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Reaction of 2-Alkoxypropenals with 2-Mercaptoethanol*

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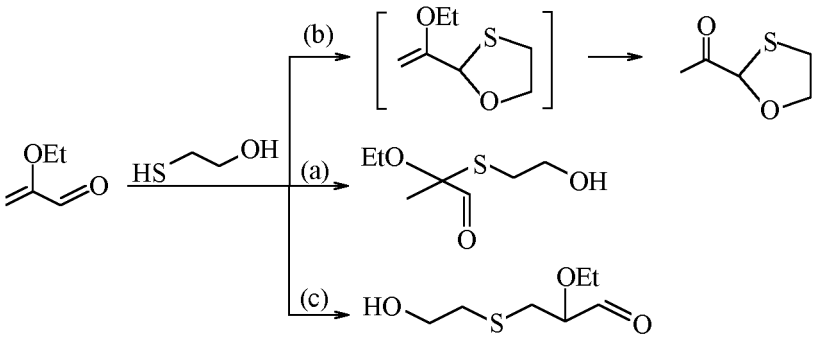
Abstract—The reaction between 2-alkoxypropenals and 2-mercaptoethanol was studied at 20 and 60°C by means of ^{1}H NMR and GC-MS methods. Under kinetically controlled conditions (20°C, 7–30 days) with no catalyst the addition of 2-mercaptoethanol to 2-alkoxypropenals occurs along Markownikoff rule. The arising 2'-hydroxyethylthio-2-alkoxypropanal undergoes isomerization into the 2-hydroxy-3-alkoxy-3-methyl-1,4-oxathiane that at heating in the presence of catalytic amounts of acids is converted into 2-methyl-2-formyl-1,3-oxathiolane. The reaction of 2-alkoxypropenals with 2-mercaptoethanol at heating (60°C, 3 h) in the presence of acids affords 2-methyl-2,2'-bi(1,3-oxathiolane) even at 2-mercaptoethanol deficit. At the double excess of the latter the 2-methyl-2,2'-bi(1,3-oxathiolane) was obtained in quantitative yield. The presumable schemes of conversion of 2-hydroxy-3-alkoxy-3-methyl-1,4-oxathiane into 2-methyl-2-formyl-1,3-oxathiolane and 2-acetyl-1,3-oxathiolane are discussed.

The reactions of mercapto groups of glutathione [1] and cysteine [2] with α,β-unsaturated aldehydes govern the biological activity of the latter.

2-Alkoxypropenals combine in their structure the fragments of the vinyl ether and the acrolein. Depending on a reagent or reaction conditions this highly reactive bonds system with electron-donor and electron-acceptor substituents can react in three directions: Markownikoff addition [3], Michael addition [4], and addition to the carbonyl group [4, 5].

The target of this study was elucidation of the regiodirection in reaction of 2-alkoxypropenals with a bifunctional reagent, 2-mercaptoethanol, in the neutral and acidic media. If the substrate molecule is regarded as an α-formyl-substituted vinyl ether then the expected reaction would be addition of the sulfhydryl group along Markownikoff rule as in reactions with thiols [3] and alcohols [6] (path *a*). However further route of the reaction remained unclear. If the system under study is regarded as an acryl one then it is presumable that occurs 1,2-addition [7, 8, 9] in the presence of acids (path *b*) or 1,4-addition [10] in the absence of a catalyst (path *c*); the latter direction is characteristic of unsubstituted acrolein in reactions with thiols [7, 10], dithiols [10], or diols [11].



