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Abstract

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Synthesis of Polyene Aldehydes and Ketones by Condensation of Aldehyde Acetals with Vinyl and Isopropenyl Ethers

Polyene aldehydes and ketones are widely known. Some of them (citral, farnesal) occur in nature; others are intermediates in the synthesis of isoprenoids, to the study of which a series of communications from our laboratory has been devoted [1]. Much less attention has been paid to the investigation and synthesis of polyene carbonyl compounds of unbranched structure, although they undoubtedly may be stages in the synthesis of such important natural substances as fatty acids and sugars.

Practically the only method for obtaining polyenals of unbranched structure is the method of polycondensation of aldehydes. Thus, in the condensation of acetaldehyde with crotonaldehyde (or in the polycondensation of crotonaldehyde itself) in the presence of salts of secondary amines, Kuhn and Fischer [2] obtained a mixture of polyenals, both open-chain and cyclic, together with a considerable amount of high-molecular products. Separation of this mixture presented great difficulties, especially since the highly unsaturated aldehydes are extremely sensitive to atmospheric oxygen and to heating. Attempts at selectively carrying out the reaction [3] did not give positive results—the yield of polyenals amounted to no more than 20%.

The purpose of the present work is to extend the condensation of acetals with vinyl ethers [4] to the preparation of polyene aldehydes and ketones with a normal carbon chain.

By condensation of the acetal of crotonaldehyde (I) with vinylethyl ether in the presence of zinc chloride, the acetal of 3-ethoxyhex-4-enal (II) was obtained; on saponification it gives sorbic aldehyde (III). This reaction can be carried out in one stage without isolating acetal (II), and the yield of sorbic aldehyde in this case reaches 75%. Sorbic aldehyde (III), after its conversion into the acetal (IV), can be introduced into the next condensation with vinylethyl ether, and after saponification octatrien-2,4,6-al (V) is obtained in 71% yield. By such successive chain extension, decatetraen-2,4,6,8-al (VI) and dodecapentaen-2,4,6,8,10-al (VII) were synthesized. The intermediate acetals were obtained in high yield by the action of tetraethoxysilane on the aldehydes, according to a method developed earlier in our laboratory [5].

$$CH_3CH{=}CHCH(OC_2H_5)_2\ (I)\ \xrightarrow{CH_2{=}CHOC_2H_5}$$

$$\rightarrow\ CH_3CH{=}CHCH(OC_2H_5)CH_2CH(OC_2H_5)_2\ (II) \rightarrow$$

$$\xrightarrow{H^+}\ CH_3(CH{=}CH)_2CHO\ (III)\ \xrightarrow{Si(OC_2H_5)_4}\ CH_3(CH{=}CH)_2CH(OC_2H_5)_2\ (IV) \rightarrow$$

$$\rightarrow\ CH_3(CH{=}CH)_3CHO\ (V) \rightarrow CH_3(CH{=}CH)_4CHO\ (VI) \rightarrow CH_3(CH{=}CH)_5CHO\ (VII)$$

All stages proceed in high yields (70-80%); thus, this method has undeniable advantages over Kuhn’ s method.

It turned out that, analogously to vinyl ethyl ether, isopropenyl ethyl ether also reacts with acetals, and this opened a new route for the synthesis of polyene ketones. Thus, condensation of the acetal of crotonaldehyde (I) with isopropenyl ethyl ether leads to the ketal 4-ethoxyhepten-5-one-2 (VIII), which after saponification gives heptadien-3,5-one-2 (IX) in 51% yield. According to the same scheme, from the acetals of sorbic aldehyde and octatrien-2,4,6-al, nonatrien-3,5,7-one-2 (X) and undecatetraen-3,5,7,9-one-2 (XI) were synthesized.

$$CH_3CH{=}CHCH(OC_2H_5)_2\ (I)\ \xrightarrow{CH_2{=}C(CH_3)OC_2H_5}$$

$$arrow\ CH_3CH{=}CHCH(OC_2H_5)CH_2C(OC_2H_5)_2CH_3\ (VIII)\ \xrightarrow[51\%]{H^+}\ CH_3(CH{=}CH)_2COCH_3\ (IX)$$

$$CH_3(CH{=}CH)_2CH(OC_2H_5)_2\ (IV)\ \xrightarrow[62\%]{}\ CH_3(CH{=}CH)_3COCH_3\ (X)$$

$$CH_3(CH{=}CH)_3CH(OC_2H_5)_2\ \xrightarrow[54\%]{}\ CH_3(CH{=}CH)_4COCH_3\ (XI)$$

The structure of the ketones obtained was proved by hydrogenation to the corresponding saturated ketones, identified in the form of their derivatives.

