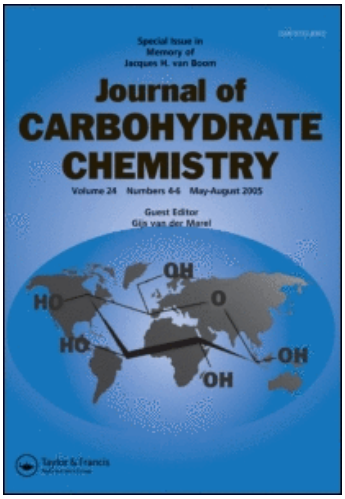

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SYNTHESIS OF THE FOUR CONFIGURATIONAL ISOMERS OF N-BENZOYL-2,3,6-TRIDEOXY-3-C-METHYL-3-AMINO-L-HEXOSE FROM THE (2S,3R)-DIOL OBTAINED FROM α-METHYLCINNAMALDEHYDE BY FERMENTATION WITH BAKER'S YEAST

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ABSTRACT

The erythro and threo chiral C_5 methyl ketones (4) and (5), prepared from the (2S,3R)-methyl diol (1b), were converted into the phenylsulfenimines (6) and (7), which, in turn, on reaction with allylmagnesium bromide, yielded after acid hydrolysis and benzoylation, the diastereoisomeric C_8-N-aminodiol derivatives (9) and (11), with threo stereochemistry relative to positions 4 and 5. Ozonolysis of (9) and (11) yielded the L-arabino and L-xylo 3-C-methyl branched aminodeoxysugar derivatives (13) and (15), respectively. Using diallylzinc as the reagent, the diastereoisomeric erythro products (8) and (10) were obtained. The latter materials gave the L-ribo- and L-lyxo-(L-vancosamine) derivatives (12) and (14) upon ozonolysis. The ^1H and ^{13}C NMR spectra of the four isomeric aminodeoxysugar derivatives (12)—(15) were discussed.

 0732-8303/83/0203-0225$3.50/0

INTRODUCTION

For some years now we have been using the (2S,3R)-diols (1), prepared from cinnamaldehyde and α-methylcinnamaldehyde, respectively, by fermentation with baker's yeast, as starting materials in the synthesis of enantiomerically pure forms of natural products.[1,2] The synthetic applications of compounds (1) involved, in most instances, as key intermediates the C_4 and C_5 chiral carbonyl compounds (2) and (4), extruded by ozonolysis from protected forms of (1), and their α-epimers (3) and (5), prepared from (2) and (4) by treatment with potassium carbonate in methanol. The synthetic significance of compounds (2), (3), (4) and (5) rests on the high degree of stereocontrol exerted by the two chiral centers embedded in the pentacyclic ketal framework in the addition of nucleophiles onto the sp^2 carbon of these compounds or of their transformation products. In this context, we refer now to the synthesis of the N-benzoyl derivatives of the four configurational isomers of 2,3,6-trideoxy-3-C-methyl-3-amino-L-hexose from the erythro and threo phenylsulfenimines (6) and (7) and addition of a C_3 allylic anion equivalent.†

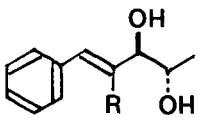
RESULTS AND DISCUSSION

Therefore, the ketones (4) and (5) could be converted in ca. 60-70% yield into the corresponding phenylsulfenimines (6) and (7) by treatment with $(C_6H_5S)_2$, $AgNO_3$ and ammonia in methanol.[3] However, ^1H NMR studies and GLC analysis indicated that the phenylsulfenimine derived from the erythro ketone (4) contained ca. 30% of the

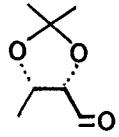
†For a preliminary account of part of this work, see: G. Fronza, C. Fuganti, P. Grasselli and G. Pedrocchi-Fantoni, Tetrahedron Lett., 5073 (1981).

threo isomer (7), formed at some stage of the sequence by α-epimerization under the basic conditions used in its preparation. Addition experiments were carried out on the above phenylsulfenimines (6) and (7) with both diallylzinc[4] and allylmagnesium bromide in ether.

The general procedure required addition of the appropriate phenylsulfenimine in ether to ca. 2 mol equiv of the organometallic reagent at -78 °C or at -15 °C. Work-up was carried out with NH_4Cl solution, and the nitrogen-sulfur bond present in the adducts was hydrolyzed with 6N HCl. The resulting amine(s) was (were) benzoylated under basic conditions to give the C_8-N-adducts as N-benzoyl derivatives (8)—(11) in ca. 30-40% overall yield. Ozonolysis of the terminal vinyl group of compounds (8)—(11) gave rise to the required isomeric N-benzoylaminodeoxy sugars (12)—(15). When the latter were present in admixture, separation was achieved by fractional crystallization and by SiO_2 column chromatography.



