3,4-PHOSPHOLANEDIOL 1-OXIDES AND THEIR DERIVATIVES

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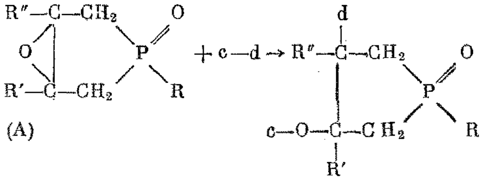
It is known [1] that compounds containing the epoxide group can, as a rule, undergo three types of transformations: 1) opening of the epoxide ring and formation of addition products; 2) isomerization to carbonyl compounds; 3) isomerization to unsaturated alcohols. However, data in the literature on this question are insufficient for α-epoxides of heterocycles and they are mainly concerned with α-epoxides of alkylfuryl alcohols and α-epoxides of sulfolenes [2, 3]. In agreement with these data, attempts of Azanovskaya and Pansevich-Kolyada [2] to isolate products from the reaction of epoxides of alkylfuryl alcohols with alcohols, amines, and water ended in failure: although the reaction went, the products formed could not be isolated. In the case of α-epoxides of sulfolenes, their reactions with hydrogen halides, water, ammonia, and certain other reagents were studied. Here, smooth opening of the epoxide ring [3] was observed with formation of only addition products. It is natural to expect that the presence of other hetero atoms in the ring, and in particular a phosphorus atom, would in some degree affect the course of the process. In the light of what has been presented above, we thought it of interest to study the chemical behavior of α-epoxides of phosphorus-containing heterocyclic compounds in the reactions indicated. We chose as the object of the investigation 3,4-epoxyphospholane 1-oxides (A), which are bicyclic systems consisting of condensed oxirane and phospholane fragments, the preparation of which we reported recently [4]. Data on this question are absent in the literature.

Data concerning reactions of (A) with alcohols and water in the presence of catalysts of acid character, organic acids, and hydrogen halides, are presented in this communication. Transformations under conditions of basic catalysis and also reactions with amines will be reported in subsequent publications. Upon reaction of (A) with alcohols the main course of reaction was found to be opening of the α-epoxide ring with formation of addition products [5]. In the case of unsymmetrical (A), only one compound was isolated, for which we propose the structure having a secondary hydroxyl group on analogy with the product of the opening of the α-epoxide of methylcyclopentene under conditions of acid catalysis [6]. In rare cases the reaction was complicated by isomerization to the unsaturated alcohols; however, the latter (based on IR spectral data) were formed as small admixtures. The compounds obtained react with acetic anhydride, exchanging the hydroxyl group for an acetate group. Analogous transformations are also observed upon reaction of (A) with organic acids and hydrogen halides. In these cases the reaction is directed exclusively in the direction of formation of derivatives 3,4-phospholanediol 1-oxide, and the isomerization reaction is not observed. With the exception of the bromohydrin, the compounds obtained were found to be stable and, in the case of liquid products, did not decompose upon distillation. Reaction of (A) with water also proceeds smoothly and leads to 3,6-phospholanediol 1-oxides.

On the basis of what has been stated above, we concluded that all the processes studied by us proceeded by the scheme



(A)

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The compounds obtained are presented in Table 1. They are viscous colorless oils or crystalline substances having quite high melting points, frequently poorly soluble in water and organic solvents. The compounds do not give a qualitative reaction for epoxide oxygen [7].

IR spectra were taken with the purpose of establishing the structure of the compounds obtained. Absorption in the 840-850 cm^{-1} region (characteristic for the α-epoxide ring of phosphorus-containing epoxides [8]) was absent in the spectra. Absorption in the 3250-3400 cm^{-1} region (OH stretching vibrations) was present for all of the compounds [except (XV)], and (IX)-(XII) and (XV) absorbed in the 1720-1740 cm^{-1} region (C = O stretching vibrations). A very weak absorption characteristic for the double bond situated in an α,β-position to the phosphoryl group appeared in the spectra of compounds (VI) and (VII). All of these data confirm the structures proposed by us for the adducts obtained. We have found a method [5] which makes it possible to obtain 3,4-phospholanediol 1-oxides and some of their derivatives easily and simply.

EXPERIMENTAL

The starting 3,4-epoxyphospholane 1-oxides were prepared by the method described earlier [4].

Reaction with Alcohols. A mixture of the 3,4-epoxyphospholane 1-oxide (A), excess alcohol, and 1-2 drops of H_2SO_4 or 5-7 drops of BF_3 etherate or 5 drops of H_3PO_4 was boiled for 6-24 h with a reflux condenser, then neutralized with $NaHCO_3$ or $Ba(OH)_2$, and filtered from the precipitate. All volatile products were distilled in vacuum. The crystalline residue was recrystallized from a suitable solvent and liquids were distilled in vacuum. Analyses and constants of the compounds obtained are indicated in Table 1.

