REFERENCES

1. Bobek M., Farkaš J., Šorm F.: *3rd Symposium on the Chemistry of Heterocyclic Compounds, Brno, 1969*; Abstracts of Papers N-7.
2. Montgomery J. A., Hewson K.: J. Heterocycl. Chem. *7*, 443 (1970).
3. Bobek M., Farkaš J., Šorm F.: This Journal *34*, 1684 (1969).
4. Bobek M., Farkaš J., Šorm F.: This Journal *34*, 247 (1969).
5. Lister J. H.: Revs Pure Appl. Chem. (Australie) *11*, 178 (1961).
6. Vince R., Donovan J.: J. Med. Chem. *12*, 175 (1969).
7. Defaye J., Reyners T.: Bull. Soc. Chim. Biol. *50*, 1625 (1968).

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AMINO SUGARS. XXV.*

REACTION OF METHYL-6-DEOXY-2,3-O-ISOPROPYLIDENE-4-O-METHANESULFONYL-α-L-TALOPYRANOSIDE WITH AMMONIA AND HYDRAZINE

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In previous papers[1-3] we studied the reaction of methyl-2,3-O-isopropylidene-4-O-methanesulfonyl-α-L-rhamnopyranoside (*VIII*) with sodium azide and hydrazine with the aim of preparing the corresponding 4-amino sugar. However, in agreement with the investigations of other authors[4,5] the substitution had an anomalous course, accompanied by ring rearrangement. In order to check the effect of steric conditions on the course of this substitution reaction we synthesized methyl-6-deoxy-2,3-O-isopropylidene-4-O-methanesulfonyl-α-L-talopyranoside (*V*) which differs from rhamnopyranoside *VIII* only by its inverse configuration at $C_{(4)}$ and we also followed its reaction with ammonia and hydrazine.

As a starting compound for the synthesis of talopyranoside *V* we chose methyl-2,3-O-isopropylidene-α-L-rhamnopyranoside (*I*). Overend and coworkers[6,7] oxidised it with chromium trioxide in pyridine and obtained methyl-6-deoxy-2,3-O-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (*II*) and found that its reduction takes place stereospecifically to methyl-6-deoxy-2,3-O-isopropylidene-α-L-talopyranose (*IV*). We endeavoured to carry out the oxidation with a mixture of dimethyl sulfoxide and acetic anhydride. However, we isolated methyl-2,3-O-isopropylidene-4-O-methylthiomethyl-α-L-rhamnopyranoside (*III*) in 53% yield as the main product. The formation of methylthiomethyl ethers during the oxidation of alcohols with the mentioned reagent is known[8], but if they are formed at all, then only in low yields. We obtained an incompletely pure

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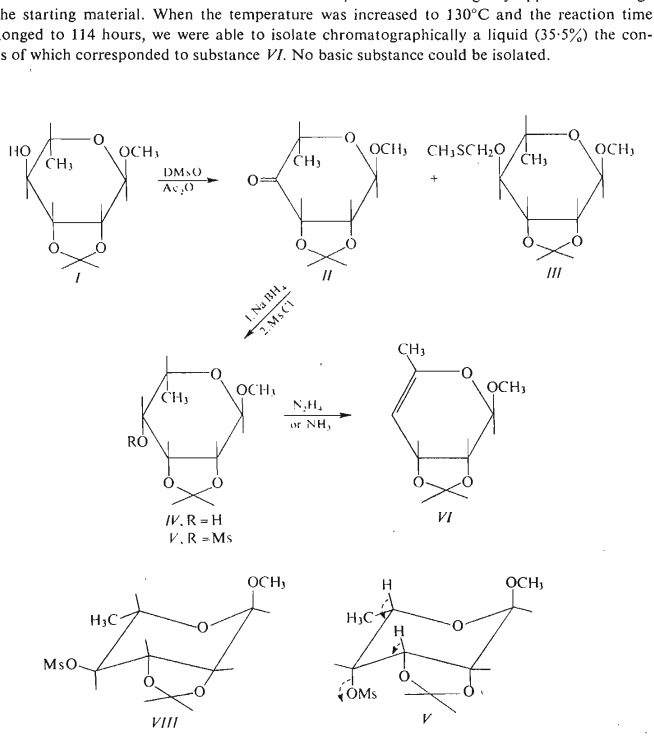
4-keto sugar *II* displaying absorption at 1 750 cm^{-1} in a 23% yield. On reduction with sodium boro-hydride and mesylation mesyl derivative *V* was obtained.

