CHEMISTRY OF ACETALS

COMMUNICATION 13. STUDY OF THE HYDROLYSIS OF SOME DIACETALS BY MEANS OF GAS-LIQUID CHROMATOGRAPHY

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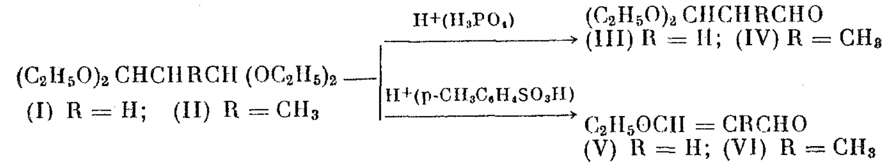
In a previous communication [1] we described the hydrolysis of the diacetals (I) and (II) of malonaldehyde and methylmalonaldehyde. It was shown that preferential formation of 3,3-diethoxypropionaldehyde (III) [and 3,3-diethoxy-2-methylpropionaldehyde (IV), respectively] occurs in hydrolysis in presence of phosphoric acid, whereas preferential formation of 3-ethoxyacrolein (V) [and 3-ethoxy-2-methylacrolein (VI), respectively] occurs in hydrolysis in presence of p-toluenesulfonic acid:



$$(C_2H_5O)_2CHCHRCH(OC_2H_5)_2 \xrightarrow{H^+(H_3PO_4)} (C_2H_5O)_2CHCHRCHO$$

(I) $R = H$; (II) $R = CH_3$ → (III) $R = H$; (IV) $R = CH_3$

$$(C_2H_5O)_2CHCHRCH(OC_2H_5)_2 \xrightarrow{H^+(p\text{-}CH_3C_6H_4SO_3H)} C_2H_5OCH = CRCHO$$

(V) $R = H$; (VI) $R = CH_3$

With the object of further clarifying the proposed scheme of transformations we studied the character of the hydrolysis of these diacetals, and also of dimethylmalonaldehyde bis(diethyl acetal) (VII), as a function of the time of heating, using gas-liquid chromatography for the analysis of the mixture formed. As the stationary liquid phase we used a silicone elastomer supported on sodium chloride [2, 3], and this permitted the precise separation and identification of all the products that could be formed in the course of the hydrolysis.

It was found that the hydrolysis of malonaldehyde diacetal (I) with an equimolecular amount of water in presence of 6-10% of phosphoric acid in the water phase at 100° leads in the initial stages of the reaction (after 5-10 minutes) only to the formation of 3,3-diethoxypropionaldehyde (III). Only in the course of further heating (after 15 minutes) can the formation of 3-ethoxyacrolein (V) be detected, and the amount of this gradually increases. Typical chromatograms of the hydrolyzates of (I) obtained after different times of heating are shown in Fig. 1.

Analogous results were obtained in a study of the course of hydrolysis of malonaldehyde bis(diethyl acetal) (I) by observations on the intensity of absorption at 242.5 mμ. As will be seen from the table, at the initial stages of reaction 3-ethoxyacrolein (V) is almost absent.

The hydrolysis of (I) at 100° in presence of p-toluenesulfonic acid (3% on the aqueous phase) is very rapid, and already five minutes after the start of the reaction about 60% of the diacetal is hydrolyzed with formation of a mixture of the hydrolysis products (III) and (V) (Fig. 2). Under such conditions, therefore, the initial reaction products cannot be obtained. However, when the process is carried out at a lower temperature (55°), the rate of hydrolysis is greatly reduced. By observing the change in the character of the hydrolysis with time under these conditions, we showed that in the first stages (1-2 hours) 3,3-diethoxypropionaldehyde (III) is again formed exclusively and that only after hydrolysis for a longer time (3-5 hours) does 3-ethoxyacrolein (V) make its appearance in the reaction mixture. However, as we stated previously [1], at low temperature the total yield of reaction products is small, and even after six hours much of the diacetal (I) is recovered unchanged.

