CROATICA CHEMICA ACTA CCACAA 58 (3) 321—330 (1985)

CCA-1585

YU ISSN 0011-1643
UDC 547.81
Original Scientific Paper

Preparation of the Chiral Diol (2*R*,3*R*)-2-Hydroxymethyl-3--hydroxy-tetrahydropyran from D-Glucose *via* Reductive Rearrangement of Pseudo-D-glucal Triacetate

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Received February 7, 1985

Hydrogenation of D-glutal triacetate (*1*) and pseudo-D-glucal triacetate (*2*) into (2*R*,3*R*)-2-acetoxymethyl-3-acetoxy-tetrahydropyran (*4*) and the rearrangement of *1* into *2* were investigated. On hydrogenation, at high catalyst-to-substrate ratio and in the presence of a great excess of diethylamine, compound *1* afforded diacetate *4* in a mixture with triacetate *6*, while *2* was quantitatively converted into *4* under standard catalyst-to-substrate ($\sim 1:80$) ratio. It was established that hydrogenation of both isomers proceeds through the same intermediate 4,6-di-O-acetyl-1,2,3-trideoxy-D-erythro-hex-1-enitol (*3*) which was fully characterised from its ^{1}H- and ^{13}C-NMR spectra. When hydrogenation of *2* was performed with platinum on carbon in acetonitrile, compound *3* was isolated in 83% yield. The thermal and Lewis acid catalysed rearrangement of *1* into *2* was examined; only zinc(II) chloride in acetic anhydride gave preparatively acceptable yields (60—70%) of *2*. It was demonstrated that with Zn(II) or Mo(VI) ions in Ac_2O an $1 \leftrightharpoons 2$ equilibrium in favour of *2* was attained.

INTRODUCTION

Related to another synthetic project, larger quantities of the chiral diol (2*R*,3*R*)-2-hydroxymethyl-3-hydroxy-tetrahydropyran (*5*) were required.

This compound was first described by Bergmann[1], and later by Lemieux et al.[2] Its diacetate derivative *4* was prepared by Gray and Barker[3], who also carried out a brief study of the conversion of D-glucal triacetate (*1*) into *4*. Bergmann already observed[1] that pseudo-D-glucal triacetate (*2*) was more prone to hydrogenation and hydrogenolysis into *4* than the isomeric *1*. The latter compound afforded *4* in low yields[3] ($< 20\%$) only when large quantities of the noble metal catalysts were used[3]; e. g. per 100 mg of *1* were needed 145 mg of 10% Pt/C in the presence of a large (10—15 fold) excess of diethylamine[2,3].

We have undertaken this study in order to find the optimal conditions for preparation of the chiral diol *5* and to clarify the pathway of hydrogenation of the isomeric glucals *1* and *2*; the former is readily available from D-glucose[4,5].

RESULTS AND DISCUSSION

In the first series of experiments (Table I, no. 1—5) an attempt was made to convert D-glucal triacetate *1* into the diacetate *4* at lower catalyst- and base-to-substrate ratios than those in the original paper[3].

TABLE I

Catalytic Hydrogenation of the Compounds 1 *and* 2

Exp. No.	Starting compound (mmol)	Catalyst (mmol × 10^{-2})	Et_2NH (mmol)	Solvent	Time hr	Mol. ratio catalyst/ substrate	Product	Yield %
1	*1* (1.5)	Pt/C 17	5.0	EtOH	14	1/8.5	4	44.6
2	*1* (1.5)	Pt/C 7.5	5.0	EtOH	14	1/20	4	48
3	*1* (7.5)	Pt/C 25	22.0	EtOH	16	1/30	4, 6 (2.7 : 1.0)[b]	59[c]
4	*1* (2.0)	Pt/C 5.0	0.5	EtOH 90%	48	1/40	4, 6 (3.0 : 1.0)[b]	62[c]
5	*1* (2.0)	Pt/C 5.0	2.5	EtOH 90%	48	1/40	4, 6 (3.5 : 1.0)[b]	61.5[c]
6	*2* (1.24)	Pt/C 1.7	—	EtOH 90%	100 min[a]	1/73	4	88.8
7	*2* (1.03)	Pt/C 2.6	—	AcOH	45 min[a]	1/40	4	quant.
8	*2* (1.07)	Pt/C 2.7	—	MeCN	46	1/40	3	83
9	*2* (0.68)	Pt/C 1.0	—	EtOH 90%	65 min[a]	1/68	4	quant.
10	*2* (0.75)	Pd/C 1.0	—	EtOH 90%	20 min[a]	1/75	4	quant.
11	*2* (0.79)	Pd/C 1.0	—	AcOH	20 min[a]	4	1/79	quant.
12	*2* (0.88)	Pd/C 1.0	—	MeCN	5	1/88	(*3*) → *4*	76

