Hydrolysis of 2-alkoxyalk-2-enals

T. N. Mamashvili, N. A. Keiko, G. I. Sarapulova, and M. G. Voronkov*

Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 ul. Favorskogo, 664033 Irkutsk, Russian Federation. Fax: +7 (395 2) 35 6046. E-mail: admin@irioch.irk.ru

Hydrolysis of 2-alkoxyalk-2-enals with equimolar amount of water (in an organic solvent) and with an excess of water has been studied with the aim of synthesizing 2-oxopropanal (methylglyoxal). 2-Oxopropanal obtained in an excess of water exists in the hydrate form. In organic solvents, the cyclic trimer of 2-oxopropanal, 2,4,6-triacetyl-1,3,5-trioxane, predominates (NMR data).

Key words: 2-alkoxyalk-2-enals, hydrolysis, 2-oxopropanal (methylglyoxal), 2,4,6-triacetyl-1,3,5-trioxane.

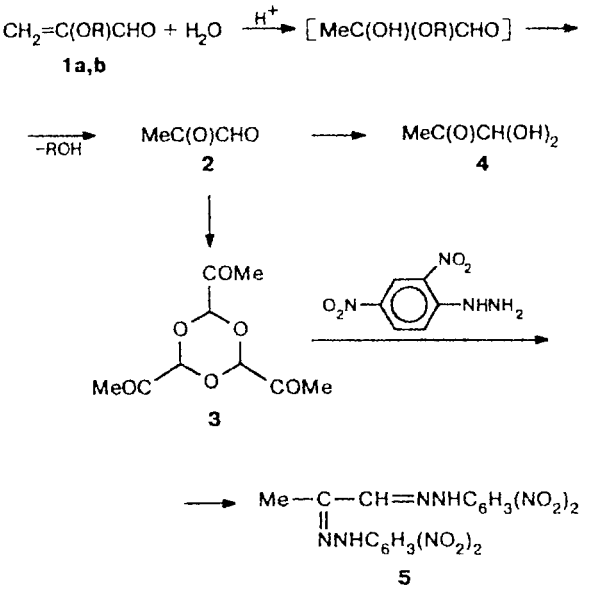
The C=C bond in α,β-unsaturated carbonyl compounds containing an electron-donor alkoxy group in the α-position is polarized towards the C_β atom (see NMR data in the Experimental Section). Hence, electrophilic reagents add to such molecules according to the Markownikoff rule similarly to addition to alkyl vinyl ethers.[1]

We have studied hydrolysis of 2-alkoxy-2-alkenals (**1a,b**) in an acid medium with the aim of synthesizing 2-oxopropanal (methylglyoxal) (**2**). Methylglyoxal is a low-molecular-weight cell growth regulator, including tumor cells,[2,3] and a valuable starting compound in organic synthesis.[4]

Methylglyoxal is usually obtained and used in the form of 30—40% aqueous solutions, which makes it possible to avoid its irreversible polymerization, which easily occurs upon concentration of the solution. It should be emphasized that the difficulties in the studies of methylglyoxal are associated with the fact that it is very hygroscopic, readily gives mono- and dihydrate forms in aqueous solutions,[5—7] and is prone to enolization.[5]

To obtain dilute solutions of methylglyoxal, hydrolysis of 2-alkoxypropenals **1a,b** (Scheme 1) was carried out in a tenfold excess of water in the presence of catalyst (HCl or a cation-exchange resin KU-2). The reaction was considered completed when the band assigned to the π—π*-transition of the initial alkenals **1a,b** (250 nm) disappeared in the UV spectra of the reaction mixture and the band assigned to the n—π*-transition at 285 nm (typical of methylglyoxal) appeared[7]; this was observed in *ca.* 3 h at 40 °C for ethoxypropenal **1b** and in 10 h for methoxypropenal **1a**. The absence of the band at 430 nm, which is typical of the conjugated α-oxo aldehyde system,[7] indicates that methylglyoxal exists in a monomeric hydrate form (**4**) in an excess of water. In the IR spectra of the reaction mixture there were no vibrations of C=C and C=O bonds (1610 and 1700 cm^{-1}, respectively) typical of 2-alkoxypropenals, and a band due to the newly formed carbonyl group appeared at 1730 cm^{-1}.

Scheme 1



R = Me (**a**), Et (**b**)

Methylglyoxal dilute aqueous solutions are not very suitable for its subsequent transformations, which are usually carried out in aprotic solvents. We have studied the removal of water from methylglyoxal aqueous solutions by conventional procedures (distillation or azeotropic distillation) and have found that it leads to significant losses of methylglyoxal due to its decomposition and extensive polymerization. This prompted us to investigate the possibility of hydrolysis of 2-alkoxypropenals

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1a,b with an equimolar amount of water in an organic solvent (MeCN, dioxane, and DMSO).

