Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 774–786

Synthesis of and NMR studies on the four diastereomeric 1-deoxy-D-ketohexoses

Nigel A. Jones,[a] Sarah F. Jenkinson,[a] Raquel Soengas,[a] Mette Fanefjord,[a] Mark R. Wormald,[b] Raymond A. Dwek,[b] Gullapalli P. Kiran,[c] Rao Devendar,[c] Goro Takata,[c] Kenji Morimoto,[c] Ken Izumori[c] and George W. J. Fleet[a,*]

[a]*Chemistry Research Laboratory, Department of Chemistry, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK*
[b]*Glycobiology Institute, Department of Biochemistry, Oxford University, South Parks Road, Oxford OX1 3QU, UK*
[c]*Rare Sugar Research Centre, Kagawa University, 2393 Miki-cho, Kita-gun, Kagawa 761-0795, Japan*

Received 18 February 2007; accepted 25 February 2007

Abstract—The four 1-deoxy-D-ketohexoses—1-deoxy-D-psicose, 1-deoxy-D-fructose, 1-deoxy-D-sorbose and 1-deoxy-D-tagatose—were synthesised by methyl lithium addition to suitably protected and readily available pentonolactones. The 1-deoxy-L-ketohexoses are available from the enantiomeric lactones. The NMR studies on aqueous solutions of each diastereomer show that the relative amounts of open chain ketones, α- and β-pyranoses, and α- and β-furanoses vary considerably; at least four different species are identifiable from each equilibrium.

1. Introduction

The availability of rare monosaccharides has been transformed by the demand for alternative foods which qualify as GASF (generally regarded as a safe food).[1] Izumoring is a biotechnological concept, which allows the green production of any of the isomeric hexoses.[2] Inexpensive chemical production of D-tagatose by the calcium(II) isomerisation of D-galactose has led to a drop in price from around $10,000 to $5 per kilogram.[3] A considerable amount of ingenious effort has been invested in the chemical synthesis of rare sugars and their potential uses as starting materials for bioactive compounds,[4] but for large scale synthesis a biotechnological approach is likely to be both more economically efficient and environmentally friendly.

D-Tagatose has GASF status and is used as a low calorie sweetener.[5] D-Psicose, readily available from D-fructose by the action of D-tagatose epimerase,[6] shows promise as a healthy food substitute.[7] Rare monosaccharides have been found to possess interesting biological activity. For example, 2-deoxy-L-ribose suppresses tumour growth, showing potential in antitumour therapy.[8] Intraperitoneal administration of L-glucose enhanced memory in mice by acting peripherally and its effect depended on cholinergic mechanisms;[9] L-glucose has been used in the development of glycoconjugate vaccines against diseases caused by *Shigella sonnei*.[10] D-Allose is an inhibitor of segmented neutrophile production and lowered platelet count without detrimental clinical effects.[11] A combination of D-allose with a low dose of FK506, a frequently used potent immunosuppressant, significantly increased the rate of six-month allograft survival with reduced tissue damage. D-Allose was also reported to possess a protective effect against ischemia reperfusion.[12] D-Tagatose has been found to be an antihyperglycemic agent and therefore useful in the treatment of diabetes.[13] D-Psicose has a significant number of chemotherapeutic properties.[14]

Relatively little attention has been paid to the synthesis or structures of deoxyketoses. While they may have potential as foods, the main objective of this project is a study of their ability to interact with a wide variety of biological receptors and to determine the structure of the free sugars in solution. If they are of substantial value, it is likely that they will be prepared on a large scale by biotechnological

* Corresponding author. E-mail: george.fleet@chem.ox.ac.uk

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.02.028

Izumoring procedures[15] by a green environmentally friendly technique; the deoxyketoses reported herein have been used to confirm the structures and to provide substrates for the initial studies of the interconversions of all 1- and 6-deoxyhexoses by deoxy Izumoring.[15]

Herein we report efficient short syntheses of each of the diastereomeric D-ketohexoses by methyl lithium addition to a suitably protected lactone of an aldonic acid. 1-Deoxy-D-psicose **1**, 1-deoxy-D-fructose **2**, 1-deoxy-D-sorbose **3** and 1-deoxy-D-tagatose **4** were prepared from readily available protected lactones of D-ribonic acid **5**, D-arabinonic acid **6**, D-xylonic acid **7** and D-lyxonic acid **8**, respectively. The L-enantiomers of the starting lactones are also available, giving a formal synthesis of the four enantiomeric L-ketohexoses.

2. Results and discussion

X-ray crystallographic analysis has shown that 1-deoxy-D-sorbose[16] crystallises in the α-pyranose form (Fig. 1); two different crystalline forms of 1-deoxy-α-D-tagatopyranose (Fig. 2) have been isolated.[17] However, in solution each of the diastereomeric ketohexoses exists as an equilibrium between both anomers of the pyranose and furanose ring forms as well as the open chain form in varying proportions (Scheme 1). NMR studies on each diastereomer are presented; the pioneering work of Angyal[18] in 1976 on 1-deoxy-D-fructose, 1-deoxy-L-sorbose and 1-deoxy-L-psicose is extended.

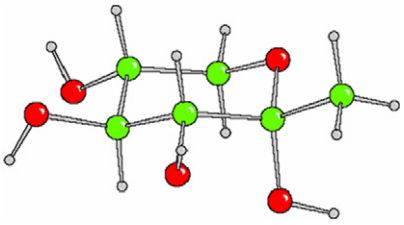


Figure 1. Crystal structure of 1-deoxy-α-D-sorbopyranose.

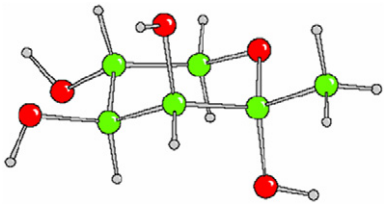


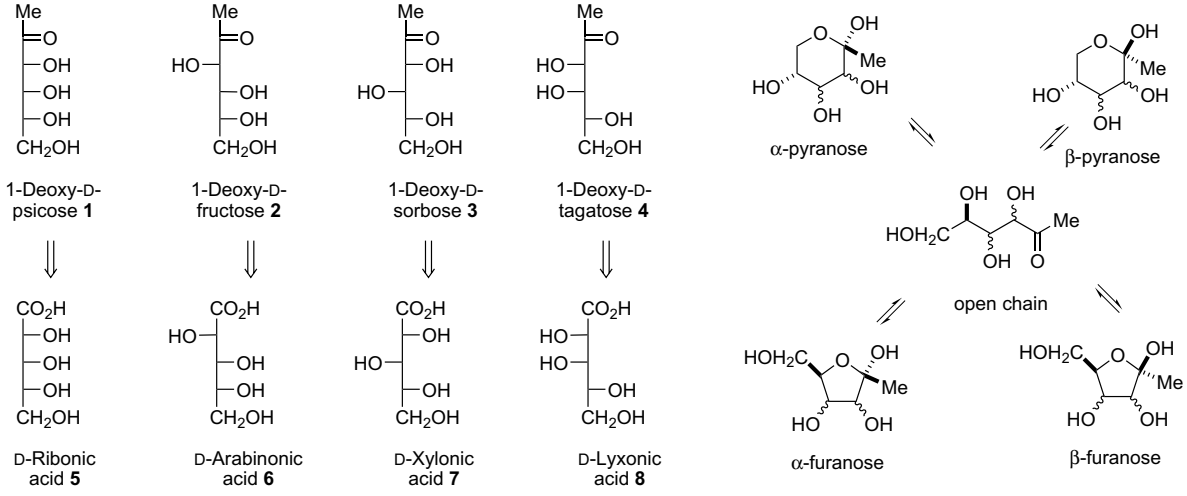
Figure 2. Crystal structure of 1-deoxy-α-D-tagatopyranose.

2.1. Synthesis of 1-deoxy ketohexoses

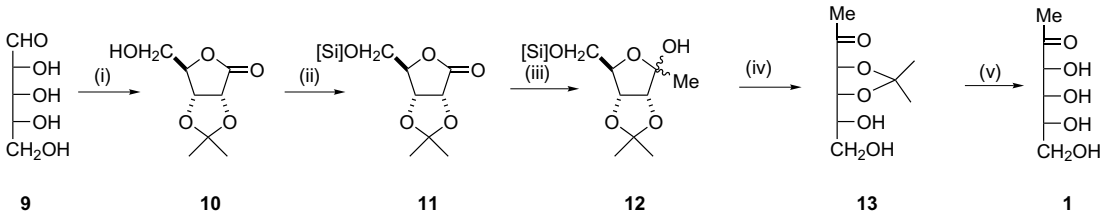
2.1.1. 1-Deoxy-D-psicose 1. 1-Deoxy-L-psicose has been synthesised in a multi-step synthesis from L-sorbose;[19] two syntheses of 1-deoxy-D-psicose **1** have been reported.[20]

D-Ribose **9** can be converted to the protected lactone **10** by oxidation with bromine and subsequent acetonation by an organic synthesis procedure in a 73% yield;[21] lactone **10** is the equivalent of a protected ribonic acid **5**. Treatment of the resulting lactone **10** with *tert*-butyldimethylsilyl chloride (TBDMSCl) and imidazole gave 5-*O*-silyl protected **11**, which with methyl lithium afforded the protected 1-deoxy-D-psicose **12** in a 96% yield over 2 steps; reaction of **10** with methyl lithium gave only low yields of the required lactol **13**, so protection of the C5 alcohol is necessary. 5-*O*-Desilylation of **12** with tetra-*n*-butylammonium fluoride (TBAF) in THF to **13**, followed by acidic hydrolysis, afforded 1-deoxy-D-psicose **1** in 51% yield over 2 steps. Removal of the 2,3-*O*-isopropylidene protecting group was also attempted with an increased reaction temperature and the use of a different acid (acetic acid) but this led to a complex mixture of products by TLC. It may be that lactols such as **13**, which can give rise to a tertiary carbocation at the anomeric centre, are more prone than most glycosides to acid catalysed decomposition. 1-Deoxy-D-psicose **1** was obtained in a 36% overall yield from D-ribose (Scheme 2).

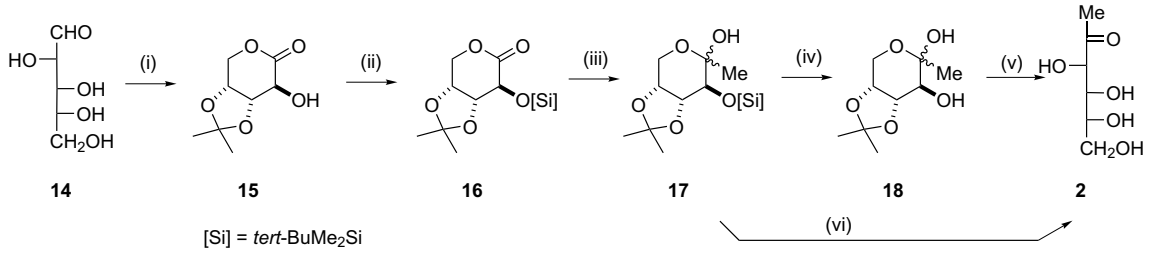
The L-enantiomer of **9** can be readily derived from D-lyxonolactone **28**[22] thus allowing access to 1-deoxy-L-psicose.



