N-OXIDES OF 3-NITROISOXAZOLINES

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Abstract

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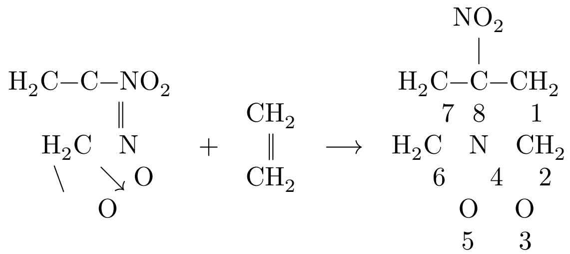
N-OXIDES OF 3-NITROISOXAZOLINES

IN THE 1,3-DIPOLAR CYCLOADDITION REACTION

(Presented by Academician I. L. Knunyants, March 22, 1965)

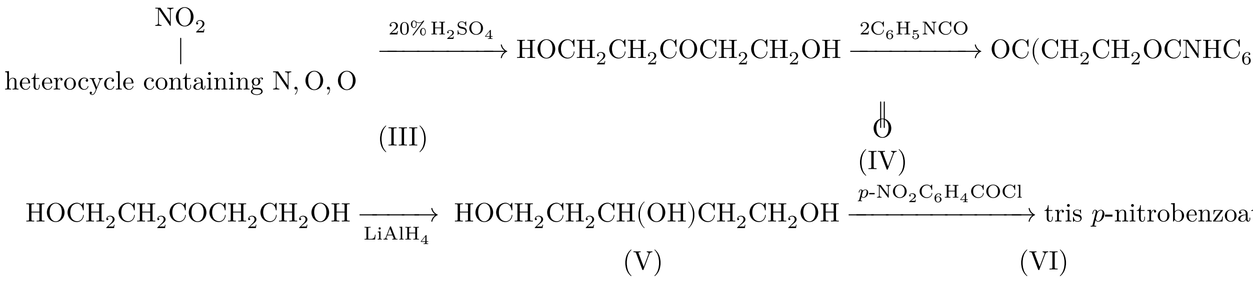
We have established that the interaction of the N-oxide of 3-nitroisoxazoline (I) with ethylene proceeds according to the scheme of 1,3-dipolar cycloaddition, and the product of this reaction is a representative of a new class of heterocyclic compounds–8-nitroisoxazolidizine (II).*



(I)

(II)

The correctness of the conclusion concerning the structure of II is confirmed by infrared-spectroscopic data (see Fig. 1) and by its chemical transformations. Thus, hydrolysis of II with 20% sulfuric acid gives pentanone-3-diol-1,5, characterized in the form of the corresponding diurethane (IV):



$$\overset{NO_2}{\underset{\text{heterocycle containing N, O, O}}{|}} \xrightarrow[(III)]{20\%\ H_2SO_4} HOCH_2CH_2COCH_2CH_2OH \xrightarrow{2C_6H_5NCO} OC(CH_2CH_2OCNHC_6$$

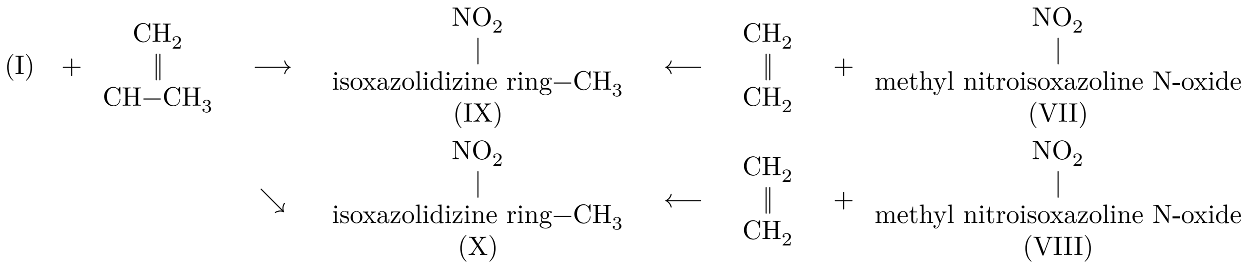
$$\underset{(IV)}{\overset{\|}{O}}$$

$$HOCH_2CH_2COCH_2CH_2OH \xrightarrow[LiAlH_4]{} \underset{(V)}{HOCH_2CH_2CH(OH)CH_2CH_2OH} \xrightarrow{p\text{-}NO_2C_6H_4COCl} \underset{(VI)}{\text{tris } p\text{-nitrobenzoa}}$$

On reduction of III with $LiAlH_4$, pentanetriol-1,3,5 (V) was obtained; the tris-*p*-nitrobenzoate (VI) of this compound proved identical with an authentic product.

To clarify the question of the structural direction of the 1,3-dipolar cycloaddition reaction, we investigated the interaction of I with propylene, as well as the interaction of the N-oxide of 4-methyl-3-nitroisoxazoline (VII) and the N-oxide of 5-methyl-3-nitroisoxazoline (VIII) with ethylene.

