DERIVATIVES OF 2-ALKOXY-5,6-DIHYDRO-2*H*-PYRAN AS STARTING MATERIALS IN THE SYNTHESIS OF MONOSACCHARIDES

PART IX*. TOTAL SYNTHESIS OF METHYL 3,4-DIDEOXY- AND 3,4,6-TRIDEOXY-D,L-HEX-3-ENOPYRANOSIDES†

A. BANASZEK AND A. ZAMOJSKI

Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw 42 (Poland)

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ABSTRACT

The synthesis of the title compounds from the butyl ester of *cis,trans*-5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylic acid, which was reduced to *cis,trans*-5,6-dihydro-6-hydroxymethyl-2-methoxy-2*H*-pyran is described. Epoxidation of the latter compound yielded four stereoisomeric epoxides, which were separated by column chromatography. Each epoxide was, in turn, treated with dimethylamine to give the corresponding methyl 3,4-dideoxy-3-dimethylamino-D,L-hexopyranoside. Hydrogen-peroxide oxidation of the aminodeoxy sugar gave the *N*-oxide, which was subjected to a Cope degradation to afford methyl 3,4-dideoxy-D,L-hex-3-enopyranoside. The same reaction scheme was applied to *trans*-5,6-dihydro-2-methoxy-6-methyl-2*H*-pyran, affording methyl 3,4,6-trideoxy-α-D,L-*erythro*- and *threo*-hex-3-enopyranosides; β anomers were obtained by acid-catalyzed anomerization. The n.m.r. data are given for unsaturated sugars and their *O*-acetyl derivatives.

INTRODUCTION

It has been shown that esters of 5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylic acid[2] (**1–3**) can be conveniently used as substrates for simple and highly stereoselective synthesis of a variety of such monosaccharides as methyl 4-deoxy-D,L-hexopyranosides[3] (**4**), methyl 4,6-dideoxy-D,L-hexopyranosides[4] (**5–7**), 1,3,6-tri-*O*-acetyl-2,4-dideoxy-D,L-hexopyranosides[5] (**8**), etc. For example, methyl 4-deoxy-α-D,L-*xylo*-hexopyranoside (**4**) was prepared from *trans*-5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylic acid (**1**) in three steps involving a lithium aluminium hydride reduction of the ester group, epoxidation of the double bond (two diastereoisomeric epoxides were formed), and acidic hydrolysis of methyl 2,3-anhydro-4-deoxy-α-D,L-*ribo*-hexopyranoside (**15**). It is noteworthy that the simplest synthesis of methyl 4-deoxy-α-D-*xylo*-hexopyranoside from methyl α-D-galactopyranoside requires, at least, five

*For Part VIII, see Ref. 1.

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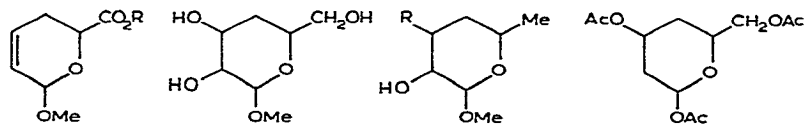


1 R = Me
2 R = Et
3 R = Bu

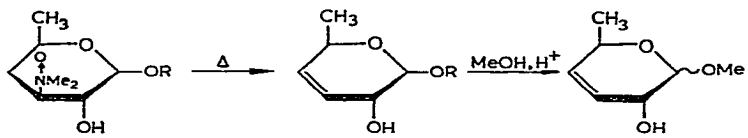
4

5 R = OH
6 R = OMe
7 R = NMe_2

8

steps[6]. Only two sugars having the structures **4–8**, D-chalcose[7] and D-desosamine[8], are known to occur in Nature; a ready access to them opens the possibility of thorough examination of their biological and physical properties.