A priori the result of interaction of aldehydes **1a,b** with equimolar amount of H_2O is not obvious. According to the electron density distribution in molecule **1**,[8] the negative charge on the carbonyl oxygen is larger than that on the C_β. This allowed us to expect that the protonation of the oxygen will be more preferable and subsequent addition of OH^- to the carbocation giving the hydrate form $CH_2{=}C(OR)CH(OH)_2$ will become the major direction of the reaction. In this case, hydration of the C=C bond will be the secondary, slower process leading to negligible formation of methylglyoxal (because of the deficiency of water).

However, complete hydration of the C=C bond proved to occur when the ratio of 2-alkoxypropenals **1a,b** and H_2O was equimolar. The hydrolysis was monitored (from the beginning to 100% conversion) by ^1H NMR (in CD_3CN) and IR spectroscopy. According to IR spectral data, the characteristic bands assigned to vibrations of the C=C and C=O groups (1610 and 1700 cm^{-1}) gradually disappeared, and a new broad asymmetrical band appeared at 1730 cm^{-1} (in CH_3CN), 1726 cm^{-1} (in DMSO), or 1734 cm^{-1} (in dioxane). We assigned this band to vibrations of the acetyl group of 2,4,6-triacetyl-1,3,5-trioxane (**3**), the product of trimerization of methylglyoxal **2**. This is confirmed by the ^1H NMR spectra which contained the signals for the acetal and acetyl protons and did not contain a signal for the aldehyde proton. Transformation of saturated aldehydes into trioxane derivatives is well known,[9] and splitting of the signals for the acetal and acetyl groups in the ^1H NMR spectra of the latter observed in some cases may be an indication of configuration nonuniformity of the trimerization product.[10] The presence of low-intense absorption at 430 nm in the UV spectrum of the reaction mixture probably indicates that monomeric methylglyoxal **2** does exist under the reported conditions. However, the absence of the signal for the aldehyde proton in the ^1H NMR spectrum suggests that the content of form **2** in the mixture is beyond the limits of sensitivity of the instrument. We can draw the conclusion that the final product of hydrolysis of alkenals **1a,b** with an equimolar amount of water is an equilibrium mixture of the monomeric form **2** and trimeric form **3** (>90%).

Compared to heterogeneous hydrolysis of propenals **1a,b** (in an excess of H_2O), hydrolysis in homogeneous solution proceeds much faster. For instance, hydrolysis of 2-ethoxypropenal **1b** is over in 45 min in MeCN, in 90 min in dioxane, and in 120 min in DMSO. Hydrolysis of 2-methoxypropenal **1a** proceeds more slowly or requires an increased amount of the catalyst: it is completed in 30 min in MeCN if the catalyst concentration is six times higher than that in the case of 2-ethoxypropenal **1b**.

The obtained solution of methylglyoxal trimeric form **3** can serve as the synthetic equivalent of methylglyoxal **2**. For example, when 2,4-dinitrophenylhydrazine was added to the solution of **3**, methylglyoxal bishydrazone (**5**) was formed, and the treatment of **3** with formaldehyde and ammonia gave 4(5)-methylimidazole.[11]

Experimental

^1H and ^{13}C NMR spectra (89.95 MHz and 22.49 MHz, respectively) were recorded on a JEOL 90-Q spectrometer (HMDS was used as the internal standard). When the process was monitored by ^1H NMR spectroscopy, hydrolysis of substrate in CD_3CN was carried out directly in an NMR tube. Monitoring by IR spectroscopy was carried out on a Specord IR-75 instrument using CaF_2 cells. UV spectra were recorded on a Specord UV—VIS in quartz cells.

The initial aldehydes **1a** and **1b** were obtained by the reported procedures.[12,13]

2-Methoxypropenal (1a). ^1H NMR ($CDCl_3$), δ: 5.10 and 5.24 (both d, 2 H, $=CH_2$, J = 3.0 Hz); 3.69 (s, 3 H, OMe); 9.29 (s, 1 H, CHO).

2-Ethoxypropenal (1b). ^1H NMR (CCl_4), δ: 5.05 and 5.17 (both d, 2 H, $=CH_2$, J = 2.0 Hz); 9.20 (s, 1 H, CHO); 1.38 (t, 3 H, CH_3, J = 7.0 Hz); 3.83 (q, 2 H, CH_2, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 102.0 (C-2); 157.8 (C-3); 187.2 (CHO); 62.9 (OCH_2); 13.07 (Me).

Hydrolysis of 2-ethoxypropenal (1b) in an excess of water. Water (36 g, 2 mol) and 2 mol.% HCl were added to 2-ethoxypropenal (**1b**) (20 g, 0.2 mol) and stirred at 40 °C until a homogeneous solution was formed (for *ca.* 3 h). As a result of the reaction, *ca.* 30% aqueous-ethanolic solution of methylglyoxal hydrate was formed (**4**). UV, λ_{max}/nm: 285. According to oxime titration carried out by the known procedure, the content of the dicarbonyl compound was 98%. The solution was stirred with anion-exchange resin AV-17 (0.1 g) to remove HCl.