Scheme 1.



Scheme 2. Reagents and conditions: (i) Ref. 21 (73%); (ii) *tert*-BuMe$_2$SiCl, imidazole, DMF (98%); (iii) MeLi, THF, −78 °C (98%); (iv) TBAF, THF (79%); (v) Dowex® 50WX8-100 ion-exchange resin, water, room temperature (65%).



Scheme 3. Reagents and conditions: (i) Ref. 25 (75%); (ii) *tert*-BuMe$_2$SiCl, imidazole, DMF (90%); (ii) MeLi, THF, −78 °C (98%); (iv) TBAF, THF (69%); (v) CH_3COOH, H_2O (53%); (vi) Dowex® 50WX8-100 ion-exchange resin, water, room temperature (93%).

2.1.2. 1-Deoxy-D-fructose 2. The synthesis of **2** has previously been reported.[19,23] 1-Deoxy-D-fructose was synthesised from D-arabinose **14** as indicated in Scheme 3. The preparation of 1,5-lactone **15**—the equivalent of arabinonic acid **6**—as prepared by the procedure reported for the L-enantiomer; thus treatment of D-arabinose **14** with dimethoxypropane in DMF, in the presence of catalytic amounts of *p*-toluenesulfonic acid, gave the kinetic 3,4-monoacetonide,[24] which on oxidation with bromine afforded lactone **15** in 75% yield.[25]

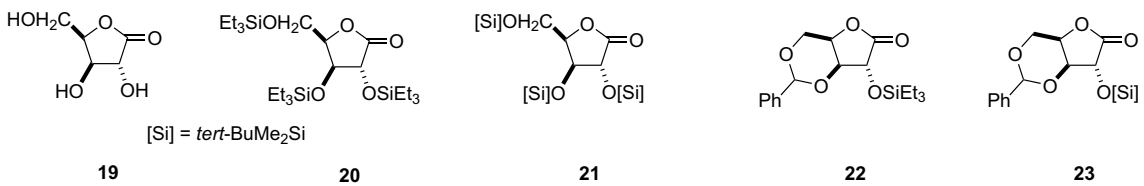
As is in the case of the synthesis of deoxypsicose **1**, protection of the remaining free OH group in **15** was necessary in order to obtain a good yield on addition of methyl lithium; only a low yield of **18** could be obtained by reaction of methyl lithium with **15**. Protection of the secondary alcohol group in **15** with TBDMS chloride gave the fully protected lactone **16** in 90% yield, which on addition of methyl lithium afforded lactol **17** (98% yield). Removal of the silyl protecting group from **17** by treatment with TBAF gave **18** in 69% yield. Acid hydrolysis of **18** with aqueous acetic acid gave deoxy fructose **2** in 53% yield. However, both the silyl and isopropylidene protecting groups in **17** can be removed by careful treatment with acidic ion-exchange resin to give the deprotected target in 93% yield.

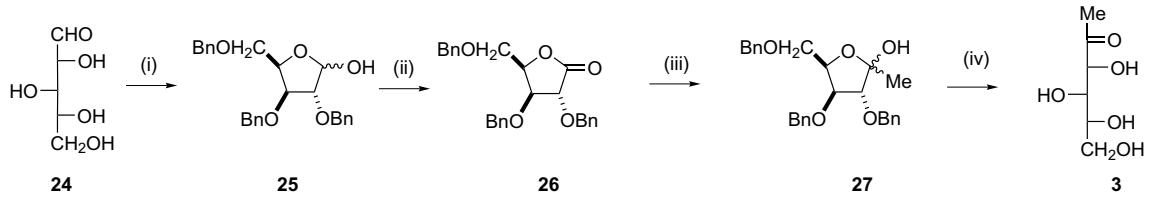
Thus the overall yield of unprotected 1-deoxy-D-fructose **2** from D-arabinose **14** is 64%. L-Arabinose is equally available as D-arabinose **14**, so that 1-deoxy-L-fructose is also readily and cheaply available.

2.1.3. 1-Deoxy-D-sorbose 3. The enantiomer 1-deoxy-L-sorbose is made by the deoxygenation of C-1 in L-sorbose,[19] and the synthesis of 1-deoxy-D-sorbose has also been reported.[23b]

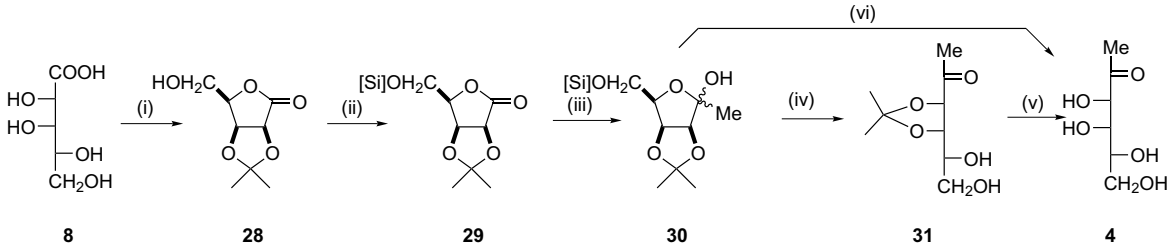
A number of protected derivatives of xylonolactone **19** with a silyl protecting group at C-2 are readily available. However, the reaction of any of the pertriethyl silyl ether **20**, the perTBDMS silyl ether **21**, and the 3,5-*O*-benzylidene silyl ethers **22** and **23** with methyl lithium all gave very low yields of the addition compounds with either methyl lithium or methyl magnesium bromide. Accordingly benzyl protecting groups were used in the synthesis of 1-deoxy-D-sorbose **3** (Scheme 4).

D-Xylose **24** can be converted to the tribenzyl furanose **25** in an overall yield of 60% by literature procedures.[26] Oxidation of **25** by dimethyl sulfoxide and acetic anhydride afforded lactone **26**[27] in 97% yield. The addition of methyl lithium to lactone **26** gave the protected furanose **27**[28] (81% yield) from which the benzyl protecting groups were removed by palladium catalysed hydrogenolysis to give 1-deoxy-D-sorbose **3** (86%). The overall yield of deoxyketose **3** from D-xylose **24** is 41%.





Scheme 4. Reagents and conditions: (i) Ref. 26 (60%); (ii) Ac_2O, DMSO (97%); (iii) MeLi, THF (81%); (iv) $Pd(OH)_2$, H_2, dioxane (86%).



Scheme 5. Reagents and conditions: (i) Ref. 31 (60%); (ii) *tert*-$BuMe_2SiCl$, imidazole, DMF (90%); (iii) MeLi, THF, −78 °C (97%); (iv) TBAF, THF (96%); (v) Dowex® 50WX8-100 ion-exchange resin, water, 45 °C (98%); (vi) Dowex® 50WX8-100 ion-exchange resin, water, 45 °C (97%).

2.1.4. 1-Deoxy-D-tagatose 4. The literature procedures for the synthesis of 1-deoxy-D-tagatose **4** use either starting materials that are not readily available or involve several synthetic steps.[20b,29] 1-Deoxy-D-tagatose **4** can be prepared from D-lyxonic acid **8**, a high yield product of alkaline oxygenation of D-galactose[30] (Scheme 5).

The crude D-lyxonic acid **8** can be converted to isopropylidene lactone **28** in 60% yield.[31] 5-*O*-Silylation of the primary alcohol in **28** gave the fully protected lactone **29**, which with methyl lithium afforded the protected tagatopyranose **30** in 89% yield over 2 steps. Initially the silyl ether in **30** was removed by treatment with TBAF to ketal **31**; subsequent acid hydrolysis of **31** gave 1-deoxy-D-tagatose **4** in 94% over two steps. However, treatment of **30** with Dowex® 50WX8-100 ion-exchange resin removed both the silyl and isopropylidene protecting groups, directly producing 1-deoxy-D-tagatose **4** in 98% yield. The overall yield of 1-deoxy-D-tagatose **4** from the protected lyxonolactone **28** is 87%.

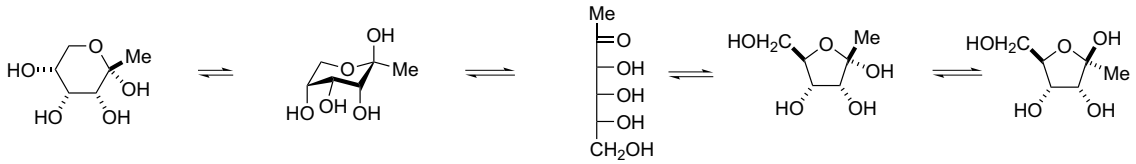
2,3-*O*-Isopropylidene-L-lyxono-1,5-lactone, the enantiomer of **28**, may be prepared on a multi-kilogram scale from D-ribonolactone **10**;[22,32] thus 1-deoxy-L-tagatose may also be prepared efficiently by this procedure.

2.2. NMR Studies on aqueous solutions of 1-deoxy-D-ketohexoses

NMR analyses were carried out on **1**, **2**, **3** and **4** in D_2O solution, pD = 5.0, at a temperature of 30 °C. All four compounds gave complex spectra with either four (**3**) or five (**1**, **2** and **4**) different forms present, corresponding to the α- and β-anomers of the furanose and pyranose forms, and the open chain keto-form. In most cases, the H3–H6/H6′ proton spin-systems could be identified in the COSY spectra and the equivalent carbon shifts determined directly from the HSQC spectrum. The C1 and C2 carbons were identified in the HMBC spectra, usually from cross-peaks between the C2 carbon and the H1 and H3 protons. The keto-form of each compound could be easily identified by the chemical shift of the C2 carbon. In all cases, the two pyranose forms could be identified by the C2 to H6/H6′ cross-peaks in the HMBC spectra. The furanose forms could then be identified by elimination, and some also gave C2 to H5 cross-peaks in the HMBC spectra. The anomericities of the pyranose and furanose forms were identified by the pattern of NOE peaks from the H1 protons in the NOESY spectra. For the pyranose forms, the ring conformations could be determined from the values of the $^3J_{HH}$ coupling constants, where available. The relative proportions of each form were determined from the peak integrals in the 1D ^{1}H NMR spectra. For compounds **1**, **2** and **3**, many ^{13}C assignments have been reported[18] although some of these were uncertain and for **3** only three forms were reported. Our assignments are in general agreement with the previous values and resolve almost all the uncertainties.

