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Abstract

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CONDENSATION OF ACETALS WITH ETHOXYISOPRENE

A NEW METHOD FOR THE SYNTHESIS OF POLYENE ALDEHYDES OF THE ISOPRENOID TYPE

In recent years simple vinyl ethers have been successfully used for the synthesis of polyene aldehydes in a number of carotenoids ([1,2]). Simple diene ethers had never previously been used for the preparation of aldehydes.

We decided to use, for the synthesis of polyene aldehydes of the isoprenoid type, ethoxyisoprene (3-methyl-1-ethoxybutadiene-1,3), recently obtained in our laboratory ([3]). The use of ethoxyisoprene would make it possible to lengthen the polyene chain at once by 5 carbon atoms, with the introduction of two double bonds and a methyl group in the position required for isoprenoids.

We have established that, under the influence of zinc chloride or boron trifluoride, acetals add to ethoxyisoprene I in the 1,4-position; in this process, with high yield, α,β-unsaturated ether acetals are formed, which then are smoothly converted, depending on the reaction conditions, into ether aldehydes and into polyenals.

We studied this reaction in detail with the acetal of dimethylacrolein aldehyde II as an example. On interaction of acetal II with ethoxyisoprene I under the influence of zinc chloride at room temperature, a mixture of ether acetals III, IV, V was obtained in an overall yield of 89%.

$$R = C_2H_5$$

$$\mathrm{II} + \mathrm{I} \longrightarrow \left[\begin{array}{lcccc} \mathrm{III}\ (44\%) & \xrightarrow[90\%]{1\%\, H_3PO_4} & \mathrm{VI} & \xrightarrow[92\%]{CH_3C_6H_4SO_3H} & \mathrm{IX} \\ \mathrm{IV}\ (30\%) & \xrightarrow{95\%} & \mathrm{VII} & \xrightarrow{65\%} & \mathrm{X} \\ \mathrm{V}\ (15\%) & \longrightarrow & \mathrm{VIII} & & \end{array} \right]$$

$$\xrightarrow[89\%]{CH_3COONa + CH_3COOH}$$

Formation of ether acetal IV is explained by the fact that the ether acetal III formed in the reaction in turn adds to a second molecule of ethoxyisoprene.

In an analogous manner ether acetal V is formed from ether acetal IV and ethoxyisoprene.

In the condensation of ether acetal III, isolated in pure form, with ethoxyisoprene I in the presence of zinc chloride, ether acetals IV and V were obtained in yields of 41 and 25.5%, respectively.

The formation of high-molecular-weight ether acetals is explained by the fact that, as a result of addition of an unsaturated acetal to ethoxyisoprene, an unsaturated ether acetal is also formed, which quite readily enters into reaction with a second molecule of ethoxyisoprene, etc. In order for the principal reaction products to be the ether acetals formed by addition of one and two molecules of ethoxyisoprene to the acetal, it is necessary to use an excess of the latter.

The ether acetals are quite stable compounds, distilling in vacuo at 0.1 mm without decomposition, and their separation presents no difficulty.

We found that ether acetals, under the action of 1% orthophosphoric acid, are quantitatively saponified to ether aldehydes.

From ether acetals III, IV, and V there were obtained 4-ethoxycitral VI, 4,8-diethoxyfarnesal VII, and 2,6,10,14-tetramethyl-4,8,12-triethoxyhexadecatetraen-2,6,10,14-al-16 (VIII).

Ether aldehydes, under the action of *p*-toluenesulfonic acid in toluene, are readily converted into polyenals. By this method, dehydrocitral IX (yield 92%) and farnesinal X (yield 65%) were obtained from ether aldehydes VI and VII.

Dehydrocitral was also obtained directly from ether acetal III in 89% yield by heating the latter with a mixture of sodium acetate and acetic acid. It was not possible to convert ether acetal IV into farnesinal X by this route.

The use of ethoxyisoprene makes it possible to lengthen the carbon chain by 5 carbon atoms with introduction of two double bonds and an aldehyde group conjugated with them (in the case of addition of one molecule of ethoxyisoprene), and by 10 carbon atoms with introduction of four double bonds and an aldehyde group conjugated with them (in the case of addition of two molecules of ethoxyisoprene), which constitutes a new simple method for the synthesis of polyene aldehydes of the isoprenoid type.

