Organic Chemistry

Reactions of alcohols with α-alkoxyacroleins at room temperature

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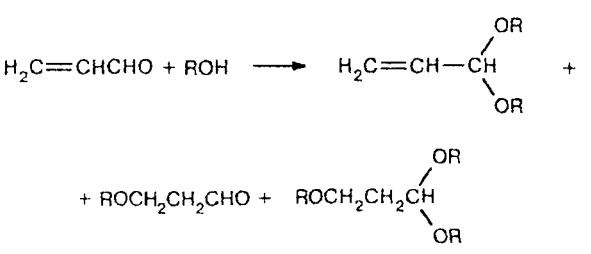
The first stage of the reactions of alcohols with α-alkoxyacroleins in an acidic medium at 20 °C under kinetically controlled conditions is the Markovnikoff addition at the C=C bond to form 2,2-dialkoxypropanals (methylglyoxal ketals). Under conditions of thermodynamic control, subsequent acetalization of the aldehyde group occurs to form 1,1,2,2-tetraalkoxypropanes. When the duration of the reaction is further increased in the absence of a water acceptor, the ketal group undergoes hydrolysis and methylglyoxal acetals are formed. A method was developed for the preparation of methylglyoxal ketals.

Key words: α-alkoxyacroleins, alcohols, addition, acetals, methylglyoxal ketals, direction of polarization of the activated C=C bond.

It is known[1] that the reactions of 2-alkenals, for example, of acrolein, with alcohols in an acidic medium afford acetals. Due to the π,π-conjugation in the classical acrylic system, these reactions are often accompanied by nucleophilic 1,4-addition to form 3-alkoxypropanals and their acetals (Scheme 1).

Scheme 1



The reactions of α-alkoxyacroleins with alcohols (Scheme 2) in the presence of acids with azeotropic distillation with benzene of water that liberated were accompanied by hydrolysis of the vinyl ether to form 1,1-dialkoxypropanones (methylglyoxal acetals) (**4**) as the major product (the yields were up to 70%).[2]

An attempt to detect possible intermediates **2** or **3** by spectral methods was unsuccessful.

In this work, we studied this reaction at room temperature with the aim of determining the direction and the rate of the attack of an alcohol on particular centers of polydentate α-alkoxyacrolein molecules. The compounds that formed were identified by GLC-mass spectrometry.

The reaction of α-methoxyacrolein with a twofold excess of methanol (Scheme 3) was carried out in the presence of TsOH (5 mol.%). Binding of water that liberated upon formation of the acetal was effected by 3A molecular sieves added to the reaction mixture.

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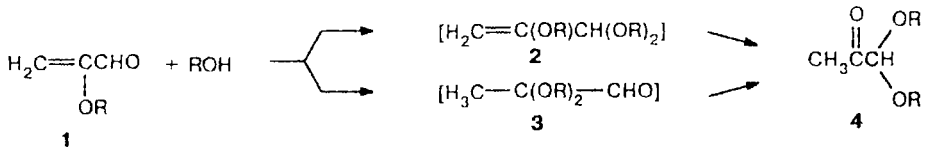
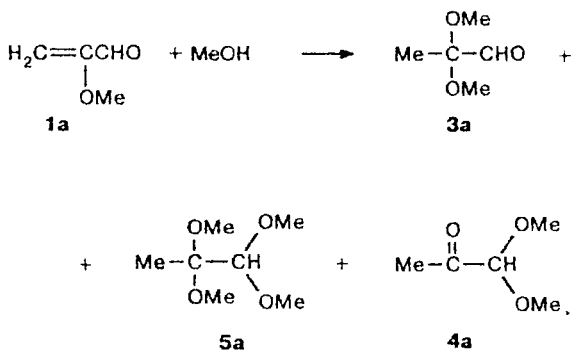
Scheme 2



During the first hour, only addition of methanol at the C=C bond occurred and the content of 2,2-dimethoxypropanal (methylglyoxal ketal) (**3a**) in the mixture was 5%. Products **2** or **4** were not formed. After 1 day, the content of ketal **3a** reached 50%. The contents of the compounds in the mixture were determined by GLC-mass spectrometry after neutralization of the acid. The ratio of the initial and resulting compounds, which was determined by GLC-mass spectrometry, was confirmed by ^{1}H NMR spectroscopy.