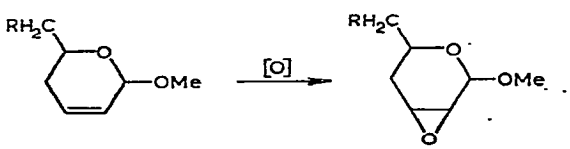
Compounds **4–8** have one structural feature in common: the methylene group in position 4. This group, stemming from the starting esters, prohibits the use of **1–3** for the synthesis of monosaccharides that possess a substituent at C-4. We investigated, therefore, methods which could lead to a suitable transformation of **1–3**. Numerous experiments with "allylating" reagents, such as *N*-bromosuccinimide, *N,N'*-dibromo-5,5-dimethylhydantoin, selenium dioxide, lead tetraacetate, 2-methyl-2-propyl perbenzoate, oxygen, cuprous chloride, etc. were unsuccessful*. Addition of bromine to the double bond in **1** and in related compounds gave a series of stereoisomeric dibro-



9 10 11

R = macro ring of oleandomycin or erythromycin A

motetrahydropyrans. Debromination failed, however, to yield the desired 4,5-unsaturated allyl bromides[9]. Celmer[10], and Jones and Rowley[11] found that pyrolysis of desosamine *N*-oxide (**9**) lead to the unsaturated compound **10** with a C-3–C-4 double

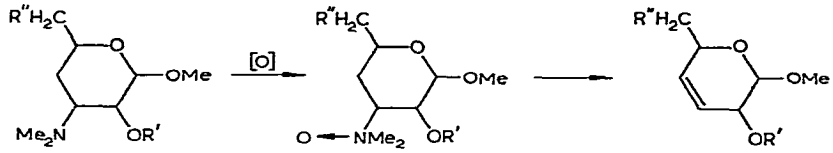


12 R = H
13 R = OH

14 α-anomer, *ribo*, R = H
15 R = OH
16 β-anomer, *ribo*, R = OH
17 α-anomer, *lyxo*, R = H
18 R = OH
19 β-anomer, *lyxo*, R = OH

*Other reactions were observed, *e.g.* additions to the double bond, cleavage of the dihydropyran ring, etc.

bond in the pyranose ring. Therefore, we investigated the reaction sequence **12** to **52** which was shown to be valid. Starting with the butyl ester of *cis, trans* 5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylic acid (**3**) all four diastereoisomeric methyl 3,4-dideoxy-D,L-hex-3-enopyranosides (**38, 43, 47, 52**) could be synthesized. 5,6-Dihydro-2-methoxy-6-methyl-2*H*-pyran (**12**) was used for the synthesis of all diastereoisomeric methyl 3,4,6-trideoxy-D,L-hex-3-enopyranosides (**36, 41, 45, 50**). Compounds of both syntheses were obtained in good yields. This permits the introduction of suitable substituents at C-3 and C-4 by addition to the double bond.



20–27 **28–35** **36–53**

20	α-anomer, *xylo*,	R′ = R″ = H	**37**		R′ = Ac, R″ = H
21		R′ = H, R″ = OH	**38**		R′ = H, R″ = OH
22		R′ = Ac, R″ = OAc	**39**		R′ = H, R″ = OAc
23	β-anomer, *xylo*,	R′ = H, R″ = OH	**40**		R′ = Ac, R″ = OAc
24	α-anomer, *arabino*,	R′ = R″ = H	**41**	β-anomer, *erythro*,	R′ = R″ = H
25		R′ = H, R″ = OH	**42**		R′ = Ac, R″ = H
26		R′ = Ac, R″ = OAc	**43**		R′ = H, R″ = OH
27	β-anomer, *arabino*,	R′ = H, R″ = OH	**44**		R′ = Ac, R″ = OAc
28	α-anomer, *xylo*,	R′ = R″ = H	**45**	α-anomer, *threo*,	R′ = R″ = H
29		R′ = H, R″ = OH	**46**		R′ = Ac, R″ = H
30		R′ = Ac, R″ = OAc	**47**		R′ = H, R″ = OH
31	β-anomer, *xylo*,	R′ = H, R″ = OH	**48**		R′ = H, R″ = OAc
32	α-anomer, *arabino*,	R′ = R″ = H	**49**		R′ = Ac, R″ = OAc
33		R′ = H, R″ = OH	**50**	β-anomer, *threo*,	R′ = R″ = H
34		R′ = Ac, R″ = OAc	**51**		R′ = Ac, R″ = H
35	β-anomer, *arabino*,	R′ = H, R″ = OH	**52**		R′ = H, R″ = OH
36	α-anomer, *erythro*,	R′ = R″ = H	**53**		R′ = Ac, R″ = OAc

