ELECTROCHEMICAL BROMOALKOXYLATION OF 2-ALKOXY-Δ^5-DIHYDROPYRANS

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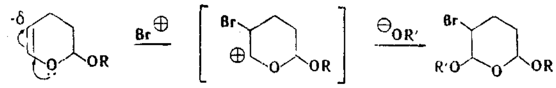
A number of 2,6-dialkoxy-3-bromotetrahydropyrans were obtained by the electrochemical bromomethoxylation of 2-alkoxy-Δ^5-dihydropyrans. An assumption regarding the stereospecificity of the electrochemical and chemical bromoalkoxylation was stated on the basis of the dehydrobromination and hydrogenation of the compounds obtained and on the basis of the results of gas-liquid chromatography: the reaction proceeds as cis and trans addition at the multiple bond, and the alkoxy group occupies only the trans position with respect to the alkoxy group already present in the ring. The isomeric 2,6-dialkoxy-Δ^4-dihydropyrans are formed along with 2,6-dialkoxy-Δ^3-dihydropyrans in the dehydrobromination of 2,6-dialkoxy-3-bromotetrahydropyrans.

2,6-Dialkoxy-Δ^3-dihydropyrans, which are promising intermediates for organic synthesis, are obtained from 2-alkoxy-Δ^5-dihydropyrans (adducts in the diene synthesis of acrolein and vinyl alkyl ethers) by the action on the latter of N-bromosuccinimide in alcohol solution and subsequent dehydrobromination with alcoholic alkali [1].

We have investigated the possibility of obtaining 2,6-dialkoxy-3-bromotetrahydropyrans by electrochemical bromoalkoxylation of 2-alkoxy-Δ^5-dihydropyrans in alcoholic ammonium bromide solutions. Two variants of the mechanism of the electrochemical bromoalkoxylation can be proposed.

1. The bromine formed as a result of the electrolysis of ammonium bromide adds to the double bond to form 2-alkoxy-5,6-dibromotetrahydropyrans. The bromine atoms in the compound obtained are nonequivalent: the acetal bromine is exchanged for an alkoxy group of the alcohol. The hydrogen bromide evolved is neutralized by the ammonia formed on the cathode, and the ammonium bromide again undergoes electrolysis.

2. The bromine formed in the electrolysis of ammonium bromide undergoes heterolytic cleavage to give $Br^{\oplus}$. The polarization of the double bond causes electrophilic addition of $Br^{\oplus}$ in the 3 position. An alkoxide ion ($^{\ominus}OR'$), in competition with Br^-, adds to the resulting carbonium ion.



I $R=R'=CH_3$; II $R=R'=C_2H_5$; III $R=C_2H_5$, $R'=CH_3$; IV $R=C_4H_9$, $R'=CH_3$; V $R=R'=C_4H_9$

Despite a previous study [2] of the alkoxylation of 2,3-dibromotetrahydropyrans, the second mechanism seems more likely, since the concentration of $^{\ominus}OR$ ions is much higher than the $Br^{\ominus}$ concentration. An indirect confirmation of this is the absence of 2,3-dibromotetrahydropyrans in the reaction products. Electrochemical alkoxylation of furan proceeds via a similar mechanism [3].

Electrochemical and chemical means were used to obtain 2,6-dimethoxy-, 2,6-diethoxy-, 2-methoxy-6-ethoxy-, and 2-methoxy-6-butoxy-3-bromotetrahydropyrans (I-IV). The gas-liquid chromatograms of the reaction products demonstrated that two isomers, which appear as two incompletely separated peaks, are obtained in all cases. The peaks diverge better as the volume of the alkoxy groups increases. The

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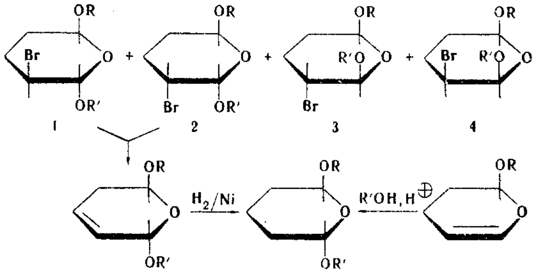
isomer ratio in the mixture varies as a function of the method – electrochemical or chemical – used to obtain them. For 2,6-diethoxy-3-bromotetrahydropyran (II) obtained by electrochemical and chemical bromoalkoxylation of 2-ethoxy-Δ^5-dihydropyran, the isomer ratio is 4 : 6 in the first case and 7 : 3 in the second case. About the same isomer ratio is also observed in the preparation of other 2,6-dialkoxy-3-bromotetrahydropyrans by these methods.