Scheme 3



When a substantial excess of methanol (1 : 17.6) was used, 1,1,2,2-trimethoxypropane (**5a**) was formed. After 1 day, the contents of compounds **3a** and **5a** in the reaction mixture reached 45 and 34%, respectively.

The reaction of α-methoxyacrolein with a fourfold excess of methanol in the absence of a water acceptor (3A molecular sieves) afforded ketal **3a**, methylglyoxal acetal (**4a**), and tetramethoxypropane **5a** in a ratio of 1 : 1 : 2. The reaction was complicated by the formation of methylglyoxal and its trimer.[3] Apparently, ketal **3a** was also involved in trimerization.

After 1 day, the reaction of α-ethoxyacrolein with anhydrous ethanol (taken in a ratio of 1 : 2) in the presence of TsOH and molecular sieves afforded compounds **3b**, **4b**, and **5b** (Scheme 4). Their contents in the reaction mixture were 49, 3, and 41%, respectively. In the absence of molecular sieves, the content of acetal **4b** in the reaction mixture reached 30% after 20 days, while the contents of **3b** and **5b** decreased to zero. The mixture contained also several minor nonidentified components (apparently, with the trioxane structure).

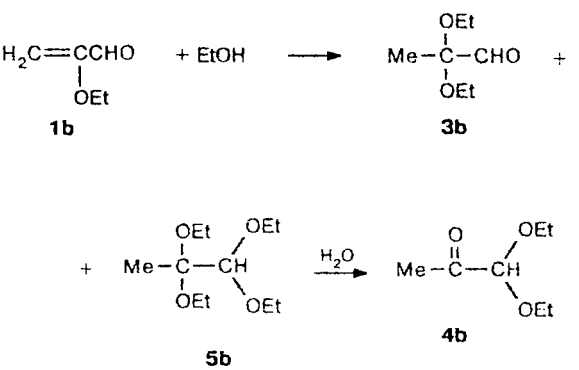
Taking into account the higher tendency of ketals to undergo hydrolysis compared to acetals,[4] one can suggest that **4b** was formed from **5b**. The same acetal **4b** was formed when an excess of ethanol, which has not been preliminarily dried, was used in the absence of a drying agent. After 1 day, the ratio of acetals **3b** : **4b** : **5b** was 2 : 42 : 7.

Apparently, the sequence of the processes that occurred in the reaction of butanol with α-ethoxyacrolein, is identical to that observed in the case of the above-described alcohols. However, the reaction with butanol was complicated by the formation of mixed acetals. Because of this, when a 2—5-fold excess of butanol was used in the presence of TsOH and 3A molecular sieves, the derivatives shown in Scheme 5 were obtained in variable amounts depending on the reaction time (their percentage in the mixture after 1 day with the use of a twofold excess of BuOH is given in parentheses).

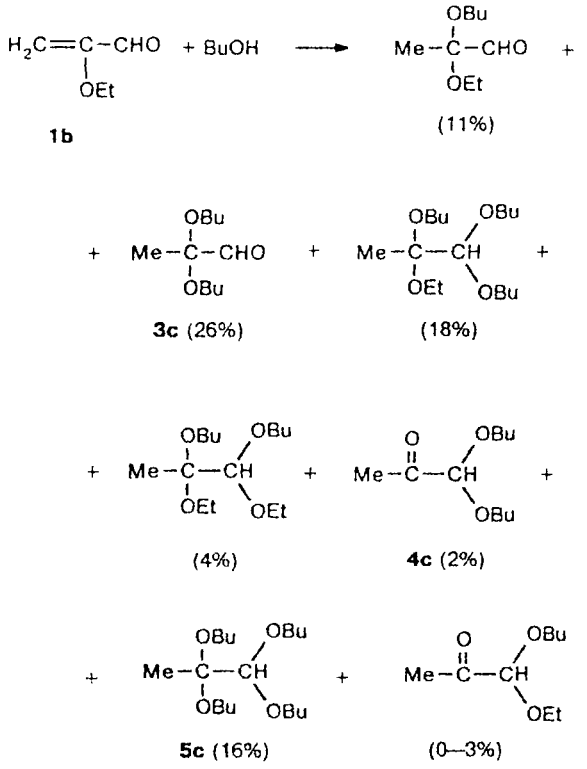
We succeeded in suppressing the formation of mixed acetals by using a 30-fold excess of butanol. In this case, only three compounds (**3c**, **4c**, and **5c**) were obtained. After 1 day, their ratio in the mixture was 25 : 7 : 55. Apparently, the reaction reached the equilibrium because this ratio remained unchanged after 3 days. This reaction in the absence of a water acceptor afforded compounds **3c**, **4c**, and **5c** in a ratio of 17 : 12 : 51.