Preparation of 1,4-Diethoxy-3-phospholanol 1-Oxide (I). From 16.2 g of (A) ($R = OC_2H_5$, $R' = R'' = H$), 12.6 g of ethanol, and 2 drops of conc. H_2SO_4 after boiling for 24 h, subsequent neutralization with $Ba(OH)_2$, filtration from the precipitate, and distillation of the liquid residue in vacuum we obtained 8.9 g of (I).

Preparation of 1,4-Diethoxy-4-methyl-3-phospholanol 1-Oxide (II). From 12.6 g of (A) ($R = OC_2H_5$, $R' = CH_3$, $R'' = H$), 30 ml of C_2H_5OH, and 7 drops of BF_3 etherate after boiling for 6 h and subsequent distillation we obtained 7.82 g of (II) (method a).

b. From 17.6 g of (A) ($R = OC_2H_5$, $R' = CH_3$, $R'' = H$), 55.2 g of ethanol, and 1 drop of conc. H_2SO_4 after boiling for 7 h, neutralization with $NaHCO_3$, filtration, and distillation of the liquid residue in vacuum we obtained 7.0 g (yield 31.5%) of (II). Yield of (II) in Table 1 is given for method a.

Preparation of 4-Methoxy-3,4-dimethyl-1-phenyl-3-phospholanol 1-Oxide (III). From 1.1 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$), 20 g of CH_3OH, and 2 drops of conc. H_2SO_4 after boiling for 13 h with a reflux condenser and removal of alcohol in vacuum, filtration of the crystalline residue, and recrystallization of it from acetone we obtained 1.23 g of (III).

Compounds (IV) and (V) were obtained analogously.

Preparation of 4-Methyl-1,4-dipropoxy-3-phospholanol 1-Oxide (VI). From 7.0 g of (A) ($R = OC_3H_7$, $R' = CH_3$, $R'' = H$), 30 ml of propyl alcohol, and 7 drops of BF_3 etherate after boiling for 6 h and subsequent distillation we obtained 1.1 g of (VI).

Preparation of 1,4-Dibutoxy-3,4-dimethyl-3-phospholanol 1-Oxide (VII). From 9.55 g of (A) ($R = OC_4 \cdot H_9$, $R' = R'' = CH_3$), 20 ml of butyl alcohol, and 5 drops of 65% H_3PO_4 after boiling for 16 h, neutralization with $NaHCO_3$, filtration from the residue, and subsequent distillation we obtained 2.7 g of (VII).

Reaction with Acetic Anhydride

Preparation of 1,4-Diethoxy-3-acetoxyphospholane 1-Oxide (XV). A mixture of 7.6 g of (I), 10 ml of abs. benzene, 6 ml of $(CH_3CO)_2O$, and 1 drop of conc. H_2SO_4 was held at room temperature for 48 h and then heated at 80°C for 1 h. Subsequent distillation in vacuum yielded 6.3 of product (XV).

Reaction with Hydrogen Halides

Preparation of 4-Chloro-3,4-dimethyl-1-phenyl-3-phospholanol 1-Oxide (XIII). We dissolved 1 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$) in ether and the solution was saturated with HCl. An oil precipitated which hardened upon rubbing with a glass rod. We obtained 1.15 g of (XIII).

