706	46.8	0

[a] 1 au. = 627.5095 kcal mol^{-1}.

[b] Structures were named similarly to the rotamers of the corresponding starting structures involved in prototropic rearrangement.

[c] Relative to structure **8**.

The probability of isomerization of **1** following pathway (1) can also decrease owing to the existence of an alternative reaction channel. The alternative process begins with the prototropic rearrangement followed by cleavage of the weak N—O bond, cyclization, and transformation of isomer **1** into pyrroles.[2,3]



We assume that by choosing appropriate condensed medium (see below) or substituents at the N atom one can make the initial stage of process (2) (*i.e.*, the sigmatropic shift) difficult or impossible, thus increasing the probability of reaction (1).

As mentioned above, the necessary stereochemical condition for an increase in the probability of rearrangement of the type (1) consists of deviation of the LEP of the N atom out of the plane passing through the heavy atoms. This requires an increase in the fraction of the

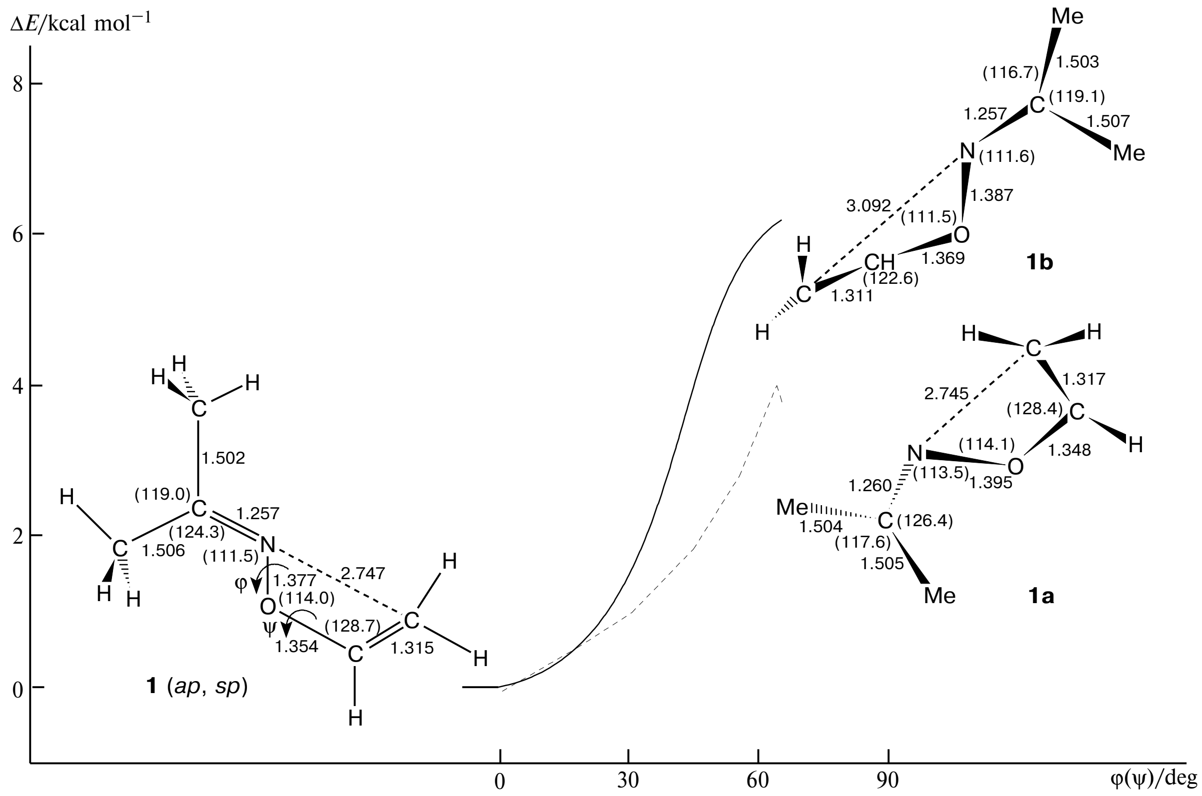


Fig. 1. Energy profile of the PES of compound **1** as function of the angle of rotation about the N—O bond (φ, structure **1a**) and C—O bond (ψ, structure **1b**). The total energy of the (*ap*, *sp*) conformer was taken as zero. The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses.

staggered (*ap*, *sp*) conformer. However, the rotational mobility of compound **1** is due to both rotation about the N—O bond (this favors rearrangement (1) and is characterized by variation of the angle φ) and rotation about the C—O bond (this hinders rearrangement (1) and is characterized by variation of the angle ψ) (see Fig. 1). This brings up the question: can thermal vibrations stimulate the initial stage of this rearrangement?

