4- AND 5-HYDROXYLAMINOTHIAZOLIDINE-2-TIIONES.  
REACTION WITH 4-NITROBENZALDEHYDE

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Stable nitrones are formed in the condensation of 5-hydroxylaminothiazolidine-2-thiones with 4-nitrobenzaldehyde. At the same time, nitrones obtained from the isomeric 4-hydroxylaminothiazolidine-2-thiones, as well as 4-hydroxylaminoimidazolidin-2-one, can undergo rearrangement to E- or Z-O-substituted 4-nitrobenzaldoximes, depending on the structure and the reaction conditions.

In a continuation of our research on the synthesis and study of the reactivities of hydroxylaminothia(imida)zolidine-2-thiones(ones) [1, 2] we examined their reaction with 4-nitrobenzaldehyde.

Thus, regardless of the structures of substituents R1--R4, 5-hydroxylaminothiazolidine-2-thiones I react with the aldehyde to give stable [N-(thiazolidine-2-thion-5-yl)-C-(4-nitrophenyl)]nitrones Ila,b [1] and Iic,d; it is best to carry out the reaction in the presence of 4-toluenesulfonic acid (TSA).

In the case of the isomeric 4-hydroxylaminothiazolidine-2-thiones III, however, the corresponding nitrones Va-e can be obtained only in the absence of TSA and when R1 = H. Similar conditions are also necessary for the formation of nitron VI from 4-hydroxylaminoimidazolidin-2-one IV.

A completely different situation arises when the reaction of 4-hydroxylamo derivatives III and IV with the aldehyde is carried out in the presence of TSA and, in the case of the sterically hindered hydroxamines IIf, g (R1 = CH3), also without it. Although they do have the empirical formulas of the corresponding nitrones, the UV spectra (ethanol) of the resulting VIIa-g and VIII do not contain the absorption at 340-350 nm that is characteristic for nitrones [1], a 0.1-0.4 ppm shift of the signal of the azomethine proton to weaker field as compared with the PMR spectra of nitrones III is observed in their PMR spectra, and the IR spectra (KBr) do not contain bands of stretching vibrations of an N–O bond but do contain bands at 900-1000 cm⁻¹, which are more characteristic for the vibrations of an oxime group [3]. In addition, VII and VIII do not react with sodium borohydride [3].

An O-substituted 4-nitrobenzaldoxime structure can be assigned to VII and VIII on the basis of these data. The alternative synthesis of VIIc and VIII by the reaction of, respectively, 4-hydroxythiazolidine-2-thione IXa and 4-hydroximidazolidin-2-one IXc with E-4-nitrobenzaldoxime [2] makes it possible to conclude that the oxime group of derivatives VII and VIII has an E configuration.
We also established that, in contrast to nitrones II, nitrones V and VI undergo rearrangement to the corresponding oximes VII and VIII when they are heated in the presence of TSA.

In addition, we noted that, according to TLC data, hydroxy products IX and the E-4-nitrobenzaldoxime are present in the reaction mixtures in all cases involving the formation of oximes, while carrying out the rearrangement of nitrone Vb (R4 = CH3) in the presence of hydroxy derivative IXb (R4 = CH2C6H5) leads to a mixture of oximes VIIb and VIIe.

The results obtained attest that nitrones V and VI, like 4-hydroxylamino derivatives III and IV [1, 2, 4], under acid-catalysis conditions, in contrast to isomeric compounds I and II, undergo hydrolysis to the corresponding 4-hydroxy derivatives IX, which are known [2] to readily react with one another (acid catalysis) to give oximes VII and VIII (see Scheme 1).

The formation of oximes VIIf, g (R1 = CH3) also in the absence of TSA is evidently due to the instability of the resulting nitrones as a consequence of the greater steric hindrance. In the case of hydroxylamine IIIh [R1 + R2 = (CH2)4], however, 4-thiazoline-2-thione X was isolated instead of the expected nitrone or oxime [1].

The properties of nitrone Va (R4 = H) should be dealt with separately. In contrast to the rest of the synthesized nitrones, which can be recrystallized from alcohol, nitrone Va is converted to 4-ethoxythiazolidine-2-thione XI and the thermodynamically less favorable Z-4-nitrobenzaldoxime XII upon brief heating in alcohol. However, heating in dry acetonitrile is accompanied by its rearrangement to a substituted 4-nitrobenzaldoxime with a Z configuration of the oxime group (Z-VIIa). At the same time, the oxime obtained in the condensation of hydroxylamine IIIa with the aldehyde in the presence of TSA has an E configuration (E-VIIa). The E- and Z-isomeric assignments were made from PMR spectroscopic data. Thus the signal of the H-C=N proton of oxime E-VIIa is located at weaker field by 0.62 ppm as compared with the corresponding signal of Z-VIIa; this is due to the anisotropic deshielding effect of the OH group, which is cis-oriented with respect to it [5] (see Scheme 2).

The reduction of nitrone Va with sodium borohydride does not lead to the expected N,N-disubstituted hydroxylamine. The Z-4-nitrobenzaldoxime and 5,5-dimethylthiazolidine-2-thione (XIII) are isolated in this case.

Such properties of nitrone Va are evidently associated with the presence of a labile hydrogen atom in the 3 position of the heteroring. It may be assumed that the intermediate formation of a 3-thiazoline-2-thione (A) and Z-benzaldoxime XII occurs during the examined reactions. Thiazoline A reacts with alcohol to give ethoxy derivative XI, while it is reduced by sodium borohydride to give XIII. Oxime Z-VIIa evidently can also be formed in the reaction

Scheme 1