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Structure and Stability of Isoxazoline Compounds

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Abstract—Structure of isoxazoline compounds formed via the reaction of alkyl-substituted benzonitrile oxides with ethylene was determined by X-ray diffraction method. Isoxazoline ring is flattened, the bond lengths in it depend slightly on the nature of substituents (CH_3, C_2H_5) and their position in the benzene ring and the angle of rotation relative to the isoxazoline ring. The connection N–O has a length 1.422 Å. Thermal decomposition of isoxazolines in a liquid phase (160–280°C) is accompanied by the release of acetaldehyde and aromatic nitrile. Both the structure of the cycle and its stability is practically independent of the structure of an aromatic substituent. The rate constant of the initial stage is characterized by the low significance of kinetic parameters, E = 104±8 kJ mol^{-1} and log a(A/c) = 7.2±0.8. The results obtained are rationalized in terms of biradical mechanism of isoxazoline ring-opening that includes an efficient recombination of the biradical and its disappearance as a result of synchronous multi-center rearrangement with the release of acetaldehyde.

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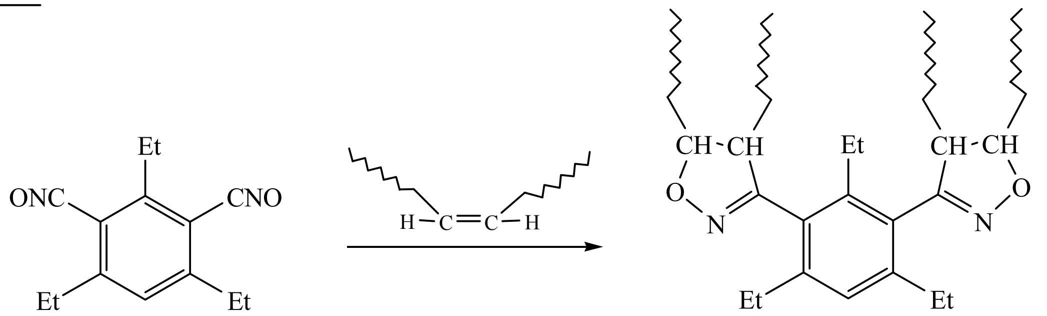
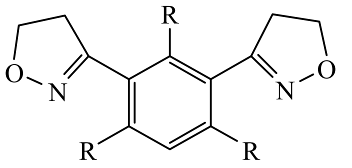
A process of flow-temperature solidifying of rubber based on the addition reaction of aromatic dinitrile oxides on the double C=C bond has been suggested in 1968 [1].

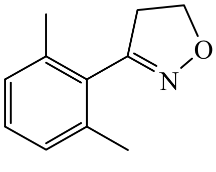


After synthesis of thermally stable and suitable for technical applications sterically screened dinitrile oxides of 2,4,6-triethylbenzene-1,5-dinitrile oxide type [2] the method was developed and, in particular, was used to of the polymer binders of solid rocket fuels [3–5]. The formation of isoxazoline ring as a cross-linking fragment of the binder means an appearance of new structural component in the rocket fuel which may affect the degradation of the cross-linked polymer and the stability of the composition as a whole. Therefore, the problem of thermal stability of isoxazolines deserves detailed study. There is no information in the literature on the kinetics of decomposition of pure isoxazolines or their solutions in neutral media. In this regard, we undertook a detailed kinetic study of the decomposition of a simple isoxazoline ring formed as a result of addition of a nitrile oxide group to ethylene in two bifunctional compounds **I** and **II** simulating the structure of cross-linked rubbers, and of two mono-functional isoxazolines **III** and **IV** differing in the degree of steric shielding of the five-membered ring with alkyl groups of the substituted aromatic moieties.

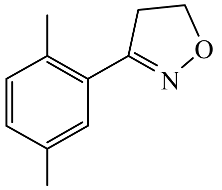
Structure of isoxazolines. The structures of compounds **III** and **IV** were determined by XRD analysis. The information on the structure of **I** is given in [6]. The general view of the molecules and the bond lengths of the isoxazoline rings are given in the figure.



