Synthesis of 6-Deoxy-6-phenylphosphonoyl-D-fructopyranoses: The First Phosphorus-in-the-Ring Analogues of a Ketose

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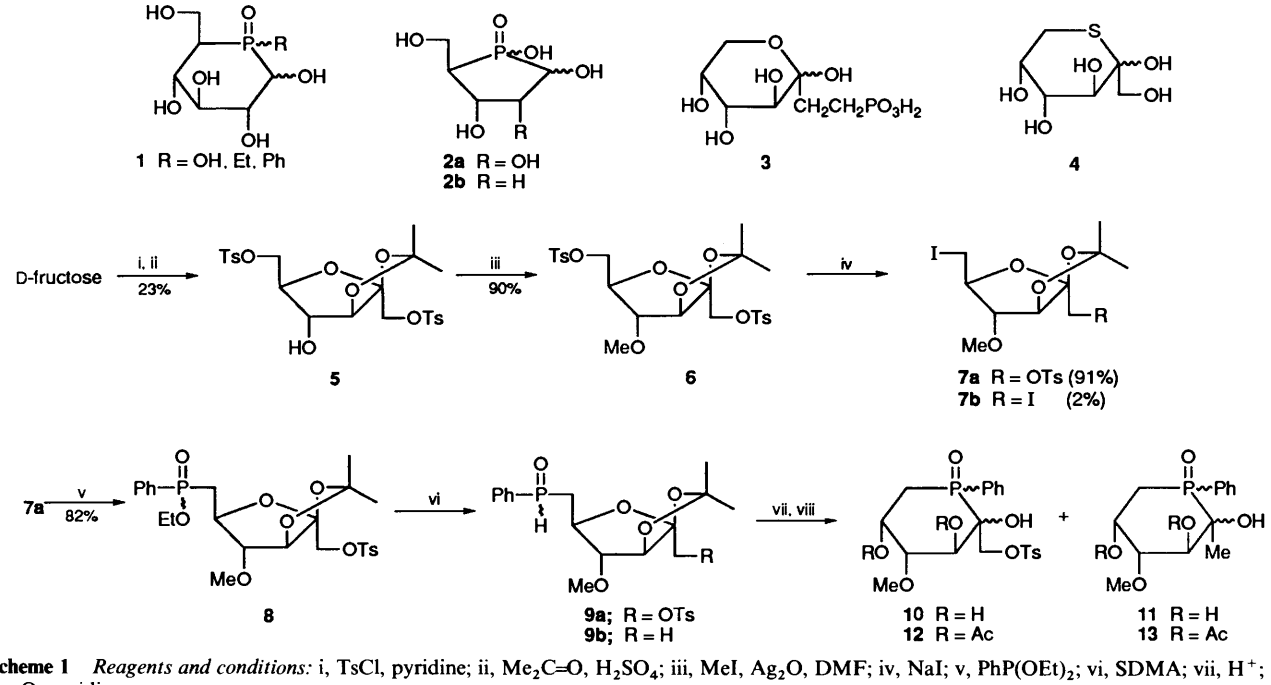
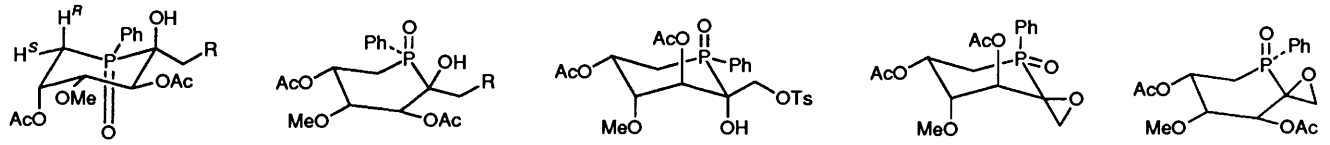
The title sugar analogues were synthesized through three routes, by starting with three kinds of 6-*O*-tosyl-D-fructofuranoses. (i) Treatment of the known 2,3-*O*-isopropylidene-1,6-di-*O*-tosyl-β-D-fructofuranose successively with methyl iodide–silver oxide, sodium iodide and diethyl phenylphosphonite provided 6-deoxy-6-[(ethoxy)phenylphosphinoyl]-2,3-*O*-isopropylidene-4-*O*-methyl-1-*O*-tosyl-β-D-fructofuranose in 67% overall yield. This was reduced with sodium dihydrobis-(2-methoxyethoxy)aluminate, followed by hydrolysis with acid, to afford a mixture of the 4-*O*-methyl-1-*O*-tosyl and 1-deoxy-4-*O*-methyl derivatives of the title compound. (ii) Treatment of D-fructose with 2-methoxypropene in the presence of TsOH and then with TsCl in pyridine afforded 1,3-*O*-isopropylidene-6-*O*-tosyl-α-D-fructofuranose (35% yield). This was subjected to the same five-step conversion, to give the 4-*O*-methyl derivatives of the title compound. (iii) Treatment of D-fructose with 2,2-dimethoxypropane–$SnCl_2$ and then with TsCl–pyridine gave 1,2-*O*-isopropylidene-6-*O*-tosyl-β-D-fructofuranose (23% yield). This was elaborated, in three steps, to either the 3,4-di-*O*-acetyl-6-deoxy-6-[(ethoxy)phenylphosphinoyl] derivative (84% yield) or the 3,4-bis-*O*-(tetrahydropyran-2-yl) congener (54% yield), both of which furnished, in two steps, the unsubstituted title compound. The products obtained in the three approaches (i–iii) were converted into the corresponding per-*O*-acetates, whose structures and conformations [$^2C_5$(D), $^5C_2$(D), or $B_{3,6}$] were established by spectroscopy.

We have prepared various sugar analogues having a phosphorus atom in the hemiacetal ring[1] because of an appreciable interest in their chemical and biochemical properties. Although a number of phosphorus-in-the-ring aldose analogues, *e.g.*, D-glucose **1**,[2,3] D-ribofuranose **2a**,[4] and 2-deoxy-D-ribofuranose **2b**,[5] were synthesized, no such analogues of a ketose type have been reported in detail yet. Meanwhile, in chemical modifications of D-fructose, various analogues having a C–P bond on a side-chain, *e.g.*, compound **3**,[6] have been prepared. A sulfur-in-the-ring analogue of D-fructopyranose, compound **4**,[7,8] showing various antiradiation properties, has also been reported. We now describe our detailed study on the synthesis and characterization of some 6-deoxy-6-phosphonoyl-D-fructopyranoses by employing phenylphosphonoyl [>P(O)Ph] as a model functional group.[9] These compounds are the first example of phosphorus-in-the-ring sugar analogues of a ketose type.

6-*O*-Tosyl-D-fructofuranose derivatives can be perceived as important starting materials for the introduction of a phosphonoyl group onto the C-6 atom; the phosphorus subsequently becomes the ring-phosphorus atom in our present synthetic scheme. We have devised three different approaches, starting from three different 6-*O*-tosyl-D-fructofuranoses (the 2,3-*O*-, 1,3-*O*-, and 1,2-*O*-isopropylidene derivatives **5**, **17a** and **25a**), as will be explained in Schemes 1, 2 and 3, respectively.



Scheme 1 *Reagents and conditions:* i, TsCl, pyridine; ii, $Me_2C{=}O$, H_2SO_4; iii, MeI, Ag_2O, DMF; iv, NaI; v, $PhP(OEt)_2$; vi, SDMA; vii, H^+; viii, Ac_2O, pyridine



12a R = OTs
13a R = H

12b R = OTs
13b R = H

12c

16a

16b

Chart 1 Structures and favourable conformations of 6-deoxy-6-phenylphosphonoyl-D-fructopyranoses from Scheme 1

Starting material for the first approach (Scheme 1), 2,3-*O*-isopropylidene-1,6-di-*O*-tosyl-β-D-fructofuranose **5**, was prepared from D-fructose according to a reported method.[10] To facilitate characterization of the products in the subsequent steps, methylation of the 4-hydroxy group of compound **5** was performed by use of MeI–Ag_2O, providing 4-*O*-methyl compound **6**. Treatment of compound **6** with sodium iodide gave exclusively the 6-iodo compound **7a** (91% yield), although a trace amount of 1,6-diiodo compound **7b** (2%) was also isolated. Compound **7a** was elaborated to the key intermediate, 6-deoxy-6-[(ethoxy)phenylphosphinoyl] derivative **8** (82%), by the Michaelis–Arbuzov reaction with diethyl phenylphosphonite; besides phosphinate ester **8**, a minor amount of 6-deoxy compound **14** (4%) was produced.

14 **15**

Compound **8** was then reduced with sodium dihydrobis-(2-methoxyethoxy)aluminate (SDMA) to give the 6-deoxy-6-phenylphosphinoyl derivative **9a*** together with a minor amount of 1,6-dideoxy-6-phenylphosphinoyl derivative **9b**. This mixture was immediately treated with 0.5 mol dm^3 hydrochloric acid at 90 °C under argon, to afford a crude mixture of 6-deoxy-4-*O*-methyl-6-phenylphosphonoyl-1-*O*-tosyl-D-fructopyranoses **10** and their 1,6-dideoxy compounds **11**.

These products were characterized after having been converted into the corresponding 3,5-di-*O*-acetyl derivatives **12** and **13** by the usual method. By purification on a silica gel column, the presence of the following eight compounds was confirmed: the 6-deoxy-6-[(*R*)-phenylphosphonoyl]-1-*O*-tosyl-β-D-fructopyranose **12a** (15% overall yield from **8**), the P(*S*)-β-isomer **12b** (12%), the P(*S*)-α-isomer **12c** (4.3%), the 1,6-dideoxy-6-[(*R*)-phenylphosphonoyl]-β-D-fructopyranose **13a** (2.2%), the P(*S*)-β-isomer **13b** (6.9%), the 1,2-anhydro-6-deoxy-6-[(*R*)-phenylphosphonoyl]-β-D-fructopyranose **16a** (0.8%), and the P(*S*)-β-isomer **16b** (3.3%). Some of these minor products were not completely separable, whereupon the product proportions were based on the ^1H and ^{31}P NMR spectra (see the Experimental section). Structures and preferable conformations of the above products were established on the basis of 500 MHz ^1H NMR spectral data (see Chart 1 shown above).

The 1,2-anhydro compounds **16a** and **16b** appeared to be derived from compounds **12** (or **10**) as a result of elimination of the tosyl ester by the action of pyridine. Indeed, treatment of compounds **12a** and **12b** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1 mol equiv.) gave the corresponding epoxides **16a** and **16b**, respectively. In contrast, treatment of compound **12b** with 2 mol equiv. of DBU resulted in the formation of the 5,6-dideoxyhex-5-enopyranose **15**.

As the second approach (Scheme 2), D-fructose was converted into 1,3-*O*-isopropylidene-6-*O*-tosyl-α-D-fructofuranose **17a** (35% yield) by treatment with 2-methoxypropene in the presence of toluene-*p*-sulfonic acid (TsOH) † and then with tosyl chloride in pyridine. Minor proportions of 1,3-*O*-isopropylidene-4,6-di-*O*-tosyl-α-D-fructofuranose **17b** (3%), 4,5-*O*-isopropylidene-1-*O*-tosyl-β-D-fructopyranose **18a** (15%), and its 1,3-di-*O*-tosyl derivative **18b** (2%) were also produced.