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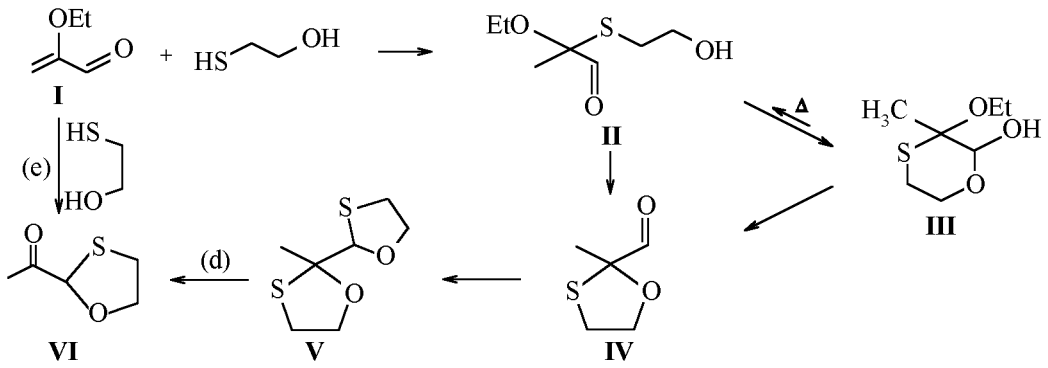


The reaction was studied by an example of 2-ethoxypropenal. The reaction progress was monitored by ^{1}H NMR and GC-MS methods. In the absence of catalyst at room temperature the reaction of 2-ethoxypropenal (**I**) and 2-mercaptoethanol occurs with heat evolution. Therewith in the first stage the sulfhydryl group of the reagent adds to the double bond of the substrate along the Markownikoff rule. Then follows an intramolecular addition of the hydroxy group of intermediate **II** to the carbonyl group yielding 2-hydroxy-3-methyl-3-ethoxy-1,4-oxathiane (**III**).

This sequence of stages is evidenced by disappearance in the IR spectrum of the reaction mixture of the absorption bands belonging to 2-ethoxypropenal ($\nu_{C=C}$ 1610 and $\nu_{C=O}$ 1710 cm^{-1}) and appearance of a single broad band of the OH group (3350 cm^{-1}). The structure of cyclic semiacetal **III** was also confirmed by the data of ^{1}H NMR spectrum and GC-MS. According to ^{1}H NMR semiacetal **III** arises in two diastereomeric forms in the ratio from 1:14 to 3:1 depending on the preparation conditions (see Experimental). The semiacetal **III** formation to complete consumption of the initial reactants in the absence of a catalyst takes two months at 20°C and 5 h at 60°C. Therewith in the cold semiacetal **III** forms regiospecifically and diastereoselectively, and at heating its content in the reaction mixture in 3 h amounts to 60% (see the table, run no. 2a) and further its content decreases presumably due to the thermal isomerization into semithioketal **II** that subsequently is converted through intramolecular *trans*-acetalization into a cyclic semithioketal of methylglyoxal, 2-methyl-2-formyl-1,3-oxathiolane (**IV**). Besides at heating is also observed formation of an admixture of isomeric methylglyoxal thioacetal, 2-acetyl-1,3-oxathiolane (**VI**). According to ^{1}H NMR data after 5 h of heating the reaction mixture contains compounds **III**, **IV**, and **VI** in 3:7:1 ratio. The formation of thioacetal **VI** may be rationalized by assumption that in a small amount arises a bicyclic methylglyoxal acetal, 2-methyl-2,2'-bi(1,3-oxathiolane) (**V**), whose ketal fragment suffers hydrolysis under the reaction conditions (path *d*). In the absence of an acid catalyst a hydrolysis of the vinyloxy group of the initial substrate **I** and formation of thioacetal at the aldehyde group to afford thioacetal **VI** is less probable (path *e*). An intramolecular rearrangement of semiacetal **III** into acetal **VI** along the scheme given above is also presumable.

At cautious evaporation from the reaction mixture of the solvent (ether, benzene) or at keeping the reaction mixture without solvent for 6–7 days semiacetal **III** crystallized. Therefore we were able to purify it and to have good elemental analyses. In the ^{1}H NMR spectrum of the crystalline substance as a rule appear signals corresponding to one of the diastereomers. The thermal stability of this cyclic semiacetal was sufficiently high to be heated to 100°C (in DMSO) for 1 min in the NMR tube; no changes in the spectrum was observed after such treatment. However at heating in benzene at 70°C for 2 h one diastereomer to 60% is converted into the other diastereomeric form.