Study of the hydrolysis of methylmalonaldehyde bis(diethyl acetal) (II) in presence of phosphoric acid at 100° showed that, in this case also, at the early stages of reaction only 3,3-diethoxy-2-methylpropionaldehyde (IV) is formed [formation on the chromatogram of one peak at $t_R = 0.34$ due to (IV)] [1]. In presence of p-toluenesulfonic acid the diacetal (II) is hydrolyzed rapidly with exclusive formation of 3-ethoxy-2-methylacrolein (VI), but at a lower temperature (about 50°) the initial formation of (IV) with its subsequent rapid conversion into (VI) can again be observed. The difference in the behaviors of the diacetals (I) and (II) in hydrolysis in presence of p-toluenesulfonic acid is shown particularly clearly when a mixture of them is hydrolyzed at 100°. It was found that in this case even after five minutes from the start of the hydrolysis methylmalonaldehyde diacetal (II) is completely converted into 2-ethoxy-2-methylacrolein (VI), whereas the diacetal (I) is not hydrolyzed completely and gives a mixture of (III) and (V) (Fig. 3A). For comparison we give the chromatogram of the hydrolyzate formed in presence of phosphoric acid (Fig. 3B).

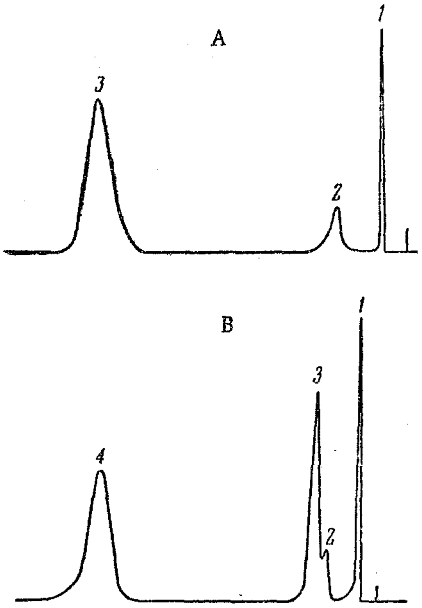


Fig. 1. Chromatograms of hydrolyzates of malonaldehyde bis(diethyl acetal). Hydrolysis conditions: ratio of (I) to water = 1 : 1; 100°; alcohol distilled off; 6% of H_3PO_4 in aqueous phase. Chromatography conditions: 100°; consumption of helium 75 ml/min. A) 5 min after start of hydrolysis: peak (1), alcohol; peak (2), $(C_2H_5O)_2CHCH_2CHO$; peak (3), $(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2$. B) 25 min after start of hydrolysis: peak (1), alcohol; peak (2), $C_2H_5OCH = CHCHO$; peak (3), $(C_2H_5O)_2CHCH_2CHO$; peak (4), $(C_2H_5)_2CHCH_2CH(OC_2H_5)_2$.

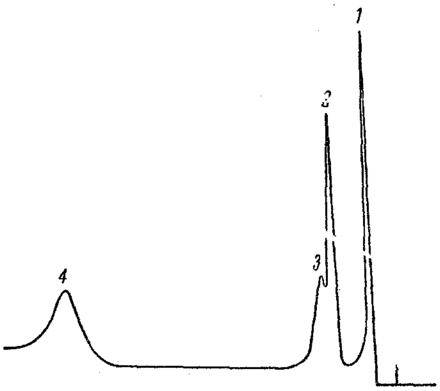


Fig. 2. Chromatogram of the hydrolyzate of malonaldehyde bis(diethyl acetal). Hydrolysis conditions: (I): $H_2O = 1 : 1$; 3% of $p\text{-}CH_3C_6H_4SO_3H$ in aqueous phase; 100°; 5 min. Chromatography conditions: 100°; consumption of helium 80 ml/min: peak (1), alcohol; peak (2), $C_2H_5OCH = CHCHO$; peak (3), $(C_2H_5O)_2CHCH_2CHO$; peak (4), $(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2$.