Hydrolysis of 2-ethoxypropenal (**1b**) in the presence of a KU-2 (H^+) resin was carried out similarly. Hydrolysis of 2-methoxypropenal (**1a**) in the presence of 2 mol.% HCl at 40 °C is completed in 10 h.

Hydrolysis of 2-ethoxypropenal (1b) with equimolar amount of water. Water (0.18 g, 0.01 mol), MeCN (10 mL), and 0.56 mol.% HCl were added to 2-ethoxypropenal (**1b**) (1 g, 0.01 mol) and stirred at 40 °C. IR (for the reaction mixture after 45 min), ν/cm^{-1}: 1730 (CH_3CO). ^1H NMR (for the reaction mixture carried out in the tube, after 45 min, CD_3CN), δ: 2.17 and 2.19 (both s, 9 H, CH_3CO); 4.74 and 4.80 (both s, 3 H, OCHO). ^{13}C NMR (for the reaction mixture after 45 min, CD_3CN), δ: 23.72 (CH_3); 95.62 (OCHO); 204.44 (C=O). Hydrolysis in dioxane was carried out in a similar way. IR (for the reaction mixture after 90 min), ν/cm^{-1}: 1734 br (CH_3CO). Hydrolysis in DMSO was carried out similarly. IR (for the reaction mixture after 120 min), ν/cm^{-1}: 1726 (CH_3CO). The solutions were stirred with ion-exchange resin AV-17 (0.01 g) to remove HCl.

Hydrolysis of 2-methoxypropenal (1a) with equimolar amount of water. Water (0.02 g, 1.1 mmol), MeCN (1 mL), and 3.27 mol.% HCl were added to 2-methoxypropenal (**1a**) (0.01 g, 1.1 mmol) and stirred at 40 °C. IR (for the reaction mixture after 30 min), ν/cm^{-1}: 1730 (CH_3CO). ^1H NMR (for the reaction mixture carried out in the tube, after 30 min, CD_3CN), δ: 4.71 (s, 3 H, OCHO); 2.15 (s, 9 H, CH_3CO).

Reaction of a solution of trioxane 3 with 2,4-dinitrophenylhydrazine. A solution of 2,4-$(NO_2)_2C_6H_3NHNH_2$ (3.96 g, 0.02 mol) in EtOH (acidified with HCl) was added to an

aliquot of the reaction product in MeCN containing *ca.* 0.0216 g (3.3 mmol) of trioxane **3**, and the resulting mixture was heated for 15 min at 60 °C. An orange precipitate of methylglyoxal bis-2,4-dinitrophenylhydrazone **5** that formed was filtered off. Yield 0.037 g (86%). The precipitate was recrystallized from $C_6H_5NO_2$ to give a product with m.p. 296 °C that is consistent with the literature data.[13] A specimen prepared by mixing **5** with an authentic product obtained from methylglyoxal (Aldrich) gave no depression of m.p.

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Reaction of methyl iodide with organylethynyl silatranylmethyl chalcogenides

M. S. Sorokin, M. G. Voronkov, and V. A. Lopyrev*

Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 ul. Favorskogo, 664033 Irkutsk, Russian Federation. Fax: +7 (395 2) 35 6046

The reactivity of organylethynyl silatranylmethyl chalcogenides $RC{\equiv}CYCH_2Si(OCH_2CH_2)_3N$ (R = Ph, Me_3Si; Y = S, Se, Te) in the reaction with methyl iodide depending on the nature of the chalcogen Y, the substituent R at the triple bond, and the reaction conditions was studied.

Key words: 1-organylethynyl silatranylmethyl chalcogenides, methyl organylethynyl silatranylmethyl telluronium iodide, dimethyl silatranylmethyl selenonium and telluronium iodides, ^1H NMR and IR spectra.

The extremely high electron-donor effect of silatranyl $-Si(OCH_2CH_2)_3N$ ($\sigma^* = -3.49$)[1] and silatranylmethyl $-CH_2Si(OCH_2CH_2)_3N$ ($\sigma^* = -2.24$)[1,2] groups ensures high nucleophilicity of the S and Se atoms in phenyl silatranylmethyl chalcogenides $PhYCH_2Si(OCH_2CH_2)_3N$ (Y = S, Se) in their reactions with MeI leading to the corresponding iodides $I^-(Me)PhY^+CH_2Si(OCH_2CH_2)_3N$.[3,4]

In a continuation of these studies, we investigated the reactivity of organylethynyl silatranylmethyl chalcogenides $RC{\equiv}CYCH_2Si(OCH_2CH_2)_3N$ (R = Ph, Y = S (**1**); R = Ph, Y = Se (**2**); R = Ph, Y = Te (**3**); R =

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