CHEMISTRY OF ACETALS

COMMUNICATION 2. REACTION OF ACETAL WITH DIKETENE AND WITH ACETOACETIC ESTER

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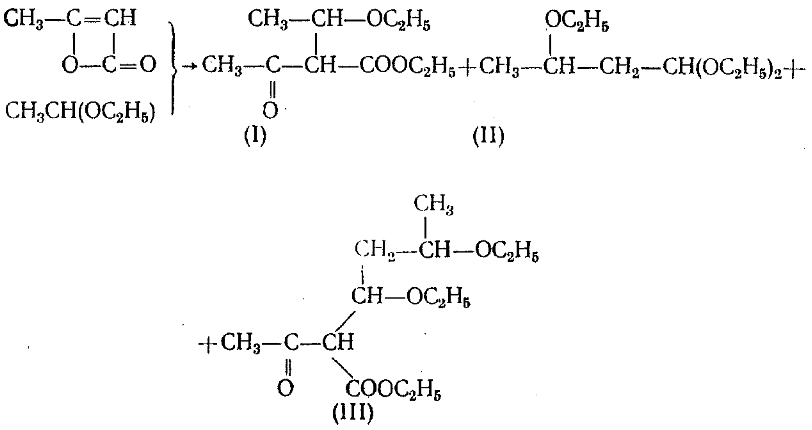
Continuing the study of the conversions of acetals [1], we decided to investigate the reactions of acetal with diketene and with acetoacetic ester for their subsequent use as a new method of lengthening carbon chains. It was found that the reaction of acetal with diketene in the presence of boron trifluoride etherate forms a mixture of products and the determination of their structures and the probable scheme for their formation is the subject of the present communication.

From the reaction products of diketene and acetal we isolated three products: 2-(1'-ethoxy)ethylacetoacetic ester (I), 1,1,3-triethoxybutane (II), and 2-(1',3'-diethoxy)butylacetoacetic ester (III).

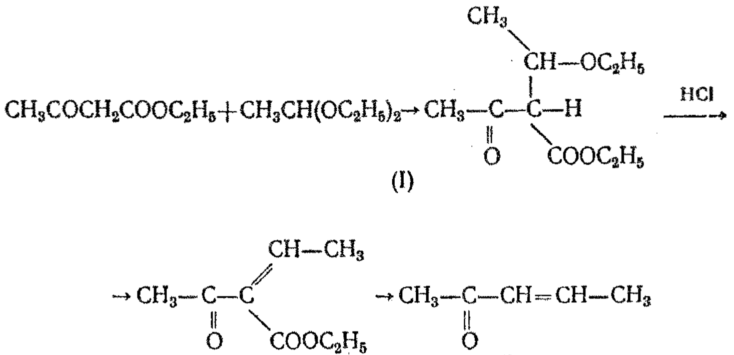


(I) (II) (III)

The main reaction product was 2-(1'-ethoxy)ethylacetoacetic ester (I) and this was formed in up to 50% yield as a result of direct alkylation of diketene with the formation of a new carbon—carbon bond. Its structure was established by acid hydrolysis to ethylideneacetoacetic ester (IV) and ethylideneacetone (V), which were characterized through crystalline 2,4-dinitrophenylhydrazones and spectra.

A conclusive demonstration of the structure of the ester (I) was obtained by studying the reaction of acetal with acetoacetic ester. As we showed for the first time, this reaction in the presence of such a catalyst as BF_3 etherate gives up to 70% yield of 2-(1'-ethoxy)ethylacetoacetic ester (I). This reaction evidently may be a general method of lengthening a carbon chain. (See scheme on next page).

As will be shown below, under the conditions of the reaction of diketene with acetal there is elimination of alcohol from the acetal so that 2-(1'-ethoxy) ethylacetoacetic ester (I) may be formed both by direct reaction



$$CH_3COCH_2COOC_2H_5 + CH_3CH(OC_2H_5)_2 \rightarrow CH_3-\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3\diagdown CH-OC_2H_5}{|}}{C}(-H)\diagdown COOC_2H_5 \xrightarrow{HCl}$$

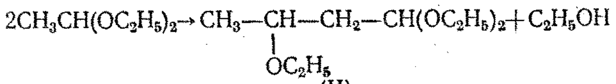
(I)

$$\rightarrow CH_3-\underset{\underset{O}{\|}}{C}-C(=CH-CH_3)\diagdown COOC_2H_5 \rightarrow CH_3-\underset{\underset{O}{\|}}{C}-CH=CH-CH_3$$

(IV) (V)

of acetal with diketene and by a secondary reaction of acetal with acetoacetic ester, obtained by the reaction of diketene with alcohol. It might also be considered that 2-(1'-ethoxy)ethylacetoacetic ester (I) could be formed by the reactions of acetal with 3-ethoxycrotonic ester, acetoacetic ester with vinyl ether [2], or, finally, diketene with vinyl ether. Special experiments showed that in the first two cases the reaction gives only insignificant yields while in the latter case there is vigorous polymerization of vinyl ether and decomposition of diketene to acetone. Thus, these reactions cannot explain the formation of 2-(1'-ethoxy)ethylacetoacetic ester (I).

