

# Ketoacetal Chemistry: I. Reactions of 4,4-Diethoxy-2-trimethylsilyloxy-1-butene with Dialdehydes Acetals

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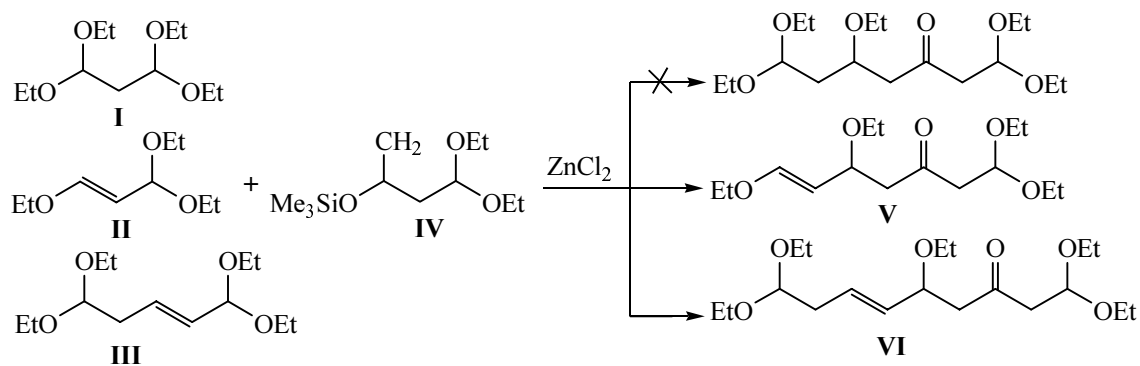
**Abstract**—Condensation of 4,4-diethoxy-2-trimethylsilyloxy-1-butene with malonic and glutaric aldehydes tetraethyl acetals and  $\beta$ -ethoxyacrolein diethyl acetal catalyzed by zinc chloride was investigated. Synthesis of 1,1,5,7-tetraethoxy-6-hepten-3-one and 1,1,5,7,7-pentaethoxy-6-nonen-3-one was performed.

Ketoacetals are well studied compounds that are extensively used in the organic synthesis.  $\alpha$ -Keto-acetals were described by Tamura *et al.* [1, 2] and Niecco *et al.* [3] and served as precursors in the synthesis of many biologically active compounds. Even more examples are known of application of  $\beta$ -keto-acetals [4–6]. These compounds are prepared both by traditional procedures, e.g., by Claisen condensation, and also by more modern methods: with the use of stable enol forms of carbonyl compounds [7–10] that has considerably extended the range of the structures obtained. Ketoacetals with the other reciprocal positions of the carbonyl functions ( $\gamma$ ,  $\delta$ , and  $\epsilon$ ) are less understood [11], and even less studies concern the preparation methods and chemical properties of ketodiacetals. These compounds are promising for a wide application because their potential is a lot larger than that of their electronic analogs, bisaminoketones, which are already extensively used [12].

The study of ketodiacetals is hampered by the lack of accessible preparation methods. The only existing publication [13] describes the preparation 1,1,5,5-tetraethoxy-3-pentanone and 1,1,5,5-tetraethoxy-2,4-trimethylene-3-pentanone, but the applied method of ketones alkylation with triethyl orthoformate in the presence of *N,N*-diisopropylamine in dichloromethane at  $-78^\circ\text{C}$  is unsuitable for preparation of unsymmetrical ketoacetals and those of versatile structure, and besides the yields of compounds obtained were small.

We formerly demonstrated [14, 15] that the first synthesized silyl enol ethers containing an acetal group could be regarded as convenient initial compounds for preparation of  $\beta,\beta'$ -ketodiacetals by reaction with the triethyl orthoformate in the presence of zinc chloride.

The goal of the present study was testing the possibility of performing a similar reaction with dialdehydes acetals to obtain ketodiacetals with various reciprocal positions



of the carbonyl functions. As the study objects we chose acetals of malonic aldehyde **I**,  $\beta$ -ethoxyacrolein **II**, and glutaconic aldehyde tetraethyl acetal (**III**).