Experimental part

In all condensation experiments a freshly prepared 10% solution of zinc chloride in ethyl acetate was used. Hydrolysis of the ethoxyacetals, distillation, and crystallization of the polyene compounds were carried out in an atmosphere of nitrogen.

Condensation of the acetal of crotonaldehyde (I) with vinyl ethyl ether. To a mixture of 31 g of the acetal of crotonaldehyde (I) and 5 ml of a zinc chloride solution, 16 g of vinyl ethyl ether was added with stirring at such a rate that the temperature of the reaction mass did not rise above 45°. After addition of the ether, the reaction mass was stirred for about one hour; then the temperature was raised to 50-60° and stirring was continued for another 1.5 hours. The reaction product was diluted with an equal volume of ether, washed with 5% caustic soda solution, and dried over ignited potash. After fractionation, 37.2 g (79% of theory) of the acetal of 3-ethoxyhexen-4-al (II) was obtained, b.p. 95-100°/12 mm; n_D^{20} 1.4248; d_4^{20} 0.8908.

Found, %: C 66.61; 66.68; H 11.24; 11.11
$C_{12}H_{24}O_3$. Calculated, %: C 66.64; H 11.14

Preparation of sorbic aldehyde (III). 22 g of acetal (II) and 45 ml of a mixture prepared from 80 ml of acetic acid, 22 g of anhydrous sodium acetate, and 13 ml of water were heated with stirring in an atmosphere of nitrogen for 3.5-4 hours at 85-90°. The mixture was cooled, poured into 150 ml of ice water, the upper layer was separated, and the aqueous layer was extracted with ether. The ether and the main quantity of acetic acid were distilled off in vacuo; the residue was carefully neutralized by shaking with a solution of sodium bicarbonate, and after drying and fractionation, 8.1 g (83% of theory) of sorbic aldehyde was obtained, b.p. 65-67°/15 mm and n_D^{20} 1.5354. $\lambda_{\max}$ (in ethanol) 271.5 mμ.

If the condensation and hydrolysis are carried out successively without isolation of the intermediate acetal (II), the overall yield of sorbic aldehyde reaches 75%.

Acetal of sorbic aldehyde (IV). A mixture of 96 g of sorbic aldehyde (III), 260 g (25% excess) of tetraethoxysilane, 32 ml of absolute alcohol, and 6 ml of 85% phosphoric acid was left for 3 days in a closed vessel at 20°. The reaction mass obtained was shaken vigorously in a separatory funnel with 1 l of 30% caustic soda solution for 10-15 min; the upper layer was separated and the aqueous portion was extracted with ether. The ethereal extract, combined with the main product, was washed with water, dried with potash, and fractionated. 144 g (85% of theory) of the acetal of sorbic aldehyde (IV) was obtained, b.p. 99-100°/21 mm; n_D^{17} 1.4560; d_4^{20} 0.8831.

Found, %: C 70.49; 70.61; H 10.60; 10.60
$C_{10}H_{18}O_2$. Calculated, %: C 70.50; H 10.66

Preparation of octatrien-2,4,6-al (V). To a mixture of 58 g of acetal (IV) and 11 ml of zinc chloride solution, 28.8 ml of vinyl ethyl ether was added under the conditions described for the preparation of acetal (II). After completion of the reaction, 32.8 g of anhydrous sodium acetate, 275 ml of acetic acid, and 25 ml of water were added to the product obtained, and the mixture was heated in a stream of nitrogen at 90-95° for one hour. After the usual work-up and distillation, 34.4 g (71% of theory) of octatrien-2,4,6-al (V) was obtained, b.p. 64-69°/0.4 mm; m.p. 57-58° (from petroleum ether), which agrees with the literature data (^{2}). The 2,4-dinitrophenylhydrazone melts at 188-189° (from methanol-ethyl acetate). λ_{max} (in isooctane) 370.5; 389 and 404 mμ (^{3}).