Protection of the 4-hydroxy and anomeric 2-hydroxy group of the major product **17a** was performed by the use of MeI–Ag_2O, to give the methyl 4-*O*-methyl-D-fructofuranoside **19**. By following the synthetic scheme analogous to that used for compound **10**, we prepared 6-deoxy-4-*O*-methyl-6-phenylphosphonoyl-D-fructopyranoses **23** from glycoside **19** by the sequence **19** ⟶ 6-iodo **20** ⟶ 6-[(ethoxy)phenylphosphinoyl] **21** ⟶ 6-phenylphosphinoyl **22** ⟶ **23**. Compounds **23** were converted into the tri-*O*-acetyl derivatives **24** for characterization. Chromatography of triacetate **24** on a column of silica gel afforded 1,3,5-tri-*O*-acetyl-6-deoxy-4-*O*-methyl-6-[(*R*)-phenylphosphonoyl]-β-D-fructopyranose **24a** (16% overall yield from **21**), the 6-P(*S*)-β-isomer **24b** (13%), the 6-P(*S*)-α-isomer **24c** (3.2%), and the 6-P(*R*)-α-isomer **24d** (4.7%). A small amount of 1,2,3,5-tetra-*O*-acetyl-6-deoxy-4-*O*-methyl-6-[(*S*)-phenylphosphonoyl]-α-D-fructopyranose **24c'** was also isolated (4.1% yield); for structures and conformations of compounds **24a–d** and **24c'**, see Chart 2.

These successful syntheses of 4 (or 1,4-di)-*O*-substituted D-fructopyranose analogues **10** and **23** prompted us to study the preparation of 4-*O*-unsubstituted compounds **30** by the third approach (Scheme 3). Namely, acetonation of D-fructose with 2,2-dimethoxypropane and tin chloride,‡ followed by tosylation with tosyl chloride and pyridine, provided the desired starting material, 1,2-*O*-isopropylidene-6-*O*-tosyl-β-D-fructofuranose **25a** in 23% yield, along with minor amounts of 3,6-di-*O*-tosyl, 4,6-di-*O*-tosyl and 3,4,6-tri-*O*-tosyl derivatives **25b** (1.7%), **25c** (0.6%) and **25d** (0.5%), as well as the 1,3-*O*-isopropylidene compound **17a** (2.0%).

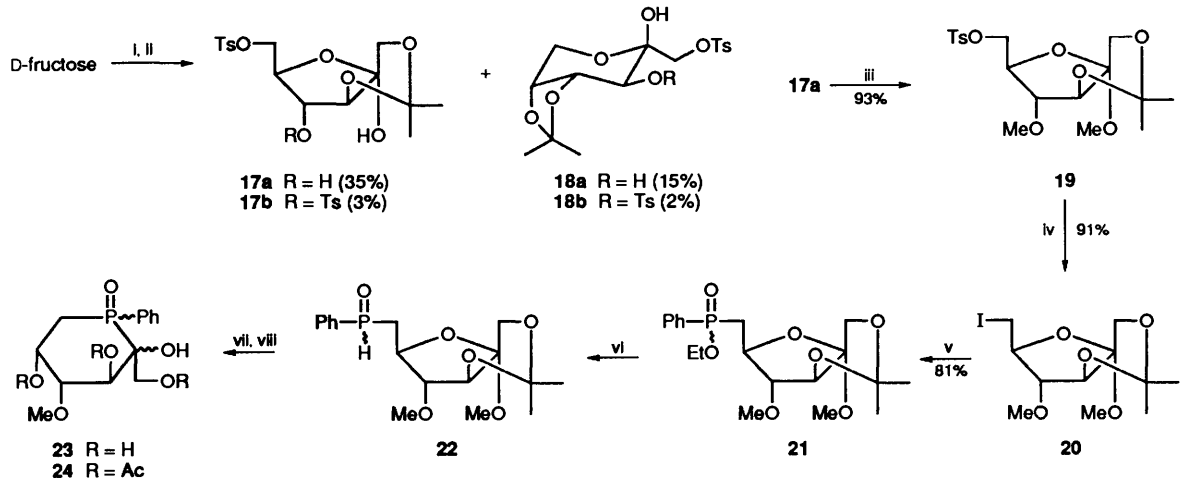
Compound **25a** was treated with acetic anhydride–pyridine to furnish 3,4-di-*O*-acetyl derivative **26a**, which was converted into the 6-iodo compound **27a**. This was elaborated to the key precursor 6-[(ethoxy)phenylphosphinoyl] compound **28a** together with minor amounts of the 6-deoxy compound **32** (2%).

By the same procedures as described above, compound **28a** was converted into the 6-deoxy-6-phenylphosphonoyl-D-fructopyranoses **30** *via* the 6-phenylphosphinoyl-D-fructofuranose intermediate **29**. The structure of products **30** was similarly established by derivatization into the corresponding tetra-*O*-acetates **31**. Column chromatography of tetraacetates **31** afforded 1,3,4,5-tetra-*O*-acetyl-6-deoxy-6-[(*R*)-phenylphosphonoyl]-β-D-fructofuranose **32a** (13% from overall yield from **28a**), its 6-P(*S*)-α-isomer **32c** (5.9%), and its 1,2,3,4,5-penta-*O*-acetate **32c'** (5.7%); for structures and conformations of products **31**, see Chart 2.

* Although phosphinate **8** was reduced with SDMA into the corresponding phosphine (6-PHPh), it was easily oxidized to phosphine oxide **9a** during work-up; *cf.* ref. 3.

† A synthesis of 2,4,6-tri-*O*-acetyl-1,3-*O*-isopropylidene-α-D-fructofuranose has been reported but without detailed experimental procedures (see ref. 11).

‡ The reported procedure for the preparation of 1,2-*O*-isopropylidene-β-D-fructofuranose was slightly modified (see ref. 12).



Scheme 2. *Reagents and conditions:* i, CH_2=C(OMe)Me, TsOH; ii, TsCl, pyridine; iii, MeI, Ag_2O, DMF; iv, NaI; v, $PhP(OEt)_2$; vi, SDMA; vii, H^+; viii, Ac_2O, pyridine

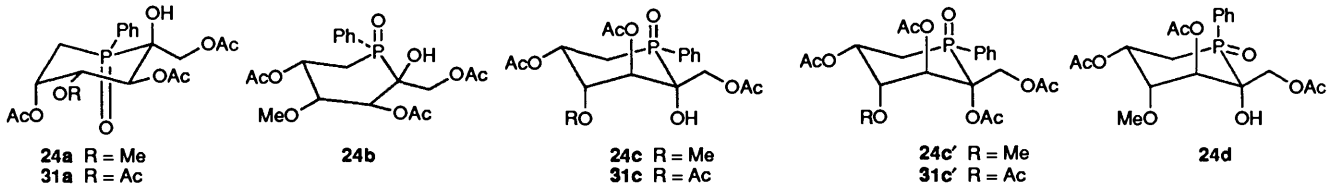
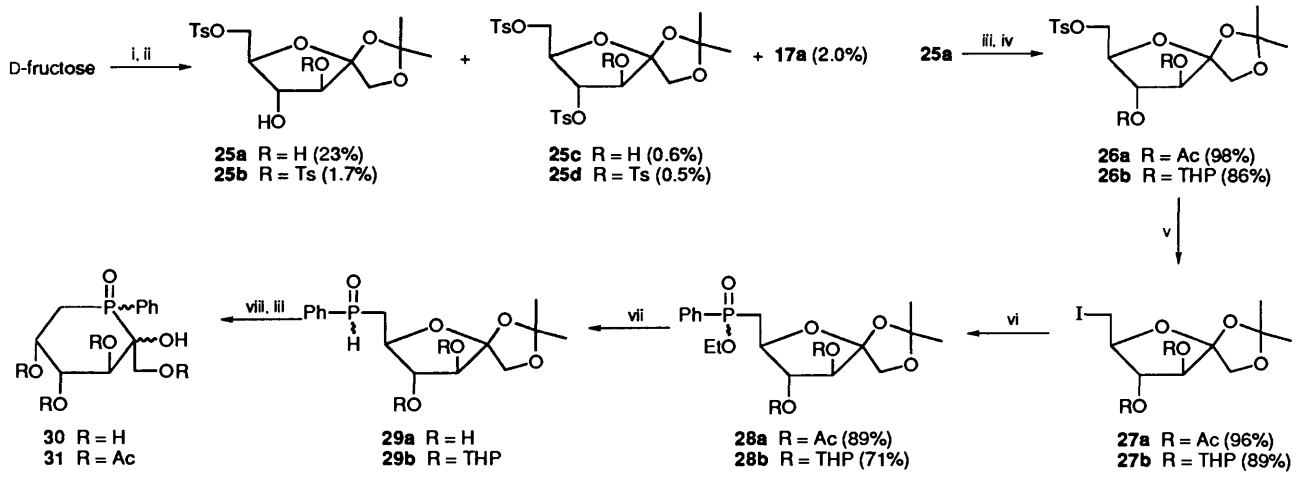
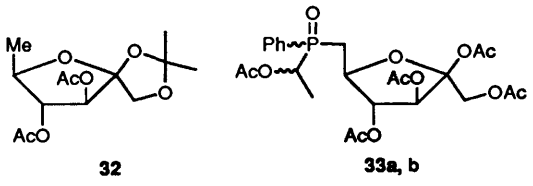


Chart 2 Structures and favourable conformations of 6-deoxy-6-phenylphosphonoyl-D-fructopyranoses from Scheme 2

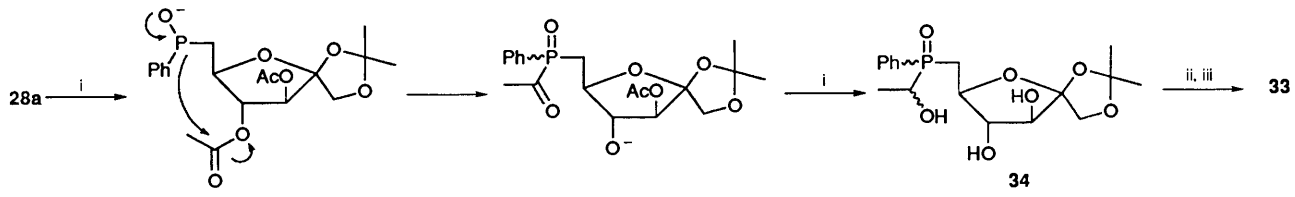


Scheme 3 *Reagents and conditions:* i, $Me_2C(OMe)_2$, $SnCl_2$; ii, TsCl, pyridine; iii, Ac_2O, pyridine; iv, DHP, PPTS; v, NaI; vi, $PhP(OEt)_2$; vii, SDMA; viii, H^+



As by-products in this three-step conversion (**28a** ⟶ **31**), two isomers of 1,2,3,4-tetra-*O*-acetyl-6-[(1-acetoxyethyl)phenylphosphinoyl]-β-D-fructofuranose, **33a** (1.9% from **28a**) and **33b** (2.8%), were isolated, although the configurations of the phosphorus atom and its α-position remained to be established. A possible pathway for the formation of pentaacetates **33** from compound **28a** is illustrated in Scheme 4. Migration of the 4-*O*-acetyl group to a reduced 6-phenylphosphino group and the subsequent reduction would give 6-[(1-hydroxyethyl)phenylphosphinoyl] compounds **34**, which would then be converted into peracetates **33** by hydrolysis and then acetylation.