Hence, from the results obtained we may clearly conclude that the first stage of the hydrolysis of the diacetals (I) and (II) consists in the hydrolysis of one acetal grouping with formation of the aldehydo-acetals (III) and (IV):

$$(C_2H_5O)_2CHCHRCH(OC_2H_5)_2 + H_2O \rightarrow (C_2H_5O)_2CHCHRCHO$$

$$\text{(I) } R = H; \quad \text{(II) } R = CH_3; \quad \text{(III) } R = H; \text{ (IV) } R = CH_3$$

Apart from their formation in this way we cannot exclude the possibility that these compounds may be formed also as a result of the hydrolysis of the original diacetals (I) and (II) to the corresponding dialdehydes with subsequent transacetalization by the scheme:

$$(C_2H_5O)_2CHCHRCH(OC_2H_5)_2 \xrightarrow{H_2O} HOCCHRCHO$$

$$HOCCHRCHO + (C_2H_5O)_2(CHCHRCH\ OC_2H_5)_2 \xrightarrow{H^+} (C_2H_5O)_2CHCHRCHO.$$

We succeeded in showing that such transacetalization does actually occur when a mixture of the diacetal (II) and methylmalonaldehyde is heated and when a mixture of dimethylmalonaldehyde bis(diethyl acetal) (VII) and dimethylmalonaldehyde is heated in presence of traces of phosphoric acid or p-toluenesulfonic acid at 100° for

20-30 minutes. With the aid of gas-liquid chromatography we showed that in the course of these treatments diacetal and dialdehyde peaks disappear or are greatly reduced in size and new peaks appear corresponding to aldehydo-acetals (Fig. 4). However, if such a reaction occurs in the course of the hydrolysis, its importance in the formation of partial-hydrolysis products is probably small as the formation of considerable amounts of malonaldehydes when there is a deficiency of water is not very likely. The 3-ethoxyacrolein (V) and 3-ethoxy-2-methylacrolein (VI) formed as a result of the hydrolysis of the diacetals (I) and (II) are undoubtedly the products of the secondary reaction:

Accumulation of 3-Ethoxyacrolein (V) in the Hydrolysis of Malonaldehyde Bis(diethyl acetal) (I) with an Equimolecular Amount of Water (6% of H_3PO_4 on aqueous phase, 100°)

Hydrolysis time (min)	Content * of (V) (%)	Hydrolysis time (min)	Content * of (V) (%)
5	0.9	20	3.4
10	1.3	25	4.25
15	1.6	30	6.9

*Determined from value of ε at λ_{max} 242.5 mμ.

$$(C_2H_5O)_2CHCHRCHO \xrightarrow{-C_2H_5OH} C_2H_5OCH=CRCHO\cdot$$

$$(V)\ R=H;\ (VI)\ R=CH_3; \qquad (III)\ R=H;\ (IV)\ R=CH_3$$

Actually, after a pure sample of (III) had been heated with traces of p-toluenesulfonic acid at 100° for 20 minutes, the peak of (III) on the chromatogram had completely disappeared and two new peaks, corresponding to 3-ethoxyacrolein (V) and malonaldehyde diacetal (I), made their appearance. There can be no doubt that the last was formed as a result of the ready acetalization of the original aldehydo-acetal (III) by the alcohol eliminated (Fig. 5). The elimination of alcohol from (III) occurs also on heating with traces of phosphoric acid, but in this case the process is considerably slower and in the course of 20-30 minutes no appreciable amounts of (III) and (I) are formed.

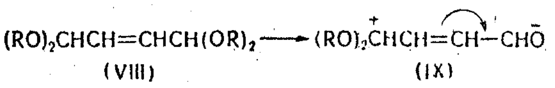
When the aldehydo-acetal molecule contains no hydrogen atom capable of being eliminated, the hydrolysis of the diacetal with an equimolecular amount of water stops at the stage of the formation of the aldehydo-acetal. For example, the hydrolysis of dimethylmalonaldehyde bis(diethyl acetal) (VII) proceeds both in presence of phosphoric acid and in presence of p-toluenesulfonic acid. A typical chromatogram of the hydrolyzate of (VII) obtained in presence of phosphoric acid is given in Fig. 6. Hydrolysis in presence of p-toluenesulfonic acid differs only in its greater speed.

It is characteristic that in the case of the diacetal (VII), in addition to 3,3-diethoxy-2,2-dimethylpropionaldehyde, small amounts of dimethylmalonaldehyde are formed, and the latter may be the main product in hydrolysis with excess of water.

