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O.N. Chupakhin on his 70th Anniversary

## Reaction of 2,3-Epoxypropyl Ethers with 1-Butanol

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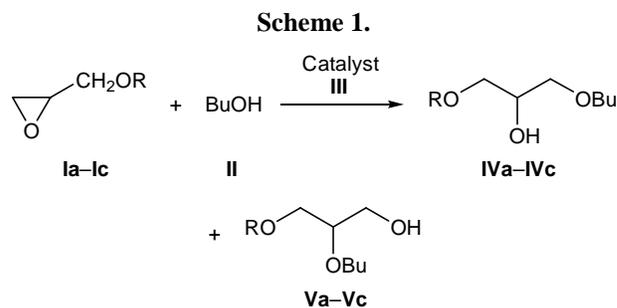
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**Abstract**—Nucleophilic opening of the oxirane ring in 2,3-epoxypropyl ethers with alcohols in the presence of titanium alkoxides and other catalysts was studied. The mechanism of catalysis by titanium alkoxides was discussed on the basis of comparison with acid–base catalysts.

Addition of alcohols to alkyl 2,3-epoxypropyl ethers in the presence of sodium alkoxides yields 1,3-dialkoxy-2-propanols, while under catalysis with boron trifluoride–ether complex insignificant amounts of 2,3-dialkoxy-1-propanol are also formed [1]. In the reaction of 2,3-epoxypropyl phenyl ether with 1-butanol, 2-butoxy-3-phenoxy-1-propanol was isolated together with the major product, the corresponding secondary alcohol [2]. It should be noted that no quantitative estimation of the product ratio was performed in [1, 2]. Kuvamura [3] reported on the formation of secondary alcohol as the only product in the presence of sulfuric acid. Caron and Sharpless in their classical work [4] showed that titanium isopropoxide ensures highly selective ring opening in 2,3-epoxy-1-hexanol with a large number of nucleophiles; on the other hand, the corresponding methyl ether failed to react under analogous conditions. It is known that organic titanium compounds act as curing agents toward epoxy resins, i.e., they are capable of catalyzing opening of epoxy ring with hydroxy compounds [5].

The goal of the present work was to compare the efficiency and selectivity of oxirane ring opening in 2,3-epoxypropyl ethers in the presence of titanium alkoxides and other catalysts. We examined the reaction of 2,3-epoxypropyl ethers with 1-butanol as a model. The reactions were carried out at different reactant ratios using titanium butoxide, sulfuric acid (protic acid), boron trifluoride–ether complex (Lewis acid), and benzyldimethylamine (base) as catalysts. Titanium butoxide was added in both catalytic and

equimolar amounts with respect to the substrate. The products were identified by GLC. Generally, the reaction can occur both according to the Krasuskii rule and contrary to it (Scheme 1). The results are summarized in Table 1.



I, IV, V, R = C<sub>4</sub>H<sub>9</sub> (a), CH<sub>2</sub>=CHCH<sub>2</sub> (b), C<sub>6</sub>H<sub>5</sub> (c).

It is seen that titanium butoxide at 140°C exhibits a weak catalytic activity in the reaction of butyl 2,3-epoxypropyl ether with 1-butanol, as compared to acid and base catalysts. The overall yield of dialkoxypropanols ranges from 9 to 16%, and a considerable amount of the initial ether is recovered from the reaction mixture. Probable isomerization products, such as butoxyacetone and 3-butoxypropanal were not detected. The yield increases in going to boron trifluoride–ether complex and benzyldimethylamine as catalysts. The maximal yield was obtained in the presence of sulfuric acid. Taking into account that the substrate conversion was complete (initial butyl 2,3-epoxypropyl ether was not detected among the

**Table 1.** Reactions of 2,3-epoxypropyl ethers **I** with 1-butanol (**II**) in the presence of catalysts **III**; temperature 140°C

