REDUCTION OF DIALKOXYDIHYDROFURANS, DIALKOXYTETRAHYDROFURANS, DIALKOXYDIHYDROPYRANS, AND DIALKOXYTETRAHYDROPYRANS WITH $LiAlH_4 \cdot AlCl_3$ COMPLEX

R. I. Kruglikova and L. N. Kralinina

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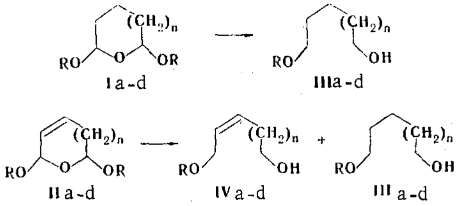
The reduction of 2,5-dimethoxytetrahydrofurans, 2,5-dimethoxydihydrofurans, 2,6-dialkoxytetrahydropyrans, and 2,6-dialkoxydihydropyrans with mixtures of $LiAlH_4$ and $AlCl_3$ with various component ratios (3 : 1, 1 : 1, and 1 : 3) proceeds with ring opening and the formation of aliphatic ω-alkoxy alcohols. Hydrogenolysis of 2,5-dimethoxy-2,5-dihydrofuran and 2,6-dialkoxy-Δ^3-dihydropyrans is accompanied by a partial reduction of the double bond and the formation of unsaturated alkoxy alcohols and their saturated analogs. A possible mechanism for the hydrogenolysis is discussed.

Acetals and ketals, both open-chain and cyclic types, are resistant to the action of $LiAlH_4$. This makes it possible in the α-alkoxyfuran and α-alkoxypyran series to reduce different functional groups without involvement of the heteroring [1-3]. The addition of aluminum chloride to $LiAlH_4$ changes the character of the reducing agent and the reaction mechanism and makes it possible to reduce acetals to give high yields of simple ethers. In the reduction of 2-alkoxytetrahydrofurans and 2-alkoxytetrahydropyrans with $LiAlH_4 \cdot AlCl_3$, the reaction proceeds at both the endo and exo acetal bonds, and the ratio of reaction products depends on the character of the alkoxy group [4-6].

We have investigated the reduction of 2,5-dimethoxytetrahydrofuran (Ia), 2,5-dimethoxydihydrofuran (IIa), 2,6-dialkoxytetrahydropyrans (Ib-d), and 2,6-dialkoxy-Δ^3-dihydropyrans (IIb-d) with mixtures of $LiAlH_4$ and $AlCl_3$ with various component ratios (3 : 1, 1 : 1, and 1 : 3) (the electrophilicity of the reducing agents increases in the same order [7]). The reduction of I and II proceeds with opening of the heterorings and formation of aliphatic ω-alkoxy alcohols (III, IV).



I-IVa R = CH_3, n = 0; I-IV b R = CH_3, n = 1; I-IV c R = C_2H_5, n = 1; I-IV d R = C_4H_9, n = 1

The different ratios of lithium aluminum hydride and aluminum chloride do not affect the direction of the reaction but have an appreciable effect on the reaction rate and the yields of final products. Reduction with a mixture of equimolecular amounts of lithium aluminum hydride and aluminum chloride is the optimum reaction for obtaining ω-alkoxy alcohols. When the electrophilicity of the system is lower ($3LiAlH_4 : AlCl_3$), the reaction proceeds slowly even on heating in tetrahydrofuran. When the amount of aluminum chloride is greater ($LiAlH_4 : 3AlCl_3$), the reaction proceeds rapidly and completely but is accompanied by appreciable

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TABLE 1. Effect of the Ratio of Lithium Aluminum Hydride and Aluminum Chloride on the Composition of the Reaction Products (in ether)

Starting compound	$LiAlH_4$: $AlCl_3$	Reaction time, h	Overall yield, %	Reaction product composition (from results of GLC), %		
				starting material	IV	III
Id	3 : 1	1	28	74	—	26
	1 : 1	1	90	2	—	98
	1 : 3	1	50	—	—	100
IId	3 : 1	1	61	11	63	26
	1 : 1	1	92	—	75	25
	1 : 3	1	48	—	54	46
IIa	3 : 1	4	32	65	32	3
	1 : 1	4	86	3	90	7
	1 : 3	4	47	—	80	20

TABLE 2. Composition of the Products Obtained in the Reduction with $3LiAlH_4 : AlCl_3$

Starting compound	Reaction time, h	Solvent	Reaction product composition (from GLC), %		
			starting compound	IV	III
Ia	25	Tetrahydrofuran	20	—	80
IIa	12	"	35	53	12
	50	"	~2	84	16
Id	4	Ether	—	—	100
IId	3	"	—	85	15
	3	Tetrahydrofuran	—	73	22
	8	"	—	68	32
IIb	3	"	—	92	8
IIc	3	"	—	91	9

Note: The amount of $LiAlH_4$ with respect to 1 mole of material to be reduced was 1.5 moles.