Experimental Part

Condensation of dimethylacrolein aldehyde acetal II with ethoxyisoprene I. To a mixture of 204 g (1.3 mole) of acetal II and 13 ml of a 10% solution of zinc chloride in ethyl acetate at 20° over 2.5 hr with stirring, 35.6 g (0.32 mole) of ethoxyisoprene I was added; the temperature thereby rose to 27°. The reaction mass was then stirred for 1.5 hr at room temperature and 45 min at 35–40°, after which it was diluted with ether, washed with 5% caustic soda solution, with water, dried over potassium carbonate, and distilled in vacuo. Obtained:

1) 159 g of the starting acetal II with b.p. 65–68°/24 mm, n_D^{18} 1.4215;
2) 38.0 g (yield 44%)* of 2,6-dimethyl-4,8,8-triethoxyoctadiene-2,6 III as a colorless liquid with b.p. 80–81°/0.1 mm, n_D^{20} 1.4517, d_4^{20} 0.9120; *MR* found 79.82, calculated 80.08.

Found, %:	C 71.28; 71.20;	H 11.10; 11.11
$C_{16}H_{30}O_3$. Calculated, %:	C 71.08;	H 11.19

3) 18.0 g (yield 30%) of 2,6,10-trimethyl-4,8,12,12-tetraethoxydodecatriene-2,6,10 IV with b.p. 124–126°/0.04 mm, n_4^{20} 1.4618, d_4^{20} 0.9200; *MR* found 114.3; calculated 113.59.

Found, %:	C 72.24; 72.26;	H 10.91; 10.91
$C_{23}H_{42}O_4$. Calculated, %:	C 72.18;	H 11.06

* Yield calculated on ethoxyisoprene.

4) 7.8 g (yield 15%) of 2,6,10,14-tetramethyl-4,8,12,16,16-pentaethoxyhexadecatetraene-2,6,10,14 **V** as a yellowish, slightly mobile liquid with b.p. 164–168°/0.07 mm, n_D^{20}1.4710, d_4^{20}0.9298.

	Found, %:	C 73.00; 72.84;	H 11.04; 10.84
$C_{30}H_{54}O_5$.	Calculated, %:	C 72.85;	H 11.00

Condensation of 2,6-dimethyl-4,8,8-triethoxyoctadiene-2,6 III with ethoxyisoprene I. By the procedure described above, from 12 g (0.044 mole) of ether acetal **III**, 2.5 g (0.022 mole) of ethoxyisoprene, and 0.6 ml of a 10% solution of zinc chloride in ethyl acetate, 7.8 g of the starting ether acetal **III**, 3.45 g of ether acetal **IV**, and 1.4 g of ether acetal **V** were obtained.

4-Ethoxycitral VI. A mixture of 8.1 g of ether acetal **III**, 1 g of 1% orthophosphoric acid, and 2.5 ml of ethyl alcohol was stirred in a stream of nitrogen for 1.5 h at room temperature. After 15 min the reaction mass became homogeneous. The mixture was diluted with ether, washed with a 5% solution of sodium bicarbonate, then with water, dried with magnesium sulfate, and distilled in vacuo in a stream of nitrogen.

5.3 g of 4-ethoxycitral **VI** was obtained as a colorless liquid (turning yellow on standing) without the odor of lemon peel, with b.p. 58–60°/0.06 mm, n_D^{20}1.4762, d_4^{20}0.9247; *MR* found 59.89, calculated 58.34.
$\lambda_{\max}$ (in ethanol) 240 mμ ($\lg\varepsilon$ 4.132), 327 mμ ($\lg\varepsilon$ 1.956).

	Found, %:	C 73.29; 73.46;	H 10.10; 9.98
$C_{12}H_{20}O_2$.	Calculated, %:	C 73.41;	H 10.27

Dehydrocitral IX. a) A mixture of 3.2 g of 4-ethoxycitral **VI**, 50 ml of abs. toluene, and 5 mg of *p*-toluenesulfonic acid was heated in a stream of nitrogen on a Wood' s metal bath at a bath temperature of 110-130°. During this process a slow distillation of toluene with alcohol occurred; after 20 min the distillation of alcohol ceased (test for alcohol content in the distillate according to Chugaev—Tserevitinov).