When reacting talopyranoside *V* with sodium azide we had already observed[9] that the yield of the corresponding methyl-4-azido-4-deoxy-2,3-O-isopropylidene-α-L-rhamnopyranoside was very low. This was confirmed in the work by Brimacomb, Ching, and Stacey[10], who were able to isolate the product of pyranoside (*VI*) in addition to azide. We carried out the reaction of *V* with ammonia in an autoclave at 80°C for 18 hours, without observing any appreciable change of the starting material. When the temperature was increased to 130°C and the reaction time prolonged to 114 hours, we were able to isolate chromatographically a liquid (35·5%) the contants of which corresponded to substance *VI*. No basic substance could be isolated.



The reaction of talopyranoside *V* with hydrazine and subsequent chromatography on silica gel gave a liquid in 39—50% yield the analysis of which corresponded to olefin *VI*, but its optical rotation, $[\alpha]_{578}$ −143° (*c* 0·48, chloroform) differed considerably from the value $[\alpha]_{578}^{25}$ −193° (*c* 1, chloroform) corresponding to substance *VI* (ref.[11]). Its IR spectrum was similar to that

of the product of ammonolysis, but it also contained maxima at 843, 1 337, and 1 707 cm^{-1} (measured in chloroform). The UV-spectrum in ethanol also showed differences in ε-values (calculated for the molecular weight 200·1). The substance from ammonolysis had λ_{max} 216 nm (ε 2522·6) and 264 nm (ε 124·5), the one from hydrazinolysis had λ_{max} 215·5 nm (ε 2724·8) and 264 nm (ε 140,3). The NMR spectra have shown that the product of hydrazinolysis contains predominantly the olefin *VI* accompanied by a smaller proportion of another substance which could not be analysed because of its low concentration. Gas chromatography combined with mass spectrography showed that it is a mixture containing approx. 80% of olefin *VI* (*m/e* 200, the spectrum identical with the spectrum of the product of ammonolysis) and 15% of a substance with a maximum mass peak at *m/e* 140, agreeing with formula $C_7H_8O_3$. To a certain extent the mass spectrum was similar to those of 2-methoxy-6-methyl-4-pyrone and 4-methoxy-6-methyl-2-pyrone.

From the NMR spectrum it follows that pyranosides *V* and *VIII* are in 1C conformation (see Scheme[1]). From comparison we see that in talopyranoside *V* the conditions for substitution are much better than in rhamnopyranoside *VIII*. As the mesyloxy group is axial, the antiperiplanar arrangement of the $C_{(5)}$-O and $C_{(4)}$-OSO_2R bonds enabling the rearrangement of the ring in rhamnoside *VIII* is not present in compound *V*. In addition to this, steric hindrances are also absent in *V* (the substitution takes place from that side of the ring which is opposite to the methyl and O-isopropylidene groups) and the axial position of the mesyloxy group is advantageous for the S_N2 substitution. Hence, the substitution should take place smoothly. However, there is another feature, very suitable for an elimination reaction, *i.e.* the diaxial arrangement of the mesyloxy group at $C_{(4)}$ and the hydrogen atoms at $C_{(3)}$ and $C_{(5)}$. From the paper of Brimacomb and coworkers[10] and the results presented here it can be demonstrated that this fact has a decisive influence on the course of the reactions with nucleophilic reagents. In the reaction of talopyranoside *V* with the azide ion[10] the nucleophilicity of which is high but the basicity low, elimination already prevails over substitution. In the reaction of *V* with ammonia and hydrazine no product of substitution can be isolated. The basicity of these reagents is evidently so high that elimination becomes the dominant reaction. Moreover, in the case of hydrazinolysis a deeper degradation of the molecule takes place, as can be inferred from the presence of a substance of molecular weight 140.

The stability of olefin *VI* toward catalytic hydrogenation is also very conspicuous. The reduction on platinum and palladium were unsuccessful. Hydrogenation at 90°C and 100 at pressure, with Raney nickel catalyst, also left the double bond intact.

EXPERIMENTAL

Melting points were determined on a Kofler block and they were not corrected. The boiling points were not corrected either The samples for analysis were dried at room temperature at 0.1 Torr for 10 hours. The NMR spectrum was measured on a HA-100 apparatus in deuteriochloroform, using tetramethylsilane as internal standard, IR spectra were measured on a Perkin-Elmer spectrophotometer, model 325. UV spectra were taken on a Beckmann DK 1 apparatus and mass spectra were measured on a LKB 9000 spectrometer.