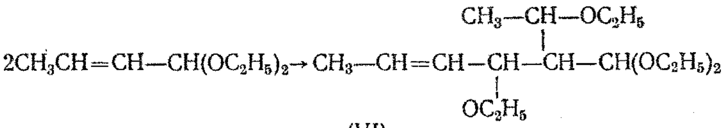
The formation of 1,1,3-triethoxybutane (II) by the reaction of diketene and acetal is extremely interesting. It is readily seen that this product could only be formed by dimerization of the starting acetal under the action of boron trifluoride. Despite the fact that the possibility of such dimerization under the action of catalysts has been reported previously in a patent [3], we considered it necessary to study it in more detail as it is of great independent interest. It was found that under the conditions we developed (see experimental section) with BF_3 or a mixture of BF_3 and $ZnCl_2$ as the catalyst, acetal is dimerized in up to 40% yield (on the acetal reacting) to form 1,1,3-triethoxybutane (II), whose structure was readily demonstrated by its conversion to crotonaldehyde 2,4-dinitrophenylhydrazone.



$$2CH_3CH(OC_2H_5)_2 \rightarrow CH_3-\underset{\underset{OC_2H_5}{|}}{CH}-CH_2-CH(OC_2H_5)_2 + C_2H_5OH$$

(II)

As we showed, in the case of unsaturated acetals, the dimerization may also proceed without the elimination of alcohol. Thus, as a result of addition at the double bond, crotonaldehyde acetal gives up to a 50% yield of 2-(1'-ethoxy)-1,1,3-triethoxy-4-hexene (VI), whose structure was demonstrated by conversion to 2-ethylhexanal, the 2,4-dinitrophenylhydrazone of which did not depress the melting point of an authentic sample.



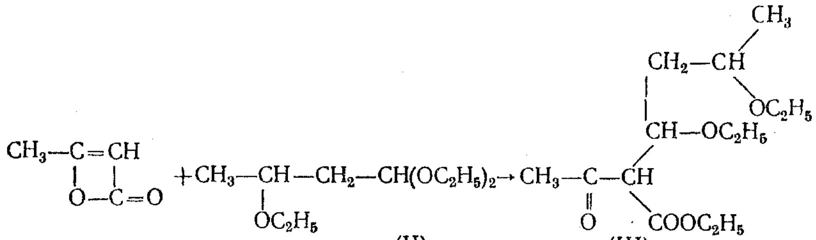
$$2CH_3CH=CH-CH(OC_2H_5)_2 \rightarrow CH_3-CH=CH-\underset{\underset{OC_2H_5}{|}}{CH}-\overset{\overset{CH_3-CH-OC_2H_5}{|}}{CH}-CH(OC_2H_5)_2$$

(VI)

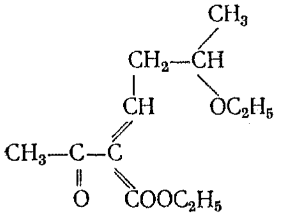
Both these modes of dimerization of acetals are of very great interest for the synthesis of polyene compounds.

It was most difficult to isolate and demonstrate the structure of the third product from the reaction of diketene and acetal, which was found to decompose partly even during vacuum distillation; however, we were able to demonstrate that it was the product from the addition of one molecule of diketene to 1,1,3-triethoxybutane (II). (See scheme on next page).

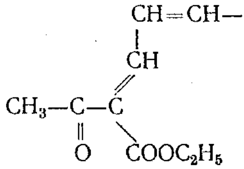
In accordance with the rule established above for the addition of acetal to diketne, it may be considered that this product had structure (III), though the 2,4-dinitrophenylhydrazone obtained from it (m.p. 130-131°) corresponded in analysis to the product from the elimination of one molecule of alcohol(VII). (See scheme on next page).



(II) (III)



(VII)



(VIII)

The unsaturated keto ester (VII) could also be obtained in low yield by the direct reaction of diketene with 1,1,3-triethoxybutane and the infrared spectrum confirmed that it had the structure (VII). However, the 2,4-dinitrophenylhydrazone obtained from it had m.p. 185- 186° and corresponded in analysis to the 2,4-dinitrophenylhydrazone of the diene keto ester (VIII); its ultraviolet spectrum had λ_{max} 370 mμ (in heptane), which demonstrates that it contained a carbonyl group conjugated with a diene system. All the data examined above show that the product (III) actually has the structure assigned to it.