As should be expected at vacuum distillation semiacetal **III** is decomposed yielding 2-hydroxyethylthio-2-ethoxypropanal (**II**). It is evidenced by ^{1}H NMR spectrum of the freshly distilled fraction. In the spectrum besides the weak signals of semiacetal **III** appears a signal with the chemical shift δ 9.65 ppm not observed in the other compounds obtained in this series of transformations; the signals inherent to the cyclic conformations of compound **III** (groups SCH_2 and OCH_2) nearly completely disappear, and are present the signals from the group –OCH_2CH_2S– subjected to free rotation (2.8 m CSH_2 and 3.7 m OCH_2). In the IR spectrum is observed an absorption band of the carbonyl group (1740 cm^{-1}) and a strong band

Reaction of 2-mercaptoethanol with 2-ethoxypropenal at equimolar ratio

Run no.	Catalyst	Solvent (molecular sieves)	*T*, °C	Reaction time	Reaction products and their ratio in the reaction mixture, mol%, (^{1}H NMR data)			
					III	**IV**	**V**	**VI**
1	–	Benzene	20	60 days	Quantitative			
2a	–	Benzene	60	3 h	58	4		1
2b	–	Benzene	60	5 h	27	64		9
3	–	–	20	4 days	70	30		
4	CF_3COOH (5 mol%)	Benzene	20	24 h	80	15		
5	*p*-TsOH (1 mol%)	Ether	20	5 h	82	15		
6	*p*-TsOH (5 mol%)	Ether	50	3 h	5		80	
7[a]	*p*-TsOH (7 mol%)	Ether mol. sieves 4A	20	7 days			Quantitative	
8[a]	*p*-TsOH (5 mol%)	Benzene	60	2 h			Quantitative	

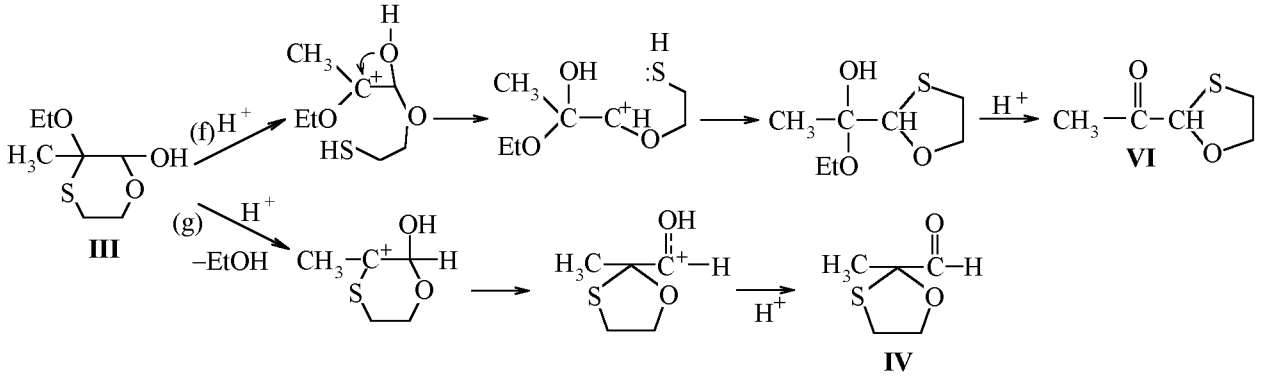
[a] Double (molar) excess of 2-mercaptoethanol.

