separated to give 2.75 g (55%) of a product with mp 117-118°C and R_f 0.91 [Silufol UV-254, chloroform—ethanol (20:1)]. Found: N 5.6; S 12.6%. $C_{13}H_{17}NO_2S$. Calculated: N 5.6; S 12.7%.

1-Phenyliminobutan-3-one (VII). A mixture of 0.5 g (0.0025 mole) of thiazole IV, 5 g of Raney nickel, and 30 ml of absolute alcohol was refluxed for 6 h, after which it was filtered. The alcohol was removed from the filtrate, and the residue was distilled to give 0.11 g (30%) of a product with bp 123-125°C (2-3 mm) (bp 128-134°C (2-5 mm) [5]).

4-Methyl-2-mercaptoacetoacetanilide (VIII). A solution of 3.1 g (0.024 mole) of AAE in 5 ml of o-xylene was added in the course of 15 min to a refluxing solution of 3 g (0.02 mole) of 5-methyl-2-aminothiophenol in 30 ml of o-xylene, and the mixture was heated for 2 h. It was then cooled, and anilide VIII was separated to give 1.4 g (32%) of a product with mp 176-178°C (from ethanol) and R_f 0.70 [Silufol UV-254, chloroform—alcohol (20:1)]. Found: N 6.4; S 14.3%. $C_{11}H_{13}NO_2S$. Calculated: N 6.3; S 14.3%.

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THERMAL ISOMERIZATION OF 5-METHOXY-3-ARYLISOXAZOLES TO METHYL 3-ARYL-2H-AZIRINE-2-CARBOXYLATES

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UDC 547.717.786:542.952

The thermal isomerization of 5-methoxy-3-arylisoxazoles to methyl 3-aryl-2H-azirine-2-carboxylates was subjected to a kinetic study. A correlation between the isomerization rate constants and the σ^+ constants of the substituents in the aromatic ring is observed. The enthalpies of formation of a number of isoxazoles and 2H-azirines were calculated. The effect of the nature of the substituents on the mutual isomerization of isoxazoles and azirines is discussed. The results make it possible to refute the approved and previously proposed diradical mechanism for the isomeric transformations and are in agreement with a nitrene mechanism for the formation of azirines.

When isoxazoles containing alkoxy [1, 2], alkylthio [2], and amino [3, 4] groups in the 5 position are heated, they undergo isomerization to the corresponding derivatives of 2H-azirine-2-carboxylic acids.

In the present research we made a kinetic study of the thermal isomerization of 5-methoxy-3-arylisoxazoles (Ia-e) to methyl 3-aryl-2H-azirine-2-carboxylic acids (IIa-e). Isoxazoles Ia-e were synthesized by the method in [2] from the corresponding isoxazolones obtained by the method in [5]. Azirines IIa-e were obtained from isoxazoles Ia-e by the method in [2].

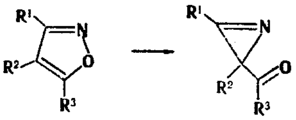
A. A. Zhdanov Leningrad State University, Leningrad 199004. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1053-1056, August, 1978. Original article submitted August 1, 1977.

0009-3122/78/1408-0843$07.50

TABLE 1. Enthalpies of Formation of Isoxazoles Ia, f-u and Azirines IIa, f-u (kJ·mole^{-1})

Letter index of the compound	Isoxazole I		Azirine II, ΔH^0_f calc	$\Delta\Delta H^0_f$ (II←I)
	ΔH^0_fexp	ΔH^0_f calc (±13)		
a	—	−9	44	−35
f	—	52	87	35
g	20±3	20	53	33
h	139±6	149	187	38
i	15±3	20	37	17
j	−18±4	−13	2	15
k	99±8	117	137	20
l	21±3	24	32	8
m	—	−153	−123	30
n	−20±4	−45	−26	19
o	160±6	149	163	14
p	107±8	117	133	16
q	—	−106	−144	−38
r	—	69	66	−3
s	—	56	11	−45
t	5±3	−9	−51	−42
u	—	62	8	−54

An analysis of the literature data on the thermal conversion of isoxazoles I to azirines II showed that the possibility of isomerization is determined by the nature of substituent R^3.



I II

I, II a $R^1=C_6H_5$, $R^2=H$, $R^3=OCH_3$; b $R^1=p\text{-}CH_3OC_6H_4$, $R^2=H$, $R^3=OCH_3$; c $R^1=p\text{-}CH_3C_6H_4$, $R^2=H$, $R^3=OCH_3$; d $R^1=p\text{-}ClC_6H_4$, $R^2=H$, $R^3=OCH_3$; e $R^1=p\text{-}BrC_6H_4$, $R^2=H$, $R^3=OCH_3$; f $R^1=R^2=R^3=H$; g $R^1=CH_3$, $R^2=R^3=H$; h $R^1=C_6H_5$, $R^2=R^3=H$; i $R^1=R^2=H$, $R^3=CH_3$; j $R^1=R^3=CH_3$, $R^2=H$; k $R^1=C_6H_5$, $R^2=H$, $R^3=CH_3$; l $R^1=NH_2$, $R^2=H$, $R^3=CH_3$; m $R^1=H$, $R^2=COCH_3$, $R^3=CH_3$; n $R^1=R^2=R^3=CH_3$; o $R^1=R^2=H$, $R^3=C_6H_5$; p $R^1=CH_3$, $R^2=H$, $R^3=C_6H_5$; q $R^1=R^2=H$, $R^3=OCH_3$; r $R^1=R^2=H$, $R^3=SCH_3$; s $R^1=R^2=H$, $R^3=NH_2$; t $R^1=R^2=CH_3$, $R^3=NH_2$; u $R^1=R^2=H$, $R^3=N(CH_3)_2$