R in <b>I</b>	Catalyst <b>III</b>	Molar ratio <b>I:II:III</b>	Overall yield ( <b>IV + V</b> ), %	Ratio <b>IV:V</b> , %
Butyl	–	1:4:0	4.5	95:5
Butyl	H <sub>2</sub> SO <sub>4</sub>	1:4:0.06	64.0	78:22
Butyl	BF <sub>3</sub> –Et <sub>2</sub> O	1:4:0.06	39.0	85:15
Butyl	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>3</sub> ) <sub>2</sub>	1:4:0.06	43.0	98:2
Butyl	Ti(OC <sub>4</sub> H <sub>9</sub> ) <sub>4</sub>	1:4:0.06	9.1	90:10
Butyl	Ti(OC <sub>4</sub> H <sub>9</sub> ) <sub>4</sub>	1:4:1	16.0	88:12
Butyl	Ti(OC <sub>4</sub> H <sub>9</sub> ) <sub>4</sub>	1:0:1	9.8	60:40
Allyl	Ti(OC <sub>4</sub> H <sub>9</sub> ) <sub>4</sub>	1:4:1	15.0	91:9
Phenyl	Ti(OC <sub>4</sub> H <sub>9</sub> ) <sub>4</sub>	1:4:1	15.0	94:6

products), the low yields may be due to concurrent polymerization of butyl 2,3-epoxypropyl ether. This was confirmed by the presence of a considerable amount of undistillable products.

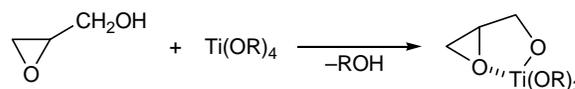
The yield of the addition products increases with rise in the amount of titanium butoxide from catalytic to equimolar. In the absence of 1-butanol, the yield decreases, indicating that the addition of titanium butoxide itself is ineffective. The addition of 1-butanol in the absence of a catalyst occurs with a very poor yield. The nature of the R radical in 2,3-epoxypropyl ether almost does not affect the yield.

Under catalysis by benzyldimethylamine, the major product is 1,3-dialkoxy-2-propanol, whereas almost no primary alcohol is formed. The yield of the latter increases in the presence of sulfuric acid. Boron trifluoride–ether complex occupies an intermediate place between the base and acid catalysts; it approaches titanium butoxide in the selectivity but is superior to Ti(OBu)<sub>4</sub> in the product yield. Increase in the amount of titanium butoxide from catalytic to equimolar almost does not affect the product ratio. The high selectivity in the absence of a catalyst is likely to result from leaching of glassware. The substituent in the substrate has no appreciable effect on the product ratio.

**Table 2.** Reaction of butyl 2,3-epoxypropyl ether (**Ia**) with 1-butanol (**II**) in the presence of titanium butoxide at 200°C

Molar ratio <b>Ia:II:III</b>	Overall yield ( <b>IV + V</b> ), %	Ratio <b>IV:V</b> , %
1:4:0	21	97:3
1:4:0.06	51	88:12
1:4:1	52	92:8
1:0:1	23	72:28

In order to raise the yield of the addition products, the reaction of 2,3-epoxypropyl ethers with 1-butanol was carried out at higher temperature. The results given in Table 2 show that the overall yield of products **IV** and **V** in the reaction catalyzed by titanium butoxide considerably increases as the temperature rises from 140 to 200°C; the above relations holding in the selectivity of the process are generally conserved.

**Scheme 2.**

Reactions of titanium alkoxides with 2,3-epoxy-1-propanol involve intermediate formation of a complex shown in Scheme 2 [4]. Such structure cannot be obtained from 2,3-epoxypropyl ethers. Let us consider possible mechanisms of alcohol addition to 2,3-epoxypropyl ethers in the presence of titanium alkoxides with account taken of the complexing power of the catalyst toward the substrate and the product ratio. Gut [6] studied complex formation in the system Ti(OMe)<sub>4</sub>–MeOH and found that the dissociation constant of the alkoxide is so small that it could not be measured.