[a] Time at which the theoretical amount of hydrogen was consumed, [b] Ratio *4 : 6* determined after quantitative separation on silicagel column, eluent *A*, [c] Total yield of *4* + *6*.

Hydrogenation was monitored by t.l.c. of the reaction mixture and by the hydrogen uptake. In the experiments 3—5 (Table I) *4* ($Rf \sim 0.35$, solvent methylene chloride) and *6* ($Rf \sim 0.25$) were quantitatively separated; traces of the unreacted *1* ($Rf \sim 0.3$) and the side-product *3* ($Rf \sim 0.4$) were identified. Spectral and analytical data of the isolated *3* revealed the presence of two acetoxy groups and one double bond. However, when compound *2* was hydrogenated with platinum on carbon in acetonitrile (no. 8, Table I), the same compound *3* was isolated. Thus, the problem of localisation of the double bond in *3* arose. Confirmation for the 1,2-double bond position in *3* was obtained after detailed analyses of its ^{1}H-NMR and ^{13}C-NMR spectra. Comparing the ^{1}H-NMR spectrum of *3* with that of (*2R,3R*)-2-methyl-3-acetoxy-2,3-dihydro pyran[6] (deacetoxy congener of *3*) the ring proton signals for C(1)-H (6.35 ppm, sextet), C(4)-H (5.02 ppm, sextet), and C(2)-H (4.70 ppm octet), could be assigned. The vinylic and allylic constants of *3* were as follows: C(4)-H; $J_{4,5} = = 6.1$ Hz, $J_{4,3pa} = J_{4,3pe} = 7.4$ Hz, C(2)-H; $J_{2,3pa} = 3.2$ Hz, $J_{2,3pe} = 4.4$ Hz, C(1)-H; $J_{1,2} = 6.10$ Hz, $J_{1,3pa} = J_{1,3pe} = 1.95$ Hz (notation following an earlier suggested pattern[7]). Irradiation of C(2)-H at 4.70 ppm decoulped the C(1)-H sextet into triplet. These results strongly indicated, but did not definitely prove, the 1,2-position of the double bond in *3*. Definite confirmation was provided by the ^{13}C-NMR spectrum of *3* which was compared with those of the two isomers *1* and *2* (Figure 1).

Unsaturated carbons in *3* revealed the signals at 97.67 ppm and 142.67 ppm, in close vicinity to the signals for the unsaturated carbons in *1*. Their assignation was performed according to earlier suggestions.[8,9]

The experiments with the pseudo-D-glucal triacetate *2* revealed that this isomer was quantitatively hydrogenated into *4* with platinum on carbon when 90% ethanol and acetic acid were used as solvents (Table I). The formation of *3* in acetonitrile (exp. no. 8) was shown to be a consequence of autoinhibition of the catalyst which slowly converted acetonitrile into ethylamine. In a blank experiment, i. e. in hydrogenation of the solvent under the same conditions, the ^{1}H-NMR spectrum confirmed the presence of ethylammonium ion. Paladium on carbon turned to be more resistant to the same inhibitory effect; on prolonged hydrogenation in acetonitrile, *3* was slowly hydrogenated into *4* (exp. no. 12).

