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A New Approach to 6-Deoxy-*D*-allofuranose- and 6-Deoxy-*L*-talofuranose Derivatives from 1,2 : 5,6-Di-O-isopropylidene α-*D*-Glucofuranose

Virág Zsoldos-Mády[a] and **Erich Zbiral**[b,*]

[a] Central Research Institute for Chemistry, Hungarian Academy of Sciences, H-1525 Budapest, Hungary

[b] Institut für Organische Chemie, Universität Wien, A-1090 Wien, Austria

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3-O-Acetyl-1,2-O-isopropylidene-α-*D*-allofuranose (**2b**) was prepared from 1,2 : 5,6-di-O-isopropylidene-α-*D*-allofuranose (**1b**). Treatment of **2b** with triphenylphosphine-diethyl azodicarboxylate afforded regio- and stereospecifically the 5,6-epoxy-α-*D*-allo derivative (**3**). The other diastereomeric compound, 5,6-epoxy-1,2-O-isopropylidene-β-*L*-talofuranose (**6**) was also prepared stereoselectively from **2b** *via* the intermediates **5a** and **5b**. The epoxy sugars **3** and **6** were converted with lithium aluminum hydride to the corresponding 6-deoxy-1,2-O-isopropylidene-α-*D*-allofuranose (**4a**) and -β-*L*-talofuranose (**7a**) derivatives. Hydrolysis of **4a** and **7a** afforded 6-deoxy-*D*-allose and 6-deoxy-*L*-talose, respectively. The corresponding 3,5-di-O-acetyl- (**4b** and **7b**) and the 3,5-O-(tetraisopropyldisiloxane-1,3-diyl) derivatives (**4c** and **7c**) are also described. Selective removal of the isopropylidene group and subsequent acetylation offers a convenient route to prepare sugar derivatives containing furanose ring, like **8b**, as a suitable precursor for nucleoside analogs.

(Keywords: Synthesis of 5,6-anhydro-1,2-O-isopropylidene-α-D-allofuranose and 5,6-anhydro-1,2-O-isopropylidene-β-L-talofuranose; Stereospecific transformation of 5,6-dihydroxy sugar derivative into 5,6-epoxy sugar derivative; Transformation of 6-O-t-butyldimethylsilyl-5-O-tosyl sugar derivative into 5,6-epoxy sugar derivative)

Ein neuer Zugang zu 6-Desoxy-α-D-allofuranose- und 6-Desoxy-β-L-talofuranosederivaten ausgehend von 1,2 : 5,6-Di-O-isopropyliden-α-D-glucofuranose

1,2 : 5,6-Di-O-isopropyliden-α-*D*-allofuranose (**1b**) wird zunächst in das 3-O-Acetyl-1,2-O-isopropylidenderivat **2b** übergeführt, aus welchem beim Umsatz mit

* Herrn Prof. Dr. *K. Komarek* mit den besten Wünschen zum 60. Geburtstag gewidmet.

Hilfe von Triphenylphosphin-Azodicarbonsäureester das 5,6-Epoxy-α-*D*-allozuckerderivat **3** regio- und stereospezifisch entsteht. Das andere diastereomere Derivat, die 5,6-Epoxy-1,2-OL-isopropyliden-β-*L*-talofuranose (**6**) wurde auch aus **2b** über die Zwischenprodukte **5a** und **5b** stereoselektiv hergestellt. Die Epoxyzucker **3** und **6** wurden mit $LiAlH_4$ in die entsprechenden 6-Desoxy-1,2-O-isopropyliden-α-*D*-allofuranose (**4a**) bzw. -β-*L*-talofuranose (**7a**) umgewandelt. Hydrolyse von **4a** und **7a** ergab 6-Deoxy-*D*-allose bzw. 6-Desoxy-*L*-talose. Die entsprechenden 3,5-Di-O-acetyl- (**4b** und **7b**) und 3,5-O-(Tetraisopropyldisiloxan-1,3-diyl)-derivate (**4c** und **7c**) werden ebenfalls beschrieben. Verbindung **4c** konnte in das 1 β,2-Di-O-acetylderivat (**8b**) umgewandelt werden, welches unmittelbar für Nucleozidsynthesen eingesetzt werden kann.

Introduction

The title compounds, regarded as derivatives of *D*-ribofuranose where the pro-(*R*)-H or the pro-(*S*)-H of the CH_2OH group is replaced by a methyl group, consitute a pair of epimers. In the studies on modified nucleoside analogs of biological interest [1] the derivatives of 6-deoxy-*D*-allofuranose and 6-deoxy-*L*-talofuranose have recently received special interest [2, 3]. Therefore, methods for the large-scale preparation of the corresponding sugar precursors are required.

El Khadem and *Nelson* [5] described a seven-step procedure, starting from *D*-ribose, for both 6-deoxy-*D*-allo- and 6-deoxy-*L*-taloepimers, suitable for the synthesis of nucleoside analogs. The procedure resulted in a mixture of C-5 epimers (*D*-allo: *L*-talo ~ 2:1), requiring subsequent separation of the isomers.

In an earlier work [4a] the corresponding 6-deoxyhexofuranosyl derivatives were prepared from *L*-rhamnose only in low yield. Recently, 6-deoxy-*L*-talose and its pyranosyl derivatives have been prepared [4b] from *L*-rhamnose in an eleven-step procedure.