EXPERIMENTAL

Reaction of diketene with acetal. To a mixture of 41 g of acetal and 5 ml of BF_3 etherate was added a solution of 16.8 g of diketene in 30 g of acetal at such a rate that the temperature did not rise above 40-50°. On the following day the mixture was neutralized with sodium bicarbonate and extracted with ether and the extract dried with magnesium sulfate and distilled. Two successive distillations yielded: 1) 2 g of a fraction with b.p. up to 60° (20 mm) n_D^{20} 1.4022, containing 1,1,3-triethoxybutane (II). The 2,4-dinitrophenylhydrazone obtained from this fraction had m.p. 187-188° and did not depress the melting point of crotonaldehyde 2,4-dinitrophenylhydrazone. 2) 20.4 g of a fraction with b.p. 88-94° (4 mm); n_D^{20} 1.4306; 3) 8.8 g of a fraction with b.p. 108-118° (3 mm); n_D^{20} 1.14418. Fraction 2 was redistilled to yield 19.7 g of 2-(1'-ethoxy)ethylacetoacetic ester (I) with b.p. 84-85° (3 mm); n_D^{21} 1.4292. Found: C 59.73; 59.81; H 8.83; 8.77; (OC_2H_5) 42.5%. $C_{10}H_{18}O_4$. Calculated: C 59.38; H 8.97; (OC_2H_5) 44.6%*.

The 2,4-dinitrophenylhydrazone obtained from (I)** (orange needles with m.p. 163-164° from alcohol) did not depress the melting point of ethylideneacetoacetic ester 2,4-dinitrophenylhydrazone (IV) [5]. Found: C 50.31; 51.21; H 4.91; 5.04; N 17.17; 17.18%. $C_{14}H_{16}N_4O_6$. Calculated: C 50.00; H 4.80; N 16.66%.

Fraction 3 changed on redistillation and we could only isolated from it a small amount of a product with b.p. 80-81° (1 mm); n_D^{20} 1.4482, which corresponded in analysis to 2-(1',3'-diethoxy)butylacetoacetic ester (III). Found: C 61.33; 61.45; H 8.76; 8.70; (OC_2H_5) 46.9%. $C_{14}H_{26}O_5$. Calculated: C 61.29; H 9.55; (OC_2H_5) 49.2%.

After chromatography on Al_2O_3, the 2,4-dinitrophenylhydrazone obtained from this fraction had m.p. 131-132° (from ligroin—benzene) and corresponded in composition to the 2,4-dinitrophenylhydrazone of (VII); λ_{max} 355 mμ (in heptane). Found: C 52.46; 52.55; H 5.60; 5.77%. $C_{18}H_{24}N_4O_7$. Calculated: C 52.80; H 5.86%.

Acid hydrolysis of 2-(1'-ethoxy)ethylacetoacetic ester (I). A mixture of 16 g of 2-(1'-ethoxy)ethylacetoacetic ester (I) and 50 ml of 2 N HCl was heated at 60° for 18 hr. The mixture was neutralized with bicarbonate and carefully extracted with ether (in a percolator). The ether layer was dried and distilled. We isolated 2.5 g of a substance with b.p. 68—85°, from which we obtained a 2,4-dinitrophenylhydrazone with m.p. 159-160° (from

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*It has been found [4] that the normal method of analysis for ethoxyl groups gives an error of 2-3% with a similar type of compound. This was confirmed by a special series of analyses, that were kindly carried out by N. L. Shitikova.

**The 2,4-dinitrophenylhydrazones of the ethoxy derivatives precipitated from 2 N HCl as oils. To obtain crystals, it was necessary to extract with ether, dry with $MgSO_4$, and distill the ether from the extract. If this was insufficient it was necessary to use chromatography on Al_2O_3.

ethyl acetate) that did not depress the melting point of ethylideneacetone (V) 2,4-dinitrophenylhydrazone [6]. Found: N 20.80; 20.85%. $C_{11}H_{12}N_4O_4$. Calculated: N 21.22%.

In addition to ethylideneacetone, redistillation of the higher-boiling fractions yielded 3.1 g of ethylideneacetoacetic ester (IV) with b.p. 86-88° (7 mm); n_D^{20} 1.4474 [2]. Found: C 61.44; 61.39; H 8.07; 8.07%. $C_8H_{12}O_3$. Calculated: C 61.52; H 7.75%. The 2,4-dinitrophenylhydrazone obtained from it had m.p. 161-162° (from alcohol) and did not depress the melting point of an authentic sample.