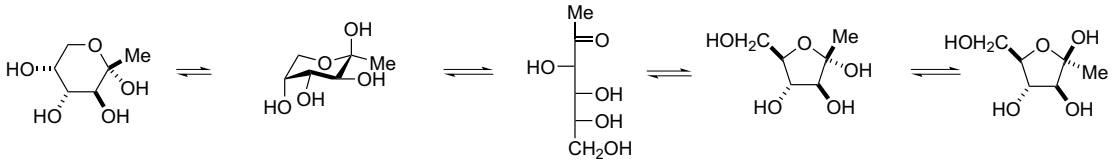
The ^{13}C and ^{1}H chemical shifts and $^{2/3}J_{HH}$ coupling constants, and the proportions of each form, for **1**, **2**, **3** and **4**, are given in Tables 1–3. The 1D ^{1}H NMR spectra are shown in Figure 3.

2.2.1. 1-Deoxy-D-psicose. The 1D ^{1}H NMR spectrum of **1** shows four forms at similar concentrations and one form at about one third the concentration of the rest, later identified as the keto-form. All five spin-systems could be identified in the COSY spectrum, except for the H6 protons of the keto-form. Complete ^{1}H and ^{13}C assignments of all five forms could be made, expect for the C6 of the β-furanose and keto-forms (the peaks are at 63.58 ppm and 63.63 ppm but could not been specifically assigned) and the H6/H6′ of the keto-form. The α-pyranose, β-pyranose and β-furanose forms could be identified by cross-peaks from the C2 resonance in the HMBC spectrum. The NOESY spectrum identified the α-pyranose and α-furanose forms through strong H1 to H3 and weak H1 to H4 NOEs, and so the β-pyranose and β-furanose could be identified



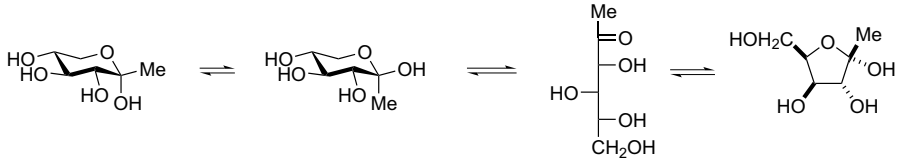
by elimination. For the β-pyranose form, the $^{3}J_{HH}$ coupling constants are only consistent with a $^{2}C_{5}$ ring conformation. A $^{5}C_{2}$ conformation would give a *trans*-di-axial H5–H6 proton pair leading to a very large coupling constant, which is not observed. The α-pyranose form shows different couplings between H3, H4 and H5, suggesting that the ring conformation is different to the β-pyranose form, but the H5 to H6/H6′ couplings could not be resolved and so the ring conformation could be determined unambiguously. It is interesting to note that the four pyranose and furanose forms all have similar concentrations and thus stabilities.

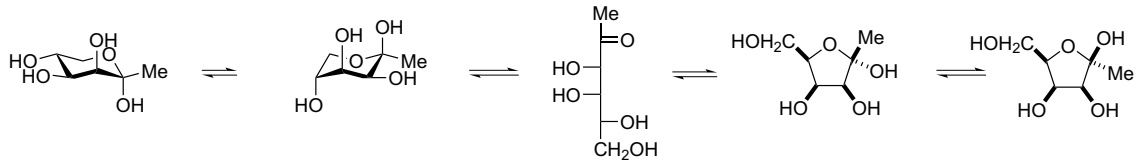
2.2.2. 1-Deoxy-D-fructose. The 1D ^{1}H NMR spectrum of **2** shows one major form, later identified as the β-pyranose, another at about one tenth the concentration, later identified as the β-pyranose, and two more at about one twentieth of the concentration, later identified as the α-furanose and keto-forms. If the β-furanose form is present, it is at less than one hundredth the concentration of the α-pyranose (the signal-to-noise limit of the spectra). The major form gives a ^{1}H NMR spectrum that is strongly coupled, with the exception of the H3 peak. The approximate ^{1}H chemical shifts of the other resonances could be measured from the HSQC spectrum, where the overlapping peaks are pulled apart in the ^{13}C dimension. The large H3 coupling indicates that H3 and H4 are *trans*-di-axial. This allows the ring conformation to be modelled and approximate J_{HH} values to be estimated. Accurate ^{1}H chemical shifts and J_{HH} coupling constants were obtained by simulating



and four more at about one tenth of the concentration. All five spin-systems could be identified in the COSY spectrum, except for the H3 proton of one form, later identified as the α-pyranose. Complete ^{1}H and ^{13}C assignments of all five forms could be made. The H3 of the α-pyranose could only be assigned by elimination of all other peaks in the HSQC spectrum. The α-pyranose, β-pyranose and β-furanose forms could be identified by cross-peaks from the C2 resonance in the HMBC spectrum. The NOESY spectrum identified the β-pyranose and β-furanose forms through strong H1 to H3 NOEs, and so the α-pyranose and α-furanose could be identified by elimination. For the β-pyranose form, the $^{3}J_{HH}$ coupling constants are only consistent with a $^{2}C_{5}$ ring conformation. A $^{5}C_{2}$ conformation would give a *trans*-di-axial H5–H6 proton pair leading to a very large coupling constant, which is not observed. The couplings of the α-pyranose could not be resolved and so the ring conformation could not be determined unambiguously.

2.2.3. 1-Deoxy-D-sorbose. The 1D ^{1}H NMR spectrum of **3** shows one major form, later identified as the α-pyranose, the 1D ^{1}H NMR spectrum and optimising the parameters to match the observed spectrum (Fig. 4). The three minor spin-systems could be identified completely in the COSY spectrum and complete ^{1}H and ^{13}C assignments made. The C5 resonance of the β-pyranose is coincident with the C5 of the dominant α-pyranose and this assignment was confirmed by an HSQC–TOCSY. The α-pyranose and β-pyranose forms could be identified by cross-peaks from the C2 resonance in the HMBC spectrum. The NOESY spectrum identified the α-pyranose and α-furanose forms through strong H1 to H3 NOEs, and the β-pyranose by a strong H1 to H6′ NOE. For both the α- and β-pyranose forms, the large $^{3}J_{HH}$ coupling constants are only consistent with the $^{5}C_{2}$ ring conformation, which gives H3, H4 and H5 as all axial. For the β-pyranose, this results in the C1 methyl group being axial, consistent with the observed H1 to H6′ NOE. The $^{5}C_{2}$ conformation places the C3OH, C4OH and C5OH groups equatorial, and for the β-anomer putting the methyl group equatorial does not compensate for placing these three groups axial. However, the axial methyl group does explain the α:β anomer ratio of 10:1.





2.2.4. 1-Deoxy-D-tagatose. The 1D ^{1}H NMR spectrum of **4** shows one major form, later identified as the α-pyranose, another at about one quarter the concentration, later identified as the β-pyranose, and three more at about one fortieth of the concentration. All five spin-systems could be identified in the COSY spectrum, except for the H5 and H6/H6′ of the keto-form. Complete ^{1}H and ^{13}C assignments of all five forms could be made, expect for the H5 and H6/H6′ of the keto-form. The C5 and C6 of the keto-form could only be assigned by elimination of all other peaks in the 1D ^{13}C spectrum. The α-pyranose and β-pyranose forms could be identified by cross-peaks from the C2 resonance in the HMBC spectrum. The NOESY spectrum identified the α-pyranose form through the weak H1 to H5 NOE, and the β-pyranose form through the weak H1 to H4 NOE. One of the furanose forms shows a stronger H1 to H3 NOE than the other, suggesting that it is the β-anomer. The conformation of this was obtained by comparing the ^{13}C chemical shifts of the two pyranose forms versus the reported shifts of the two pyranose forms of D-tagatose.[33] With the exception of the C3 resonance of the β-furanose (75.55 ppm in **4** vs 71.7 ppm reported for D-tagatose), the match between the 1-deoxy-D-tagatose and D-tagatose pyranose ^{13}C chemical shifts is very accurate. For the α-pyranose form, the $^{3}J_{HH}$ coupling constants are only consistent with a $^{5}C_{2}$ ring conformation. This gives a *trans*-di-axial H5–H6′ proton pair leading to a very large coupling constant, which is observed. The β-pyranose form shows very different couplings between H4, H5, H6 and H6′, only consistent with an equatorial H5 and thus a $^{2}C_{5}$ ring conformation. Both these conformations place the C1 methyl groups equatorial. This gives C3OH as axial and C4OH and C5OH as equatorial for the α-anomer, whereas for the β-anomer C4OH and C5OH are axial and C3OH is equatorial. This explains the α:β anomer ratio of 4:1.

3. Conclusion

Efficient syntheses of the four diastereomeric 1-deoxy-D-ketohexoses have allowed the investigation of the

Table 1. ^{13}C chemical shifts of 1-deoxy-hexuloses (referenced to acetone at 30.90 ppm)

	Percentage	^{13}C chemical shift (ppm)					
		C1	C2	C3	C4	C5	C6
1-Deoxy-psicose **1**							
α-Furanose	21	24.35	103.60	74.89	71.13	83.84	62.09
β-Furanose	20	21.88	106.63	76.72	71.92	83.08	63.6[a]
α-Pyranose	25	24.35	98.67	70.55	72.10	66.74	58.89
β-Pyranose	27	24.86	99.15	73.87	65.81	69.16	64.70
Keto	~7	27.04	213.00	79.63	72.90	70.69	63.6[a]
1-Deoxy-fructose **2**							
α-Furanose	~7	22.39	105.82	82.99	77.09	81.91	61.80
β-Furanose	14	24.45	102.17	80.78	75.29	81.06	63.27
α-Pyranose	~3	18.92	99.94	73.52[b]	71.57	67.63	64.10
β-Pyranose	69	25.23	98.79	72.66	70.15	69.86	63.89
Keto	~7	26.30	214.17	77.52	71.44	71.28	63.48
1-Deoxy-sorbose **3**							
α-Furanose	~2.5	24.42	101.80	80.09	75.99	77.84	61.25
β-Furanose	<0.8	—	—	—	—	—	—
α-Pyranose	86	25.12	98.37	75.67	74.34	70.29	62.30
β-Pyranose	~8	17.89	100.17	76.45	74.68	70.29[c]	64.48
Keto	~3.5	26.44	213.35	78.27	71.94	72.95	62.90
1-Deoxy-tagatose **4**							
α-Furanose	~2	22.49	105.92	77.64	71.94	79.23	60.70
β-Furanose	~2	18.69	103.16	75.55	71.83	80.01	61.62
α-Pyranose	75	24.74	98.90	73.56	71.47	66.70	62.83
β-Pyranose	19	24.35	99.31	68.86	71.56	69.75	61.04
Keto	~2	27.71	215.24	77.24	71.72	71.21[d]	63.17[d]

Percentages were estimated from peak area in the ^{1}H 1D spectrum.

[a] The β-furanose-C6 is either 63.58 ppm or 63.63 ppm. The other can be assigned to keto-C6 by elimination in the 1D ^{13}C spectrum.

[b] Assigned by elimination in the 2D HSQC spectrum.