To estimate the effect of variation of the angles φ and ψ on the energy of the system, we varied them independently with full optimization of the rest geometric parameters. According to calculations, rotation about the C—O bond leads to a greater (by a factor of about 1.5) increase in the total energy of the system (see Fig. 1, structure **1b**) as compared to rotation about the N—O bond (see Fig. 1, structure **1a**), thus favoring rearrangement (1). This rearrangement is also favored by a virtually planar structure of the rest part of the molecular skeleton (except for the varied fragment, the N—O—C—C (structure **1a**) and C—O—N—C (structure **1b**) torsion angles are 0.03° and 181.19°, respectively). For rotation about the N—O bond, this at least does not lead to an increase in the distance between the N and C_β atoms in the vinyl fragment (see Fig. 1). Moreover, according to calculations, an increase in the angle φ leads to substantial weakening of the N—O bond (*cf.* 1.377 Å for the (*ap*, *sp*) rotamer of molecule **1** and 1.395 Å for structure **1a**) and strengthening of the C—O bond (*cf.* 1.355 Å for the (*ap*, *sp*) rotamer of molecule **1** and 1.348 Å for structure **1a**).

Analysis of the dipole moments of structures **1** (*ap*, *sp*), **1a**, and **1b** (2.05, 3.03, and 1.41 D, respectively) showed that variation of the angle φ leads to an increase while that of the angle ψ leads to a decrease in the polarity of the molecular system. Hence an increase in the solvent polarity must lead to a decrease in the activation barrier to rotation about the N—O bond, thus favoring reaction (1) and making rotation about the C—O bond difficult.

The structure of the transition state (TS) **3** of rearrangement **1** → **2** obtained by moving along the gradient line connecting the stationary states **1** (*ap*, *sp*) and **2** (*ap*, *sp*) is shown in Fig. 2.

For this TS (see Fig. 2), the angle φ is 102.1° and lies within the limits of optimum spatial orientation of the LEP. Polarity of TS **3** appreciably increases (μ = 4.88 D) and a strong charge separation occurs, the positive charge being more delocalized than the negative charge. In this connection, one can suggest that an increase in the solvent polarity and electrophilicity can lead not only to an increase in the initial fraction of staggered (*ap*, *sp*) conformer of **1** but also to an increase in the rate of rearrangement (1).

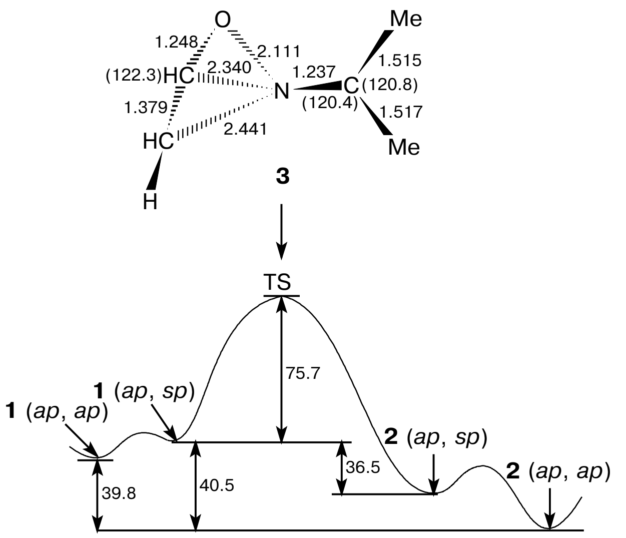


Fig. 2. Schematical representation of the energy profile of rearrangement **1** → **2**. The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses. Figures in the structure-energy diagram are given in kcal mol^{-1}.

Unlike structure **1** for which only two stable rotamers have been predicted,[6] our study of the PES of compound **2** revealed three stationary states (Fig. 3). The energy difference between the most stable (*ap*, *ap*) and (*ap*, *sp*) conformers is small ($\Delta E \approx 4$ kcal mol^{-1}). The former structure is more stable; however, its skeleton is slightly nonplanar (the torsion angles in the C—C—N—C and N—C—C—O chains are 172.9° and 171.1°, respectively), whereas the other structures have planar skeletons. The end product of rearrangement (1) undergoes relatively easy transformation into a more stable state (**2** (*ap*, *sp*) → **2** (*ap*, *ap*)), which increases the overall energy balance of reaction **1** (*ap*, *ap*) → **2** (*ap*, *ap*) up to 39.8 kcal mol^{-1} (see Table 1, Fig. 2).