In no case was the formation of a product of type **2** observed. Therefore, the Markovnikoff addition of alcohols is the fastest reaction and it is the first stage in the process of conversions. The formation of ketals **3** strongly suggests that the OR group exerts the predominant electronic effect on the double C=C bond, *i.e.*, the conjugation typical of the acrylic system is not manifested in this case. The reaction under consideration offers possibilities of preparing methylglyoxal ketals **3**, which, to our knowledge, are unavailable by other methods. These compounds are relatively storage-stable and can be distillated, although ketals can undergo conver-

Scheme 4



Scheme 5



sions to isomeric acetals in the presence of an excess of alcohol in an acidic medium[5] or thermal decomposition to the initial compounds.[6]

Experimental

The ^{1}H NMR spectra were recorded on JEOL FX-90Q (89.95 MHz) and Varian VXR-500S (500 MHz) spectrometers in $CDCl_3$ at ~20 °C with HMDS as the internal standard. The mass spectra were obtained on a Hewlett—Packard HP5971A GLC-mass spectrometer (EI, 70 eV) equipped with a mass-selective detector, an HP-5890 chromatograph, and an Ultra-2 column (5% phenylmethylsilicone); the evaporator temperature was 250 °C, the column thermostat temperature was increased from 40 to 180 °C with a rate of 15 deg min^{-1}.

Addition of methanol to α-methoxyacrolein. 2,2-Dimethoxypropanal (3a). Methanol (1.79 g, 56 mmol), ether (57.4 mL), and freshly calcined 3A molecular sieves (3 g) were added to α-methoxyacrolein[7] (2.39 g, 27.8 mmol). Then TsOH (0.241 g, 5 mol.%) was added. The reaction mixture was kept at ~20 °C for 1 day. Then the acid was neutralized with potassium carbonate and ether was evaporated. The content of 2,2-dimethoxypropanal **3a** in the reaction mixture was 50%.

Distillation of the reaction mixture gave ketal **3a** in a yield of 0.77 g (23%), b.p. 49—50 °C (50 Torr). Found (%): C, 50.62; H, 8.40. $C_5H_{10}O_3$. Calculated (%): C, 50.84, H, 8.53. ^{1}H NMR, δ: 1.15 (s, 3 H, Me); 3.12 (s, 6 H, OMe); 9.27 (s, 1 H, CHO). MS, *m/z* (I_{rel} (%)): 103 [M − Me]$^+$ (1), 89 [M − CHO]$^+$ (33), 87 [M − MeO]$^+$ (10), 75 (2), 49 (41), 43 (100), 31 (15).

1,1,2,2-Tetramethoxypropane (5a). Methanol (15.20 g, 475 mmol) and freshly calcined 3A molecular sieves (3 g) were added to α-methoxyacrolein (2.26 g, 26 mmol). Then TsOH (0.172 g, 3.8 mol.%) was added. The reaction mixture was kept at ~20 °C for 2 days. Then the acid was neutralized with K_2CO_3 and the reaction mixture was distilled. Compound **5a** was obtained in a yield of 2.62 g (60%), b.p. 50—52 °C (10 Torr). Found (%): C, 50.92; H, 9.69. $C_7H_{16}O_4$. Calculated (%): C, 51.20; H, 9.82. ^{1}H NMR, δ: 1.26 (s, 3 H, Me); 3.25 (s, 6 H, OMe); 3.51 (s, 6 H, OMe); 4.19 (s, 1 H, CH). MS, *m/z* (I_{rel} (%)): 149 [M − Me]$^+$ (1), 133 [M − MeO]$^+$ (28), 89 [M − CH(OMe)$_2$]$^+$ (95), 75 [M − MeC(OMe)$_2$]$^+$ (59), 59 (37), 47 (37), 43 (100), 31 (36).

Reaction of methanol with α-methoxyacrolein in the absence of a water acceptor. Methanol (2.65 g, 80 mmol), ether (30 mL), and TsOH (137 mg, 4 mol.%) were added to α-methoxyacrolein (1.88 g, 20 mmol). The reaction mixture was kept for 12 days. GLC-mass spectrometry showed that the ratio of acetals **3a**, **4a**, and **5a** was 1 : 1 : 2. **Methylglyoxal dimethylacetal 4a.** MS, *m/z* (I_{rel} (%)): 87 [M − OMe]$^+$ (12), 75 [M − MeCO]$^+$ (100), 59 (43), 47 (61), 43 [M − CH(OMe)$_2$]$^+$ (52), 31 (57).