[c] Could only be assigned in the 2D HSQC-TOCSY spectrum.

[d] Assigned by elimination in the 1D ^{13}C spectrum.

Table 2. ^{1}H chemical shifts of 1-deoxy-hexuloses (referenced to acetone at 2.220 ppm)

	Percentage	^{1}H chemical shift (ppm)					
		H1	H3	H4	H5	H6	H6′
1-Deoxy-psicose **1**							
α-Furanose	21	1.453	3.856	4.091	4.066	3.714	3.640
β-Furanose	20	1.473	3.865	4.349	3.950	3.782	3.644
α-Pyranose	25	1.376	3.488	4.131	3.824	3.788	3.600
β-Pyranose	27	1.476	3.627	4.008	3.899	4.025	3.751
Keto	~7	2.268	4.398	4.085	3.774	nd	nd
1-Deoxy-fructose **2**							
α-Furanose	~7	1.408	3.963	3.914	4.000	3.744	3.666
β-Furanose	14	1.467	3.858	4.055	3.825	3.750	3.652
α-Pyranose	~3	1.357	3.67[a]	3.799	3.950	3.826	3.699
β-Pyranose	69	1.459	3.580	3.804	3.973	3.994	3.625
Keto	~7	2.279	4.590	4.036	3.766	3.849	3.677
1-Deoxy-sorbose **3**							
α-Furanose	~2.5	1.486	3.869	4.363	4.226	3.755	3.674
β-Furanose	<0.8	—	—	—	—	—	—
α-Pyranose	86	1.438	3.256	3.584[b]	3.586[b]	3.663[b]	3.632
β-Pyranose	~8	1.388	3.315	3.491	3.634	3.872	3.376
Keto	~3.5	2.288	4.424	4.088	3.838	3.752	3.65[c]
1-Deoxy-tagatose **4**							
α-Furanose	~2	1.453	3.984	4.541	4.244	3.771	3.700
β-Furanose	~2	1.442	3.974	4.3608	4.122	3.858	3.748
α-Pyranose	75	1.429	3.721	3.856	3.794	3.697	3.593
β-Pyranose	19	1.412	3.729	3.958	3.899	4.120	3.520
Keto	~2	2.307	4.293	3.807	nd	nd	nd

Percentages were estimated from peak area in the ^{1}H 1D spectrum.
[a] Assigned by elimination in the 2D HSQC spectrum.
[b] H4, H5, H6 and H6′ are strongly coupled, assignments are based on simulation of the 1D spectrum.
[c] Could only be assigned from a partially overlapping peak in the 2D spectra.

possibility of Izumoring technology to be extended to 1- and 6-deoxyhexoses; biological evaluation of the deoxy-monosaccharides is currently in progress. The structure of the free sugars, though a complex mixture of four or five species, has been elucidated and may help to understand features about the structures of other novel monosaccharides in aqueous solution and thus their biological activity.

4. Experimental

4.1. General experimental

All commercial reagents were used as supplied. Tetrahydrofuran and *N*,*N*-dimethylformamide were purchased dry from Aldrich chemical company in sure-seal bottles. Methanol and pyridine were purchased dry from the Fluka chemical company in sure-seal bottles over molecular sieves. All other solvents were used as supplied (Analytical or HPLC grade), without prior purification. The reactions were performed under an atmosphere of either nitrogen or argon, unless stated otherwise. Thin layer chromatography (TLC) was performed on aluminium sheets coated with 60 F_{254} silica. Sheets were visualised using a spray of 0.2% w/v cerium(IV) sulfate and 5% ammonium molybdate in 2 M sulfuric acid. Flash chromatography was performed on Sorbsil C60 40/60 silica. Melting points were recorded on a Kofler hot block and are uncorrected. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are quoted in g 100 mL^{-1}. Elemental analyses were performed by the microanalysis service of the Inorganic Chemistry Laboratory, Oxford. Infrared spectra were recorded on a Perkin–Elmer 1750 IR Fourier Transform spectrophotometer using thin films on NaCl plates (thin film). Only the characteristic peaks are quoted. Low resolution mass spectra (*m*/*z*) were recorded on VG MassLab 20–250, Micromass BIOQ-II, Micromass Platform 1, Micromass TofSpec 2E, or Micromass Autospec 500 OAT spectrometers and high resolution mass spectra (HRMS *m*/*z*) on a Micromass Autospec 500 OAT spectrometer. The techniques used were electrospray (ESI), chemical ionisation (CI NH_3), or atmospheric pressure chemical ionisation (APCI). Nuclear magnetic resonance (NMR) spectra were recorded on Bruker AMX 500 (^{1}H: 500 MHz and ^{13}C: 125.7 MHz) and Bruker DPX 400 and DQX 400 spectrometers (^{1}H: 400 MHz and ^{13}C: 100.6 MHz) in the deuterated solvent stated. For spectra recorded in D_2O acetone was used as an internal reference. Residual signals from other solvents were used as an internal reference. NMR spectra for **1**, **2**, **3** and **4** were recorded on a Varian UnityINOVA 500 (^{1}H—500 MHz: ^{13}C—125 MHz) spectrometer, in D_2O, pD = 5.0 ± 0.1, with a probe temperature of 30 °C. Chemical shifts were measured relative to internal standards (^{1}H—acetone at 2.220 ppm: ^{13}C—acetone at 30.9 ppm). Two-dimensional gradient COSY, HSQC, HMBC and HSQC–TOCSY spectra were used to aid assignment of ^{1}H and ^{13}C spectra. NOESY spectra were

Table 3. Two and three-bond J_{HH} values of 1-deoxy-hexuloses

	Percentage	J_{HH} (Hz)				
		H3–H4	H4–H5	H5–H6	H5–H6′	H6–H6′
1-Deoxy-psicose **1**						
α-Furanose	21	5.7	4.2	3.4	4.6	12.4
β-Furanose	20	4.8	7.6	nd	6.3	12.2
α-Pyranose	25	2.9	2.7	nd	nd	nd
β-Pyranose	27	3.4	3.4	1.6	2.3	12.7
Keto	~7	3.1	nd	nd	nd	nd
1-Deoxy-fructose **2**						
α-Furanose	~7	6.6[a]	4.6[a]	nd	nd	nd
β-Furanose	14	8.1	7.3	nd	nd	nd
α-Pyranose	~3	nd	nd	nd	nd	nd
β-Pyranose	69	10.1	3.5	0.9	1.6	12.8
Keto	~7	1.5	9.2	nd	nd	nd
1-Deoxy-sorbose **3**						
α-Furanose	~2.5	6.5	6.6	3.8	6.2	12.3
β-Furanose	<0.8	—	—	—	—	—
α-Pyranose	86	9	9[b]	5[b]	10[b]	11[b]
β-Pyranose	~8	9.4	9.2	5.6	10.3	11.9
Keto	~3.5	2.3	6.3	3.9	6.2	12.0
1-Deoxy-tagatose **4**						
α-Furanose	~2	5.3	5.3	nd	nd	nd
β-Furanose	~2	4.5	4.5	nd	nd	nd
α-Pyranose	75	3.3	9.6	5.6	10.8	10.8
β-Pyranose	19	3.3	4.6	2.0	2.7	13.1
Keto	~2	7.1	nd	nd	nd	nd

Percentages were estimated from peak area in the ^{1}H 1D spectrum.
[a] H4 appears as a 6.6 Hz/4.6 Hz doublet of doublets, but H3 and H5 cannot be resolved in the 1D ^{1}H spectrum.
[b] H4, H5, H6 and H6′ are strongly coupled, J values are based on simulation of the 1D spectrum.

recorded with a 400 ms mixing time. 1D ^{1}H NMR spectral simulations were performed using the program gNMR (Cherwell Scientific Publishing). All chemical shifts (δ) are quoted in ppm and coupling constants (J) in Hz.

4.2. 1-Deoxy-D-psicose 1

4.2.1. 5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-D-ribono-1,4-lactone 11. *tert*-Butyldimethylsilyl chloride (8.1 g, 53.8 mmol) was added to a stirred solution of lactone **10**[21] (5.0 g, 26.9 mmol), imidazole (3.66 g, 53.8 mmol) and DMF (45 mL) and stirred at room temperature for 16 h. The reaction mixture was concentrated in vacuo, water (15 mL) was added and the compound was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 7:1→4:1) affording compound **11** as a white solid (7.9 g, 98%); mp 70–71 °C [lit.[34] mp 69–70 °C]; $[\alpha]_D^{23} = -49.0$ (c 1.16, $CHCl_3$) {lit.[34] $[\alpha]_D^{25} = -46.6$ (c 0.80, $CHCl_3$)}; ν_{max} (film): 1775 cm^{-1} (CO); δ_H (400 MHz, $CDCl_3$): 0.06 (3H, s, $SiCH_3$), 0.08 (3H, s, $SiCH_3$), 0.88 (9H, s, *t*-Bu), 1.40 (3H, s, CH_3), 1.48 (3H, s, CH_3), 3.81 (1H, d, $J_{5a,5b} = 11.3$ Hz, H-5a), 3.88 (1H, dd, $J_{4,5b} = 1.9$ Hz, $J_{5a,5b} = 11.3$ Hz, H-5b), 4.61–4.63 (1H, m, H-4), 4.70–4.74 (2H, m, H-2, H-3); δ_C (100 MHz, $CDCl_3$): −5.8 ($SiCH_3$), −5.6 ($SiCH_3$), 18.2 ($SiC(CH_3)_3$), 25.6 (CH_3), 25.8 (*t*-Bu), 26.8 (CH_3), 63.0 (C-5), 75.8 (C-2), 78.5 (C-3), 82.3 (C-4), 113.0 (CMe_2), 174.2 (C-1); HR CI-MS: found m/z 320.1891 $[M+NH_4]^+$, calcd for $C_{14}H_{30}O_5SiN$: 320.1893. Found: C, 55.68, H, 8.65; $C_{14}H_{26}O_5Si$ requires C, 55.60, H, 8.67.

