Cheletropic Decomposition of Cyclic Nitrosoamines Revisited: The Nature of the Transition States and a Critical Role of the Ring Strain†

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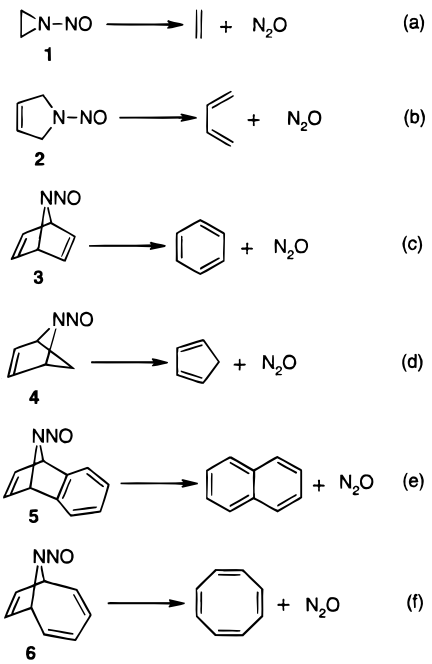
The cheletropic decompositions of 1-nitrosoaziridine (**1**), 1-nitroso-Δ^3-pyrroline (**2**), 7-nitroso-7-azabicyclo[2.2.1]hepta-2,5-diene (**3**), and 6-nitroso-6-azabicyclo[2.1.1]hexa-4-ene (**4**) have been studied theoretically using high level ab initio computations. Activation parameters of the decomposition of nitrosoaziridine **1** were obtained experimentally in heptane ($\Delta H^{\ddagger}_{298} = 18.6$ kcal mol^{-1}, $\Delta S^{\ddagger}_{298} = -7.6$ cal mol^{-1} K^{-1}) and methanol (20.3 kcal mol^{-1}, 0.3 cal mol^{-1} K^{-1}). Among employed theoretical methods (B3LYP, MP2, CCD, CCSD(T)//CCD), the B3LYP method in conjunction with 6-31+G*, 6-311+G**, and 6-311++G(3df,2pd) basis sets gives the best agreement with experimental data. It was found that typical *N*-nitrosoheterocycles **2**−**4** which have high N−N bond rotation barriers (>16 kcal mol^{-1}) extrude nitrous oxide via a highly asynchronous transition state with a planar ring nitrogen atom. Nitrosoaziridine **1**, with a low rotation barrier (<9 kcal mol^{-1}) represents a special case. This compound can eliminate N_2O via a low energy linear synperiplanar transition state ($\Delta H^{\ddagger}_{298} = 20.6$ kcal mol^{-1}, $\Delta S^{\ddagger}_{298} = 2.5$ cal mol^{-1} K^{-1}). Two higher energy transition states are also available. The B3LYP activation barriers of the cheletropic fragmentation of nitrosoheterocycles **2**−**4** decrease in the series: **2** (58 kcal mol^{-1}) ≫ **3** (18 kcal mol^{-1}) > **4** (12) kcal mol^{-1}. The relative strain energies increase in the same order: **2** (0 kcal mol^{-1}) ≪ **3** (39 kcal mol^{-1}) < **4** (52 kcal mol^{-1}). Comparison of the relative energies of **2**−**4** and their transition states on a common scale where the energy of nitrosopyrroline **2** is assumed as reference indicates that the thermal stability of the cyclic nitrosoamines toward cheletropic decomposition is almost entirely determined by the ring strain.

Introduction

Secondary *N*-nitrosoamines are notorious carcinogens and mutagens that can be seriously hazardous to human health.[1a−e] These compounds can enter from a polluted environment[1d] or they can be formed in vivo in a reaction of nitrous acid with a secondary amine. For instance, nitrite-cured food[2] can be a source of nitrous acid, and NH-heterocycles frequently used as drug components can play the role of the amine reactant. Carcinogenic nitrosoamines undergo metabolic activation, the key step of which is α-hydroxylation catalyzed by the cytochrome P450 dependent enzyme system.[1e] However, some nitrosoheterocycles are thermally unstable to cheletropic decomposition,[3] and may be transformed to the relatively harmless products, N_2O and alkene, by a nonenzymatic route (Scheme 1). *N*-Nitroso-substituted aziridines (such as **1**) and larger unsaturated heterocycles (like **2**−**6**) are candidates for this alternative decomposition pathway but not all undergo it.

Scheme 1



In principle, an "orbital symmetry allowed" pathway can always be found in a cycloelimination reaction, with a predictable alteration of the stereochemical course

† Dedicated to Professor Remir G. Kostyanovsky on the occasion of his 65th birthday.

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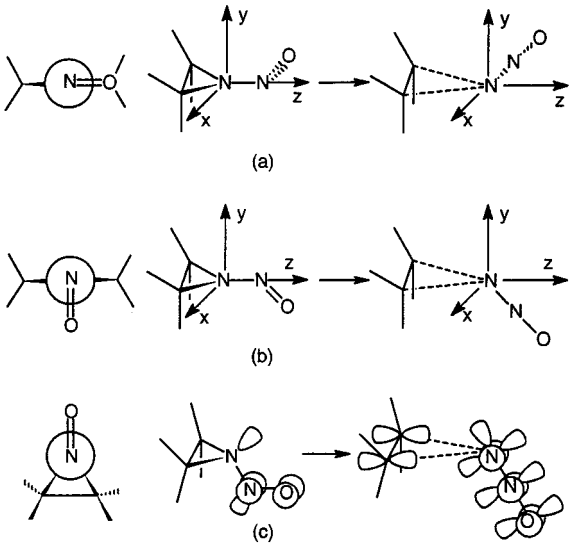
Chart 1



depending on the number of endocyclic π-bonds.[3] However, while stereochemical integrity is well maintained in a few cases, such as SO_2 elimination from cyclic unsaturated sulfones, interpretation of most cheletropic reactions in terms of orbital symmetry control is problematic. Three-membered rings appear to decompose readily by a "forbidden" pathway, the situation is less clear for other leaving groups, and activation barriers for "forbidden" pathways are often just a few kcal mol^{-1} higher than "allowed" pathways.[3b]

Nitrous oxide elimination from compounds such as nitrosoheterocycles **1**−**6** is a case in point. Previous experimental studies[4−8] of the thermal stability of compounds **1**, **2**, **5**, **6** suggests that not all such classes of nitrosoheterocycles are able to undergo fast cheletropic fragmentation. Rapid decomposition was observed only for nitrosoaziridine **1**[4a,b] and its derivatives,[4c,d] and for 7-nitroso-7-azabenznorbornadiene **5**[5] (benzo derivative of **3**), at a temperature below 0 °C and at 45 °C, respectively. On the other hand, 1-nitroso-Δ^3-pyrroline (**2**)[6] and 9-nitroso-9-azabicyclo[4.2.1]nona-2,4,7-triene (**6**)[7] resist the cycloelimination of N_2O. Nitrosopyrroline **2** was less than half decomposed by heating for 1 h at 200 °C.[6] From the main products of thermolysis[6] of **2**, pyrrole, and a polymer, one can conclude that the decomposition does not proceed by the cheletropic pathway. Similarly, bicycle **6** gave[7] a polymer and only traces of N_2O after 30 min at 198 °C.