RESULTS AND DISCUSSION

The synthesis of the *cis,trans*-isomer mixture of the butyl ester of 5,6-dihydro-2-methoxy-2*H*-pyran-6-carboxylic acid (**3**) and its reduction to *cis,trans*-5,6-dihydro-6-hydroxymethyl-2-methoxy-2*H*-pyran (**13**) was described in earlier papers of this series[1,2]. Epoxidation of **13** gave all four stereoisomeric epoxides **15, 16, 18,** and **19**, which were separated chromatographically into pure components[1]. The configuration of epoxides **15, 16, 18, 19** was established by the interpretation of the n.m.r. spectra[1]. Each compound (**15, 16, 18,** and **19**) was treated with an aqueous solution of dimethylamine to give, in high yield, the corresponding methyl 3,4-dideoxy-3-dimethylamino-D,L-hexopyranoside **21, 23, 25,** and **27**. In the case of both anomers **15** and **16** having the *ribo* configuration, a small amount of methyl 2,4-dideoxy-2-dimethylamino-D,L-hexopyranosides, **54** and **55**, was formed beside the stereoisomeric **21** and **23**. The results of the opening of the oxirane ring of **15, 16, 18,** and **19** are reported in Table I.

TABLE I

REACTION PRODUCTS OF STEREOISOMERIC EPOXIDES WITH 20% AQUEOUS DIMETHYLAMINE AT 20°

Epoxide	*Reaction time (h)*	*Products*	*Yield (%)*	*M.p.*[a]	*Formula*	*Analysis*[a]							
						Calc.				*Found*			
						C	*H*	*Cl*	*N*	*C*	*H*	*Cl*	*N*
α, *Ribo* (15)[b]	48	α, *xylo* (21)	84	210–212	$C_9H_{20}ClNO_4$	44.71	8.30	14.70	5.81	44.80	8.43	14.72	5.67
		α, *arabino* (54)	10	167–169[c]	*ibid.*					44.31	8.25	14.68	5.63
β, *Ribo* (16)[d]	48	β, *xylo* (23)	73	187–188	*ibid.*					44.21	8.36	14.46	6.05
		β, *arabino*[e] (55)	15	121–123	$C_9H_{19}NO_5$	48.85	8.66		6.33	48.89	8.56		6.41
α, *Loxo* (18)	12	α, *arabino* (25)	100	132–133	$C_9H_{20}ClNO_4$	44.71	8.30	14.70	5.81	44.45	8.21	15.13	6.07
β, *Loxo* (19)	12	β, *arabino* (27)	100	94–95	*ibid.*					44.42	8.35	14.46	5.52

[a]Of hydrochlorides. [b]With 60% aqueous dimethylamine for 8 h at 40–50°, *ca.* 72% of **21** and 28% of **54** were formed. [c]M.p. of free aminosugar: 123–125°. [d]With *ca.* 60% aqueous dimethylamine at 40–50°, 55% of **23** and 45% of **55** were formed. [e]M.p. (dec.) and analysis of *N*-oxide.

TABLE II

YIELDS, M.P., B.P., AND ANALYTICAL DATA OF METHYL 3,4-DIDEOXY- AND 3,4,6-TRIDEOXY-D,L-HEX-3-ENOPYRANOSIDES AND THEIR *O*-ACETYL DERIVATIVES

