intensity greater than the standard deviation estimated from counting statistics. The structure was solved by direct methods (MULTAN 78)[24] and refined by least-squares methods (ORFLS).[25] Hydrogen atoms were located from a difference Fourier synthesis. Parameters refined in the last cycles were positional parameters for all atoms, isotropic thermal parameters for the hydrogen atoms, and anisotropic thermal parameters for the other atoms. The resulting $R$ factor was 3.5%. The drawing of the structure was made with the ORTEP program.[26]

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**Registry No.** 1, 37639-57-9; 2, 80242-89-3; 3, 80242-90-6; 4, 80242-91-7; 5, 80242-94-0; 6, 80242-92-8; 7, 80242-93-9; 8, 37639-56-8; 9, 80242-95-1; 10, 80242-96-2; 11, 36715-94-3; 12, 80242-97-3; 13, 80242-98-4; 14, 80242-99-5; 15, 80243-00-1; 16, 80243-01-2; 17, 80243-02-3.

**Supplementary Material Available:** X-ray structure, fractional atomic coordinates, mean square amplitudes of thermal vibration, bond distances, and bond angles of 17 (18 pages). Ordering information is given on any current masthead page.

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# Kinetic Evidence for the Intermediacy of 1-Azirines in the Gas-Phase Thermal Isomerization of 3*H*-Isoxazoles to α-Carbonylacetonitrile Derivatives

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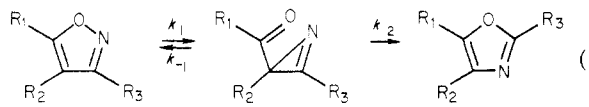
Thermal isomerization of 5-methylisoxazole and 5-amino-4-methylisoxazole to acetylacetonitrile and 2-cyanopropionamide, respectively, was studied in a flow system. The activation parameters are reported. According to the experimental results, a concerted 1,3 sigmatropic shift to 1-azirines is proposed as the rate-limiting step in these reactions. A general reaction mechanism for the isomerization of isoxazoles into 1-azirines, oxazoles, and α-carbonylacetonitrile derivatives is discussed.

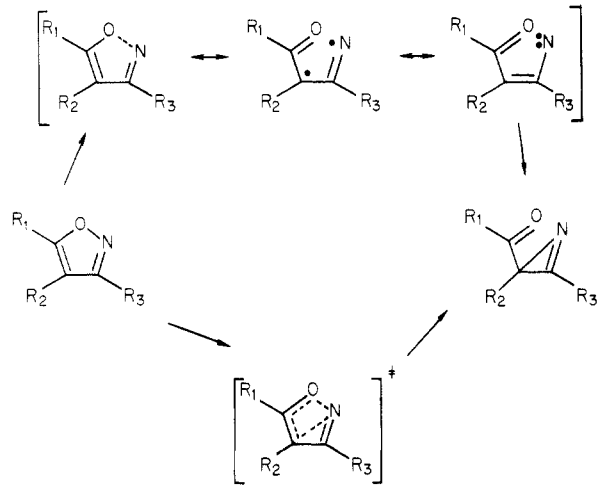
We have recently reported[2a,b] that in the gas-phase thermal isomerization of isoxazole derivatives to 1-azirines and oxazoles, the rate-limiting step is the formation of 1-azirines and its activation energy depends largely on substitution at position 5 of the isoxazole derivative (eq 1).



(1)

Moreover, we found that this effect can be rationalized through the incidence of the substituents on the HOMO of the migrating framework (MF) for the 1,3 sigmatropic shift. The $E_a$ of the isomerization depends on the energy of the HOMO of the MF as predicted with the donor–acceptor model suggested by Epiotis.[3] The kinetic results lead us to suggest two alternative reaction pathways (eq 2).