4.2.2. 6-*O*-*tert*-Butyldimethylsilyl-1-deoxy-3,4-*O*-isopropylidene-D-psicofuranose 12. Methyl lithium (1.6 M) in Et_2O (5.0 mL, 7.94 mmol) was added dropwise to a stirred solution of fully protected lactone **11** (2.18 g, 7.22 mmol) and THF (20 mL) at −78 °C. The reaction was stirred at this temperature for 1.5 h; water (20 mL) was slowly added and the mixture was allowed to warm to room temperature. The product was extracted with EtOAc (3 × 30 mL), dried ($MgSO_4$) and concentrated in vacuo to afford lactol **12** as a colourless oil (2.25 g, 98%); A/B = 1:5 (from integration of ^{1}H NMR signals); $[\alpha]_D^{21} = -13.1$ (c 0.99, $CHCl_3$) {lit.[35] $[\alpha]_D^{23} = -10.0$ (c 1.5, $CHCl_3$)}; ν_{max} (film): 3406 cm^{-1} (OH); δ_H (400 MHz, $CDCl_3$): 0.14 (3H, s, $SiCH_3$), 0.15 (3H, s, $SiCH_3$), 0.94 (9H, s, *t*-Bu), 1.35 (3H, s, CH_3), 1.51 (3H, s, CH_3), 1.52 (3H, s, CH_3), 3.72 (1H, dd, $J_{5,6a} = 2.1$ Hz, $J_{6a,6b} = 11.1$ Hz, H-6a), 3.76 (1H, dd, $J_{5,6b} = 2.1$ Hz, $J_{6a,6b} = 11.1$ Hz, H-6b), 4.26–4.28 (1H, m, H-5), 4.45 (1H, d, $J_{3,4} = 5.9$ Hz, H-3), 4.80 (1H, dd, $J_{3,4} = 5.9$ Hz, $J_{4,5} = 1.0$ Hz, H-4); δ_C (100 MHz, $CDCl_3$): −5.8 ($SiCH_3$), −5.7 ($SiCH_3$), 18.2 ($SiC(CH_3)_3$), 21.2 (CH_3), 25.2 (CH_3), 25.8 (CH_3), 26.6 (*t*-Bu), 64.9 (C-6), 82.0 (C-4), 85.8 (C-5), 88.0 (C-3), 106.6 (C-1), 112.4 (CMe_2); HR CI-MS: found m/z 317.1790 $[M-H]^-$, calcd for $C_{15}H_{29}O_5Si$: 317.1784. Found: C, 56.60; H, 9.49; $C_{15}H_{30}O_5Si$ requires C, 56.57; H, 9.49.

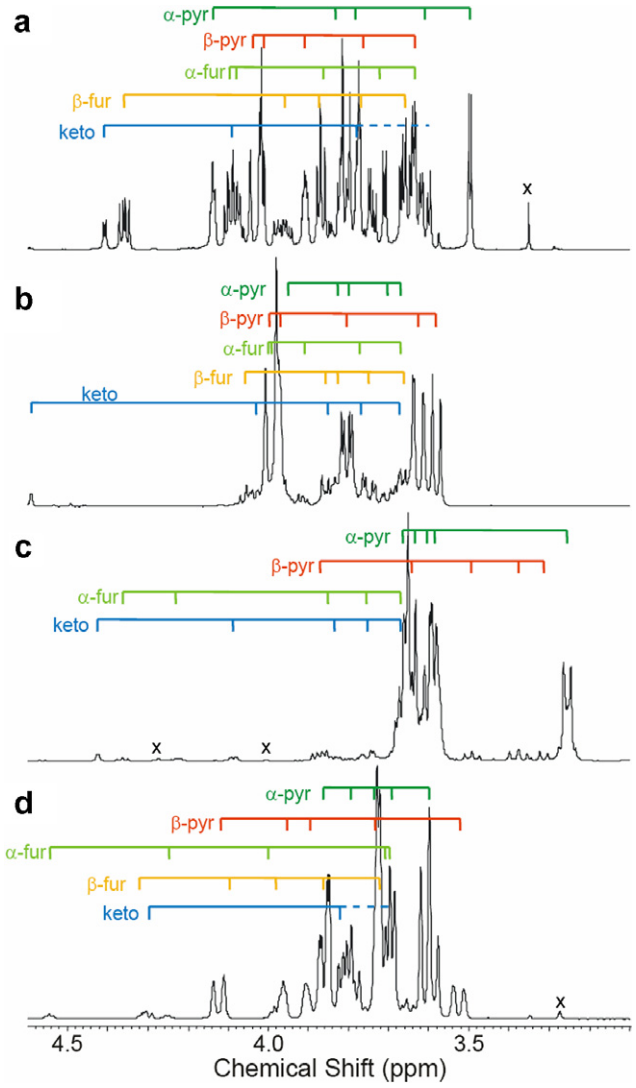


Figure 3. 1D ^{1}H NMR spectra of (a) **1**, (b) **2**, (c) **3** and (d) **4**, showing the spin-systems for the α-pyranose, β-pyranose, α-furanose, β-furanose and keto-forms.

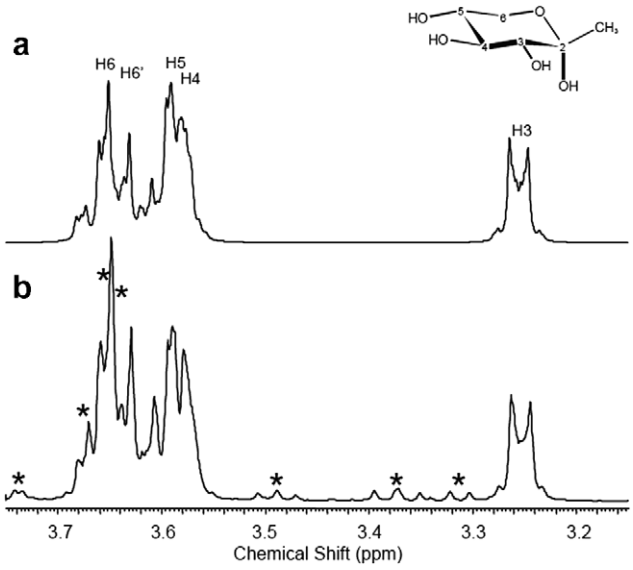


Figure 4. (a) Simulated 1D ^{1}H NMR spectrum of the α-pyranose form of 1-deoxy-D-sorbose, **3**, used to obtain the peak chemical shifts and J_{HH} values. (b) Experimental ^{1}H NMR spectrum of 1-deoxy-D-sorbose, **3**. The major component is the α-pyranose form. * marks peaks assigned to the minor component spin-systems.

4.2.3. 1-Deoxy-3,4-*O*-isopropylidene-D-psicose 13. A 1 M solution of TBAF in THF (9.0 mL, 9.0 mmol) was added to a stirred solution of compound **12** (2.2 g, 6.91 mmol) in THF (20 mL). The reaction was stirred at room temperature for 16 h and then concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 3:1→1:2) affording compound **13** as a white solid (1.1 g, 79%); A/B = 14:1 (from integration of ^{1}H NMR signals); mp 72–74 °C; $[\alpha]_D^{21} = -15.0$ (*c* 1.11, $CHCl_3$); ν_{max} (film): 3406 cm^{-1} (OH); δ_H (400 MHz, $CDCl_3$): 1.34 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.75 (2H, m, H-6a, H-6b), 4.29–4.31 (1H, m, H-5), 4.48 (1H, d, $J_{3,4} = 5.9$ Hz, H-3), 4.90 (1H, d, $J_{3,4} = 5.9$ Hz, H-4); δ_C (100 MHz, $CDCl_3$): 22.3 (CH_3), 24.9 (CH_3), 26.5 (CH_3), 63.7 (C-6), 82.1 (C-4), 86.2 (C-5), 87.0 (C-3), 106.8 (C-1), 112.4 (*C*Me$_2$); HR CI-MS: found *m/z* 203.0911 $[M-H]^-$, calcd for $C_9H_{15}O_5$: 203.0919. Found: C, 52.75; H, 7.89; $C_9H_{16}O_5$ requires C, 52.93; H, 7.90.

4.3. 1-Deoxy-D-psicose 1

A mixture of compound **13** (2.5 g, 12.3 mmol) and Dowex® 50WX8-100 ion-exchange resin (0.18 g) in water (25 mL) was stirred for 16 h at room temperature, filtered and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 1:1→MeOH/EtOAc 1:9) affording 1-deoxy-D-psicose **1** as a white solid (1.29 g, 65%); mp 99–100 °C [lit.[36] mp 97–98 °C]; $[\alpha]_D^{21} = +1.0$ (*c* 0.99, H_2O) {lit.[20a] $[\alpha]_D^{30} = +1.5$ (*c* 5, H_2O), lit.[36] $[\alpha]_D^{20} = -0.1$ (*c* 0.88, H_2O)}. The NMR of compound **1** is discussed above; HR ESI-MS: found *m/z* 163.0600 $[M-H]^-$, calcd for $C_6H_{11}O_5$: 163.0601.

4.4. 1-Deoxy-D-fructose 2

4.4.1. 2-*O*-*tert*-Butyldimethylsilyl-3,4-*O*-isopropylidene-D-arabinono-1,5-lactone 16. *tert*-Butyldimethylsilyl chloride (8.3 g, 55 mmol) was added to a solution of lactone **15** (9.58 g, 50 mmol) and imidazole (7.70 g, 113 mmol) in dry DMF (90 mL) and the reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was purified by flash column chromatography (cyclohexane/EtOAc 5:1) to afford the fully protected lactone **16** as a white solid (13.8 g, 90%); mp 86–88 °C; ν_{max} (film): 1757 cm^{-1} (CO); $[\alpha]_D^{21} = -87.2$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$): 0.13 (3H, s, CH_3), 0.15 (3H, s, CH_3), 0.89 (9H, s, *t*-Bu), 1.35 (3H, s, CH_3), 1.44 (3H, s, CH_3), 4.30 (1H, d, $J_{2,3} = 2.9$ Hz, H-2), 4.35 (1H, dd, $J_{4,5a} = 1.8$ Hz, $J_{5a,5b} = 12.1$ Hz, H-5a), 4.42 (1H, dd, $J_{2,3} = 2.9$ Hz, $J_{3,4} = 7.5$ Hz, H-3), 4.49 (1H, a-dt, $J = 1.9$ Hz, $J_{3,4} = 7.5$ Hz, H-4), 4.73 (1H, dd, $J_{4,5b} = 2.0$ Hz, $J_{5a,5b} = 12.1$ Hz, H-5b); δ_C (100 MHz, $CDCl_3$): −5.4 ($SiCH_3$), −5.2 ($SiCH_3$), 18.0 ($SiC(CH_3)_3$), 24.1 (CH_3), 25.5 (*t*-Bu), 26.0 (CH_3), 67.4 (C-5), 70.3

(C-2), 71.3 (C-4), 76.4 (C-3), 110.4 (*C*Me$_2$), 168.6 (C-1); HR ESI-MS: found *m/z* 303.1623 [M+H]$^+$, calcd for $C_{14}H_{27}O_5Si$: 303.1622.