1 a R= H
b R= Me



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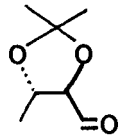

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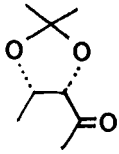

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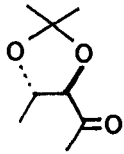
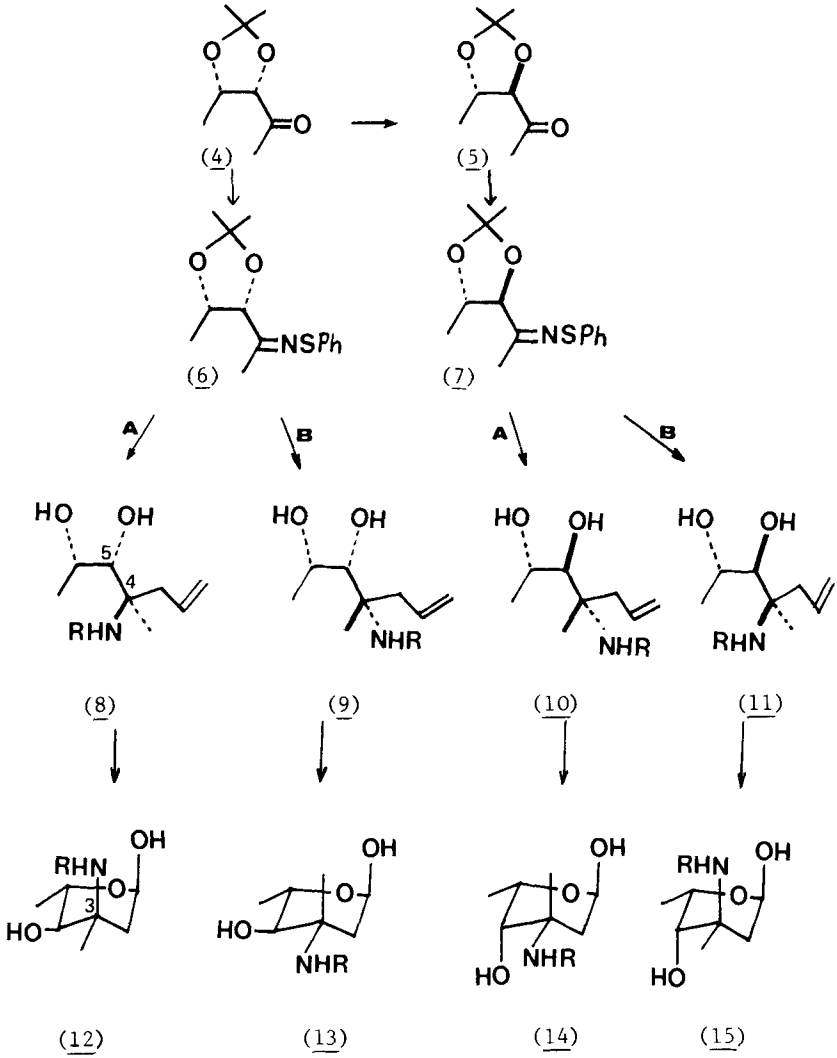


5

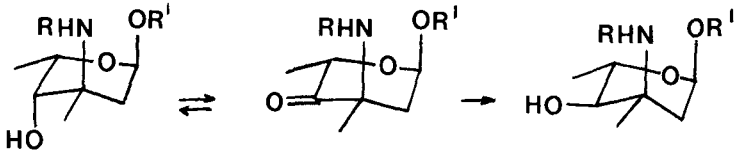
Generally speaking, addition of the C_3 allylic nucleophile to the re face of the carbon-nitrogen bond of (6) and (7) is expected to produce the (4R,5R,6S)-C_8-N-adduct (8) and the (4S,5S,6S)-isomer (10), respectively. The latter materials give rise, in turn, to the L-ribo- and L-lyxoaminosugar derivatives (12) and (14). When the above process proceeds on the si face of (6) and (7), the (4S,5R,6S)-C_8-N-adduct (9) and its (4R,5S,6S)-isomer (11) are obtained, respectively. The latter products yield on ozonolysis the L-arabino- and L-xylo derivatives (13) and (15) as indicated in Scheme 1.

The structural assignement for compounds (12)—(15) was made as follows. The L-xylo derivative (15), obtained as the almost exclusive product in the addition of allylmagnesium bromide to the threo phenylsulfenimine (7), was identified on the basis of its physical constants and comparison with an authentic sample isolated from antibiotic A35515B.[5] The isomer obtained as the major product in the addition of diallylzinc to the phenylsulfenimine (6) was recognized as the L-ribo product (12) by comparison of its methyl glucoside with an authentic sample prepared from the L-xylo isomer (15) by inverting the configuration at position 4. This was achieved by converting (15) into the glucoside (16), followed by oxidation with pyridinium chlorochromate in the presence of 3 Å molecular sieves[6] to give the ketone (17) in ca. 60% yield. The latter material on lithium tri-sec-butylborohydride (L-Selectride) reduction gave (16) and the L-ribo isomer (18), mp 142 °C, $[\alpha]_D^{20}$ = -76°, separated by SiO_2 chromatography, in ca. 80% overall yield, as indicated in Scheme 2. ^{1}H NMR studies on the above products (see later) confirmed the inversion of configuration in position 4 of compund (18) in respect to the starting material (16). The



