

Mechanisms of [1,3]-Sigmatropic Migrations of the Nitroso Group in the ON–X–CH=X Systems (X = O, S, Se, NH, CH₂)

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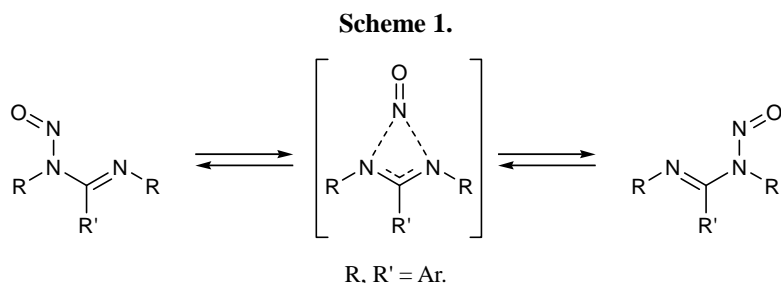
Abstract—[1,3]-Sigmatropic migrations of the nitroso group in the systems ON–X–CH=X (X = O, S, Se, NH, CH₂) were studied by MP2(fc)/6-311+G** and B3LYP/6-311+G** quantum-chemical calculations. The energy barrier in the process was estimated at 2.4 (2.5), 20.0 (25.0), and 22.3 (23.4) kcal/mol for X = O, NH, and CH₂, respectively. The energy minima for X = S and X = Se correspond to cyclic structures with two-coordinate NO group, which are more stable than acyclic structures by 9.3 (4.3) (X = S) or 13.1 (5.7) kcal/mol (X = Se).

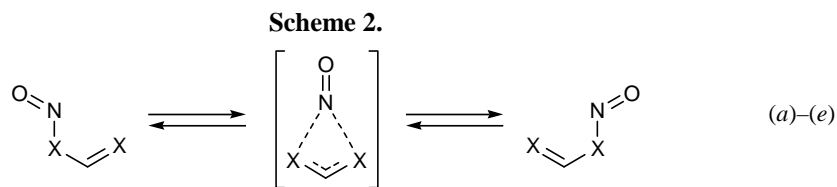
At present, a large number of biochemical studies deal with properties of compounds containing a nitroso group due to their important role in the regulation of vital processes in humans and animals [1–3]. In keeping with the results of biological studies [2, 4], transfer of a nitroso group from one biomolecule to another involves mainly nucleophilic substitution at the nitrogen atom of that group; here, electronegative sulfur [1] and oxygen atoms [5] act as nucleophiles.

Stereochemical and energetic parameters of biochemical processes with participation of nitroso groups can be estimated most accurately by studying simple model reactions in which the nucleophilic species is simulated by a single electronegative atom and the nucleofugal center is the same as in model nucleophile. These structural requirements become maximally rigorous in such systems where both nucleophile and nucleofuge belong to a single molecule, i.e., when intramolecular migration of NO group between N, O, S, or Se atoms is concerned.

Mikhailov *et al.* [6] described the synthesis of *N*-nitrosoarene-carboximidamide derivatives and studied the reaction shown in Scheme 1. However, we have found no published experimental data on rearrangements of nitrosyl formate or nitrosyl dithioformate derivatives. Quantum-chemical calculations of biological systems capable of involving any rearrangements with participation of NO groups (NO group transfer) are strongly complicated due to large size of the corresponding structures; therefore, such studies are few in number. Santillan *et al.* [7] examined the formation of HNO from *N*-methylguanidine and peroxyformic acid as a process simulating oxidation of L-arginine *in vivo* to produce NO. However, the authors did not perform a detailed analysis of the mechanisms of elementary stages of the process. The energies of bonds between the NO group and N, O, and S atoms in various simple organic molecules were studied in [4, 8].

We previously performed *ab initio* calculations of the simplest degenerate bimolecular reactions like





a: X = O; *b*: X = S; *c*: X = Se; *d*: X = NH; *e*: X = CH₂.

$X^- + X'NO \rightarrow X'^- + XNO$ ($X = H, F$) [9]. However, these reactions turned out to be inappropriate model for studying nucleophilic substitution at the nitrogen atom of nitroso group, for hydride ion attacked hydrogen rather than nitrogen atom and the attack by fluoride ion was directed at the double bond. Intramolecular sigmatropic shift of the nitroso group in *N*-nitrosoformimidamide $O=N-NH-CH=NH$ was studied in [10] by the MINDO/3 semiempirical method which could not provide adequate description of the reaction mechanism owing to its known imperfections [11].