Attempts to rationalize the nature of transition states for cheletropic fragmentation of cyclic nitrosoamines such as **1**, **2**, **5**, and **6** have a long history.[3−8] Woodward and Hoffmann[3a] proposed two alternative cheletropic transition states for nitrosoaziridine **1**, one with a planar configuration in which the departure of the NNO fragment proceeds by a nonlinear pathway in the plane of the three-membered ring (Chart 1a), and an alternative mode which requires prior rotation about the N−N bond (Chart 1b).

Freeman and Graham[8] and, subsequently, Mock and Isaac[3b,7] believed that the ability of a cyclic nitrosoamine to adopt the antiperiplanar (*ap*) conformation about the N−N bond with a pyramidal ring nitrogen (Chart 1c) is a key factor for the extrusion of N_2O. In their opinion, the *ap* conformation is most appropriate for the molecular orbital correlation between the initial nitrosoheterocycle and nitrous oxide. Adoption of such a conformation for the unstrained nitrosoamines **2** and **6** would entail an energy cost of ca. 23 kcal mol^{-1}, the estimated value[3b,7] of the barrier for rotation about the N−N bond in **2** and **6**. This places a minimum value for the barrier hindering cheletropic decomposition of unstrained cyclic nitrosoamines. However, the *ap* conformation should be accessible for nitrosoaziridine **1**,[3b,7] which could have a pyramidal configuration of the ring nitrogen atom and a low rotation barrier due to the weakened n_N-π^*_{NO} conjugation. Mock and Isaac[3b,7] considered the influence of the ring strain on the rate of the cycloelimination of N_2O from nitrosoaziridine **1**, but regarded the stereoelectronic factor to be dominant.

Later, the assumptions about the pyramidal configuration of nitrosoaziridines and their relatively low barriers for the rotation (ca. 4 kcal mol^{-1})[9c] and inversion (ca. 8 kcal mol^{-1})[9c] were confirmed experimentally[9a−c] and theoretically.[9c,d] However, there are no such data for compounds **2**−**6** in the literature. No theoretical studies of the structure and energy of transition states for the extrusion of N_2O from nitrosoheterocycles that are formally capable of cheletropic fragmentation have been reported.

We undertook the current high level computational study of cyclic nitrosoamines **1**−**4** in order to answer two questions:

Is the ability to adopt the *ap* conformation about the N−N bond a crucial factor for the cheletropic decomposition of nitrosoheterocycles?

What is the role of ring strain in influencing the propensity of nitrosoheterocycles to undergo cheletropic fragmentation?

In answer to the first question, the structures of the ground states of nitrosoheterocycles **1**−**4** were studied, and their rotation and inversion barriers were calculated. Then the structures and energetics of the transition states for cheletropic decomposition were determined.

An answer for the second question was obtained from calculations of isodesmic reactions, in which the least-strained nitrosopyrroline **2** was used as the reference compound.

In the experimental part, we measured kinetics of the decomposition of nitrosoaziridine **1** in heptane and methanol within the temperature range from 10 to 36 °C in order to obtain values of the activation energy and enthalpy. These values were needed for verification of theoretical data and choosing the most economical and, at the same time, accurate method for calculation of the activation barriers for the cheletropic fragmentation of cyclic nitrosoamines.

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Table 1. Potential Energy Barriers[a] (kcal mol^{-1}) for the Rotations about the N−N Bond and the Inversion of the Ring Nitrogen in Nitrosoheterocycles 1−4

compound theoret level	ring N inversion ($\mathbf{TS_{inv}}$)	*syn* rotation about N−N bond (*sp*-$\mathbf{TS_{rot}}$)	*anti* rotation about N−N bond (*ap*-$\mathbf{TS_{rot}}$)	compound theoret level	ring N inversion ($\mathbf{TS_{inv}}$)	*syn* rotation about N−N bond (*sp*-$\mathbf{TS_{rot}}$)	*anti* rotation about N−N bond (*ap*-$\mathbf{TS_{rot}}$)
1				**3**			
B3LYP/6-31+G*	5.8	8.8	5.1	B3LYP/6-31+G*	0.7	27.7	18.7
B3LYP/6-311+G**	5.8	8.7	4.8	B3LYP/6-311+G**	0.6	26.8	18.2
2				**4**			
B3LYP/6-31+G*	0.0	29.4	24.4	B3LYP/6-31+G*	2.8	25.3	16.7
B3LYP/6-311+G**	0.0	29.0	23.8	B3LYP/6-311+G**	2.7	24.8	16.3

[a] Relative to the ground states, including 0.98 × ΔZPVE.

Table 2. Relative Energies[a] (kcal mol^{-1}) of the Initial Compound, Products, and Transition States for the Cheletropic Decomposition of 1-Nitrosoaziridine (1)

species	B3LYP/A[b]	B3LYP/B[b]	B3LYP/C[b]	MP2/A[b]	MP2/B[b]	CCSD(T)/A//CCD/A[b]
1	0.0	0.0	0.0	0.0	0.0	0.0
sp-$\mathbf{TS_{lin}}$-**1**	20.9	20.4	20.4	25.8	26.9	22.6
ap-$\mathbf{TS_{lin}}$-**1**	42.1	41.3	41.7	53.5	54.5	46.8
$\mathbf{TS_{nonlin}}$-**1**	49.0	47.8	48.4	46.3	43.6	47.8
$CH_2{=}CH_2 + N_2O$	−27.2	−31.2	−32.3	−35.0	−36.7	−27.3

[a] Including 0.98 × ΔZPVE and 0.967 × ΔZPVE for the B3LYP and MP2 [CCSD(T)] calculations, respectively. [b] Basis set "A" is 6-31+G(d), "B" is 6-311+G(d,p), and "C" is 6-311++G(3df,2pd).