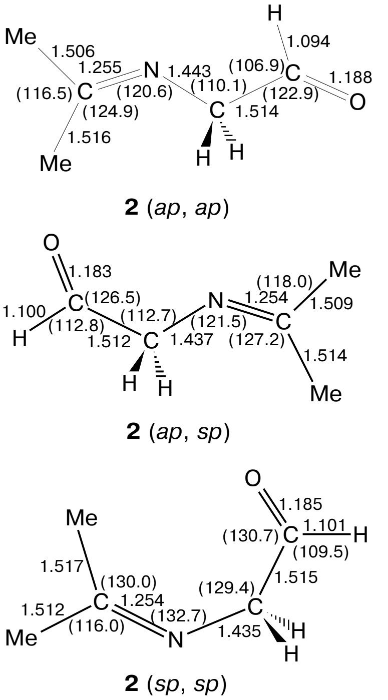
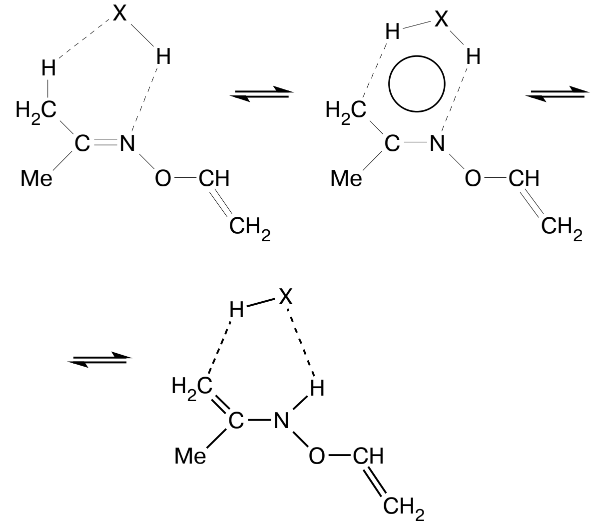


Fig. 3. Molecular structures and geometric parameters of the rotamers of compound **2**. The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses.

Reaction (2) begins with proton transfer (**1** → **A**). However, the main parameters related to the height of the energy barrier to proton transfer[8,17,18] suggest that the probability of intramolecular 1,3-shift is low since suprafacial 1,3-sigmatropic shifts are symmetry forbidden.[13,15] This is also confirmed by the results obtained in this work. According to calculations, the intramolecular migration requires the overcoming of a rather high activation barrier (Fig. 4). The ease of rearrangement (2) in the condensed phase in the KOH/DMSO system can suggest that transformation **1** → **A** occurs involving mediators following the mechanism shown below:



X = KO

This rearrangement requires the transfer of two protons rather than one proton; however, the height of the activation barrier decreases in this case by nearly an order of magnitude (see Fig. 4, 5). This becomes possible owing to more favorable conditions for the closure of H-bridges and, thus, proton transport along them in the associates as compared to the isolated forms of compound **1**.

The results obtained suggest that by choosing appropriate condensed medium one can block the initial stage of rearrangement (2) and, hence, increase the probability of reaction (1). Stationary states of the structures of the type A are ~15 kcal mol^{-1} less stable than those of the initial conformers of **1** (see Table 1). Since they are prone to intramolecular cyclization[2] and the barrier to transformation **1** → **A** is high (see Fig. 4), preparative