The structure of the unsaturated intermediate *3* indicates that hydrogenation of *2*, but not of *1*, proceeds under allylic rearrangement. Presumably, this process occurs in concert with hydrogen transfer from the catalyst surface, i. e. during hydrogenolysis of the acetoxy group on C(1) (A in the Scheme 1). A similar mechanism was proposed[10,11] for deuterolysis of 2,3-unsaturated compounds *9* and *10* with lithium aluminium deuteride that afforded congener of *3* monodeuterated at C(3). However, isomeric compound *3A* was described recently as the only product when hydrogenolysis of *1*, *8* and *9* was performed with triethylsilane in the presence of bortrifluorid-diethyletherate[10]. The surprising opposite regioselectivity of this reaction is in keeping with the HSAB interpretation of the Lewis-acid catalyzed nucleophilic rearrangements of glycals[13].

After that, the conditions for an efficient preparation of pseudo-D-glucal triacetate *2* were sought. The long known[3,14] hydrolytic rearrangement of *1* into *2*, *via* pseudo-D-glucal diacetate *8*, proved impractical at the large scale.

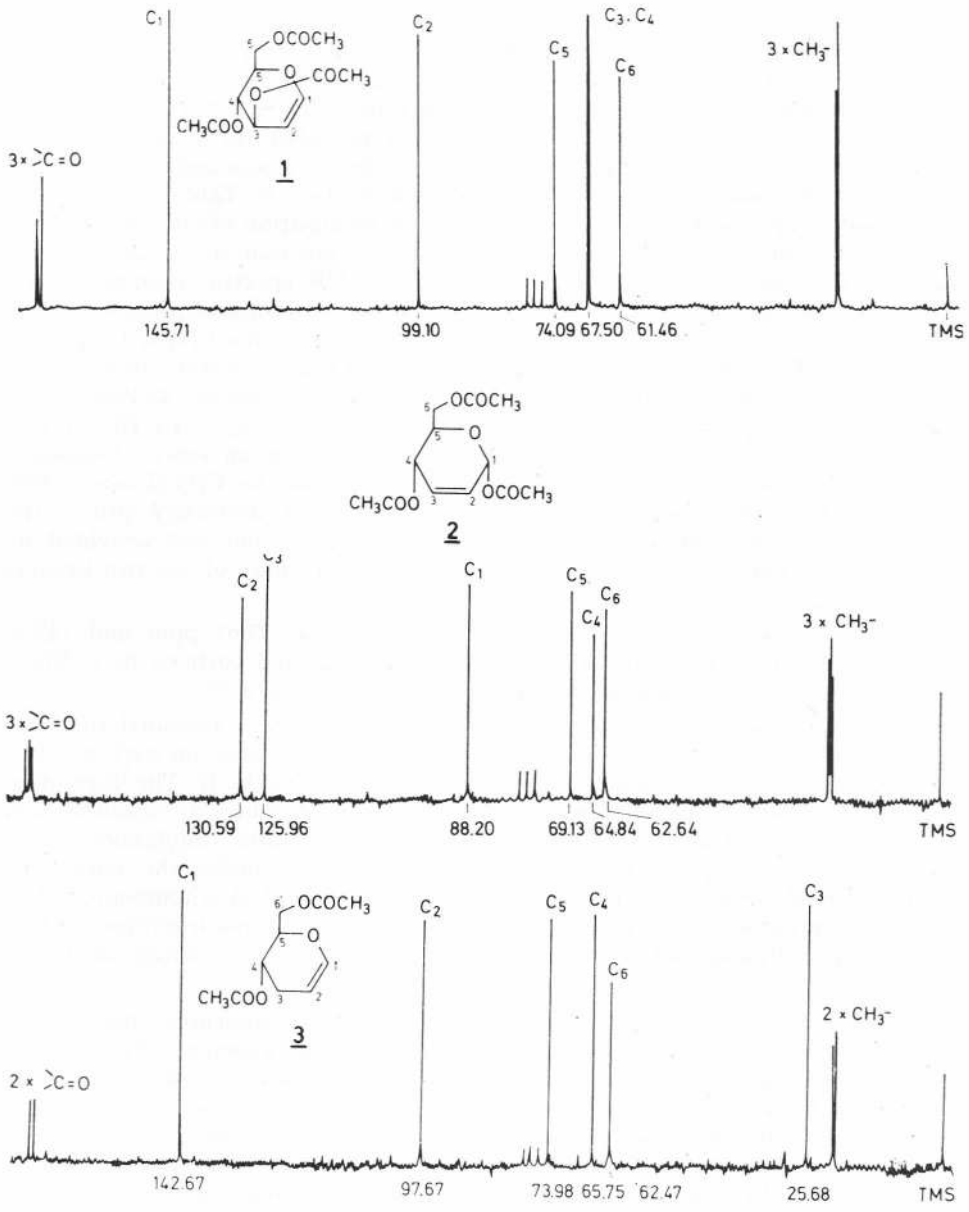


Figure 1. ^{13}C-NMR spectra of the compounds *1*, *2* and *3*.

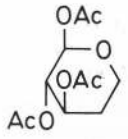
The yields of *2* were highly time-dependent as already noticed by others[14], and never exceeded 40%. Prolonged heating of *1* (2—3 hrs), required in order to consume the starting material, led to the formation of side-products, the double unsaturated compound *7* being regularly isolated. Its non-acetylated derivative was found in acid catalysed reaction of D-glucal triacetate with water[15]. When we performed acetylation of *8* in the presence of sodium-acetate

trihydrate, the ring opening took place, followed by acetylation at C(5) and *cis/trans* isomerisation to afford unsaturated aldehyde *11* in a good yield. This compound was purified by chromatography on silica gel and fully characterized. An earlier report[12] cited the use of dimethylsulfoxide-impregnated paper for purification of *11* which was identified as the dinitrophenylhydrazone derivative.