Table 3. Calculated Activation Parameters[a] for the Cheletropic Decomposition of 1-Nitrosoaziridine (1) via the Lowest Energy Transition State *sp*-$\mathbf{TS_{lin}}$-1

level	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$
B3LYP/6-31+G*	2.7	21.1	20.3
B3LYP/6-311+G**	2.5	20.6	19.9
B3LYP/6-311++G(3df,2pd)	2.8	20.6	19.8
MP2/6-31+G*	3.8	26.2	25.0
MP2/6-311+G**	5.8	27.2	25.5
CCSD(T)/6-31+G*//CCD/6-31+G*	2.7	22.1	21.3

[a] At 298 K; $\Delta S^{\ddagger}$ in cal mol^{-1} K^{-1}, $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ in kcal mol^{-1}.

Table 4. Experimental Rate Constants and Activation Parameters[a] for the Cheletropic Decomposition of 1-Nitrosoaziridine (1)

T (K)	$10^4 \times k$ (s^{-1})	$\Delta G^{\ddagger}_T$ (kcal mol^{-1})
	In Heptane	
283	4.76 ± 0.05	20.83
285	6.51 ± 0.06	20.80
287	7.60 ± 0.04	20.86
289	10.0 ± 0.1	20.86
291	11.96 ± 0.05	20.90
293	17.4 ± 0.3	20.83
295	19.99 ± 0.07	20.90
297	23.0 ± 0.1	20.96
299	30.2 ± 0.1	20.94
301	36.8 ± 0.3	20.97
303	44.0 ± 0.8	21.00
305	57.4 ± 0.9	20.98
307	76.8 ± 0.5	20.95
309	86.5 ± 0.9	21.01
	$E_a{}^b = 19.2 \pm 0.6$, ln $A^b = 26.6 \pm 1.1$, $\Delta H^{\ddagger} = 18.6 \pm 0.6$, $\Delta S^{\ddagger} = -7.6 \pm 2.2$	
	In Methanol	
283	12.3 ± 0.1	20.29
285	18.34 ± 0.07	20.22
287	22.2 ± 0.3	20.25
289	29.5 ± 0.4	20.23
291	36.5 ± 0.3	20.26
293	41.0 ± 0.5	20.33
295	59.5 ± 0.4	20.26
297	86 ± 2	20.18
299	103.0 ± 0.7	20.21
301	122 ± 2	20.25
303	148 ± 3	20.27
305	184 ± 3	20.28
	$E_a{}^b = 20.9 \pm 1.1$, ln $A^b = 30.6 \pm 2.0$, $\Delta H^{\ddagger} = 20.3 \pm 1.1$, $\Delta S^{\ddagger} = 0.3 \pm 3.9$	

[a] At 298K; $\Delta S^{\ddagger}$ in cal mol^{-1} K^{-1}, E_a, and $\Delta H^{\ddagger}$ in kcal mol^{-1}. [b] As estimated from a ln k versus [(1/*T*), K^{-1}] plot.

Computational Methods

All ab initio calculations presented here were performed with the Gaussian 94[10a] and Gaussian 98[10b] systems of programs. The geometry optimizations were carried out at various levels of theory including the B3LYP, MP2, and CCD methods with the internal 6-31+G*, 6-311+G**, and 6-311++G(3df,2pd) basis sets, using procedures implemented in the Gaussian molecular orbital packages. The CCD/6-31+G* energies were refined by single-point calculations at the CCSD(T)/6-31+G* level of theory. The methods and basis sets used for the calculations of each specific reaction system are shown in Tables 1−6. Vibrational frequency calculations were performed on all stationary points at the B3LYP and MP2 levels, and transition structures were characterized by a single imaginary frequency, whereas initial compounds and products had none. Zero-point corrections (ΔZPVE) were scaled by 0.98 for the B3LYP and by 0.967 for the MP2 level.[11] In the cases of the MP2, CCD, and CCSD(T) calculations, the frozen core approximation was used. Total energies and ZPVEs of all species are given in Tables S-1 to S-5 of the Supporting Information.

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Table 5. Relative Energies[a] (kcal mol^{-1}) of the Initial Compound, Products, and Transition State for the Cheletropic Decomposition of 1-Nitroso-Δ^3-pyrroline (2)

species	B3LYP/ 6-31+G*	B3LYP/ 6-311+G**	MP2/ 6-31+G*
2	0.0	0.0	0.0
TS-2	58.2	56.8	63.8
SP-2[b]	74.4	72.7	84.7
cis-butadiene + N_2O	4.4	0.4	1.3

[a] Including 0.98 × ΔZPVE and 0.967 × ΔZPVE for the B3LYP and MP2 calculations, respectively. [b] A second-order saddle point obtained under C_s symmetry constraint.

Table 6. Relative Energies[a] (kcal mol^{-1}) of the Initial Compounds, Products, and Transition States for the Cheletropic Decomposition of 7-Nitroso-7-azabicyclo[2.2.1]hepta-2,5-diene (3) and 6-Nitroso-6-azabicyclo[2.1.1]hex-4-ene (4)

species	B3LYP/ 6-31+G*	B3LYP/ 6-311+G**
3	0.0	0.0
TS-3	18.3	17.6
benzene + N_2O	−71.8	−74.3
4	0.0	0.0
TS-4	12.6	12.0
cyclopentadiene + N_2O	−49.3	−53.5

[a] Including 0.98 × ΔZPVE.

The intrinsic reaction coordinate (IRC)[12] path was traced in order to check the B3LYP/6-31+G* energy profiles for all cheletropic fragmentations. Both singlet and triplet stabilities of the RB3LYP and RHF solutions for the B3LYP and MP2 transition structures have been checked.[13] Heat capacities and entropy corrections were made using scaled B3LYP and MP2 frequencies and standard statistical procedures within the rigid rotator−harmonic oscillator model[14] to determine enthalpies and free energies for the cheletropic decompositions of nitrosoaziridine **1** at 289K.

Throughout the text, bond lengths are in angstroms and bond angles in degrees.