TABLE 1

Compound	R	R′	R″	c	d	Catalyst	Found, %	Bp, °C (p, mm Hg)	mp, °C	n_D^{20}	d_4^{20}	Found Calculated, %				Empirical formula
												MR	C	H	P	
I	OC_2H_5	H	H	OH	OC_2H_5	H_2SO_4	43	148—150 (0,04)	—	1,4757	1,1726	50,00 49,85	45,84 46,15	8,19 8,17	15,05 14,90	$C_8H_{17}O_4P$
II	OC_2H_5	H	CH_3	OH	OC_2H_5	H_2SO_4	50	139—139,5 (0,02)	—	1,4733	1,1411	54,65 54,47	48,66 48,64	8,45 8,55	14,12 13,94	$C_9H_{19}O_4P$
III	C_6H_5	CH_3	CH_3	OH	OCH_3	H_2SO_4	96,8	—	238—239	—	—	—	61,37 61,41	7,43 7,48	12,27 12,22	$C_{13}H_{19}O_3P$
IV	C_6H_5	CH_3	CH_3	OH	OC_2H_5	H_2SO_4	94	—	232—233	—	—	—	62,62 62,68	7,80 7,83	11,66 11,57	$C_{14}H_{21}O_3P$
V	C_6H_5	CH_3	CH_3	OH	OC_4H_9	H_2SO_4	90,7	—	201—202	—	—	—	—	—	10,62 10,47	$C_{16}H_{25}O_3P$
VI	OC_3H_7	H	CH_3	OH	OC_3H_7	Эфират BF_3	10	155—157 (0,05)	—	1,4657	1,0743	64,41 63,71	—	—	12,23 12,39	$C_{11}H_{23}O_4P$
VII	OC_4H_9	CH_3	CH_3	OH	OC_4H_9	H_3PO_4	21	149—149,5 (0,045)	—	1,4751	1,0660	76,63 77,56	57,27 57,50	9,93 9,92	10,96 10,62	$C_{14}H_{29}O_4P$
VIII	C_6H_5	CH_3	CH_3	OH	OH	H_2SO_4	92,5	—	239—240	—	—	—	59,83 60,00	7,09 7,08	12,65 12,90	$C_{12}H_{17}O_3P$
IX	OC_2H_5	CH_3	CH_3	OH	CH_3COO	H_2SO_4	40,6	162,5—163 (0,035)	—	1,4720	—	—	—	—	12,36 12,39	$C_{10}H_{19}O_5P$
X	C_6H_5	CH_3	CH_3	OH	CH_3COO	H_2SO_4	91,8	—	224—225	—	—	—	59,53 59,57	6,95 6,73	11,03 10,98	$C_{14}H_{19}O_3P$
XI	C_6H_5	CH_3	CH_3	OH	$ClCH_2COO$	—	63,5	—	220—221	—	—	—	53,41 53,09	5,85 5,68	—	$C_{14}H_{18}O_3PCl$
XII	C_6H_5	CH_3	CH_3	OH	Cl_3CCOO	—	81,7	—	185—186	—	—	—	43,71 43,64	4,16 4,15	7,70 8,03	$C_{14}H_{16}O_3PCl_3$
XIII	C_6H_5	CH_3	CH_3	OH	Cl	—	91,3	—	208	—	—	—	—	—	12,00 11,97	$C_{12}H_{16}O_2PCl$
XIV	C_6H_5	CH_3	CH_3	OH	Br	—	95	—	185 (разл.)	—	—	—	47,43 47,52	5,28 5,28	10,34 10,23	$C_{12}H_{16}O_2PBr$
XV	OC_2H_5	H	H	CH_3COO	OC_2H_5	H_2SO_4	70	110—111 (0,035)	—	1,4639	1,1601	59,45 59,22	48,19 48,00	7,63 7,60	12,28 12,39	$C_{10}H_{19}O_5P$

Preparation of 4-Bromo-3,4-dimethyl-1-phenyl-3-phospholanol 1-Oxide (XIV). We dissolved 1 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$) in 5 ml of distilled H_2O. To the solution we added 5 ml of 48% HBr. An oil precipitated which solidified upon rubbing with a glass rod. We obtained 1.3 g of product (XIV). After washing with water and acetone with recrystallization from acetone-n-heptane, 5 : 1, we obtained colorless crystals (dec. t. 185°) which turned brown under the influence of light.

Reaction with Organic Acids

Preparation of 4-Acetoxy-3,4-dimethyl-1-phenyl-3-phospholanol 1-Oxide (X). A mixture of 1.95 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$), 20 ml of anh. CH_3COOH, and 2 drops of H_2SO_4 was heated at 50° for 72 h. The excess CH_3COOH was distilled in vacuum. The solid was filtered off, washed with ether, and recrystallized from acetone. We obtained 2.25 g of product (X).

Preparation of 3,4-Dimethyl-1-phenyl-4-(trichloroacetoxy)-3-phospholanol 1-Oxide (XII). A mixture of 0.6 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$), 0.7 g of the anhydride of CCl_3CO_2H in 12 ml of abs. C_6H_6 was boiled for 15 h. The solvent was removed in vacuum. The residue was recrystallized from acetone-methylene chloride, 5 : 1. We obtained 0.85 g of product (XII).

Compound (XI) was obtained analogously.

Preparation of 4-Acetoxy-1-ethoxy-3,4-dimethyl-3-phospholanol 1-Oxide (IX). We held 14 g of (A) ($R = OC_2H_5$, $R' = R'' = CH_3$), 70 ml of anhyd. CH_3COOH, and 3 drops of H_2SO_4 at room temperature for 288 h, after which the CH_3COOH was removed in vacuum. The residue was diluted with ether and washed with an aqueous solution of K_2CO_3 to a neutral reaction. The ether layer was separated from the aqueous layer and the latter was extracted two times with ether.

The extracts were combined with the ether layer and dried over Na_2SO_4. After filtration from the drying agent the solvent was removed in vacuum and the residue was subjected to distillation. We obtained 10.2 g of product (IX).

Reaction with Water

Preparation of 3,4-Dimethyl-1-phenyl-3,4-phospholanediol 1-Oxide (VIII). A mixture of 0.6 g of (A) ($R = C_6H_5$, $R' = R'' = CH_3$), 4 ml of H_2O, and 1 drop of conc. H_2SO_4 was boiled for 13 h. The precipitated crystals were filtered off, washed with water, and recrystallized from dioxane. We obtained 0.6 g of product (VIII).

CONCLUSIONS

Upon reaction of 3,4-epoxyphospholane 1-oxides with alcohols and water in the presence of catalysts having acid character, organic acids, and hydrogen halides, opening of the α-epoxide ring occurs with formation of addition products.

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