TABLE 3. Properties of the Products of the Reduction with $3LiAlH_4 : AlCl_3$

Starting compound	Reaction product		Bp, °C (mm)	n_D^{20}	Empirical formula	Found, %		Calc., %	
	composition	ratio				C	H	C	H
Ia	IIIa	100	70—71 (10)*	1,4285	—	—	—	—	—
Ic	IIIc	100	110—111 (35)*	1,3598	—	—	—	—	—
Id	IIId	100	110—111 (8)*	1,4352	—	—	—	—	—
IIa	IVa : IIIa	84 : 16	64—66 (8)	1,4410	84% $C_5H_{10}O_2$; 16% $C_5H_{12}O_2$	58,41	9,91	58,61	10,03
IIb	IVb : IIIb	92 : 8	78—79 (1)	1,4450	92% $C_6H_{12}O_2$; 8% $C_6H_{14}O_2$	61,65	10,53	61,96	10,36
IIc	IVc : IIIc	91 : 9	125—127 (35)	1,4470	91% $C_8H_{14}O_2$; 9% $C_7H_{16}O_2$	63,81	11,25	64,42	10,96
IId	IVd : IIId	85 : 15	95—97 (3)	1,4463	85% $C_9H_{18}O_2$; 15% $C_9H_{20}O_2$	68,17	11,68	68,18	11,69

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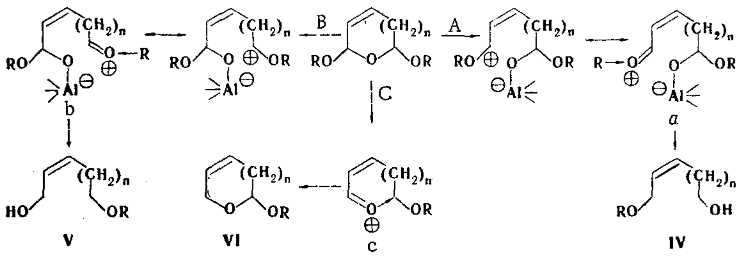
* Literature data: IIIa: bp 80-82° (14 mm), n_D^{20} 1.4242 [10]; IIIc: bp 60° (0.5 mm), n_D^{25} 1.4263 [6]; IIId: bp 120° (10 mm), n_D^{20} 1.4376 [4].

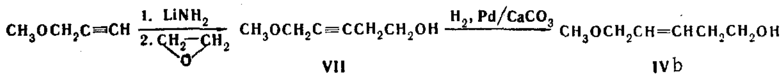
resinification of the products, which lowers the overall yield (Table 1). In order to ascertain how the structure of the starting dialkoxy-substituted heterocycles affects the reaction rate and yield, the latter were reduced with the least active system ($3LiAlH_4 : AlCl_3$) (Table 2). Intermediate reduction products were not detected in any of the experiments. The reactivity of II is higher than that of the corresponding I (just as in the case of the Grignard reaction [8, 9]). The reactivities of the dialkoxydihydro- and dialkoxytetrahydrofurans are considerably lower than the reactivities of the corresponding pyrans (this was not observed with respect to the Grignard reaction).

In the reduction of IIa-d, a certain amount of saturated alkoxy alcohols (III), which were identical to those that are formed in the reduction of I, was obtained along with unsaturated IV. The yield of saturated alcohol increases as the electrophilicity of the reducing mixture increases. It was shown that III are saturated analogs of IV, since the corresponding III is formed when a mixture of alcohols III and IV is hydrogenated over finely granulated Raney nickel.

The idea that the mechanism of the hydrogenolysis of acetals with metal hydrides is similar to the mechanism of acid hydrolysis and proceeds through a step involving the formation of an oxonium ion, the stability of which (and, consequently, the direction of the reaction) depends on the electron-donor properties of the adjacent substituents, was stated in [6]. According to this mechanism, the reduction of both I and II should proceed only at the endo acetal bond, since in this case the charge of the oxonium ion formed is compensated by the positive inductive effect of the alkyl group, while an oxonium ion containing a group with a negative inductive effect should be formed in the hydrogenolysis at the exo acetal bond. In addition, the endo acetal bonds in IIb-d are nonequivalent, and two other possible hydrogenolysis paths (A and B) should be considered for them. Oxonium ions *a* and b contain identical electron-donor substituents R. However, there is a conjugation in cation *a*, which should stabilize it and favor reaction via path A. Compounds IV, V, or VI might have been formed in the subsequent transformation of cations *a*, b, and c. The fact that only alkoxy alcohols III and IV are formed in the reduction of I and II confirms the proposed mechanism; the direction of the reaction is due to the polar effect of the substituents, and steric factors do not play a substantial role in this case.



