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REACTIONS OF ACETALS WITH ALKYL 2-BROMOVINYL ETHERS

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In a number of previous communications we have shown that the reaction of acetals with α , β -unsaturated ethers, discovered in 1939 by Mueller-Cunradi and Pieroh [1], can be extended to various types of these compounds, of which both the acetal component and the ether can be varied [2-4]. A further development of this reaction is the reaction of acetals with alkyl 2-bromovinyl ethers, described in this paper.

We have found that in the reaction of benzaldehyde diethyl acetal with 2-bromovinyl ethyl ether in presence of boron trifluoride an addition product is formed in good yield in accordance with the same scheme as in the case of ethyl vinyl ether [2]. Analogous reaction occurs also with 2-bromovinyl butyl ether.

$$C_{6}H_{5}-CH (OC_{2}H_{5})_{2} + CHBr=CHOR \xrightarrow{BF_{3}} C_{6}H_{5}-CH (OC_{2}H_{5})-CHBr-CH (OC_{2}H_{5}) - CHBr-CH (OC_{2}H_{$$

in which $R = C_2H_5$ (Ia) and C_4H_9 (Ib).

This reaction shows a number of peculiar features. Unlike the reaction with ethyl vinyl ether, which we studied in detail previously [2], in this case the formation of products of the addition of two or more molecules of the unsaturated ether to the original acetal is not observed. This is to be explained by the fact that in the bromo acetals (I), arising from the reaction, the halogen in the α -position relative to the carbonyl group stabilizes alkoxy groups, making their mobility low. This results in the complete passivity of the bromo acetals (I) in condensation with unsaturated ethers, so that products of further condensation are not formed. Also, these acetals show an extraordinary stability to hydrolysis: the preparation of the corresponding bromo aldehyde $-\alpha$ -bromo- β -ethoxyhydrocinnamaldehyde (II) - from the bromo acetals (I) can be carried out only under severe conditions (long boiling with 10% HC1). Even then, hydrolysis is not complete, and part of the acetal is recovered.

$$C_{6}H_{5}-CH (OC_{2}H_{5})-CHBr-CH \begin{pmatrix} OC_{2}H_{5} \\ \\ OR \end{pmatrix} C_{6}H_{5}-CH (OC_{2}H_{5})-CHBr-CHC \\ (II) \qquad (II)$$

For comparison we may note that the corresponding unhalogenated acetal $-\beta$ -ethoxyhydrocinnamaldehyde diethyl acetal - is hydrolyzed to β -ethoxyhydrocinnamaldehyde in 100% yield when boiled with 2% HCl.

The bromine atom stabilizes not only the acetal, but also the corresponding aldehyde (II). Despite severe hydrolysis conditions the elimination of the ethoxy group and resinification are not observed. In acetals we met a similar example of the effect of a halogen atom on the mobility of alkoxy groups in an attempt to condense bromo-acetaldehyde with ethyl vinyl ether. Under the usual condensation conditions no addition product was obtained. It is known that the hydrolysis of this acetal also goes with great difficulty [5]. Thus, in these examples, and in a number of others, there is a clear relation between the tendency for an acetal to hydrolyze and its reactivity toward α , β -unsaturated ethers.

In the work of Hoaglin and Hirsh [6] it was observed that in the condensation of acetals with alkyl vinyl ethers containing various alkoxy groups, mixtures of reaction products are formed as a result of the migration of the alkoxy groups. Thus, in the condensation of acetaldehyde dibutyl acetal with ethyl vinyl ether a mixture of products was obtained including compounds with all the possible arrangements of butoxy and ethoxy groups. In condensations with alkyl 2-bromovinyl ethers the migration of alkoxy groups was not observed, and the bromo acetal (Ib) was the only product of the reaction of benzaldehyde diethyl acetal with 2-bromovinyl butyl ether.

As a representative of aliphatic acetals in the reaction with 2-bromovinyl butyl ether we used acetaldehyde diethyl acetal:

$$CH_{3}-CH (OC_{2}H_{5})_{2} + CHBr=CHOC_{4}H_{9} \rightarrow CH_{3}-CH (OC_{2}H_{5}) - CHBr-CH (OC_{4}H_{9})$$
(III)

In this case condensation with more sluggish than with benzaldehyde acetal, but again only one condensation product was formed -2-bromo-3-ethoxybutyraldehyde butyl ethyl acetal (III).