	R^1	R^2	R^3	R^4	R^5	*Yield* (%)	*M.p.* (°)	*B.p.* (°)[a]	*Formula*	*Analysis*			
										Calc.		*Found*	
										C	*H*	*C*	*H*
36	H	OMe	H	OH	CH_3	68		130 (20)	$C_7H_{12}O_3$	58.32	8.39	57.93	8.61
37	H	OMe	H	OAc	CH_3	90		130 (25)	$C_9H_{14}O_4$	58.05	7.58	57.88	7.81
38	H	OMe	H	OH	CH_2OH	67	68–70		$C_7H_{12}O_4$	52.49	7.55	52.43	7.68
39	H	OMe	H	OH	CH_2OAc	64		100 (0.05)	$C_9H_{14}O_5$	53.46	6.98	53.36	7.03
40	H	OMe	H	OAc	CH_2OAc	83		130–140 (0.05)	$C_{11}H_{16}O_6$	54.09	6.60	54.03	6.54
41[b]	OMe	H	H	OH	CH_3	100	44–45		$C_7H_{12}O_3$	58.32	8.39	58.07	8.36
42	OMe	H	H	OAc	CH_3	95	66–67		$C_9H_{14}O_4$	58.05	7.58	58.21	7.69
43	OMe	H	H	OH	CH_2OH	59		130 (0.02)	$C_7H_{12}O_4$	52.49	7.55		
44	OMe	H	H	OAc	CH_2OAc	89	59–60		$C_{11}H_{16}O_6$	54.09	6.60	54.11	6.66
45	H	OMe	OH	H	CH_3	76		120 (15)	$C_7H_{12}O_3$	58.32	8.39	58.19	8.56
46	H	OMe	OAc	H	CH_3	79		125 (15)	$C_9H_{14}O_4$	58.05	7.58	58.10	7.89
47	H	OMe	OH	H	CH_2OH	66	63–64		$C_7H_{12}O_4$	52.49	7.55	52.50	7.72
48	H	OMe	OH	H	CH_2OAc	38	43–45		$C_9H_{14}O_5$	53.46	6.98	53.16	6.97
49	H	OMe	OAc	H	CH_2OAc	80		130 (0.2)	$C_{11}H_{16}O_6$	54.09	6.60	54.03	6.65
50	OMe	H	OH	H	CH_3	8		120 (12)	$C_7H_{12}O_3$	58.32	8.39	58.51	8.20
51	OMe	H	OAc	H	CH_3	50			$C_9H_{14}O_4$	58.05	7.58		
52	OMe	H	OH	H	CH_2OH	64		130 (0.02)	$C_7H_{12}O_4$	52.49	7.55		
53	OMe	H	OAc	H	CH_2OAc	76		130 (0.03)	$C_{11}H_{16}O_6$	54.09	6.60	53.82	6.63

[a]Pressure in mm indicated in parenthesis. [b]Obtained by anomerization of the α anomer and separation of the mixture.

TABLE III

N.M.R. DATA OF METHYL 3,4-DIDEOXY- AND 3,4,6-TRIDEOXY-D,L-HEX-3-ENOPYRANOSIDES AND THEIR *O*-ACETYL DERIVATIVES[a]

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*OMe*	*OAc*	$J_{1,2}$	*Other coupling constants (Hz)*
36	4.80	4.20[b]	5.63		4.20	1.21	3.50		3.7	$J_{5,6}$ 6.8
37	4.94	5.18	5.46	5.73	4.19	4.19	1.20	2.05	4.1	$J_{3,4}$ 10.6
38	4.81	4.12[b]	5.64		4.12	3.58	3.44		3.8	
39[c]	4.80	4.10[d]	5.63		4.10	4.10	3.45	2.04	4.1	
40[e]	5.03	5.23	5.64	5.78	4.31	4.10	3.43	2.05 2.08	4.0	$J_{3,4}$ 10
41	4.30	4.05	5.69		4.35	1.26	3.55		6.5	
42	4.51	5.15	5.60	5.83	4.35	1.30	3.48	2.07	5.8	$J_{3,4}$ 10.2
43	4.38	4.05	5.75		4.32	3.65	3.55		5.8	
44	4.54	5.05	5.79		4.40	4.10	3.43	2.05	4.8	
45	4.55	3.58	5.74		4.17	1.25	3.42		3.2[f]	
46	4.72	4.87	5.75	5.96	4.29	1.31	3.47	2.08	2.7[f]	
47	4.77	3.85[g]	5.85	5.97	4.10	3.85	3.47		2.6[f]	$J_{3,4}$ 10.6
48[c]	4.68	3.73	5.77	5.98	4.15[h]	4.15	3.40	2.05	3.3[f]	
49	4.71	4.83	5.88		4.30	4.15	3.40	2.05	2.5[f]	
50	4.51	3.98	5.75		4.27	1.30	3.55		2.6	
51	4.50	5.02	5.75		4.22	1.31	3.40	2.02	2.7	
52	4.48	3.95	5.74	5.91	4.23	3.62	3.50		2.7	$J_{3,4}$ 10
53[i]	4.73	5.22	5.92		4.38	4.18	3.50	2.07 2.09	3.0	

[a]In $CDCl_3$ solution, δ scale, first-order coupling constants are given. [b]Together with H-5. [c]The position of the acetyl group was determined by the downfield shift of the H-6 proton. [d]Together with H-5, H-6, and H-6'. [e]Lit.[15]: H-1, 5.10; $J_{1,2}$ 4.2 Hz. [f]Broad singlet, w/2 is given. [g]Together with H-6 and H-6'; centre of a multiplet. [h]Together with H-6 and H-6'. [i]Lit.[15]: H-1, 4.76; $J_{1,2}$ 2.8 Hz.