Thus I→II isomerization occurs when R^3 = OAlk, SC_4H_9, and NH_2 [1-4], whereas conversion to azirines is not observed when R^3 = H, Alk, C_6H_5, and $COCH_3$ [6]. Moreover, azirine IIh gives isoxazole Ih in 80% yield when it is heated to 200°C [7]. To ascertain the possible reason for the effect of the nature of the substituents on the isomerization of isoxazoles I to azirines II, we compared the enthalpies of formation of the corresponding isoxazoles and azirines. The enthalpies of formation of isoxazoles Ia, f-u were calculated with allowance for the bond increments [8] and the heats of combustion of isoxazoles Ig-*l*, n-p, t [9-11]. With the exception of In, the calculated enthalpies of formation of these isoxazoles were in agreement with the experimentally measured values within the limits of the measurement errors (see Table 1).

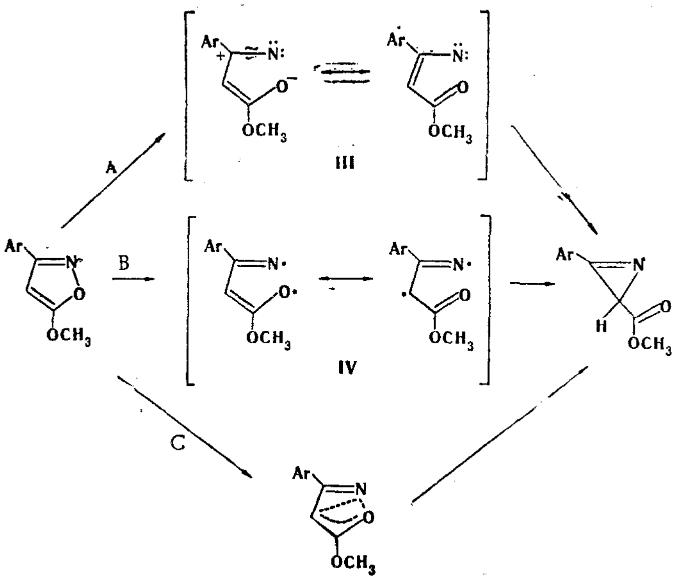
The enthalpies of formation of azirines IIa, f-u were calculated with allowance for the increments for the substituents [8] and the enthalpy of formation of 2H-azirine (ΔH_f° 204 kJ·mole^{-1}), which in turn was estimated from quantum-chemical calculations of 1H-azirine, 2H-azirine, and 2H-diazirine [12] and the enthalpy of formation of 2H-diazirine [13]. The results of the calculations are presented in Table 1. The heat effect for the isomerization of isoxazoles I to azirines II is also presented in Table 1. It is apparent from the data presented in Table 1 that, in agreement with the above statements, substituent R^3 has the greatest influence on the heat effect in the I→II isomerization; the isomeric conversion of isoxazoles Ia, q-u, for which R^3 = OAlk, SAlk, and NH_2, to azirines is exothermic, whereas the conversion of isoxazoles If-p is endothermic. The ability of the isoxazoles to undergo isomerization to azirines decreases in the I series with R^3 substituents in the order $N(CH_3)_2 > NH_2 > OCH_3 > SCH_3$. Depending on the nature of substituent R^3, for azirines II one should observe preferred isomerization to isoxazoles in the order $H > CH_3 > C_6H_5$.

In order to ascertain the mechanism of the isomeric transformations we made a kinetic study of the thermal isomerization of isoxazoles Ia-e to azirines IIa-e. The isomerization kinetics were studied in C_2Cl_4 solutions at 165-185°C for isoxazole Ia and at 180°C for isoxazoles Ib-e. The isomerization is a first-order reaction. The isomerization rate constants are presented in Table 2.

TABLE 2. Rate Constants for the Isomerization of Isoxazoles Ia-e to Azirines IIa-e

Isoxazole	Temp., °C	$k \cdot 10^5$, sec^{-1}
Ia	165	0,68±0,04
Ia	170	1,13±0,06
Ia	175	1,56±0,13
Ia	180	2,9±0,2
Ia	185	4,9±0,5
Ib	180	11,1±0,8
Ic	180	2,9±0,3
Id	180	1,85±0,17
Ie	180	1,44±0,11

Two mechanisms that include the formation of nitrene particle III (A) [7] or diradical IV (B) [1-4, 6] are proposed in the literature for the I→II isomeric transformation. One should also take into account the possibility of reaction via a 1,3-sigmatropic antarafacial shift (C).