Therefore, we turned our attention to another approach for the preparation of compounds **30**; namely, from precursor 3,4-bis-*O*-(tetrahydropyran-2-yl) congener **28b** (Scheme 3) instead of 3,4-di-*O*-acetyl compounds **28a**. Tetrahydropyranylation of compound **25a** by treatment with dihydropyran (DHP) in the presence of pyridinium toluene-*p*-sulfonate (PPTS) provided the bis-THP ether **26b**, which was converted into phosphinoate **28b** *via* the 6-iodo compound **27b** by the same procedures described above. Alternatively, phosphinate **28b** could be prepared also from diacetate **28a** in 85% yield by deacetylation and then tetrahydropyranylation. Compound **28b** was converted into the anticipated product **30** *via* 6-phenylphosphinoyl intermediate **29b** by the same procedures as described



Scheme 4 *Reagents and conditions:* i, H^-; ii, H^+; iii, Ac_2O, pyridine

above. After tetra-*O*-acetylation of compound **30**, compounds **31a** (16% from **28b**), **32c** (14%), and **32c'** (4.3%) were obtained, free from the formation of by-products **33**.

^1H *NMR Spectral Analysis of the* 6-*Deoxy*-6-*phenylphosphonoyl*-D-*fructopyranose Derivatives.*—During the course of the structural assignments of these new phosphorus-in-the-ring sugar analogues, the precise parameters of their ^1H NMR spectra were obtained and these are summarized in Table 1. As the parameters for 6-deoxy-6-phosphonoyl-D-fructopyranoses have become available for the first time in the present study, some of the characteristic features of these compounds are discussed here in detail in conjunction with the conformational studies.

(1) Among these D-fructopyranose derivatives, the group of compounds **12a**, **13a**, **24a** and **31a** characteristically show large values of $J_{3,4}$ (9.8–10.3 Hz) and $J_{5,P}$ (28–29 Hz) and small values of $J_{5,6S}$ (4.3–4.7 Hz) and $J_{3,P}$ (0.5–1.0 Hz), whereas another group of compounds **12c**, **16a**, **24c**, **c'**, **d** and **31c**, **c'**, exhibit opposite magnitudes of the corresponding coupling constants: namely, relatively small values of $J_{3,4}$ (4.2–6.1 Hz) and $J_{5,P}$ (3.5–8.3 Hz) and large values of $J_{5,6S}$ (11.4–13.0 Hz) and $J_{3,P}$ (18–22 Hz). It has been reported that β-D-fructopyranose derivatives exist in the $^2C_5$ conformation, whereas α-D-fructopyranose derivatives exist in the dominant $^5C_2$ (an admixture with a minor portion of $^2C_5$) conformation.[8,13] Therefore the former group of compounds (**12a**, **24a**, **31a**) can be assigned to be β-anomers exclusively in the $^2C_5$ conformation, whereas the latter compounds are assigned to be α-anomers in the $^5C_2$ conformation.[14] It should be noted, however, that the 1,2-anhydro-β-D-fructopyranose **16a**, which was derived from β-anomer **12a**, exists in the $^5C_2$ conformation (see later). The structural assignment of compound **12a** was supported by an NOE enhancement between 3-H and 1-H_2 protons.

(2) As for the orientation of the ring P=O group, the small $J_{6R,P}$ values (6.8–7.3 Hz) for **12a**, **13a**, **24a**, and **31a** indicate the *anti* connection of H^R–C^6–P=O;[3,14] thus an axial P=O. On the other hand, while the small $J_{6S,P}$ values (3.2–5.1 Hz) for **12c**, **24c**, **c'** and **31c**, **c'** indicate the alternative axial orientation of the ring P=O group; an equatorial orientation for P=O is assignable for compounds **16a** and **24d** on the basis of their large $J_{6S,P}$ values (18.3–18.6 Hz).[3,14]

(3) Compounds **12b**, **13b**, **16b** and **24b** have moderate or intermediate magnitudes of $J_{3,P}$ (12–15 Hz) and $J_{5,P}$ (15–19 Hz), seemingly suggesting an equilibrium mixture of $^2C_5$ and $^5C_2$ conformers.* However, such an averaging between these conformers is excluded by taking into account the large $J_{5,6S}$ values (8.7–9.8 Hz) and the small $J_{6S,P}$ values (6.0–7.7 Hz) for these compounds, which instead indicate the *anti* connection of H–C^5–C^6–H^S and H^S–C^6–P=O, respectively. Therefore, these compounds are presumed to be (*S*)-phenylphosphonoyl-β-isomers that exist preponderantly in the $B_{3,6}$ (or readily variable $^PS_3$) conformation, most likely as a result of quasi-equatorial orientations of all steric groups as illustrated in Chart 3. The

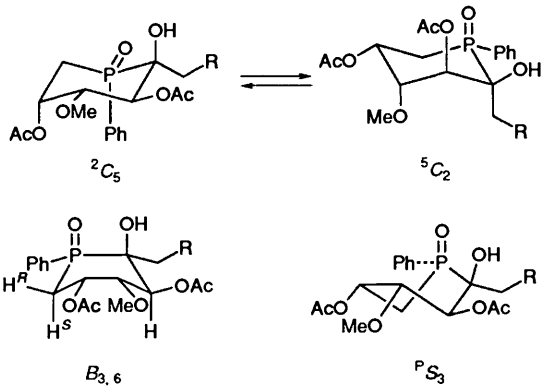


Chart 3 Unfavourable ($^2C_5$ and $^5C_2$) and favourable conformations ($B_{3,6}$ and $^PS_3$) for compounds **12b** (R = OTs), **13b** (R = H) and **24b** (R = OAc)

conformation of compound **12b** was confirmed by an NOE enhancement between the 3-H and 6-H^S protons.

(4) It is noteworthy that compound **12b** was converted into the corresponding epoxide **16b** with retention of conformation, while epoxide **16a** has the reversed conformation compared with its precursor **12a**.

The present work therefore demonstrates that phosphorus-in-the-ring ketose analogues can readily be prepared from appropriate precursors and that these analogues possess some characteristic physicochemical features. Extension of this work, including preparative studies on other D-fructose derivatives (such as those having a hydroxyphosphonoyl group in the ring), as well as biological evaluation of the compounds, is in progress.

Experimental

M.p.s were determined with a Yanagimoto MP-S3 instrument and are uncorrected. All reactions were monitored by TLC (Merck silica gel 60F, 0.25 mm) with an appropriate solvent system [AcOEt (Solvent A); (1 : 1) AcOEt–hexane (Solvent B); (1 : 2) AcOEt–hexane (Solvent C); (1 : 4) AcOEt–hexane (Solvent D); and (19 : 1) AcOEt–EtOH (Solvent E)]. Components were detected by exposing the plates to UV light and/or spraying them with 20% sulfuric acid–ethanol, with subsequent heating. Column chromatography was performed on Wako C-200 silica gel. Optical rotations were measured with a Nihon-Bunko DIP-370 polarimeter at 27 °C, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. The ^1H and ^{31}P NMR spectra were measured in $CDCl_3$ with Varian VXR-500 (500 MHz for ^1H) and VXR-200 (81 MHz for ^{31}P) spectrometers at 21 °C, unless otherwise stated. Chemical shifts are reported as δ-values relative to tetramethylsilane (internal standard for ^1H) and 85% phosphoric acid (external standard for ^{31}P). *J*-Values are given in Hz. The assignments of all signals were made by employing a first-order analysis with the aid of decoupling techniques and, if necessary, 2D COSY and NOEDS measurements. The mass spectra (EI, unless otherwise specified) were taken on an A.E.I. MS 50 ultra-high-resolution instrument and are given in terms of *m/z* (relative intensity) compared with the base peak.

* We postulated the existence of an equilibrium mixture of compound **24b** in ref. 9, but we revise its conformation to that illustrated in Chart 2.

Table 1 ^{1}H and ^{31}P NMR parameters for compounds **12**, **13**, **16**, **24** and **31** in $CDCl_3$

(a) Chemical shifts (δ)

Compounds	1-H	1-H′	3-H	4-H	5-H	6-H^S	6-H^R	2-OH	4-OMe	OAc[a] (1-OTs)[b]	PPh (*o*, *m*, *p*)	^{31}P
12a	4.41	4.34	5.86	3.83	5.66	2.49	2.51	3.62	3.44	2.17, 2.12 (7.45, 7.26, 2.44)	7.78, 7.44, 7.57	31.4
12b	4.26	3.56	5.68	3.90	5.65	2.71	2.51	4.18	3.50	2.16, 2.07 (7.54, 7.21, 2.40)	7.77, 7.49, 7.60	31.8
12c	4.59[c]	3.88	5.41	4.04	5.67	2.92	2.25	4.54[c]	3.67	2.08, 2.06 (7.67, 7.28, 2.41)	7.85, 7.48, 7.58	33.1
13a	1.31		5.80	3.81	5.73	2.53	2.55	2.45[d]	3.43	2.20, 2.16	7.87, 7.52. 7.60	34.4
13b	1.27		5.46	3.89	5.67	2.71	2.48	3.75	3.49	2.22, 1.97	7.87, 7.54, 7.74	36.4
16a	3.63	3.00	4.92	3.67	5.26	2.78	3.03		3.56	2.17, 1.51	8.01, 7.55, 7.59	20.8
16b	2.96	2.86	5.23	3.84	5.77	2.98	2.48		3.51	2.22, 1.84	7.78, 7.54, 7.60	26.8
24a	4.58	4.45	5.91	3.83	5.68	2.46	2.44	4.02	3.44	2.20, 2.17, 1.32	7.92, 7.50, 7.56	29.8
24b	4.27	3.87	5.73	3.93	5.69	2.74	2.54	4.29	3.49	2.21, 2.08, 1.89	7.88, 7.54, 7.62	32.4
24c	4.64	4.03	5.43	4.01	5.73	2.94	2.29	4.64	3.70	2.20, 2.10, 1.81	7.93, 7.50, 7.58	32.7
24c′	4.64	4.60	6.11	3.90	5.76	2.85	2.39		3.59	2.23, 2.09, 2.04, 1.86	7.75, 7.50, 7.55	29.0
24d	4.20	4.05	5.61	3.79	5.56	2.89	2.64	4.43	3.63	2.17, 2.03, 1.85	7.91, 7.54, 7.61	31.9
31a	4.54	4.44	6.04	5.55	5.59	2.43	2.58	4.02		2.19, 2.11, 2.03, 1.32	7.92, 7.50, 7.57	29.7
31c	4.56	4.24	5.39	5.45	5.84	2.97	2.25	3.52		2.23, 2.21, 2.00, 1.76	7.95, 7.53, 7.61	33.0
31c′	4.65	4.62	5.97	5.58	5.85	2.73	2.51			2.20, 2.16, 2.07, 2.03, 1.85	7.82, 7.53, 7.59	28.4

(b) Coupling constants (Hz)