In theory, four geometrical isomers (1-4) can be obtained in the bromoalkoxylation of 2-alkoxy-Δ^5-dihydropyran. It has been assumed that electrophilic addition to a multiple bond proceeds as trans addition [4]. However, studies that demonstrate that electrophilic addition can also proceed in the cis position have recently appeared [5]. In particular, chloronitrosation and chlorination of Δ^2-dihydropyran give a mixture of cis and trans isomers [6]. On the basis of these results, the formation of isomers 2 and 4 cannot be excluded.

The alkaline dehydrobromination of I, II, and V via the method in [1] gives the corresponding 2,6-dialkoxy-Δ^3-dihydropyrans, which give one peak on the gas-liquid chromatograms. The hydrogenation of these products over Raney nickel gave 2,6-dimethoxy-, 2,6-diethoxy-, and 2,6-dibutoxytetrahydropyrans, which also emerge on the gas-liquid chromatogram as a symmetrical peak. The same dialkoxytetrahydropyrans were also obtained in the addition of the corresponding alcohols to 2-alkoxy-Δ^5-dihydropyrans under conditions where, as shown in [7,8], the trans isomers are formed. This series of successive transformations demonstrated that both the chemical and electrochemical bromoalkoxylation of 2-alkoxy-Δ^5-dihydropyrans proceed as cis and trans addition of bromine and the alkoxy group to the double bond, and the entering alkoxy group occupies the trans position with respect to the alkoxy group already present in the ring (isomers 1 and 2). Isomers 1 and 2 cannot be separated, and their configurations were not established, but, considering the steric hindrance, which may determine the stereospecificity of the chemical and electrochemical bromoalkoxylation, it can be assumed that structure 2 corresponds to the isomer formed in greater amounts during chemical bromoalkoxylation, while structure 1 corresponds to the predominant isomer formed during electrochemical bromoalkoxylation.

Two isomers that differ with respect to the position of the multiple bond are formed in the alkaline dehydrobromination of 2,6-dialkoxy-3-bromotetrahydropyrans having different alkoxy groups. Thus 2-methoxy-6-butoxy-Δ^3-dihydropyran and 2-methoxy-6-butoxy-Δ^4-dihydropyran are formed in a ratio of 3 : 1 in the dehydrobromination of IV. The composition of this mixture was confirmed by introducing it into the Grignard reaction with methylmagnesium iodide, as a result of which alcohols previously synthesized from 2,6-dimethoxy- and 2,6-dibutoxy-Δ^3-dihydropyrans [9] were obtained. The dehydrobromination of III gives 2-methoxy-6-ethoxy-Δ^3-dihydropyran (85%) and 2-methoxy-6-ethoxy-Δ^4-dihydropyran (15%). Similar isomerization of the multiple bond during dehydrobromination was also noted in [10].

Thus the electrochemical bromoalkoxylation of 2-alkoxy-Δ^5-dihydropyrans does not differ substantially with respect to geometrical specificity from their bromoalkoxylation with N-bromosuccinimide in alcohol. Electrochemical bromoalkoxylation gives satisfactory results in the case of methoxylation, somewhat poorer results in the case of ethoxylation, and has advantages over the chemical method in the preparation of bromo derivatives of pyran with different alkoxy groups. Thus 20-30% transalkoxylation occurs in the preparation of 2-methoxy-6-butoxy-3-bromotetrahydropyran by the chemical method, and 2,6-dimethoxy-3-bromotetrahydropyran is formed as a side product. Transalkoxylation is almost completely excluded in electrochemical bromoalkoxylation, since the pH of the medium is maintained at practically a neutral level during the electrolysis. About 5% 2,6-dimethoxy-3-bromotetrahydropyran is present in the products of the electrochemical bromomethoxylation of 2-butoxy-Δ^5-dihydropyran.

2,6-Dialkoxy-3-bromotetrahydropyrans are obtained in lower yields (40-50%) in the electrochemical method than in bromoalkoxylation with N-bromosuccinimide (60-70%). This is possibly a consequence of the imperfect construction of the electrolyzer.