All the data examined show that in the hydrolysis of malonaldehyde diacetals with one molecular proportion of water the first and most rapid reaction is the formation of aldehydo-acetals, which under more severe conditions are then capable of not so much the hydrolysis of the second acetal grouping as the limination of a molecule of alcohol. On the basis of the experimental material with which we are now acquainted we may conclude that such selective hydrolysis of the diacetals of β-dicarbonyl compounds has a fairly general character. Thus, the bis(diethyl acetal)s of acetoacetaldehyde, 3-oxovaleraldehyde, 3-oxohexanal, and benzoylacetaldehyde, even when hydrolyzed with excess of water, give only keto-acetals [4]. The cause of such selectivity of hydrolysis in diacetals is probably the primary formation, in the process of their hydrolysis, of the electron-attracting aldehyde group in the β-position to the acetal grouping, as a result of which the rate of hydrolysis of the latter is greatly reduced. On several occasions we have been able to show that the hydrolysis of acetals containing an electron-attracting grouping in the β-position to the acetal grouping is slow. It is not without interest that these same compounds generally do not react with vinyl ethers under the usual conditions [6]. For example, we have shown that the hydrolysis of the diethyl acetals of bromoacetaldehyde and ethoxyacetaldehyde is slow and incomplete; the same acetals do not react with ethyl vinyl ether in presence of zinc chloride or boron trifluoride etherate. The hydrolysis of the following is slow and incomplete:

glyoxal bis(diethyl acetal), acetoacetaldehyde diethyl acetal, propiolaldehyde diethyl acetal, and fumaraldehyde bis(diethyl acetal). The same compounds do not react with ethyl vinyl ether under the usual conditions [5].

On the basis of the above considerations it may be suppose that the diacetal of fumaraldehyde (VIII) will be capable of selective hydrolysis when treated with an equimolecular amount of water, for in the initially formed aldehydo-acetal (IX) the acetal grouping will be stabilized because of the attraction of the electrons to the aldehyde grouping.



$$\underset{\text{(VIII)}}{(RO)_2CHCH{=}CHCH(OR)_2} \longrightarrow \underset{\text{(IX)}}{(RO)_2\overset{+}{C}HCH{=}CH{-}CH\overset{-}{O}}$$

A study of this question was of interest from the point of view of synthesis because the monoacetal of fumaraldehyde (IX) may be an interesting starting compound for the preparation of unsymmetrical polyenic compounds. With this object we synthesized the diacetal (VIII; R = CH_3) by the action of bromine on a methanolic solution of furan [6]. Previously, we prepared the bis(diethyl acetal) of malealdehyde (VIII, R = C_2H_5) by the selective hydrogenation of the diacetal of 2-butynedial [7] over Lindlar's catalyst, and it was shown that, according to the infrared spectrum, this diacetal contained some trans isomer (fumaraldehyde diacetal) as impurity. It was therefore of interest to determine the confirguration of the diacetal (VIII; R = CH_3) formed by the cleavage of the furan ring, and for this purpose we studied its infrared spectrum in the region of the nonplanar deformations of C–H bonds (700-1100 cm^{-1}). It was found that this product had the trans configuration and was therefore fumaraldehyde diacetal. In Fig. 7 we show the infrared spectra of the previously prepared diacetal (VIII; R = C_2H_5) and of the diacetal (VIII; R = CH_3) prepared in the present work; these leave no doubt about the configuration of each of these diacetals.

