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SYNTHESIS OF 3-OXA-1,5-KETO ALCOHOLS AND INVESTIGATION OF THEIR TAUTOMERIC TRANSFORMATIONS

It was shown earlier that γ-keto alcohols can be synthesized by catalytic hydrogenolysis of acetates of furyl alcohols (^{1}). The same method was used in the present work to obtain the previously difficultly accessible and hitherto unstudied 3-oxa-1,5-keto alcohols. For this purpose, acetates of monofurfuryl ethers of 1,2-glycols (I) were prepared and hydrogenated over Pt–C at 180° and normal pressure:

(reaction scheme)
hydrogenolysis of C–O bond 1,2 $\longrightarrow$ (II) $\longrightarrow$ (III)
hydrogenolysis of C–O bond 1,5 $\longrightarrow$ (VI)
where $R_1 = H,\ C_2H_5; \quad R_2 = H,\ CH_3.$

As is evident from the scheme, the main reaction is hydrogenolysis of the furan ring at the C–O bond 1,5, as a result of which acetates of 5-keto-3-oxa-octanols-1 (VI) are obtained in yields of 65-70%. Hydrogenolysis of the C–O bond 1,2 leads to the formation of acetates of 3-oxa-heptanols-1 (II) in yields of 12-15%. In addition to these two reactions, cleavage of the ether bond in the side chain was also observed, leading to the formation of α-alkylfurans (IV), 5-7%, and products of their hydrogenolysis—aliphatic ketones (V), 7-8%. In the preceding work (^{2}) it was noted that the presence of an alkyl radical adjacent to the ether oxygen in the side chain of furyl ether alcohols sharply weakens the ether bond and promotes its hydrogenolysis. In contrast, during hydrogenation of acetates of ether alcohols such an influence of the alkyl radical was not observed. In addition, during hydrogenation of monofurfuryl ethers of 1,2-glycols only selective hydrogenolysis of the furan ring at the C–O bond 1,5 occurred, whereas during hydrogenation of the acetates hydrogenolysis of the ring at the C–O bond 1,2 was also appreciably observed.

The acetates obtained (II and VI) were subjected to transesterification with methanol in the presence of hydrochloric acid. The acetates (II) were converted rather smoothly into the corresponding 3-oxa-heptanols-1 (III).

From the products of methanolysis of the keto alcohol acetates (VI), two fractions were isolated which, as a result of careful chemical and spectral examination, were identified as the tautomeric cyclo- and oxo-forms of 5-keto-3-oxa-octanols-1. This type of tautomerism is a well-known fact for γ- and δ-hydroxy aldehydes and hydroxy ketones; moreover, in the case of hydroxy aldehydes the cyclic form proves to predominate ([3],[4]), while hydroxy ketones exist mainly in the open form ([5],[6]). One–

···however, these forms could be isolated in pure form only in isolated cases (7, 8). In this connection, the fact that in our case it proved possible to separate the oxo- and cyclo-forms by simple distillation is of considerable interest, since their boiling points differ substantially.

Under conditions of methanolysis in an acidic medium, an equilibrium is established between the oxo- and cyclo-forms; this equilibrium is fixed by treatment of the reaction mixture with alkaline agents, and upon distillation approximately equal amounts of the oxo- and cyclo-forms are obtained. The isolated tautomers can be converted into one another by boiling in methanol in the presence of hydrochloric acid.

$$\mathrm{C_3H_7{-}C(=O){-}CH(R_1){-}OCH_2{-}CH(R_2){-}OCOCH_3} \quad \mathrm{(VI)}$$

$$\Big\downarrow \begin{matrix}\mathrm{[H]} \\ \mathrm{CH_3OH}\end{matrix}$$

$$\begin{gathered}\mathrm{C_3H_7{-}C(=O){-}CH(R_1){-}OCH_2{-}CH(R_2){-}OH} \quad \mathrm{(VII)} \rightleftarrows \mathrm{(VIII)} \\ \text{where } R_1 = \mathrm{H},\ \mathrm{C_2H_5}; \qquad R_2 = \mathrm{H},\ \mathrm{CH_3};\end{gathered}$$

$$\Big\downarrow -\mathrm{H_2O}$$

$$\mathrm{(IX)}$$

Both the oxo- and cyclo-forms, on heating in the presence of NaH_2PO_4, are converted into the same 1,4-dioxene. In addition, treatment of (VII) and (VIII) with a solution of 2,4-dinitrophenylhydrazine gives the same products. Substantial confirmation of the existence of 5-keto-3-oxa-octan-1-ol in two tautomeric forms is provided by spectral analysis. In the IR spectrum of the oxo-form (VII), bands characteristic of the carbonyl and hydroxyl groups were observed (1726 and 3450 cm^{-1}, respectively). In the spectrum of the cyclo-form (VIII), the band characteristic of the carbonyl group was absent; however, it appeared in the spectrum of the product obtained after boiling the cyclo-form in methanol in the presence of hydrochloric acid. All these tautomeric transformations were observed for 5-keto-3-oxa-octan-1-ol and 1-methyl-5-keto-3-oxa-octan-1-ol. 4-Ethyl-5-keto-3-oxa-octan-1-ol acetate, on methanolysis, was converted into 4-ethyl-5-keto-3-oxa-octan-1-ol and 2-propyl-3-ethyl-1,4-dioxene-2.