On the basis of low $A$ factors obtained, we proposed that the rate-determining step can hardly be attributed to a simple ring opening and then, in the stepwise mechanism, the transition state of the rate-limiting step must be attributed to the vinyl nitrene closure. On the other hand,



(2)

the concerted pathway is supported by both the activation parameters and the theoretical analysis, since whichever the reaction mode is (supra with inversion or supra with retention), the thermal 1,3 sigmatropic shift shows a net pericyclic bonding along the reaction coordinate.[3]

Continuing with our studies on the thermal behavior of isoxazoles in the gas phase, we studied the thermal reaction of 5-methylisoxazole **I** and 5-amino-4-methylisoxazole **2** to evaluate the influence of groups attached to position 3 of the isoxazole ring, by measuring the incidence of change of amino and methyl groups by hydrogen. The product analysis in both cases showed quantitative isomerization to the α-carbonylacetonitrile derivatives. Here

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Table I. Reactions of 5-Methylisoxazole

| temp, °C (±0.5 °C) | carrier | $k$, $s^{-1}$ [a] |
|---|---|---|
| 530 | nitrogen | 3.36 ± 0.07 |
| 540 | nitrogen | 4.27 ± 0.25 |
| 550 | nitrogen | 6.50 ± 0.31 |
| 565 | nitrogen | 9.73 ± 0.11 |

[a] Averaged over at least three determinations, contact times from $10^{-1}$ to $10^{-2}$ s and pressures from 0.2 to 0.1 torr.

Table II. Reactions of 5-Amino-4-methylisoxazole

| temp, °C (±0.5 °C) | carrier | $k$, $s^{-1}$ [a] |
|---|---|---|
| 387 | toluene | 7.07 ± 0.18 |
| 398 | toluene | 10.1 ± 0.1 |
| 408 | toluene | 14.3 ± 0.7 |
| 425 | toluene | 21.1 ± 0.6 |

[a] Averaged over at least three determinations, contact times ranged between $10^{-1}$ to $10^{-2}$ s and pressures from 0.1 to 0.6 torr.

Table III. Arrhenius Parameters for 1 and 2

| compd | log $A$ | $E_a$, kcal/mol |
|---|---|---|
| 1 | 11.9 ± 0.4 | 41.8 ± 0.4 |
| 2 | 9.0 ± 0.4 | 26.1 ± 0.3 |

we report the kinetic results of these isomerizations, and on the basis of the activation parameters, the intermediacy of 1-azirines is proposed.

## Results

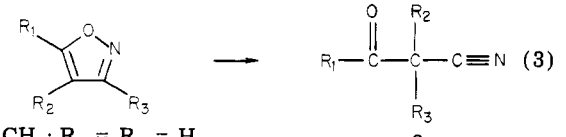
Reactions were carried out in a flow system previously described.[2]

**5-Methylisoxazole.** The only product formed was identified as acetylacetonitrile (3, eq 3). The reaction was unaffected by changing the surface/volume ($S/V$) ratio and using dry air or toluene as carrier instead of oxygen-free dry nitrogen. The specific rate constants were calculated following the decrease in 1 by UV, using water as solvent [max 221 nm (log $\epsilon$ 3.671)], according to:

$$k = (u/V_0) \ln (A_0/A_t)$$

where $u$ is the flow rate, $V_0$ is the reactor volume, and $A_0$ and $A_t$ are the absorbances of 1 at time 0 and $t$, respectively. Results are given in Table I. Arrhenius parameters obtained by the least-squares method are shown in Table III.

**5-Amino-4-methylisoxazole.** The only product formed was identified as 2-cyanopropionamide 4 (eq 3). The reaction rate was unaffected when the $S/V$ ratio was modified by packing the reaction vessel. We chose toluene as the carrier to avoid the fall-off region due to the poor collisional efficiency of nitrogen under the reaction conditions and simultaneously to check the absence of a radical chain. The specific rate constants are given in Table II and were calculated as stated above for 1 by UV, using water as solvent [max 256 nm (log $\epsilon$ 3.872)]. Arrhenius parameters calculated by the least-squares method are given in Table III.



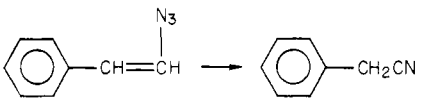
(3)