Experimental Section

1-Nitrosoaziridine (1). A solution of ClNO (0.0327 g, 0.5 mmol) in absolute heptane (1 mL) was added to aziridine (0.0431 g, 1 mmol) in absolute heptane (4 mL) with cooling (−78 °C) and stirring. After 15 min at −40 to −30 °C, the precipitate was filtered at the same temperature. The resulting solution was kept at −78 °C and was used for preparation of heptane and methanol solutions with an initial concentration of 2×10^{-2} M of **1** for kinetic measurements.

Kinetics. The progress of the decomposition of nitrosoaziridine **1** was followed at 454 nm in a thermostatically controlled spectrophotometer cell (±0.1 °C, 1 cm). Rate constants were extracted from a single-exponential trace of the change in absorbance vs time. Activation parameters were obtained from the slope and intercept on the ordinate of the best straight line plot of ln k vs T^{-1}. The rate constants and activation parameters are given in Table 4 along with the error margins at the 95% confidence limit.

Results and Discussion

Structure and Intramolecular Dynamics of Cyclic Nitrosoamines 1−4. The ring nitrogen atom is pyramidal in optimized structures of the ground states of nitrosoheterocycles **1**, **3**, and **4** (Figures 1, 3, 4, S-1, S-3, S-4, Table S-6). For nitrosopyrroline **2**, the B3LYP method predicts a planar configuration (Figures 2,S-2), while the MP2 method yields a slightly pyramidal one. The out-of-plane angle (angle α in Figures 1−4, S-1 to S-4, Table S-6) between the N−N bond and the C1N1C2 plane is a good measure of the pyramidality of the ring nitrogen. For the MP2 structure of nitrosopyrroline **2**, α = 10.4° and for the B3LYP structure α = 0.0°. Nitrosoaziridine **1** is the most nonplanar (α = ca. 54°) and bicycles **4** (α = ca. 36°) and **3** (α = ca. 30°) are less so. Despite the high pyramidality, a synclinal (*sc*) conformation about the N−N bond (Chart 2a) was found to be the ground state for nitrosoheterocycles **1**, **3**, and **4** apparently driven by the requirement to maximize the n_N-π^*_{NO} conjugation at the pyramidal ring nitrogen atom.

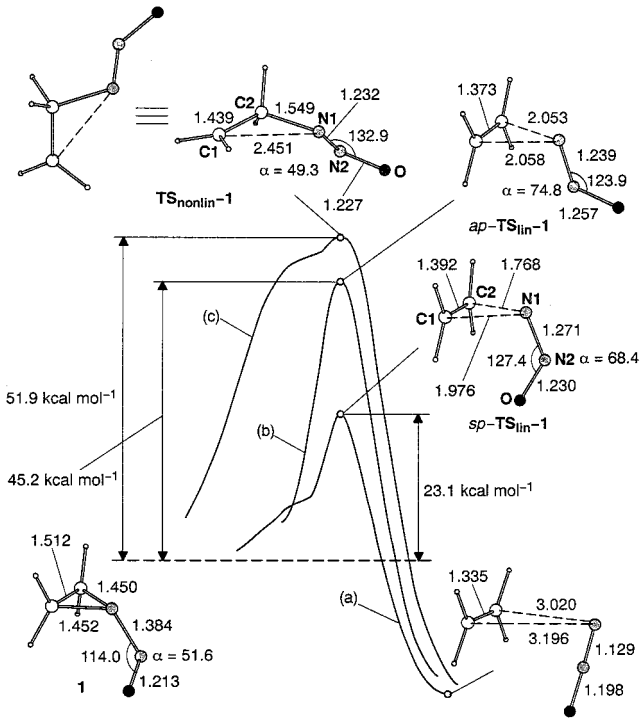

Figure 1. B3LYP/6-31+G* structures of nitrosoaziridine **1** and its transition states for the cheletropic fragmentation and graphic representations of the potential energy curves for the linear (a,b) and nonlinear pathways (c) of this fragmentation derived with the IRC-B3LYP/6-31+G* calculations. The IRC relative energies are not ZPVE corrected.

The B3LYP method, using the 6-31+G* and 6-311+G** basis sets, was used to determine the barriers to rotation about the N−N bond via syn- and antiperiplanar transition states (*ap*- and *sp*-**TS$_{rot}$**) (Chart 2b,c, Figures S-1 to S-4). The values for cyclic nitrosoamines **1**−**4** are listed in Table 1. For the pyramidal compounds **1**, **3**, and **4** transition states for the ring nitrogen inversion (**TS$_{inv}$**) (Figures S-1, S-3, S-4) were also calculated.

As one can see from Table 1, the highly pyramidal nitrosoaziridine **1** and the planar nitrosopyrroline **2** represent two extreme cases. The aziridine is characterized by quite low and similar inversion and rotation barriers. The B3LYP method gives a rather different ratio of these barriers for **1** in comparison with the HF/6-31G* and MP2/6-31+G**//HF/6-31G* methods used earlier.[9c] However, it is important that all methods predict the stereochemical flexibility for nitrosoaziridine

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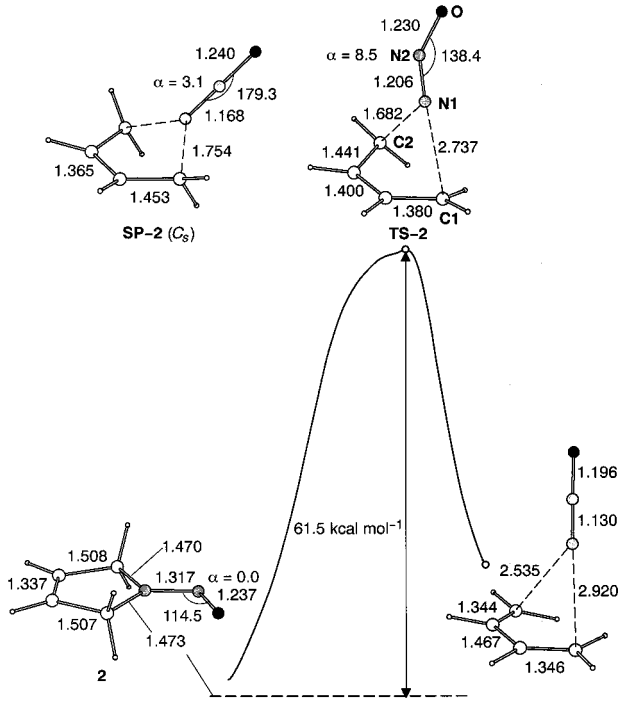


Figure 2. B3LYP/6-31+G* structures of nitrosopyrroline **2**, its second-order saddle point, and transition state for the cheletropic fragmentation and graphic representation of the potential energy profile for this fragmentation derived with the IRC-B3LYP/6-31+G* calculations. The IRC relative energies are not ZPVE corrected.

