Preparation of 2,3-di-*O*-methylglyceraldehyde and its β-elimination product 2-methoxypropenal

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2,3-Di-*O*-methylglyceraldehyde has been prepared both from racemic glyceraldehyde and its enantiomers through dimethyl acetal and its di-*O*-methyl derivative. The prepared compound was submitted to β-elimination reaction in alkali medium to yield 2-methoxypropenal.

Из рацемического глицеральдегида и из его обоих энантиомеров был синтезирован через диметилацеталь и его ди-*O*-метилпроизводное 2,3-ди-*O*-метилглицеральдегид, который далее использовался при синтезе 2-метоксипропеналя посредством реакции β-элиминирования в щелочной среде.

Due to wide spectrum of concurrent acid-base catalyzed reactions of unsubstituted saccharides, exact study of the individual reactions is almost impossible and the task of finding methods applicable for this study is not an easy one. The individual enantiomers of 2,3-di-*O*-methylglyceraldehyde and the β-elimination product, 2-methoxypropenal, were shown to be suitable model compounds for studying some of these reactions. 2,3-Di-*O*-methyl-D-glyceraldehyde is the oxidation product 1,2,5,6-tetra-*O*-methyl-D-mannitol with lead(IV) acetate [1] or sodium periodate [2]. 2-Methoxypropenal can be prepared by Mannich reaction from methoxyacetaldehyde and formaldehyde in the presence of dialkylammonium chloride [3, 4]. In the present work we focused our attention to the preparation of the above-mentioned derivatives of trioses both from optically pure and racemic glyceraldehyde.

Treatment of optically pure or racemic glyceraldehyde with anhydrous methanol in the presence of hydrogen chloride gave the corresponding dimethyl acetal in 70% yield. Under the given reaction conditions the concentration of the optically pure glyceraldehyde monomer was apparently sufficient for the required course of the reaction, *i.e.* for the formation of dimethyl acetal. When racemic glyceraldehyde was the starting compound for the preparation of dimethyl acetal, initiation of decomposition of its relatively stable dimer forms was ensured by addition of a small amount of sodium hydrogen carbonate. In its absence a mixture of

by-products is formed and consequently, the yield of dimethyl acetal is lower and its isolation more complicated.

The isolated dimethyl acetals were than methylated with methyl iodide (serving also as the solvent) in the presence of sodium hydride. Complete methylation was achieved within 4 days. The resulting product, 2,3-di-*O*-methylglyceraldehyde dimethyl acetal, was obtained in 62% yield after distillation.

In the further step 2,3-di-*O*-methylglyceraldehyde dimethyl acetal was hydrolyzed with diluted hydrochloric acid. After neutralization, extraction, and distillation under reduced pressure, the released 2,3-di-*O*-methylglyceraldehyde was obtained in 72% yield (31% with regard to the starting glyceraldehyde).

At last, 2,3-di-*O*-methylglyceraldehyde was submitted to β-elimination reaction in alkali medium. By treatment with alkali at pH 12 and 25°C for 90 min, one molecule of methanol was quantitatively eliminated under the formation of 2-methoxypropenal which was isolated from the reaction mixture in 69% yield. Preparation of 2-methoxypropenal, the achiral compound, directly from racemic 2,3-di-*O*-methylglyceraldehyde dimethyl acetal without isolation of the intermediate (2,3-di-*O*-methylglyceraldehyde) was shown to be advantageous. After hydrolysis of dimethyl acetal in acid medium, the reaction solution was titrated to the required alkalinity for β-elimination reaction.

Experimental

Specific optical rotations were measured on a Perkin—Elmer, type 141, polarimeter and the u.v. spectra on a Specord UV VIS (Zeiss, Jena) spectrophotometer. Conversions of the individual compounds were followed on an LP-7 polarograph (Prague). The samples withdrawn in preset time intervals were recorded in buffer solution (0.25 mol dm^{-3} ammonium sulfate — 0.05 mol dm^{-3} ammonia) from — 1.0 V against a saturated calomel electrode at 20°C. The purity of the prepared compounds was followed by thin-layer chromatography on Silufol plates in the system chloroform—acetone—*n*-hexane (5:2:3, v/v). The compounds were detected with anilinium hydrogen phthalate or diphenylamine.

Glyceraldehyde dimethyl acetal

The mixture of D-glyceraldehyde (10 g, product of Fluka, 10% water content), anhydrous sodium sulfate (10 g), and methanol (200 cm^3) was stirred at room temperature for 2 h. Then acetyl chloride (8 cm^3) was added and the mixture was stirred for 1 h. At last, the reaction mixture was neutralized with potassium hydrogen carbonate. The formed salts were filtered off and washed with a small amount of methanol. The combined filtrates were evaporated and distillation of the residue under reduced pressure gave D-glyceraldehyde dimethyl acetal (9.5 g, 70%) of b.p. 116—118°C at 1.6 kPa, R_f 0.18, and $[\alpha]_D^{24} = +23°$ (*c* 2, water); Ref. [5] gives b.p. 127—129°C at 2.26 kPa and $[\alpha]_D^{15} = +21.2°$ (*c* 18, water).