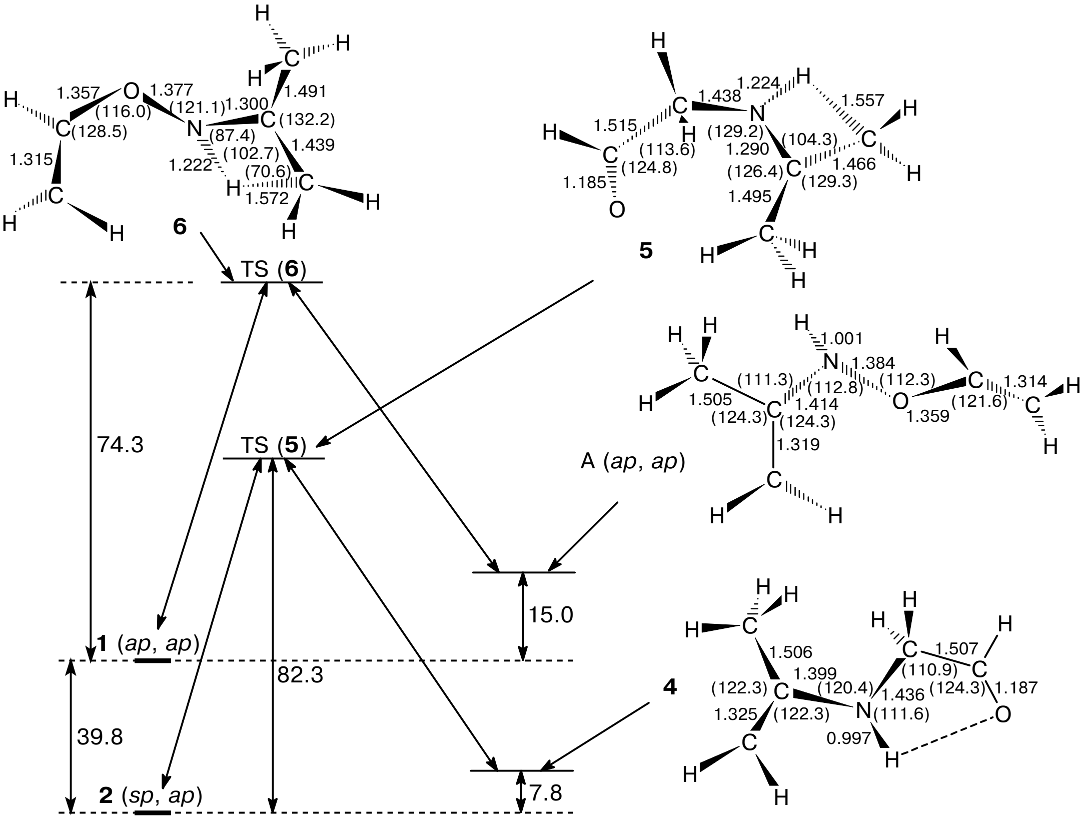


Fig. 4. Schematical representation of the mechanisms of intramolecular prototropic rearrangements of compounds **1** (**1** (*ap*, *ap*) → **6** → **A** (*ap*, *ap*)) and **2** (**2** (*sp*, *ap*) → **5** → **4**). The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses. Figures in the structure-energy diagram are given in kcal mol^{-1}.