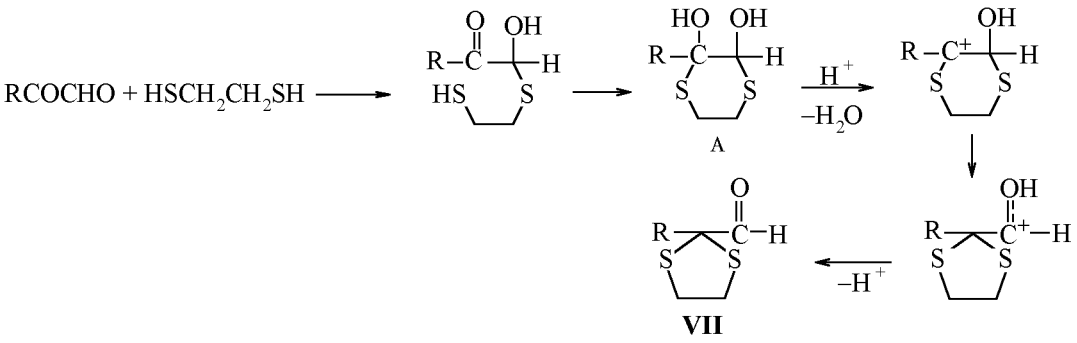
of associated OH group (3430 cm^{-1}). Presumably the GC-MS method also registered isomer **II** as the main peak with the molecular weight 178 (90% of the fraction) since the temperature in the vaporizer and the column of the mass spectrometer is sufficiently high (250°C and 70–280°C respectively).

The heating of semiacetal **III** to 100°C in DMSO in the presence of 5 mol% of p-TsOH within 5 min resulted in conversion of compound **III** into acetals **IV** and **VI** at the ratio (**III**) : (**IV**) : (**VI**) of 1 : 4 : 1. The similar high yield of ketal **IV** (67%) was obtained at heating semiacetal **III** to 60°C for 3 h in the presence of *p*-TsOH. The latter two observations suggest that alongside the previously mentioned possible paths leading to monocyclic acetals **IV** and **VI** may additionally occur due to intramolecular rearrangements of acetal **III** depicted in the scheme.

The mechanism similar to the path *g* was previously assumed to explain the formation of cyclic dithioketal of methylglyoxal **VII** in the reaction of alkylglyoxals with ethanedithiol proceeding via intermediate semiketal (A) [11]. The formation of the hypothetical intermediate (A) was not proved spectrally or by its isolation.

In our series of conversions that undergoes methylglyoxal semiacetal **III** in the absence of Brønsted acids their role is apparently played by the sulfhydryl group of 2-mercaptoethanol. This assumption was proved experimentally. The heating of the reaction mixture at 60°C for 5 h (see the table, run





no. 2b) results in reaction products among which acetal **IV** amounts to 64%. The similar heating of an individual diastereomerically pure semiacetal **III** led only to its isomerization to 66% into the other diastereomer.

To increase the yield of thioketal **IV** and accelerate its formation we studied catalysis by acids of the reaction between 2-mercaptoethanol and 2-ethoxypropenal. This reaction in the presence of trifluoroacetic acid (5 mol%) in benzene at 20°C in 24 h gives rise to a mixture of acetals **III** and **IV** in 5:1 ratio at complete consumption of the initial compounds. The reaction catalyzed by *p*-toluenesulfonic acid (*p*-TsOH) (1 mol%) at 20°C in 5 h afforded crystalline semiacetal **III** in 72% yield. The mother liquor according to GC-MS data contained equal weights of semiacetal **III** and ketal **IV**. The yield of the latter same as in the preceding experiment was around 15%. The attempt to separate the products by rectification furnished ketal **IV** in 7% yield and a fraction containing according to GC-MS data two isomers of molecular weight 178. They are probably isomers **II** and **III**. Overall yield amounts to 65%.

On heating equimolar mixture of the initial reagents to 50°C for 3 h in the presence of *p*-TsOH (5 mol%) without solvent arose a mixture of products where by GC-MS data the main component (80% of the mixture) was 2-methyl-2,2'-bi(1,3-oxathiolane) (**V**), and the ratio thereof with its three isomers was 37:5:4:3. These are presumable diastereomers pairs of structures **V** and **VIII**.