Compound	$J_{1,1'}$	$J_{1,P}$	$J_{1',P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,6R}$	$J_{5,6S}$	$J_{5,6R}$	$J_{5,P}$	$J_{6S,6R}$	$J_{6S,P}$	$J_{6R,P}$
12a	11.5	4.7	12.2	9.8	0.8	2.8	0	4.7	3.2	28.4	15.6	14.8	7.3
12b	10.2	6.8	6.5	6.8	14.7	2.4	0.5	9.6	3.9	15.3	14.6	6.0	20.1
12c	10.5	2.0	2.9	4.2	21.9	2.0	1.5	12.8	4.0	4.0	14.3	5.1	19.0
13a		12.4		10.2	1.0	2.7	0	4.3	3.5	28.5	15.5	15.0	6.9
13b		13.8		7.3	12.0	2.9	0.5	8.7	3.4	18.8	14.7	7.4	19.5
16a	5.6	4.5	2.7	5.0	20.0	2.2	1.3	12.4	3.8	3.9	14.3	18.3	17.0
16b	5.0	3.6	4.0	7.0	11.6	2.3	0.9	9.8	3.3	15.3	14.6	7.7	19.5
24a[e]	12.5	17.3	2.9	10.0	0.5	3.0	0	4.4	3.4	29.4	15.7	14.6	7.2
24b[e]	11.9	8.8	6.8	7.0	14.0	2.7	0.8	9.2	3.9	16.2	14.9	6.2	19.9
24c	12.1	7.0	3.0	4.2	22.2	2.0	1.5	12.8	3.8	3.5	14.5	4.7	18.6
24c′	12.6	5.6	8.5	5.1	21.9	1.9	1.5	12.5	3.9	4.4	14.4	3.3	19.7
24d	11.8	6.8	5.8	6.0	19.7	2.3	1.0	11.4	3.9	8.0	14.6	18.6	13.7
31a	12.5	17.0	3.2	10.3	0.5	3.0	0	4.3	3.0	28.9	15.8	14.3	6.8
31c	12.2	9.4	2.9	4.0	21.1	2.6	1.3	13.0	3.5	4.4	14.0	5.1	18.2
31c′	12.6	8.0	5.9	6.1	17.6	2.6	1.0	12.1	4.2	8.3	15.0	3.2	19.8

[a] 3-, 5-OAc for **12**, **13** and **16**, 1-, 3-, 5-OAc for **24a–d**, 1-, 2-, 3-, 5-OAc for **24c′**, 1-, 3-, 4-, 5-OAc for **31a**, **c**, and 1-, 2-, 3-, 4-, 5-OAc for **31c′**. [b] 1-$OSO_2C_6H_4Me$-p ($J_{2',3'}$ 8.2–8.4 Hz) for **12a–c**. [c] $^3J_{1,OH}$ 1.7 Hz. [d] $J_{P,OH}$ 3.9 Hz. [e] Close reexamination of the parameters (with the aid of simulation analysis) resulted in slight modification of some of the previously reported values (ref. 9).

2,3-O-*Isopropylidene*-4-O-*methyl*-1,6-*di*-O-*tosyl*-β-D-*fructofuranose* **6**.—To a solution of compound **5**[10] (700 mg, 1.32 mmol) in dry dimethylformamide (DMF) (3.0 cm^3) were added methyl iodide (0.80 cm^3, 9.5 mmol) and silver oxide (510 mg, 2.20 mmol). The mixture was stirred in the dark at 25 °C for 20 h, then was filtered, and the residue was extracted several times with CH_2Cl_2. The combined extracts were filtered to remove white precipitates and were then concentrated under reduced pressure. The residue was dissolved with CH_2Cl_2 and the solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was readily crystallized from methanol to give *title compound* **6** (647 mg, 90%), m.p. 109–111 °C [Found: C, 53.2; H, 5.4%; ($M^+ - CH_3$), 527.1048. $C_{24}H_{30}O_{10}S_2$ requires C, 53.12; H, 5.57%; (M − 15), 527.1045]; R_f 0.75 (Solvent B); $[\alpha]_D$ +17 (*c* 1.41, $CHCl_3$); δ_H 1.30 and 1.35 (3 H each, 2 × s, CMe_2), 2.44 (6 H, s, C_6H_4Me), 3.31 (3 H, s, 4-OMe), 3.74 (1 H, d, $J_{4,5}$ 1.0, $J_{3,4}$ ~0, 4-H), 4.05 and 4.07 (1 H each, 2 × d, $J_{1,1'}$ 10.9, 1-H_2), 4.09–4.14 (3 H, m, 5-H and 6-H_2), 4.51 (1 H, s, 3-H) and 7.33, 7.33, 7.765 and 7.77 (2 H each, 4 × d, *J* 8.3, C_6H_4); *m*/*z* 527 ($M^+ - CH_3$, 27%), 387 (33), 357 (9), 323 (17), 299 (7), 281 (16), 155 (62), 109 (80) and 91 (100).

Acetonation and Subsequent Tosylation of D-*Fructose*.—(A). *Procedure by use of* 2-*methoxypropene*–TsOH. To a solution of D-fructose (500 mg, 2.78 mmol) in dry DMF (10 cm^3) at −5 °C were added 2-methoxypropene (0.50 cm^3, 5.22 mmol) and TsOH (2 mg). The mixture was stirred at this temperature for 5 h. Anhydrous sodium carbonate (100 mg) was added and the cold mixture was stirred vigorously for 3 h before being filtered, and the filtrate was evaporated under reduced pressure. The residue was chromatographed on a short-path silica gel column with (9:1) $CHCl_3$–MeOH as eluent to give a syrup (450 mg), R_f 0.23–0.18 [(9:1) $CHCl_3$–MeOH].

This syrup was dissolved in dry pyridine (5 cm^3) and tosyl chloride (480 mg, 2.18 mmol) was added to the solution at 0 °C. The mixture was stirred at 20 °C for 12 h, diluted with a small amount of water at 0 °C, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and the solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was separated by column chromatography into two fractions, A and B.

Fraction A [R_f 0.39 (Solvent B)] gave a 3:2 mixture of 1,3-*O*-isopropylidene-4,6-di-*O*-tosyl-α-D-fructofuranose **17b** and 4,5-*O*-isopropylidene-1,3-di-*O*-tosyl-β-D-fructopyranose **18b**. Each compound was separated by fractional recrystallization from AcOEt–hexane.

Compound **17b**: syrup (48 mg, 3.3%); δ_H 1.21 and 1.33 (3 H each, 2 × s, CMe_2), 2.44 and 2.48 (3 H each, 2 × s, C_6H_4Me), 2.81 (1 H, br s, 2-OH), 3.70 and 3.78 (1 H each, 2 × d, $J_{1,1'}$ 12.5, 1-H_2), 3.99 (1 H, dd, $J_{6,6'}$ 10.3, $J_{5,6'}$ 6.7, 6-H′), 4.02 (1 H, dd, $J_{5,6}$ 6.1, 6-H), 4.13 (1 H, br s, $J_{3,4}$ 0.5, 3-H), 4.33 (1 H, td, $J_{4,5}$ 2.1, 5-H), 4.58 (1 H, br d, 4-H) and 7.33, 7.40, 7.74 and 7.81 (2 H each, 4 × d, *J* 8.4, C_6H_4).

Compound **18b**: needles (34 mg, 2.3%) m.p. 114–116 °C; $[\alpha]_D$ −73 (*c* 1.24, $CHCl_3$); δ_H 1.26 and 1.41 (3 H each, 2 × s, CMe_2),

2.45, 2.46 (3 H each, 2 × s, C_6H_4Me), 3.45 (1 H, d, $J_{3,OH}$ 1.4, 3-OH), 3.96 (1 H, br d, $J_{6,6'}$ 13.6, $J_{5,6'}$ 0.5, 6-H'), 4.01 and 4.31 (1 H each, 2 × d, $J_{1,1'}$ 10.7, 1-H_2), 4.07 (1 H, dd, $J_{5,6}$ 2.7, 6-H), 4.20 (1 H, br dd, $J_{4,5}$ 5.6, 5-H), 4.28 (1 H, dd, $J_{3,4}$ 7.3, 4-H), 4.48 (1 H, dd, 3-H) and 7.32, 7.36, 7.80 and 7.805 (2 H each, 4 × d, J 8.4, C_6H_4).

Fraction B [R_f 0.20 (Solvent B)] gave a mixture (552 mg) of 1,3-O-*isopropylidene*-6-O-*tosyl*-α-D-*fructofuranose* **17a** and 4,5-*O*-isopropylidene-1-*O*-tosyl-β-D-fructopyranose **18a**. Each compound was separated by fractional recrystallization from AcOEt–hexane.

Compound **17a**: prisms (366 mg, 35%), m.p. 107–108 °C [Found: C, 51.2; H, 6.0%; ($M^+ - CH_3$), 359.0781. $C_{16}H_{22}O_8S$ requires C, 51.33; H, 5.92%; (M − 15), 359.0800]; $[\alpha]_D$ +13 (*c* 1.36, $CHCl_3$); δ_H 1.24 and 1.44 (3 H each, 2 × s, CMe_2), 2.44 (3 H, s, C_6H_4Me), 2.87 (1 H, br d, $J_{4,OH}$ 4.6, 4-OH), 3.59 (1 H, br s, 2-OH), 3.76 and 3.85 (1 H each, 2 × d, $J_{1,1'}$ 12.4, 1-H_2), 4.09 (1 H, br s, $J_{3,4}$ 0.5, 3-H), 4.11 (1 H, br dd, $J_{4,5}$ 1.0, 4-H), 4.13 (2 H, d, $J_{5,6}$ 6.8, 6-H_2), 4.40 (1 H, td, 5-H) and 7.34 and 7.80 (2 H each, 2 × d, J 8.5, C_6H_4); *m/z* 359 ($M^+ - CH_3$, 0.2%), 256 (0.8), 172 (71), 155 (12), 107 (38) and 91 (100).

Compound **18a**: prisms (152 mg, 15%), m.p. 104–105 °C; $[\alpha]_D$ −12 (*c* 0.71, $CHCl_3$); δ_H 1.34 and 1.45 (3 H each, 2 × s, CMe_2), 2.45 (3 H, s, C_6H_4Me), 2.54 (1 H, br d, $J_{3,OH}$ 6.7, 3-OH), 3.44 (1 H, br s, 2-OH), 3.66 (1 H, br t, $J_{3,4}$ 7.0, 3-H), 3.91 (1 H, br d, $J_{6,6'}$ 13.6, $J_{5,6'}$ 0.5, 6-H'), 4.05 and 4.20 (1 H, each, 2 × d, $J_{1,1'}$ 10.3, 1-H_2), 4.08 (1 H, d, $J_{5,6}$ 2.3, 6-H), 4.20–4.23 (2 H, m, 4- and 5-H) and 7.35 and 7.80 (2 H each, d, J 8.6, C_6H_4).

(B) *Procedure by use of* 2,2-*dimethoxypropane*–$SnCl_2$. A mixture of D-fructose (5.00 g, 27.8 mmol), 2,2-dimethoxypropane (12.0 cm^3, 97.9 mmol), and tin(II) chloride (30 mg) suspended in dry 1,2-dimethoxyethane (DME) (300 cm^3) was refluxed for 25 min. The reaction was terminated by the addition of pyridine (0.2 cm^3) followed by removal of the solvent under reduced pressure. The residue was purified by short-path column chromatography and was then treated with tosyl chloride (5.0 g, 2.4 mmol) and dry pyridine (50 cm^3) as described above. Separation by column chromatography gave five fractions, A–E.

Fraction A [R_f 0.56 (Solvent B)] gave 1,2-*O*-isopropylidene-3,4,6-tri-*O*-tosyl-β-D-fructofuranose **25d** (94 mg, 0.5%) as prisms, m.p. 157–158 °C (from AcOEt–hexane); $[\alpha]_D$ −17 (*c* 0.54, $CHCl_3$); δ_H 1.28 and 1.30 (3 H each, 2 × s, CMe_2), 2.44, 2.46 and 2.46 (3 H each, 3 × s, C_6H_4Me), 3.96 and 4.00 (1 H each, 2 × d, $J_{1,1'}$ 9.7, 1-H_2), 4.03 (1 H, dd, $J_{6,6'}$ 10.5, $J_{5,6'}$ 7.3, 6-H'), 4.06 (1 H, dd, $J_{5,6}$ 3.7, 6-H), 4.14 (1 H, ddd, $J_{4,5}$ 5.2, 5-H), 4.76 (1 H, dd, $J_{3,4}$ 6.9, 4-H), 4.93 (1 H, d, 3-H) and 7.32, 7.335, 7.34, 7.65, 7.75 and 7.76 (2 H each, 6 × d, J 8.3, C_6H_4).