In the present work we examined model systems in which intramolecular migration of nitroso group is possible (Scheme 2, reactions *a–e*). *Ab initio* (MP2(fc)/6-311+G**; hereinafter MP2) [12] and DFT (B3LYP/6-311+G**) [13] calculations were performed with the use of GAUSSIAN 94 software package [14] and PC GAMESS 6.2 program based on the GAMESS code (US) [15]. Geometric parameters of structures corresponding to stationary points on the potential energy surfaces (PES) were optimized to a gradient value of 4.5×10^{-4} hartree/bohr. The calculated con-

figurations were checked for relevance to stationary points by calculation of harmonic frequencies. A minimum neighboring to a given transition state was localized by descent along the minimal energy path. The energies of vertical triplet transitions were calculated for all structures, and in all cases they exceeded 32 kcal/mol; therefore, only the singlet potential energy surfaces are considered below. Natural bond orbital (NBO) analysis was performed using a built-in program [16] in GAMESS software.

Migration of the nitroso group in nitrosyl formate. According to the calculations, the stable configuration is structure **I** which is characterized by anomalously long single N–O bond, 1.684 (MP2) or 1.601 Å (DFT). Migration of the nitroso group occurs through transition state **II** with a C_s symmetry (Fig. 1), and the activation barrier is extremely low, 2.4 (MP2) or 2.5 kcal/mol (DFT). The energies and geometric parameters of the calculated structures are given in Table 1 and Fig. 2. The low activation barrier can be rationalized in terms of strong destabilization of the initial state with respect to molecules having standard

Table 1. Total energies (E , a.u.), relative energies of isomeric structures (E_{rel} , kcal/mol), relative energies with correction for zero-point vibration energy [$(E + ZPE)_{rel}$, kcal/mol], and minimal or imaginary vibration frequencies (ω_1/ω_{im} , cm^{-1}) of structures **I–XII**, calculated by the MP2 and DFT methods

Structure no.	E		E_{rel}		$(E + ZPE)_{rel}$		ω_1/ω_{im}	
	MP2	DFT	MP2	DFT	MP2	DFT	MP2	DFT
I (X = O)	–318.46205	–319.12787	0	0	0	0	14.7	36.5
II (X = O)	–318.45826	–319.12386	2.4	2.5	2.4	2.7	$i^*203.8$	$i^*39.5$
III (X = S)	–963.53510	–965.05861	9.3	4.3	7.9	3.5	$i^*175.3$	$i^*135.3$
IV (X = S)	–963.55000	–965.06542	0	0	0	0	216.2	103.5
V (X = Se)	–4968.03000	–4971.72475	11.3	5.7	10.0	4.9	$i^*168.3$	$i^*130.6$
VI (X = Se)	–4968.04800	–4971.73383	0	0	0	0	190.1	90.4
VII (X = NH)	–278.66405	–279.37727	0	0	0	0	92.3	142.8
VIII (X = NH)	–278.63234	–279.33751	19.9	25.0	18.8	23.5	186.4	$i^*218.6$
IX (X = NH)	–278.63216	–	20.0	–	18.7	–	$i^*209.7$	–
X (X = CH ₂)	–246.58094	–247.26157	0	0	0	0	43.2	55.7
XI (X = CH ₂)	–246.54579	–247.22435	22.1	23.4	20.8	22.2	145.6	$i^*232.8$
XII (X = CH ₂)	–246.54543	–	22.3	–	21.5	–	$i^*210.2$	–