A= $Zn(CH_2CH=CH_2)_2$; B= $BrMgCH_2CH=CH_2$; R= COC_6H_5

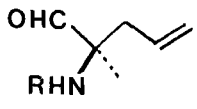
Scheme 1



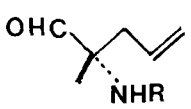
16 17 18

R= COC_6H_5 ; R^1= Me

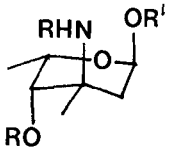
Scheme 2



19 R= COC_6H_5



20 R= COC_6H_5



21 R= COC_6H_5 ; R^1= Me

L-arabino configuration (13) was assigned to the product obtained from the addition of allylmagnesium bromide to the erythro phenylsulfenimine (6) because it gave at positions 3 and 4 epimers in respect to the L-xylo isomer (15). Indeed, the (4R,5S,6S)-adduct (11), the chemical precursor of (15), on oxidation with 1 mol equiv of HIO_4 in dry tetrahydrofuran gave rise to the (2R)-aldehyde (19), $[\alpha]_D^{20}$ = +13.5°, whereas the N-benzoyl aminodiol yielding (13) under the same conditions afforded the (2S)-aldehyde (20), $[\alpha]_D^{20}$ = -14°. Thus the aminodeoxysugar derivative (13) must hold a (3S) absolute configuration. The equatorial orientation of

the hydroxyl group in position 4 of (13) is supported by ^{1}H NMR studies (see later). Inversion of configuration at position 4 of the L-arabino framework of (13) via the 4-O-mesyl derivative of the methyl glucoside, followed by acetate displacement and acid hydrolysis, yielded the L-lyxo product (14), mp 155 °C, $[\alpha]_D^{20} = -85°$. The latter physical constants are in agreement with those of the product obtained as the major isomer in the addition of diallylzinc to the threo phenylsulfenimine (7).

The steric outcome of the present experiments (Table 1) indicate a dramatic change in the mode of addition of diallylzinc and allylmagnesium bromide in ether onto the sp^2 carbon of the phenylsulfenimines (6) and (7). With the former reagent the 4,5-erythro adducts (8) and (10) are preferred over the 4,5-threo isomers (9) and (11), which indeed become the almost exclusive educts using the second reagent.

Mechanistic considerations are outside the purposes of the present preparative work. Most economically, the erythro mode of addition can be explained with the Felkin's model,[7] whereas the threo one invokes control by metal chelation.[8] The major synthetic

TABLE 1. Ratios of the 4,5-erythro/4,5-threo Products in the addition of the C_3 Allylic Nucleophiles onto the Phenylsulfenimines (6) and (7) as Determined from the Weights of the Aminodeoxysugar Derivatives (12)—(15)

Substrate	$Zn(CH_2CH=CH_2)_2$	$BrMgCH_2CH=CH_2$
(6)	70:30	5:95
(7)	75:25	5:95

significance of the present work is represented by the fact that, at our choice, depending upon the reagent used, the phenylsulfenimine (7) can be converted (path B) into the N-benzoyl 2,3,6-trideoxy-3-C-methyl-3-amino-L-xylohexose (15), or (path A) into the N-benzoyl 2,3,6-trideoxy-3-C-methyl-L-lyxohexose (14) (N-benzoyl-L-vancosamine),[9] the latter being accompanied by (15). Similarly, the phenylsulfenimine (6), present in the 7:3 mixture of (6) and (7), yields (path A) N-benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-ribohexose (12), close to ca. 30% (13), and (path B) N-benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-arabinohexose (13).

Discussion of The NMR Spectra

We report here the analysis of the ^{1}H and ^{13}C NMR spectra of the aminosugar derivatives (12)—(15) in order to determine the structure and the conformation in solution of these biologically important derivatives and to outline the spectral features which allow an easy identification of these compounds. Just after the dissolution in dimethylsulfoxide the L-ribo (12), L-lyxo (14) and L-xylo (15) isomers exist as α-pyranoses, whereas the L-arabino (13) derivative exists as a mixture of α- and β-pyranose and α- and β-furanose ring forms. During ca. one month all compounds gave rise to a mixture of pyranoid and furanoid structures, showing generally a preponderance of the β-pyranose form (see Table 3 for relative proportions of the various ring forms). The furanoid forms exist in rather small amount (8-18%), and precise NMR data could not be extracted from the spectra.

The most crucial point of the structure elucidation of these amino sugars is the determination of the configuration at the quaternary carbon C-3 and both the ^{13}C and ^{1}H NMR spectra show some characteristic features which allow one to deduce the

stereochemistry at this chiral center. It is known[10] that the ^{13}C chemical shift of an axial methyl group is shifted downfield by about 2 ppm by a syn axial hydroxyl group (δ syn axial effect). In fact by comparing (Table 2) the β- and α-anomers of the L-arabino (13) and L-lyxo (14) compounds, the Me-3 group is shifted to lower field by 2.0 and 1.9 ppm, respectively, while for the L-ribo (12) and the L-xylo (15) isomers it shows only a small upfield effect by 0.3 and 0.6 ppm. Moreover, the carbon resonance of axial methyl groups occurs generally ca. 6 ppm at higher fields than that of their equatorial counterparts, owing to the γ-gauche interaction with the ring carbons.[11] This effect is apparent for the Me-3 resonance going from the β-L-ribo (12b) to the β-L-arabino (13b) isomers. For the α-anomers the upfield effect is only

TABLE 2. ^{13}C NMR Chemical Shifts of the 3-Benzoylamino-3-C-methyl 2,3,6-trideoxyhexoses.[a,b]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	Me-3
12a	90.0	40.3	55.9	78.6	64.6	18.0	23.5
12b	91.8	40.7	56.3	76.9	69.8	18.5	23.8
13a	89.9	c	56.6	75.1	64.6	18.7	19.9
13b	91.7	43.7	57.3	74.9	69.8	18.9	17.9
14a	90.0	35.2	54.3	71.2	62.6	17.4	23.2
14b	91.2	c	56.0	70.0[d]	68.1[d]	17.6	21.3
15a	92.2	36.9	57.1	67.9[d]	68.3[d]	17.3	23.2

a. Designations a and b indicate α- and β-anomer, respectively.

b. Chemical shifts (in ppm) from internal Me_4Si; solvent: $(CD_3)_2SO$.

c. Peaks not assigned.

d. Assignments may be interchanged.