On the chromatogram among the impurities is clearly seen the methylglyoxal diethylacetal. It can be generated by hydrolytic decomposition of the vinyloxy group of substrate **I** or of the ketal fragment in thioketal **II** followed by acetal formation at the aldehyde group with the liberated ethanol. Thus at heating the reaction mixture in the presence of acids into the reaction are involved the carbonyl groups of compounds **I** and **II**, and methylglyoxal bisacetal (**V**) becomes the principal reaction product even at deficit of 2-mercaptoethanol in the reaction mixture.

To optimize the yield of bisacetal **V** we carried out the reaction with double molar excess of 2-mercaptoethanol with respect to 2-ethoxyacrolein in the presence of *p*-TsOH (7 mol%) at 20°C. According to ^{1}H NMR and GC-MS data after 7 days the only reaction product was bisacetal **V**, yield quantitative (see the table, run no. 17). At 60°C the same result was attained in 2 h (run no. 8).

Thus in the reaction under investigation 2-ethoxypropenal behaved as a vinyl ether with an α-carbonyl group and as a chemical equivalent of methylglyoxal. The study of methylglyoxal thioacetals as models of natural analogs is especially interesting for the methylglyoxal is one of metabolites of glyoxalase system and is widely spread in the cells of living organisms, in particular, it reacts with the sulfhydryl group of glutathione and takes part in controlling the cell growth [12].

EXPERIMENTAL

^{1}H NMR spectra were registered on spectrometer Bruker DPX-400 (400 MHz) from solutions in DMSO and $CDCl_3$, internal reference HMDS. IR spectra were measured on spectrometer Specord 75IR. GC-MS measurements were carried out on Hewlett-Packard HP 5971A instrument (electron impact at 70 eV, mass-selective detector), chromatograph HP-5890, column Ultra-2 (stationary phase 5% of phenylmethylsilicone), vaporizer temperature 250°C, oven temperature 70–280°C, heating rate 20 deg min^{-1}.

Preparation of 2-hydroxy-3-methyl-1,4-oxathiane (III) at 20°C in benzene (Procedure A). To a solution of 0.5 ml (4.85 mmol) of 2-ethoxypropenal in 1 ml of benzene was added 0.34 ml (4.85 mmol) of

2-mercaptoethanol. The mixture was left standing at 20°C till complete consumption of the initial compounds (monitoring by ^{1}H NMR and GC-MS). After standing for 2 months from the mixture precipitated crystals. The crystalline compound is one of diastereomers of semiacetal **III**, the mother liquor contained a mixture of diastereomers **III** in 1 : 3 ratio (see spectra below). Yield quantitative.

Reaction of 2-ethoxypropenal with 2-mercaptoethanol at heating. (Procedure B). To a solution of 2 ml (19.5 mmol) of 2-ethoxypropenal in 6 ml of benzene was added 1.36 ml (19.5 mmol) of 2-mercaptoethanol. The mixture was heated to 60°C for 3 h. As showed ^{1}H NMR spectrum, after 3 h in the mixture were still present the initial compounds, and the reaction products **III**, **IV**, and **VI** were in the ratio 58 : 4 : 1. The heating to 60°C was continued for 2 h more, the initial compounds were totally consumed, and the products were present in the ratio (**III**) : (**IV**) : (**VI**) = 3 : 7 : 1. After evaporation of benzene in 7 days from the reaction mixture was isolated 0.81 g (23%) of colorless needle-like crystals of compound **III** as a pure diastereomer, mp 102°C. ^{1}H NMR spectrum, DMSO, δ, ppm: 1.16 s [3H, CH_3(Et), *J* 7.0 Hz], 1.29 s (3H, CH_3), 2.23 d.d.d [1H, SCH_2 (H_e), J_{AB} 13.2, $^3J_{e\text{-}a}$ 2.3, $^3J_{e\text{-}e}$ 3.1 Hz], 2.8 d.d.d [1H, SCH_2 (H_a), $^2J_{AB}$ 13.2, $^3J_{a\text{-}a}$ 11.3, $^3J_{e\text{-}a}$ 3.1 Hz), 3.50 and 3.73 two d.q [2H, OCH_2(Et), $^2J_{AB}$ 9.15, ^3J 7.0 Hz], 3.61 d.t [1H, CH_2O (H_e), $^3J_{e\text{-}a}$ 11.5, $^3J_{e\text{-}e}$ 3.1, $^3J_{e\text{-}a}$ 3.1 Hz], 4.1 t.d [1H, CH_2O (H_a), $^2J_{a\text{-}e}$ 11.5, $^3J_{a\text{-}a}$ 11.3, $^3J_{a\text{-}e}$ 2.3 Hz], 4.55 d (1H, C<u>H</u>OH, ^3J 5.2 Hz), 6.48 d (1H, CHO<u>H</u>, ^3J 5.2 Hz).^{13}C NMR spectrum (DMSO), δ_C, ppm: 16.16 [CH_3(Et)], 22.25 (CH_3C), 24.51 (SCH_2), 57.18 and 58.51 (OCH_2), 82.88 (SCO), 93.84 (OCO). Mass spectrum, *m/z* (I_{rel}, %): 178 (1) $[M]^+$, 151 (1), 149 (19) $[M–CHO]^+$, 133 (3) $[M–OEt]^+$, 105 (64), 104 (49) $[M–CHO–OEt]^+$, 89 (9), 77 (11) $[SCH_2CH_2OH]^+$, 61 (51), 43 (100) $[CH_3CO]^+$. Found, %: C 47.22; H 8.07; S 18.23. $C_7H_{12}O_3S$. Calculated, %: C 47.19; H 7.87; S 17.98.