I, II



III



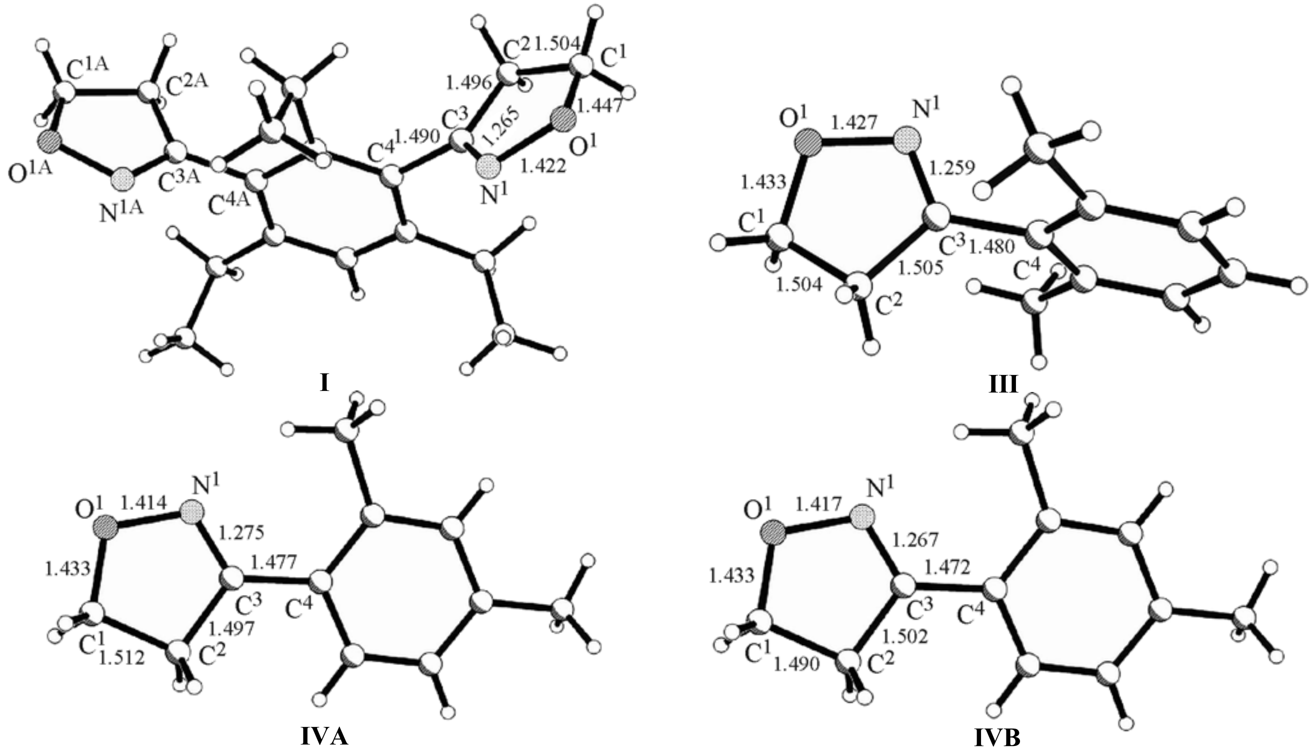
IV

I, R = C_2H_5; **II**, R = CH_3.

In the molecules of compound **I** and **III** the planes of benzene and isoxazoline rings are almost orthogonal. The dihedral angle between the planes is 84.6° and 85.4°, respectively. Isoxazoline ring has an *envelope* conformation and is strongly flattened. Thus, in the molecule of **III** the atom C is deviated from the plane of other four atoms by 0.34 Å, and the bend on the line O···C^2 is 22.2°.

A single crystal of connection of compound **IV** is built of two crystallographically independent molecules **A** and **B**. The isoxazoline ring in them is materially flat. The atom C^1 is out of plane of the other ring atoms by 0.11 and 0.03 Å for **A** and **B**, respectively, and the bend at the line O···C^2 is 7.4° and 1.8°, respectively. The torsion angle $N^1C^3C^4C^9$ characterizing the rotation of the isoxazoline ring relative to benzene moiety is equal to 4.3° (**B**) and 17.9° (**A**).