Fraction B [R_f 0.50 (Solvent B)] gave 1,2-*O*-isopropylidene-3,6-di-*O*-tosyl-β-D-fructofuranose **25b** (256 mg, 1.7%) as needles, m.p. 125–126 °C (from AcOEt–hexane); $[\alpha]_D$ −40 (*c* 1.45, $CHCl_3$); δ_H 1.29 and 1.33 (3 H each, 2 × s, CMe_2), 2.45 and 2.47 (3 H each, 2 × s, C_6H_4Me), 2.93 (1 H, d, $J_{4,OH}$ 3.0, 4-OH), 3.69 and 3.92 (1 H each, 2 × d, $J_{1,1'}$ 9.6, 1-H_2), 4.02 (1 H, q, $J_{4,5} = J_{5,6} = J_{5,6'} = 6.2$, 5-H), 4.14 (2 H, d, 6-$H_2$), 4.37 (1 H, ddd, $J_{3,4}$ 7.3, 4-H), 4.52 (1 H, d, 3-H) and 7.34, 7.38, 7.79 and 7.82 (2 H each, 4 × d, J 8.1, C_6H_4).

Fraction C [R_f 0.47 (Solvent B)] gave 1,2-O-*isopropylidene*-4,6-*di*-O-*tosyl*-β-D-*fructofuranose* **25c** (86 mg, 0.6%) as needles, m.p. 111–112 °C (from benzene) [Found: ($M^+ - CH_3$), 513.0879. $C_{23}H_{28}O_{10}S_2$ requires (M − 15), 513.0889]; δ_H 1.36 and 1.40 (3 H each, 2 × s, CMe_2), 2.37 (1 H, br d, $J_{3,OH}$ 9.2, 3-OH), 2.46 and 2.47 (3 H each, 2 × s, C_6H_4Me), 3.98 and 4.06 (1 H each, 2 × d, $J_{1,1'}$ 9.4, 1-H_2), 4.05 (1 H, dd, $J_{6,6'}$ 10.4, $J_{5,6'}$ 6.5, 6-H'), 4.09 (1 H, dd, $J_{5,6}$ 4.2, 6-H), 4.12 (1 H, br dd, $J_{3,4}$ 6.5, 3-H), 4.14 (1 H, td, $J_{4,5}$ 5.5, 5-H), 4.60 (1 H, dd, 4-H) and 7.35, 7.37, 7.77 and 7.80 (2 H each, 4 × d, J 8.3, C_6H_4); *m/z* 513 ($M^+ - CH_3$, 2.4%), 373 (4.4), 172 (52), 155 (19), 107 (33) and 91 (100).

Fraction D [R_f 0.39 (Solvent B)] gave a further crop of compound **17a** (208 mg, 2.0%).

Fraction E [R_f 0.10 (Solvent B)] gave 1,2-O-*isopropylidene*-6-O-*tosyl*-β-D-*fructofuranose* **25a** (2.38 g, 23%) as needles, m.p. 108–110 °C (from AcOEt–hexane) [Found: ($M^+ - CH_3$), 359.0785. $C_{16}H_{22}O_8S$ requires (M − 15), 359.0800]; δ_H 1.39 and 1.41 (3 H each, 2 × s, CMe_2), 2.25 and 2.63 (1 H each, 2 br s, 3- and 4-OH), 2.45 (3 H, s, C_6H_4Me), 3.92 (1 H, d, $J_{3,4}$ 7.4, 3-H), 3.95 (1 H, dt, $J_{4,5}$ 6.8, $J_{5,6'}$ 5.5, $J_{5,6}$ 5.1, 5-H), 4.01 and 4.07 (1 H each, 2 × d, $J_{1,1'}$ 9.5, 1-H_2), 4.06 (1 H, t, 4-H), 4.12 (1 H, dd, $J_{6,6'}$ 10.4, 6-H'), 4.15 (1 H, dd, 6-H), 7.35 and 7.80 (2 H each, 2 × d, J 8.2, C_6H_4); *m/z* 359 ($M^+ - CH_3$, 0.7%), 257 (1.3), 172 (45), 107 (21), 91 (59) and 58 (100).

Methyl 1,3-O-*Isopropylidene*-4-O-*methyl*-6-O-*tosyl*-α-D-*fructofuranoside* **19**.—By use of the same procedures as those for preparation of compound **6**, compound **17a** (256 mg, 0.684 mmol) was treated with methyl iodide (0.60 cm^3, 8.6 mmol) and silver oxide (520 mg, 2.24 mmol) at 20 °C for 10 h. Purification by column chromatography gave *glycoside* **19** (256 mg, 93%) as a syrup [Found: ($M^+ - CH_3$), 387.1115. $C_{26}H_{26}O_8S$ requires (M − 15), 387.1115]; R_f 0.51 (Solvent B); $[\alpha]_D$ +34 (*c* 1.23, $CHCl_3$); δ_H 1.29 and 1.41 (3 H each, 2 × s, CMe_2), 2.45 (3 H, s, C_6H_4Me), 3.23 and 3.35 (3 H each, 2 × s, OMe), 3.49 (1 H, br d, $J_{4,5}$ 4.4, $J_{3,4}$ 0.5, 4-H), 3.70 and 3.85 (1 H each, 2 × d, $J_{1,1'}$ 12.2, 1-H_2), 4.00 (1 H, br s, 3-H), 4.09 (1 H, td, $J_{5,6}$ 5.5, 5-H), 4.18 (2 H, d, 6-H_2) and 7.35 and 7.83 (2 H each, 2 × d, J 8.3, C_6H_4); *m/z* 387 ($M^+ - CH_3$, 5.6%), 330 (55), 298 (12), 283 (10), 239 (16), 155 (52), 111 (79), 91 (58) and 73 (100).

3,4-*Di*-O-*acetyl*-1,2-O-*isopropylidene*-6-O-*tosyl*-β-D-*fructofuranose* **26a**.—Compound **25a** (366 mg, 0.978 mmol) was dissolved in a mixture of dry pyridine (3.0 cm^3) and acetic anhydride (1.0 cm^3) at 0 °C. The mixture was stirred at 20 °C overnight, diluted with a small amount of cold water, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and the solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by column chromatography to give the *diacetate* **26a** (440 mg, 98%) as needles, m.p. 91–92 °C (from cyclohexane) (Found: C, 52.2; H, 5.6%; M^+, 458.1264. $C_{20}H_{26}O_{10}S$ requires C, 52.39; H, 5.72%; M, 458.1247); R_f 0.42 (Solvent C); $[\alpha]_D$ −26 (*c* 2.03, $CHCl_3$); δ_H 1.32 and 1.37 (3 H each, 2 × s, CMe_2), 2.06 and 2.10 (3 H each, 2 × s, OAc), 2.45 (3 H, s, C_6H_4Me), 4.05 and 4.12 (1 H each, 2 × d, $J_{1,1'}$ 9.4, 1-H_2), 4.12 (1 H, dt, $J_{5,6'}$ 7.9, $J_{4,5}$ 4.9, $J_{5,6}$ 4.5, 5-H), 4.21 (1 H, dd, $J_{6,6'}$ 10.3, 6-H'), 4.30 (1 H, dd, 6-H), 5.17 (1 H, dd, $J_{3,4}$ 6.5, 4-H), 5.31 (1 H, d, 3-H) and 7.34 and 7.80 (2 H each, 2 × d, J 8.1, C_6H_4); *m/z* 458 (M^+, 1.2%), 443 (59), 281 (12), 211 (100), 169 (40), 155 (71) and 109 (65).

1,2-O-*Isopropylidene*-3,4-*bis*-O-(*tetrahydropyran*-2-*yl*)-6-O-*tosyl*-β-D-*fructofuranose* **26b**.—A solution of diol **25a** (558 mg, 1.49 mmol) and DHP (800 mg, 9.51 mmol) in dry CH_2Cl_2 (5 cm^3) containing PPTS (90 mg, 0.36 mmol) was stirred for 12 h at 20 °C. The solution was diluted with diethyl ether, washed once with half-saturated brine to remove the catalyst, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by short-path column chromatography to give a diastereoisomeric mixture of compound **26b** (695 mg, 86%) as a syrup, R_f 0.43–0.40 (Solvent C). Recrystallization of this mixture from cyclohexane gave one *pure isomer* as prisms (110 mg), m.p. 119–121 °C [Found: ($M^+ - CH_3$), 527.1965. $C_{26}H_{38}O_{10}S$ requires (M − 15), 527.1951]; δ_H 1.33 and 1.39 (3 H each, 2 × s, CMe_2), 1.48–1.80 (12 H, m, 3- and 4-OCH[CH_2]$_3$), 2.43 (3 H, s, C_6H_4Me), 3.38, 3.50, 3.72 and 3.88 (1 H each, 4 × m, 3- and 4-$OCCH_2$), 4.00 and 4.12 (1 H each, 2 × d, $J_{1,1'}$ 9.1, 1-H_2), 4.02 (1

H, dd, $J_{6,6'}$ 7.8, $J_{5,6'}$ 6.0, 6-H'), 4.07 (1 H, ddd, $J_{5,6}$ 9.5, $J_{4,5}$ 2.1, 5-H), 4.11 (1 H, dd, 6-H), 4.14 (1 H, d, $J_{3,4}$ 9.4, 3-H), 4.36 (1 H, dd, 4-H), 4.57 and 4.83 (1 H each, 2 × br t, J 3.5, 3- and 4-OCH) and 7.31 and 7.79 (2 H each, 2 × d, J 8.3, C_6H_4); *m/z* 527 ($M^+ - CH_3$, 0.9%), 343 (1.8), 257 (1.8), 169 (3.4), 109 (11) and 85 (100).

Preparation of 6-*Deoxy*-6-*iodo*-D-*fructofuranoses* **7a, b**, **20** *and* **27a, b**.—(A) *Procedure for compounds* **7a, b**. A solution of ditosyl ester **6** (834 mg, 1.54 mmol) and sodium iodide (460 mg, 3.08 mmol) in dry acetone (15 cm^3) was heated in a sealed tube at 90–100 °C for 12 h. The resulting sodium toluenesulfonate was filtered off and the filtrate was evaporated under reduced pressure. The residue was separated by column chromatography to give 6-*deoxy*-6-*iodo*-2,3-O-*isopropylidene*-4-O-*methyl*-1-O-*tosyl*-β-D-*fructofuranose* **7a** (698 mg, 91%) and its 1,6-dideoxy-1,6-diiodo analogue **7b** (16 mg, 2%).