Finally, we examined the direct isomerization of *1* into *2*. Ferrier had found[16] *2* as an intermediate in the borontrifluoride-diethyletherate catalysed dimerization of *1*, and concluded[17] that the isomerization $1 \rightarrow 2$ could be achieved either thermally or under acid catalysis. Since this reaction belongs to the group of 3,3-sigmatropic rearrangements of glucals[18], we first examined the thermal rearrangement. Screening of several solvents and temperature intervals revealed a very slow formation of *2* and the presence of numerous side-products (see experimental). Among the acid catalysts tried, boron trifluoride diethyletherate led to polymerization of the starting material, whereas aluminium(III) chloride was inefficient. Since methanesulfonic acid was found very efficient in isomerasing 2-hydroxy-D-glucal and 2-hydroxy-D-galactal tetraacetates[19,20], its catalytic properties were examined in acetic anhydride and acetic acid at ambient temperature and ca. 100 °C. In acetic acid and at ambient temperature D-glucal triacetate reacted extremely slowly, at ca. 100 °C decomposition of *1* prevailed. In acetic anhydride at room temperature no reaction of *2* was noticed, and at ca. 100 °C a very slow formation of *2* was observed. Pseudo-D-glucal triacetate *2* did not give any detectable yield of *1* in either of the two solvents at ambient temperature, whereas in both solvents at ca. 100 °C about 20% of *2* was converted into *1*. The above results revealed a quite different response of *1* and *2* to the catalytic action of methanesulphonic acid than that exerted by their 2-acetoxy analogs[19,20]. It is interesting that silicagel (Merck 60F-254, for column chromatography) catalysed the rearrangement $1 \rightarrow 2$ in boiling toluene to an equilibrium ratio of approx. 1.5 : 1, reached after 3—4 hrs. Mo(VI) ions (molibdic acid) in boiling acetic anhydride led to the *1/2* ratio of $\sim$ 1 : 1.5 after ca. 10—15 min. The same ratio was achieved when *2* was submitted to isomerization.