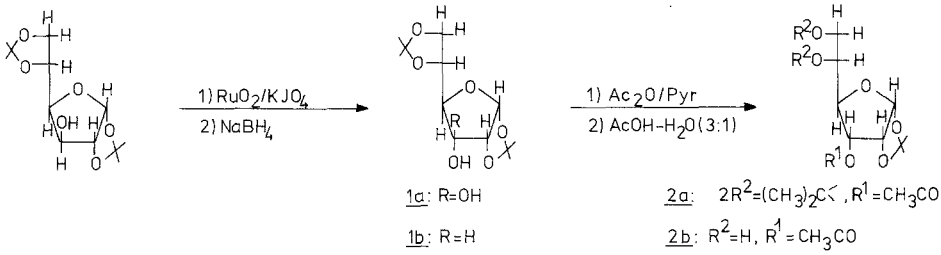
In this paper we describe a new and convenient synthetic route suitable for a large-scale stereoselective preparation of both of the desired 6-deoxyhexofuranose derivatives from the easily available 1,2:5,6-di-O-isopropylidene-α-*D*-glucofuranose [6].

Results and Discussion

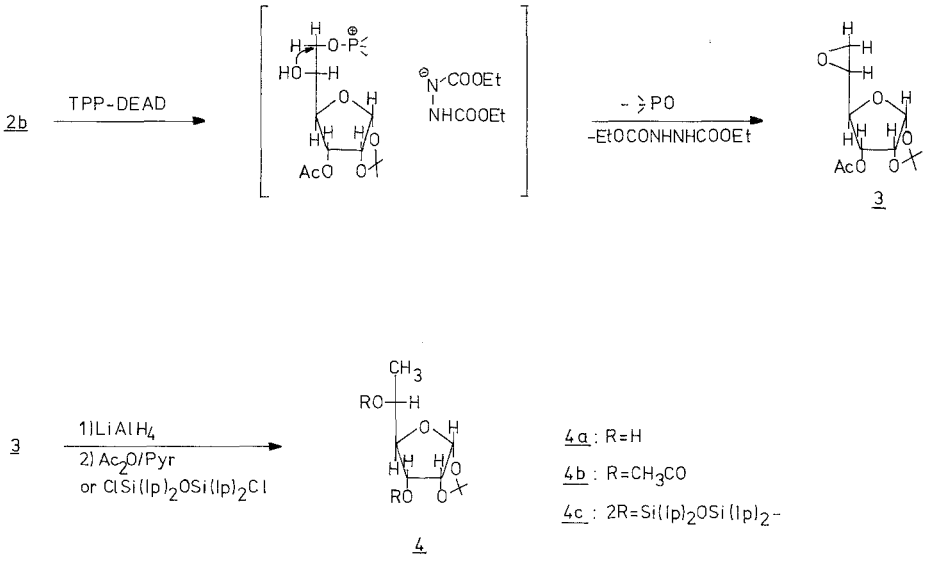
1,2:5,6-Di-O-isopropylidene-α-*D*-glucofuranose [6] was converted into 1,2-O-isopropylidene-3-O-acetyl-α-*D*-allofuranose (**2b**) [10] as presented in Scheme 1. By minor modification of the described procedures [7–10], **2b** was obtained in 75% overall yield, even on a large scale.

The oxidation of diacetone-glucofuranose can be performed by several reagents [7, 8]. Using ruthenium tetroxide [7], **1a** was obtained in 89% yield. Reduction of **1a** with sodium borohydride [7] gave the *D*-allo derivative **1b** and subsequent acetylation afforded almost quantitatively the 3-O-acetyl derivative **2a**. Selective hydrolysis of the latter was carried