Compound **7a**: needles, m.p. 66–67 °C (from AcOEt–hexane) [Found: C, 41.2; H, 4.5%; ($M^+ - CH_3$), 482.9980. $C_{17}H_{23}IO_7S$ requires C, 40.97; H, 4.65%; (M − 15), 482.9974]; R_f 0.39 (Solvent D); $[\alpha]_D$ +7.3 (*c* 2.15, $CHCl_3$); δ_H 1.33 and 1.51 (3 H each, 2 × s, CMe_2), 2.45 (3 H, s, C_6H_4Me), 3.32 (1 H, dd, $J_{6,6'}$ 9.8, $J_{5,6'}$ 5.5, 6-H'), 3.37 (1 H, t, $J_{5,6}$ 9.6, 6-H), 3.38 (3 H, s, OMe), 3.91 (1 H, d, $J_{4,5}$ 1.1, $J_{3,4}$ ~0, 4-H), 4.08 (2 H, s, 1-H_2), 4.21 (1 H, ddd, 5-H), 4.55 (1 H, s, 3-H) and 7.34 and 7.78 (2 H each, 2 × d, J 8.2, C_6H_4); *m/z* 483 ($M^+ - CH_3$, 21%), 409 (5), 270 (20), 237 (18), 155 (29), 91 (38) and 85 (100).

Compound **7b**: needles, m.p. 39–40 °C (from AcOEt–hexane); R_f 0.65 (Solvent D); δ_H 1.44 and 1.56 (3 H each, 2 × s, CMe_2), 3.37 (1 H, dd, $J_{6,6'}$ 9.7, $J_{5,6'}$ 5.6, 6-H'), 3.39 (1 H, dd, $J_{5,6}$ 9.2, 6-H), 3.41 and 3.53 (1 H each, 2 × d, $J_{1,1'}$ 10.7, 1-H_2), 3.45 (3 H, s, OMe), 3.91 (1 H, dd, $J_{4,5}$ 1.9, $J_{3,4}$ 0.9, 4-H), 4.26 (1 H, ddd, 5-H) and 4.60 (1 H, br s, 3-H).

(B) *Procedure for compounds* **20** *and* **27a, b**. A solution of 6-*O*-tosyl compound (1.00 mmol) and sodium iodide (750 mg, 5.00 mmol) in dry acetone (10 cm^3) was heated in a sealed tube at 100 °C for 5 h. The reaction mixture was worked up as described above (Procedure A).

Methyl 6-*deoxy*-6-*iodo*-1,3-O-*isopropylidene*-4-O-*methyl*-α-D-*fructofuranoside* **20**: syrup (91% yield from **19**) [Found: ($M^+ - OCH_3$), 327.0099. $C_{11}H_{19}IO_5$ requires (M − 31), 327.0095]; R_f 0.38 (Solvent D); δ_H 1.38 and 1.45 (3 H each, 2 × s, CMe_2), 3.29 and 3.43 (3 H each, 2 × s, OMe), 3.37 (2 H, d, $J_{5,6}$ 6.3, 6-H_2), 3.53 (1 H, dd, $J_{4,5}$ 4.7, $J_{3,4}$ 1.1, 4-H), 3.79 and 3.91 (1 H each, 2 × d, $J_{1,1'}$ 12.2, 1-H_2), 4.03 (1 H, td, 5-H) and 4.09 (1 H, d, 3-H); *m/z* 327 ($M^+ - OCH_3$, 2.8%), 286 (100), 239 (22), 159 (21), 149 (40), 85 (26) and 73 (96).

3,4-*Di*-O-*acetyl*-6-*deoxy*-6-*iodo*-1,2-O-*isopropylidene*-β-D-*fructofuranose* **27a**: needles (96% yield from **26a**), m.p. 80–81 °C (from AcOEt–hexane) (Found: C, 37.9; H, 4.8%; M^+, 414.0169. $C_{13}H_{19}IO_7$ requires C, 37.70; H, 4.62%; M, 414.0176); R_f 0.55 (Solvent C); δ_H 1.36 and 1.53 (3 H each, 2 × s, CMe_2), 2.09 and 2.12 (3 H each, 2 × s, OAc), 3.40 (1 H, dd, $J_{6,6'}$ 10.2, $J_{5,6'}$ 8.1, 6-H'), 3.50 (1 H, dd, $J_{5,6}$ 6.6, 6-H), 4.09 and 4.12 (1 H each, 2 × d, $J_{1,1'}$ 9.5, 1-H_2), 4.16 (1 H, ddd, $J_{4,5}$ 4.0, 5-H), 5.29 (1 H, dd, $J_{3,4}$ 6.1, 4-H) and 5.32 (1 H, d, 3-H); *m/z* 414 (M^+, 6.3%), 399 (100), 339 (37), 297 (30), 237 (45), 171 (43), 129 (29), 117 (37) and 72 (60).

6-*Deoxy*-6-*iodo*-1,2-O-*isopropylidene*-3,4-*bis*-O-(*tetrahydropyran*-2-*yl*)-β-D-*fructofuranose* **27b**: syrup (89% yield from **26b**); R_f 0.45–0.42 (Solvent C). Recrystallization of this syrup from hexane gave one pure isomer (10% yield) as needles, m.p. 116–118 °C [Found: ($M^+ - CH_3$), 483.0897. $C_{19}H_{31}IO_7$ requires (M − 15), 483.0880]; δ_H 1.45 and 1.57 (3 H each, 2 × s, CMe_2), 1.50–1.82 (12 H, m, 3- and 4-O-CH[CH_2]$_3$), 3.35 (1 H, dd, $J_{6,6'}$ 10.2, $J_{5,6}$ 9.3, 6-H'), 3.51, 3.52, 3.85 and 3.90 (1 H each, 4 m, 3- and 4-OCHOCH_2), 3.62 (1 H, dd, $J_{5,6}$ 2.9, 6-H), 4.04 (1 H, ddd, $J_{4,5}$ 5.5, 5-H), 4.08 (1 H, dd, $J_{3,4}$ 7.4, 4-H), 4.09 and 4.15 (1 H each, 2 × d, $J_{1,1'}$ 9.1, 1-H_2), 4.18 (1 H, d, 3-H) and 4.65 and 4.86 (1 H each, 2 × br t, J 3.5, 3- and 4-OCH); *m/z* 483 ($M^+ - CH_3$, 0.8%), 171 (2.3) and 85 (100).

General Procedures for the Preparation of 6-*Deoxy*-6-[(R *and* S)-(*ethoxy*)*phenylphosphinoyl*]-D-*fructofuranoses* **8**, **21** *and* **28a, b**.—A mixture of the 6-deoxy-6-iodo compound (2.0 mmol) and diethyl phenylphosphonite (4.0 cm^3, 21 mmol) was heated at 150 °C for 6–10 h under argon and was then concentrated under reduced pressure. The residue was purified by column chromatography to give 6-deoxy-6-phosphinoyl compounds.

6-*Deoxy*-6-[(*ethoxy*)*phenylphosphinoyl*]-2,3-O-*isopropylidene*-4-O-*methyl*-1-O-*tosyl*-β-D-*fructofuranose* **8**: syrup (82% yield from **7a**) (Found: M^+, 540.1573. $C_{25}H_{33}O_9PS$ requires M, 540.1583); R_f 0.47 (Solvent A); δ_P 37.9 and 38.3* (a 56:44* mixture with regard to the phosphorus atom); δ_H 1.28 and 1.29* (3 H each, 2 × t, J_{Et} 7.1, $POCH_2Me$), 1.30, 1.32,* 1.44 and 1.46* (3 H each, 4 × s, CMe_2), 2.34* and 2.43 (1 H each, td* and m, $J_{6,6'}$ 15.5,* $J_{6',P}$ 14.5,* $J_{5,6'}$ 4.5,* 6-H'), 2.44 and 2.57* (1 H each, m and td,* $J_{6,P}$ 16.0,* $J_{5,6}$ 10.3,* 6-H), 2.43* and 2.44 (3 H each, 2 × s, C_6H_4Me), 3.27 and 3.29* (3 H, 2 × s, OMe), 3.83 and 3.97* (1 H each, 2 × br s, $J_{4,5}$ 1.0, $J_{3,4}$ 0.5, 4-H), 3.86 and 3.86* (1 H each, dquint, $^2J_{H,H'}$ 10.0, $^3J_{H',P}$ 7.1, POCH'), 3.98,* 4.02, 4.03* and 4.07 (1 H each, 4 × d, $J_{1,1'}$ 10.7, 1-H_2), 4.07 and 4.07* (1 H each, dquint, $^3J_{H,P}$ 7.1, POCH), 4.22* and 4.43 (1 H each, 2 × dddd, $J_{5,6}$ 10.3* and 7.3, $J_{5,P}$ 7.0* and 8.0, $J_{5,6'}$ 4.5* and 6.1, 5-H), 4.47 and 4.48* (1 H each, 2 × br s, 3-H), 7.31,* 7.33, 7.75* and 7.77 (2 H each, 4 × d, J 8.2, C_6H_4), 7.48* and 7.49 [2 H each, 2 × m, Ph(*m*)], 7.66* and 7.66 [1 H each, m, Ph(*p*)] and 7.75* and 7.75 [2 H each, m, Ph(*o*)]; *m/z* 540 (M^+, 0.9%), 525 (2.2), 482 (1.6), 355 (3.3), 297 (54), 213 (11), 141 (34) and 85 (100).

In the preparation of compound **8**, 6-deoxy-2,3-*O*-isopropylidene-4-*O*-methyl-1-*O*-tosyl-β-D-fructofuranose **14** was obtained as a syrupy by-product (4% yield from **7a**); R_f 0.33 (Solvent D); δ_H 1.35 and 1.51 (3 H each, 2 × s, CMe_2), 1.37 (3 H, d, $J_{5,6}$ 6.7, 6-H_3), 2.44 (3 H, s, C_6H_4Me), 3.35 (3 H, s, OMe), 3.57 (1 H, dd, $J_{4,5}$ 3.1, $J_{3,4}$ 1.2, 4-H), 4.06 (1 H, qd, 5-H), 4.07 and 4.09 (1 H each, 2 × d, $J_{1,1'}$ 10.6, 1-H_2), 4.53 (1 H, d, 3-H) and 7.34 and 7.79 (2 H each, 2 × d, J 8.1, C_6H_4).

Methyl 6-*Deoxy*-6-[(*ethoxy*)*phenylphosphinoyl*]-1,3-O-*isopropylidene*-4-O-*methyl*-α-D-*fructofuranoside* **21**: syrup (81% yield from **20**) [Found: (M^+ + H), 401.1747. $C_{19}H_{29}O_7P$ requires (M + 1), 401.1729]; R_f 0.24 (Solvent A); δ_P 38.5 and 38.9* (a 1:1 mixture with regard to the phosphorus atom); δ_H 1.30 and 1.31* (3 H each, 2 × t, J_{Et} 7.1, $POCH_2Me$), 1.32, 1.33,* 1.41 and 1.41* (3 H each, 4 × s, CMe_2), 2.37 and 2.40* (1 H each, td and dd,* $J_{6',P}$ 14.4 and 15.4,* $J_{6,6'}$ 15.0, $J_{5,6'}$ 7.1 and 7.0,* 6-H'), 2.40* and 2.46 (1 H each, dd* and td, $J_{6,P}$ 15.4* and 15.6, $J_{5,6}$ 7.0* and 6.7, 6-H), 3.15, 3.19,* 3.28 and 3.38* (3 H each, 4 × s, OMe), 3.51 and 3.59* (1 H each, 2 × dd, $J_{4,5}$ 5.0 and 4.4,* $J_{3,4}$ 1.1 and 1.0,* 4-H), 3.55, 3.67,* 3.78 and 3.84* (1 H each, 2 × d, $J_{1,1'}$ 12.1, 1-H_2), 3.87–3.93 (1 H, m, POCH'), 3.97 and 3.98* (1 H each, 2 × d, 3-H), 4.07–4.13 (1 H, m, POCH), 4.13* and 4.19 (1 H each, 2 × qd, $J_{5,P}$ 7.4* and 7.6, 5-H), 7.48 [2 H, m, Ph(*m*)], 7.55 [2 H, m, Ph(*p*)] and 7.81 [1 H, m, Ph(*o*)],* the assignments of some of the δ-values may have to be interchanged; *m/z* 401 (M^+ + 1, 0.4%), 385 (4.4), 328 (2.3), 311 (51), 296 (36), 253 (7.6), 241 (18), 213 (100), 169 (20), 141 (63) and 111 (35).