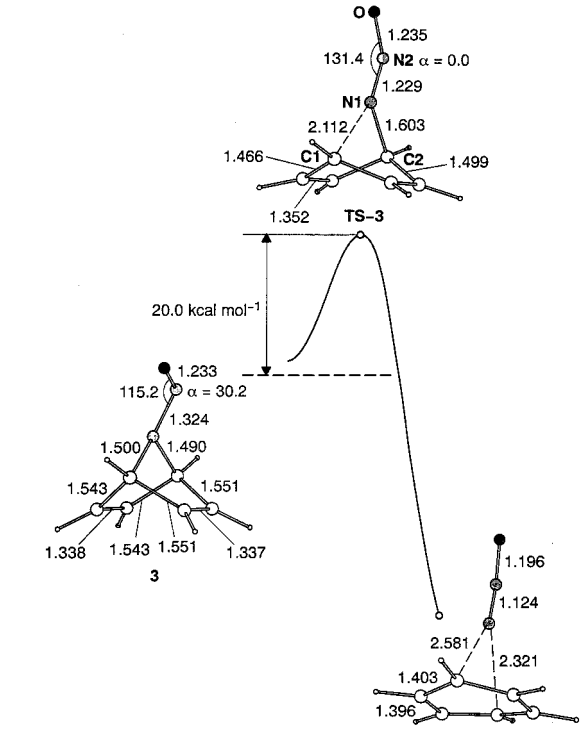


Figure 3. B3LYP/6-31+G* structures of nitrosobicycle **3** and its transition state for the cheletropic fragmentation and graphic representation of the potential energy profile for this fragmentation derived with the IRC-B3LYP/6-31+G* calculations. The IRC relative energies are not ZPVE corrected.

1. In contrast, the nitrosoamine group in nitrosopyrroline **2** is relatively rigid, with rotation barriers > 23 kcal mol^{-1}.

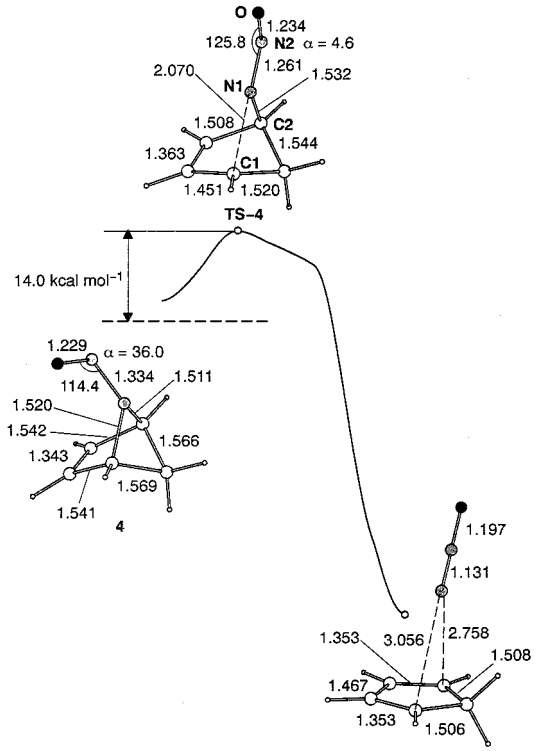
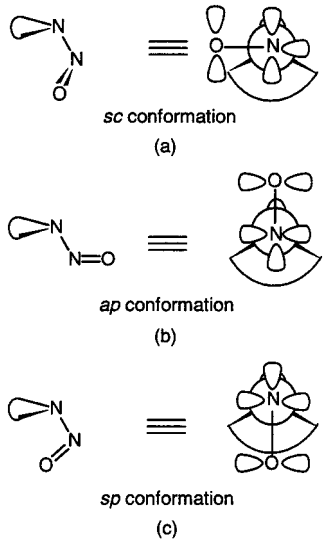


Figure 4. B3LYP/6-31+G* structures of nitrosobicycle **4** and its transition state for the cheletropic fragmentation and graphic representation of the potential energy profile for this fragmentation derived with the IRC-B3LYP/6-31+G* calculations. The IRC relative energies are not ZPVE corrected.

Chart 2



The calculated potential barriers for the internal rotation in nitrosobicycles **3** and **4** proved to be closer to that of the *planar* nitrosopyrroline **2** than to the *pyramidal* nitrosoaziridine **1** (Table 1). These compounds have relatively high rotation barriers (>16 kcal mol^{-1}) and extremely low inversion barriers(<3 kcal mol^{-1}). The ratio of the B3LYP inversion and rotation barriers in bicycle **4** which contains an azetidine ring is similar to the ratio calculated for 1-nitrosoazetidine at the HF/6-31G* level.[15]

(15) Shustov, G. V.; Rauk, A. *J. Am. Chem. Soc.* **1995**, *117*, 928.

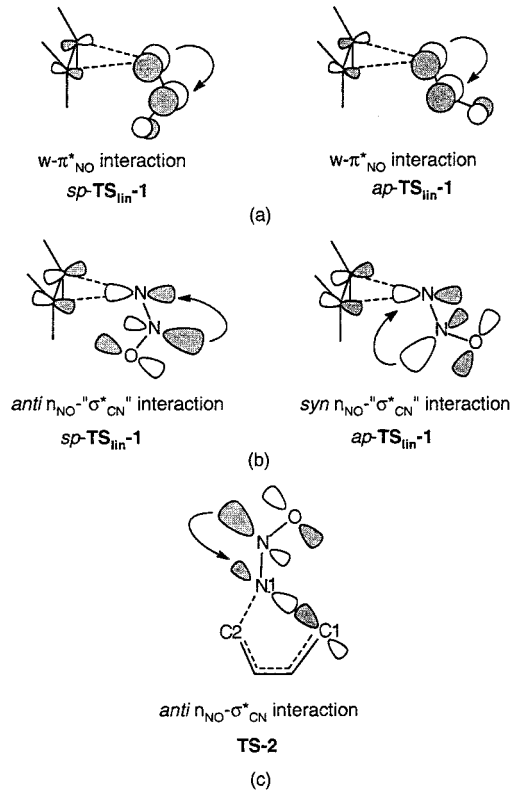
For all cyclic nitrosoamines **1**−**4**, the *sp* transition state of the rotation, *sp*-**TS$_{rot}$**, is more destabilized than its *ap*-isomer, *ap*-**TS$_{rot}$** (Table 1), due to a strong steric repulsion between the syn-oriented nitroso group and the ring.