3.6 ppm, since it is partially compensated by the downfield effect of the syn axial hydroxy group. On the contrary, the Me-3 chemical shift going from the L-xylo (15a,b) to the L-lyxo (14a,b) compounds show only small differences because the methyl group with an axial orientation lacks the γ-gauche interaction with the C-4 hydroxy group.

The proton chemical shifts and coupling constants are collected in Table 3 and Table 4, respectively. The assignement of the methylene protons H-2e and H-2a for the α-anomers was made on the basis of the smaller value of the vicinal equatorial-equatorial coupling constants (ca. 1 Hz) than the axial-equatorial one (ca. 4 Hz) and was confirmed by the existence of a long-range coupling by 1.3-1.6 Hz between H-2a and the anomeric hydroxy proton.[12] Inspection of the vicinal coupling constants reveals that all compounds are stable in the $^{1}C_{4}$ (L) conformation. Recently, a set of additivity constants have been developed,[13] which are valid for the prediction of the vicinal coupling constants for conformationally pure pyranose rings. The application of these additivity rules reproduces reasonably well the values of the coupling constants in the 3-benzoylamino-3-C-methyl-2,3,6-trideoxyhexoses, except for $^{3}J(1,2a)$. The predicted value for this coupling constant is 2.1 Hz, while we find a mean experimental value of 4.0 Hz for the α-anomers and 2.0 for the β-anomers. Similar systematic discrepancies were outlined by the authors themselves for the β-anomers of several 2-deoxypyranoses, but the reason for this anomaly remained unclear.

The long-range coupling constant $^{4}J(Me\text{-}3,H\text{-}2a)$ is particularly interesting for the determination of the stereochemistry at C-3, since only compounds with an axial orientation of the Me-3 group

TABLE 3. ^{1}H NMR Shifts of the 3-Benzoylamino-3-C-methyl-2,3,6-trideoxyhexoses.[a,b]

Compound	H-1	H-2e	H-2a	H-4	H-5	H-6	Me-3	OH-1	OH-4	NH	%
12a	5.11	2.41	1.66	3.03	3.93	1.16	1.54	6.55	5.68	7.9	15
12b	4.75	3.09	1.30	2.94	3.64	1.20	1.38	6.39	5.79	6.97	77
13a	5.11	d	d	3.60	3.80	1.17	1.55	6.06	5.57	ca7.60[e]	19
13b	4.78	2.19	2.03	3.56	3.40	1.19	1.38	6.44	5.57	7.68	71
14a	5.11	2.02	1.94	3.51	4.18	1.13	1.69	6.02	4.88	7.38	21
14b	4.75	1.98	1.71	3.50	3.76	1.15	1.53	6.84	4.82	ca7.50[e]	61
15a	5.17	1.58	1.84	3.78	4.17	1.04	1.42	6.84	4.88	8.30	42
15b	4.78	2.26	1.45	3.74	3.83	1.10	1.35	6.32	4.73	ca7.60	46
16[f]	4.85	1.69	2.07	4.16	4.13	1.19	1.70	3.43(OMe)2.8		7.88	-
18[f]	4.79	2.06	1.94	3.28	3.79	1.33	1.75	3.42(OMe)6.05		8.13	-

a. Designations a and b indicate α- and β-anomers, respectively.

b. Chemical shifts (in ppm) from internal Me_4Si; solvent $(CD_3)_2SO$, except otherwise indicated.

c. Mixture of the various ring forms after ca. one month; the remaining amount to obtain 100% is due to the furanose forms.

d. Peaks not assigned.

e. Overlapped to the aromatic signals.

f. Methyl glycosides (16) and (18) in $CDCl_3$.

TABLE 4. ^{1}H NMR Coupling constants of the 3-Benzoylamino-3-C-methyl-2,3,6-trideoxyhexoses.[a,b]

Compoud	J(1,2e)	J(1,2a)	J(2e,2a)	J(4,5)	J(5,6)	J(1,OH-1)	J(4,OH-4)	J4,2a)	J(2a,OH-1)	J(Me-3,2a)
12a	1.3	4.0	14.2	9.6	6.2	3.8	6.8	-	1.6	-
12b	1.8	9.6	13.6	9.4	6.1	6.3	6.6	-	-	-
13a	1.5	4.0	c	9.5	6.1	3.2	4.5	-	1.3	0.8
13b	2.1	9.7	13.0	9.4	6.0	6.6	4.2	-	-	0.8
14a	1.5	4.2	13.4	1.3	6.5	3.4	7.2	1.0	1.3	0.8
14b	2.3	9.8	13.0	1.2	6.4	6.6	6.9	1.0	-	0.8
15a	1.2	4.0	14.1	1.4	6.5	6.5	7.4	1.2	1.6	-
15b	2.0	9.6	13.3	1.2	6.5	6.5	7.4	1.2	-	-
16[d]	1.2	4.1	14.7	1.1	6.5	-	6.2	-	-	-
18[d]	1.1	3.9	14.8	9.5	6.2	-	6.2	-	-	-

a. Designations a and b indicate - and -anomers, respectively

b. Coupling constants in Hz; solvent $(CD_3)_2SO$ except otherwise indicated.

c. Not detected.

d. In $CDCl_3$.