3,4-*Di*-O-*acetyl*-6-*deoxy*-6-[(*ethoxy*)*phenylphosphinoyl*]-1,2-O-*isopropylidene*-β-D-*fructofuranose* **28a**: syrup (89% yield from **27a**) [Found: ($M^+ - CH_3$), 441.1320. $C_{21}H_{29}O_9P$ requires (M − 15), 441.1314]; R_f 0.40 (Solvent A); δ_P 38.2 and 39.1* (a 58:42* mixture with regard to the phosphorus atom); δ_H 1.04,* 1.27,* 1.34 and 1.41 (3 H each, 4 × s, CMe_2), 1.28* and 1.29 (3 H each, 2 × t, J_{Et} 7.1, $POCH_2Me$), 2.05, 2.08,* 2.09* and 2.10 (3

H each, 4 × s, OAc), 2.43* and 2.47 (1 H each, 2 × ddd, $J_{6,6'}$ 15.2, $J_{6',P}$ 11.0* and 14.1, $J_{5,6}$ 8.6* and 5.4, 6-H'), 2.52 and 2.56* (1 H each, 2 × ddd, $J_{6,P}$ 13.5 and 18.6,* $J_{5,6}$ 8.0 and 4.9,* 6-H), 3.84* and 3.89 (1 H each, 2 × dquint, $^2J_{H,H'}$ 10.2, $^3J_{H',P}$ 7.1, POCH'), 3.87,* 4.02, 4.04* and 4.10 (1 H each, 4 × d, $J_{1,1'}$ 9.4, 1-H_2), 4.04* and 4.10 (1 H each, 2 × dquint, $^3J_{H,P}$ 7.1, POCH), 4.39 and 4.35* (1 H each, 2 × tt, $J_{5,P}$ 8.3 and 8.4,* $J_{4,5}$ 4.7 and 5.3,* 5-H), 5.23* and 5.26 (1 H each, 2 × d, $J_{3,4}$ 6.7* and 6.5, 3-H), 5.265 and 5.35* (1 H, 2 × dd, 4-H), 7.47* and 7.48 [2 H each, 2 × m, Ph(*m*)], 7.53* and 7.55 [1 H each, 2 × m, Ph(*p*)] and 7.77 and 7.77* [2 H each, m, Ph(*o*)]; *m/z* 441 ($M^+ - CH_3$, 23%), 385 (17), 343 (21), 296 (8), 279 (100), 239 (96), 187 (11) and 141 (64).

As a by-product of compound **28a**, 3,4-*di*-O-*acetyl*-6-*deoxy*-1,2-O-*isopropylidene*-β-D-*fructofuranose* **32** was obtained as prisms (2% yield from **27a**), m.p. 60–61 °C (from AcOEt–hexane) (Found: M^+, 288.1204. $C_{13}H_{20}O_7$ requires M, 288.1209); R_f 0.47 (Solvent C); $[\alpha]_D$ −83 (*c* 1.08, $CHCl_3$); δ_H 1.36 and 1.49 (3 H each, 2 × s, CMe_2), 1.44 (3 H, d, $J_{5,6}$ 6.5, 6-H_3), 2.08 and 2.12 (3 H each, 2 × s, OAc), 4.01 (1 H, qd, $J_{4,5}$ 4.8, 5-H), 4.02 and 4.13 (1 H each, 2 × d, $J_{1,1'}$ 9.3, 1-H_2), 5.14 (1 H, dd, $J_{3,4}$ 6.1, 4-H) and 5.30 (1 H, d, 3-H); *m/z* 288 (M^+, 0.4%), 273 (35), 213 (23), 171 (12), 143 (15), 129 (23), 117 (40) and 111 (100).

6-Deoxy-6-[(ethoxy)phenylphosphinoyl]-1,2-*O*-isopropylidene-3,4-bis-*O*-(tetrahydropyran-2-yl)-β-D-fructofuranose **28b**: syrup (71% yield from **27b**); R_f 0.45 (Solvent A); δ_H 1.05, 1.26, 1.27, 1.29, 1.35, 1.36, 1.38 and 1.41 (6 H, 8 × s, CMe_2), 1.26, 1.27 and 1.30 (3 H, 3 × t, J_{Et} 7.1, $POCH_2Me$), 1.45–1.80 (12 H, m, 3- and 4-OCH[CH_2]$_3$), 2.25–2.60 (2 H, m, 6-H_2), 3.35–3.85 (4 H, m, 3- and 4-$OCHOCH_2$), 3.80–4.35 (7 H, m, 1-H_2, 3-, 4- and 5-H, and $POCH_2$), 4.61, 4.63, 4.71, 4.74, 4.77, 4.78, 4.82, 4.86, 4.91 and 4.94 (2 H, 10 × br t, *J* 3.0–3.4, 3- and 4-OCH), 7.45–7.55 [3 H, m, Ph(*m*, *p*)] and 7.72–7.80 [2 H, m, Ph(*o*)].

Preparation of Compound **28b** *from Diacetate* **28a**.—To a solution of compound **28a** (465 mg, 1.02 mmol) in absolute ethanol (2.0 cm^3) at 0 °C was added a 21% ethanolic solution of NaOEt (0.05 cm^3) and the mixture was stirred for 1 h before being neutralized with Amberlite IR-120 (H^+). The resin was filtered off and washed with ethanol. The filtrate was evaporated under reduced pressure. The residue was subjected to the same procedures described for iodide **27b** (from **26b**), thereby giving compound **28b** (468 mg, 85% from **28a**).

3,5-*Di*-O-*acetyl*-6-*deoxy*-4-O-*methyl*-6-*phenylphosphonoyl*-1-O-*tosyl*-D-*fructopyranose* **12** *and its* 1-*Deoxy- and* 1,2-O-*Anhydro Derivatives* **13** *and* **16**.—To a stirred solution of compound **8** (195 mg, 0.361 mmol) in dry toluene (2 cm^3) at −5 °C under Ar was added a solution of SDMA (3.4 mol dm^3 in toluene; 0.21 cm^3, 0.71 mmol) in dry toluene (1 cm^3) in small portions. The mixture was stirred at this temperature for 1 h. Then, water (0.2 cm^3) was added and the mixture was stirred for 30 min. The precipitate was centrifuged, and washed with several portions of benzene. The organic layers were combined, and evaporated under reduced pressure, to give a mixture of 6-deoxy-1-*O*-tosyl-6-phenylphosphinoyl compound **9a** and its 1,6-dideoxy derivative **9b** as a syrup: δ_P for **9a** 19.7 and 21.5, for **9b** 24.3 and 26.2.

The above syrup was immediately treated with propan-2-ol (2 cm^3) and 0.5 mol dm^3 hydrochloric acid (2 cm^3) at 90 °C for 5 h under argon. After cooling, the reactants were neutralized with Amberlite IRA-45. The resin was filtered off, and washed with water. The filtrate was evaporated under reduced pressure to give a mixture of 6-deoxy-4-*O*-methyl-6-phenylphosphonoyl-1-*O*-tosyl-D-fructopyranose **10** and its 1,6-dideoxy analogue **11** as a syrup.

This mixture was acetylated with acetic anhydride (1.0 cm^3) in dry pyridine (2.0 cm^3) for 12 h at 20 °C and was then concentrated under reduced pressure. The residue was separated by column chromatography with a gradient eluent of AcOEt ⟶ (19:1) AcOEt–EtOH, into four fractions, A–D.

Fraction A [R_f 0.55 (Solvent E)] gave 3,5-*di*-O-*acetyl*-6-*deoxy*-4-O-*methyl*-6-[(R)-*phenylphosphonoyl*]-1-O-*tosyl*-β-D-*fructopyranose* **12a** as needles (28.4 mg, 15% from **8**), m.p. 194–195 °C (from AcOEt–hexane) [Found: C, 53.1; H, 5.3%; ($M^+ - OC_6H_4CH_3$), 369.1092. $C_{31}H_{36}O_{11}PS$ requires C, 55.33; H, 5.41%; (M − 107), 369.1103]; $[\alpha]_D$ −91 (*c* 1.01, $CHCl_3$); ^1H and ^{31}P NMR, see Table 1; NOEDS experiment [obsd. NOEs (%) by irradiation of 3-H] 1-H = 1-H' = 2.5 and 4-H = 4.2; *m/z* 369 ($M^+ - OC_6H_4CH_3$, 5.7%), 326 (18), 284 (18), 241 (17), 202 (49), 141 (64), 125 (45) and 85 (100).

Fraction B [R_f 0.49 (Solvent E)] gave 6-P(*S*)-β-isomer **12b** as a syrup (23.8 mg, 12% from **8**); ^1H and ^{31}P NMR, see Table 1; NOEDS experiment [obsd. NOEs (%) by irradiation of 6-H^S] 3-H = 4.5, 5-H = 5.5 and 6-H^R = 21.

Fraction C [R_f 0.44 (Solvent E)] gave a syrup (9.4 mg) which consisted of 6-P(*S*)-α-isomer **12c** (4.3% from **8**) and the 1,2-anhydro-6-P(*R*)-β-D-fructopyranose **16a** (0.8%), the relative amounts being determined from the integral ratio of 4-OMe and ^{31}P signals: ^1H and ^{31}P NMR, see Table 1.

Fraction D [R_f 0.36 (Solvent E)] gave a syrup (7.4 mg) which consisted of the 1,6-dideoxy-6-P(*R*)-β-D-fructopyranose **13a** (2.2% from **8**) and the 1,2-anhydro-6-P(*S*)-β-D-fructopyranose **16b** (3.3%): ^1H and ^{31}P NMR, see Table 1.

Fraction E [R_f 0.28 (Solvent E)] gave the 1,6-*dideoxy*-6-P(S)-β-D-*fructopyranose* **13b** as a syrup (9.2 mg, 6.9% from **8**) [Found: (M^+ + H), 371.1278. $C_{17}H_{23}O_7P$ requires (M + 1), 371.1260]; ^1H and ^{31}P NMR, see Table 1; FAB *m/z* 371 (M^+ + 1, 61%), 329 (17), 311 (20), 249 (38), 235 (58), 155 (39), 125 (65) and 71 (100).

3,5-*Di*-O-*acetyl*-1,2-*anhydro*-6-*deoxy*-4-O-*methyl*-6-[(R)-*phenylphosphonoyl*]-β-D-*fructopyranose* **16a**.—To a solution of compound **12a** (5.5 mg, 0.010 mmol) in dry CH_2Cl_2 (0.20 cm^3) was added a solution of DBU (1.6 mg, 1 mol equiv.) in dry CH_2Cl_2 (0.050 cm^3). After having been stirred for 4 h at room temperature, the solution was evaporated under reduced pressure. The residue was purified by column chromatography to give *title compound* **16a** as a syrup (3.1 mg, 83%) [Found: (M^+ + H), 369.1106. $C_{17}H_{21}O_7P$ requires (M + 1), 369.1103]; R_f 0.44 (Solvent E); FAB *m/z* 369 (M^+ + 1, 100%), 327 (49), 309 (14), 293 (25), 279 (37), 251 (17), 141 (31) and 71 (48).