The structure and configuration of the aminosugars **21**, **23**, **25**, **27**, **54**, and **55** was based on analytical and spectral data, as well as on the analogy with earlier results concerning the oxirane ring opening of **14** and **17**. Compounds **21–23** and **25–27** were oxidized with hydrogen peroxide in an acetone–water mixture to give the corresponding *N*-oxides **29–31** and **33–35** in 90–100% yield. Each *N*-oxide **29–31** and **33–35** was subjected to thermal degradation at *ca.* 130–140° under diminished pressure. The elimination of N,N-dimethylhydroxylamine proceeded smoothly, and the olefins obtained were but little contaminated.

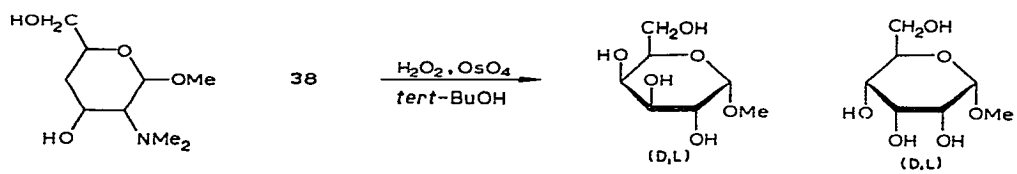
The Cope degradation was applied to the 2,6-diacetates of the *xylo*-α isomer **30** and *arabino*-α isomer **34**. The formation of olefins was accompanied by deacetylation at *O*-2, and **39** and **48** were obtained.

The synthesis of the isomeric methyl 3,4,6-trideoxy-α-D,L-hex-3-enopyranosides **36**, **45** followed the same pathway starting with *trans*-5,6-dihydro-2-methoxy-6-methyl-2*H*-pyran (**12**). The preparation of the two epoxides **14** and **17** from **12**, and their reaction with dimethylamine leading to the methyl 3,4,6-trideoxy-3-dimethylaminohexopyranosides **20** and **24** has already been described[4]. The oxidation of both aminosugars **20** and **24** to the *N*-oxides **28** and **32**, and the Cope degradation of the latter compounds were strictly analogous to the preparations described for **29** and **38** and gave methyl 3,4,6-trideoxy-D,L-hex-3-enopyranosides having the *erythro*-α (**36**) and the *threo*-α (**45**) configuration. Anomerization of both compounds **36** and **45** with methanolic hydrogen chloride, and separation of the resulting α,β-anomeric mixtures by column chromatography gave the two β anomers **41** and **50**.

The stereoisomeric compounds **38**, **39**, **43**, **47**, **48**, and **52** gave, on treatment with acetic anhydride and pyridine, the corresponding 2,6-diacetates **40**, **44**, **49**, and **53**. Similarly, compounds **36**, **41**, **45**, and **50** gave, under the same conditions, the diacetates **37**, **42**, **46**, and **51**, respectively.

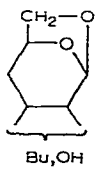
The results of the Cope elimination of **28–35** as well as the properties of **36–53** are recorded in Table II.

The structure of compounds **36–53** was deduced from the n.m.r. data (Table III). The relative stereochemistry of the substituents in **36–53** (CH_2OH or CH_3, OH, and OCH_3) was presumed to be the same as in the amino sugars **20–27**. This was shown in one case by the hydroxylation of **38** with Milas' reagent to provide a mixture of two products, which were identified as methyl α-D,L-galactopyranoside (**56**) and methyl α-D,L-allopyranoside (**57**).