(13,14) show such interaction (0.8 Hz). Compounds with an equatorial orientation of Me-3 do not exhibit any detectable coupling between Me-3 and H-2 protons because the interacting protons lack the W favorable coupling path.[14] Finally, the chemical shifts of the anomeric hydroxyls and the amide protons deserve some attention since they seem related to the stereochemistry at C-3. Equatorially anomeric hydroxy protons in dimethylsulfoxide solution resonate generally at lower field by 0.4 ppm than axial hydroxyls because of their greater ability to form intermolecular hydrogen bonds with the solvent molecules.[12] The OH-1 groups of compounds with L-arabino and L-lyxo configuration follow this general trend [see (13b) vs. (13a) and (14b) vs. (14a)], while for the L-xylo (15) and L-ribo (12) isomers the axial OH-1 resonates at lower field than the equatorial one. In addition, the amidic proton experiences an appreciable upfield shift going from the α- to the β-anomers of (12) and (15). Most probably this behaviour is due to the occurrence of an intramolecular hydrogen bonding between the axial -NH- and the axial OH-1 substituents, although this conclusion must be taken with caution since the high magnetic anisotropy of the COPh group can be misleading for the interpretation of the ^{1}H chemical shifts.

The ^{1}H chemical shifts and coupling constants of the methyl glycosides (16) and (18) are also reported in Tables 3 and 4, respectively. Compound (16) was converted into compound (18) by inverting the configuration at position 4 (see above), as it is apparent from the change of the $^{3}J(4,5)$ coupling constant.

CONCLUSIONS

The preparation of the four configurationally isomeric 3-C-methylaminodeoxy sugar derivatives (12)—(15) from the (2S,3R)-diol

(1b) through the key intermediacy of the C_5 chiral ketones (4) and (5) lends further support to the significance of the synthesis of enantiomerically pure forms of natural products by the present approach. This method, which is based on the use as starting materials of chiral products obtained by microbial transformations of non-conventional substrates, proceeds through relatively small, highly functionalized chiral synthons which are stereoselectively elongated, taking advantage of the increasing knowledge of methods for the steric control in nucleophilic addition to sp^2 carbon. Furthermore, the acyclic intermediates (8)—(11), prepared by addition of the C_3 nucleophiles onto the phenylsulfenimines (6) and (7), allow one to obtain the aminosugar derivatives (12)—(15) without any further manipulation of the chiral centers. This last feature suggests a favorable comparison of the present procedure with those recently published,[6,15] relative to the synthesis of derivatives of N-benzoyl-L-vancosamine (14), starting from L-rhamnose and D-glucose, respectively. Moreover, the conversion of (9) and (11) by periodate oxidation into the (R)- and (S)-aldehydes (19) and (20), respectively, and, by ozonolysis into the deoxysugar derivatives (13) and (15), allows one to regard these compounds as masked forms of the dialdehyde derived from N-benzoyl derivatives of (R)- and (S)-α-methylaspartic acid.

EXPERIMENTAL

The ^1H NMR spectra of the aminosugar derivatives were recorded on a Bruker CXP-300 spectrometer at a concentration of ca. 5 mg x $mL.^{-1}$ The gaussian multiplication method for resolution enhancement of the signals was employed to obtain accurate values of the coupling constants. The ^{13}C spectra were recorded on a Varian XL-100 spectrometer at a concentration of ca. 40 mg x $mL.^{-1}$

Flash chromatography was performed with Merk Silica gel (0.040-0.069 mm), and TLC with Merck HF_{254} Silica gel. GLC analyses were performed on a DANI 3800 gas chromatograph equipped with a FID detector. Organic solutions were dried over Na_2SO_4 and evaporated at reduced pressure at 40-60 °C. Analytical samples were obtained by bulb-to-bulb distillation or by crystallization.

Phenylsulfenimines (6)+(7) from (3S,4S)-3,4-isopropylidendioxypentan-3-one (4). To a solution of 13 g (0.076 mol) of $AgNO_3$ in 1200 mL of methanol in a three-necked flask equipped with a mechanical stirrer and an inlet tube were added at 0 °C, 16.6 g (0.076 mol) of $(C_6H_5S)_2$, and then dry ammonia was passed through for 30 min at 0 °C. To the above mixture were added 12 g (0.076) of (3S,4S)-3,4-isopropylidendioxypentan-3-one (4),[2] and the reaction mixture was stirred overnight at room temperature. Silver mercaptide was removed by suction filtration, and the solvent was evaporated under reduced pressure to give a residue which was redissolved in ether and filtered again. The ethereal solution was washed with water and dried. SiO_2 column chromatography with hexane-ethyl acetate (9:1)-(7:3) gave ca. 14 g (70%) of an oily product: $[\alpha]_D^{20} = -58.4°$ (c 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 90 MHz) δ 7.54-7.1 (5H,Ph,m), 4.66 and 4.46 (2H, H-4 and H-3,m), 2.04 (3H,CH_3,s), 1.42 and 1.35 (6H,2 CH_3,s), 1.14 (3H,5-Me,d). Anal. calcd for $C_{14}H_{19}NO_2S$: C, 63.35; H, 7.23; N, 5.28; S, 12.08. Found: C, 63.42; H, 7.29; N, 5.19; S, 11.90. GLC (2m x 3mm int. diam.; 10% Silicon UCC-W 982 on Chrom.W-DMCS 80-100 mesh at 210 °C) indicated the presence of a 7:3 mixture of compounds (6) and (7).