4.4.2. 3-*O*-*tert*-Butyldimethylsilyl-1-deoxy-4,5-*O*-isopropylidene-D-fructose 17. Methyl lithium (1.6 M) in Et_2O (14.5 mL, 23.0 mmol) was added dropwise to a stirred solution of the fully protected lactone **16** (6.39 g, 21 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 2 h; the reaction was then quenched by addition of water (20 mL) and then warmed to room temperature. The water phase was extracted with EtOAc (3 × 20 mL), the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford the protected lactol **17** as a white solid (6.62 g, 98%); mp 94–96 °C; ν_{max} (film): 3404 cm^{-1} (OH); $[\alpha]_D^{21} = -61.3$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$): 0.13 (3H, s, CH_3), 0.19 (3H, s, CH_3), 0.93 (9H, s, *t*-Bu), 1.36 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.53 (3H, s, CH_3), 3.62 (1H, d, $J_{3,4} = 5.8$ Hz, H-3), 3.88 (1H, d, $J_{5,6a} = 0.7$ Hz, $J_{6a,6b} = 13.3$ Hz, H6a), 4.11–4.13 (2H, m, H-4, H-6b), 4.19 (1H, ddd, $J_{5,6a} = 0.7$ Hz, $J_{5,6b} = 2.5$ Hz, $J_{6a,6b} = 6.1$ Hz, H-5); δ_C (100 MHz, $CDCl_3$): −5.2 ($SiCH_3$), −4.2 ($SiCH_3$), 18.0 (Si*C*(CH_3)$_3$), 25.7 (SiC(*C*H_3)$_3$), 25.8 (CH_3), 26.8 (CH_3) 267.6 (CH_3), 60.0 (C-6), 74.6 (C-5), 76.8 (C-3), 96.4 (C-2), 109.1 (*C*Me$_2$); HR ESI-MS: found *m/z* 341.1755 [M+Na]$^+$, calcd for $C_{15}H_{30}O_5SiNa$: 341.1760. Found: C, 56.50, H, 9.49; $C_{15}H_{30}O_5Si$ requires C, 56.57, H, 9.49.

4.5. 1-Deoxy-4,5-*O*-isopropylidene-D-fructose 18

A 1 M solution of TBAF in THF (33.0 mL, 33.0 mmol) was added to a stirred solution of silyl lactol **17** (8.85 g, 27 mmol) in dry THF (30 mL). After stirring overnight, the solvent was evaporated in vacuo and the residue was purified by flash column chromatography (cyclohexane/EtOAc 1:4) to give ketal **18** as an oil (3.91 g, 69%); ν_{max} (film): 3417 cm^{-1} (OH); $[\alpha]_D^{21} = -102.2$ (*c* 1.0, $CHCl_3$); $[\alpha]_D^{23} = -137.9$ (*c* 1.04, MeOH), $[\alpha]_D^{23} = +132$ for the L-enantiomer; δ_H (400 MHz, $CDCl_3$): 1.37 (3H, s, CH_3), 1.51 (3H, s, CH_3), 1.54 (3H, s, CH_3), 2.79 (1H, br s, OH), 2.97 (1H, br s, OH), 3.55 (1H, d, $J_{3,4} = 6.8$ Hz, H-3), 3.94 (1H, d, $J_{6a,6b} = 13.3$ Hz, H-6a), 4.13–4.18 (2H, m, H-4, H-6b), 4.22 (1H, ddd, $J_{4,5} = 5.7$ Hz, $J_{5,6a} = 0.6$ Hz, $J_{5,6b} = 2.6$ Hz, H-5). δ_C (100 MHz, $CDCl_3$): 26.3 (CH_3), 26.4 (CH_3), 28.2 (CH_3), 59.9 (C-6), 73.7 (C-5), 74.1 (C-3), 77.1 (C-4), 97.1 (C-2), 109.5 (*C*Me$_2$); HR ESI-MS: found *m/z* 227.0890 [M+Na]$^+$, calcd for $C_9H_{16}O_5Na$: 227.0895.

4.6. 1-Deoxy-D-fructose 2

Method A: Isopropylidene lactol **18** (0.51 g, 2.50 mmol) was dissolved in acetic acid/water (2:1, 9 mL), heated to 50 °C and stirred for 16 h. The reaction mixture was concentrated in vacuo and the residue was purified by flash column chromatography (EtOAc/MeOH 9:1) to afford 1-deoxy-D-fructose **2** as an oil (0.22g, 53%); R_f 0.23 (EtOAc/MeOH 9:1); $[\alpha]_D^{21} = -80.5$ (*c* 1.0, H_2O) {lit.[37] $[\alpha]_D^{23} = -82.0$ (*c* 4.4, H_2O), lit.[38] $[\alpha]_D^{23} = -81.0$ (*c* 1.5, H_2O)}. The NMR of compound **2** is discussed above; HR ESI-MS: found *m/z* 163.0601 [M−H]$^-$, calcd for $C_6H_{11}O_5$: 163.0607.

Method B: Silyl lactol **17** (2.19 g, 6.9 mmol) and Dowex® 50WX8-100 ion-exchange resin (1.0 g) were suspended in a solution of water/dioxane (2:1, 18 mL) and stirred for 40 h at room temperature. The reaction mixture was filtered and partitioned between water (15 mL) and EtOAc (15 mL). The water layer was washed with EtOAc (2 × 15 mL) and concentrated in vacuo to afford 1-deoxy-D-fructose as an oil (1.05 g, 93%), which was identical by ^{1}H NMR to the compound prepared in method A.

4.7. 1-Deoxy-D-sorbose 3

4.7.1. 2,3,5-Tri-*O*-benzyl-D-xylono-1,4-lactone 26. A mixture of acetic anhydride (8.3 mL) and dimethyl sulfoxide (5.6 mL) was added to lactol **25** (2.7 g, 6.43 mmol) and stirred at room temperature for 24 h. Water (50 mL) was added and the product extracted with CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 8:1→6:1) affording compound **26** as a colourless oil (2.62 g, 97%); $[\alpha]_D^{20} = +89.0$ (*c* 1.0, $CHCl_3$) {lit.[27] $[\alpha]_D = +95.6$ (*c* 1.13, $CHCl_3$)}; ν_{max} (film): 1789 cm^{-1} (CO); δ_H (400 MHz, $CDCl_3$): 3.72 (1H, dd, $J_{4,5a} = 3.2$ Hz, $J_{4a,5b} = 10.8$ Hz, H-5a), 3.78 (1H, dd, $J_{4,5b} = 2.8$ Hz, $J_{5a,5b} = 10.8$ Hz, H-5b), 4.38 (1H, t, $J_{2,3} = J_{3,4} = 7.2$ Hz, H-3), 4.52–4.62 (5H, m, H-2, H-4, 3 × OCH_2Ph), 4.67 (1H, d, $J_{gem} = 12.0$ Hz, OCH_2Ph), 4.71 (1H, d, $J_{gem} = 11.6$ Hz, OCH_2Ph), 5.07 (1H, d, $J_{gem} = 11.6$ Hz, OCH_2Ph); δ_C (100 MHz, $CDCl_3$): 67.1 (C-5), 72.6 (OCH_2Ph), 72.7 (OCH_2Ph), 73.6 (OCH_2Ph), 77.3 (×2), 79.4 (C-2, C-3, C-4), 127.5–128.5 (Ph), 137.1, 137.2, 137.6, (3 × quat. Ph), 173.3 (C-1); HR ESI-MS: found *m/z* 436.2113 [M+NH$_4$]$^+$, calcd for $C_{26}H_{26}O_5N$: 436.2118.

4.7.2. 3,4,6-Tri-*O*-benzyl-1-deoxy-D-sorbofuranose 27. Methyl lithium (1.6 M) in Et_2O (7.4 mL, 11.8 mmol) was added dropwise to a stirred solution of lactone **26** (4.1 g, 9.80 mmol) and THF (40 mL) at −78 °C. The reaction was stirred at this temperature for 1.5 h, water (35 mL) was slowly added and the mixture was allowed to warm to room temperature. The product was extracted with EtOAc (3 × 40 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 8:1→6:1) affording compound **27** as a colourless oil (3.46 g, 81%); A/B = 3:4 (from integration of ^{1}H NMR signals); $[\alpha]_D^{20} = -11.0$ (*c* 1.0, $CHCl_3$); ν_{max} (film): 3492 cm^{-1} (OH); δ_H (400 MHz, $CDCl_3$): 1.50 (3H, s, CH_3 B), 1.53 (3H, s, CH_3 A), 3.66 (1H, dd, $J_{5,6a} = 5.6$ Hz, $J_{6a,6b} = 9.6$ Hz, H-6a A), 3.71 (1H, dd, $J_{5,6a} = 4.4$ Hz, $J_{6a,6b} = 9.6$ Hz, H-6b A), 3.72–3.78 (3H, m, H-3 A, H-6a B, H-6b B), 3.91 (1H, d, $J_{3,4} = 2.4$ Hz, H-3 B), 4.03 (1H, dd, $J_{3,4} = 2.0$ Hz, $J_{4,5} = 4.4$ Hz, H-4 A), 4.07 (1H, dd, $J_{3,4} = 2.4$ Hz, $J_{4,5} = 4.8$ Hz, H-4 B), 4.34–4.41 (2H, m, H-5 A, H-5 B), 4.46–4.63 (12H, m, OCH_2Ph), 7.25–7.39 (30H, m, Ph); δ_C (100 MHz, $CDCl_3$): 21.5 (CH_3 B), 26.5 (CH_3 A), 68.2 (C-6 A), 68.8 (C-6 B), 73.2, 72.4, 72.7, 73.1, 73.4, 73.7 (6 × OCH_2Ph), 787.6

(C-5 A), 78.9 (C-5 B), 81.4 (C-4 B), 82.3 (C-4 A), 85.5 (C-3 A), 86.2 (C-3 B), 102.4 (C-2 A), 106.4 (C-2 B), 127.0–128.6 (Ph), 137.2–138.2 (6 × quat. Ph); HR ESI-MS: found *m/z* 457.1984 $[M+Na]^+$, calcd for $C_{27}H_{30}O_5Na$: 457.1985.

4.8. 1-Deoxy-D-sorbose 3

A solution of compound **27** (2.1 g, 4.84 mmol) in dioxane (20 mL) was hydrogenated over 20% $Pd(OH)_2$ on carbon (210 mg) for 16 h at room temperature. The mixture was filtered through Celite and concentrated in vacuo to afford 1-deoxy-D-sorbose **3** as a colourless solid (0.69 g, 86%); mp 152–154 °C [lit.[19] mp 149–151 °C (for the L-enantiomer)]; $[\alpha]_D^{20} = +49.0$ (*c* 1.0, H_2O) {lit.[19] $[\alpha]_D = -51$ (*c* 0.7, H_2O) (for the L-enantiomer)}. The NMR of compound **3** is discussed above; HR ESI-MS: found *m/z* 187.0577 $[M+Na]^+$, calcd for $C_6H_{12}O_5Na$: 187.0577.