The Nature of the Transition States for the Cheletropic Decomposition of Nitrosoheterocycles 1−4. 1-Nitrosoaziridine (1). As was indicated in the Introduction, all early attempts to rationalize the nature of the transition state for the cheletropic decomposition of cyclic nitrosoamines were based on nitrosoaziridine **1**. This compound is the simplest one in the series of nitrosoheterocycles **1**−**4** and is most appropriate for testing various levels of theory (Tables 2, 3). The experimentally measured activation parameters for the cheletropic decomposition of **1** (Table 4) give the opportunity to verify the theoretical data.

Two transition states were located, with syn- and antiperiplanar orientations of the NNO fragment, *sp*- and *ap*-**TS$_{lin}$-1**, respectively. Both correspond to a linear cycloelimination geometry. The MP2 and CCD methods predict C_s symmetry for these species (Table S-6), while the B3LYP structures of *sp*- and *ap*-**TS$_{lin}$-1**, deviate somewhat from C_s (Figure 1, Table S-6). The transition state *sp*-**TS$_{lin}$-1** is considerably more nonsymmetrical than its *ap* isomer.

The pathways of the cheletropic decomposition of nitrosoaziridine **1** via the isomeric transition states *sp*- and *ap*-**TS$_{lin}$-1** were confirmed by the IRC−B3LYP/6-31+G* calculations (Figure 1). The shoulder on the IRC curve obtained from *sp*-**TS$_{lin}$-1** (Figure 1a) is caused by an initial rotation around the N−N bond in **1** in order to adopt a conformation similar to *sp*-**TS$_{rot}$** (Chart 2c). In this conformation, the stabilizing interaction of the π-like Walsh orbital of the three-membered ring with the antibonding π^* orbital of the NO group is maximized (Chart 3a).

Chart 3



In the case of *ap*-**TS$_{lin}$-1**, rotation transition state *ap*-**TS$_{rot}$-1** was identified as a minimum during the IRC calculations toward the initial compound. This curious result indicates a bifurcation in the reaction coordinate to clockwise or anticlockwise rotation.

The calculated relative energy of the antiperiplanar transition state, *ap*-**TS$_{lin}$-1**, is twice as high as the energy of the synperiplanar isomer, *sp*-**TS$_{lin}$-1**, at all theoretical levels (Table 2). The preferable anti interaction of the n orbital of the NO group with the antibonding σ-like group orbital ("σ^*_{CN}") of the breaking CN bonds of the three-membered ring (Chart 3b) seems to be the determining factor in the stabilization of *sp*-**TS$_{lin}$-1** with respect to its anti isomer. The repulsion of the syn-nitroso group and aziridine ring, which determines the relative energies of the *sp* and *ap* isomers of the rotation transition state, **TS$_{rot}$-1**, is less important in the isomers of the transition state of the linear cheletropic fragmentation owing to the long C−N distances. The stereoelectronic situation for the w-π^*_{NO} interaction is apparently the same for both isomers of **TS$_{lin}$-1** (Chart 3a).

A transition structure for nonlinear decomposition of nitrosoaziridine **1** was also located. In contrast to the proposition of Woodward and Hoffmann,[3a] this transition state, **TS$_{nonlin}$-1**, has a pyramidal configuration of the ring nitrogen N1 (Figure 1, Table S-6). The pyramidality of this nitrogen (α = ca. 45°) is lower than in the linear transition states *sp*-**TS$_{lin}$-1** (α = ca. 69°) and *sp*-**TS$_{lin}$-1** (α = ca. 75°). The nonlinear transition state **TS$_{nonlin}$-1** was found to be even more asynchronous than *sp*-**TS$_{lin}$-1**: the ratio of the C1−N1 and C2−N1 bond distances is ca. 1.6 for **TS$_{nonlin}$-1** and ca. 1.1 for *sp*-**TS$_{lin}$-1** (Figure 1, Table S-6). As in the case of *sp*-**TS$_{lin}$-1**, the IRC-B3LYP/6-31+G* curve obtained from **TS$_{nonlin}$-1** has a shoulder. However, the origin of this shoulder is different: for **TS$_{nonlin}$-1**, it is caused by a considerable stretching of the C1−N1 bond concurrent with a relatively small change in the C2−N1 bond length. There is a noticeable charge separation between the $C1H_2$ group (+0.177e) and N1 atom (−0.255e) in **TS$_{nonlin}$-1**. Notably, and unlike *sp*- and *ap*-**TS$_{lin}$-1**, the nonlinear transition state **TS$_{nonlin}$-1** exhibits a RHF → UHF instability for both the B3LYP and MP2 structures. This may be interpreted as arising from some diradical character of this species.

Relative energies of **TS$_{nonlin}$-1** calculated at the B3LYP and CCSD(T) levels are even higher than the energies of *ap*-**TS$_{lin}$-1** (Table 2). Therefore the linear pathway via the lowest energy *sp*-**TS$_{lin}$-1** remains the most probable pathway for the cheletropic decomposition of nitrosoaziridine **1**. The B3LYP activation enthalpies (Table 3), calculated for this pathway, are in excellent agreement with the experimental values (Table 4). Good results were also obtained at the CCSD(T)/6-31+G*//CCD/6-31+G* level, while the MP2 method notably overestimates the activation enthalpy. The use of the various basis sets in the B3LYP calculations produced little change in the values of the activation parameters (Table 3).

The theoretical calculations modeling the reaction in a vacuum predict a small positive activation entropy (Table 3) that is normal for a fragmentation process. However, $\Delta S^{\ddagger}$ obtained from the kinetics of the decomposition of nitrosoaziridine **1** in methanol (Table 4), is close to zero, and the activation entropy, measured in heptane, is negative. Small or negative entropies of activation for decomposition reactions are attributed to

dipole−dipole or dipole−induced dipole interactions[16] between a polar transition state and solvent molecules. This results in increased solvent molecule order in the polar transition state relative to the less polar ground. In methanol, this effect is less pronounced than in heptane because hydrogen bonded molecules of methanol themselves are already in order.