Phenylsulfenimine (7) from (3R,4S)-3,4-isopropylidendioxypentan-3-one (5). (3R,4S)-3,4-isopropylidendioxypentan-3-one (5) was

obtained as an oil: bp 55 °C (0.1 mm Hg), $[\alpha]_D^{20}$ = +68.8° (c 1, $CHCl_3$); in ca. 80% yield from 20 g (0.12 mol) of (3S,4S)-3,4-isopropyliden-dioxypentan-3-one (4) in 200 mL of dry methanol upon stirring 3 h at room temperature with 4 g of potassium carbonate. Product (5) was isolated from the reaction mixture as follows. The potassium carbonate was filtered, and the solution was concentrated at reduced pressure to ca. 50 mL. The latter solution was diluted with 200 mL of ether, and the organic phase was washed with water. The dried organic phase was concentrated at normal pressure (Vigreux) and then distilled at 0.1 mm Hg. ^1H NMR ($CDCl_3$) δ 4.1-3.8 (2H,H-3 and H-4), 2.21 (3H,CH_3,s), 1.45 (6H,2 CH_3,s), 1.35 (3H,5-Me,d). GLC (WCOT-OV1 (0.4 micron), 25 m, from 55 °C; (3.5 °C/min) indicated a ratio (5):(4) > 9:1.

Addition of allylmagnesium bromide to the Isomeric Phenylsulfenimines (6) and (7): Preparation of the 4-benzoylamino-4-methyl-5,6-dihydroxyhept-1-enes (9) and (11). The appropriate phenylsulfenimine (6) + (7) or (7) (10 g, 0.038 mol) in 40 mL of ether was added at -15 °C to an ethereal solution of allylmagnesium bromide prepared from 9.2 g (0.076 mol) of $BrCH_2CH=CH_2$ and 2.2 g (0.09 mol) of Mg in 200 mL of ether. After 3 h at -15 °C, 50 mL of a satd soln of NH_4Cl were added, and the separated ethereal phase was washed with 3 x 30 mL of 6N HCl. The combined acid solutions were taken to dryness at reduced pressure to leave 5.6 g of a thick oily residue (75%). The latter crude materials were taken up in 40 mL of water and 10 mL of acetone and treated at 0 °C under stirring with 4.2 g (0.03 mol) of benzoyl chloride in 20 mL of acetone, while mantaining the solution at pH 8.5 by adding solid K_2CO_3. After stirring overnight, the reaction mixture was extracted with 3 x 100 mL of ethyl acetate. The dried organic phase left a residue, 3.7 g (50%), which was chromato-

graphed on SiO_2 (150 g) by eluting with increasing amounts of ethyl acetate in hexane. From the phenylsulfenimine (7), under these conditions, 3.2 g (47%) of (4R,5S,6S)-4-benzoylamino-4-methyl-5,6-dihydroxyhept-1-ene (11), a thick oil showing a small negative rotation in chloroform, was obtained: ^{1}H NMR ($CDCl_3$) δ 7.75-7.22 (5H,Ph,m), 6.67 (1H,NH), 5.9 and 5.2 (3H, CH_2=CH-), 4.03 (1H,H-6,m), 3.43 (1H,H-5,q), 2.8-2.6 (2H,CH_2), 1.42 (3H,4-Me,s), 1.27 (3H,6-Me, d). Anal. calcd for $C_{15}H_{21}NO_3$: C, 68.4; H, 8.05; N, 5.32. Found: C, 68.28; H, 8.09; N, 5.41. From the mixture of phenylsulfenimines (6)+(7), separated from ca. 30% (11), (4S,5R,6S)-4-benzoylamino-4-methyl-5,6-dihydroxyhept-1-ene (9) was obtained as an oil: $[\alpha]_D^{20}$ = -22° (C 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.75-7.22 (5H,Ph,m), 6.35 (1H, NH,s), 5.9 and 5.13 (3H, CH_2=CH-), 5.41 (1H,5-OH,d), 3.87 (1H,H-6,m), 3.48 (1H,H-5,q), 2.85-2.59 (2H,CH_2, octet), 2.3 (1H,6-OH,d), 1.48 (3H,4-Me,s), 1.26 (3H,6-Me,d).