EXPERIMENTAL

The electrochemical bromoalkoxylation was accomplished as follows. An alcohol solution of equimolecular amounts of 2-alkoxy-Δ^5-dihydropyran and ammonium bromide was electrolyzed at −15°; the calculated number of ampere-hours of electricity was passed through the solution, and it was neutralized with sodium alkoxide and distilled. The electrolyzer was a glass beaker containing a nickel cylinder (cathode) and a graphite rod (anode). Alternating line current was supplied to the electrodes through a 100-GM-20A selenium rectifier. The voltage was varied from 10 to 40 V while maintaining the current strength at 2-3 A. The solubility of ammonium bromide in the alcohol decreased as the alcohol molecular weight increased, and the electrical conductivity of the solution deteriorated. It was therefore necessary to increase the voltage, which resulted in the evolution of a large amount of heat and required vigorous cooling. This complicated reactions with C_3 and higher alcohols.

Gas-liquid chromatography (GLC) was carried out with a PAKhV-02 chromatograph with a 1-m by 6-mm column packed with 10% polyethylene glycol on Cellite-545 with helium as the carrier gas.

2,6-Dimethoxy-3-bromotetrahydropyran (I). A solution of 13.6 g (0.119 mole) of 2-methoxy-Δ^5-dihydropyran and 12.6 g (0.129 mole) of ammonium bromide in 200 ml of methanol was cooled to −20°, and 4.3 A-h of direct current was passed through it at −15°, followed by the addition of 15 ml of sodium methoxide solution from 0.3 g (0.013 g-atom) of sodium metal. Distillation of the mixture gave 12.1 g (45.4%) of I with bp 60-61° (0.2 mm) and n_D^{20} 1.4756 [1]. Gas-liquid chromatography of the product gave two incompletely separated peaks in a ratio of 1:2 (150°, helium flow rate 40 ml/min, τ 7 min 15 sec, 8 min 55 sec).

2,6-Diethoxy-3-bromotetrahydropyran (II). This compound was similarly obtained in an isomer ratio of 2:3 (120°, helium flow rate 60 ml/min, τ 9 min 10 sec, 10 min 50 sec) and had bp 75-76° (0.4 mm) and n_D^{20} 1.4666 [1].

2-Methoxy-6-ethoxy-3-bromotetrahydropyran (III). This compound was similarly obtained and had bp 72-73° (0.1 mm) and n_D^{20} 1.4694. Found: Br 33.8%. $C_8H_{15}BrO_3$. Calculated: Br 33.4%. The isomer ratio was 4:5 (150°, helium flow rate 70 ml/min, τ 4 min 5 sec, 4 min 52 sec).

2-Methoxy-6-butoxy-3-bromotetrahydropyran (IV). This compound was similarly obtained and had bp 73-74° (0.2 mm) and n_D^{20} 1.4685. Found: Br 29.9%. $C_{10}H_{19}BrO_3$. Calculated: Br 29.1%. The isomer ratio was 2:3 (150°, helium flow rate 60 ml/min, τ 9 min 40 sec, 11 min 35 sec).

2-Methoxy-6-butoxy-3-bromotetrahydropyran (IV). A solution of 64.3 g (0.423 mole) of 2-butoxy-Δ^5-dihydropyran in 50 ml of absolute methanol was cooled to −10°, and 70 g (0.393 mole) of N-bromosuccinimide was added while maintaining the temperature below 0°. The mixture was then stirred at room temperature for 3 h, the succinimide was removed by filtration, and the filtrate was made alkaline with a solution of 10 g of sodium hydroxide in 60 ml of water. The alkaline filtrate was extracted with ether, and the ether extract was dried with magnesium sulfate. Before distillation, the reaction product gave four peaks on the gas-liquid chromatogram: 19, 8, 50, and 20% (150°, helium flow rate 40 ml/min, τ 7 min 15 sec, 8 min 55 sec, 9 min 50 sec, and 12 min 10 sec). The first two peaks pertain to I, while the last two peaks are related to IV. Distillation gave 23 g of I with bp 70-73° (0.4 mm) and n_D^{20} 1.4750, and 28 g of IV with bp 78-80° (0.4 mm) and n_D^{20} 1.4634.

2,6-Dimethoxy-Δ^3-dihydropyran. This compound was obtained by alkaline dehydrochlorination via the method described in [1] and had bp 57-58° (5 mm) and n_D^{20} 1.4483 [1]. Gas-liquid chromatography gave one peak.

2,6-Diethoxy-Δ^3-dihydropyran. This compound was similarly obtained and had bp 78-79° (8 mm) and n_D^{20} 1.4425 [1]. Gas-liquid chromatography gave one peak.

2-Methoxy-6-ethoxy-Δ^3-dihydropyran. This compound was similarly obtained and had bp 68-70° (8 mm), n_D^{20} 1.4430, and d_4^{20} 0.998. Found: C 60.5; H 8.7%; MR_D 41.9. $C_8H_{14}O_3$. Calculated: C 60.70; H 8.92%; MR_D 41.52; Gas-liquid chromatography gave two peaks: 85 and 15% (120°, gas flow rate 50 ml/min, τ 2 min 35 sec, 3 min 20 sec).