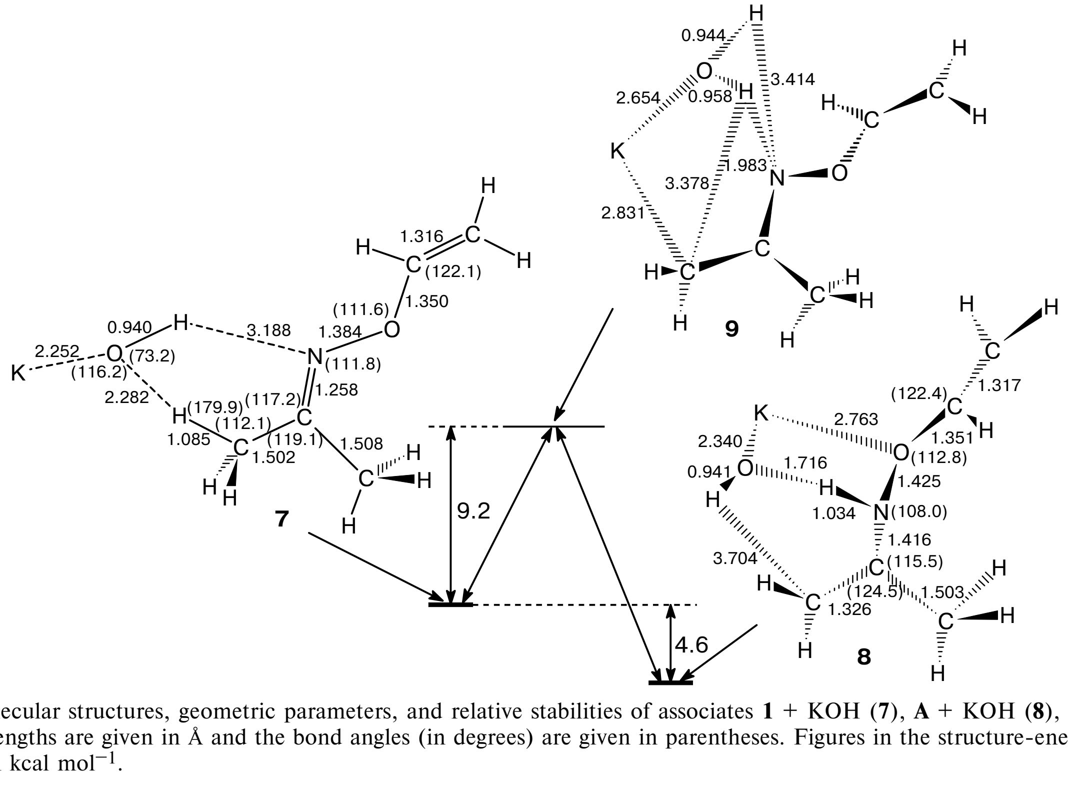


Fig. 5. Molecular structures, geometric parameters, and relative stabilities of associates **1** + KOH (**7**), **A** + KOH (**8**), and TS (**9**). The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses. Figures in the structure-energy diagram are given in kcal mol^{-1}.

isolation of these intermediates is difficult. It cannot be ruled out that structures **2** also undergo a prototropic rearrangement **2** → **4** (see Fig. 4, with structure **5** as TS) involving bases as mediators, which is analogous to transformation **1** → **A**.

The stability of compound **4** is comparable with that of isomer **2** (see Table 1) and the central part of its skeleton can be stabilized owing to the formation of a pseudo-five-membered heterocycle with a weak hydrogen bond (see Fig. 4). Despite this fact, preparative isolation of compound **4** is unlikely owing to the presence of highly reactive NH and C=O groups in the same molecule. Hydrogen bond can also be responsible for the unexpectedly low stability (ΔE = 2.9 kcal mol^{-1}) of the *anti*-conformer (rotation about the C—C bond) in which the electronegative N and O atoms are at the longest distances from each other and their dipoles are oriented in opposite directions.

Not only thermal, but also photochemical initiation of reaction (1) can favor the detection of rearrange-