Addition of ethanol to α-ethoxyacrolein. Anhydrous ethanol (0.25 g, 5.4 mmol), which has been dried with $(EtO)_4Si$, ether (9.9 mL), and freshly calcined 3A molecular sieves (~1 g) were added to α-ethoxyacrolein[8] (0.27 g, 2.7 mmol). Then TsOH (0.023 g, 4.9 mol.%) was added. The reaction mixture was kept at ~20 °C for 1 day. Then the acid was neutralized with K_2CO_3. According to the data of GLC-mass spectrometry, the reaction mixture contained 2,2-diethoxypropanal (**3b**), 1,1-diethoxypropanone (**4b**), and 1,1,2,2-tetraethoxypropane (**5b**) in a ratio of 49 : 3 : 41. Distillation gave three fractions. The first fraction with a b.p. of 30—40 °C (20 Torr) contained a mixture of isomers **3b** and **4b** in a ratio of 3 : 4. **2,2-Diethoxypropanal (3b).** ^{1}H NMR, δ: 1.19 (t, $OCH_2\underline{CH}_3$); 1.30 (s, 3 H, CH_3); 3.43—3.73 (m, $OC\underline{H}_2CH_3$); 9.43 (s, 1 H, CHO). MS, *m/z* (I_{rel} (%)): 117 [M − CHO]$^+$ (19), 101 [M − OEt]$^+$ (8), 89 [M − CHO − C_2H_4] (10), 73 (28), 61 (66), 45 (34), 43 (100). **1,1-Diethoxypropanone (4b).** ^{1}H NMR, δ: 1.17 (t, $OCH_2\underline{CH}_3$); 2.14 (s, 3 H, CH_3); 3.43—3.73 (m, $OC\underline{H}_2CH_3$); 4.48 (s, 1 H, OCHO) (*cf.* Ref. 2). MS, *m/z* (I_{rel} (%)): 103 [M − MeCO]$^+$ (24), 75 [M − MeCO − C_2H_4]$^+$ (31), 73 (29), 47 (100), 45 (42), 43 (89). The third fraction contained **1,1,2,2-tetraethoxypropane (5b),** b.p. 63 °C (2 Torr). ^{1}H NMR, δ: 1.20 (t, 6 H, $OCH_2\underline{CH}_3$, J = 7 Hz); 1.14 (t, 6 H, $OCH_2\underline{CH}_3$, J = 7 Hz); 1.29 (s, 3 H, CH_3); 3.48 (q, 2 H, $OC\underline{H}_2CH_3$); 3.53 (q, 2 H, $OC\underline{H}_2CH_3$); 3.62 (q, 2 H, $OC\underline{H}_2CH_3$); 3.70 (q, 2 H, $OC\underline{H}_2CH_3$); 4.30 (s, 1 H, OCHO). MS, *m/z* (I_{rel} (%)): 175 [M − OEt]$^+$ (6), 147 (1), 130 (2), 117 [M − CH(OEt)$_2$]$^+$ (65), 103 [M − $CH_3C(OEt)_2$]$^+$ (13), 89 (32), 75 (22), 73 (100), 61 (78), 47 (49), 45 (48), 43 (79).

In the absence of molecular sieves, the ratio of **3b** : **4b** : **5b** was 33 : 5 : 41 after 1 day. After 20 days, compounds **3b** and **5b** were absent.

Addition of butanol to α-ethoxyacrolein. *A.* Butanol (8.8 g, 0.12 mol) and freshly calcined 3A molecular sieves (~1 g) were added to α-ethoxyacrolein (0.43 g, 4.3 mmol). Then TsOH (37 mg, 4.9 mol.%) was added. The reaction mixture was kept at ~20 °C for 3 days. Then the acid was neutralized with K_2CO_3 and butanol was distilled off. The mixture was distilled. The fraction with a b.p. of 60—90 °C (1 Torr) contained (according to the ^{1}H NMR data) 2,2-dibutoxypropanal (**3c**), 1,1-dibutoxypropanone (**4c**), and 1,1,2,2-tetrabutoxypropane (**5c**) in a ratio of 1 : 1 : 2.