1, $R_1 = CH_3$; $R_2 = R_3 = H$
2, $R_1 = NH_2$; $R_2 = CH_3$; $R_3 = H$

3
4

## Discussion

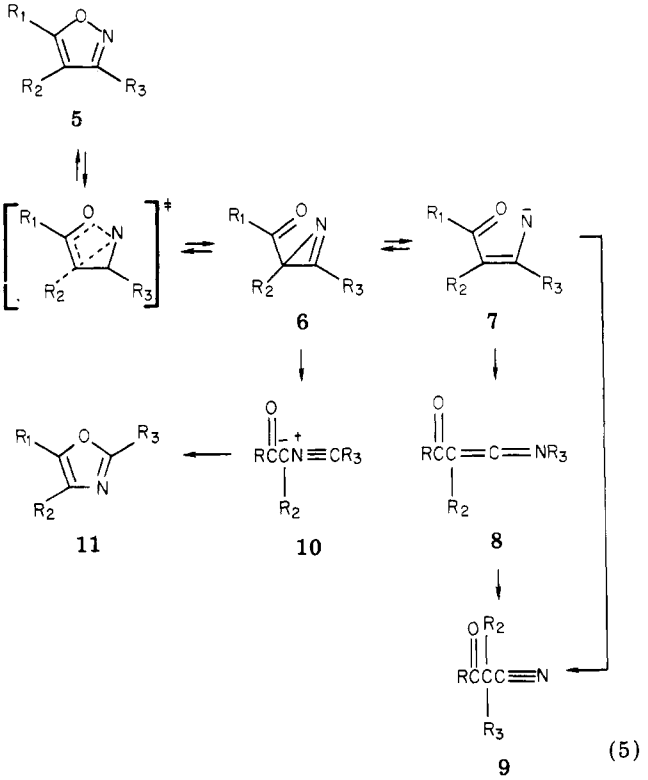
The isomerization of 1 and 2 to the α-carbonylacetonitrile derivatives agrees with the results obtained in the thermal decomposition of terminal vinyl azides, which often give nitriles as the major product. It has been strongly suggested that a vinyl nitrene is a common intermediate in these reactions.[5] However, it has been shown that the photolysis of β-styryl azides[6] at −30 °C gives 3-phenyl-1-azirines. Pyrolysis of either this azirine or the β-styryl azide at 287 °C gives phenylacetonitrile and indole, suggesting that the 1-azirine is the primary product of these reaction[7] (eq 4). On the other hand, Taniguchi[8] reported the intermediacy of vinyl nitrenes in the isomerization of 3-phenyl-1-azirine to indole.



(4)

When the isoxazoles only differ in substitution at C-3 (Table IV), it can be seen that the obtained activation parameters remain unaffected. These results indicate that whichever isomer is formed, the activation parameters are controlled essentially by the migrating framework of the 1,3 sigmatropic shift, which should lead to the 1-azirine derivative. This fact precludes to consider a simple ring opening as the rate-limiting step. So far, 1-azirines seems to be common intermediates in thermal isomerization of isoxazoles to oxazoles and α-carbonylacetonitrile derivatives.

The reaction scheme shown in eq 5 gives a satisfactory explanation to the experimental evidences up to date.



(5)

5, 6, 7, 8, 9, 10, 11

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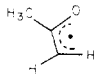
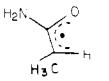
Table IV

| isoxazole | isolated product | $E_a$, kcal/mol | MF HOMO[b] | model MF |
|---|---|---|---|---|
| 3,5-dimethyl-[a] | 2,5-dimethyloxazole | 41.1 | $\alpha + 0.413\beta$ |  |
| 3-amino-5-methyl-[a] | 2-amino-5-methyloxazole | 40.2 | | |
| 5-methyl- | acetylacetonitrile | 41.8 | | |
| 5-amino-3,4-dimethyl-[a] | 3-carbamoyl-2,3-dimethyl-1-azirine | 25.8 | $\alpha + 0.222\beta$ |  |
| 5-amino-4-methyl- | 2-cyanopropionamide | 26.1 | | |

[a] From ref 2b. [b] HMO calculations were carried out by using $h_X$ and $k_{CX}$ parameters from ref 11. The methyl group was calculated as a heteroatom.

When $R_3 \neq H$ and the reaction isoxazole → 1-azirine is exothermic, the 1-azirine is isolated as the major product. When $R_3 \neq H$ and the reaction **5** → **6** is endothermic, the final product is **11**, produced via the nitrile ylide **10**. Finally, when $R_3 = H$ the reaction product is **9**, which can be formed through the ketenimine **8** or directly from **7** via a 1,2 hydrogen shift.