Alkyl substituents in the benzene cycle limit the rotational movement of the isoxazoline cycle. When there are two *ortho*-substituents in the benzene cycle, the orthogonal arrangement of the rings is achieved. At the same time, the substituents in the aromatic group have a little effect on the structure and the bond lengths of the isoxazoline ring. Regardless of the angle of rotation of the five-membered ring relative to benzene ring the bond lengths in the isoxazoline ring of different molecules are the same within the definitions error (see figure). The C^3–C^4 bond between the rings is shortened and also slightly dependent on the relative orientation of their planes. Probably, at the perpendicular location of the rings the violation of conjugation between the π-systems the benzene ring and the C=N bond is compensated by the interaction of *n*(N)σ type of an unshared electron pair of the nitrogen atom lying in the plane of the five-membered ring with



General view of molecules of compounds **I**, **III**, **IVA**, **IVB** in the crystal.

Table 1. Kinetic characteristics of decomposition of compounds **I**–**IV** in the liquid phase and in *o*-dichlorobenzene

Comp. no.	Medium	Temperature range, °C	E, kJ mol^{-1}	log (A/c^{-1})	K, s^{-1} at 200°C
I	Liquid phase	160–220	106.3	7.1	2.3×10^{-5}
	Solution	190–250	109.7	6.66	3.6×10^{-6}
II	Liquid phase	190–220	112.6	6.95	3.3×10^{-6}
	Solution	230–250	123.5	7.90	1.8×10^{-6}
III	Liquid phase	170–220	112.6	6.95	3.3×10^{-6}
	Solution	230–270	112.6	6.69	1.9×10^{-6}
IV	Liquid phase	180–230	113.0	7.03	3.6×10^{-6}
	Solution	230–270	113.4	7.02	3.2×10^{-6}

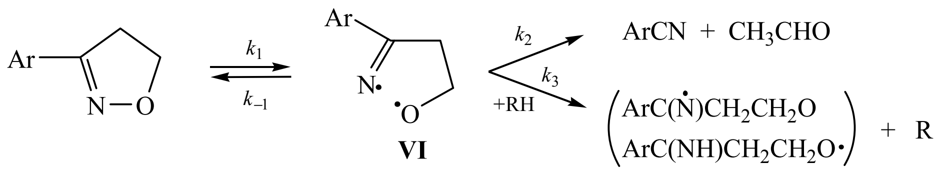
the vacant π*-orbital of benzene ring, whose symmetries coincide. It can be noted also that the N–O bond is weakened, as well as all the bonds of >C=N–O, and has a length of ~1.422 Å.

The packaging of molecules in the crystals of **I**, **III**, **IV** is loose. In all the compounds there are no intermolecular hydrogen bonds and shortened intermolecular contacts. This means that factors like the association of molecules and intramolecular spatial interactions of the atoms cannot influence the reactivity of isoxazolines and, in particular, the rate of their decomposition.

The kinetics of decomposition. The analysis of the volatile and condensed products showed that the decomposition of the isoxazoline ring in compounds **I**–**IV** results in the corresponding aromatic nitrile and acetaldehyde **V**, whose going out in the gaseous phase was manometrically measured. Thus it was established for compound **I** in the temperature range of 160–220°C and at the degree of filling of vessel with the compound (m/V, g cm^{-3}) of ~0.002 the reaction obeys the first order equation. Yield of compound **V** is 95 mol %. When the m/V value increases 10 times, the decomposition becomes autocatalytic, the yield of acetaldehyde is reduced to 65%, the initial rate remains unchanged. When the m/V values are high, the 1st order rate constants calculated by the initial rate of release of acetaldehyde on the assumption that in the early stages its yield is 1 mol per one isoxazoline ring coincided with the data obtained at low values m/V. The acceleration degree increases with decreasing temperature and increasing m/V. We conclude that acetaldehyde accelerates the decomposition of the isoxazoline ring. When dissolving compound **I** in chlorobenzene, *o*-dichlorobenzene or naphthalene, the first order reaction occurs. The rate of decomposition in these solvents is reduced 5 times compared with the melt. This means that the reaction medium contributes to the decomposition of the substance and the above-mentioned solvents are inert compounds relative to **I**. A similar effect of the m/V value on the decomposition nature was observed for other isoxazolines, but unlike compound **I** in the case of **II**–**IV** there is no significant reduction in the reaction rate when dissolving in inert solvents. These compounds react in the melt and in a solution with virtually the same rate.

