ORGANIC AND BIOLOGICAL CHEMISTRY

ISOMERIZATION OF 3,4-EPOXYPHOSPHOLANES

B. A. Arbuzov, A. P. Rakov, and A. O. Vizel' UDC 542.952.1+661.718.1

The synthesis of 3,4-epoxyphospholanes, bicyclic compounds composed of condensed phospholane and oxirane rings, was reported in [1]. Smooth opening of the α -oxide ring occurred when these compounds were reacted with certain compounds under acid catalysis conditions, with the formation of the 3,4-glycols of phospholanes or their derivatives as the addition products [2]. In some cases the process was complicated by the formation of a small amount of α , β -unsaturated alcohols as impurity.

Continuing our study of the chemical properties of 3,4-epoxyphospholanes, we also made a study of their behavior when reacted with certain nucleophilic reagents under basic catalysis conditions. The present paper is devoted to a discussion of the obtained results. As a rule, three types of transformations occurred when nucleophilic reagents were reacted with compounds containing an α -oxide ring: 1) opening of the α -oxide ring with the formation of addition products; 2) isomerization to α , β -unsaturated alcohols; 3) isomerization to carbonyl compounds [3]. The mechanism of the process, leading to the formation of addition products, reduces to attack by the nucleophilic reagent of the carbon atom having the lowest electron density, the formation of the intermediate anion, and the rapid addition of a proton. In the given case the catalytic action of bases is explained by the fact that they increase the activity of the O-H bond of the compound that condenses with the oxide [4].

Isomerization processes are observed less frequently under basic catalysis conditions than are the processes of opening of the α -oxide ring. Here isomerization products are formed frequently together with the addition products. According to the literature data [5-7], the action of bases on α -oxides reduces to attack of the hydrogen atoms, attached to the carbon atom of the oxide ring and to the carbon atom in the α -position to the oxide ring, and the first step of this reaction consists in cleavage of one of the protons by the anion of the base. The redistribution of the bonds in the formed anion, caused by the cleavage of a proton, leads to the formation of the corresponding isomerization products. The direction of the isomerization depends on the structure of the compound: the formation of carbonyl compounds occurs only in the case where the carbon atoms in the α -position to the oxide ring are devoid of hydrogen atoms; α -oxides, in whose molecules are present hydrogen atoms, attached to both the carbon atom of the oxide ring and the α -carbon atom (with respect to the oxide ring), undergo isomerization only to α , β -unsaturated alcohols.

In view of what has been said it is possible to expect the formation of products with the following structure when 3,4-epoxyphospholanes are reacted with nucleophilic reagents under basic catalysis conditions:



A. E. Arbuzov Institute of Organic and Physical Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No.1, pp.85-90, January, 1970. Original article submitted July 22, 1968.

©1970 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.



Actually, it proved that in the presence of catalysts with a basic character, in either alcohol or acetic acid medium, only isomerization processes take place, in which connection the sole products are α , β -unsaturated alcohols of type (a), (d), (g), and (h). In principle, the formation of compounds with structures (b) and (i) is possible, but the IR-spectroscopy data do not corroborate such a structure for the compounds isolated by us.

Such a well-defined course of the reaction we associate with the enhanced lability of the hydrogen atoms of the methylene groups adjacent to the strongly polar phosphoryl group. Many authors [8-16] have reported previously on the lability of the hydrogen atoms in the methylenephosphoryl group. The uniqueness of the 3,4-epoxyphospholanes consists in the fact that their methylenephosphoryl groups are found in the α -position to the carbons of the oxide ring, which favors isomerization only to α, β -unsaturated alcohols. The hydrogen atoms found attached to the carbon atoms of the oxide ring or (in the case of methyl substituents on the carbon atoms of the oxide ring) in the CH₃ group, are much less labile than the hydrogen atoms of the methylenephosphoryl group. The obtained results confirm this assumption.

A mixture of isomers with the structures (g) and (h) is formed in the case of an unsymmetrically substituted 3,4-epoxyphospholane. It proved possible to isolate these isomers in the pure state by repeated fractional distillation. The isomer with structure (g) was formed in much larger amounts than the isomer with structure (h). This can probably be explained by the fact that the hydrogen atom having an adjacent methyl group, is less available to the anion of the base during attack.