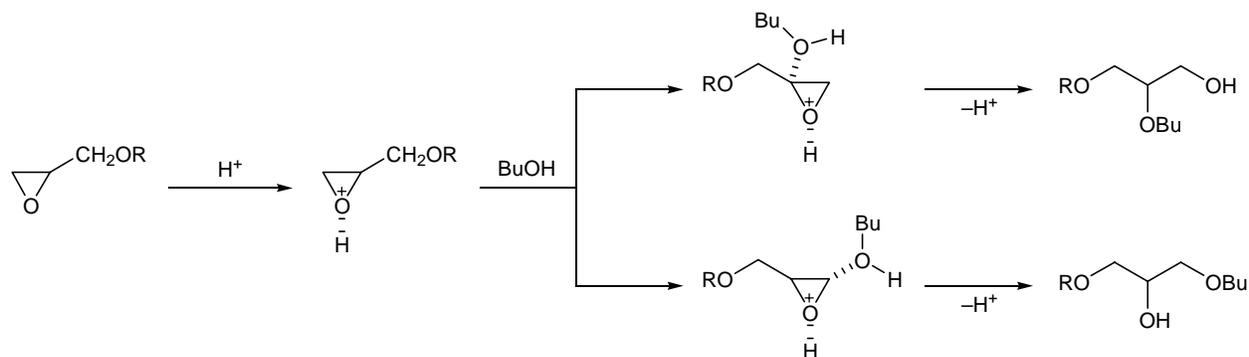


Therefore, participation of titanium alkoxides in the catalytic process as bases seems to be improbable. On the other hand, it was shown [6] that titanium methoxide with methanol forms an acidic complex:

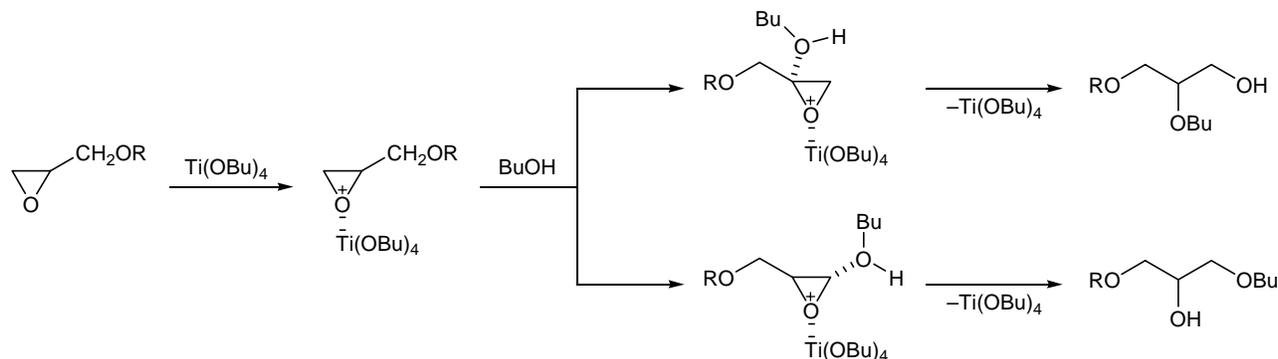


We previously studied in detail [7] complex formation in alkanol–titanium alkoxide systems and showed

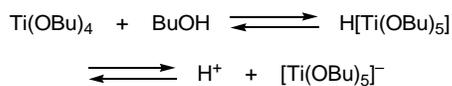
Scheme 3.



Scheme 4.



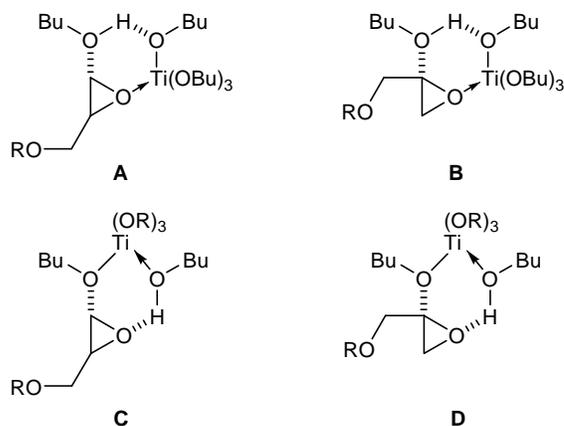
that the complex derived from 1-butanol and titanium butoxide (which is the most acidic) dissociates according to the following scheme:



Thus titanium butoxide, being a weak Lewis acid, reacts with 1-butanol to give a complex Meerwein acid, and the subsequent addition of the alcohol can follow the acid catalysis pattern (Scheme 3). However, in this case the regioselectivity should be the same as under catalysis by sulfuric acid. Provided that the amount of titanium butoxide increases (or the amount of 1-butanol decreases), the alkoxide can act as Lewis acid (Scheme 4). Then the regioselectivity should approach that observed in the presence of Lewis acids, i.e., boron trifluoride–ether complex. In fact, titanium alkoxide gives rise to higher regioselectivity, as compared to both  $\text{H}_2\text{SO}_4$  and  $\text{BF}_3\text{-Et}_2\text{O}$ .