The behavior of the bromo aldehyde and bromo acetals obtained toward 2,4-dinitrophenylhydrazine was found interesting. Thus, by the action of 2,4-dinitrophenylhydrazine sulfate on α -bromo- β -ethoxycinnamaldehyde (II) we obtained phenylpyruvaldehyde bis(2,4-dinitrophenylhydrazone) (IV), the formation of which can be represented as follows:

$$C_{6}H_{5} - CH (OC_{2}H_{5}) - CHBr - CHO \xrightarrow{(NO_{2})_{2}} C_{4}H_{3}NH - NH_{2}} \rightarrow [C_{6}H_{5} - CH (OC_{2}H_{5}) - CH - CH = N - NHC_{6}H_{3} (NO_{2})_{2}] \xrightarrow{-C_{3}H_{5}OH} NH - NH - C_{6}H_{3} (NO_{2})_{2} \rightarrow [C_{6}H_{5} - CH = C - CH = N - NHC_{6}H_{3} (NO_{2})_{2}] \rightarrow NH - NHC_{6}H_{3} (NO_{2})_{2} \rightarrow NH - NHC_{6}H_{3} (NO_{2})_{2} \rightarrow C_{6}H_{5} - CH_{2} - C - CH = N - NHC_{6}H_{3} (NO_{2})_{2} (IV)$$

The reaction of the acetal (III) with 2,4-dinitrophenylhydrazine sulfate takes a different course. In this case the elimination of hydrogen bromide probably first occurs, and then, in its place, a molecule of alcohol adds to the double bond formed. Simultaneously, the acetal grouping reacts with the hydrazine, and, as a result, acetoacetaldehyde diethyl ketal 2,4-dinitrophenylhydrazone (V) is formed.

$$CH_{3}-CH (OC_{2}H_{5}) -CHBr-CH \left\langle \begin{array}{c} OC_{2}H_{5} \\ OC_{4}H_{9} \end{array} \xrightarrow{(NO_{2})_{2} C_{9}H_{3}NH-NH_{2}} \\ -HBr \rightarrow [CH_{3}-C (OC_{2}H_{5}) =CH-CH=N-NHC_{6}H_{3} (NO_{2})_{2}] \xrightarrow{C_{2}H_{5}OH} \\ \rightarrow CH_{3}-C (OC_{2}H_{5})_{2} -CH_{2}-CH=N-NHC_{6}H_{3} (NO_{2})_{2} \\ (V) \end{array} \right\rangle$$

When the hydrazone (V) is heated with an alcoholic solution of sulfuric acid the ketal grouping is hydrolyzed with formation of a substance of m. p. 233°, probably 1-(2,4-dinitrophenyl)-5-methylpyrazone (VI):



However, the proposed structures of (V) and (VI) are only tentative, for these compounds have not been described in the literature, and we were unable to prepare them by an independent synthesis.

EXPERIMENTAL

<u>α-Bromo-β-ethoxyhydrocinnamaldehyde Diethyl Acetal (I). R = C₂H₅).</u> 18.1 g of 2-bromovinyl ethyl ether was added dropwise at 50° to 30 g of benzaldehyde diethyl acetal containing 0.5 ml of boron trifluoride etherate as catalyst; heat was liberated. When the addition of the ether was complete the mixture was kept at 50° for ten minutes and then cooled to room temperature. Three g of anhydrous sodium carbonate was added to neutralize the catalyst, and the mixture was stirred for three hours. The catalyst was then filtered off, and the reaction products were vacuum-fractionated. After the removal of excess of the original acetal we obtained 30 g (75.8%) of the addition product, α-bromo-β-ethoxyhydrocinnamaldehyde diethyl acetal; b. p. 103-105° (2 mm); d_4^{20} 1.2126; n_D^{20} 1.5010. Found: C 54.64, 54.64; H 6.96, 6.99; Br 23.98, 24.00%; MR 80.48. C₁₅H₂₃O₃Br. Calculated: C 54.36; H 7.00; Br 24.12%; MR 80.56.

