REACTION OF ETHYLENE OXIDE WITH N-PHENYLATED ISOMERS OF 1,2,4-TRIAZOLINE-3-THIONE AND 1-PHENYLTETRAZOLINE-5-THIONE

L. A. Vlasova and I. Ya. Postovskii

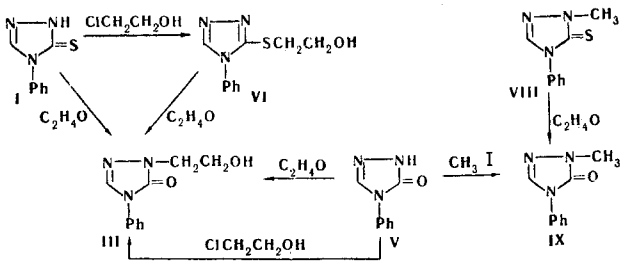
UDC 547.792.5.07

It is demonstrated that ethylene oxide forms N-β-hydroxyethyl derivatives of the corresponding triazolin-3-ones in the reaction with 1-phenyl- and 4-phenyl-1,2,4-triazolin-3-thiones and with 3-β-hydroxyethylthio derivatives of 1-phenyl- and 4-phenyl-1,2,4-triazole in acetic acid. 1-Phenyltetrazolin-5-thione reacts similarly with ethylene oxide. Under the influence of ethylene oxide, 2-methyl-4-phenyl-1,2,4-triazolin-3-thione is converted to 2-methyl-4-phenyl-1,2,4-triazolin-3-one.

In this study we set out to obtain N- and S-β-chloroethyl derivatives from Δ^2-1,2,4-triazolin-5-thione by reaction with ethylene oxide and subsequent treatment with thionyl chloride.

4-Phenyl-1,2,4-triazolin-3-thione (I) and 1-phenyl-1,2,4-triazolin-3-thione (II) were taken as model starting substances for the study of this reaction. The reaction of I and II with ethylene oxide was carried out in acetic acid at room temperature.

Instead of the expected N- or S-β-hydroxyethyl derivatives, this reaction yielded 2-β-hydroxyethyl-4-phenyl-1,2,4-triazolin-3-one (III) and 2-β-hydroxyethyl-1-phenyl-1,2,4-triazolin-3-one (IV) (ν_{CO} 1664 cm^{-1} and λ_{max} 265 nm for III, and ν_{CO} 1668 cm^{-1} and λ_{max} 280 nm for IV). Compound III was obtained independently from 4-phenyl-1,2,4-triazolin-3-one (V) and ethylene chlorohydrin in alcoholic alkali as well as from V and ethylene oxide in acetic acid.



The desired 3-β-hydroxyethylthio-4-phenyl-1,2,4-triazole (VI) and 3-β-hydroxyethylthio-1-phenyl-1,2,4-triazole (VII) were obtained by the reaction of I and II with ethylene chlorohydrin in alcoholic alkali. The sulfide structures of these compounds follow from the UV spectral data. The spectra of 3-methyl-4-phenyl-1,2,4-triazolin-3-thione (VIII), 3-methylthio-4-phenyl-1,2,4-triazole, and VI are presented in Fig. 1 for comparison.

It is interesting that sulfide derivatives VI and VII also form N-β-hydroxyethyltriazolinones III and IV on reaction with ethylene oxide. Thus the β-hydroxyethyl group is transferred from S to N in the presence of ethylene oxide with simultaneous replacement of the thiol sulfur by carbonyl oxygen when this group is attached to the sulfide sulfur. Similarly, 3-methyl-4-phenyl-1,2,4-triazolin-3-thione (VIII) reacts with excess ethylene oxide to form good yields of 2-methyl-4-phenyl-1,2,4-triazolin-3-one (IX).

S. M. Kirov Ural Polytechnical Institute, Sverdlovsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 700-703, May, 1971. Original article submitted July 21, 1970.

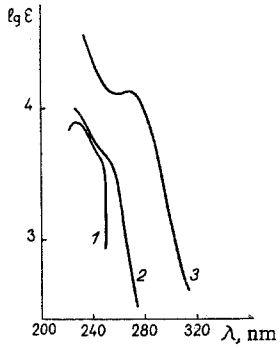
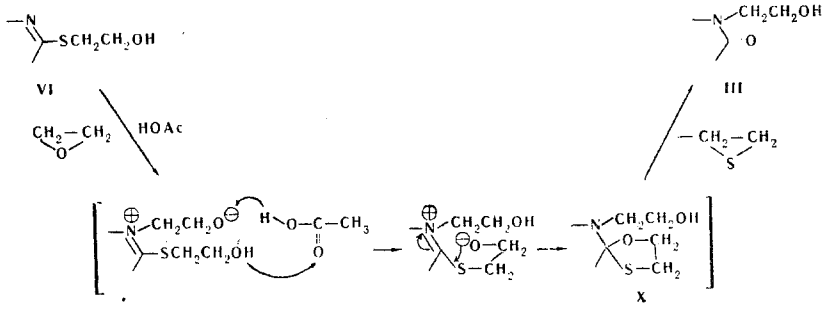


Fig. 1. UV spectra (in ethanol): 1) 3-methylthio-1,2,4-triazole; 2) 3-β-hydroxyethylthio-1,2,4-triazole; 3) 2-methyl-4-phenyl-1,2,4-triazolin-3-thione.