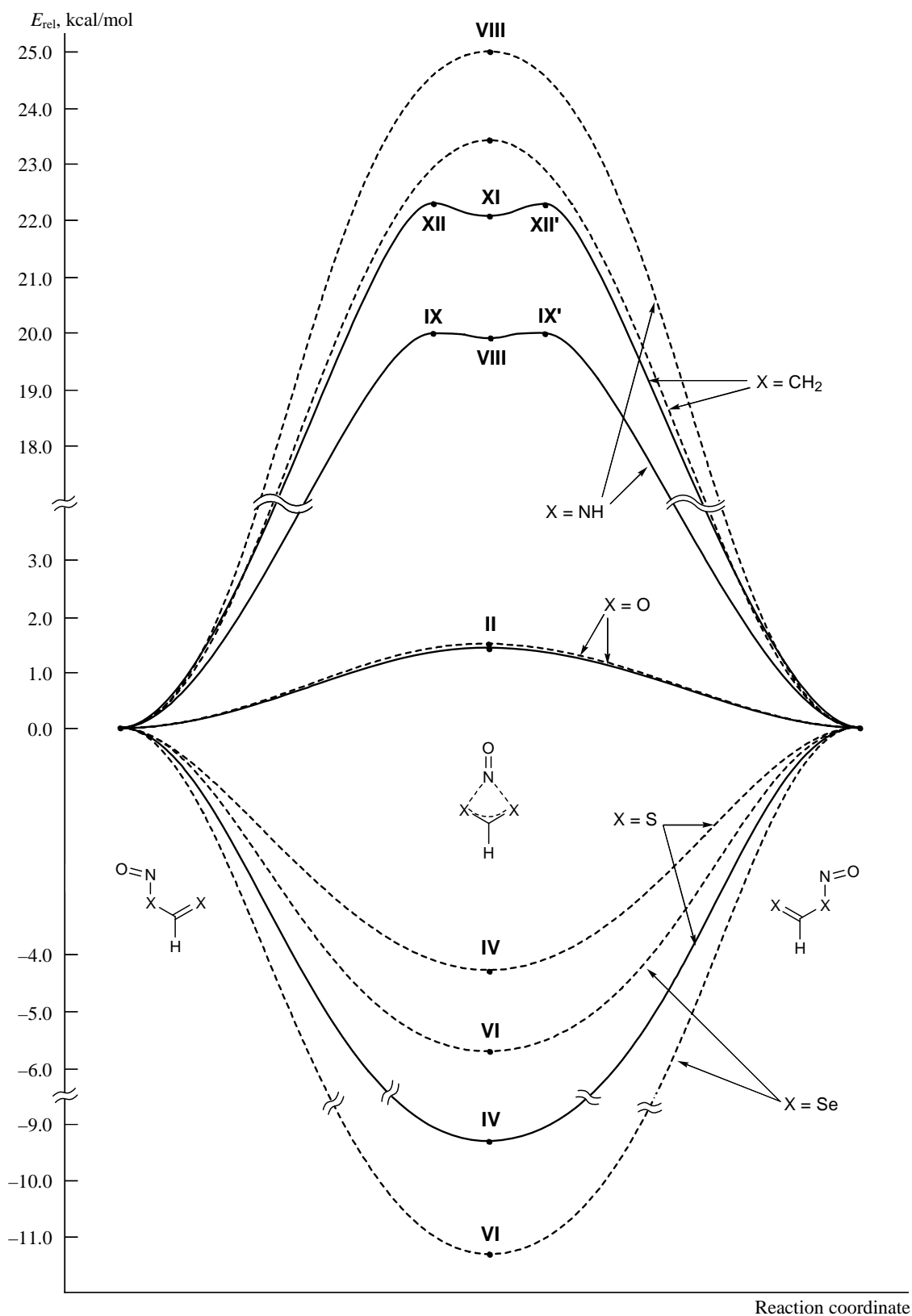


Fig. 1. Sections of the potential energy surfaces along the minimal energy path for rearrangements *a-e* (Scheme 2). Solid curves correspond to the MP2/6-311+G** data, and dashed curves, to the B3LYP/6-311+G** data. The energies of $X=CH-X-N=O$ isomers **I** ($X = O$), **III** ($X = S$), **V** ($X = Se$), **VII** ($X = NH$), and **X** ($X = CH_2$) were taken as zero values.