Schema 1

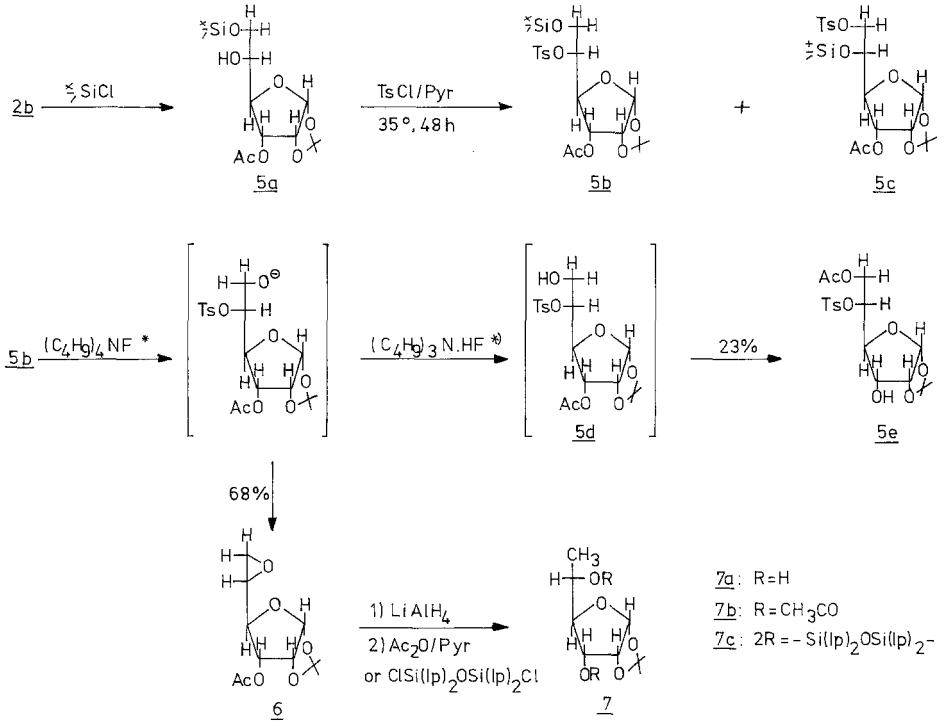


Schema 2



out with acetic acid—water (3:1) to give 3-O-acetyl-1,2-O-isopropylidene-α-*D*-allofuranose (**2b**) in 94% yield. Since in the literature for **2a** and **2b** different optical rotations are reported [9, 10], we confirmed the correct structure for **2a** and **2b** also by ^{1}H NMR spectroscopy at 250 MHz (Table 1). Compound **2b** proved to be an efficient key compound for the synthesis of both 6-deoxy-*D*-allofuranose (**4a–c**) and 6-deoxy-*L*-talofuranose (**7a–c**) derivatives *via* the corresponding epimeric 5,6-epoxy derivatives (**3** and **6**, respectively) (Scheme 2 and 3).

Schema 3



* $(C_4H_9)_3N \cdot HF$ can be formed to some extent from $(C_4H_9)_4NF$ spontaneously (see Ref. [14b]).

The 5,6-epoxy-*D*-allo derivative (**3**) was formed stereospecifically from **2b** by the triphenylphosphine—diethylazodicarboxyate (*TPP-DEAD*) technique [11] in boiling toluene. Thereby we achieved regiospecific activation at C-6. Similar specific activation of the primary CH_2OH group with *TPP-DEAD* was also recently observed [13] . In contrast, treatment of (*S*)-1,2-propanediol with this reagent resulted in [12] terminal activation only in the ratio of 5 : 1.

Reduction of **3** with lithium aluminum hydride afforded 6-deoxy-1,2-O-isopropylidene-α-*D*-allofuranose (**4a**) in 93% yield. The reaction-sequence to **4a** including six steps gave ~ 50% overall yield, based on di-O-isopropylidene-α-*D*-glucofuranose. Recently *Billich* et al. [3] described an alternative synthesis for **4a** in ~ 25% yield from the same starting material. Our new method, in addition, offers also the possibility to synthesize 6-deoxy-*L*-talofuranose derivatives stereoselectively (Scheme 3).

For the preparation of the 5,6-epoxy-*L*-talofuranose derivative (**6**), activation at C-5 was required. Therefore, the primary hydroxyl group of **2b** was selectively protected with the *tert*-butyldimethylsilyl group and **5a** subsequently tosylated. Treatment of the 6-O-tert-butyldimethylsilyl-5-O-tosyl-α-*D*-allofuranose derivative (**5b**) with tetrabutylammonium fluoride [14a] resulted in the desired 5,6-epoxy-*L*-talo compound (**6**) with inversion of configuration at C-5.

Tosylation of **5a** required slightly forced conditions (48 h, 35 °C, 1.5 eq. TsCl) and gave predominantly the expected 6-O-t-butyldimethylsilyl-5-O-tosyl derivative (**5b**) with minor amounts of by-products. Flash chromatography of the crude product resulted in a mixture of **5b** and **5c** (Scheme 3) in the ratio of 4 : 1, as shown by NMR. Recrystallization from petroleum ether afforded pure crystalline **5b** (60% yield), suitable for the synthesis of **6**. When the mixture of **5b** and **5c** (~ 4 : 1) was treated with tetrabutylammonium fluoride, a mixture of the epimeric *L*-talo- and *D*-allo epoxide derivatives (**6** and **3**) was isolated in almost the same ratio. Consequently, in **5c** the silyl substituent was bonded to C-5. Formation of this by-product in the tosylation procedure can be explained by partial migration of the *t*-butyldimethylsilyl group from C-6 to C-5 in compound **5a**. An analogous isomerization of the alkylsilyl group, induced by base, was observed previously [14a, 15a].

During the conversion of **5b** into **6** epoxy-derivative (yield 68%) a silicium-free by-product (23%) was also isolated from the reaction mixture. It was identified on the basis of microanalysis and ^{1}H NMR data (Table 1) as 6-O-acetyl-5-O-tosyl-1,2-O-isopropylidene-α-*D*-allofuranose (**5e**). The presence of the unsubstituted hydroxyl group at C-3 was shown by the increased multiplicity and significant upfield shift of H-3 (δ 4.08). The formation of **5e** from **5b** can be interpreted *via* **5d** as intermediate (Scheme 3), attributed to partial *Hofman* degradation of the reagent [14b] and subsequent acetyl migration. Tetrabutylammonium fluoride caused acyl migration also in other desilylation reactions [15b]. The by-product **5e**, however, can be converted into the desired *L*-talo-epoxide derivative (**6**) with sodium methoxide and subsequent acetylation.

Reduction of **6** gave the expected 6-deoxy-1,2-O-isopropylidene-β-*L*-talofuranose (**7a**) in good yield. The epimeric epoxy precursors (**3** and **6**) can also serve as useful starting materials for several other *D*-allofuranosyl and *L*-talofuranosyl derivatives.