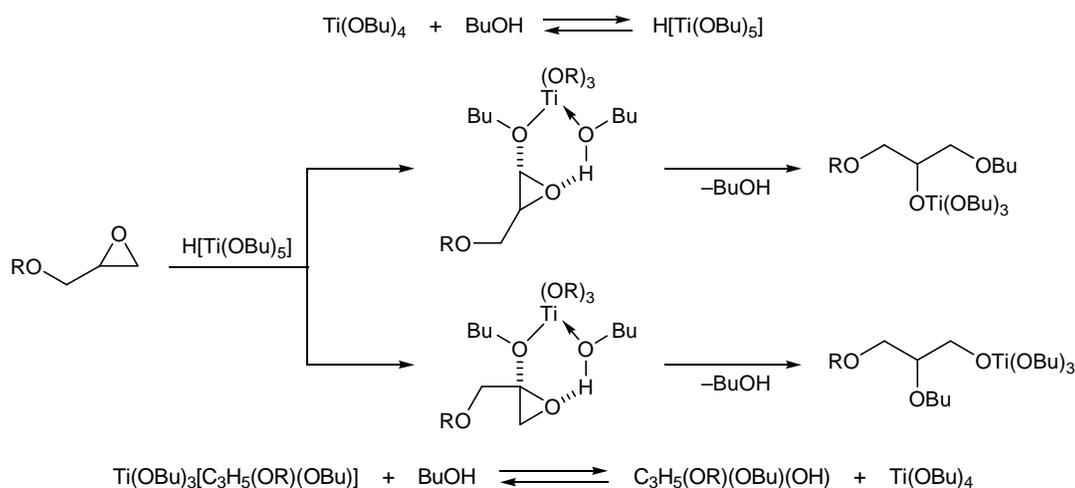
We showed in [8] that ethers, including epoxy derivatives, are capable of forming complexes with titanium butoxide, although such complexes with ethers are weaker than those derived from alcohols. Two pairs of transition complexes can be formed: with

inner-sphere coordination of epoxide and outer-sphere coordination of alcohol (**A**, **B**) and with inner-sphere coordination of alcohol and outer-sphere coordination of epoxide (**C**, **D**).



Taking into account that complexes of titanium alkoxides with alcohols are more stable, the latter version of the coordination–acid catalysis is preferred (Scheme 5). Undoubtedly, steric hindrances to formation of the complex giving rise to secondary alcohol are greater; therefore, the corresponding primary alcohol is formed as the major product.

## Scheme 5.



Thus reactions of 2,3-epoxypropyl ethers with 1-butanol in the presence of titanium alkoxides give addition products both according and contrary to the Krasuskii rule. The overall yield increases as the temperature rises, and the selectivity approaches 90%. Analysis of the selectivity observed under catalysis by titanium butoxide, base, mineral acid, and Lewis acid suggests that the coordination–acid mechanism of catalysis is preferred.

## EXPERIMENTAL

1-Butanol, titanium butoxide, and butyl, allyl, and phenyl 2,3-epoxypropyl ethers were purified by distillation prior to use. 1,3-Dibutoxy-2-propanol was synthesized as described in [9]. 2,3-Dibutoxy-1-propanol was prepared by the procedure reported in [10] from 3-butoxy-1,2-propanediol which was obtained according to [11].

GLC analysis was performed on an LKhM-8MD chromatograph equipped with a thermal conductivity detector; 2-m×3-mm column was packed with Chromaton AW-HMDS impregnated with 5% of 1,2,3-tris(β-cyanoethoxy)propane; carrier gas helium. The products were identified using authentic samples.

**Reaction of 2,3-epoxypropyl ethers with 1-butanol.** Required amounts of the reactants (Tables 1, 2) were added to 0.2 mol of 1-butanol. The mixture was heated for 10 h, cooled, and washed with dilute sulfuric acid (to remove benzyldimethylamine), a solution of sodium carbonate (to remove sulfuric acid and boron trifluoride–ether complex), or dilute (1:1)

hydrochloric acid (to remove titanium butoxide). The organic phase was separated, dried over sodium sulfate, and subjected to fractional distillation under reduced pressure. The target fraction was analyzed by GLC. The reaction at 200°C was carried out in a sealed ampule.

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