The structure of the obtained compounds (g) and (h) was established on the basis of the IR spectra, and was corroborated chemically. For this purpose we used the absorption band of the stretching vibration of the C = C bond. It is known [17] that its frequency is mainly dependent on the degree and character of the substitution of the double bond and the conjugation. In (g) and (h) the C = C bond was found in the same position to the phosphoryl group, but had a different degree of substitution. We also made use of this difference. As model compounds we took the 2-phospholenes and obtained the 2-phospholen-4-ols, the position of the double bonds in which failed to evoke doubt. Below are given the frequencies of the stretching vibrations of the C = C bonds in these compounds and the structures of the compounds themselves.



In the IR spectrum of one of the isomers isolated by us there was present intense absorption with a frequency of 1585 cm⁻¹, while the other isomer exhibited intense absorption at 1610 cm⁻¹. On the basis of the data given below we assigned structure (g) to the first compound, and structure (h) to the second compound, as respectively being compounds with an unsubstituted and substituted double bond. The validity of such an assignment was also confirmed chemically. For this purpose the compound, which was assigned structure (h), was oxidized with $K_2Cr_2O_7$ in benzene. The product that was formed here was reacted with 2,4-dinitrophenylhydrazine. As a result we isolated the 2,4-dinitrophenylhydrazone, which indicates the presence of a keto group, which could be formed from a compound with a secondary hydroxyl group according to the scheme:



The formation of carbonyl compounds of type (e) or (m), or of addition products of type (c), (f), (p) or (t), was not observed under the conditions selected by us. In all of the experiments, together with the main products, was formed a noticeable amount of polymers. As catalysts we used sodium alcoholates, triethylamine and sodium acetate. The isomerization proceeds most vigorously in the presence of sodium alcoholates. Even the addition of a small amount of such a catalyst causes a sharp rise in the temperature and a yellowing of the solution, for which reason the components were mixed using chilled water for cooling. The other catalysts fail to give a heat effect and require additional heating.

The obtained compounds are listed in Table 1, while the experimental details are described in the experimental part.

EXPERIMENTAL

The starting 3,4-epoxyphospholanes were synthesized by the previously described method [1].

<u>Preparation of 1-Ethoxy-1-oxo-2-phospholen-4-ol (I)</u>. To a solution of 23.9 g of 3-ethoxy-3-oxo-6,3oxaphosphabicyclo [3,1,0]hexane in 60 ml of absolute ethanol, using chilled water for cooling, was gradually added a solution of C_2H_5ONa (0.14 g of Na in 10 ml of absolute ethanol). When all of the alcoholate had been added the mixture was kept at room temperature for 12 h, and then it was heated under reflux for 25 h.





R´ [°] O												
r b	R	B,	в″	Yield,	Bp, °C (p, mm	n ²⁰	d20	Found /calculated				Empirical
Con			1	%	of Hg)	- D	4	MR	C, %	н, %	P, %	Iormula
I	OC₂H₅	н	н	74,0	141 - 143 (0,03)	1,4950	1,2294	$\frac{38,43}{38,53}$	$\frac{44,50}{44,44}$	$\frac{6,83}{\overline{6,79}}$	$\frac{19,02}{19,11}$	C ₆ II ₁₁ O ₈ P
11	OC_2H_5	н	CH3	53,3	116-117 (0,045)	1,4860	1,1672	$\tfrac{43,29}{43,13}$	$\tfrac{47,71}{47,72}$	$\frac{7,45}{7,44}$	$\frac{17,29}{17,59}$	$C_7H_{13}O_3P$
ш	$\mathrm{OC}_{2}\mathrm{H}_{5}$	СН₃	н	4,4	$139_{(0,035)}^{140}$	1,4960	1,1799	$\frac{43,56}{43,13}$	$\tfrac{47,92}{47,72}$	$\frac{7,49}{7,44}$	$\frac{17,60}{17,59}$	C7H13O3P
ıv	OC₂H₅	СН₃	CH₃	35,0	138—139 (0,03)	1,4908	1,1501	$\frac{47,88}{47,75}$	$\frac{50,29}{50,47}$	$\frac{7,90}{7,89}$	$\frac{16,30}{16,29}$	C ₈ H ₁₅ O ₃ P
v	C ₆ H ₅	CII3	CH3	50,0*	_	_	-	-	$\begin{array}{c} 64,71\\ \overline{64,86}\end{array}$	$\frac{6,97}{\overline{6,76}}$	$\frac{13,81}{13,96}$	C12H15O2P
		-										

* Bp, 198.5-199.5°.