L-Glyceraldehyde dimethyl acetal of b.p. 113—114°C at 1.2 kPa and $[\alpha]_D^{21} = -21°$ (c 2, water) was obtained from L-glyceraldehyde in a similar way. D,L-Glyceraldehyde dimethyl acetal of b.p. 125—127°C at 2.4 kPa was obtained from D,L-glyceraldehyde (addition of 0.1 g of sodium hydrogen carbonate to the starting reaction mixture, D,L-glyceraldehyde—absolute methanol).

2,3-Di-O-methylglyceraldehyde dimethyl acetal

D-Glyceraldehyde dimethyl acetal (9 g) was dissolved in methyl iodide (50 cm^3), sodium hydride (7.2 g) was added under cooling within 2—3 h and the reaction mixture was stirred at room temperature for 4 days (until total disappearance of the starting dimethyl acetal and its mono-*O*-methyl derivatives of R_f 0.42 and 0.48). The salts were filtered off, washed with ether (3×25 cm^3) and the combined filtrates were dried with the mixture of sodium sulfate and sodium thiosulfate for 24 h. After removal of salts, ether and the excess methyl iodide were distilled off under normal pressure. Distillation of the residue under reduced pressure resulted in 2,3-di-*O*-methyl-D-glyceraldehyde dimethyl acetal (6.7 g, 62%) of b.p. 74—75°C at 2.0 kPa, R_f 0.76, and $[\alpha]_D^{21} = +15.5°$ (c 2, water). For $C_7H_{16}O_4$ calculated: 51.20% C, 9.82% H; found: 51.21% C, 9.75 % H.

2,3-Di-*O*-methyl-L-glyceraldehyde dimethyl acetal of b.p. 65—66°C at 1.3 kPa and $[\alpha]_D^{21} = -15°$ (c 2, water) was prepared similarly from L-glyceraldehyde dimethyl acetal and 2,3-di-*O*-methyl-D,L-glyceraldehyde dimethyl acetal of b.p. 69—70°C at 1.6 kPa from D,L-glyceraldehyde dimethyl acetal.

2,3-Di-O-methylglyceraldehyde

2,3-Di-*O*-methyl-D-glyceraldehyde dimethyl acetal (6 g) was dissolved in 1 mol dm^{-3} hydrochloric acid (30 cm^3) and heated at 50°C for 150 min. Termination of the reaction was controlled polarographically (constant content of the product). The reaction mixture was neutralized with aqueous solution of sodium hydroxide to pH 7 and extracted with chloroform (10×20 cm^3). After drying the chloroform extract with calcium chloride (24 h), chloroform was distilled off. Distillation of the residue under reduced pressure gave 2,3-di-*O*-methyl-D-glyceraldehyde (3.1 g, 72%) of b.p. 47—48°C at 1.9 kPa, R_f 0.65, and $[\alpha]_D^{20} = +12.5°$ (3 min) $\rightarrow$ +6° (24 h, c 2, water), and $[\alpha]_D^{23} = +108°$ (c 2, benzene), respectively. Ref. [1] gives for 2,3-di-*O*-methyl-D-glyceraldehyde b.p. 38.5—39°C at 1.1 kPa and $[\alpha]_D = +98°$ (c 10.71, benzene); Ref. [2] gives b.p. 42°C at 1 kPa and $[\alpha]_D^{20} = +12.5°$ (c 1, water) and $[\alpha]_D^{20} = +92.7°$ (c 1, benzene), respectively.

2,3-Di-*O*-methyl-L-glyceraldehyde of b.p. 49—50°C at 2.1 kPa and $[\alpha]_D^{21} = -107°$ (c 2, benzene) was prepared from 2,3-di-*O*-methyl-L-glyceraldehyde dimethyl acetal in a similar way.

2-Methoxypropenal

Procedure A

2,3-Di-*O*-methyl-D-glyceraldehyde or 2,3-di-*O*-methyl-L-glyceraldehyde (2 g) was dissolved in 10^{-2} mol dm^{-3} aqueous solution of sodium hydroxide (20 cm^3) and allowed to stay at 25°C for 90 min. Termination of the reaction was controlled polarographically (constant content of the product and disappearance of the substrate). Then the reaction solution was neutralized with 10^{-1} mol dm^{-3} hydrochloric acid to pH 7, filtered, and extracted with ether (5 × 20 cm^3). From the dried extract (calcium chloride, 24 h), ether was distilled off through Vigreux column. Distillation of the residue under reduced pressure resulted in 2-methoxypropenal (1 g, 69%) of b.p. 36—37°C at 2.7 kPa, R_f 0.92 and λ_{max} 248 nm (log ε 3.82, water, 25°C). Ref. [3] gives for 2-methoxypropenal b.p. 32.5°C at 1.7 kPa and Ref. [4] 37—40°C at 2.7 kPa.

Procedure B

2,3-Di-*O*-methyl-D,L-glyceraldehyde dimethyl acetal (8 g) was dissolved in 1 mol dm^{-3} hydrochloric acid (50 cm^3) and heated at 50°C for 150 min. After cooling the solution, 1 mol dm^{-3} aqueous solution of sodium hydroxide (50 cm^3) was added, pH was adjusted to 12 with 0.2 mol dm^{-3} sodium hydroxide and the solution was allowed to stay at 25°C for 90 min. At last, the solution was adjusted with 0.1 mol dm^{-3} hydrochloric acid to pH 7 and the reaction mixture was worked up as in the previous case. In this way 2-methoxypropenal (2.2 g, 52%) of b.p. 35°C at 2.4 kPa was obtained.

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