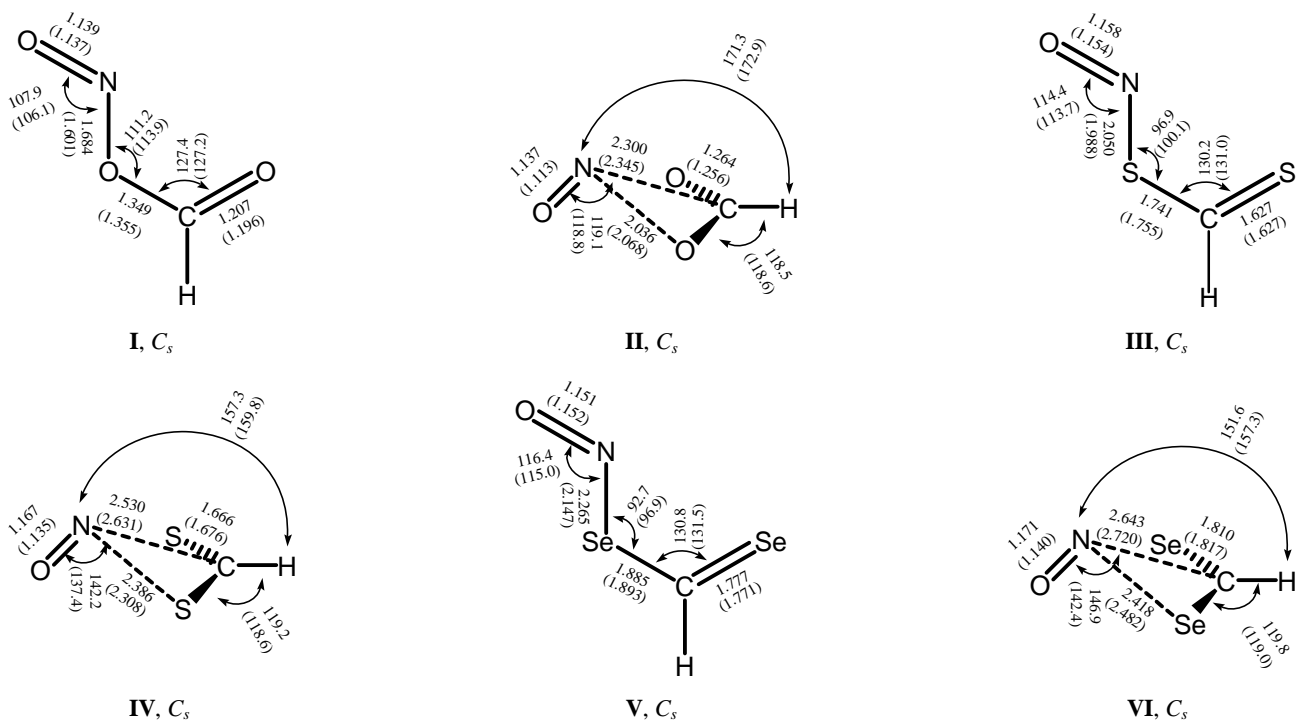


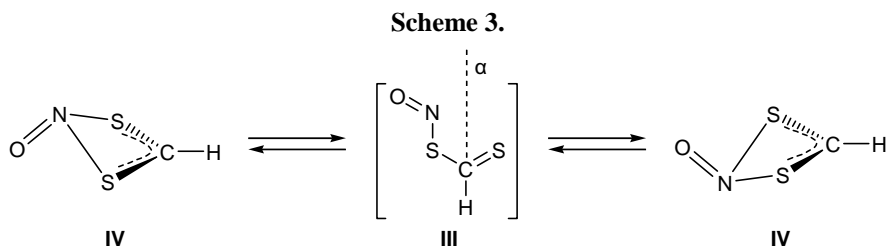
Fig. 2. Interatomic distances (Å) and bond angles (deg) in the structures corresponding to stationary points along the minimal energy paths of rearrangements *a-c* (Scheme 2), calculated by the MP2/6-311+G** and B3LYP/6-311+G** (in parentheses) methods.

covalent bonds (the sum of the covalent radii of the nitrogen and oxygen atoms is 1.36 Å [17]). In keeping with the charge distribution, transition state **II** cannot be a contact ion pair: the overall charge on the NO group does not exceed +0.29 (Table 2).

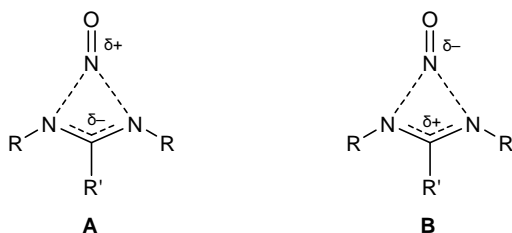
Migration of the nitroso group in nitrosyl dithioformate and nitrosyl diselenoformate. The stable structure of nitrosyl dithioformate is **IV** where the NO group is two-coordinate, unlike one-coordinate nitroso group in the initial state of nitrosyl formate (**I**). Here, transition state **III** with one-coordinate nitroso group does not correspond to migration of the nitroso group from one sulfur atom to the other, but conforms to its internal rotation about the α axis (Scheme 3), which is accompanied by displacement of the N=O bond center to the plane of the dithioformate fragment; the activation barrier to internal rotation is 9.3 (MP2) or 4.3 kcal/mol (DFT).