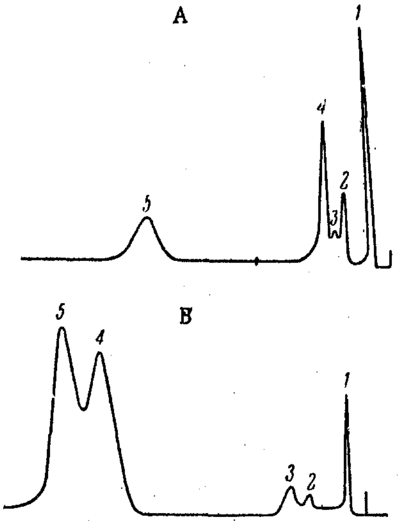


Fig. 3. A. Chromatogram of the hydrolyzate of a mixture of malonaldehyde and methylmalonaldehyde bis(diethyl acetal)s. Hydrolysis conditions: [(I) + (II)] : H_2O = 1 : 1; 100°; alcohol distilled off; 3% of p-$CH_3C_6H_4SO_3H$ in the aqueous phase; 5 min. Chromatography conditions: 104°; consumption of helium 80 ml/min: peak (1), alcohol; peak (2), $C_2H_5OCH = CHCHO$; peak (3), $(C_2H_5O)_2CHCH_2CHO$; peak (4), $C_2H_5OCH = C(CH)_3CHO$; peak (5), $(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2$. B. Chromatogram of the hydrolyzate of a mixture of malonaldehyde and methylmalonaldehyde bis (diethyl acetal)s. Hydrolysis conditions: [(I) + (II)] : H_2O = 1 : 1; 100°; 6% of H_3PO_4 in the aqueous phase; 10 min. Chromatography conditions: 100°; consumption of helium 70 ml/min: peak (1), alcohol; peak (2), $(C_2H_5O)_2CHCH_2CHO$; peak (3), $(C_2H_5O)_2CHCH(CH_3)CHO$; peak (4), $(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2$; peak (5); $(C_2H_5O)_2CHCH(CH_3)CH(OC_2H_5)_2$.

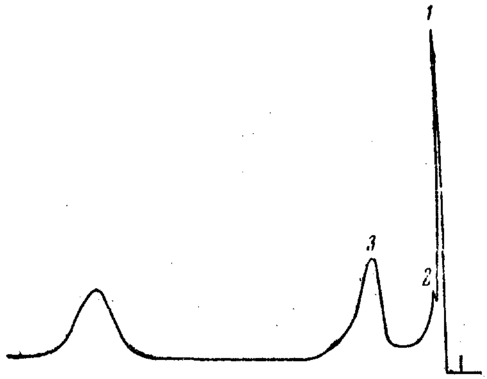


Fig. 4. Chromatogram of products of reaction between methylmalonaldehyde bis(diethyl acetal) and methylmalonaldehyde at 100° for 20 minutes in presence of traces of p-$CH_3C_6H_4SO_3H$. Chromatography conditions: 100°; consumption of helium 70 ml/min; peak (1), alcohol; peak (2), $HOCCH(CH_3)CHO$; peak (3), $(C_2H_5O)_2CHCH(CH_3)CHO$; peak (4), $(C_2H_5O)_2CHCH(CH_3)CH(OC_2H_5)_2$.

In a study of the hydrolysis of fumaraldehyde diacetal (VIII; R = CH_3) we showed that one of its acetal groupings is extremely readily hydrolyzed, even with water, with formation of 4,4-dimethoxycrotonaldehyde (X). The hydrolysis has this character not only when an equimolecular amount of water is used, but also in hydrolysis with excess of water in presence of phosphoric acid or even in absence of acid agents. Under certain conditions (see Experimental) the yield of the aldehydo-acetal (X) attains 70-75%, which makes this interesting product completely accessible. Syntheses of polyenic compounds from this substance will be published in the near future.

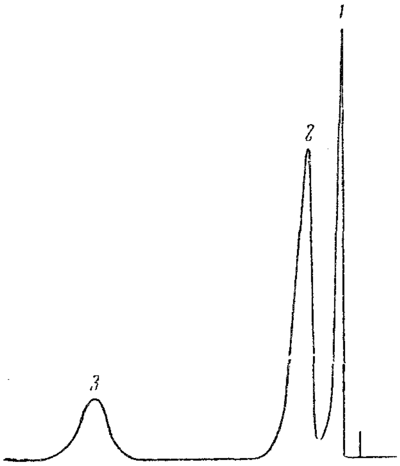


Fig. 5. Chromatogram of 3,3-diethoxypropionaldehyde after being heated at 100° for 20 minutes with traces of p-$CH_3C_6H_4SO_3H$. Chromatography conditions: 102°; consumption of helium 94 ml/min: peak (1), alcohol; peak (2), $C_2H_5OCH = CHCHO$; peak (3), $(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2$.