The interaction of VII and VIII with ethylene leads, respectively, to the formation of 1-methyl-8-nitroisoxazolidizine (IX) and 2-methyl-8-nitroisoxazolidizine (X), in which the position of the methyl groups is unambiguously determined by their position in the initial N-oxides:



$$(I) + \overset{CH_2}{\underset{CH-CH_3}{\|}} \longrightarrow \underset{(IX)}{\overset{NO_2}{\underset{\text{isoxazolidizine ring}-CH_3}{|}}} \longleftarrow \overset{CH_2}{\underset{CH_2}{\|}} + \underset{(VII)}{\overset{NO_2}{\underset{\text{methyl nitroisoxazoline N-oxide}}{|}}}$$

$$\searrow \underset{(X)}{\overset{NO_2}{\underset{\text{isoxazolidizine ring}-CH_3}{|}}} \longleftarrow \overset{CH_2}{\underset{CH_2}{\|}} + \underset{(VIII)}{\overset{NO_2}{\underset{\text{methyl nitroisoxazoline N-oxide}}{|}}}$$

IX and X are thick oils, which were purified on a column with Al_2O_3.

* For preliminary communications, see ([1]).

Gas-liquid chromatographic analysis data (see Table 1) show that each of them has a characteristic retention time; in the case of X, the chromatogram contains two distinct peaks, evidently corresponding to the cis- and trans-isomers. Chromatographic analysis of the product of the reaction of I with propylene shows that the reaction gives exclusively X (see Table 1). These results are in agreement with the data of thin-layer chromatography on Al_2O_3 (see Fig. 2).

Fig. 1. IR spectrum of 8-nitroisoxazolidine

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Figure 1: Fig. 1. IR spectrum of 8-nitroisoxazolidine

Fig. 2. a—X from the reaction of I with propylene, b—X from the reaction of VIII with ethylene, c—IX

Figure 2: Fig. 2. a—X from the reaction of I with propylene, b—X from the reaction of VIII with ethylene, c—IX

Fig. 2. *a*—X from the reaction of I with propylene, *b*—X from the reaction of VIII with ethylene, *c*—IX

Thus, the reaction of I with propylene has a clearly pronounced structural directionality.

It is interesting to note that, whereas in the interaction of VIII with ethylene the amounts of the cis- and trans-isomers formed in X are approximately the same (45 and 55%), the reaction of I with propylene leads to a clear predominance of one of the isomers in X (87 and 13%)* (see Fig. 3).

Table 1

Substance	Retention time, min	Isomer ratio, %
X from the reaction of I with propylene	33$ ‘52’ ‘, 50’ 41’ ’ $	13/87
X from the reaction of VIII with ethylene	33$ ‘42’ ‘, 50’ 30’ ’ $	45/55
IX	55$ ‘13’ ’ $	

The methyl group in VIII is remote from the reaction center and, apparently, does not exert any substantial influence on the direction of attack by the dipolarophile (“from above” or “from below”) on the 1,3-dipole. Evidently, in this case the amounts of the cis- and trans-isomers formed should be approximately equal. In the second case (the reaction of I with propylene), the methyl group is bonded to the carbon atom directly participating in the formation of the transition complex, and its influence, naturally, will be manifested to a greater extent.

The results obtained make it possible to conclude that the reaction of 1,3-dipolar cycloaddition of I with propylene, in addition to structural directionality, also possesses a definite spatial directionality.

We were unable, either by gas-liquid chromatography or by thin-layer chromatography, to separate IX; therefore the question of whether IX is a single isomer or a mixture of two isomers remains open for the time being. It should

Fig. 3. a—X from reaction I with propylene; b—X from reaction VIII with ethylene

Figure 3: Fig. 3. a—X from reaction I with propylene; b—X from reaction VIII with ethylene

be said that substituents at the 1 and 7 atoms in 8-nitroisoxazolidines will experience considerable steric hindrance with respect to

* The question of which of the isomers should be assigned the cis- or trans-configuration is under investigation.

compared with substituents located at atoms 2 and 6 of the bicycle. (In the cis* position because of the neighboring nitro group; in the trans position because of mutual repulsion. The trans substituents at atoms 1 or 7 are close together in space.)

At present, without precise data on bond lengths and angle values in the bicycles, it is difficult to estimate which of the isomers in IX should be more hindered. However, the considerations given above may explain the preferential formation of one of them.