Preparation of decatetraen-2,4,6,8-al (VI). Starting from 34 g of aldehyde (V), by the method described above, 47.6 g (87% of theory) of its acetal was obtained, b.p. 130-132°/15 mm; 74-76°/0.2 mm; n_D^{20} 1.5031; d_4^{20} 0.8971.

Found, %: C 73.03; 73.07; H 10.40; 10.31
$C_{12}H_{20}O_2$. Calculated, %: C 73.41; H 10.27

From 19.6 g of this acetal, upon condensation with vinyl ethyl ether under the conditions described above and after saponification of the reaction product by heating with sodium acetate, acetic acid, and water for 10-15 min at 75-80°, 12.2 g (83% of theory) of decatetraen-2,4,6,8-al (VI) was obtained, b.p. 112-116°/0.4 mm; m.p. 109-109.5° (from petroleum ether), which agrees with the literature data (^{6}).

Preparation of dodecapentaen-2,4,6,8,10-al (VII). From 12 g of aldehyde (VI), by the method described above, 13.2 g (72% of theory) of its acetal was obtained, b.p. 104-107°/0.1 mm; n_D^{20} 1.5205.

Found, %: C 75.60; 75.67; H 10.0; 10.0
$C_{14}H_{22}O_2$. Calculated, %: C 75.59; H 9.97

Upon condensation of 6.7 g of this acetal with vinyl ethyl ether, followed by brief saponification of the reaction product, 3.7 g (72% of theory) of dodecapentaen-2,4,6,8,10-al (VII) was obtained, m.p. 159-161° (from methanol) (^{2}).

Condensation of crotonaldehyde acetal with isopropenyl ethyl ether. The condensation was carried out analogously to the preparation of acetal (II), omitting heating at the end of the reaction. From 17 g of acetal (I), 15.5 g of 2,4,4-triethoxypent-5-ene (VIII) was obtained, b.p. 57-61°/0.1 mm; n_D^{18} 1.4300; after hydrolysis of this compound with a mixture of sodium acetate, acetic acid, and water (4 hours, 85-90°), 6.8 g (51% of theory) of heptadien-3,5-one-2 (IX) was isolated, b.p. 79-80°/18 mm; n_D^{20} 1.5182.

Found, %: C 76.50; 76.59; H 9.08; 9.17
$C_7H_{10}O$. Calculated, %: C 76.38; H 9.15

Preparation of nonatrien-3,5,7-one-2 (X). In an analogous manner, from 8.5 g of sorbic aldehyde acetal (IV), upon condensation with isopropenyl ethyl ether and saponification of the reaction product (1 hour, 80-90°), 4.2 g (62%

of theory) of nonatrien-3,5,7-one-2 (X) was obtained, b.p. 62–64°/0.2 mm; n_D^{20} 1.5453. $\lambda_{\max}$ (in ethanol) 229.5 (lg ε 4.05) and 316 (lg ε 4.23) mμ.

Its 2,4-dinitrophenylhydrazone melted at 170–172° (from ethanol-ethyl acetate); $\lambda_{\max}$ (in isooctane) 316 and 404 mμ.

Found, %: C 56.52; 56.53; H 5.02; 4.97; N 18.26; 18.29
$C_{15}H_{16}O_4N_4$. Calculated, %: C 56.93; H 5.10; N 17.72

Upon exhaustive hydrogenation of ketone (X) in the presence of palladium on strontium sulfate, 3 moles of hydrogen were absorbed, and nonanone-2 was obtained,

the semicarbazone of which melted at 120–120.5° (from aqueous methanol), which agrees with the literature data (7).

Preparation of undecatetraen-3,5,7,9-one-2 (XI). In a manner analogous to that described above, from 9.8 g of octatrien-2,4,6-al acetal there were obtained 5.2 g (64% of theory) of undecatetraen-3,5,7,9-one-2 (XI), b.p. 94–96°/0.4 mm; m.p. 101–103° (from petroleum ether) (8). $\lambda_{\max}$ (in ethanol) 243.5 (lg ε3.85) and 351 (lg ε4.62) mμ.

The 2,4-dinitrophenylhydrazone obtained from it melted at 163–164° (from methanol-ethyl acetate).

Found, %: N 16.67; 16.72
$C_{17}H_{18}O_4N_4$. Calculated, %: N 16.37

On exhaustive hydrogenation of ketone (XI), 4 moles of hydrogen were absorbed and undecanone-2 was obtained, the semicarbazone of which melted at 122–123.5° (from aqueous methanol) (7).

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