As it follows from the results of the present study of nitrosoaziridine **1**, the B3LYP method in conjunction with the 6-31+G* and 6-311+G** basis sets is the most economical and at the same time adequate method for calculation of the cheletropic fragmentation of cyclic nitrosoamines. Therefore, nitrosoheterocycles **2**, **3**, and **4** were studied mostly by means of this method.

1-Nitroso-Δ³-pyrroline (2). The transition state **TS-2** for the cycloelimination of N_2O from nitrosopyrroline **2** is characterized by an almost planar ring nitrogen atom (Figure 2): the out-of plane angle α is ca. 8° at the B3LYP level and ca. 4° at the MP2 level. Such planarity of the nitrosoamine fragment results in a high degree of asynchronicity of bond breaking because the n_{NO} orbital lying in the NNO plane interacts preferably with the σ^* orbital of the anti-oriented C1−N1 bond (Chart 2c). There is apparently no stabilizing interaction of occupied orbitals of the C−N bonds with the π^*_{NO} orbital in **TS-2** similar to the w-π^*_{NO} interaction in $\mathbf{TS_{lin}}$**-1** (Chart 2a) because these orbitals are almost orthogonal at the optimized geometry of **TS-2**.

As a result of the anti n_{NO}-σ^*_{CN} interaction, the C1−N1 bond is 60% longer than the syn-oriented C2−N1 bond. A similar ratio of the C−N bonds was observed for the nonlinear transition state $\mathbf{TS_{nonlin}}$**-1** of the fragmentation of nitrosoaziridine **1**. The IRC−B3LYP/6-31+G* potential energy profile for the extrusion of N_2O from **2** via **TS-2** is also similar to the profile derived from $\mathbf{TS_{nonlin}}$**-1** though it contains a less pronounced shoulder (Figure 2). The RB3LYP wave function for **TS-2** also suffers from a RHF → UHF instability indicative of developing diradical character.

As in the case of nitrosoaziridine **1**, the MP2 method gives a higher potential barrier for the cheletropic decomposition of nitrosopyrroline **2** than does the B3LYP method (Table 5). The lowest value of the barrier, 56.8 kcal mol^{-1}, was obtained at the B3LYP/6-311+G** level. Even this value is too high for an experimental observation of the process in a reasonable period of time at 200 °C. Thus the theoretical data on thermal stability of nitrosopyrroline **2** in the channel of the cheletropic fragmentation are consistent with the experimental finding, namely that extrusion of N_2O does not occur.[6]

We tried to locate transition states for the loss of N_2O from **2** with syn- and antiperiplanar orientations of the NO group, i.e., transition states, which are similar to *sp*- and *ap*-$\mathbf{TS_{lin}}$**-1**. The NO group can be held in such orientations only under C_s symmetry constraint. A stationary structure was found only in the case of the synperiplanar orientation. This structure, second-order saddle point **SP-2** (Figures 2, S-2), contains the almost linear NNO fragment and is characterized by two imaginary frequencies. Its relative energy is higher by 16−20 kcal mol^{-1} than the energy of **TS-2** (Table 5). Reoptimization of **SP-2** after removing the symmetry constraint led back to **TS-2**.

(16) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: New York, 1988.

7-Nitroso-7-azabicyclo[2.2.1]hepta-2,5-diene (3) and 6-Nitroso-6-azabicyclo[2.1.1]hexa-4-ene (4). Despite the moderate pyramidality of the ground states of nitrosobicycles **3** (α = ca. 30°) and **4** (α = ca. 36°), the geometries of the transition states, **TS-3** and **TS-4** (Figures 3, 4, S-3, S-4), of their cheletropic decomposition are closer to the geometry of the transition state for the *planar* nitrosopyrroline **2** than for the *pyramidal* nitrosoaziridine **1**. The ring nitrogen atoms in **TS-3** (α = 0.0°) and **TS-4** (α = ca. 4°) are even more planar than in **TS-2** (α = ca. 8°). Similar to the latter, both states are asynchronous: the C1−N1 bond *anti*-oriented with respect to the n_{NO} orbital is more stretched than the *syn*-oriented C2−N1 bond. Nevertheless, the RB3LYP wave functions for **TS-3** and **TS-4** were found to be singlet stable, and the IRC−B3LYP/6-31+G* potential energy profiles derived from these states indicate a concerted mechanism of the extrusion of N_2O.

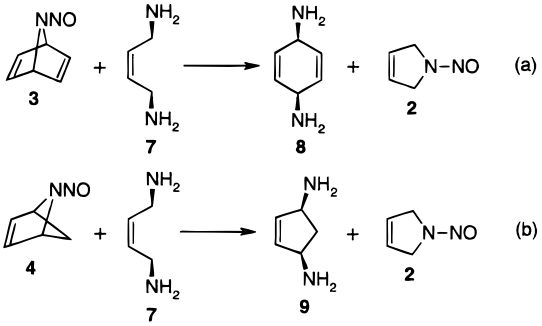
No stationary structures for the cycloelimination of N_2O from nitrosobicycles **3** and **4** were found which had a syn- or antiperiplanar conformation of the NNO fragment, despite an extensive search.

The relatively low calculated activation energy (ca. 18 kcal mol^{-1}, Table 6) for the cheletropic decomposition of nitrosobicycle **3** via the *planar* transition state **TS-3** is consistent with the experimental data[5] on the low thermal stability of its benzo derivative **5**.

Bicycle **4** contains the nitrosopyrroline **2** moiety. Nevertheless, the relative energy of transition state **TS-4** (ca. 12 kcal mol^{-1}, Table 6) is very much smaller than the energy of **TS-2** (ca. 58 kcal mol^{-1}). This dramatic decrease of the activation barrier for the decomposition of nitrosobicycle **4** must be attributed to the high ring strain of the bicyclo[2.1.1]hexene framework. Ring strain must also make a contribution in destabilization of nitrosoheterocycles **1** and **3** toward cheletropic decomposition. However, nitrosobicycle **4** compared with nitrosopyrroline **2** represents the most vivid example. We examine this question quantitatively below.

Contribution of the Ring Strain to the Barriers for Cheletropic Decomposition of Cyclic Nitrosoamines 2−4. Isodesmic reactions (Scheme 2) were calculated at the B3LYP level in order to determine the relative ring strain energies of nitrosoheterocycles **2**, **3**, and **4** in the channel of the cheletropic decomposition.