Then the mixture was cooled at room temperature, cautiously neutralized with hydrochloric acid solution, and diluted with diethyl ether. The obtained precipitate of NaCl was filtered, all of the readily volatile products were vacuum-distilled, and the residue was subjected to fractional distillation. We obtained 17.7 g (74%) of (I).

Preparation of 1-Ethoxy-1-oxo-4-methyl-2-phospholen-4-ol (II) and 1-Ethoxy-1-oxo-3-methyl-2phospholen-4-ol (III). To a solution of 38.0 g of 1-methyl-3-ethoxy-3-oxo-6,3-oxaphosphabicyclo[3,1,0]hexane in 67 ml of absolute ethanol, with cooling in a water bath, was gradually added a solution of C_2H_5ONa (0.6 g of Na in 15 ml of absolute ethanol). After adding all of the alcoholate the experiment was run as indicated above for the preparation of (I). Here we obtained 26.9 g of a mixture of (II) and (III). By repeated fractional distillation we were able to isolate 20.6 g (53.3%) of (II) and 1.7 g (4.4%) of (III).

<u>Preparation of 1-Ethoxy-1-oxo-3,4-dimethyl-2-phospholen-4-ol (IV)</u>. A mixture of 22.8 g of 1,5dimethyl-3-ethoxy-3-oxo-6,3-oxaphosphabicyclo[3,1,0]hexane, 100 ml of absolute diethyl ether, 10 ml of glacial acetic acid and 0.5 g of anhydrous sodium acetate was heated under reflux for 15 h. All of the readily volatile products were vacuum-distilled using a water-jet pump, while the residue was subjected to fractional distillation. We isolated 8.0 g (35%) of (IV). We also recovered 14.05 g of the starting oxide.

<u>Preparation of 1-Phenyl-1-oxo-3,4-dimethyl-2-phospholen-4-ol (V)</u>. A solution of 0.6 g of 1,5-dimethyl-3-phenyl-3-oxo-6,3-oxaphosphabicyclo[3,1,0]hexane and 0.4 ml of triethylamine in 5 ml of absolute ethanol was heated under reflux. All of the readily volatile products were vacuum-distilled. The residue was dissolved in CH_2Cl_2 , and the addition of ether to this solution gave a precipitate. The precipitate was filtered and recrystallized from boiling acetone. We obtained 0.3 g (50%) of (V).

Oxidation of 1-Ethoxy-1-oxo-3-methyl-2-phospholen-4-ol. To a solution of 2.1 g of (III) in 20 ml of absolute benzene was slowly added in drops, with shaking and cooling, a solution of 1.65 g of $K_2Cr_2O_7$ and 1 g of conc. H_2SO_4 in 10 ml of distilled water. Here the appearance of an intense lilac color was observed, which after some time changed to a pale yellow. Then the reaction mixture was kept at room temperature for 10 h, the benzene layer was separated, and the aqueous layer was extracted first with 30 ml of benzene, and then twice with 25-ml portions of freshly distilled CHCl₃. The extracts and benzene layer were combined, dried over anhydrous Na₂SO₄, and filtered from the drying agent. All of the readily volatile products were vacuum-distilled, using a water-jet pump first, and then an oil pump. We obtained 1.3 g of residual oil.