By removal of the isopropylidene protecting group with Amberlyst 15 acidic resin, crystalline 6-deoxy-*D*-allose [18] was formed from **4** and 6-deoxy-*L*-talose [4b] from **7**, presenting a new and convenient synthetic method for the preparation of both 6-deoxy sugars, starting from *D*-glucose.

The 6-deoxyhexofuranose derivatives (**4a** and **7a**) were reacted with

Table 1. ^{1}H *NMR parameters*[a] *of D-allofuranose and L-talofuranose derivatives in*

Chemical shifts (δ /ppm)	**1b**[c]	**2a**	**2b**[d]
H-1	5.83	5.83	5.82
H-2	4.63	4.84	4.84
H-3	(4.05)[e]	4.91	4.92
H-4	3.84	4.18	4.17
H-5	4.33	4.33	3.98
H-6a	(4.08)[e]	4.09	3.71
H-6b	(4.01)[e]	3.93	3.60
OH	2.60	–	2.87; 2.42
acetyl-CH_3	–	2.14	2.14
tosyl-CH_3	–	–	–
$C(CH_3)_2$	1.60; 1.49 1.41; 1.39	1.59; 1.45 1.37 (6H)	1.57 1.35
$SiC(CH_3)_3$	–	–	–
$Si(CH_3)_2$	–	–	–
Coupling constants (J in Hz)			
$J_{1,2}$	3.8	3.7	3.8
$J_{2,3}$	5.1	5.2	4.8
$J_{3,4}$	8.6	8.6	8.7
$J_{4,5}$	4.6	4.4	4.0
$J_{5,6a}$	(6.6)[e]	7.0	3.8
$J_{5,6b}$	(6.8)[e]	5.4	7.0
$J_{6a,6b}$	(−8.7)[e]	−8.6	−11.5
$J_{CH,OH}$	8.7	–	b. s.

[a] Assignements confirmed by spin-decoupling; data from first-order analysis; b. s.: broad singulet; c. m.: complex multiplet.
[b] Related to $CHCl_3$ (δ = 7.24 ppm).

the bifunctional 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane [16] *TIPDS*Cl_2, to prepare **4c** and **7c** 3,5-O-*TIPDS*-derivatives (Scheme 2 and 3). Removal of the isopropylidene group with trifluoroacetic acid in aqueous chloroform resulted in the 1,2-dihydroxy-*D*-allofuranose derivative (**8a**), subsequent acetylation the 1,2-di-O-acetyl-β-*D*-allofuranose derivative (**8b**) (Scheme 4). The β anomeric configuration was established from the ^{1}H NMR spectrum (Table 2), $J_{1,2} < 1$ Hz indicated unambiguously[19] *trans* orientation of H-1 and H-2. This compound can serve as a convenient starting material for the synthesis of various nucleoside analogues which will be published elsewhere.

$CDCl_3$ *solution at 250 MHz (internal standard TMS or* $CHCl_3$[b]*)*

5a[b,d]	**5b**[b]	**5e**	**3**	**6**
5.82	5.45	5.49	5.84	5.81
4.84	4.81–4.70	4.51	4.87	4.85–4.80
4.94		4.08	4.68	
4.15	4.36	3.90	4.17	4.08
3.83	4.81–4.70	5.05	3.21	3.13
3.73	3.66–3.78	4.35	2.85	2.86–2.82
3.62		4.24	2.66	
2.50	—	2.60	—	—
2.14	2.08	1.99	2.16	2.17
—	2.42	2.45	—	—
1.56	1.45	1.54	1.57	1.57
1.35	1.27	1.35	1.36	1.36
0.90	0.84	—	—	—
0.08	−0.01	—	—	—
3.8	3.6	3.7	3.9	3.7
5.0	c. m.	4.3	4.9	5.0
8.5	8.2	8.4	9.0	8.6
5.1	3.5	3.2	4.2	4.5
4.1	c. m.	3.6	4.0	3.4
6.8	c. m.	7.5	2.8	3.4
−10.0	c. m.	−12.4	−5.1	c. m.
3.7	—	8.0	—	—

[c] Data for compound **1b** in D_2O solution at 300 MHz were published [20]. We observed nearly the same values. Data in brackets are form Ref. [20].
[d] First order analysis was made after D_2O exchange.

Schema 4

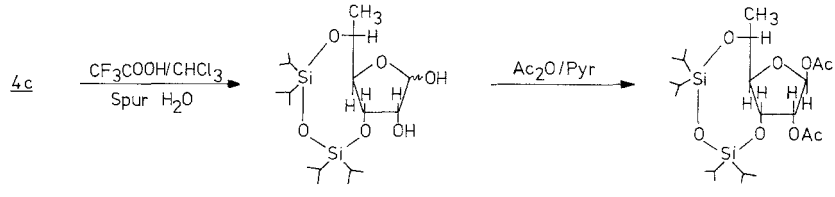


Table 2. ^{1}H *NMR parameters*[a] *of 6-deoxy-D-allofuranose and L-talafuranose derivatives in* $CDCl_3$ *solution at 250 MHz (internal standard TMS)*