Zinc(II) chloride was found to be the best catalyst. It had been already used for isomerization of D-glucal acetates[19–21], and the reversibility of this reaction was pointed out by several authors[22–24]. When either *1* or *2* were treated in acetic anhydride at ambient temperature with zinc(II) chloride, an equilibrium mixture consisting of 70—80% of *2* was reached within 10—20 min. By lowering the temperature or by dillution of acetic anhydride with benzene the isomerization rate was slowed down, and at —15 °C the reaction was completely stopped. It is interesting to note that the high ratio of *2* in equilibrium with *1* indicates that the allylic carbocation intermediate undergoes predominant acetylation at C(1), contrary to the behaviour of the intermediate *A* in hydrogenation of *1* and *2* (Scheme), which is protonated at C(3) exclusively. A rationalization of the substitution reactions of unsaturated sugars based on HSAB principle has been recently proposed by Zamojski et al.[25]

In the final step deacetylation of *4* was performed in the conventional way to give *5*.



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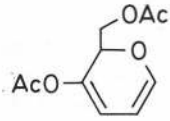

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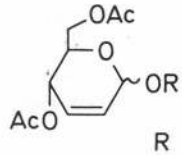
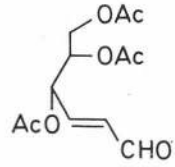


	R
8	H
9	α-OEt
10	β-OMe



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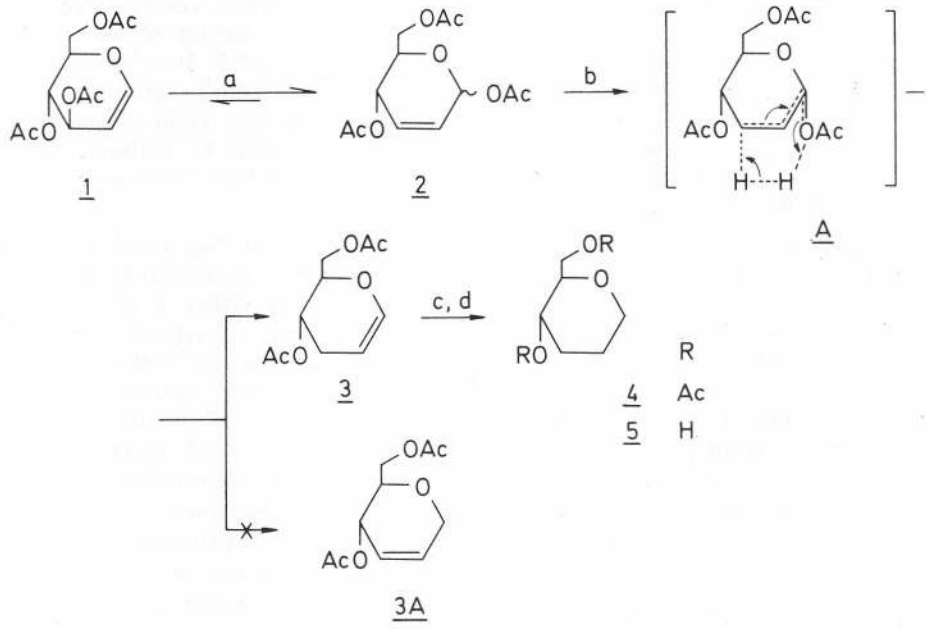
SCHEME 1.



a. $ZnCl_2$ / Ac_2O / R. T., b. Pt/C - H_2 / MeCN, c. Pd/C - H_2 / EtOH
d. NaOMe / MeOH / R. T.

EXPERIMENTAL

IR spectra were recorded with a Perkin-Elmer Model 137 spectrometer, and ^{1}H- and ^{13}C-NMR spectra with a Jeol FX 90 Q Furrier-transform spectrometer for solutions in chloroform-d, with TMS as the internal standard. TLC was performed on Merck's DC-alufolien with Kieselgel 60F-254, and column chromatography on silica gel (Merck 0.05—0.2 mm): detection on t.l.c. plates was effected by charring with sulphuric acid. Organic solutions were dried over sodium sulphate, and evaporations of the solvents were carried out at reduced pressure on a rotary evaporator. For chromatographic separations the following solvents and solvent mixtures were used: *A*-methylen-chloride; *B*-chloroform-ethylacetate-light petroleum (1 : 1 : 3); *C*-ethylether-light petroleum (2 : 1).

D-Glucal triacetate was prepared[4] from D-glucose; for hydrogenation experiments the compound was purified on a silica gel column using chloroform as eluant.