4.9. 1-Deoxy-D-tagatose 4

4.9.1. 5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-D-lyxono-1,4-lactone 29. *tert*-Butyldimethylsilyl chloride (0.23 g, 1.91 mmol) was added to a stirred solution of lactone **28** (0.3 g, 1.60 mmol), imidazole (0.13 g, 1.91 mmol) and DMF (3 mL) and stirred at room temperature for 16 h. The reaction mixture was concentrated in vacuo, water (15 mL) was added and the compound was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 7:1→4:1) affording silyl ether **29** as a white solid (0.44 g, 92%); mp 88–90 °C [lit.[39] mp 90–91 °C]; $[\alpha]_D^{21} = +58.0$ (*c* 1.0, $CHCl_3$) {lit.[39] $[\alpha]_D^{23} = +54.9$ (*c* 1.03, $CHCl_3$)}; ν_{max} (film): 1775 cm^{-1} (CO); δ_H (400 MHz, $CDCl_3$): 0.09 (6H, s, 2 × $SiCH_3$), 0.89 (9H, s, *t*-Bu), 1.38 (3H, s, CH_3), 1.45 (3H, s, CH_3), 3.93 (1H, dd, $J_{4,5a} = 6.4$ Hz, $J_{5a,5b} = 10.8$ Hz, H-5a), 3.97 (1H, dd, $J_{4,5b} = 6.0$ Hz, $J_{5a,5b} = 10.8$ Hz, H-5b), 4.49–4.54 (1H, m, H-4), 4.79–4.81 (2H, m, H-2, H-3); δ_C (100 MHz, $CDCl_3$): −5.4 ($SiCH_3$), −5.4 ($SiCH_3$), 18.3 ($SiC(CH_3)_3$), 25.8 (*t*-Bu), 26.8 (CH_3), 26.9 (CH_3), 60.9 (C-5), 75.7, 76.0 (C-2, C-3), 79.4 (C-4), 114.0 (CMe_2), 173.8 (C-1); HR ESI-MS: found *m/z* 325.1440 $[M+Na]^+$, calcd for $C_{14}H_{26}O_5SiNa$: 325.1442.

4.9.2. 6-*O*-*tert*-Butyldimethylsilyl-1-deoxy-3,4-*O*-isopropylidene-D-tagatofuranose 30. Methyl lithium (1.6 M) in Et_2O (0.8 mL, 1.27 mmol) was added dropwise to a stirred solution of the protected lactone **29** (0.35 g, 1.16 mmol) in THF (4 mL) at −78 °C. The reaction was stirred at this temperature for 1.5 h, water was slowly added (10 mL) and the mixture was allowed to warm to room temperature. The product was extracted with EtOAc (3 × 10 mL), dried ($MgSO_4$) and concentrated in vacuo to afford the protected tagatopyranose **30** as a colourless oil (0.36 g, 97%); A/B = 1:5 (from integration of ^1H NMR signals); $[\alpha]_D^{20} = +5.0$ (*c* 1.0, $CHCl_3$); ν_{max} (film): 3403 cm^{-1} (OH); δ_H (400 MHz, $CDCl_3$): 0.07 (6H, s, 2 × CH_3 A), 0.08 (6H, s, 2 × CH_3 B), 0.89 (9H, s, *t*-Bu A), 0.90 (9H, s, *t*-Bu B), 1.31 (3H, s, CH_3 A), 1.35 (3H, s, CH_3 B), 1.38 (3H, s, CH_3 B), 1.44 (3H, s, CH_3 A), 1.51 (3H, s, CH_3 A), 1.52 (3H, s, CH_3 B), 3.65–3.69 (1H, m, H-5 A), 3.80 (1H, dd, $J_{5,6a} = 6.4$ Hz, $J_{6a,6b} = 10.4$ Hz, H-6a B). 3.77–3.81 (1H, m, H-6a A), 3.88–3.94 (1H, m, H-6b A), 3.92 (1H, dd, $J_{5,6b} = 5.2$ Hz, $J_{6a,6b} = 10.4$ Hz, H-6a B), 4.15–4.19 (1H, m, H-5 B), 4.25 (1H, d, $J_{3,4} = 6.0$ Hz, H-3 A), 4.42 (1H, d, $J_{3,4} = 6.0$ Hz, H-3 B), 4.72 (1H, dd, $J_{3,4} = 6.0$ Hz, $J_{4,5} = 3.6$ Hz, H-4 A), 4.77 (1H, dd, $J_{3,4} = 6.0$ Hz, $J_{4,5} = 4.0$ Hz, H-4 B); δ_C (100 MHz, $CDCl_3$): −5.5, −5.3, −5.2 (4 × CH_3), 18.4 ($SiC(CH_3)_3$A), 18.5 ($SiC(CH_3)_3$ B), 21.0 (CH_3 A), 22.0 (CH_3 A), 22.6 (CH_3 B), 24.7 (CH_3 A), 24.9 (CH_3 B), 25.9 (CH_3 B), 25.9 (*t*-Bu A, *t*-Bu B), 60.8, 61.4 (C-6 A, C-6 B), 76.8 (C-5 A), 79.7 (C-5 B), 80.6 (C-4 A, C-4 B), 82.2 (C-3 A), 85.4 (C-3 B), 102.2 (C-2 A), 105.1 (C-2 B), 112.4 (CMe_2 B), 112.7 (CMe_2A); HR ESI-MS: found *m/z* 341.1758 $[M+Na]^+$, calcd for $C_{15}H_{30}O_5SiNa$: 341.1755.

4.9.3. 1-Deoxy-3,4-*O*-isopropylidene-D-tagatose 31. A 1 M solution of TBAF in THF (4.95 mL, 4.95 mmol) was added to a stirred solution of silyl ether **30** (1.15 g, 3.81 mmol) in THF (10 mL). The reaction was stirred at room temperature for 1 h, and concentrated in vacuo. The resulting residue was purified by column chromatography (cyclohexane/EtOAc 2:1→0:1) affording deoxytagatose **31** as a white solid (0.75 g, 96%); A/B = 1:4.4 (from integration of ^1H NMR signals); mp 119–121 °C [lit.[20b] mp 123–125 °C]; $[\alpha]_D = +21$ (*c* 1.0, $CHCl_3$) {lit.[20b] $[\alpha]_D^{25} = +16$ (*c* 1.24, $CHCl_3$)}; ν_{max} (film): 3400 cm^{-1} (OH); δ_H (400 MHz, $CDCl_3$): 1.31 (3H, s, CH_3 B), 1.37 (3H, s, CH_3 A), 1.41 (3H, s, CH_3 A), 1.49 (3H, s, CH_3 B), 1.55 (6H, s, CH_3 A, CH_3 B), 3.76–3.79 (1H, m, H-5 A), 3.89–3.94 (4H, m, H-6a A, H-6b A, H-6a B, H-6b B), 4.20–4.24 (1H, m, H-5 B), 4.32 (1H, d, $J_{3,4} = 6.0$ Hz, H-3 A), 4.47 (1H, d, $J_{3,4} = 6.0$ Hz, H-3 B), 4.78 (1H, dd, $J_{3,4} = 6.0$ Hz, $J_{4,5} = 3.6$ Hz, H-4 A), 4.84 (1H, dd, $J_{3,4} = 6.0$ Hz, $J_{4,5} = 4.0$ Hz, H-4 B); δ_C (100 MHz, $CDCl_3$): 22.2, 22.4, 24.6, 25.8, 26.0 (6 × CH_3), 61.2 (C-6 A, C-6 B), 76.7 (C-5 A), 78.7 (C-5 B), 80.3 (C-4 A), 81.2 (C-4 B), 82.6 (C-3 A), 85.5 (C-3 B), 102.6 (C-2 A), 105.2 (C-2 B), 112.8 (CMe_2B), 113.3 (CMe_2A); HR ESI-MS: found *m/z* 203.0918 $[M-H]^-$, calcd for $C_9H_{15}O_5$: 203.0914.

4.10. 1-Deoxy-D-tagatose 4

Method A: A mixture of protected compound **31** (1.29 g, 4.05 mmol) and Dowex® 50WX8-100 ion-exchange resin (0.7 g) in dioxane/water (1:1, 12 mL) was stirred for 8 h at 45 °C. The mixture was allowed to cool to room temperature, filtered and partitioned between water (40 mL) and EtOAc (40 mL). The water layer was washed with EtOAc (2 × 40 mL) and concentrated in vacuo to afford 1-deoxy-D-tagatose **4** as a white solid (0.65 g, 98%). 1-Deoxy-D-tagatose **4** was recrystallised from a mixture of EtOAc and MeOH to give colourless crystals as two polymorphs;[17] mp 136–138 °C and 143–145 °C [lit.[29a] mp 121–123 °C, lit.[29b] mp 130 °C]; $[\alpha]_D^{22} = -13$ (*c* 2.0, H_2O) {lit.[29a] $[\alpha]_D^{23} = -14$ (*c* 2.0, H_2O)}. The NMR of compound **4** is discussed above. HR ESI-MS: found *m/z* 163.0607 $[M-H]^-$, calcd for $C_6H_{11}O_5$: 163.0607.

Method B: A mixture of acetonide silyl ether **30** (0.44 g, 2.15 mmol) and Dowex® 50WX8-100 ion-exchange resin (0.7 g) in water (5 mL) was stirred for 2.5 h at 45 °C, fil-

tered and concentrated to dryness to yield 1-deoxy-D-tagatose **4** as a white solid (0.34 g, 97%), which was identical by ^{1}H NMR to the compound prepared in method A.

Acknowledgements

Financial support [to R.S.] provided through the European Community's Human Potential Programme under Contract HPRN-CT-2002-00173 and Novartis Pharma AG, Basel, Switzerland, and Idenix Montpellier, France, is gratefully acknowledged.