Both initial (**VI**) and transition states (**V**) of nitrosyl diselenoformate are very similar to the corresponding nitrosyl dithioformate structures. The calculation results are presented in Fig. 2 and Table 1. In this case, the internal rotation is characterized by an activation barrier of 11.3 (MP2) or 5.7 kcal/mol (DFT).

Migration of the nitroso group in *N*-nitrosoformimidamide. The calculation showed that stable structure **VII** is characterized by a single covalent bond between the nitroso group and one nitrogen atom of the amidine fragment. The length of that bond is 1.359 (MP2) or 1.356 Å (DFT) (Fig. 3), i.e., it is almost equal to the sum of the covalent radii of the corresponding atoms (1.4 Å [18]; cf. structure **I**). MP2 calculations identified symmetric structure **VIII** as intermediate; according to DFT calculations, structure **VIII** is a true transition state. The energy of activation of the process [20.0 (MP2) or 25.0 kcal/mol (DFT)] is



much greater than the energy of activation of reaction *a* (Scheme 2), presumably due to increased strength of the N–NO bond in structure **VII** as compared to the O–NO bond in structure **I**. Our theoretical data are consistent with the experimental energy barriers [6] of the reaction shown in Scheme 1, which range from 14 to 18 kcal/mol, depending on the donor–acceptor power of the R and R' substituents. The Mulliken charges on atoms in structures **VII** and **VIII** (Table 2) conform to the charge distribution proposed in [6] for intermediate **VIII** (**A** rather than **B**).



Factors determining the strength of the X–NO bond (X = O, NH, CH₂). Stabilization or destabilization of the X–NO bond is determined mainly by two interactions: (1) donation of electron density from the unshared electron pair on the X atom to the antibonding π -N=O orbital and (2) donation of electron

density from the unshared electron on the nitroso oxygen atom to the antibonding σ -X–N orbital. The first of these makes the X–N bond stronger at the expense of the π -N=O bond, which leads to appearance of a partial positive charge on the X atom and a partial negative charge on the oxygen atom of the nitroso group. The second factor makes the X–N bond weaker because of strengthening of the N=O bond which becomes partially triple; this is accompanied by appearance of a partial positive charge on the X atom and a partial negative charge on the nitroso group. It should be noted that free NO molecule is capable of readily losing an electron to give triple-bonded nitrosonium cation which is isoelectronic to N₂ molecule. The magnitude of the first effect in nitrosoamidine molecule **VII** (X = N) is greater by a factor of ~7 than in nitrosyl formate molecule **I** (X = O). The second effect in molecule **VII** turned out to be weaker than in **I** by a factor of ~5.

Migration of the nitroso group in 3-nitroso-propene. Taking into account that a double C=C bond can also act as nucleophile, we examined migration of the NO group along the allyl fragment (reaction *e* in Scheme 2). According to the calculations, structure **X** is the initial state in the migration process. Structure