Chemical shifts (δ/ppm)	**4a**[d]	**4b**	**4c**	**7a**[d]	**7b**	**8b**
H-1	5.83	5.81	5.68	5.83	5.85	6.03
H-2	4.60	4.84–4.79	4.54	4.60	4.82	5.29
H-3	4.10[e]		4.0	3.95[e]	4.68	4.51
H-4	3.70	4.17	3.67	3.63	4.15	3.62
H-5	4.08[e]	5.13	3.87	3.90[e]	5.04	3.85
H-6	1.29	1.27	1.31	1.32	1.34	1.27
OH	2.65; 2.37	–	–	2.59; 2.23	–	–
acetyl-CH_3	–	2.15; 2.06	–	–	2.14; 2.09	2.12; 2.04
$C(CH_3)_2$	1.61	1.57	1.58	1.60	1.58	–
	1.40	1.36	1.38	1.39	1.36	–
TIPDS ($8 \times 3H + 4H$)	–	–	1.15–0.95	–	–	1.12–0.86
Coupling constants (J in Hz)						
$J_{1,2}$	3.9	3.7	3.8	3.9	3.8	<1
$J_{2,3}$	5.3	4.8	5.0	5.1	5.0	4.9
$J_{3,4}$	8.6	8.2	8.0	8.5	9.1	7.0
$J_{4,5}$	3.9	3.9	8.4	4.2	3.2	9.4
$J_{5,6}$	6.8	6.5	6.2	6.8	6.4	6.0
$J_{CH,OH}$	10.0	–	–	10.7	–	–
	b. s.			6.6		

For footnotes [a–d] see Table 1.
[e] First order analysis from spin-decoupled spectra.

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Experimental

Collaborator: **Martina Drescher**

Melting points were determined with a *Kofler* apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 automatic polarimeter. TLC was performed with Silica gel 60 F_{254} (Merck), spots were made visible by spraying with a solution of 2% cerium nitrate in 2 *N* sulfuric acid and subsequently heating or by irradiation with a UV lamp (254 nm). Flash chromatography [17] was performed on Silica Gel (Merck, 0.04–0.063 mm) at 1.5–2 bar. The ^{1}H-NMR spectra were recorded at 250 MHz with a WM-250 Bruker spectrometer in $CDCl_3$ with *TMS* as internal standard, unless otherwise stated.

1,2 : 5,6-Di-O-isopropylidene-α-D-allofuranose (**1 b**)

Compound **1 b** was prepared by a minor modification of the procedure of *Baker* et al. [7] 1,2 : 5,6-Di-O-isopropylidene-α-*D*-glucofuranose [6] (10 g, 0.038 mol) was oxidized with ruthenium tetraoxide as described [7]. After 12 h TLC (benzene-methanol 9 : 1) indicated still starting material. By addition of further amount of potassium metaperiodate (7.0 g) and potassium carbonate (0.75) the reaction mixture was stirred for further 12 h to achieve complete oxidation. After work-up according to the literature 9.36 g (89%) crude, crystalline **1 a** was formed, suitable for further reaction.

Reduction of crude **1 a** (37.7 g, 0.137 mol) with sodium borohydride [7] gave 33.3 g (94%) crystalline **1 b**, homogeneous by TLC (ethyl acetate-petroleum ether 2 : 1), $R_f = 0.70$. The product can be used without further purification at the next step.

3-O-acetyl-1,2 : 5,6-di-O-isopropylidene-α-D-allofuranose (**2 a**)

Acetylation of **1 b** (33.3 g, 0.128 mol) was made with anhydrous pyridine (75 ml) and acetic anhydride (75 ml) for 12 h at room temperature. The mixture was poured into ice-water and stirred to 5 h. The separated crystalline product was filtered, washed with cold water and dried yielding 32 g pure **2 a**. The aqueous phase (1 000 ml) was extracted several times with ether, the combined etheric solutions were washed with 100 ml ice-cold 4% hydrochloric acid solution, with water, with saturated sodium hydrogen carbonate solution and with water again. After drying over sodium sulfate and evaporation, a further crop (5.5 g) was obtained, total yield 37.5 g (97%). Recrystallization from petroleum ether gave white crystals, 35.6 g (92%) m.p. 77–78 °C; $[\alpha]_D = +116.2°$ (*c* 1.59; $CHCl_3$). Lit. m. p.: 75–76 °C [9, 10 b]; Lit. $[\alpha]_D = +100.6°$ ($CHCl_3$) [9 a]; $+107.6°$ ($CHCl_3$) [9 b], $+64.2°$ ($CHCl_3$) [10 a].

3-O-Acetyl-1,2-O-isopropylidene-α-D-allofuranose (**2b**)

The partial hydrolysis of **2a** (5.88 g, 0.019 mol) was made with 51 ml of a mixture of acetic acid—water (3 : 1) for 24 h at room temperature. When TLC (ethyl acetate—chloroform 2 : 1) indicated incomplete reaction, a further amount of acetic acid—water (21 + 7 ml) was added, and the mixture stirred for further 12 h. After evaporation the residue was purified by flash chromatography [17] (ethyl acetate) to give 4.8 g (94%) pure **2b**, which on standing or treated with ether-hexane gave a white solid material, m.p. 68–70 °C, $R_f = 0.36$ (ethyl acetate—chloroform 2 : 1), $[\alpha]_D = +116.7°$ ($c = 0.6$, $CHCl_3$). Lit. $[\alpha]_D = +113.7°$ ($CHCl_3$) [10b], $+294.3°$ ($CHCl_3$) [10a].