The observations made in this study make it possible to propose the following scheme for the conversion of a cyclic thioamide to the corresponding N-substituted amide.

The reaction probably begins with attack of the ethylene oxide at the exocyclic sulfur atom. (Investigation of the reaction by means of thin-layer chromatography indicated that a compound with an R_f value corresponding to β-hydroxyethylthio derivative is initially formed. A sample taken after a certain time gives a second spot, in addition to this spot, with an R_f value which corresponds to the final reaction product.) The conversion of 3-β-hydroxyethylthiotriazole to 2-β-hydroxyethyl derivative of the oxygen analog may occur due to subsequent attack by ethylene oxide at the nitrogen atom of the heterocycle with participation of the solvent through a step involving an unstable spiran (X). The conversion of thione VIII to amide IX apparently proceeds similarly through attack by ethylene oxide at the thiocarbonyl carbon, spiran formation, etc.



Calculation of thio forms I and II by the MO LCAO method indicates that there is a higher negative charge on the N_2 atom in I than in II [1]. This facilitates repeated attack by ethylene oxide in VI. The observation that the VI → III conversion is accomplished more rapidly than the VII → IV conversion, according to chromatographic data, is in agreement with the calculations and the proposed reaction scheme.

We also accomplished the conversion of a cyclic thioamide to the corresponding cyclic amide for 1-phenyltetrazolin-5-thione (XI). The reaction proceeds smoothly to give 1-phenyl-4-β-hydroxyethyltetrazolin-5-one (XII).

Similar conversions were recently described for benzothiazole-2-thione and its methylthio derivative [2]. The conversion of a cyclic thioamide to a cyclic amide during reaction with excess ethylene oxide is apparently a characteristic reaction for cyclic thioamides.

EXPERIMENTAL

2-β-Hydroxyethyl-4-phenyl-1,2,4-triazolin-3-one (III). A. A total of 3.4 g (2 mmole) of I [3] was dissolved in 20 ml of acetic acid, and 30 ml of ethylene oxide was added while cooling the mixture with an ice bath. The mixture was allowed to stand for 24 h in a refrigerator and then for 3 days at room temperature. The acetic acid was removed by distillation, the residual syrup was treated with several portions of acetone, each time removing the acetone by distillation on a water bath. The residue was allowed to stand in a refrigerator until a precipitate formed; the precipitate was filtered and crystallized from ethanol–ether (1 : 1) to give 1.5 g (50%) of a product with mp 146° and R_f 0.50. Found %: C 58.4; H 5.5; N 20.1. $C_{10}H_{11}N_3O_2$. Calculated %: C 58.6; H 5.4; N 20.4.

B. A total of 1.6 g (1.0 mmole) of V [3] was dissolved in 40 ml of ethanol containing 0.4 g (1.0 mmole) of NaOH, and 0.8 g (1.0 mmole) of ethylene chlorohydrin was added. The reaction mixture was refluxed for 6 h, the NaCl was filtered, and the solvent was distilled. The residual mass was triturated with ether and crystallized from ethanol–ether (1 : 1) to give 0.45 g (30%) of a product with mp 145-146°.

C. Compound V [1.6 g (1.0 mmole)] was dissolved in 22 ml of acetic acid, and 10 ml of ethylene oxide was added. The mixture was allowed to stand for 10 h in a refrigerator and for 4 days at room temperature. The solvent was distilled, and III was extracte d from the residue with a small amount of ethanol to give 0.15 g (10%) of a product with mp 145-146°.

D. A threefold excess of ethylene oxide was added to 0.2 g (0.9 mmole) of VI in 3 ml of acetic acid, and the mixture was allowed to stand for 5 days at room temperature. The acetic acid was removed by distillation, and the residual low-melting product was dissolved in alcohol and passed through a column filled with aluminum oxide. The eluate was diluted with ether until it became turbid, and the mixture was allowed to stand in the cold. The resulting crystals were filtered to give 0.18 g (82%) of a product with mp 145-146°.

The products obtained by methods A-D did not give melting point depressions in mixed samples.