Experimental Part

Acetates of monofurfuryl ethers of 1,2-glycols were obtained by acetylation of the corresponding furan ether alcohols and had the following properties: acetate of 1-furyl-2-oxa-butan-4-ol, b.p. 115–116° (10 mm), d_4^{20} 1.1248; n_D^{20} 1.4660; MR_D 45.47. $C_9H_{12}O_4$. Calculated 45.56.

Found, %: C 58.53; 58.53; H 6.59; 6.47
Calculated, %: C 58.68; H 6.56

Acetate of 1-furyl-4-methyl-2-oxa-butan-4-ol, b.p. 122° (13 mm), d_4^{20} 1.0840; n_D^{20} 1.4609; MR_D 50.16. $C_{10}H_{14}O_4$. Calculated 50.18.

Found, %: C 60.28; 60.32; H 6.96; 7.00
Calculated, %: C 60.59; H 7.11

acetate of 1-furyl-1-ethyl-2-oxa-butanol-4, b.p. 129° (13 mm), d_4^{20} 1.0651; n_D^{20} 1.4600; MR_D 54.57. $C_{11}H_{16}O_4$. Calculated 54.80.

Found, %: C 62.03; 61.94; H 7.55; 7.46
Calculated, %: C 62.24; H 7.59

The yields were 70–85%.

Hydrogenation of the acetates of monofurfuryl ethers of 1,2-glycols was carried out in a flow system over platinized charcoal (5% Pt) at 180° and normal pressure. This gave acetates of 3-oxa-heptanols-1 and acetates of 5-keto-3-oxa-octanols-1, whose properties are given in Table 1.

Table 1

Properties of 5-keto-3-oxa-octanols-1 and their acetates

No.	Compound	B.p., °C (mm)	d_4^{20}	n_D^{20}	Found C, %	Found H, %	Found MR_D	Calculated C, %	Calculated H, %	Calculated MR_D	Gross formula
1	$C_3H_7-C(=O)-CH_2-O-CH_2-CH_2-OH$	122–123 (10)	1.0349	1.4471	[illegible]	[illegible]	37.74	57.51	9.65	37.70	$C_7H_{14}O_3$
2	$C_3H_7-C(=O)-CH_2-O-CH_2-CH_2-OCOCH_3$	114 (6)	1.0376	1.4345	[illegible]	[illegible]	47.28	57.42	8.56	47.07	$C_9H_{16}O_4$

No.	Compound	B.p., °C (mm)	d_4^{20}	n_D^{20}	Found C, %	Found H, %	Found MR_D	Calculated C, %	Calculated H, %	Calculated MR_D	Gross formula
3	$C_3H_7C(=O)-CH_2OCH_2CH(OH)CH_3$	120–121 (9)	1.0162	[illegible]	[illegible]	[illegible]	[illegible]	59.97	10.06	42.32	$C_8H_{16}O_3$
4	$C_3H_7-C(=O)-CH_2OCH(CH_3)CH_2OCOCH_3$	127 (8)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	59.36	8.97	51.68	$C_{10}H_{18}O_4$
5	$C_3H_7-C(=O)-CH(C_2H_5)OCH_2CH_2OH$	121–122 (8)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	62.03	10.41	46.94	$C_9H_{18}O_3$
6	$C_3H_7-C(=O)-CH(C_2H_5)OCH_2CH_2OCOCH_3$	105 (5)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	61.08	9.32	56.30	$C_{11}H_{20}O_4$

Methanolysis of acetates of 3-oxa-heptanols-1 and acetates of 5-keto-3-oxa-octanols-1.