Treatment of the kinetic data for the isomerization of isoxazole Ia (Table 2)* gave the following activation parameters for the process: $\Delta H^{\neq}$ = 159 ± 4 kJ·mole^{-1}, and $\Delta S^{\neq}$ = 15 ± 8 J·mole^{-1}·deg^{-1} (180°C). Thus the enthalpy of activation of the isomerization is in agreement with the energy of dissociation of the N—O bond, which is 151-167 kJ·mole^{-1} [15], and the entropy of activation is positive. At the same time, the enthalpy of activation for 1,3-sigmatropic rearrangements of the C—C bond is 167-209 kJ·mole^{-1} lower than the energy of dissociation of the C—C bond, and the entropy of activation is negative [16]. On the basis of this, concerted mechanism C can be excluded from consideration. A comparison of the isomerization constants of isoxazoles Ia-e at 180°C (Table 2) shows that the introduction of donor substituents in the aromatic ring facilitates isomeric transformation. A correlation between the isomerization rate constants and the σ^+ substituent constants is observed:

$$\lg k(\mathrm{sec}^{-1}) = -(0.128 \pm 0.002) - (0.854 \pm 0.006)\sigma^+,\ s_0 = 0.131,\ r = 0.933$$

This result indicates that a positive charge in direct polar conjugation with the substituent in the aromatic ring develops on the reaction center in the transition state. It is easy to see that this effect should occur in nitrene particle III but not in diradical IV. Consequently, the isomerization of isoxazoles Ia-e to azirines IIa-e evidently proceeds

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*In the present research we were able to obtain more accurate data than that obtained in a previous communication [14] owing to expansion of the temperature range and an increase in the number of check points.

through a step involving the formation of nitrene III. The formation of azirines from vinylnitrenes has been previously observed in more than one instance [17].

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4 were recorded with a Varian HA-100 D-15 spectrometer with tetramethylsilane as the internal standard. The UV spectra of solutions of the compounds in ethanol were obtained with a Perkin–Elmer M-402 spectrophotometer. The IR spectra of solutions of the compounds in CCl_4 were recorded with a UR-20 spectrometer. The constants and spectral characteristics of the known isoxazoles Ia-d and azirines IIa-d are in agreement with the literature data [2, 18].

5-Methoxy-3-(p-bromophenyl)isoxazole (Ia). An ether solution containing ∿0.8 g (0.019 mole) of diazomethane was added dropwise to 3 g (0.012 mole) of 3-(p-bromophenyl)isoxazol-5-one [5], after which the solvent was removed, and the residue was recrystallized from methanol to give 2.1 g (66%) of isoxazole Ie with mp 124°C. PMR spectrum, δ: 4.05 (s, 3H, OCH_3), 5.52 (s, 1H, 4-H), and 7.7 ppm (m, 4H, C_6H_4). IR spectrum: 840, 911, 953 w, 972, 995, 1020, 1032, 1053 w, 1081 s, 1186 w, 1300, 1308, 1440 s, 1485, 1523 w, 1580, 1620 s, 2840 w, 2890 w, 2950, and 3010 cm^{-1}. UV spectrum: λ_{max} 248 nm (log ε 4.28). Found: C 47.6; H 3.2; Br 31.7; N 5.4%. $C_{10}H_8BrNO_2$. Calculated: C 47.3; H 3.2; Br 31.4; N 5.5%.

Methyl 3-(p-bromophenyl)-2H-azirine-2-carboxylate (IIe). A 2-g (0.008 mole) sample of isoxazole Ie was heated at 200°C for 30 min, after which it was subjected to vacuum distillation [bp 130-135°C (0.6 mm)] and recrystallized from methanol to give 1.4 g (70%) of azirine IIe with mp 76°C. PMR spectrum, δ: 2.75 (s, 1H, 2-H), 3.70 (s, 3H, OCH_3), and 7.8 ppm (m, 4H, C_6H_4). IR spectrum: 838 s, 870 w, 921 w, 988, 1010, 1020, 1040, 1076 s, 1104 w, 1127 w, 1190 s, 1209 s, 1280 s, 1308 w, 1350 s, 1408, 1444, 1490, 1597, 1748 s, 1782 s, 2854 w, 2960, 3005 w, and 3035 cm^{-1}. UV spectrum: λ_{max} 259 nm (log ε 4.25). Found: C 47.0; H 3.2; Br 31.5; N 5.6%. $C_{10}H_8BrNO_2$. Calculated: C 47.3; H 3.2; Br 31.4; N 5.5%.

Method for the Measurement of the Rate Constants for the Thermal Isomerization of Isoxazoles Ia-e. A 0.05 M solution of isoxazole I in tetrachloroethylene was heated in sealed ampuls in a thermostat (±0.1°C). The ampuls were opened at definite intervals, and the IR spectra were recorded. The concentration of isoxazole I in the samples was determined from the intensity of the absorption bands at 1575-1587 cm^{-1}, which are characteristic for isoxazoles Ia-e. The rate constants and activation parameters were calculated by the method in [19]. The constants and parameters were calculated by the method of least squares with an ODRA-1204 computer.

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