Preparation of 2-(1'-ethoxy) ethylacetoacetic ester (I). To a mixture of 26 g (0.2 mole) of acetoacetic ester and 70.8 g (0.6 mole) of acetal was added 5 ml of BF_3 etherate and the reaction mixture left at room temperature for a day. The reaction product was neutralized with solid sodium bicarbonate, filtered, and distilled. We isolated 38.8 g of the starting acetal and 12.0 g of acetoacetic ester. Two distillations of the residue yielded 15.9 g of 2-(1'-ethoxy) ethylacetoacetic ester (I) with b.p. 70-73° (1.5 mm); n_D^{20} 1.4276 which represents 78% on the acetoacetic ester reacting. The 2,4-dinitrophenylhydrazone obtained from it had m.p. 163-165° and did not depress the melting point of ethylideneacetoacetic ester 2,4-dinitrophenylhydrazone. In addition to this dinitrophenylhydrazone, we also isolated a small amount of an isomeric 2,4-dinitrophenylhydrazone as yellow needles with m.p. 121-122° (from alcohol), the ultraviolet spectrum of which showed the absence of conjugation (λ_{max} 346 mμ). Found: C 50.05; 49.85; H 4.73; 4.60%. $C_{14}H_{16}N_4O_4$. Calculated: C 50.00; H 4.80%.

Dimerization of acetal. A mixture of 35.4 g of acetal, 3 g of anhydrous $ZnCl_2$, and 3 ml of BF_3 etherate was left at room temperature for three days and then neutralized with dry sodium bicarbonate, filtered, and distilled. We isolated 6.6 g of the starting acetal, 7.1 g of 1,1,3-triethoxybutane (II) with b.p. 68-73° (8 mm); n_D^{20} 1.4062 [7] and 4.3 g of higher-boiling products. The 1,1,3-triethoxybutane obtained was characterized as crotonaldehyde 2,4-dinitrophenylhydrazone with m.p. 186-188° (λ_{max} 355 mμ), which did not depress the melting point of an authentic sample. In addition to this dinitrophenylhydrazone, we were able to isolate a very small amount of 3-ethoxybutyraldehyde 2,4-dinitrophenylhydrazone as fine golden platelets with m.p. 79-80° (from aqueous alcohol). Found: C 48.15; H 5.53%. $C_{12}H_{16}N_4O_5$. Calculated: C 48.64; H 5.44%.

Dimerization of crotonaldehyde acetal. To 14.4 g of crotonaldehyde acetal was carefully added 0.5 ml of BF_3 etherate with cooling. After the vigorous reaction, the mixture was neutralized with sodium bicarbonate, filtered, and distilled. Two distillations yielded 7.3 g of the dimer (VI) with b.p. 105-108° (3 mm); n_D^{17} 1.4366. Found: C 66.40; 66.64; H 10.83; 10.80; (OC_2H_5) 59.3%. $(C_8H_{16}O_2)$. Calculated: C 66.63; H 11.18; (OC_2H_5) 62.6%.

Reaction of diketene with 1,1,3-triethoxybutane (II). To a mixture of 7.6 g (0.08 mole) of diketene and 15.5 g (0.08 mole) of 1,1,3-triethoxybutane was added 3 ml of BF_3 etherate at such a rate that the temperature did not rise above 30°. After 2 hr, the reaction product was neutralized with dry sodium bicarbonate, filtered, and distilled. We obtained 3.4 g of acetoacetic ester (confirmed by preparation of the 2,4-dinitrophenylhydrazone) and 8.5 g of a fraction with b.p. 94-140° (1.5 mm); n_D^{20} 1.4502; two distillations of the latter yielded a product with b.p. 87-91° (1 mm); n_D^{20} 1.4626, which corresponded in analysis to the substance (VII). Found: C 62.73; 62.68; H 8.59; 8.66%. $C_{12}H_{20}O_4$. Calculated: C 63.2; H 8.76%.

The infrared spectrum of this compound had absorption bands at 1640 and 1725 cm^{-1}, which confirmed that it contained carbonyl and carboxyl groups conjugated with a double bond. The 2,4-dinitrophenylhydrazone obtained from it formed dark red needles with m.p. 185-186° (from alcohol) and corresponded in analysis to the 2,4-dinitrophenylhydrazone of the diene keto ester (VIII), as was confirmed by the ultraviolet spectrum: λ_{max} 370 mμ (in heptane). Found: 52.88; 53.12; H 5.06; 5.28%. $C_{16}H_{18}N_4O_6$. Calculated: C 53.1; H 4.96%.

SUMMARY

1. The reaction of acetal with diketene in the presence of BF_3 etherate gives as the main product 2-(1'-ethoxy)ethylacetoacetic ester (I). 1,1,3-Triethoxybutane (II) and 2-(1',3'-diethoxy) butylacetoacetic ester (III) are formed as by-products.

2. The reaction of acetal with acetoacetic ester was studied and found to give a good yield of 2-(1'-ethoxy) ethylacetoacetic ester (I).

3. On the example of acetaldehyde and crotonaldehyde acetals it was shown that acetals may be dimerized to compounds which could be of interest for the synthesis of polyene compounds.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**