Methyl-6-deoxy-2,3-O-isopropylidene-4-O-methanesulfonyl-α-L-talopyranoside (*V*)

A solution of 2·14 g of rhamnoside *I* in 29·5 ml of dry dimethyl sulfoxide was additioned with 19·5 ml of acetic anhydride and heated at 30°C for 24 hours. Acetic anhydride was evaporated *in vacuo* (0·5 Torr) at 50°C and the residue was dissolved in 100 ml of chloroform. Water (100 ml) was added to this solution and the mixture was shaken under gradual addition of 2M-K_2CO_3 until the aqueous layer had a constant pH 8 (uptake approximately 50 ml of the carbonate). The aqueous layer was extracted twice with 100 ml of chloroform. The combined chloroform

extracts were washed with three 100 ml portions of water and dried over magnesium sulfate. After the evaporation of the solvent the residual oil (2·66 g) was chromatographed on a silica gel CH column (40–100 μ, 10% water). Light petroleum–benzene mixture (1 : 10) (450 ml) eluted 1·45 g (53%) of chromatographically pure methyl-2,3-O-isopropylidene-4-O-methylthiomethyl-α-L-rhamnopyranoside (*III*), b.p. 85°C/0·08 Torr, $[\alpha]_D^{20}$ −224° (*c* 1·09, ethanol). For $C_{12}H_{22}O_5S$ (278·4) calculated: 51·78% C, 7·97% H, 11·52% S; found: 51·70% C, 8·02% H, 11·49% S. Further 400 ml of the eluate contained 0·49 g of a less pure substance with a distinct absorption at 1750 cm^{-1} (C=O), corresponding to the value given for methyl-2,3-O-isopropylidene-6-deoxy-α-L-*lyxo*-hexopyranosid-4-ulose (*II*) (ref.[6]).

To a stirred solution of 0·49 g of keto derivative *II* in 17 ml of 70% aqueous ethanol sodium boro-hydride (0·43 g) was added at 0°C over 30 minutes. The mixture was stirred for another 30 minutes, diluted with 27 ml of water and extracted 5 times with 13 ml portions of chloroform. The combined extracts were dried over magnesium sulfate, filtered and evaporated to dryness. The residue (0·38 g of a syrup) was dissolved in 2 ml of pyridine, the solution cooled util solid, and 0·18 ml methanesulfonyl chloride were added to it. After 12 hours standing at −5°C the mixture was evaporated to dryness, the crystalline residue was dissolved in 25 ml of chloroform, and the solution was washed with water, dilute sulfuric acid, sodium hydrogen carbonate, and water, and dried over magnesium sulfate. After the evaporation of the solvent and crystallisation from ethanol 0·32 g of talopyranoside *V* were obtained, m.p. 117–118°C, $[\alpha]_D^{20}$ −20° (*c* 0·7, ethanol). Literature[10] gives m.p. 116–117°C, $[\alpha]_D$ −19 ± 1° (*c* 0·6, chloroform), and lit.[12] m.p. 116–117·5°C $[\alpha]_D$ +20·2° (*c* 0·8, methanol) for the D-enantiomer.

Reaction of Talopyranoside *V* with Ammonia

a) A mixture of pyranoside *V* (1·00 g), methanol (30 ml), and liquid ammonia (30 ml) was heated in an autoclave at 80°C for 18 hours. After the evaporation of the solvent 0·98 g of the starting substance were recovered.