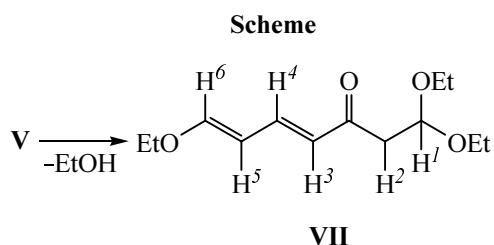
The reaction with the two former acetals would give oxo-substituted derivatives of 1,7-dialdehydes, and with the latter acetal a derivative of 1,9-dialdehyde would be obtained.

Malonic aldehyde tetraacetal (**I**) is known [16] to be a compound of low reactivity that reluctantly reacts with unsubstituted or alkyl-substituted alkyl enol ethers. We showed before that the condensation with compound **I** afforded fair yields only at bringing into the reaction either alkyl enol ethers with electron-acceptor substituents [17] or silyl enol ethers [18]. These facts are understandable for only enol ethers possessing as high stability as those mentioned can survive the prolonged reaction under stringent conditions used in this condensation.

We failed to find appropriate conditions for 4,4-diethoxy-2-trimethylsilyloxy-1-butene (**IV**) condensation with malonic aldehyde tetraethyl acetal (**I**): Neither the variation of reaction temperature (from room temperature to 60°C), nor the use of more catalyst (from 0.3 mol to 1 mol), nor the increased reaction time resulted in the target product. In all cases the unreacted diacetal **I** was recovered nearly quantitatively.

The acetals of  $\alpha,\beta$ -unsaturated aldehydes are known to be more reactive with respect to nucleophilic substitution than their saturated analogs. Therefore we attempted to prepare the desired oxo derivative of 1,7-dialdehyde by condensation with  $\beta$ -ethoxyacrolein diethyl acetal (**II**). Actually, its condensation with 4,4-diethoxy-2-trimethylsilyloxy-1-butene (**IV**) was successful: compound **V** was obtained in a 71.5% yield in 1 h. The reaction occurred at  $-2\dots-5^\circ\text{C}$  and equimolar amounts of acetal **II**, silyl enol ether **IV**, and catalyst ( $\text{ZnCl}_2$ ). The reaction product was obtained as a mixture of *E*- and *Z*-isomers in the ratio 7:3 (identical to the isomer ratio in the initial acetal **II**).

Ketoacetal **V** is stable at storage in a refrigerator, but at dissolution in deuteriochloroform at room temperature it relatively quickly spontaneously undergoes dealkoxylation affording a diene along the scheme:



The formation of diene structure **VII** was observed in the  $^1\text{H}$  NMR spectrum. In the  $^1\text{H}$  NMR spectrum of diene **VII** the proton signals appeared in the following order,  $\delta$ , ppm:  $\text{H}^3$  (6.07),  $\text{H}^4$  (7.19),  $J_{\text{H}^3\text{H}^4}$  15.3 Hz;  $\text{H}^5$  (5.67),  $\text{H}^6$  (6.92),  $J_{\text{H}^5\text{H}^6}$  12.5 Hz. The location of signals from protons  $\text{H}^1$  and  $\text{H}^2$  (4.95 and 2.84 ppm) changed insignificantly.

Under similar conditions we also carried out the condensation of silyl enol ether **IV** with glutaconic aldehyde tetraethyl acetal (**III**). The reaction product formed in a 85% yield in 0.5 h at  $0\dots-2^\circ\text{C}$ . The condensation occurred selectively at the  $\alpha,\beta$ -unsaturated acetal group. The second acetal fragment did not take part in the reaction as evidenced by the signal of the acetal proton  $\text{H}^8$  which appeared as a triplet in the region of 4.49 ppm

In the IR spectra of synthesized ketoacetals **V** and **VI** the characteristic absorption bands of  $\text{C}=\text{O}$  groups vibrations appeared in the region 1720 (**V**) and 1710  $\text{cm}^{-1}$  (**VI**).