3-O-Acetyl-5,6-anhydro-1,2-O-isopropylidene-α-D-allofuranose (**3**)

To the stirred solution of 1.69 g (6.45 mmol) **2b** in 65 ml anhydrous toluene was added 2.3 g triphenylphosphine and 3.2 g molecular sieves 4 Å and under argon atmosphere 1.48 g diethyl azodicarboxylate was injected into the mixture. After boiling for 4.5 h TLC (petroleum ether—ethyl acetate 1 : 1) showed complete reaction. After cooling the solvent was evaporated, and the residue triturated with ether. The undissolved triphenylphosphinoxide was filtered, the etheric solution was evaporated. Flash chromatography with petroleum ether—ethyl acetate (5 : 1) resulted in 1.25 g (80%) pure **3**, homogeneous by TLC, $R_f = 0.7$ (petroleum ether—ethyl acetate 1 : 1) which from petroleum ether solidified; m.p.: 77–78 °C.

$C_{11}H_{16}O_6$. Calcd.: C 54.09, H 6.60. Found: C 54.05, H 6.61.

6-Deoxy-1,2-O-isopropylidene-α-D-allofuranose (**4a**)

To a solution of **3** (448 mg, 1.8 mmol) in 24 ml anhydrous tetrahydrofuran was added 233 mg (6.1 mmol) lithium aluminum hydride and the mixture was refluxed for 3 h, by which time TLC indicated complete reaction. Dry ethyl acetate was added to the suspension, and refluxed further for 1 h. When cooled, 8 ml 2.5 *N* sodium hydroxide was poured into the reaction mixture. Extraction was made once with ethyl acetate, three times with dichloromethane, the combined organic solutions were dried over sodium sulfate and evaporated to give 380 mg (93%) product, homogeneous by TLC ($R_f = 0.5$; ethyl acetate). Recrystallization from ethyl acetate, precipitated with petroleum ether gave white crystals, m.p. 113–114 °C. Lit. [3] m.p.: 115 °C.

$C_9H_{16}O_5$. Calcd.: C 52.93, H 7.90. Found: C 53.43, H 7.96.

6-Deoxy-3,5-di-O-acetyl-1,2-O-isopropylidene-α-D-allofuranose (**4b**)

Acetylation of compound **4a** (0.1 g, 0.49 mmol) was made in a mixture of dry pyridine (1 ml) and acetic anhydride (0.7 ml) for 16 h at room temperature. The solvent was evaporated by an oil-pump, and the residue was triturated with petroleum ether, filtered and evaporated to give 128 mg (91%) syrup, homogeneous by TLC ($R_f = 0.6$; petroleum ether—ethyl acetate 7 : 3) and pure by NMR.

6-Deoxy-3,5-O-(tetraisopropyldisiloxane-1,3-diyl)-1,2-O-isopropylidene-α-D-allofuranose (**4c**)

Compound **4a** (323 mg, 1.6 mmol) was dissolved in 15 ml dry dimethyl formamide. To the solution 0.48 g imidazole and 0.55 ml (1.75 mmol) *TIPDS*Cl_2

was added at 0 °C. The reaction mixture was allowed to warm to room temperature. After 12 h *DMF* was removed by oil-pump, the residue was dissolved in ether, extracted with saturated sodium chloride solution and with saturated sodium hydrogen carbonate solution. The etheric layer was dried over sodium sulfate and evaporated. The residue was purified by flash-chromatography (petroleum ether—ethyl acetate 19 : 1) resulting in 428 mg (60%) crystalline **4 c**. Recrystallization from ethanol by precipitation with water gave pure crystals, m.p. 74–76 °C; $R_f = 0.73$ (petroleum ether—ethyl acetate 7 : 1).

$C_{21}H_{42}O_6Si_2$. Calcd.: C 56.46, H 9.48. Found: C 56.38, H 9.40.

3-O-Acetyl-6-O-t-butyldimethylsilyl-1,2-O-isopropylidene-α-D-allofuranose (**5 a**)

Imidazole (1.8 g, 2 eq.) and *t*-butyldimethylchlorosilane (2.0 g; 1 eq.) in 15 ml dry dimethylformamide was dried over molecular sieves 4 Å for 12 h. Under ice-cooling 3.5 g (13.4 mmol) **2 b** was added to the dry reagent solution and allowed to stand at 4 °C for 16 h. After evaporation of the *DMF* by oil-pump the residue was dissolved in water and extracted several times with ether. The etheric solution was dried over sodium sulfate, evaporated and purified by flash-chromatography with the eluant petroleum ether—ethyl acetate (5 : 1) resulting in 3 g (60%) pure **5 a** which solidified on standing. $R_f = 0.54$ (petroleum ether—ethyl acetate 2 : 1), $[\alpha]_D = +89°$ (*c* 0.4; $CHCl_3$).

$C_{17}H_{32}O_7Si$. Calcd.: C 54.23, H 8.57. Found: C 54.32, H 8.38.