54 α–anomer, *arabino*
55 β–anomer, *arabino*

The rearrangement of an epoxide into an allylic alcohol can be realized (see Singh and Brown[13] and review in Ref. 14) by one-step, base-catalyzed isomerization. Therefore, the reaction of the epoxides **14–19** with butyllithium was investigated. At 0° no reaction was observed. At 30°, methyl 2,3-anhydro-4-deoxy-α-D,L-*ribo*-hexopyranoside (**15**) gave a mixture of products which contained the desired methyl 3,4-dideoxy-α-D,L-*erythro*-hex-3-enopyranoside (**38**) in traces only (t.l.c.). Two main components of this mixture were isolated to which, on the basis of i.r. and n.m.r. spectra, the structures of 1,6-anhydro-3(or 2)-*C*-butyl-3(or 2),4-dideoxy-β-D,L-hexopyranose (**58**) and methyl 3,6-anhydro-4-deoxy-α-D,L-*xylo*-hexopyranoside (**59**) were ascribed. The reaction of methyl 2,3-anhydro-4-deoxy-β-D,L-*ribo*-hexopyranoside (**16**) with butyllithium at 30° took an analogous course to give, among others, a compound which was presumed to be methyl 3,6-anhydro-4-deoxy-β-D,L-*xylo*-hexopyranoside (**60**). The presence of methyl 3,4-dideoxy-β-D,L-*erythro*-hex-3-enopyranoside (**43**) in the reaction mixture could be detected only by t.l.c.



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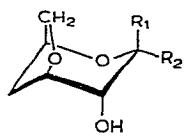

59 R_1 = H, R_2 = OMe

60 R_1 = OMe, R_2 = H

Treatment of epoxides **14**, **17**, and **19** with butyllithium gave mixtures of compounds that were not further investigated. Only in the case of methyl 2,3-anhydro-4-deoxy-α-D,L-*lyxo*-hexopyranoside (**18**) was the expected allylic alcohol **47** obtained as a single product (yield 80%). On the basis of these results we think that the reaction pathway just described, although having more steps than that of isomerization, seems to be a dependable method for the preparation of all stereoisomeric methyl hex-3-enopyranosides.

Preliminary experiments[16] have shown that the double bond in all stereoisomeric compounds **36–53** can be epoxidized or hydroxylated. We hope to accomplish the total synthesis of a variety of hexoses with this approach which has been initiated by Brown and coworkers[17].

EXPERIMENTAL

General. — Silica gel (diam. 0.08 mm, Merck), was used for column chromatography, and Silica gel G (Merck) for t.l.c. The n.m.r. spectra were recorded on Varian HR-60/IL and Jeolco JNM-4H-100 spectrometers, chloroform-*d* being the solvent and tetramethylsilane the internal standard. Spectral and analytical determinations were performed in the Physicochemical Department of this Institute.

Methyl 3,4-dideoxy-3-dimethylamino-α-D,L-xylo-*hexopyranoside* (**21**). — A solution of methyl 2,3-anhydro-4-deoxy-α-D,L-*ribo*-hexopyranoside[1] (**15**, 8 g) in 20%

aqueous dimethylamine (30 ml) was kept at room temp. After 48 h, t.l.c. in 40:9:1 chloroform–methanol–ammonia showed the presence of two products. Evaporation of the reaction mixture under reduced pressure gave an oily residue. It was separated on a silica gel column with 94:5:1 chloroform–methanol–ammonia as eluant to give first **54** (1.0 g), followed by **21** (8.6 g). The latter compound was distilled at 130–140°/0.01 mm. Both amino sugars formed crystalline hydrochlorides on treatment with a methanolic solution of hydrogen chloride. Melting points and analyses of the hydrochlorides are recorded in Table I.

*Methyl 2,6-di-*O*-acetyl-3,4-dideoxy-3-dimethylamino-α-*D,L*-xylo-hexopyranoside* (**22**). — Acetylation of **21** with acetic anhydride and pyridine gave an oil, which was distilled at 140–150°/0.08 mm.

Anal. Calc. for $C_{13}H_{23}NO_6$: C, 53.96; H, 8.01; N, 4.84. Found: C, 54.3; H, 8.10; N, 4.98.

*Methyl 3,4-dideoxy-3-dimethylamino-β-*D,L*-xylo-hexopyranoside* (**23**). — A solution of methyl 2,3-anhydro-4-deoxy-β-D,L-*ribo*-hexopyranoside[1] (**16**, 0.8 g) in 20% aqueous dimethylamine (5 ml) was kept at room temp. After 48 h the reaction mixture was concentrated under reduced pressure. The oily residue consisting of two products (t.l.c.) was distilled at 130–140°/0.06 mm. This mixture was oxidized to give the *N*-oxides, as described in the following paragraphs. They were separated on a silica gel column with 85:12:3 chloroform–methanol–ammonia. Hydrogenation of the *N*-oxides in the presence of a platinum catalyst afforded the corresponding amino sugars.