Addition of Diallylzinc to the Phenylsulfenimines (6) and (7): Preparation of the 4-Benzoylamino-4-methyl-5,6-dihydroxyhept-1-enes (8) and (10). To a solution of diallylzinc, prepared by addition of 27 g (0.2 mol) of anhydrous zinc chloride in 150 mL of ether at 0 °C to allylmagnesium bromide obtained, in turn, from 21.6 g (0.18 mol) of $BrCH_2CH=CH_2$ and 5.7 g (0.25 mol) of Mg in 250 mL of ether, were added 26 g (0.1 mol) of the phenylsulfenimine (7) at -78 °C under nitrogen. After stirring 3 h at that temperature, the reaction mixture was quenched with 50 mL of satd soln of NH_4Cl, and the ethereal solution was separated. Starting from this point ahead, the N-benzoyl derivatives of the C_8-N-adducts were isolated in ca. 40% overall yield, following the reaction sequence reported for the preparation of (11). In the present case, a mixture of (10) and (11) was obtained, which we were unable to separate by SiO_2 column

chromatography. From the relative intensities of the C-4 methyl signals which appeared at δ 1.52 and 1.42, respectively, it was shown that we were dealing with a ca. 7:3 mixture of (10) and (11). The ratio determined by ^{1}H NMR studies was later confirmed (see below) from the weights of the aminosugar derivatives (14) and (15), isolated in pure forms from the ozonolysis of the mixture (10) + (11). By repeating the above sequence with the 7:3 mixture of (6) and (7), the N-benzoyl derivatives (12), (13), (14) and (15) were obtained. As judged from the relative intensities of the peaks of the C-4 methyl groups in the NMR spectrum of the crude mixture, compound (8), whose C-4 methyl group gives a signal at δ 1.5, represented ca. 60% of the whole. SiO_2 column chromatography allowed a rough separation of the mixture of (10)+(11) from (8)+(9). Repeated chromatography of the latter mixture yielded a sample of (8), which still contained ca. 10% of (9) (from ^{1}H NMR studies): oil, $[\alpha]_D^{20} = -16°$ (c 0.5, $CHCl_3$).

N-Benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-lyxohexose (14) (N-benzoyl-L-vancosamine) and N-Benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-xylohexose. Ozonized oxygen was passed through a solution of 2.6 g (0.01 mol) of the mixture of (10)+(11), obtained by addition of diallylzinc onto the phenylsulfenimine (7), in 60 mL of methanol at -40 °C. At the end of the absorption, the excess ozone was purged with nitrogen, and 2 mL of Me_2S in 10 mL of methanol were added, and the reaction mixture was subsequently kept at room temperature overnight. The residue obtained on evaporation of the solvent, once taken up with warm ethyl acetate-methanol, separated on cooling to yield 400 mg (16%) of N-benzoyl 2,3,6-trideoxy-3-C-methyl-3-amino-L-xylohexose (15): mp 230-233

°C; $[\alpha]_D^{20}$ = -61.3° (c 0.5, MeOH); (for ^{1}H NMR data, see general part). Anal. calcd for $C_{14}H_{19}O_4N$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.51; H, 7.14; N, 5.33.

Compound (15) was converted into the methyl N,O-dibenzoylglycoside (21) as follows. A solution of 300 mg of (15) (0.0011 mol) in 10 mL of methanol, containing 1 mL of methanol saturated with dry HCl, was kept at room temperature overnight. Then solid potassium carbonate was added, and the filtered solution was taken to dryness. The residue, dissolved in 5 mL of dry pyridine, was treated with 1 mL of benzoyl chloride for two days at room temperature. The reaction mixture was poured into ice-water and was extracted with 3 x 50 mL of ethyl acetate. The residue obtained upon evaporation of the solvent was chromatographed on SiO_2 to give with ethyl acetate-hexane (6:4), 260 mg (45%) of the crystalline N,O-dibenzoate of the methyl glycoside of 2,3,6-trideoxy-3-C-methyl-3-amino-L-xylohexose (21): mp 177 °C; $[\alpha]_D^{20}$ = -188° (c 1, MeOH), these physical constants being well in agreement with those of an authentic sample.[5] The mother liquors from which separated compound (15) were taken to dryness and chromatographed on SiO_2 column to give, with increasing amounts of ethyl acetate in hexane, 200 mg (8%) of compound (15), and subsequently, 1.47 g (60%) of N-benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-lyxohexose (14) (N-benzoyl-L-vancosamine): mp 155 °C, $[\alpha]_D^{20}$ = -86.6° (c 0.5, MeOH); (for the ^{1}H NMR, see general part). Anal. calcd for $C_{14}H_{19}O_4N$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.41; H, 7.16; N, 5.20. The yield of compounds (14) and (15) from the mixture of (10) and (11) was ca. 80%, and the (14):(15) ratio, ca. 7:3. Compound (15) was obtained in pure form in ca. 80% yield on ozonolysis of pure (11), prepared by addition of allylmagnesium bromide onto the phenylsulfenimine (7).

N-Benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-arabinohexose (13). The N-benzoylamino diol (9), obtained from the addition of allylmagnesium bromide to the mixture of (6)+(7) followed by separation from accompanying (11), yielded on ozonolysis, as reported above, N-benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-arabinohexose as a thick oil which solidified on standing: $[\alpha]_D^{20}$ = -5.1° (c 0.5, MeOH) (for the ^{1}H NMR data, see general part).

N-Benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-ribohexose (12). The N-benzoyl aminodiol (8), containing ca. 10% of the isomeric material (9), was ozonized as above to give 75% yield of N-benzoyl-2,3,6-trideoxy-3-C-methyl-3-amino-L-ribohexose (12) in admixture with ca. 10% of (13), as indicated from ^{1}H NMR studies (see general part): oil; $[\alpha]_D^{20}$ = -39° (c 0.5, MeOH). The latter mixture, on treatment with methanolic HCl, as reported above for the conversion (15)—(21), gave, after SiO_2 column purification, the methyl glycoside (16) (60%): mp 142 °C, $[\alpha]_D^{20}$ = -75.8° (c 0.5, $CHCl_3$). Anal. calcd for $C_{15}H_{21}O_4N$: C, 64.48; H, 7.59; N, 5.01. Found: C, 64.56; H, 7.51; N, 4.89. (for ^{1}H NMR data, see general part).