3-O-Acetyl-6-O-t-butyldimethylsilyl-1,2-O-isopropylidene-5-O-tosyl-α-D-allofuranose (**5 b**)

Procedure A (on a smaller scale)

To a solution of **5 a** (1.0 g, 2.6 mmol) in 5 ml anhydrous pyridine was added under ice cooling 0.7 g (3.7 mmol) freshly crystallized *p*-toluenesulfonyl chloride in 5 ml anhydrous pyridine. The mixture was kept at 35 °C (at lower temperature the reaction is very slow), after 24 h TLC (petroleum ether—ethyl acetate 7 : 3) indicated still incomplete reaction. Additional 0.1 g *Ts*Cl in 1 ml pyridine was added to the mixture, and it was kept at 35 °C for further 24 h. Then the solvent was evaporated by oil-pump, and the residue was purified by flash-chromatography with petroleum ether—ethyl acetate (7 : 3). The main fraction ($R_f = 0.6$)—on the basis of the NMR spectrum—proved to be a mixture of **5 b** and **5 c** (ratio cca. 4 : 1). Recrystallization from petroleum ether gave pure **5 b** (0.84 g; 60%) in white crystals, m.p. 85–86 °C, $[\alpha]_D = +61.3°$ (*c* 1; $CHCl_3$).

$C_{24}H_{38}O_9SSi$. Calcd.: C 54.33, H 7.22. Found: C 54.01, H 7.28.

In the mother liquor **5 b**, **5 c**, and a third still unidentified product was detected by NMR.

Procedure B (on a larger scale, without chromatography)

A mixture of **5 a** (8.2 g, 0.022 mol) and 5.7 g (0.03 mol) *Ts*Cl in 30 ml anhydrous pyridine was kept at 35 °C for 48 h, then it was poured onto ice, and stirred for 1 h. The aqueous solution was extracted several times with ether, washed with ice-cold 1% hydrochloric acid solution, with water, with saturated $NaHCO_3$ solution, and dried over sodium sulfate. After evaporation a mixture of **5 b** and **5 c** (10 g) remained, TLC showed one spot ($R_f = 0.6$) only. Recrystallization from methanol—water (5 : 1) resulted in 5.1 g pure **5 b** (44%), m.p. 80–82 °C. After the

second crystallization the m.p. rose to 85–86 °C. From the mother liquor a mixture was got (4 g), the main component was **5c**, but **5b** and also a third unidentified product was detectable by NMR.

Significant ^{1}H NMR data of **5c** in $CDCl_3$ at 250 MHz (related to $CHCl_3$, $\delta = 7.24$ ppm): δ 5.71 (1 H, $J_{1,2} = 3.6$ Hz, H-1), 4.82–4.70 (2 H, m), 4.18–4.09 (2 H, m), 3.99 (1 H, dd, $J = 5.0$ Hz and 10.4 Hz), 3.80 (1 H, dd, $J = 7.14$ and 10.4 Hz), 2.45 (3 H, s, tosyl-CH_3), 2.05 (3 H, s, acetyl-CH_3), 1.50 and 1.30 (3 H, s each, isopropylidene CH_3), 0.80 (9 H, s, *tert*-butylsilyl), 0.00 (6 H, s, dimethylsilyl). Evaluation was made from the mixture of **5b** and **5c**.

Synthesis of 3-O-acetyl-5,6-anhydro-1,2-O-isopropylidene-β-L-talofuranose (**6**)

To a solution of **5b** (10.3 g, 19.4 mmol) in 350 ml anhydrous tetrahydrofuran (*THF*) was added a $\sim 0.7\,M$ solution (55 ml) of tetrabutylammonium fluoride (*TBAF*) in *THF* under argon. *TBAF* was prepared [14] from $(C_4H_9)_4NF \cdot 3\,H_2O$ by drying over molecular sieves 4 Å in dry *THF*. After 16 h TLC (petroleum ether—ethyl acetate 7 : 1) indicated no more starting material ($R_f = 0.62$).

Beside the main product **6** ($R_f = 0.44$), a minor product (**5e**; $R_f = 0.18$) also appeared. A saturated sodium chloride solution was added to the mixture and extracted several times with ether. The organic layer was dried over sodium sulfate and evaporated to give 5.8 g syrup. Flash-chromatography with petroleum ether—ethyl acetate (7 : 1) resulted in 3.2 g (68%) pure **6** as main product, crystallized from petroleum ether, m.p.: 90–91 °C.

$C_{11}H_{16}O_6$. Calcd.: C 54.09, H 6.60. Found: C 54.38, H 6.60.

The less moving component (1.8 g; 23%) proved to be 6-O-acetyl-1,2-O-isopropylidene-5-O-tosyl-α-*D*-allofuranose (**5e**).

$C_{18}H_{24}O_9S$. Calcd.: C 51.92, H 5.81. Found: C 51.25, H 5.83.

When in the same procedure a mixture of **5b** and **5c** (ratio cca. 4 : 1) was treated with tetrabutylammonium fluoride, after chromatography the main fraction was a mixture of **6** and **3** (ratio cca. 4 : 1 by NMR). In the second fraction **5e** is the major product.

6-Deoxy-1,2-O-isopropylidene-β-L-talofuranose (**7a**)

Compound **6** (1.4 g, 5.7 mmol) in 30 ml anhydrous tetrahydrofuran was added to a suspension of 0.855 g lithium aluminum hydride in 45 ml anhydrous tetrahydrofuran. The reaction mixture was refluxed for 1.5 h and allowed to stand at room temperature overnight. Then 18 ml dry ethyl acetate was added to the mixture and refluxed for 1 h. After cooling it was treated with 100 ml ether and 38 ml 10% ammonium chloride solution and extracted.

To the aqueous layer saturated sodium chloride solution was added. After filtration it was *in vacuo* concentrated and extracted several times with chloroform. The combined organic solutions were dried over sodium sulfate and evaporated. The resulting syrup was dissolved in ethyl acetate and ether, and a few drops of petroleum ether was added to it till turbidity. After cooling 0.92 g (79%) white crystals separated, m.p.: 94 °C.