Hydrogenation of D-*Glucal Triacetate* (1)

Apparatus. — A two-necked flask was joined to a standard, closed-system hydrogenation assambly, the second neck closed by the rubber septum. At regular time intervals samples were taken inserting a syringe needle, and immerging the glass capillary into the reaction solution, during which time the hydrogen inlet was closed.

General Procedure (for experiments 1—5, Table I)

A solution of *1* and diethylamine and ethanol (5 ml) was added to a stirred suspension of the prehydrogenated catalyst in the same solvent (5 ml), and the hydrogenation reaction was allowed to proceed at room temperature and atmospheric pressure for 14—18 hrs; after the first 3—6 hrs a lag period in the hydrogen uptake was regularly noticed. T.l.c. (solvent *A*) revealed a relatively fast hydrogenolysis of *1* ($Rf \sim 0.3$), and accumulation of the intermediate *3* ($Rf \sim 0.4$) and the side product *6* ($Rf \sim 0.25$). Complete hydrogenation of *3* into *4* ($Rf \sim 0.35$) required prolonged periods of time, and the hydrogen consumption was above the theoretical values (> 30—50%). After filtration of the catalyst and spilling with ethanol, the filtrate was evaporated and the product mixture was separated by column chromatography. The yields of the separated *4* and *6* are given in Table I.

*Hydrogenation of 2 in Acetonitrile. Preparation of 4,6-di-O-acetyl-1,2,3-trideoxy-*D-*rythro-hex-1-enitol* (3)

Compounds *2* (293.8 mg, 1.07 mmola) was dissolved in acetonitrile (3 ml) and added to prehydrogenated platinum on carbon (54.0 mg, 10% Pt/C) in acetonitrile (5 ml). Hydrogenation was carried out for 46 hrs, whereafter the catalyst was filtered off, the filtrate concentrated, and the crude *3* purified by chromatography on silicagel (30 g, solvent system *B*) to afford 192.8 g (83%) of the pure *3*. The analytical sample was distilled in the metal-block, bp. 160—163 °C/0.18 mmHg. IR (neat): 2970, 1750, 1662, 1378, 1245, 1105, 742, 612 cm^{-1}. ^{1}H-NMR (δ in ppm): 1.9—2.6 (m, 2H, C(3)-2H), 2.02 and 2.09 (two s, 6H, $2 \times CH_3CO$), 3.9—4.4 (m, 3H), 4.70 (octet, C(2)-H, $J_{2,3pa} = 3.2$ Hz, $J_{2,3pe} = 4.4$ Hz), 5.02 (sextet, C(4)-H, $J_{4,5} = 6.1$ Hz, $J_{4,3pa} = J_{4,3pe} = 7.4$ Hz), 6.35 (sextet, C(1)-H, $J_{1,2} = 6.10$ Hz, $J_{1,3pa} = J_{1,3pe} = 1.95$ Hz). $[\alpha]_D = +108.3$ (c = 1.2 in $CHCl_3$).

Anal. for $C_{10}H_{14}O_5$ (214.22) calc'd.: C 56.07; H 6.59%
found: C 55.89; H 6.62%.

Blank Hydrogenation of Acetonitrile

Acetonitrile (10 ml) was hydrogenated in the presence of platinum on carbon (20.6 mg) for 75 hrs, during which period 82 ml (ca. 3.5 mmol) were consumed. After removal of the catalyst, trifluoroacetic acid (0.5 ml) was added to the solution and the solvent was evaporated. The residual oil was dissolved in 0.5 ml of $CDCl_3$.

^{1}H-NMR spectrum revealed strong signals at 1.33 ppm (triplet), and 3.22 ppm (double quartet) characteristic for ethylamine trifluoroacetate.