3,5-*Di*-O-*acetyl*-1,2-*anhydro*-6-*deoxy*-4-O-*methyl*-6-[(S)-*phenylphosphonoyl*]-β-D-*fructopyranose* **16b** *and* 3-O-*Acetyl*-1,2-*anhydro*-5,6-*dideoxy*-4-O-*methyl*-6-[(S)-*phenylphosphonoyl*]-β-D-threo-*hex*-5-*enopyranos*-2-*ulose* **15**.—The same procedure as described above was employed. Compound **12b** was treated with DBU (1 mol. equiv.) to give compound **16b** as prisms (m.p. 119–120 °C) in 85% yield; R_f 0.36 (Solvent E).

When 2 mol equiv. of DBU were employed for the above reaction, *compound* **15** was isolated as a syrup in 80% yield [Found: (M^+ + H), 309.0912. $C_{15}H_{17}O_5P$ requires (M^+ + 1), 309.0892]; R_f 0.36 (Solvent E); δ_P 16.5; δ_H 2.09 (3 H, s, OAc), 2.90 (1 H, dd, $J_{1,1'}$ 4.9, $J_{1',P}$ 3.1, 1-H'), 3.19 (1 H, t, $J_{1,P}$ 4.2, 1-H), 3.52 (3 H, s, OMe), 4.30 (1 H, ddt, $J_{3,4}$ 8.3, $J_{4,P}$ 3.9, $J_{4,5}$ 2.5, $J_{4,6}$ 1.9, 4-H), 5.40 (1 H, dd, $J_{3,P}$ 2.1, 3-H), 6.34 (1 H, ddd, $J_{5,6}$ 13.0, $J_{6,P}$ 10.7, 6-H), 6.98 (1 H, ddd, $J_{5,P}$ 42.2, 5-H), 7.54 [2 H, m, $J_{o,m}$ 7.7, $J_{m,p}$ 7.3, $J_{m,P}$ 3.3, Ph(*m*)], 7.61 [1 H, m, $J_{p,P} = J_{o,p}$ = 1.4, Ph(*p*)] and 7.78 [2 H, m, $J_{o,P}$ 12.4, Ph(*o*)]; FAB *m/z* 309 (M^+ + 1, 76%), 293 (34), 279 (59), 267 (47), 249 (40), 219 (20), 141 (61) and 71 (100).

1,3,5-*Tri*-O-*acetyl*-6-*deoxy*-4-O-*methyl*-6-*phenylphosphonoyl*-D-*fructofuranose* **24**.—By the use of the same procedures as

described for compound **12** (from **8**), compound **21** (130 mg, 0.325 mmol) was converted into a mixture of triacetates **24a–d** and **24c'** *via* intermediates **22** and **23**. The mixture was separated by column chromatography into five fractions, A–E.

Fraction A [R_f 0.49 (Solvent E)] gave the 6-[(S)-*phenylphosphonoyl*]-β-D-*fructofuranose* **24b** as a syrup (19.0 mg, 13% from **21**) [Found: (M^+ + H), 429.1318. $C_{10}H_{25}O_9P$ requires (M^+ + 1), 429.1314]; ^1H and ^{31}P NMR, see Table 1; *m/z* 429 (M^+ + 1, 2.2%), 368 (19), 326 (9.2), 308 (9.2), 295 (52), 271 (36), 266 (53), 235 (48), 223 (45), 125 (52) and 71 (100).

Fraction B [R_f 0.45 (Solvent E)] gave 6-*P*(R)-β-D-*isomer* **24a** as needles (22.7 mg, 16% from **21**), m.p. 182–183 °C (from AcOEt–hexane) [Found: C, 53.4; H, 5.9%; (M^+ + H), 429.1309. $C_{19}H_{25}O_9P$ requires C, 53.27; H, 5.88%; (M^+ + 1), 429.1314]; $[\alpha]_D$ −33 (*c* 0.84, $CHCl_3$); ^1H and ^{31}P NMR, see Table 1; *m/z* 429 (M^+ + 1, 0.8%), 368 (9.9), 326 (7.7), 308 (4.7), 295 (32), 271 (28), 266 (41), 235 (44), 223 (39), 125 (45) and 71 (100).

Fraction C [R_f 0.41 (Solvent E)] gave a syrup (11.0 mg) which consisted of 6-P(*S*)-α-isomer **24c** (3.2% from **21**) and 6-P(*R*)-α-isomer **24d** (4.7%): ^1H and ^{31}P NMR, see Table 1.

Fraction D [R_f 0.37 (Solvent E)] gave the 1,2,3,5-*tetra*-O-*acetyl*-6-*P*(S)-α-*derivative* **24c'** as a syrup (6.3 mg, 4.1% from **21**) [Found: (M^+ + H), 471.1428. $C_{21}H_{27}O_{10}P$ requires (M + 1), 471.1420]; ^1H and ^{31}P NMR, see Table 1; *m/z* 471 (M^+ + 1, 0.8%), 428 (0.9), 368 (15), 326 (6.8), 308 (22), 295 (41), 271 (25), 266 (45), 235 (36), 223 (32), 125 (38) and 71 (100).

1,3,4,5-*Tetra*-O-*acetyl*-6-*deoxy*-6-*phenylphosphonoyl*-D-*fructopyranose* **31** *and* 6-[(1-*Acetoxyethyl*)*phenylphosphonoyl*]-1,2,3,4-*tetra*-O-*acetyl*-6-*deoxy*-β-D-*fructofuranose* **33**.—Similar procedures to those for compound **12** (from **8**) were employed. Thus, compound **28a** (621 mg, 1.36 mmol) was treated with SDMA (5.8 mmol) at −5 °C for 1.5 h, to give diol **29**, which, upon hydrolysis, yielded 6-deoxy-6-phenylphosphonoyl-D-fructopyranose **30** as a syrup. This was converted into a mixture of tetraacetates, which were separated by column chromatography into three fractions, A–C.

Fraction A [R_f 0.59 (Solvent E)] gave one isomer of the 6-[(2-*acetoxyethyl*)*phenylphosphonoyl*]-β-D-*fructofuranose* **33a** as a syrup (13.7 mg, 1.9% from **28a**) [Found: (M^+ − CH_3CO), 499.1367. $C_{24}H_{31}O_{12}P$ requires (M − CH_3CO), 499.1370]; δ_P 35.4; δ_H 1.31 (3 H, dd, $^3J_{H,P}$ 14.8, $^3J_{H,H}$ 6.9, PCMe), 2.04, 2.05, 2.09, 2.095 and 2.10 (3 H each, 5 × s, OAc), 2.41 (1 H, td, $J_{6',P}$ 15.2, $J_{6,6'}$ 15.1, $J_{5,6'}$ 3.4, 6-H'), 2.58 (1 H, ddd, $J_{5,6}$ 9.5, $J_{6,P}$ 6.6, 6-H), 4.28 and 4.56 (1 H each, 2 × d, $J_{1,1'}$ 12.0, 1-H_2), 4.80 (1 H, tdd, $J_{5,P}$ 8.7, $J_{4,5}$ 6.7, 5-H), 5.06 (1 H, dd, $J_{3,4}$ 4.2, 4-H), 5.55 (1 H, quint, $^2J_{H,P}$ 6.8, PCH), 5.76 (1 H, d, 3-H), 7.52 [2 H, m, $J_{o,m}$ 8.4, $J_{m,p}$ 7.4, $J_{m,P}$ 3.0, Ph(*m*)], 7.59 [1 H, m, $J_{o,p} = J_{p,P}$ = 1.5, Ph(*p*)] and 7.79 [2 H, m, $J_{o,P}$ 11.0, Ph(*o*)]; *m/z* 499 (M^+ − CH_3CO, 0.3%), 483 (8.2), 455 (8.7), 427 (11), 413 (27), 338 (17), 294 (30), 251 (100), 235 (25), 211 (188) and 125 (59).

Fraction B [R_f 0.52 (Solvent E)] gave a syrup (137 mg) which consisted of the 6-[(R)-*phenylphosphonoyl*]-β-D-*fructopyranose* **31a** (13% from **28a**), its 6-P(*S*)-α-isomer **31c** (5.9%), and another isomer of the β-D-fructofuranose **33b** (2.8%). Compound **31a** was separated by fractional recrystallization from AcOEt–hexane, m.p. 232–233 °C [Found: C, 52.7; H, 5.65%; (M^+ + H), 457.1259. $C_{20}H_{25}O_{10}P$ requires C, 52.64; H, 5.62%; (M + 1), 457.1264]; ^1H and ^{31}P NMR for **31a**, **c**, see Table 1; δ_P for **33b** 34.0; δ_H for **33b** 1.38 (3 H, dd, $^3J_{H,P}$ 14.5, $^3J_{H,H}$ 7.0, PCH*Me*), 2.03, 2.05, 2.06, 2.09 and 2.13 (3 H each, 5 × s, OAc), 2.52 (1 H, ddd, $J_{6,6'}$ 15.4, $J_{6',P}$ 10.9, $J_{5,6'}$ 5.4, 6-H'), 2.69 (1 H, ddd, $J_{6,P}$ 11.6, $J_{5,6}$ 6.7, 6-H), 4.30 and 4.50 (1 H each, 2 × d, $J_{1,1'}$ 12.0, 1-H_2), 4.72 (1 H, dq, $J_{5,P}$ 11.3, $J_{4,5}$ 6.4, 5-H), 5.08 (1 H, dd, $J_{3,4}$ 3.7, 4-H), 5.35 (1 H, qd, $^2J_{H,P}$ 1.0, PCH), 5.67 (1 H, d, 3-H), 7.52 [2 H, m, Ph(*m*)], 7.55 [1 H, m, Ph(*p*)] and 7.73 [2 H, m, Ph(*o*)]; *m/z* for **31a** 457 (M^+ + 1, 1.5%), 413 (26), 399 (29), 371 (10), 354 (14), 294 (75), 252 (100), 235 (70), 211 (63), 193 (30), 141 (41) and 125 (67).

Fraction C [R_f 0.45 (Solvent E)] gave the 1,2,3,4,5-*tetra*-O-*acetyl*-6-*P*(S)-α-*derivative* **31c'** as a syrup (35.2 mg, 5.7% from **28a**) [Found: (M^+ + H), 499.1379. $C_{22}H_{27}O_{11}P$ requires (M + 1), 499.1369]; ^1H and ^{31}P NMR, see Table 1; *m/z* 499 (M^+ + 1, 1.8%), 456 (1.7), 413 (8.1), 397 (16), 354 (17), 337 (19), 294 (84), 279 (20), 252 (100), 235 (76), 211 (46), 141 (40) and 125 (70).

When compound **28b** was subjected to the same procedures as described above, compounds **31a** (16% from **28b**), **31c** (14%) and **31c'** (4.3%) were obtained without formation of compound **33** [Found for **31c**: (M^+ + H), 457.1272. $C_{20}H_{25}O_{10}P$ requires (M + 1), 457.1264]; *m/z* 457 (M^+ + 1, 1.8%), 413 (3.4), 297 (7.5), 354 (15), 337 (12), 294 (78), 252 (100), 235 (82), 211 (27), 193 (32), 141 (34) and 125 (62).

Acknowledgements

We are grateful to the SC-NMR Lab., Okayama University, for the NMR measurements, and to the Saneyoshi Scholarship Foundation for a research grant (to T. H.) which partially supported this work.

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Paper 3/00837A
Received 11*th February* 1993
Accepted 25*th February* 1993