*Methyl 3,4-dideoxy-3-dimethylamino-β-*D,L*-arabino-hexopyranoside* (**27**). — A solution of methyl 2,3-anhydro-4-deoxy-β-D,L-*lyxo*-hexopyranoside[1] (**19**, 0.5 g) in 20% aqueous dimethylamine (5 ml) was kept at room temp. and, after 24 h, the solvent was evaporated. The oily residue was distilled at 130°/0.01 mm to give a quantitative yield. A sample of **27** was treated with methanolic hydrogen chloride to form the crystalline hydrochloride reported in Table I.

*Methyl 3,4-dideoxy-3-dimethylamino-α-*D,L*-arabino-hexopyranoside* (**25**). — This compound was prepared from methyl 2,3-anhydro-4-deoxy-α-D,L-*lyxo*-hexopyranoside[1] (**18**, 12 g) as described for **27**. After evaporation of the solvent the oily residue was distilled at 135°/0.05 mm; the crystalline hydrochloride is reported in Table I.

*Methyl 2,6-di-*O*-acetyl-3,4-dideoxy-3-dimethylamino-α-*D,L*-arabino-hexopyranoside* (**26**). — Acetylation of **25** with acetic anhydride and pyridine gave an oil, which was distilled at 165°/0.05 mm.

Anal. Calc. for $C_{13}H_{23}NO_6$: C, 53.96; H, 8.01; N, 4.84. Found: C, 53.80; H, 7.88; N. 4.86.

N-*Oxides of methyl 3,4-dideoxy- and 3,4,6-trideoxy-3-dimethylamino-*D,L*-hexopyranosides* (**28–35**). — The *N*-oxides were prepared by dissolving the amino sugars (**20–27**, respectively, 10 mmoles) in acetone (30 ml) and adding 5% aqueous hydrogen peroxide (10 ml). After 48 h at room temp., when t.l.c. showed the absence of the starting material, the solvents were evaporated *in vacuo*, the temp. not exceeding 40°, and the residue was dried *in vacuo* over phosphorus pentoxide. The *N*-oxides **28**, **29**, and **32** were solids, whereas **30**, **31**, **33**, **34**, and **35** were syrups.

Crude **29** was crystallized from methanol–acetone, m.p. 180° (dec.).

Anal. Calc. for $C_9H_{19}NO_5 \cdot H_2O$: C, 45.17; H, 8.85; N, 5.88. Found: C, 45.32; H, 8.72; N, 5.71.

*Methyl 3,4-dideoxy-*D,L*-hex-3-enopyranosides* (**38, 39, 43, 47, 48,** and **52**). — The *N*-oxides (**29, 30, 31, 33, 34,** and **35**, respectively *ca.* 10 mmoles) were slowly heated in a distilling apparatus to 130–140° under a reduced pressure of 0.2–0.3 mm, and then distilled under 0.01–0.02 mm. The distillate was purified by chromatography on silica gel with ether as the eluent for **38, 43, 47,** and **52**, and 1:1 hexane–ether for **39** and **48**. The 2,6-di-*O*-acetyl derivatives of **38, 39, 43, 47, 48,** and **52** were prepared by acetylation at room temp. with acetic anhydride and pyridine to give **40, 44, 49,** and **53**. The yields, m.p. (or b.p.), and analytical and n.m.r. data of these compounds are reported in Tables II and III.

*Methyl 3,4,6-trideoxy-α-*D,L*-hex-3-enopyranosides* (**36** *and* **45**). — The *N*-oxides (**28** and **32**, respectively, *ca.* 10 mmoles) were slowly heated in a distilling apparatus to 120–130° under reduced pressure (20–30 mm). The distillate was purified by chromatography on silica gel with 1:1 hexane–ether as the eluent. The 2-*O*-acetyl derivatives of **36** and of **45** were prepared by acetylation with acetic anhydride and pyridine to give **37** and **46**, respectively. The yields, m.p. (or b.p.), and analytical and n.m.r. data of these compounds are reported in Tables II and III.

*Methyl 3,4,6-trideoxy-β-*D,L-erythro-*hex-3-enopyranoside* (**41**). — A solution of **36** (0.1 g) in 1% methanolic hydrogen chloride (10 ml) was kept for 60 h at room temp. The starting material was transformed (t.l.c.) into the β-anomer **41**. The solution was neutralized with barium carbonate, filtered, and evaporated, and the residue was sublimed at 100°/15 mm.