From the experimental results, it seems that the 1,2 hydrogen shift in the nitrene intermediate has a lower energy barrier than the C–C rupture of the 1-azirine to give the nitrile ylide. But, when $R_3 = CH_3$, $NH_2$, the 1,2 shift requires more energy than the C–C rupture of the 1-azirine ring.

For all the studied isoxazoles, according to the kinetic results, the rate-limiting step can be attributed to the 1-azirine formation, and the oxazole and α-carbonylacetonitrile isomers come from the corresponding 1-azirine.

## Experimental Section

Proton nuclear magnetic resonance spectra were recorded on a Varian T-60 spectrometer and chemical shifts are quoted in δ (parts per million) downfield from tetramethylsilane. Ultraviolet spectra were run on a Beckman Model 24 spectrophotometer. Infrared spectra were obtained on a Beckman IR 8 spectometer. Vapor phase chromatography was performed on a Varian Aerograph Series 2400. Melting points are uncorrected and were determined by the capillary method. Solvents were analytical reagents or otherwise purified by standard methods.

5-Amino-4-methylisoxazole was obtained according to the literature[9] by reaction of 3-aminoisobutyronitrile with $H_2O_2$ in the presence of $Na_2WO_4 \cdot 2H_2O$ as catalyst in methanol. The reaction products were separated by column chromatography on silica gel and sublimation in vacuo.

5-Methylisoxazole was commercially available from Fluka.

Gas-phase reactions were carried out in a Vycor glass reactor (30-cm length and 1.2-cm internal diameter). The reactor was "seasoned" by the thermal decomposition of *n*-butyl bromide at 500 °C. Heating was performed in a Lindberg heavy duty Model 55035 tube furnace. The products were obtained from the trap after reaction tube at the liquid air temperature. In all runs the mass balance between the weight of sample used and the quantitative analysis of the reaction products was higher than 97%.

**5-Amino-4-methylisoxazole.** The products trapped were eluted with water. Compound **2** was removed from the mixture by extraction with chloroform from the aqueous solution. Evaporation in vacuo of the water extract gave **4** as a residue: white crystals (mp 94–96 °C); IR (KBr) 3400, 3200, 2200, 1650, 1300 $cm^{-1}$; NMR ($Me_2SO$-$d_6$) δ 7.6 (br s, 2 H), 3.6 (q, 1 H), 1.2 (d, 3 H).

When **4** was heated under the same conditions as those used for **2**, no reaction was observed and **4** was recovered quantitatively. Hence, an equilibrium must be rejected. This result agrees with the relative thermodynamic stabilities of acetonitrile and the isomeric 1-azirine.[12]

**5-Methylisoxazole.** The trapped products were extracted with chloroform to prevent polymerization of **3**.[10] The removal of **1** from the reaction mixture was impossible due to the polymerization of **3**. For this reason, it was necessary to carry out a reaction to completion to identify **3**, which afforded the following spectral results: IR (KBr) 2900, 2200, 1730, 1650, 1350, 1300 $cm^{-1}$; NMR (chloroform-*d*) δ 2.3 (s, 3 H), 3.4 (s, 2 H); mass spectrum, *m/e* 83 ($M^{+\cdot}$, 10.6), 57 (M – CN, 25.3), 55 (M – $CNH_2$, 16.5), 43 (M – $C_2NH_2$, 100).

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**Registry No.** 1, 5765-44-6; 2, 35143-75-0; 3, 2469-99-0; 4, 71565-78-1.

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# Two-Step Route toward Some [4.3.2]Propellanes and Their Conversion into Stable Tricyclic Cations

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The synthesis of 1,4-tetramethylene(Dewar benzene) (**2**, a [4.2.2]propellane) and its conversion to the [4.3.2]propellanes **3** and **10** are described. Reaction of alcohol **10** with $FSO_3H/SO_2ClF$ at low temperature (–135 °C) yielded tricyclic cation **12**, which rearranged at –75 °C to a mixture of three isomeric cations. The structures and rearrangements of the cations were studied with $^1H$ and $^{13}C$ NMR spectroscopy and deuterium labeling.

The multifarious chemistry derived from hexamethyl(Dewar benzene) (**1**), as reported by Schäfer and Hellmann,[2] Hogeveen and Kwant,[3] and others formed an impetus for us to develop a synthetic route toward per-

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