References

1. Skytte, U. P. *Cereal Foods World* **2002**, *47*, 224.
2. (a) Izumori, K. *J. Biotech.* **2006**, *124*, 717–722; (b) Granstrom, T. B.; Takata, G.; Tokuda, M.; Izumori, K. *J. Biosci. Bioeng.* **2004**, *97*, 89–94; (c) Izumori, K. *Naturwissenschaften* **2002**, *89*, 120–124; (d) Morimoto, K.; Park, C. S.; Ozaki, M.; Takeshita, K.; Shimonishi, T.; Granstrom, T. B.; Takata, G.; Tokuda, M.; Izumori, K. *Enzyme Microb. Technol.* **2006**, *38*, 855–859.
3. Beadle, J. R.; Saunders, J. P.; Wajda, T. J. US Patent 5078796, 1992.
4. (a) Ahmed, M. M.; O'Doherty, G. A. *J. Org. Chem.* **2005**, *70*, 10576–10578; (b) Ahmed, M. M.; O'Doherty, G. A. *Carbohydr. Res.* **2006**, *341*, 1505–1521; (c) Davies, S. G.; Nicholson, R. L.; Smith, A. D. *Synlett* **2002**, 1637–1640; (d) Davies, S. G.; Nicholson, R. L.; Smith, A. D. *Org. Biomol. Chem.* **2005**, *3*, 348–359; (e) Enders, D.; Chow, S. *Eur. J. Org. Chem.* **2006**, 4578–4584; (f) Enders, D.; Grondal, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 1210–1212; (g) Enders, D.; Grondal, C.; Vrettou, M. *Synthesis-Stuttgart* **2006**, 3597–3604; (h) Grondal, C.; Enders, D. *Tetrahedron* **2006**, *62*, 329–337; (i) Harris, J. M.; Keranen, M. D.; Nguyen, H.; Young, V. G.; O'Doherty, G. A. *Carbohydr. Res.* **2000**, *328*, 17–36; (j) Jiang, L. J.; Zhang, Z. G. *Chin. J. Org. Chem.* **2006**, *26*, 618–626; (k) Majewski, M.; Nowak, P. *J. Org. Chem.* **2000**, *65*, 5152–5160; (l) Northrup, A. B.; MacMillan, D. W. C. *Science* **2004**, *305*, 1752–1755; (m) Northrup, A. B.; Mangion, I. K.; Hettche, F.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 2152–2154; (n) Takeuchi, M.; Taniguchi, T.; Ogasawara, K. *Chirality* **2000**, *12*, 338–341; (o) Timmer, M. S. M.; Adibekian, A.; Seeberger, P. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 7605–7607; (p) Zhao, G. L.; Liao, W. W.; Cordova, A. *Tetrahedron Lett.* **2006**, *47*, 4929–4932.
5. (a) Levin, G. V. *J. Med. Food* **2002**, *5*, 23–36; (b) Howling, D.; Callagan, J. L. PCT Int. App. WO 2000042865, 2000; (c) Bertelsen, H.; Jensen, B. B.; Buemann, B. *World Rev. Nutr. Diet.* **1999**, *85*, 98–109.
6. Yoshihara, K.; Shinohara, Y.; Hirotsu, T.; Izumori, K. *J. Biosci. Bioeng.* **2006**, *101*, 219–222.
7. (a) Sun, Y. X.; Hayakawa, S.; Ogawa, M.; Izumori, K. *Food Control* **2007**, *18*, 220–227; (b) Matsuo, T.; Izumori, K. *Biosci., Biotechnol., Biochem.* **2006**, *70*, 2081–2085; (c) Matsuo, T.; Shirai, Y.; Izumori, K. *FASEB J.* **2006**, *20*, A594; (d) Matsuo, T.; Tanaka, T.; Hashiguchi, M.; Izumori, K.; Suzuki, H. *Asia Pac. J. Clin. Nutr.* **2003**, *12*, 225–231; (e) Matsuo, T.; Tanaka, T.; Hashiguchi, M.; Izumori, K.; Suzuki, H. *J. Nutr. Sci. Vitaminol.* **2002**, *48*, 512–516; (f) Matsuo, T.; Baba, Y.; Hashiguchi, M.; Takeshita, K.; Izumori, K.; Suzuki, H. *J. Clin. Biochem. Nutr.* **2001**, *30*, 55–65.
8. Nakajima, Y.; Gotanda, T.; Uchimiya, H.; Furukawa, T.; Haraguchi, M.; Ikeda, R.; Sumizawa, T.; Yoshida, H.; Akiyama, S. *Cancer Res.* **2004**, *64*, 1794–1801.
9. Simonsson, E.; Karlsson, S.; Ahren, B. *Diabetes* **1998**, *47*, 1436–1443.
10. (a) Feng, L.; Senchenkova, S. N.; Yang, J. H.; Shashkov, A. S.; Tao, J.; Guo, H. J.; Zhao, G.; Knirel, Y. A.; Reeves, P.; Wang, L. *J. Bacteriol.* **2004**, *186*, 383–392; (b) Hajko, J.; Liptak, A.; Pozsgay, V. *Carbohydr. Res.* **1999**, *321*, 116–120.
11. (a) Kimura, S.; Zhang, G. X.; Nishiyama, A.; Nagai, Y.; Nakagawa, T.; Miyanaka, H.; Fujisawa, Y.; Miyatake, A.; Nagai, T.; Tokuda, M.; Abe, Y. *J. Hypertens.* **2005**, *23*, 1887–1894; (b) Sui, L.; Dong, Y. Y.; Watanabe, Y.; Yamaguchi, F.; Hatano, N.; Izumori, K.; Tokuda, M. *Anticancer Res.* **2005**, *25*, 2639–2644; (c) Hossain, M. A.; Izuishi, K.; Tokuda, M.; Izumori, K.; Maeta, H. *J. Hepatobil. Pancreatic. Surg.* **2004**, *11*, 181–189.
12. (a) Hossain, M. A.; Wakabayashi, H.; Izuishi, K.; Okano, K.; Yachida, S.; Tokuda, M.; Izumori, K.; Maeta, H. *J. Biosci. Bioeng.* **2006**, *101*, 369–371; (b) Sui, L.; Dong, Y. Y.; Watanabe, Y.; Yamaguchi, F.; Hatano, N.; Tsukamoto, I.; Izumori, K.; Tokuda, M. *Int. J. Oncol.* **2005**, *27*, 907–912.
13. (a) Zehner, L.; Levin, G. V.; Saunders, J. P.; Beadle, J. R. US Patent 5356879, 1994; (b) Donner, T. W.; Wilber, J. F.; Ostrowski, D. *Diabetes Obes. Metab.* **1999**, *1*, 285–291.
14. (a) Menavuvu, B. T.; Poonperm, W.; Leang, K.; Noguchi, N.; Okada, H.; Morimoto, K.; Granstrom, T. B.; Takada, G.; Izumori, K. *J. Biosci. Bioeng.* **2006**, *101*, 340–345; (b) Takata, M. K.; Yamaguchi, F.; Nakanose, Y.; Watanabe, Y.; Hatano, N.; Tsukamoto, I.; Nagata, M.; Izumori, K.; Tokuda, M. *J. Biosci. Bioeng.* **2005**, *100*, 511–516.
15. (a) Izumori, K. In *Proc. 3rd Symp. Internat. Soc. Rare Sugars*, 2006; p 34; (b) Gullapalli, P. K.; Granstrom, T. B.; Morimoto, K.; Takata, G.; Fleet, G. W. J.; Izuishi, K. In *Proc. 3rd Symp. Internat. Soc. Rare Sugars*, 2006; p 56; (c) Shiji, T.; Morimoto, K.; Granstrom, T. B.; Takata, G.; Fleet, G. W. J.; Izumori, K. In *Proc. 3rd Symp. Internat. Soc. Rare Sugars*, 2006; p 64.
16. Jones, N. A.; Fanefjord, M.; Jenkinson, S. F.; Fleet, G. W. J.; Watkin, D. J. *Acta Crystallogr., Sect. E* **2006**, *62*, o4663–o4665.
17. Jones, N. A.; Jenkinson, S. F.; Soengas, R.; Izumori, K.; Fleet, G. W. J.; Watkin, D. J. *Acta Crystallogr., Sect. C* **2007**, *63*, o7–o10.
18. Angyal, S. J.; Bethell, G. S.; Cowley, D. E.; Pickles, V. A. *Aust. J. Chem.* **1976**, *29*, 1239–1247.
19. James, K.; Angyal, S. J. *Aust. J. Chem.* **1972**, *25*, 1967–1977.
20. (a) Wolfrom, M. L.; Thompson, A.; Evans, E. F. *J. Am. Chem. Soc.* **1945**, *67*, 1793–1797; (b) Cubero, I. I.; Poza, D. G. *Carbohydr. Res.* **1985**, *138*, 139–142.
21. Williams, J. D.; Kamath, V. P.; Morris, P. E.; Townsend, L. B. *Org. Syn.* **2005**, *82*, 75–80.
22. Kold, H.; Lundt, I.; Pedersen, C. *Acta Chem. Scand.* **1994**, *48*, 675–678.
23. (a) Thiem, J.; Rasch, D.; Paulsen, H. *Chem. Ber.* **1976**, *109*, 3588–3597; (b) Aparicio, F. J. L.; Cubero, I. I.; Guillen, M. G. *An. Quim. Ser. C* **1983**, *79*, 307–309.
24. (a) Ohle, H.; Berend, G. *Ber.* **1927**, *60*, 810–814; (b) Thompson, D. K.; Hubert, C. N.; Wightman, R. H. *Tetrahedron* **1993**, *49*, 3827–3840.
25. Stewart, A. J.; Evans, R. M.; Weymouth-Wilson, A. C.; Cowley, A. R.; Watkin, D. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2002**, *13*, 2667–2672.
26. (a) Barker, R.; Fletcher, H. G. *J. Org. Chem.* **1961**, *26*, 4605–4609; (b) Postema, M. H. D.; Calimente, D.; Liu, L.; Behrmann, T. L. *J. Org. Chem.* **2000**, *65*, 6061–6068.
27. Calzada, E.; Clarke, C. A.; Roussin-Bouchard, C.; Wightman, R. H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 517–518.

28. Shiozaki, M. *Carbohydr. Res.* **2002**, *337*, 2077–2088.
29. (a) Wolfrom, M. L.; Bennett, R. B. *J. Org. Chem.* **1965**, *30*, 1284–1287; (b) Dills, W. L.; Covey, T. R. *Carbohydr. Res.* **1981**, *89*, 338–341.
30. Humphlett, W. J. *Carbohydr. Res.* **1967**, *4*, 157–164.
31. Fleet, G. W. J.; Petursson, S.; Campbell, A. L.; Mueller, R. A.; Behling, J. R.; Babiak, K. A.; Ng, J. S.; Scaros, M. G. *J. Chem. Soc., Perkin Trans. 1* **1989**, 665–666.
32. (a) Batra, H.; Moriarty, R. M.; Penmasta, R.; Sharma, V.; Stanciuc, G.; Staszewski, J. P.; Tuladhar, S. M.; Walsh, D. A. *Org. Process Res. Dev.* **2006**, *10*, 484–486; (b) Batra, H.; Moriarty, R. M.; Penmasta, R.; Sharma, V.; Stancuic, G.; Staszewski, J. P.; Tuladhar, S. M.; Walsh, D. A. *Org. Process Res. Dev.* **2006**, *10*, 887–892.
33. Angyal, S. J.; Bethell, G. S. *Aust. J. Chem.* **1976**, *29*, 1249–1265.
34. Kaskar, B. *Synthesis* **1990**, 1031–1032.
35. Wilcox, C. S.; Cowart, M. D. *Carbohydr. Res.* **1987**, *171*, 141–160.
36. Šmejkal, J.; Farkaš, J. *Coll. Czech. Chem. Commun.* **1963**, *28*, 1345–1347.
37. Haylock, C. R.; Melton, L. D.; Slessor, K. N.; Tracey, A. S. *Carbohydr. Res.* **1971**, *16*, 375–382.
38. Dills, W. L.; Meyer, W. L. *Biochemistry* **1976**, *15*, 4506–4512.
39. Clinch, K.; Evans, G. B.; Fleet, G. W. J.; Furneaux, R. H.; Johnson, S. W.; Lenz, D. H.; Mee, S. P. H.; Rands, P. R.; Schramm, V. L.; Tayler Ringia, E. A.; Tyler, P. C. *Org. Biomol. Chem.* **2006**, *4*, 1131–1139.