The parameters of the Arrhenius equation for the rate constants of the non-catalytic decomposition step in the liquid phase and in one of the inert solvent (*o*-dichlorobenzene) at a concentration of 1 wt % by weight and a comparison of the rate constants at 200°C are shown in Table 1. It can be seen that all compounds in the melt and in solution decompose with almost equal rates. The maximal difference is less than 2 times. Only compound **I** in the melt has a higher decom-position rate. In all cases, almost the same activation energy was observed: E 104±8 kJ mol^{-1} and log (A/c) = 7.2±0.8. Such a low value of the pre-exponential factor cannot match any elementary reaction and demonstrates the complex mechanism that includes reversible and consecutive stages. The data on the composition of products, kinetic parameters, the catalytic action of acetaldehyde and the influence of the reaction medium can be and explainned in terms of the biradical mechanism of decomposition of the five-membered cyclic compounds [7], which corresponds to the scheme bellow.

The first step is the cleavage of the N–O bond, which is the weakst in the ring. The biradical **VI** formed recombines with recovery of the starting compound, or is destroyed by the synchronous rearrangement with the release of acetaldehyde and the formation of aromatic nitrile. In addition, the



The scheme of the stages of isoxazoline conversation.

bimolecular decomposition of the biradical **VI** is possible as a result of the break off its by the radical centers of the hydrogen atoms from the medium molecules RH. In the inert solvents reaction (3) does not occur. The observed rate constants k_{obs} and the kinetic parameters E_{obs} and A_{obs} are connected with the parameters of the individual stages approximately as follows:

$$k_{obs} = k_1k_2/k_{-1},\ E_{obs} = E_1 + E_2 - E_{-1},\ A_{obs} = A_1A_2/A_{-1}.$$

The activation energies of the secondary processes are low. Therefore we can assume that $E_{obs} \approx E_1$. The constancy of E_{obs} in the series of compounds **I**–**IV** corresponds to the same length of N–O bond in these compounds. The retardation of internal rotation around the C^3–C^4 (due to conjugation of the C=N bond with the benzene ring) and the C^2–C^3 bonds (due to the steric effect of the alkyl substituent in the *ortho*-position of the benzene group) promotes biradical recombination. Low pre-exponential factor is the result of a high rate of recombination of the biradical **VI** and low values A_2 of a multi-center synchronous decomposition of the biradical, which includes 1,2-migration of the hydrogen through the triangular transition state.

Acceleration of decomposition under action of acetaldehyde and the decomposition rate of compound **I** in the liquid phase, which is increased as compared with the compounds **II**–**IV**, are due to the proceeding of reaction (3), whose rate depends on the reactivity (primarily the strength) of the C–H bond in the molecules RH and on their concentrations. In the methyl groups of compound **I**, where the reaction (3) is unnoticeable yet, the bond dissociation energy D(C–H) can be estimated at 290 kJ mol^{-1} (less than in mesitylene due to the influence of the extended system of the π-bonds). For the methylene groups in **I** the value D(C–H) is lower by at least 20 kJ mol^{-1} than that