The crystals obtained in this run were dissolved in DMSO, and the solution was heated in the NMR tube to 100°C for 1 min; no changes in the ^{1}H NMR spectrum appeared after heating.

The benzene solution of these crystals was heated to 60–70°C for 2 h. On evaporating the solution the ^{1}H NMR spectrum revealed the presence of two diastereomers of compound **III** in 1 : 2 ratio, and the new diastereomer prevailed. Its ^{1}H NMR spectrum, DMSO, δ, ppm: 1.15 t [3H, CH_3(Et), ^3J 7.0 Hz], 1.26 s (3H, CH_3), 2.19 d.t [1H, SCH_2 (H_e), $^2J_{a\text{-}e}$ 13.4, ^3J 2.1 Hz], 2.76 d.d.d [1H, SCH_2 (H_a), $^2J_{a\text{-}e}$ 13.4, $^2J_{a\text{-}a}$ 11.9, $^3J_{a\text{-}e}$ 3.2 Hz], 3.41 and 3.70 two d.q [2H, OCH_2(OEt), $^2J_{AB}$ 11.0, ^3J 7.1 Hz], 3.76 t.d [1H, CH_2O (H_a), $^2J_{a\text{-}e}$ = $^3J_{a\text{-}a}$ = 11.8 Hz, $^3J_{a\text{-}e}$ 2.1 Hz], 4.15 d.d.d [1H, CH_2O (H_e), $^2J_{e\text{-}a}$ 11.8, $J_{e\text{-}a}$ 3.3, $J_{e\text{-}e}$ 2.2 Hz), 4.59 d (1H, C<u>H</u>OH, $^3J_{CH\text{-}OH}$ 8.2 Hz), 6.14 d (1H, O<u>H</u>, ^3J 8.2 Hz).

Conversion of semiacetal III into ketal IV at heating in the presence of acids. The solution in DMSO of crystalline semiacetal **III** prepared along procedure B was heated for 5 min in an NMR tube in the presence of 5 mol% of *p*-TsOH. According to the ^{1}H NMR spectrum in the resulting solution the ratio of compounds **III : IV : VI** = 1 : 4 : 1. The following signals in the ^{1}H NMR spectrum in DMSO were assigned to compound **VI**, δ, ppm: 2.16 s (3H, CH_3) and 5.22 s (1H, OCHS); in $CDCl_3$, δ, ppm: 2.18 s (3H, CH_3CO) and 5.38 s. (1H, OCHS); the OCH_2 and SCH_2 signals are overlapped by stronger resonances of isomer **IV**. Mass spectrum, *m/z* (I_{rel}, %): 132 (3) $[M]^+$, 89 (57) $[M–CH_3CO]^+$, 61 (90), 45 (65), 43 (100) $[CH_3CO]^+$. The spectra of isomer **IV** are given below.