Rearrangements of 1 *and* 2

(a) In Acetic Anhydride with Zinc(II) Chloride

To a solution of *1* (20.5 g, 75.3 mmol) in acetic anhydride (70 ml), a suspension of dry zinc(II) chloride (1.08 g) in aceticanhydride (20 ml) was added. The reaction mixture was vigorously stirred at ambient temperature for 20 min, whereupon it was poured on ice-water (0.5 l), extracted with chloroform (3 × 200 ml) and the combined extracts were washed with satd. aqueous bicarbonate and water, and dried. On evaporation of the solvent the residual oil was repeatedly evaporated with toluene to remove traces of acetic acid and then passed through the silica gel column with solvent system *C* to give 3.25 g (16%) of the starting *1*, a mixture (0.96 g) of *1* and *2* and 11.7 g (67.8%) of the pure *2*.

(b) Other Atttempts

Attempts at thermal rearrangement of *1* in tetrahydrofurane, dioxane, benzene, toluene, acetic acid and benzyne (bp. 180—200 °C) at the temperature 65—200 °C failed. The rearrangement was monitored by t.l.c. (5 min intervals) and by ^{13}C-NMR (30 min intervals) following the appearance of characteristic signals for *1* at (δ in ppm); 145.7 (C(1)), 99.1 (C(2)), and 74.1 (C(5)), and for *2*; 130.6 (C(2)), 126.0 (C(3)), and 69.1 (C(5)).

Treatment of *2* (269 mg, 1.0 mmol) in 3 ml of acetic anhydride with zinc(II) chloride (114 mg) for ~ 2 hrs at ambient temperature led to a mixture of *1* and *2* (~ 1 : 3), as determined on chromatographic separation.

Treatment of *1* (3.22 g, 1.2 mmol) with molibdic acid (55 mg, 0.34 mmol; Aldrich) in refluxing acetic anhydride (40 ml) for 30 min afforded, after work-up as described in (a) compound *2* (1.40 g, 52%) and unreacted 1 (0.88 g); were isolated; the ratio *1/2* 39 : 61.

Treatment of *2* (97 mg) with molibdic acid (10 mg) in refluxing acetic anhydride (2.0 ml) under the same conditions as described for *1* led to the same *1/2* ratio ~ 1 : 1.5.

(2R,3R)-*2-Hydroxymethyl-3-hydroxy-tetrahydropyran* (5)*

A stirred solution of the diacetate *4* (650 mg, 3.0 mmol) in methanol (10 ml) was treated overnight with sodium methoxyde (50 mg) at ambient temperature. The solution was adjusted to pH 5.5—6.0 by addition of Dowex 50W—X8 (methanol wet, H^+), the resin was filtered off, washed with methanol, and the combined filtrate and washing were evaporated to dryness to afford 373 mg (94%) of pure *5*, bp. 150—155 °C/0.16 mm Hg (metal block). IR (film): 3400 broad, 2970, 2930, 1460, 1440, 1380, 1350, 1280, 1080, 1050, 985, 950, 866 cm^{-1}. ^{1}H-NMR (δ in ppm): 1—1.5 (m, 3H), 1.6—1.9 (m, 1H), 2.3 (broad s, ca. 2H, 2 × OH, dissapp. on addu. of D_2O) 2.6—3.5 (m, 6H). $[\alpha]_D = +25.5°$ (c = 1.37 in $CHCl_3$).

Anal. for $C_{16}H_{12}O_3 \times 1/3\ H_2O$ (138.16) calc'd.: C 52.16; H 9.22%
found: C 52.28; H 9.15%

*4,6-Di-O-acetyl-1,5-anhydro-1,2,3-trideoxy-*D*-erythro-hex-1,3-dienitol* (7)

Compound *1* (9.0) dissolved in 180 ml of water, was heated under reflux for 2 hrs, during which time the spot of the starting *1* (*Rf* ~ 0.4, solvent *B*) disappeared. Water was removed by repeated evaporation in vacuo with ethanol and toluene, and the residual oil (5 g) was acetylated by dissolution in acetic anhydride (40 ml) and addition of sodium acetate trihydrate (10 g). After stirring overnight at ambient temperature, the reaction mixture revealed three spots (*Rf* ~ 0.7 (7), *Rf* ~ 0.4 (*2*),

* Note. In view of the forthcoming papers in this series the nomenclature based on the fully hydrogenated pyran ring has been used for compound *5*.