In a flask fitted with a reflux condenser, 20 g of acetate, 40 ml of methyl alcohol, and 1.5-2 ml of hydrochloric acid were mixed. The solution was boiled for three hours, then cooled, and saturated soda solution was added until a weakly alkaline reaction was obtained. The precipitated salt was filtered off, dried with magnesium sulfate, and distilled under reduced pressure. As a result of methanolysis of the acetates of 3-oxa-heptanols-1 (II), the corresponding alcohols were obtained: 3-oxa-heptanol-1, b.p. 74° (20 mm), d_4^{20} 0.9014; n_D^{20} 1.4198; MR_D 33.16. $C_6H_{14}O_2$. Calculated 33.07. 1-Methyl-3-oxa-heptanol-1, b.p. 68° (15 mm), d_4^{20} 0.8886; n_D^{20} 1.4180; MR_D 37.49. $C_7H_{16}O_2$. Calculated 37.69. 4-Ethyl-3-oxa-heptanol-1, b.p. 82-83° (17 mm), d_4^{20} 0.8954; n_D^{20} 1.4275; MR_D 41.97. $C_8H_{18}O_2$. Calculated 42.31.

From the acetates of 5-keto-3-oxa-octanol-1 and 1-methyl-5-keto-3-oxa-octanol-1, the corresponding 1,5-keto alcohols (VII) were obtained in 30–40% yield (properties in Table 1), and their cyclic forms (VIII) in 35–40% yield: 2-propyl-2-hydroxy-1,4-dioxane, b.p. 84–85° (13 mm), d_4^{20} 1.0150; n_D^{20} 1.4355, and 2-propyl-6-methyl-2-hydroxy-1,4-dioxane, b.p. 80° (10 mm), d_4^{20} 0.9820; n_D^{20} 1.4320.

From the acetate of 4-ethyl-5-keto-3-oxa-octanol-1, 4-ethyl-5-keto-3-oxa-octanol-1 and the product of its dehydration, 2-propyl-3-ethyl-1,4-dioxene-2, were obtained.

Conversion of 5-keto-3-oxa-octanols-1 and 2,6-dialkyl-oxy-1,4-dioxanes into homologs of 1,4-dioxene.

On distillation of 5-keto-3-oxa-octanols-1 and 2,6-dialkyl-2-oxy-1,4-dioxanes on a rectification column at atmospheric pressure in the presence of NaH_2PO_4, the corresponding homologs of 1,4-dioxene are formed: (IX) 2-propyl-1,4-dioxene-2, b.p. 67° (22 mm), d_4^{20} 0.9740; n_D^{20} 1.4440; 2-propyl-6-methyl-1,4-dioxene-2, b.p. 59° (17 mm); d_4^{20} 0.9395; n_D^{20} 1.4382; 2-propyl-3-ethyl-1,4-dioxene-2, b.p. 60-61°

(8 mm), d_4^{20} 0.9446; n_D^{20} 1.4480.

Hydrolysis of homologs of 1,4-dioxene. In a flask fitted with a reflux condenser, 3 g of the substance, 1 ml of HCl, and 30 ml of water were mixed and heated for 2–3 hr. After cooling, an aqueous-alcoholic solution of 2,4-dinitrophenylhydrazine was added. From the hydrolysis product of 2-propyl-1,4-dioxene-2, 2,4-dinitrophenylhydrazone of 5-keto-3-oxa-octanol-1 was obtained; it crystallized from methanol as orange needles with m.p. 123–124°.

$C_{13}H_{18}O_6N_4$. Found, %: C 48.12; 47.91; H 5.40; 5.30; N 17.44; 17.40
Calculated, %: C 47.84; H 5.56; N 17.16

On treatment of the hydrolysates of 2-propyl-6-methyl-1,4-dioxene-2 and 2-propyl-3-ethyl-1,4-dioxene-2 with a solution of 2,4-dinitrophenylhydrazine, a poorly crystallizing oil precipitated. After boiling in methanol and double recrystallization from toluene, dark-red needles were obtained: osazone of 1-methyl-5-keto-3-oxa-octanol-1, m.p. 228–229°.

$C_{20}H_{22}O_9N_8$. Found, %: N 22.12, 22.01.
Calculated, %: N 21.63

and osazone of 4-ethyl-5-keto-3-oxa-octanol-1, m.p. 258–259°.

$C_{21}H_{24}O_9N_8$. Found, %: N 21.59, 21.49.
Calculated, %: N 21.04

When 5-keto-3-oxa-octanol-1 was treated with a solution of 2,4-dinitrophenylhydrazine, products identical with the products from the homologs of 1,4-dioxene were obtained. Mixed samples gave no depression of the melting point.

By hydrogenation of acetates of monofurfuryl ethers of 1,2-glycols over Pt–C, acetates of 5-keto-3-oxa-octanols-1 were obtained in 65–70% yields.

On methanolysis of acetates of 5-keto-3-oxa-octanols-1, tautomeric oxo and cyclic forms of 5-keto-3-oxa-octanols-1 are formed, which were isolated in pure form.

Both tautomeric forms, on heating with NaH_2PO_4, are converted into the corresponding homolog of 1,4-dioxene.

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