*Methyl 3,4,6-trideoxy-β-*D,L-threo-*hex-3-enopyranoside* (**50**). — A solution of **45** (1.44 g) in 1% methanolic hydrogen chloride (50 ml) was heated at reflux for 3 h. The mixture of anomers formed was separated on silica gel with 1:1 benzene–ether as eluent to give 1 g (70%) of **45** and 0.12 g (8.3%) of **50**.

Reaction of **38** *with Milas' reagent*[17]. — To a solution of **38** (1.0 g) in 6% hydrogen peroxide in 2-methyl-2-propanol (5 ml) was added osmium tetroxide (10 mg). After 48 h at room temp. t.l.c. showed the presence of two new, high-polar compounds. These compounds were identified (t.l.c., i.r.) as methyl α-D,L-galactopyranoside (**56**) and methyl α-D,L-allopyranoside (**57**).

Attempted rearrangement of epoxides **14–19** *with butyllithium.* — Each epoxide (*ca.* 0.1 g) was dissolved in hexane (5 ml) or ether and treated at 0° with a double molar amount of a 20% solution of butyllithium in hexane. No change of the starting material was observed (t.l.c.) after 24 h. At 30°, the formation of the following new products was observed:

(*a*) The substances obtained from the epoxides **14, 17,** and **19** were not identical (t.l.c.) with **36, 45,** and **52**, respectively, and therefore they were not investigated further.

(*b*) From the reaction mixture of **15** two products were isolated and characterized by means of the i.r. and n.m.r. spectra:

Compound **58**: i.r. spectra: ν_{max}^{film} 3500, 1080, 1040, 980, 930, and 900 cm^{-1}; n.m.r. data (chloroform-*d*): δ 5.25 (m, 2 protons, H-1 and OH), 4.59 (m, 1 proton, H-5), 3.90 (q of d, 1 proton, $J_{5,6exo}$ 6.0 Hz, $J_{6exo,6endo}$ 7.0 Hz, $J_{4,6exo}$ 1.7 Hz, H-6exo), 3.62 (d of d, 1 proton, $J_{5,6endo}$ 1.8 Hz, H-6endo), 2.70 (d of m, 1 proton, $J_{4a,4e}$ 15.5 Hz, H-4e), 1.95–2.1 (m, 10 protons, H-4a and C_4H_9).

Compound **59**: i.r. spectra: ν_{max}^{film} 3500, 1200, 1140, 1050, 1020, 980, 965, 920, 910, 880, 865, 830, 765, and 710 cm^{-1}; n.m.r. data (chloroform-*d*): δ 4.68 (d, 1 proton, $J_{1,2}$ 3.0 Hz, H-1), 4.48 (m, 2 protons, H-5 and OH), 4.03 (pd, 1 proton, $J_{6,6'}$ 10.0 Hz, H-6), 3.4–3.85 (m, 3 protons, H-2, H-3, and H-6'), 3.52 (s, 3 protons, OMe), 2.50 (d of t, 1 proton, $J_{4a,4e}$ 12.2 Hz, H-4e), 1.60 (d of q, 1 proton, H-4a).

Compound **38** was present (t.l.c.) only in trace amount.

(*c*) *Compound* **16** gave **60** (after column chromatography); i.r. spectra: ν_{max}^{KBr} 3450, 1110, 1090, 1050, 1040, 1015, 980, 950, 925, 900, 885, 850, 795, and 770 cm^{-1}; n.m.r. data (chloroform-*d*): δ 4.45 (s, 1 proton, H-1), 4,10 (d, 1 proton, $J_{6,6'}$ 9.4 Hz, H-6), 3.33 (s, 3 protons, OMe), multiplets centered at 3.10, 3.60, and 4.35 corresponding to five protons (H-2, H-3, H-5, H-6', and OH), 2.35 (d, 1 proton, $J_{4a,4e}$ 12.5 Hz, H-4e), 1.60 (d of m, 1 proton, H-4a).

Compound **43** was present in trace amount only (t.l.c.).

(*d*) *Compound* **18** gave after 5 h at 30° *ca.* 80% of **47**, which was identical in every respect with the substance obtained by the Cope degradation of **33**.

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