2-β-Hydroxyethyl-1-phenyl-1,2,4-triazolin-3-one (IV). A. A total of 2.6 g (1.47 mmole) of II [4] was dissolved in 40 ml of acetic acid, and 20 ml of ethylene oxide was added with cooling. The reaction mixture was allowed to stand for a week at room temperature. The solution was evaporated on a water bath, and the syrupy residue was treated with 20 ml of dry benzene. The resulting fine flakes were filtered to give 2.1 g (70%) of a product with mp 213-214° (from ethanol) and R_f 0.45. Found %: C 58.9; H 5.4. $C_{10}H_{11}N_3O_2$. Calculated %: C 58.5; H 5.4.

B. Compound VII [0.5 g (2.27 mmole)] was dissolved in 5 ml of acetic acid, and 1 ml of ethylene oxide was added with cooling. The mixture was allowed to stand for 5 days at room temperature. The solvent was removed by distillation, and the residue was crystallized from ethanol to give 0.3 g (63%) of a product with mp 214-215°. The product did not depress the melting point of the product obtained by method A.

3-β-Hydroxyethylthio-4-phenyl-1,2,4-triazole (VI). A total of 3.4 g (2.0 mmole) of I was dissolved in 15 ml of ethanol containing 0.8 g (2.0 mmole) of NaOH, and 2.0 g (2.5 mmole) of ethylene chlorohydrin was added. After 20-30 min the NaCl was filtered, and the solution was refluxed for 1 h. The ethanol was removed by distillation, and the residual syrup was treated with 50 ml of acetone. The acetone was removed by distillation, and the residue was allowed to stand in the cold, after which 5 ml of cold acetone was added, and the resulting precipitate was filtered and crystallized from benzene–petroleum ether (2:1) to give 3.2 g (85%) of a product with mp 116° and R_f 0.81. Found %: C 54.5; H 5.2; S 14.4. $C_{10}H_{11}N_3OS$. Calculated %: C 54.3; H 5.0; S 14.5.

3-β-Hydroxyethylthio-1-phenyl-1,2,4-triazole (VII). Compound II [1.7 g (1.0 mmole)] was dissolved in 20 ml of ethanol containing 0.4 g (1.0 mmole) of NaOH and 0.5 ml of H_2O, and 1.3 g (1.6 mmole) of ethylene chlorohydrin was added. The mixture was refluxed for 2 h, the NaCl was filtered, and the solution was evaporated until crystallization commenced to give 1.8 g (82%) of a product with mp 73° [from benzene–petroleum ether (3:1)] and R_f 0.81. Found %: C 54.2; H 5.0; N 19.2. $C_{10}H_{11}N_3OS$. Calculated %: C 54.3; H 5.0; N 18.9.

2-Methyl-4-phenyl-1,2,4-triazolin-3-one (IX). A total of 0.5 g (2.6 mmole) of VIII [6] was dissolved in 5 ml of acetic acid, and 2 ml of ethylene oxide was added. The mixture was allowed to stand at room temperature for a week and was then concentrated to one third of its initial volume. The mixture was cooled, and the oily crystals were filtered and pressed on a porous plate. They were then crystallized from water–ethanol (14:1) to give 0.35 g (70%) of a product with mp 157° (158° [5]). The product did not depress the melting point of the substance obtained by the method in [5].

4-β-Hydroxyethyl-1-phenyltetrazolin-5-one (XII). Product XI [2.6 g (1.45 mmole)] was dissolved in acetic acid, and 20 ml of ethylene oxide was added with cooling. The mixture was allowed to stand for a week at room temperature. The solvent was removed by distillation, and the residue was stored in a refrigerator. The resulting crystals were filtered and pressed on a porous plate to give 2.1 g (70%) of a product which was crystallized from benzene to give a material with mp 144°. Found %: C 52.1; H 4.8. $C_9H_{10}N_4O_2$. Calculated %: C 52.4; H 5.0.

The chromatography was carried out on Beckmann II aluminum oxide for chromatography (neutral) in a loose layer. The solvent was chloroform–benzene–ethanol (1:1:2). The UV spectra of alcohol solutions were obtained with an SF-4 spectrophotometer, while the IR spectra of mineral oil suspensions were obtained with a UR-20 spectrometer.

LITERATURE CITED

1. E. G. Kovalev and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 1138 (1970).
2. P. Sohar, G. H. Denny, and R. D. Babson, J. Heterocycl. Chem., 5, 769 (1968).
3. M. Pesson, G. Polmanss, and S. Dupin, Comptes Rend., 248, 1677 (1959).
4. E. G. Kovalev and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 740 (1968).
5. M. Pesson and S. Dupin, Bull. Soc. Chim. France, No. 2, 250 (1962).
6. I. L. Shegal and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 133 (1965).