$C_9H_{16}O_5$. Calcd.: C 52.94, H 7.90. Found: C 53.43, H 7.96.

6-Deoxy-3,5-di-O-acetyl-1,2-O-isopropylidene-α-L-talofuranose (**7b**)

Acetylation of compound **7a** (213 mg, 1.04 mmol) was made in a mixture of 2 ml dry pyridine and 1.5 ml acetic anhydride at room temperature for 12 h. The

mixture was poured into ice-water, extracted severall times with ether. The etheric phase was washed with ice-cold 1% hydrochloric acid, water, saturated sodium hydrogen carbonate solution and dried over sodium sulfate. After evaporation the residue was filtered through a silica gel column (from 15 g Kieselgel, Merck, 0.04–0.063 mm) with petroleum ether—ethyl acetate (7 : 1), then (1 : 1). After evaporation 280 mg (93%) pure syrup was obtained. From petroleum ether by partial evaporation compound **7 b** crystallized, m.p. 65 °C, $R_f = 0.67$ (petroleum ether—ethyl acetate 1 : 1).

$C_{13}H_{20}O_7$. Calcd.: C 54.16, H 6.99. Found: C 54.02, H 6.93.

6-Deoxy-3,5-O-(tetraisopropyldisiloxane-1,3-diyl)-1,2-O-isopropylidene-β-L-talofuranose (**7 c**)

Compound **7 a** (180 mg, 0.88 mmol) was dissolved in 8 ml dry *DMF*, 264 mg imidazole and 0.304 ml (0.968 mmol) *TIPDS*Cl_2 was added to the solution at 0 °C. The reaction mixture was kept at room temperature overnight. It was worked up as described for **4 c**. After flash chromatography (petroleum ether—ethyl acetate 19 : 1) 356 mg (92%) pure product was isolated which on standing solidified. $R_f = 0.63$ (petroleum ether—ethyl acetate 19 : 1).

$C_{11}H_{42}O_6Si_2$. Calcd.: C 56.46, H 9.48. Found: C 56.32, H 9.47.

6-Deoxy-3,5-O-(tetraisopropyldisiloxane-1,3-diyl)-D-allofuranose (**8 a**)

To a solution of **4 c** (200 mg, 0.448 mmol) in 3 ml moist chloroform (shaken with water, dried over sodium sulfate for 15 min) was added 100 mg (0.877 mmol) trifluoroacetic acid and the mixture was stirred for 4 days at room temperature. After evaporation of the solvent the residue was dissolved in chloroform, washed with saturated sodium hydrogen carbonate solution and with saturated sodium chloride solution. The organic layer was dried over sodium sulfate and evaporated. The crude product was purified by flash-chromatography (petroleum ether—ethyl acetate 7 : 1) giving a homogeneous syrup, yield 130 mg (71%). $R_f = 0.3$ (petroleum ether—ethyl acetate 7 : 1).

6-Deoxy-1,2-di-O-acetyl-3,5-O-(tetraisopropyldisiloxane-1,3-diyl)-β-D-allofuranose (**8 b**)

Compound **8 a** was acetylated with a mixture of 1 ml dry pyridine and 1 ml acetic anhydride for 2 days at room temperature. The reaction mixture was evaporated using an oil-pump. Ice was added to the residue and it was extracted several times with ether. The organic layer was extracted with cold 1 *N* HCl solution and with saturated sodium hydrogen carbonate solution, dried over sodium sulfate and evaporated. Filtration through a silica gel column (prepared from 12 g adsorbent) with petroleum ether—ethyl acetate (19 : 1) resulted in 100 mg (64%) pure product.

$C_{22}H_{42}O_8Si_2$. Calcd.: C 53.84, H 8.63. Found: C 53.62, H 8.66.

6-Deoxy-D-allose

Compound **4 a** (149 mg, 0.68 mmol) was dissolved in 10 ml of dist. water and heated at 90 °C for 2 h with 1 ml Amberlyst 15 acidic ion-exchange resin. After evaporation by oil pump a crystalline mass (107 mg, 95%) remained, homogeneous by TLC (ethyl acetate—ethanol—water 7 : 2 : 1). The crystals were

dissolved in ethanol and precipitated with acetone and a few drops of ether to give white needles, m.p.: 139–142 °C, $[\alpha]_D = -3.4 \rightarrow +1.9°$ (*c* 1, water).

Lit. [18] m.p.: 140–143 °C, $[\alpha]_D = \pm 0$.

6-Deoxy-L-talose

Compound **7a** (140 mg, 0.68 mmol) was dissolved in 10 ml dist. water and heated at 90 °C for 2 h with 1 ml Amberlyst 15 acidic ion-exchange resin. After evaporation (oil pump) a crystalline mass (110 mg, 98%) remained, homogeneous by TLC (ethyl acetate—ethanol—water 7:2:1). The crystals were dissolved in ethanol, precipitated with acetone and ether to give white needles, m.p.: 124–126 °C, $[\alpha]_D = -17.3 \rightarrow -20.7°$ (*c* 0.52, water). Lit. m.p.: 116–118 °C [18]; 126–127 °C [4b]. Lit. $[\alpha]_D = -20.5°$ (*c* 2.28, water) [4b, 18].

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