Reaction of 2-ethoxypropenal (I) with 2-mercaptoethanol without solvent. To 3.59 g (35.9 mmol) of aldehyde **I** was added 2.51 ml (35.9 mmol) of 2-mercaptoethanol. The reaction mixture was heated to 50°C. After 12 days the vacuum distillation of the reaction mixture afforded 2.2 g (yield 35%) of the fraction with bp 98–101°C (1 mm Hg), n_D^{20} 1.5139. According to GC-MS data the fraction contained 70% of compound with molecular weight *M* 178. Mass spectrum, *m/z* (I_{rel}, %): 178 (1) $[M]^+$, 150 (2) $[M–CH_2CH_2]^+$, 132 (1) $[M–EtOH]^+$, 103 (32) $[M–CHO–EtOH]^+$, 85 (9), 75 (25), 72 (22), 61 (52), 59 (26), 45 (58) $[EtO]^+$, 29 (100) $[CHO]^+$. The molecular weight and the fragmentation pattern correspond to 2'-hydroxyethylthio-2-ethoxypropanal (**II**). In the IR spectrum of the compound (from thin film) were observed absorption bands at 3440 cm^{-1} (OH), 1710 cm^{-1} (CHO), 1080 cm^{-1} (C–O–C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.37 s (3H, CH_3), 9.65 s (1H, CHO), 2.8 m (SCH_2), 3.68 m (OCH_2), are present poorly resolved signals from EtO group.

Reaction of 2-ethoxypropenal (I) with 2-mercaptoethanol in the presence of acids. (a) In the presence of CF_3COOH. To a solution of 0.5 ml (4.85 mmol) of 2-ethoxypropenal in 3 ml of benzene was added 27 mg (5 mol%) of CF_3COOH and 0.34 ml

(4.85 mmol) of 2-mercaptoethanol. The mixture self-heated to 30°C. After keeping the mixture for 24 h at 20°C according to ^{1}H NMR data the yield of semiacetal **III** was 80%, that of 2-methyl-2-formyl-1,3-oxathiolane (**IV**) 15%.

(b) In the presence of *p*-TsOH. To a solution of 4.94 ml (49 mmol) of 2-ethoxypropenal in 20 ml of anhydrous ether was added 0.42 g (5 mol%) of *p*-TsOH and 3.96 ml (49 mmol) of 2-mercaptoethanol. The mixture self-heated to 30°C. After 5 h at 20°C precipitated crystals of semiacetal **III**. They were filtered off and dried in a vacuum. They weighed 1.65 g. The evaporation of the mother liquor provided more 4.7 g of compound **III** crystals, overall yield 72%. In the IR spectrum of the crystals (pelleted with KBr) the absorption bands of C=O and C=C groups were lacking, and was observed a strong narrow band at 3330 cm^{-1} with a shoulder at 3340 cm^{-1}. According to ^{1}H NMR data the diastereoisomer excess in the sample of compound **III** obtained was 80%.

The distillation of the mother liquor after neutralization with potassium carbonate provided the fraction of 2-methyl-2-formyl-1,3-oxathiolane (**IV**) , bp 44°C (2 mm Hg), n_D^{20} 1.4917. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.67 s (3H, CH_3); 3.11 and 3.17 q.t (q AB, split in t) (2H, CH_2S, ^2J 10.35, $^3J_{SH_a\text{-}CH_2O}$ 5.65, $^3J_{SH_c\text{-}CH_2O}$ 6.17 Hz); 4.30 and 4.33 d.d.d (2H, CH_2O, ^2J 9.2, ^3J 5.65, ^3J 6.1 Hz); 9.19 s (1H, CHO). Mass spectrum, *m/z* (I_{rel}, %): 103 (29) $[M–CHO]^+$, 61 (11), 59 (34), 43 (100) $[CH_3CO]^+$. Found, %: C 45.07; H 6.24; S 23.90. $C_5H_8O_2S$. Calculated, %: C 45.45; H 6.05; S 24.26.