Hence the condensation of 4,4-diethoxy-2-trimethylsilyloxy-1-butene (**IV**) with dialdehydes acetals afforded in good yields previously unknown diacetals of 1,7- and 1,9-ketodialdehydes.

## EXPERIMENTAL

$^1\text{H}$  NMR spectra were registered on a spectrometer Bruker WM-250 at operating frequency 250 MHz from 10% solutions in deuteriochloroform. IR spectra were recorded on a Shimadzu IR-435 instrument from thin films. TLC was carried out on Silufol UV-254 plates using solvent system petroleum ether–ethyl acetate, 2:1, development in iodine vapor and by calcination. The column chromatography was performed on silica gel (Kieselgel 60), gradient elution with a mixture petroleum ether–ethyl acetate, from 100:1 to 10:1.

**1,1,5,9,9-Pentaethoxy-6-nonen-3-one (VI).** To a solution of 0.54 g (0.0022 mol) of 1,1,5,5-tetraethoxy-2-pentene (**III**) in 63 ml of 20% solution of zinc chloride (0.0022 mol) in ethyl acetate was added dropwise while stirring at  $0\dots-2^\circ\text{C}$  0.51 g (0.0022 mol) of 4,4-diethoxy-2-trimethylsilyloxy-1-butene (**IV**). The reaction mixture was stirred at this temperature for 0.5 h till complete consumption of compound **IV** (TLC monitoring). Then the reaction mixture was diluted with an equal volume of ethyl ether, washed with a saturated solution of sodium hydrogen carbonate and water. The washings were extracted with ethyl ether, the ether solution was dried

over sodium sulfate. On removing the solvent the residue was subjected to column chromatography. We obtained 0.65 g (85%) of 1,1,5,9,9-pentaethoxy-6-nonen-3-one (VI),  $R_f$  0.66.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.37 t (2H,  $J$  5.9 Hz), 2.49 d.d (1H,  $J$  15.75, 4.6 Hz), 2.76 d.d (1H,  $J$  15.75, 4.6 Hz), 2.77 d (2H,  $J$  5.9 Hz), 4.15 m (1H), 4.49 t (1H,  $J$  5.9 Hz), 4.92 t (1H,  $J$  5.9 Hz), 5.40 d.d (1H,  $J$  15.1 Hz), 5.65 m (1H). Found, %: C 69.38; H 10.01.  $\text{C}_{19}\text{H}_{36}\text{O}_6$ . Calculated, %: C 69.29; H 10.08.

**1,1,5,7-Tetraethoxy-6-hepten-3-one (V).** Likewise from 4,4-diethoxy-2-trimethylsilyloxy-1-butene (IV) and  $\beta$ -ethoxyacrolein diethyl acetal (II) within 1 h at  $-2\text{...}-5^\circ\text{C}$  was obtained 1,1,5,7-tetraethoxy-6-hepten-3-one (V). Yield 71.4%,  $R_f$  0.64.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.51 d.d (1H,  $J$  15.76, 4.6 Hz), 2.78 d (2H,  $J$  5.7 Hz), 2.79 d.d (1H,  $J$  15.76, 4.6 Hz), 4.07 m (0.7H), 4.29 d.d (0.3H,  $J$  6.06, 7.35 Hz), 4.60 d.d (0.7H,  $J$  7.88, 14.92 Hz), 4.74 m (0.3H), 4.93 t (1H,  $J$  5.7 Hz), 6.08 d (0.3H,  $J$  7.35 Hz), 6.44 d (0.7H,  $J$  14.92 Hz). Found, %: C 62.51; H 9.78.  $\text{C}_{15}\text{H}_{28}\text{O}_5$ . Calculated, %: C 62.47; H 9.79.

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