Conversion of the N-Benzoyl-L-xyloderivative (15) into the methyl glycoside (18). The N-benzoyl derivative (15), (0.85 g, 0.003 mol), was converted to 620 mg (70%) of the oily methyl glycoside (16), as reported above: $[\alpha]_D^{20}$ = -69.6° (c 0.5, $CHCl_3$). A solution of the latter material, 0.62 g (0.0022 mol) in 4 mL of anhydrous CH_2Cl_2 was added to a stirred solution of 2 g of pyridinium chlorochromate and 1.6 g of 3 A molecular sieves in 15 mL of CH_2Cl_2. After 3 h at room temperature, the reaction mixture was diluted with 40 mL of dry ether and filtered through a short Florisil column. The residue obtained upon evaporation of the solvents was chromatographed on SiO_2, obtaining with hexane-ethyl acetate (7:3), 0.34 g (60%) of the oily ketone (17): $[\alpha]_D^{20}$ = -115° (c 0.5, $CHCl_3$). Anal. Calcd for

$C_{15}H_{19}O_4N$: C, 64.95; H, 6.92; N, 5.05. Found: C, 64.88; H, 6.81; N, 5.09. A 50 mL three-necked flask equipped with a dropping funnel, a stirring bar and a gas inlet tube was flushed with N_2 and charged with 5 mL of anhydrous THF and 2 mL of 1M L-Selectride (Aldrich). To this solution at -10 °C, 0.28 g (0.001 mol) of the above ketone (17) in 5 mL of THF was added. After 3 h at -10 °C, 0.5 mL of 3M NaOH and 2.5 mL of 30% H_2O_2 were added. The reaction mixture was saturated with K_2CO_3 and diluted with $CHCl_3$. The filtered solution gave a residue, which on chromatography, afforded, using increasing amounts of ethyl acetate in hexane, 0.12 g (42%) of crystalline (18): mp 140-141 °C; $[\alpha]_D^{20}$ = -76.1° (c 0.5, $CHCl_3$), identical with the product obtained on ozonolysis of (8), and 0.1 g (35%) of the L-xylo isomer (16).

Conversion of the N-Benzoyl-L-arabino Derivative (13) into the L-lyxo isomer (14). The N-benzoyl amino deoxysugar (13) was converted into the corresponding glycoside as reported above, in 70% yield. The product was shown by ^1H NMR studies to be a mixture of α- and β-isomers. This material, 1g (0.003 mol) was treated in 10 mL of dry pyridine with 2 g (0.017 mol) of methanesulfonyl chloride for two days at 0 °C. The reaction mixture was poured in ice-water, extracted with ethyl acetate (3 x 50 mL) and taken to dryness. The residue was chromatographed on a short SiO_2 column with ethyl acetate-hexane (1:1) to give 0.54 g of the unstable 4-O-mesylate which was immediately boiled with 8 mL of water, containing 1 g (0.012 mol) of sodium acetate. After 1 h the cooled reaction mixture was extracted with 3 x 50 mL of ethyl acetate, and the residue obtained upon evaporation of the solvent was treated overnight with 10 mL of a 1:1 mixture of methanol and 0.1N HCl at room temperature. After that time, TLC analysis indicated complete hydrolysis of the glycoside. Most of the methanol was evaporated

at reduced pressure, and the residue was extracted with 4 x 30 mL of ethyl acetate. On evaporation, a residue was obtained, upon SiO_2 chromatography afforded ca. 70 mg of the L-lyxo compound (14), mp 153 °C, $[\alpha]_D^{20}$ = -86.6° (c 0.5, MeOH). The overall yield of the conversion (13)—(14) resulted ca. 5%.

(2R)- and (2S)-2-Benzoylamino-2-methyl-pent-4-en-1-al (19) and (20). The N-benzoylamino diol (11), (2.6 g, 0.001 mol) in 20 mL of dry THF was added at once to 2.26 g (0.001 mol) of periodic acid in 150 mL of THF under stirring at room temperature. After 2 min, 0.5 mL of ethylene glycol was added to the cloudy reaction mixture, and the filtered reaction mixture was diluted with ice-water and extracted with 2 x 100 mL of ethyl acetate. SiO_2 chromatographic purification of the residue obtained upon evaporation of the solvent, yielded ca. 1.8 g (83%) of the (2R)-aldehyde (19) as an oil which solidified on standing: $[\alpha]_D^{20}$ = +13.5° (c 1, EtOH); ^{1}H NMR ($CDCl_3$) δ 9.53 (1H,HC=O,s), 7.9-7.4 (5H,Ph,m), 6.5 (1H,NH,m), 5.8 and 5.16 (3H,CH_2=CH-), 2.78-2.6 (2H,CH_2,m), 1.5 (3H,CH_3,s). From the N-benzoylamino diol (9), the (2S)-aldehyde (20) was obtained, identical in every respect to (19), but showing $[\alpha]_D^{20}$ = -14° (c 1, EtOH).

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