Fig. 3. *a*—X from reaction I with propylene; *b*—X from reaction VIII with ethylene

It should be noted that, in principle, the methyl group at the 1st carbon atom in 8-nitroisoxazolidines may be in either the cis or the trans position. This was established by us through the reaction of N-oxide of 4,4-dimethyl-3-nitroisoxazoline (XI) with styrene, which leads to 1,1-dimethyl-6-phenyl-8-nitroisoxazolidine (XII).

$$\text{(XI)} + CH_2{=}CH{-}C_6H_5 \longrightarrow \text{(XII)}$$

Chromatographic analysis was carried out on a "Pye" argon chromatograph with a β-ionization detector. The detector voltage was 750 V, sensitivity $×$1. A column 120 cm long and 4 mm in diameter was packed with glass beads of size 140–160 mm with 0.2% stationary phase, for which polyethylene glycol succinate was used. The column temperature was 135°, and the carrier-gas pressure at the column inlet was 0.8 atm, at the outlet 8 mm Hg.

Preparation of 8-nitroisoxazolidines. 26.4 g (0.2 mole) of (I) in 200 ml of benzene are kept in a rotating autoclave (at 50° under an ethylene pressure of 20–30 atm for 4–5 hr). (As the ethylene is absorbed, it was pumped in to the initial pressure.) The benzene is evaporated and II is isolated. Yield 28 g (88%), mp 58–59° (from 75% alcohol).

Found, %: C 37.73; 37.70; H 5.21; 5.15; N 17.60; 17.70
$C_5H_8N_2O_4$. Calculated, %: C 37.50; H 5.04; N 17.50

IR spectrum in cm^{-1}: 1560, 1360 (NO_2); 1030 (O—N—O).

* The relation to the nitro group at the 8-carbon atom is meant.

Under analogous conditions, from 5 g of (VII) 5.5 g (92%) of IX are obtained; n_D^{20} 1.4875; d_4^{20} 1.3258.

Found, %: C 41.25; 41.00; H 5.95; 5.82; N 16.23; 16.29
$C_6H_{10}N_2O_4$. Calculated, %: C 41.38; H 5.79; N 16.09

IR spectrum in cm^{-1}: 1550, 1360 (NO_2); 1015 ($\text{O—}\overset{|}{\text{N}}\text{—O}$).

From 0.72 g of VIII, 0.8 g (86%) of X are obtained; n_D^{20} 1.4818; d_4^{20} 1.2960.

Found, %: C 40.99; 41.07; H 5.85; 5.82; N 16.35; 16.33
$C_6H_{10}N_2O_4$. Calculated, %: C 41.38; H 5.79; N 16.09

IR spectrum in cm^{-1}: 1550, 1360 (NO_2); 1010 ($\text{O—}\overset{|}{\text{N}}\text{—O}$).

The reaction of I (1 g) with propylene was carried out under the same conditions. The initial propylene pressure was 6 atm. Yield of X 1.1 g (85%); n_D^{20} 1.4840; d_4^{20} 1.2993.

Found, %: C 41.57; 41.56; H 6.05; 5.97; N 16.25; 16.20
$C_6H_{10}N_2O_4$. Calculated, %: C 41.38; H 5.79; N 16.09

IR spectrum in cm^{-1}: 1555; 1355 (NO_2); 1025 ($\text{O—}\overset{|}{\text{N}}\text{—O}$).

0.2 g of XI and 2 ml of styrene are kept for 36 h at $\sim 20°$, and, after dilution of the reaction mixture with hexane, 0.3 g (90%) of XII is obtained, m.p. 131-132° (from 80% alcohol).

Found, %: C 58.74; 58.65; H 6.01; 6.10; N 10.94; 10.98
$C_{13}H_{16}N_2O_4$. Calculated, %: C 59.08; H 6.10; N 10.60

IR spectrum in cm^{-1}: 1560, 1365 (NO_2); 1015 ($\text{O—}\overset{|}{\text{N}}\text{—O}$).

Saponification of II with sulfuric acid. 0.32 g (0.002 mole) of II and 5 ml of 20% H_2SO_4 are kept at 45° until complete dissolution of II (2-3 h). The solution is neutralized with sodium bicarbonate and evaporated to dryness in vacuo. The dry residue is extracted with alcohol and, after evaporation of the alcohol, 0.17 g of III (70%) is isolated. Treatment of III with phenyl isocyanate gives the corresponding diurethane (IV), m.p. 164-165° (from alcohol).

Found, %: C 64.23; 64.36; H 5.84; 5.79; N 7.89; 8.09
$C_{19}H_{20}N_2O_5$. Calculated, %: C 64.03; H 5.65; N 7.86

IR spectrum in cm^{-1}: 3370 (—NH—); 1720 (C=O).

Reduction of III with $LiAlH_4$ leads to the formation of (V), which was characterized by us as the tris-*p*-nitrobenzoate (VI), m.p. 120-121° (from acetone).

Found, %: C 55.30; 55.25; H 3.98; 4.10
$C_{26}H_{21}O_{12}N_3$. Calculated, %: C 54.95; H 3.73

Lit. (²), m.p. 121–122°.

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CITED LITERATURE

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Note: Figure translations are in progress. See original paper for figures.