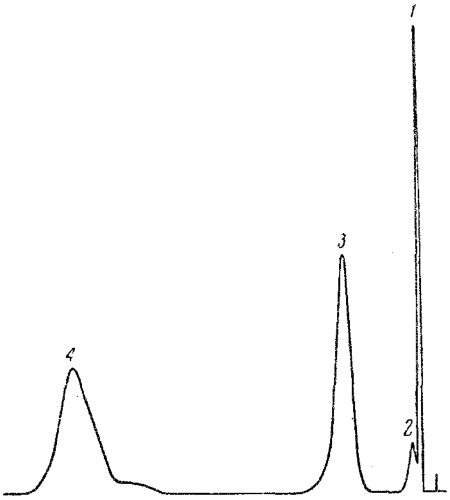


Fig. 6. Chromatogram of the hydrolyzate of dimethylmalonaldehyde bis(diethyl acetal) (for conditions see Experimental). Chromatography conditions: 100°; consumption of helium 65 ml/min: peak (1), alcohol; peak (2), $HOCC(CH_3)_2CHO$; peak (3), $(C_2H_5O)_2CHC(CH_3)_2CHO$; peak (4), $(C_2H_5O)_2CHC(CH_3)_2CH(OC_2H_5)_2$.

For the study of the hydrolysis of fumaraldehyde diacetal we made use of gas-liquid chromatography. In Fig. 8 we give typical chromatograms of hydrolyzates. As will be seen from these chromatograms, the hydrolysis of the trans diacetal (VIII; R = CH_3) is accompanied by the formation of a very small amount of a cyclic product, 2,5-dihydro-2,5-dimethoxyfuran, which may arise as the result of the partial isomerization of the original diacetal or of 4,4-dimethoxycrotonaldehyde into the cis form with subsequent cyclization. The fact that in the hydrolysis of fumaraldehyde diacetal (VIII; R = CH_3) the cyclic product is formed only as an impurity confirms again the trans configuration of the diacetal, for in the opposite case (cis configuration) the formation of a furan derivative in the hydrolysis process would undoubtedly form the main reaction.

EXPERIMENTAL

A mixture of equimolecular amounts of the diacetal and water containing 6% of phosphoric acid or 3% of p-toluenesulfonic acid was heated in a boiling water bath or at 55 ± 1° with good stirring in a flask fitted with a condenser set for distillation. Test samples were taken at definite intervals of time. Hydrolyzate samples were shaken for 0.5-1 hour with ground sodium bicarbonate or calcium carbonate for the neutralization of the catalyst, and were then filtered and used directly for gas-liquid chromatography. A gas-liquid chromatograph constructed in our laboratory was used [8]. The column was 5 m in length and was filled with 1% of silicone elastomer supported on sodium chloride; the carrier gas was helium.

Hydrolysis of Glyoxal Bis(diethyl acetal). A vigorously stirred mixture of 14 g of the bis(diethyl acetal) and 10 ml of a 3% solution of p-toluenesulfonic acid or a 6% solution of phosphoric acid was heated in a boiling water bath. After 3-5 hours the reaction mixture was neutralized by stirring it with ground calcium carbonate and extracted with ether. The ethereal solution was dried with magnesium sulfate. After fractionation we isolated 11.5 g of unchanged original bis(diethyl acetal), b.p. 65-68° (3 mm) and n_D^{19} 1.4060.

Preparation of 3,3-Diethoxy-2,2-dimethylpropionaldehyde. 10 g of dimethylmalonaldehyde bis(diethyl acetal) was stirred vigorously with 0.54 ml of 6% phosphoric acid in a boiling water bath for 30 minutes with removal of alcohol by distillation. The mixture was cooled, 1 g of calcium carbonate powder was added, and the mixture was stirred for 30 minutes, filtered, and fractionally distilled. We isolated 3.7 g of 3,3-diethoxy-2,2-dimethylpropionaldehyde; b.p. 70-72° (8 mm); n_D^{22} 1.4158. Found: C 59.11; 59.05; H 11.06; 11.10%. $C_9H_{18}O_3$. Calculated: C 59.23; H 11.18%.