Scheme 2



Nitrosopyrroline **2** was used as the reference compound, as it is expected to have the least ring strain. Other components of the isodesmic reactions, *cis*-diamines **7**−**9** (Figure S-5), were chosen for a close modeling of the stereoelectronic situation that exists in the skeletons of nitrosoheterocycles **2**−**4**. Hence the heats of the isodesmic reactions may be interpreted as the exces-

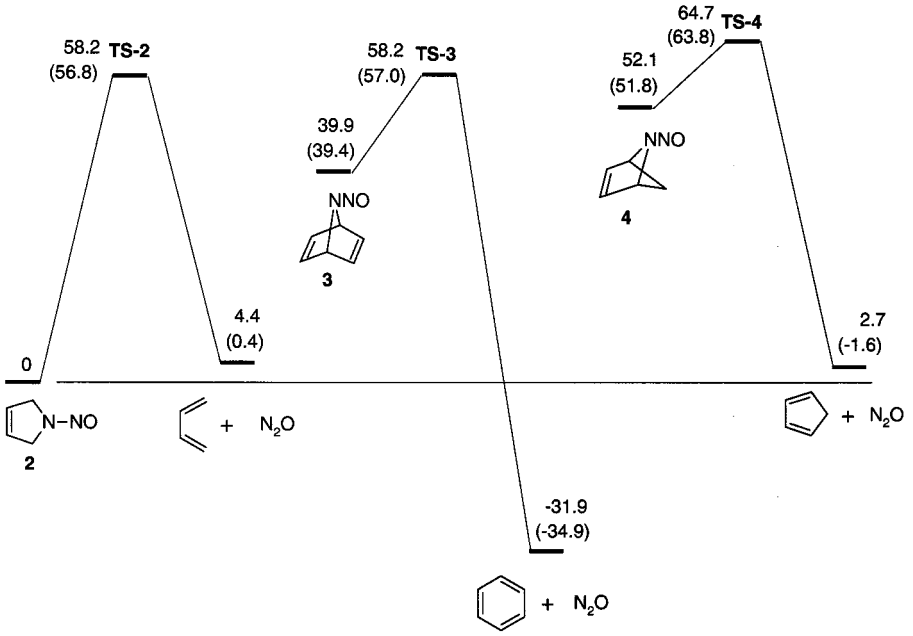


Figure 5. Schematic presentation of the B3LYP relative energies (including 0.98 × ΔZPVE) of nitrosoheterocycles **2**−**4**, their transition states and products of the cheletropic decompositions on a common scale calculated with the 6-31+G* and 6-311+G** (in parentheses) basis sets.

sive strain energies of cyclic nitrosoamines **3** and **4** with respect to nitrosopyrroline **2**.

Nitrosoaziridine **1** was deliberately excluded from the consideration because its lowest energy transition state *sp*-$\mathbf{TS_{lin}}$-**1** substantially differs from transition states **TS-2**, **TS-3**, and **TS-4** owing to the strong influence of the orbitals of the three-membered ring (vide supra). **TS-2**, **TS-3**, and **TS-4** have the following common key features: considerably asynchronous cleavage of the C−N bonds, an almost planar endocyclic nitrogen atom, and disrotatory motion of the CH(R′)R groups connected with this atom.

According to calculated heats of the isodesmic reactions, the relative strain energies increase in the series: **2** (0 kcal mol^{-1}) ≪ **3** (39) < **4** (52). The activation barriers of the cheletropic fragmentation decrease in the same order: **2** (58 kcal mol^{-1}) ≫ **3** (18) > **4** (12).

The relative energies of nitrosoheterocycles **2**−**4**, their transition states, and products of the nitrous oxide extrusion are shown in Figure 5 on a common scale where the energy of the ground state of nitrosopyrroline **2** is assumed as zero. As one can see from Figure 5, the thermal stability of the cyclic nitrosoamines in the channel of the cheletropic decomposition is almost entirely determined by the ring strain of the starting material since the energies of the transitions structures are almost the same.

Conclusions

Ring strain is the critical factor for the cheletropic decomposition of cyclic nitrosoamines. This strain destabilizes the ground state of the nitrosoamines and increases the electron donor and acceptor abilities of the CN bonds. As a result, the activation barrier for the cheletropic fragmentation decreases with increasing ring strain of the cyclic nitrosoamine.

The ability of nitrosoheterocycles to adopt a syn- or antiperiplanar conformation about the N−N bond is not a necessary condition for an easy extrusion of nitrous oxide. The cheletropic fragmentation proceeds via a highly asynchronous transition state with a (more or less) planar ring nitrogen atom. The aziridine system is an exception (see below).

1-Nitrosoaziridine with the highly pyramidal and stereochemically mobile NNO group represents a special case owing to special properties of the three-membered ring. Besides the low rotation barriers (<9 kcal mol^{-1}), this ring offers the low energy σ^*-like and high energy π-like (Walsh) *group* orbitals for the interactions with the n_{NO} and π^*_{NO} orbitals of the nitroso group, respectively. Larger rings do not have such properties and, therefore, conclusions made from the consideration of 1-nitrosoaziridine may not be applied for larger cyclic nitrosoamines.

There are three pathways for the cycloelimination of N_2O from 1-nitrosoaziridine: two linear paths via transition states with the syn- and antiperiplanar orientations of the NO group and a nonlinear pathway via a highly asynchronous transition state. In contrast to the transition states of other cyclic nitrosoamines, all three transition states of nitrosoaziridine **1** have the pyramidal ring nitrogen. The synperiplanar transition state is the lowest energy transition state for the cheletropic decomposition of 1-nitrosoaziridine.

The activation barriers calculated at the B3LYP level are in excellent agreement with the experimental data on the thermal stability of cyclic nitrosoamines in the channel of cheletropic decomposition.

Acknowledgment. The financial support of the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

Supporting Information Available: Tables S-1, S-2, S-3, and S-4 showing total energies and zero-point corrections of all studied species, Table S-6 showing selected geometrical parameters of nitrosoaziridine **1** and its transition states for the cheletropic fragmentation calculated at the various levels of theory. Figure S-1 containing B3LYP structures of the inversion and rotation transition states of nitrosoaziridine **1**, Figures S-2, S-3, S-4, S-5 containing calculated structures of all other studied species. . This material is available free of charge via the Internet at http://pubs.acs.org.

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