Reaction of 2-ethoxypropenal with equimolar amount of 2-mercaptoethanol at heating. To 1 ml (9.7 mmol) of 2-ethoxypropenal was added 83 mg (5 mol%) of *p*-TsOH and 0.68 ml (9.7 mmol) of 2-mercaptoethanol. The reaction mixture was heated to 50°C for 3 h. According to GC-MS data the content in the mixture of four isomers of molecular weight 192 amounted to 80%, their ratio was 37:5:4:3.

Reaction of 2-ethoxypropenal (I) with excess 2-mercaptoethanol. (a) At 20°C. To a solution of 1 ml (9.7 mmol) of aldehyde I in 5 ml of ether was added 1.36 ml (19.6 mmol) of 2-mercaptoethanol, 0.11 g (7 mol%) of *p*-TsOH, and 1 g of freshly calcined molecular sieves 4A. After standing for 7 days at 20°C according to the data of ^{1}H and GC-MS the reaction mixture was a solution of 2-methyl-2,2'-bi(1,3-oxathiolane) (**V**). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.71 s (3H, CH_3); 2.59 d.d.d (2H, SCH_2, ^2J 13.5, ^3J 7.0, ^3J 2.7 Hz), 2.84 d.d.d (2H, SCH_2, ^2J 13.5, ^3J 7.0, ^3J 3.1 Hz), 3.96 and 4.30 two d.d.d (4H, OCH_2, ^2J 12.0, ^3J 7.0, ^3J 3.1 Hz); 3.81 s (1H, CH). According to GC-MS the substance contained two diastereomers of molecular weight 192 in 95:5 ratio. Mass spectrum of the major diastereomer, *m/z* (I_{rel}, %): 192 (7) $[M]^+$, 164 (1) $[M–CH_2CH_2]^+$, 116 (3) $[M–2(CH_2)_2]^+$, 103 (5) $[CH_3\text{-}CSCH_2CH_2O]^+$, 88 (11) $[CSCH_2CH_2O]^+$, 76 (4), 61 (12) $[SCHO]^+$, 45 (32), 43 (100) $[CH_3CO]^+$.

(b) At heating. To a solution of 0.24 g (5 mol%) of *p*-TsOH in benzene was added 2 ml (28.2 mmol) of 2-mercaptoethanol and 1.5 ml (14.1 mmol) of 2-ethoxypropenal. The reaction occurred with heat evolution (up to 60°C). Then the reaction mixture was heated to 80°C for 2 h. According to GC-MS and ^{1}H NMR data the only product in solution was bicyclic acetal **V**. In 1 h the mixture separated in two layers. The bottom layer was removed. After neutralization with potassium carbonate in the upper benzene layer began crystals formation. The crystals according to ^{1}H NMR spectrum consist of one diastereomer of bicyclic compound **V**, mp 78°C. ^{1}H NMR spectrum (DMSO), δ, ppm: 1.58 s (3H, CH_3); 2.6 and 2.76 d.d.d (2H, SCH_2, ^2J 13.3, ^3J 7.0, ^3J 2.9 Hz), 2.76 d.d.d (2H, SCH_2, ^2J 13.3, ^3J 7.2, ^3J 2.9 Hz), 3.84 d.d.d (2H, OCH_2, ^2J 12.1, ^3J 7.0, ^3J 2.9 Hz); 3.99 s (1H, CH); 4.15 d.d.d (2H, OCH_2, ^2J 12.1, ^3J 7.2, ^3J 2.9 Hz). Found, %: C 44.28; H 6.27; S 33.96. $C_7H_{12}O_2S_2$. Calculated, %: C 43.72; H 6.29; S 33.96.

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