2,2-Dibutoxypropanal (3c). ^{1}H NMR, δ: 1.32 (s, 3 H, CH_3); 9.46 (s, 1 H, CHO). The assignment of the signals in

the ^{1}H NMR spectrum was made taking into account the relative contents of the compounds in the mixture and the effects of the substituents. MS, *m/z* (I_{rel} (%)): 173 [M − CHO]$^+$ (8), 129 [M − OBu]$^+$ (5), 117 [M − CHO − C_4H_8]$^+$ (9), 111 (2), 85 (2), 73 (40), 61 (100), 57 (57), 43 (61), 41 (53). **1,1-Dibutoxypropanone (4c)**. ^{1}H NMR, δ: 2.16 (s, 3 H, CH_3); 4.46 (s, 1 H, OCHO). MS, *m/z* (I_{rel} (%)): 159 [M − MeCO]$^+$ (5), 129 [M − OBu]$^+$ (2), 103 [M − MeCO − C_4H_8]$^+$ (6), 57 (100), 43 (27), 41 (35). **1,1,2,2-Tetrabutoxypropane (5c)**. ^{1}H NMR, δ: 1.27 (s, 3 H, CH_3); 4.27 (s, 1 H, OCHO). MS, *m/z* (I_{rel} (%)): 259 [M − OBu]$^+$ (3), 203 [M − OBu − C_4H_8]$^+$ (1), 186 [M − 2 OBu]$^+$ (2), 173 [M − CH(OBu)$_2$]$^+$ (39), 159 [M − MeC(OBu)$_2$]$^+$ (2), 117 (23), 61 (75), 57 (100), 41 (61).

B. Butanol (1.29 g, 17.4 mmol), ether (10 mL), and freshly calcined 3A molecular sieves (2 g) were added to α-ethoxyacrolein (0.87 g, 8.7 mmol). Then TsOH (75 mg, 5 mol.%) was added. The reaction mixture was kept at ~20 °C for 1 day. The acid was neutralized with K_2CO_3. According to the data of GLC-mass spectrometry, the reaction mixture contained 2-butoxy-2-ethoxypropanal, 1-butoxy-1-ethoxypropanone, 2,2-dibutoxypropanal (**3c**), 1,1-dibutoxypropanone (**4c**), 1,2-dibutoxy-1,2-diethoxypropane, 1,1,2-tributoxy-2-ethoxypropane, and 1,1,2,2-tetrabutoxypropane (**5c**).

2-Butoxy-2-ethoxypropanal. MS, *m/z* (I_{rel} (%)): 145 [M − CHO]$^+$ (8), 129 [M − OEt]$^+$ (1), 101 [M − OBu]$^+$ (11), 89 [M − CHO − C_4H_8]$^+$ (44), 73 (25), 61 (100), 57 (22), 45 (20), 43 (79), 41 (31). **1-Butoxy-1-ethoxypropanone**. MS, *m/z* (I_{rel} (%)): 131 [M − MeCO]$^+$ (12), 101 [M − BuO]$^+$ (15), 89 (3), 75 (17), 73 (77), 57 (33), 45 (100). **1,2-Dibutoxy-1,2-diethoxypropanone**. MS, *m/z* (I_{rel} (%)): 231 [M − OEt]$^+$ (2), 203 [M − OBu]$^+$ (2), 145 [M − CH(OEt)OBu]$^+$ (14), 117 (100), 101 (16), 89 (68), 73 (45), 61 (83), 57 (64). **1,1,2-Tributoxy-2-ethoxypropane** was isolated by distillation in a mixture with tetrabutoxypropane; b.p. of the fraction was 100–110 °C (1 Torr). ^{1}H NMR, δ: 1.28 (s, CH_3); 4.29 (s, OCHO). MS, *m/z* (I_{rel} (%)): 259 [M − OEt]$^+$ (1), 231 [M − OBu]$^+$ (3), 203 [M − OEt − C_4H_8]$^+$ (1), 186 [M − OEt − OBu]$^+$ (1), 175 [M − OBu − C_4H_8]$^+$, 173 (7), 159 [M − MeC(OEt)OBu]$^+$ (2), 158 [M − 2 OBu]$^+$ (2), 145 [M − CH(OBu)$_2$]$^+$ (51), 103 (8), 101 (18), 89 (84), 73 (14), 61 (74), 57 (100), 43 (46), 41 (76).

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