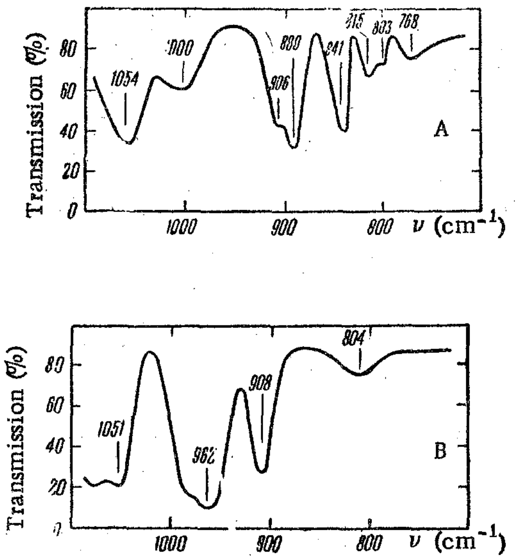


Fig. 7. Absorption spectrograms in the range 700-1100 cm^{-1} for malealdehyde bis(diethyl acetal) (A) and fumaraldehyde bis(dimethyl acetal) (B).

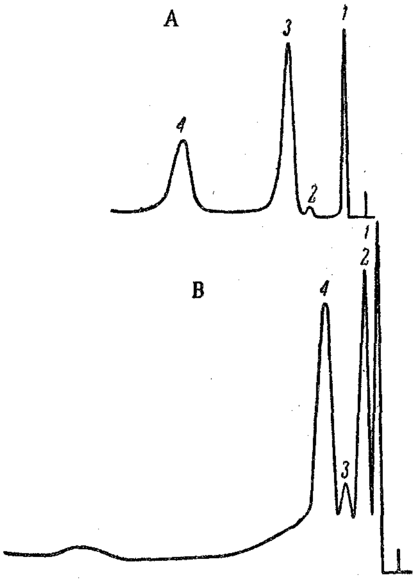


Fig. 8. A. Chromatogram of the hydrolyzate of fumaraldehyde bis(dimethyl acetal) (for conditions see Experimental). Chromatography conditions: 100°; consumption of helium 70 ml/min. B. Chromatogram of the hydrolyzate of fumaraldehyde bis(dimethyl acetal) (excess of water used). Peak (1), alcohol; peak (2), fumaraldehyde; peak (3), 2,5-dihydro-2,5-dimethoxyfuran; peak (4), 4,4-dimethoxycrotonaldehyde.

Preparation of Dimethylmalonaldehyde. 10 g of dimethylmalonaldehyde bis(diethyl acetal) was stirred vigorously with 6 ml of 6% phosphoric acid or 3% p-toluenesulfonic acid in a boiling water bath with removal of alcohol by distillation. After one hour the mixture was neutralized by stirring it with calcium carbonate; it was carefully extracted with ether, and the extract was dried with magnesium sulfate. By fractionation we isolated 2 g of the dialdehyde; b.p. 45-47° (1 mm); 63-65° (7 mm); n_D^{20} 1.4168. Found C 59.78; 59.61; H 7.94; 7.87%; $C_5H_8O_2$. Calculated: C 59.98; H 8.05%.

Preparation of 4,4-Dimethoxycrotonaldehyde. The hydrolysis of fumaraldehyde bis(dimethyl acetal) was carried out as described above. From 52.8 g of the acetal and 3 ml of phosphoric acid we obtained 26.7 g of 4,4-dimethoxycrotonaldehyde, b.p. 72-80° (11 mm) and n_D^{18} 1.4358. The structure of the product was confirmed by its reactions, which will be described in the next communication. Infrared spectra were determined on liquid samples with an IKS-12 apparatus having an NaCl prism.

SUMMARY

1. Gas-liquid chromatography (column containing a silicone elastomer on a sodium chloride support) was applied in a study of the hydrolysis of some diacetals.

2. The first stage in the hydrolysis of malonaldehyde diacetals is unsymmetrical hydrolysis at one of the acetal groupings with formation of 3,3-diethoxypropionaldehydes. Secondary products of this reaction are 3-ethoxyacroleins formed by the elimination of a molecule of alcohol from 3,3-diethoxypropionaldehydes.

3. It was shown that intermolecular transacetalization occurs between diacetals and dialdehydes.

4. It was proved that the 2-butendial diacetal prepared by the cleavage of furan has the trans configuration (fumaraldehyde diacetal). Its partial hydrolysis of 4,4-dimethoxycrotonaldehyde was studied.

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