and $Rf \sim 0.25$ (*11*) — solvent *B*). The crude product mixture was purified on a silicagel column (380 g — solvent *B*) affording 99 mg of pure 7 in the fractions 8—13 (10 ml per fraction), b. p. 90—100 °C/0.01 mm Hg metal block). IR (film): 2960, 2930, 2860, 1750, 1510, 1440, 1375, 1160, 1050, 950, 875, 820, 750, 650, 610 cm^{-1}. ^{1}H-NMR (δ in ppm): 2.06, 2.09 (two s, 2x, CH_3CO), 4.42 (d, 1H, $J = 1.2$ Hz), 4.49 (s, 1H), 6.11 (m, 1H), 6.37 (m, 2H), 7.4 (q, 1H, $J = 1.2$ Hz).

Anal. for $C_{10}H_{12}O_5$ (212.50) calc'd.: C 56.60; H 5.70%
found: C 56.74; H 5.88%.

3,4,5-Triacetoxy-hex-2-en-1-al (11)

Continuing chromatographic separation described for 7, compound *2* (0.7 g) was isolated in the fractions 44—50, then 5.30 g (59%) of pure *11* were obtained. The analytical sample was obtained on distillation in a metalblock, b. p. 155—160 °C/0.01 mm Hg. IR (film): 2960, 2840, 2750, 2440, 1755, 1700, 1655, 1440, 1380, 1230, 1130, 1050, 980, 700, 610 cm^{-1}. ^{1}H-NMR (δ in ppm): 2.06, 2.09, 2.15 (three s, $3 \times CH_3CO$), 4.24 (t, 2H, $J = 5.3$ Hz, 5.28 (m, 1H, $J = 10.2$ Hz), 5.76 (m, 1H, $J = 4.8$ Hz), 6.26 (m, 1H, $J = 15.8$ Hz), 6.76 (q, 1H, $J = 15.8$ Hz), 9.59 (d, 1H, $J = 5.3$ Hz).

Anal. for $C_{12}H_{16}O_7$ (272.26) calc'd.: C 52.64; H 5.92%
found: C 53.07; H 5.75%.

Acknowledgement. — We thank Dr. D. Keglević for helpful discussions during preparation of the manuscript. Dr. B. Klaić helped us by interpreting of some ^{1}H-NMR off resonance experiments; ^{1}H-NMR, ^{13}C-NMR, and IR spectra were determined by Ing. B. Metelko and Mrs. M. Brozinčević.

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SAŽETAK

Priprava hiralnog diola (*2R,3R*)-2-hidroksimetil-3-hidroksi-tetrahidropirana iz D-glukoze reduktivnom pregradnjom pseudo-D-glukal triacetata

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Istraživana je hidrogenacija D-glukal-triacetata (*1*) i pseudo-D-glukal-triacetata (*2*) u (*2R,3R*)-2-acetoksimetil-3-acetoksi-tetrahidropiran (*4*), kao i pregradnja *1* u *2*. Hidrogenacijom uz visok omjer katalizator-supstrat i u prisustvu velikog suviška dietilamina spoj *1* davao je diacetat *4* u smjesi s triacetatom *6*, dok je *2* kvantitativno prelazio u *4* uz standardan omjer ($\approx 1:80$) katalizator-supstrat. Hidrogenacija obaju izomera ide preko istog intermedijara, 4,6-di-O-acetil-1,2,3-trideoksi-D-*eritro*-heks-1-enitola (*3*), koji je potpuno karakteriziran ^{1}H- i ^{13}C-NMR spektrima. Kada je hidrogenacija *2* provedena uz platinu na ugljenu u acetonitrilu, spoj *3* izoliran je u 83%-tnom iskorištenju. Istraživane su termička i Lewis-ovim kiselinama katalizirana pregradnja *1* u *2*; preparativno prihvatljiva iskorištenja (60—70%) dobivena su samo upotrebom cink(II)-klorida u anhidridu octene kiseline. Pokazano je da u nazočnosti Zn(II) i Mo(VI) u Ac_2O dolazi do uspostavljanja ravnoteže $1 \rightleftharpoons 2$ u korist izomera *2*.