<u>α-Bromo-β-ethoxyhydrocinnamaldehyde Butyl Ethyl Acetal (I), $R = C_4H_9$.</u> 0.5 ml of boron trifluoride etherate was added to 18 g of benzaldehyde diethyl acetal, and then at 50° 5.5 g of 2-bromovinyl butyl ether was added dropwise. The reaction went just as in the case of 2-bromovinyl ethyl ether. By the fractionation of the reaction products we obtained 8.8 g (83.3%) of α-bromo-β-ethoxyhydrocinnamaldehyde butyl ethyl acetal; b. p. 135-136° (3 mm); d_4^{20} 1.1713; n_D^{20} 1.4978. Found: C 56.58, 56.42; H 7.34, 7.16; Br 22.22, 22.23%; MR 89.89. $C_{17}H_{27}O_3Br$. Calculated: C 56.82; H 7.57; Br 22.24%; MR 89.80.

 $\frac{2-\text{Bromo-3-ethoxybutyraldehyde Butyl Ethyl Acetal (III).}{23.6 \text{ g of acetaldehyde diethyl acetal, and then 9 g of 2-bromovinyl butyl ether was added dropwise at 50°. By the fractionation of the reaction products we obtained 11 g (74%) of 2-bromo-3-ethoxybutyaldehyde butyl ethyl acetal; b. p. 76-77° (2 mm); d²⁰₄ 1.1384; n²⁰_D 1.4487. Found: C 48.05, 48.15; H 8.43, 8.26; Br 27.38, 27.28%; MR 70.42. C₁₂H₂₅O₃Br. Calculated: C 48.19; H 8.43; Br 26.74%; MR 70.31.$

<u>α-Bromo-β-ethoxyhydrocinnamaldehyde (II).</u> A mixture of 16 g of α-bromo-β-ethoxyhydrocinnamaldehyde diethyl acetal and 20 ml of 10% HCl was boiled for one hour under a column, and in the course of this time 2.5 g of alcohol distilled off. The mixture was extracted with ether. After the usual treatment we obtained 8.5 g (66%) of α-bromo-β-ethoxyhydrocinnamaldehyde; b. p. 94-98° (2 mm); d_4^{20} 1.3211; n_D^{20} 1.5336. Found: C 51.79, 51.80; H 5.32, 5.23; Br 29.83, 29.75%; MR 60.46. C₁₁H₂₃O₂Br. Calculated: C 51.38; H 5.10; Br 31.08%; MR 58.82.

By the action of 2,4-dinitrophenylhydrazine sulfate on α -bromo - β -ethoxyhydrocinnamaldehyde we obtained a crystalline substance, which corresponded in analysis and melting point to phenylpyruvaldehyde bis(2,4-dinitrophenylhydrazone) and gave a qualitative reaction for an osazone (violet color with alcoholic alkali). The substance had m. p. 228-230°; for phenylpyruvaldehyde bis(2,4-dinitrophenylhydrazone) the literature [7] gives m. p. 231-232°. Found: C 49.20, 49.05; H 3.22, 3.19; N 22.25, 22.02%. C₂₁H₁₆N₈O₈. Calculated: C 49.61; H 3.17; N 22.04%.

By the action of 2,4-dinitrophenylhydrazine sulfate on 2-bromo-3-ethoxybutyraldehyde butyl ethyl acetal we obtained crystals of m. p. 115-116° (from alcohol), which corresponded in analysis to acetoacetaldehyde diethyl ketal 2,4-dinitrophenylhydrazone (V). Found: C 49.20, 49.10; H 5.89, 6.10; N 16.52, 16.53%. $C_{14}H_{20}N_4O_6$. Calculated: C 49.40; H 5.92; N 16.46%.

0.3 g of the hydrazone (V) was dissolved in 25 ml of alcohol, and 5 ml of concentrated sulfuric acid was added to the solution. The mixture was boiled for 30 min. When it cooled, crystals separated which after recrystallization from a 1:1 mixture of alcohol and benzene had m. p. 232-233° and corresponded in analysis to 1-(2,4-dinitrophenyl)-5-methylpyrazole (VI). Found: C 48.17, 48.38; H 3.53, 3.66%. $C_{10}H_8N_4O_4$. Calculated: C 48.39; H 3.25%.

SUMMARY

A study was made of the condensation of benzaldehyde and acetaldehyde acetals with alkyl 2-bromovinyl ethers, as a result of which bromo ethoxy acetals of general formula $RCH(OC_2H_5)CHBrCH(OR')_2$ (R = C₆H₅ and CH₃) were formed.

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