b) A mixture of pyranoside *V* (1·00 g), methanol (30 ml), and liquid ammonia (30 ml) was heated in an autoclave at 130°C for 118 hours. After the evaporation of the solvent under reduced pressure the residue was distributed between 20 ml of water and 20 ml of chloroform, and filtered through a sintered glass filter. The chloroform layer was dried over magnesium sulfate, filtered and evaporated. The residue was a brown liquid (0·39 g) which was chromatographed on a silica gel CH column (24 g) (40–100 μ, 10% of water). Benzene–light petroleum mixture (9 : 1) eluted 0·24 g (35·5%) of methyl-4,6-dideoxy-2,3-O-isopropylidene-β-D-*erythro*-4-hexenopyranoside (*VI*), b.p. 87°C/11 Torr, $[\alpha]_{578}$ −193° (*c* 0·57, chloroform), $[\alpha]_D$ −185° (*c* 0·57, chloroform, calculated from the values at 578 and 546 nm), IR spectrum (chloroform): ν 1670 cm^{-1} (C=C), UV spectrum (ethanol): λ_{max} 216 nm (ε 2522·6) and 264 nm (ε 124·5). Lit. gives b.p. 46–48°C/0·1 Torr, $[\alpha]_D$ −195° (*c* 1, chloroform), IR spectrum ν 1673 cm^{-1} (C=C) (ref.[10]), and b.p. 93–96°C/13 Torr, $[\alpha]_{578}^{25}$ +193° (*c* 1, chloroform) for the enantiomer[11]. For $C_{10}H_{16}O_4$ (200·1) calculated: 60·00% C, 8·05% H; found: 59·89% C, 8·29% H.

Reaction of Talopyranoside *V* with Hydrazine

Pyranoside *V* (1·00 g) and 96% hydrazine (5 ml) were refluxed at 130–140°C (under exclusion of moisture). An oil separated out. After cooling the mixture was extracted four times with 10 ml portions of ether. The combined extracts were washed with 50% KOH (1·4 g solid KOH) and dried over magnesium sulfate. After the evaporation of the solvent the residual liquid was diluted with a small amount of light petroleum. The unreacted pyranoside *V* crystallised out and it was

filtered off. When the reaction time was 1 hour 31·5% of the starting material were isolated, at 2 hours reaction time the yield was 4—9%, at 3 hours 7%, and at 5 hours 0%. The filtrate was concentrated *in vacuo* at 40°C and the residual liquid was chromatographed on a silica gel column (24 g) (40—100 μ, 10% of water). The column was eluted with benzene and 10 ml fractions were collected. The course of the chromatography was followed by thin-layer chromatography on Kieselgel MN in benzene–ethanol (100 : 1). A chromatographically pure liquid was isolated, b.p. 93°C/11 Torr, $[\alpha]_{578}$ −143°(*c* 0·48, chloroform). Its yield at 1 hour reaction time was 39%, at 2 hours it was 44—50%, and at 5 hours 39%. IR spectrum in chloroform contained in addition to maxima found in the spectrum of *VI* also maxima at 843, 1337, and 1707 cm^{-1}, UV spectrum (ethanol) λ_{max} 215·5 nm (ε 2724·8), and 264 nm (ε 140·3). The values given for *VI* are in the section on ammonolysis. The NMR spectrum showed that olefin *VI* predominates: τ 5·51 (H-1), 6·12 (H-2), 5·51 (H-3), 5·15 (H-4), 8·21 ($CH_3C=$), 6·46 (OCH_3), 8·55 and 8·64 ($C(CH_3)_2$), $J_{1,2} = 6·5$, $J_{2,3} = 6·0$, $J_{3,4} = 4·0$, $J_{4,6} = 1·05$ and $J_{3,6} = 1·15$ Zz. For $C_{10}H_{16}O_4$ (200·1) calculated: 60·00% C, 8·05% H; found: 60·02% C, 8·16% H.

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REFERENCES

1. Jarý J., Novák P., Ksandr Z., Samek Z.: Chem. Ind. (London) *1967*, 1490.
2. Jarý J., Novák P.: This Journal *33*, 1744 (1968).
3. Jarý J., Novák P., Samek Z.: Ann. *740*, 98 (1970).
4. Stevens C. L., Glinski R. P., Taylor K. G., Blumbergs P., Sirokman S.: J. Am. Chem. Soc. *88*, 2073 (1966).
5. Hanessian S.: Chem. Commun. *1966*, 796.
6. Collins P. M., Overend W. G.: J. Chem. Soc. *1965*, 1912.
7. Gunner S. W., Overend W. G., Williams N. R.: Carboh. Res. *4*, 498 (1967).
8. Albright J. D., Goldman L.: J. Am. Chem. Soc. *87*, 4214 (1965).
9. Novák P.: *Thesis*. Institute of Chemical Technology, Prague 1968.
10. Brimacombe J. S., Ching O. A., Stacey M.: J. Chem. Soc. (C) *1969*, 1270.
11. Lehmann J.: Angew. Chem. *77*, 863 (1965).
12. Stevens C. L., Glinski R. P., Taylor K. G.: J. Org. Chem. *33*, 1586 (1968).

Translated by Ž. Procházka.