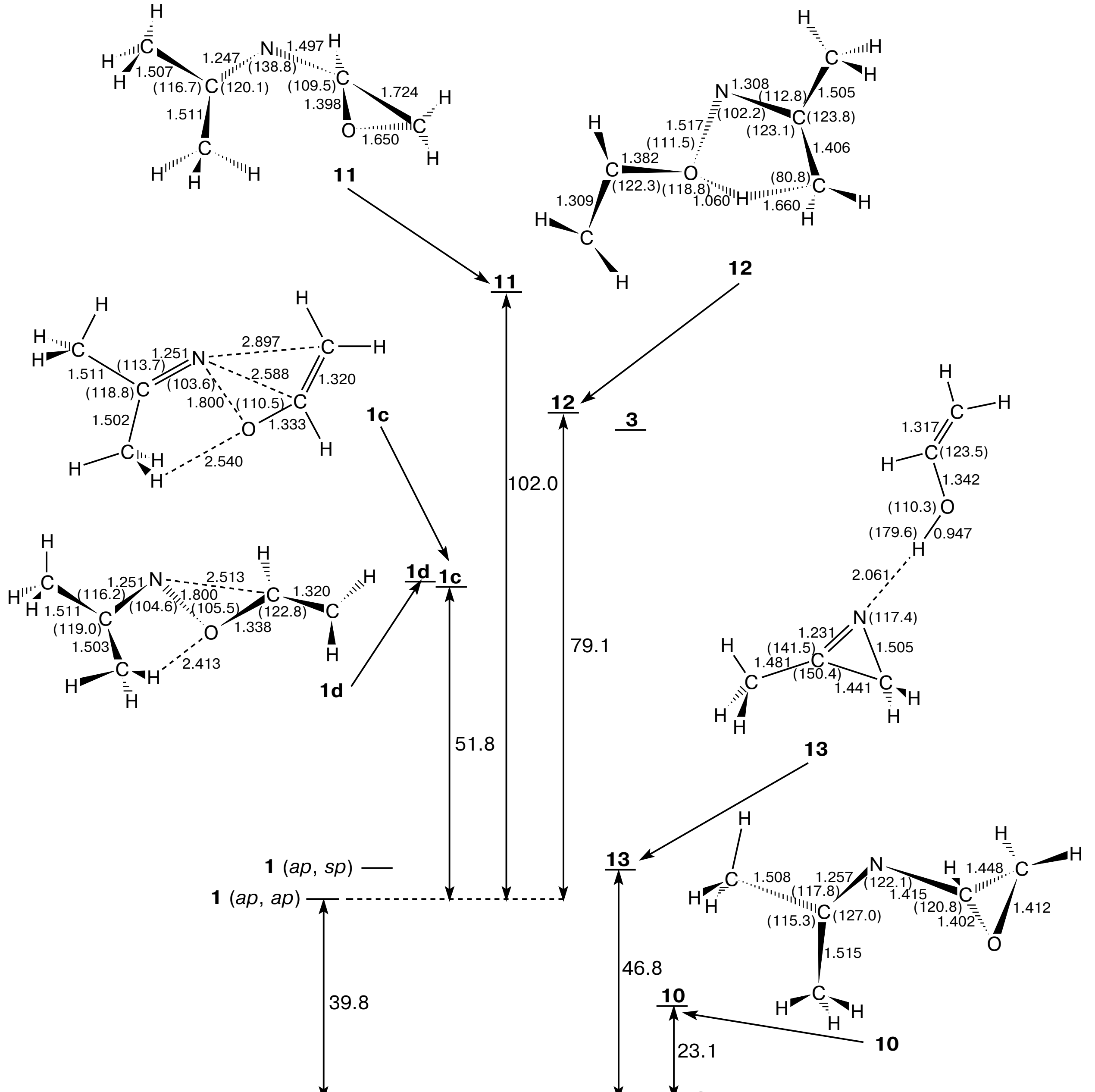


Fig. 6. Molecular structures and geometric parameters of metastable structures (**1c**, **1d**), TS (**11**, **12**), and end products (**10**, **13**) and structure-energy diagram of their transformations. The bond lengths are given in Å and the bond angles (in degrees) are given in parentheses. Figures in the structure-energy diagram are given in kcal mol^{-1}. The relative position of the TS **3** of rearrangement **1** → **2** is shown.

ments of the type **1** → **2**. For instance, the well-known isoxazole-oxazole rearrangement,[16] which begins with cleavage of the N—O bond upon irradiation with light (λ = 253.7 nm), initiates the interaction between the N atom and the vinyl fragment. However, studies of the dynamics of photoinduced molecular transformations both in the gas phase and in the condensed phase require a correct determination of the PES topology for the ground and excited states and, which is at least equally important, of their relative arrangement over a rather wide range of variation of the intrinsic coordinates.[11]

Nevertheless, in order to assess the possibility of the formation of the intermediates and end products, initiated by dissociation of the N—O bond and taking into account a hypothetical character of rearrangements (owing to the lack of experimental data), we used the following approach. The starting point was a metastable product corresponding to structure **1** with the cleaved N—O bond; however, the "pseudo"-(*ap*, *ap*) and "pseudo"-(*ap*, *sp*) conformations of the constituent fragments (Fig. 6, structures **1d** and **1c**, respectively) were retained. Thus we restricted ourselves to either diabatic interconversions or thermochemical transformations which begin with the formation of a pre-dissociation state for compound **1** with respect to the N—O bond.

We analyzed a number of PES regions with close values of activation parameters for metastable structures **1d** and **1c** and found that transformation **1d** → **2** is the most probable in the absence of external trapping agents. In this case, transition-state geometry obtained by moving along the gradient line connecting the points **1d** and **2** (*ap*, *sp*) fully corresponds to the TS structure of transformation **1** (*ap*, *sp*) → **2** (*ap*, *sp*). This points to the fact that multichannel rearrangement **1** → **2** is impossible in this region of structural rearrangements.

Moving *via* TS **11**, structure **1d** can arrive at yet another stationary state, **10** (see Fig. 6). However, the probability of this transformation is low taking into account the ratio of activation barriers. Energetically, more favorable is the rearrangement of structure **1c** resulting in associate **13** of azirine with vinyl alcohol (see Fig. 6). This pseudoelimination reaction, which begins with deformation of the N—O bond, involves prototropic migration of a proton of the methyl group as the limiting stage. However, in this case the proton migrates to the O atom (see Fig. 6, with structure **12** as TS) rather than to the N atom as in reaction (2). This is followed by a barrierless closure of the azirine ring and the formation of thermally labile 2*H*-azirine and vinyl alcohol (structure **13**).

The results of our studies of the PES of intramolecular rearrangements in *O*-vinylacetoximes give some reasons to hope that rearrangements of the type (1) can be experimentally detected. This can favor the development of new methods for the synthesis of compounds of the type **10**.

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