In order to prove the position of the multiple bond in IV, we carried out the alternative synthesis of IVb via a scheme similar to that in [10] from methyl propargyl ether and ethylene oxide with subsequent hydrogenation of VII on a Lindlar catalyst.



$$CH_3OCH_2C{\equiv}CH \xrightarrow[2.\ CH_2-CH_2\ (O)]{1.\ LiNH_2} \underset{VII}{CH_3OCH_2C{\equiv}CCH_2CH_2OH} \xrightarrow{H_2,\ Pd/CaCO_3} \underset{IVb}{CH_3OCH_2CH{=}CHCH_2CH_2OH}$$

The formation of IIIa along with IVa in the reaction of mixtures of lithium aluminum hydride and aluminum chloride with IIa is not unexpected, since allyl alcohols are capable of being reduced to saturated alcohols under similar conditions. Although this had not previously been noted in the literature, allyl ethers can also apparently undergo similar reduction. In the reaction of $LiAlH_4 \cdot AlCl_3$ with a mixture of IVd and IIId, the component ratio in the mixture changes, and the percentage of saturated IIId increases. The formation of III as a side product in the preparation of IV by reduction of II with mixtures of $LiAlH_4$ and $AlCl_3$ with various component ratios cannot be avoided under the investigated conditions.

EXPERIMENTAL

The gas-liquid chromatographic analysis of the reaction products was performed with an LKhM-7A chromatograph with a 2-m by 6-mm column packed with 10% polyethylene glycol on Cellite 545 and helium as the carrier gas.

5-Butoxy-1-pentanol (IIId). A 1.44-g (0.0108 mole) sample of anhydrous $AlCl_3$ and 1.23 g (0.0324 mole) of $LiAlH_4$ were dissolved in 60 ml of absolute ether, a solution of 5 g of Id in 10 ml of absolute ether was then added dropwise, and the mixture was refluxed for 4 h and cooled. Water (2 ml), 11 ml of 15% aqueous sodium hydroxide, and 6 ml of water were added successively, and the precipitated salts were removed by filtration and washed with ether. The ether solution was dried with magnesium sulfate and distilled to give 2.7 g (78%) of IIId.

Compounds Ia and IIa-d were similarly obtained. The effect of the $LiAlH_4$ to $AlCl_3$ ratio on the composition of the reaction products is presented in Table 1. The effect of a change in the conditions (reaction time and temperature) as well as the structure of the starting heterocycle on the composition of the reaction products is shown in Table 2. The properties of the products are given in Table 3.

5-Ethoxy-1-pentanol (IIIc). A 1-g sample of IVc containing 9% IIIc was hydrogenated over finely granulated nickel in 50 ml of ethanol. Removal of the catalyst and distillation gave 0.7 g of IIIc.

5-Methoxy-3-pentyn-1-ol (VII). A cooled solution of 15 g (0.34 mole) of ethylene oxide in 50 ml of absolute ether was added dropwise to a solution of 2.5 g (0.358 mole) of lithium in 300 ml of liquid ammonia, and the mixture was allowed to stand overnight and was then decomposed with water. The aqueous mixture was extracted with ether, and the extract was dried with magnesium sulfate and distilled to give 16 g (41.2%) of VII with bp 98-99° (10 mm) and n_D^{20} 1.4600. Found: C 62.75; H 8.87%. $C_6H_{10}O_2$. Calculated: C 63.15; H 8.76%.

5-Methoxy-3-penten-1-ol (IVb). A 12-g sample of VII was hydrogenated in 100 ml of methanol with 0.3 g of a Lindlar catalyst until the calculated amount of hydrogen had been absorbed (2360 ml) to give 9.3 g (75%) of a product with bp 85-86° (1.5 mm) and n_D^{20} 1.4460, which gave two peaks on the chromatogram in a ratio of 90 : 10 that correspond to the IVb and IIIb obtained in the reduction of Ib with a mixture of $LiAlH_4$ and $AlCl_3$.

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