<u>Preparation of 2,4-Dinitrophenylhydrazone (VI)</u>. To a solution of 0.5 g of the product from the preceding reaction in 15 ml of ethanol was added a solution composed of 0.4 g of 2,4-dinitrophenylhydrazine, 2 ml of conc. H_2SO_4 , 5 ml of H_2O and 15 ml of ethanol. A yellow precipitate began to deposit within 5 min after mixing, and the precipitation was practically ended in 5 h. After 10 h the precipitate was filtered, washed twice with a little water, recrystallized from boiling ethanol, and washed with ether. We isolated 0.85 g of a product (81.7%) with mp 184-185°. Found: C 44.10; H 4.44; P 8.47%. $C_{13}H_{15}N_4O_6P$. Calculated: C 44.05; H 4.23; P 8.75%. The IR spectra confirm the structure of the hydrazone.

In conclusion the authors sincerely express their gratitude to Z. G. Isaeva for a number of valuable suggestions, made during the course of the work and in interpreting the results.

CONCLUSIONS

1. In the presence of catalysts of basic character, 3,4-epoxyphospholanes are isomerized to 2-phospholen-4-ols.

2. Unsymmetrical 3,4-epoxyphospholanes form a mixture of isomers, with a substantial predominance of the isomer containing a tertiary hydroxyl group.

LITERATURE CITED

- B. A. Arbuzov, L. A. Shapshinskaya, A. P. Rakov, A. O. Vizel¹, and N. P. Kulikova, USSR Patent No.212258 (December 19, 1966); Byull. Izobr. No.9 (1968); B. A. Arbuzov, L. A. Shapshinskaya, A. P. Rakov, A. O. Vizel, and N. P. Kulikova, Izv. Akad. Nauk SSSR, Ser. Khim., 1313 (1968).
- 2. B. A. Arbuzov, L. A. Shapshinskaya, A. P. Rakov, A. O. Vizel', and N. P. Kulikova, USSR Patent No. 225187 (June 12, 1967); Byull. Izobr., No. 27 (1968).
- 3. A. Weissburger (editor), Heterocyclic Compounds with Three- and Four-Membered Rings, Part I, New York - London - Sydney (1964), p. 1.

- 4. M. S. Malinovskii, Olefin Oxides and Their Derivatives [in Russian], Goskhimizdat (1961), p. 30.
- 5. Z. G. Isaeva and B. A. Arbuzov, Synthetic Products from Rosin and Turpentine [in Russian], Nauka i Tekhnika, Minsk (1964), p. 203.
- 6. J. K. Crandall and Luan-Ho Chang, J. Org. Chem., 32, 435 (1967).
- 7. Some Problems in Organic Chemistry [in Russian], Izd. Kazansk. Gos. Univ. (1964), p. 161.
- 8. A. E. Arbuzov and A. I. Ruzumov, Zh. Russ. Fiz.-Khim. Obshchvesta, 61, 623 (1929); Selected Works [in Russian], Izd. AN SSSR (1952), p. 312.
- 9. A. E. Arbuzov, Selected Works [in Russian], Izd. AN SSSR (1952), p. 19; A. L. Troitskaya, Tr. Kazansk. Khim.-Tekhnol. Inst., 83, 228 (1957).
- A. N. Pudovik and N. M. Lebedeva, Dokl. Akad. Nauk SSSR, <u>90</u>, 799 (1953); M. I. Kabachnik, T. Ya. Medved, and E. I. Magrosov, Dokl. Akad. Nauk SSSR, 162, 339 (1965).
- 11. A. N. Pudovik, Usp. Khim., 23, 547 (1954).
- 12. N. Kreutzkamp, Ber., 88, 195 (1955); Angew. Chem., 69, 393 (1957).
- 13. L. Horner, H. Hoffmann, and H. G. Wippel, Ber., 91, 61 (1958).
- 14. L. Horner, H. Hoffmann, H. G. Wippel, and G. Klahre, Ber., 92, 2499 (1959).
- 15. F. F. Blicke and S. Raines, J. Org. Chem., 29, 2036 (1964).
- 16. A. V. Dombrovskii and G. V. Grinev, Ukr. Khim. Zh., 34, 171 (1968).
- 17. L. J. Bellamy, Infrared Spectra of Complex Molecules [Russian translation], IL (1963), p. 54.
- 18. H. Weitkamp and F. Korte, Z. Anal. Chem., 204, 245 (1964).
- 19. U. Hasserodt, K. Hunger, and F. Korte, Tetrahedron, 19, 1563 (1963).