The reaction mass was cooled, washed with a 5% solution of sodium bicarbonate, then with water, dried, and distilled in vacuo in a stream of nitrogen. 2.25 g of dehydrocitral **IX** with b.p. 57-60°/0.05 mm was obtained; upon cooling it crystallized. After two recrystallizations from petroleum ether, light-yellow crystals of **IX** with m.p. 39-40° were isolated, which corresponds to the literature data (4).

b) A mixture of 10 g of ether acetal **III**, 3.2 g of sodium acetate, 2 ml of water, and 30 ml of acetic acid was heated at 95° in a stream of nitrogen with stirring for 5 h. After cooling, the reaction mass was poured onto ice, and the separated oil was extracted with petroleum ether. The extract was washed with a 5% solution of sodium bicarbonate, then with water, dried, and distilled in vacuo in a stream of nitrogen. 4.8 g of dehydrocitral **IX** was obtained with b.p. 64-65°/0.06 mm; m.p. **IX** 39-40° (from petroleum ether).

2,6,10-Trimethyl-4,8-diethoxydodecatrien-2,6,10-al-12 (4,8-diethoxyfarnesal) VII. A mixture of 6.5 g of ether acetal **IV**, 0.75 g of 1% orthophosphoric acid, and 1.75 ml of ethyl alcohol was shaken in a closed flask at room temperature. After 10 min the separation into layers disappeared; after standing for 1.5 h, the mixture was subjected to the usual work-up and distilled in vacuo in a stream of nitrogen. 5.02 g of 4,8-diethoxyfarnesal (**VII**) was obtained as a yellowish liquid with b.p. 114-115°/0.04 mm, n_D^{20}1.4875, d_4^{20}0.9419; MR found 94.28, calculated 91.84.

	Found, %:	C 73.99; 74.13; H 10.43; 10.44
$C_{19}H_{32}O_3$.	Calculated, %:	C 73.98; H 10.46

Farnesinal X. A mixture of 2 g of undistilled 4,8-diethoxyfarnesal **VII**, 50 ml of abs. toluene, and 6 mg of *p*-toluenesulfonic acid was heated in an atmosphere of nitrogen on a Wood' s metal bath at a bath temperature of 120-125°. In this process,

slow distillation of toluene with the alcohol took place, while at the same time toluene was added to the flask so that the volume of the reaction mixture remained constant. After 1 hour the distillation of the alcohol ceased (test for alcohol content in the distillate by Chugaev—Tserevitinov). After the usual work-up and distillation in vacuo under nitrogen, 0.85 g of a substance was obtained, b.p. 115—120°/0.5 mm, which began to crystallize during distillation. After two recrystallizations from ethyl alcohol, farnesinal X was isolated as yellow leaflets, m.p. 119–120°, in agreement with the literature data (^{4}).

$$\lambda_{\text{max . (in ethanol)}} 239\,\text{m}\mu\ (\lg \varepsilon 3.92).$$

Found, %:	C 83.40; H 9.41
$C_{15}H_{20}O$. Calculated, %:	C 83.23; H 9.32

2,6,10,14-Tetramethyl-4,8,12-triethoxyhexadecatetraen-2,6,10,14-al-16 VIII. A mixture of 3 g of ether acetal V, 0.75 g of 1% orthophosphoric acid, and 1.75 ml of ethyl alcohol was shaken in a closed flask at room temperature.

After 1.5 hours the mixture was subjected to the usual work-up. 1.9 g of ether aldehyde VIII was obtained as a thick yellow liquid, b.p. 158–162°/0.1 mm, $n_D^{20} 1.4954$, $d_4^{20} 0.9452$.

Found, %:	C 74.06; 74.30; H 10.24; 10.20
$C_{26}H_{54}O_6$. Calculated, %:	C 74.27; H 10.54.

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Note: Figure translations are in progress. See original paper for figures.