Table 2. Crystallographic parameters for structures **III**, **IV**

Parameter	**IV**	**III**
M	175.22	175.22
T, K	293(2)	293(2)
Radiation	Mo	Mo
Space group	P212121	P212121
a, Å	7.322(1)	7.721(2)
b, Å	13.931(2)	9.869(2)
c, Å	18.807(3)	12.823(3)
V, Å^3	1918.4(5)	977.1(3)
Z	8	4
d, g cm^{-3}	1.213	1.191
μ, mm^{-1}	0.078	0.076
F(000)	752	376
Crystal size, mm	0.7×0.6×0.6	0.8×0.6×0.5
Range of data collection, deg	1.82–25.00	2.60–25.98
Index ranges	$-1 \le h \le 8, -1 \le k \le 16, -22 \le l \le 1$	$-9 \le h \le 9, 0 \le k \le 12, 0 \le l \le 15$
Reflections collected/independent	2603/2417	1312/1209
R_{int}	0.0269	0.0156
Completeness, %	99.8	100.0
Refined parameters	236	118
GOOF F^2	1.038	1.084
R-Factors on $I > 2\sigma(I)$	R_1 0.0512, wR_2 0.1462	R_1 0.0508, wR_2 0.1334
R-Factors on all reflections	R_1 0.0629, wR_2 0.1566	R_1 0.0572, wR_2 0.1371
CCDC	828197	828198

for the methyl groups in compound **II**. Apparently, such decrease in D(C–H) value is sufficient for reaction (3) to be competitive with reaction (2). The action of aldehyde may also be due to the low strength of the C–H in this compound. In addition, the C–H bond in aldehydes is highly polar, which increases its reactivity.

The presented mechanism allows the prediction the change of the stability of the isoxazoline ring of the cross-linked polymer. Due to an increase in the medium viscosity the coefficients of rotational and translational diffusion of the biradical **VI** will decrease. As a result, an increase in the rate of recombination and the decrease in the rate of bimolecular capture of the biradical with medium molecules will be observed. Finally, the isoxazoline ring in the solidified polymer may be more stable than in compound **I**. Furthermore, the decomposition of the isoxazoline ring formed when attaching the nitrile oxide group to the long-chain olefin will not afford the reactive aldehyde as from **I**, but a ketone having stronger C–H bonds, which will lead to a decrease in the rate of reaction of the biradical **VI** with the decomposition products.

From the standpoint of long-term storage, isoxazoline compounds studied have a relatively high stability. Thus, the time of 1% degradation of compound **I** in closed vessels at 60 and 40°C is 1 and 11 years, respectively.

EXPERIMENTAL

Isoxazolines were synthesized by bubbling ethylene through 30% solution of the corresponding nitrile oxide in chloroform at room temperature. The reaction progress was monitored by IR spectroscopy by the disappearance of the absorption bands of CNO group at 1321 and 2294 cm^{-1}. The reaction proceeds quantitatively. Recrystallization from chloroform affords compounds **I** (mp 75°C), **II** (mp 165–169°C), **III** (mp 73–74°C), and **IV** (mp 50–52°C).

The products were analyzed by GC-MS using a Clarus-500 Perkin Elmer instrument [capillary column (l 30 m, d 0.25 mm), the adsorbent Elite-5MS, carrier gas helium, flow rate 1 ml min^{-1}, the evaporator temperature 120°C, column temperature 75°C].

Kinetic measurements were carried out by means of manometric device, designed for pressures up to 100 at. The reactor was a glass ampule of 0.5–5.0 ml capacity, equipped with a sickle membrane with an arrow and was placed into a metal housing with a window to observe the arrow deflection. The pressure was measured by a compensation method. This technique allows to perform experiments at high temperatures in almost all solvents, as well as to measure the kinetics of decomposition at high degrees of filling of the vial with the material.

A set of experimental X-ray diffraction reflections was obtained on an automatic four circle diffractometer KM-4 (KUMA DIFFRACTION) with χ-geometry by ω/2θ scanning at monochromatic MoK_α-radiation. Table 2 shows the crystallographic parameters for the investigated crystals. The structures were solved by the direct method using SIR92 program [8], followed by a series of calculations of electron density maps. The hydrogen atoms were set geometrically. Complete anisotropic (non-hydrogen atoms) refinement by the least-squares method was performed by SHELXL-97 software [9]. Corrections for extinction were not introduced.

Full information on the investigated structures was deposited in the Cambridge Crystallographic Data Center.

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