2-Methoxy-6-butoxy-Δ^3-dihydropyran. This compound was similarly obtained and had bp 62-63° (0.8 mm), n_D^{20} 1.4468, and d_4^{20} 0.987. Found: C 64.7; H 9.7%; MR_D 50.39. $C_{10}H_{18}O_3$. Calculated: C 64.79; H 9.58%; MR_D 49.7. Gas-liquid chromatography gave two peaks: 75 and 25% (120°, gas flow rate 50 ml/min, τ 7 min 10 sec, 8 min, 50 sec).

2,6-Diethoxytetrahydropyran. A 2-g (11.6 mmole) sample of 2,6-diethoxy-Δ^3-dihydropyran was hydrogenated over Raney nickel in 50 ml of ethanol. Distillation of the reaction mixture gave 1.6 g (78%) of 2,6-diethoxytetrahydropyran with bp 78-80° (18 mm) and n_D^{20} 1.4295 that was identical to the compound obtained via the method in [7]. Gas-liquid chromatography gave one peak.

2,6-Dimethoxytetrahydropyran. This compound was similarly obtained and had bp 62-63° (20 mm) and n_D^{20} 1.4283. Gas-liquid chromatography gave one peak.

2,6-Dibutoxytetrahydropyran. This compound was similarly obtained and had bp 133-135° (10 mm) and n_D^{20} 1.4364. It was identical to the compound obtained via the method in [7]. Gas-liquid chromatography gave one peak.

2-Methoxy-6-butoxytetrahydropyran. This compound was similarly obtained and had bp 100-101° (10 mm), n_D^{20} 1.4332, and d_4^{20} 0.956. Found: C 63.8; H 10.8%; MR_D 51.1. $C_{10}H_{20}O_3$. Calculated: C 63.90; H 10.63%; MR_D 51.11. Gas-liquid chromatography gave one peak.

2-Alkoxy-3-hepten-6-ols. A 4-g (0.022 mole) sample of 2-methoxy-6-butoxydihydropyran (containing the Δ^3 and Δ^4 isomers in a ratio of 3 : 1) in 15 ml of absolute ether was added to a solution of methylmagnesium iodide, obtained from 1.22 g (0.05 g-atom) of magnesium and 7.15 g (0.05 mole) of methyl iodide in 50 ml of absolute ether, and the mixture was refluxed for 3 h. The solution was then decomposed with ammonium chloride solution and extracted with ether. The extract was dried with magnesium sulfate and distilled to give 0.99 g (31.8%) of 2-methoxy-3-hepten-6-ol with bp 46-47° (0.13 mm) and n_D^{20} 1.4461. It was identical to the compound obtained in the reaction of 2,6-dimethoxy-Δ^3-dihydropyran with methylmagnesium iodide [8]. Also obtained was 1.23 g (40%) of 2-butoxy-3-hepten-6-ol with bp 61-62° (0.18 mm) and n_D^{20} 1.4483, which was identical to the compound obtained from the reaction of 2,6-dibutoxy-Δ^3-dihydropyran with methylmagnesium iodide [8].

LITERATURE CITED

1. S. M. Makin, V. M. Likhosherstov, and M. I. Shelemina, Zh. Obshch. Khim., 34, 1809 (1964).
2. J. Korte, A. Bilow, and R. Heinz, Tetrahedron, 18, 657 (1962).
3. N. K. Kochetkov, L. I. Kudryashov, N. V. Molodtsov, and E. D. Khomutova, Zh. Obshch. Khim., 31, 3909 (1961).
4. O. A. Reutov, Theoretical Foundations of Organic Chemistry [in Russian], Izd. MGU, Moscow (1964), p. 231.
5. I. Saunders, Ionic Reactions in the Aliphatic Series [Russian translation], Mir, Moscow (1967), p. 32.
6. N. S. Zefirov, N. M. Shekhtman, and R. A. Karakhanov, Zh. Organ. Khim., 3, 1925 (1967).
7. R. H. Hall and B. K. Horve, J. Chem. Soc., 2480 (1951).
8. A. Kankaanperä and K. Müki, Acta Chem. Scand., 23, 1471 (1969).
9. L. N. Kralinina, R. I. Kruglikova, and T. P. Tarulina, Khim. Geterotsikl. Soedin., 311 (1970).
10. M. Cahu and G. Descotes, Bull. Soc. Chim. France, 2975 (1968).