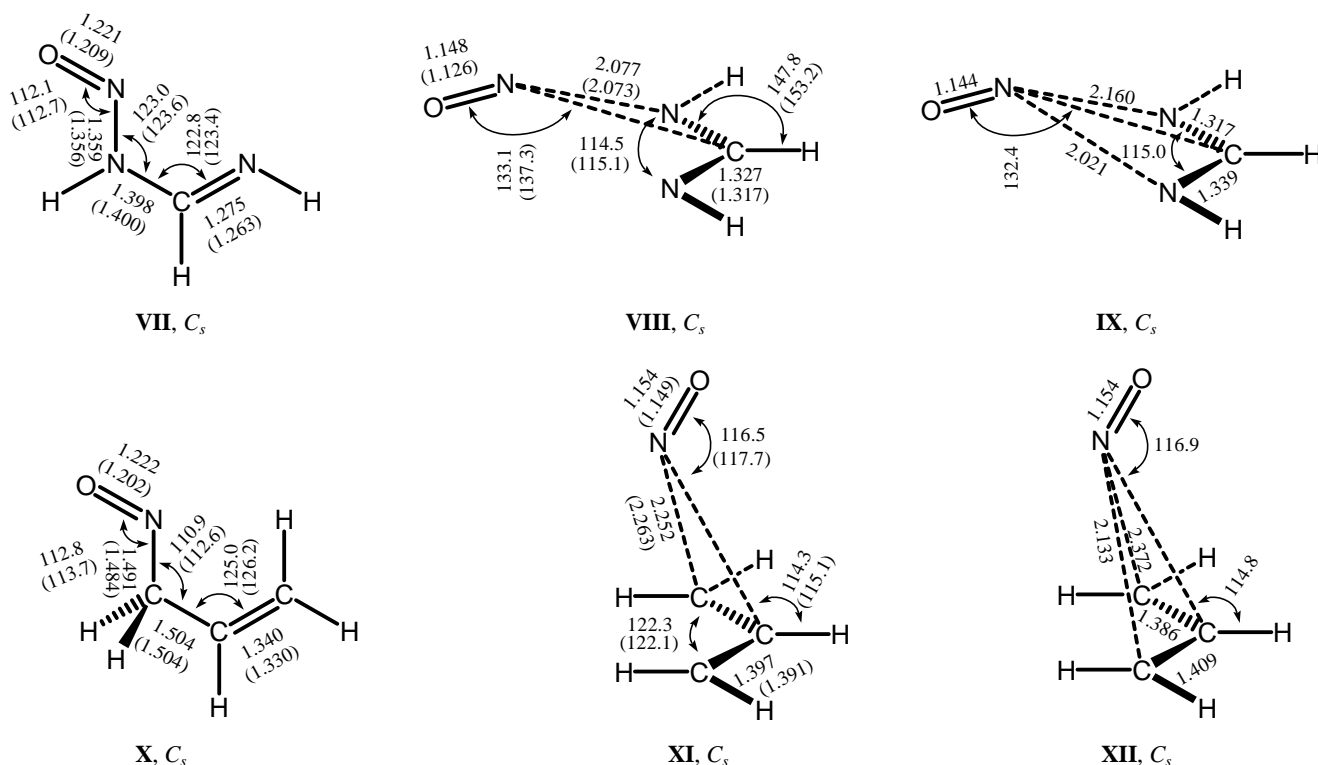


Fig. 3. Interatomic distances (Å) and bond angles (deg) in the structures corresponding to stationary points along the minimal energy paths of rearrangements *d* and *e* (Scheme 2), calculated by the MP2/6-311+G** and B3LYP/6-311+G** (in parentheses) methods.

Table 2. Mulliken charges on atoms in structures corresponding to stationary points on the minimal energy paths of reactions *a*, *d*, and *e* (Scheme 2), calculated by the MP2/6-311+G** and B3LYP/6-311+G***^a methods

Reaction	Initial state				Transition state				Intermediate		
	N	O	-Nu-	=Nu	N	O	-Nu-	=Nu	N	O	Nu
<i>a</i> (X = O)	-0.01 (-0.02)	+0.26 (+0.17)	-0.16 (-0.10)	-0.28 (-0.29)	-0.03 (+0.04)	+0.32 (+0.24)	-0.22 (-0.25)	-	-	-	-
<i>d</i> (X = NH)	-0.09 (-0.11)	-0.04 (-0.08)	-0.13 (-0.06)	-0.35 (-0.37)	+0.06 (+0.12)	+0.27 (+0.17)	-0.38 (-0.42)	-0.43 (-0.42)	+0.05	+0.26	-0.40
<i>e</i> (X = CH ₂)	-0.05 (-0.04)	-0.01 (-0.06)	-0.49 (-0.43)	-0.36 (-0.36)	+0.03 (+0.03)	+0.16 (+0.06)	-0.54 (-0.46)	-0.49 (-0.46)	+0.03	+0.17	-0.52

^a In parentheses.

XI with a C_s symmetry was identified as intermediate (MP2) or true transition state along the NO migration path (DFT). The minimal energy profile of reaction *e* is shown in Fig. 1. Attempted optimization with conservation of the C_2 symmetry led to several stationary points with a C_{2v} symmetry, which were identified as hills ($\lambda > 1$) on the PES of 3-nitrosopropene.

We can conclude that migrations of the nitroso group in chalcogen-containing systems (X = O, S, Se) are characterized by extremely low activation barriers which disappear for X = S and X = Se, leading to the most stable structures with two-coordinate NO group. The barriers to 1,3-migration of the nitroso group in the amidine (X = NH) and allyl systems (X = CH₂) are relatively high: they exceed 20 kcal/mol.

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