HPLC): $^{31}P[^1H]$ NMR δ -34.5 (d, P_γ), 10.4 (d, P_α), 22.2 (dd, P_β); $J_{P_\alpha-P_\gamma}$ = 19.4 Hz, $J_{P_\beta-P_\alpha}$ = 28.8 Hz (Figure 1). The NMR spectrum (Figure 1) is indistinguishable from a commercial sample of ATP-γ-S; the chemical shifts and the P-P coupling constants are in good agreement with literature values.[39]

ATP-γ-S, Tetrasodium Salt. The second half of the glycerokinase-treated reaction mixture (1.4 L, 33 mmol of ATP-γ-S) was adsorbed on Dowex 1 (900 g, 200-400 mesh, CO_3^{2-} form, supported in a 1-L filter) and washed as above with 4 L of 0.01 M HCl-0.2 M NaCl. The resin was washed with an additional 2 L of doubly distilled water, before the ATP-γ-S was desorbed by washing with 4 L of saturated aqueous $(NH_4)_2CO_3$ (~2 M). Most of the $(NH_4)_2CO_3$ was removed by addition of Dowex-50 W (H^+ form, ~2000 g) until the pH reached 3-4 at 0 °C. The mixture was filtered to separate the resin and the pH adjusted immediately to 7.5 by addition of NaOH (2 M). Most of the yellow color present in the solution was removed by passing the solution through charcoal (only ~25 g of acidic charcoal, since ATP-γ-S adsorbs on charcoal), and the solution was concentrated at reduced pressure to a final volume of ~500 mL. Addition of 3 L of ice-cold acetone followed by filtration afforded 15.8 g of solid containing 83% by weight ATP-γ-S, tetrasodium salt (21.3 mmol, 65% isolated yield, 53% overall reaction based on ADP), <1% by weight ATP tetrasodium salt and 8% by weight ADP disodium salt (determined by HPLC).

(39) Jaffe, E. K.; Cohn, M. *Biochemistry* **1978**, *17*, 652-657.

Registry No. ATP-γ-S, 35094-46-3; DHA, 96-26-4; DHAP, 57-04-5; ADP, 58-64-0; ATP-γ-S·2Ba, 88453-51-4; ATP-γ-S·4Na, 88453-52-5; GAPDH, 9001-50-7; PGK, 9001-83-6; LDH, 9001-60-9; GK, 9030-66-4; PK, 9001-59-6; TIM, 9023-78-3; ATP, 56-65-5; NAD, 53-84-9; D-glyceraldehyde-3-phosphate, 591-57-1; phosphorothioic acid, 13598-51-1; 1-(thiophospho)-3-phospho-D-glycerate, 88548-22-5.

Synthesis of 1,2,3,5-Tetra-*O*-acetyl-4-deoxy-4-*C*-[(*RS*)-ethylphosphinyl]-α,β-D-ribo- and -L-lyxofuranoses and Their Structural Analysis by 400-MHz Proton Nuclear Magnetic Resonance

Hiroshi Yamamoto,[1a] Yuhji Nakamura,[1a] Saburo Inokawa,*[1a] Mitsuji Yamashita,[1b] Margaret-Ann Armour,[1c] and Thomas T. Nakashima[1c]

Department of Chemistry, Faculty of Science, Okayama University, Okayama 700, Japan, Department of Synthetic Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432, Japan, and Department of Chemistry, The University of Alberta, Edmonton, Alberta T6G 2G2, Canada

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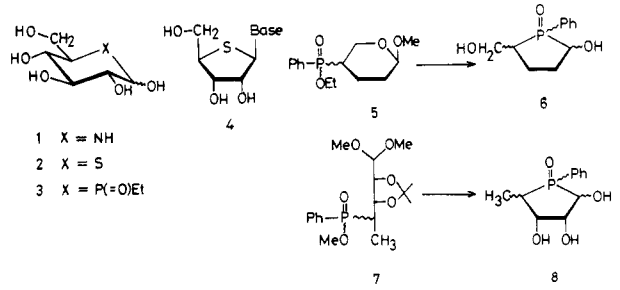
Treatment of 2,3,5-tri-*O*-benzyl-β-D-ribofuranose with 2,4-pentanediol gave 1',3'-dimethyl-1',3'-propanediyl acetal (**10**), which subsequently led to various 4-deoxy-4-*C*-(methoxyphosphinyl)-4-*C*-[(*p*-tolylsulfono)-hydrazino]-D-*erythro*-pentose derivatives (**14**, **19-21**). The reductive removal of the 4-*C*-(*p*-tolylsulfono)hydrazino group from these intermediates to obtain the open-chain precursors was found to be unsatisfactory. Methyl 2,3-*O*-isopropylidene-α-L-lyxopyranoside (**24**) was successfully converted into methyl 4-deoxy-2,3-*O*-isopropylidene-4-*C*-(methoxyethylphosphinyl)-β-D-ribo- and -α-L-lyxopyranoside (**28**), which in turn was led to the title compounds (**31-34**). The structures of these products were established on the basis of mass and 400 MHz ^1H NMR spectra. A possible reaction pathway for the predominant formation of these 4-deoxy-4-*C*-phosphinyl-D-ribofuranoses is discussed.

A large number of monosaccharides having nitrogen or sulfur in the hemiacetal ring [e.g., analogues (1,[2] 2,[3] 4[4]) of

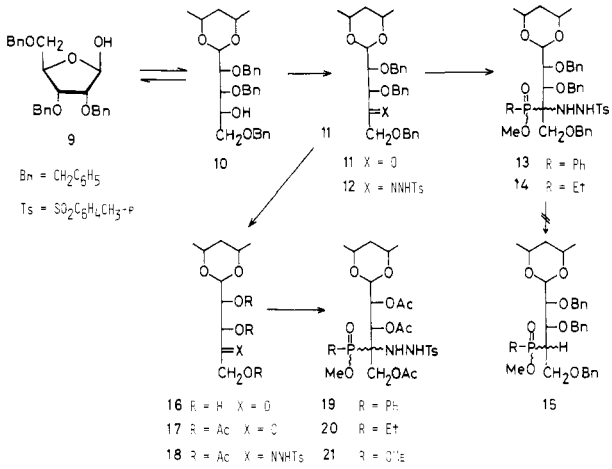


D-glucopyranose and D-ribofuranose] have been synthesized mostly in the interest of a wide variety of their pharmacological activities.[5] Thus, sugar analogues with cyclically held phosphorus are also considered to be of interest from the viewpoint of the potential utility of their biological activities as well as their physicochemical properties.[6] In our effort to prepare such pyranoid compounds, we recently reported[7,8] various 5-deoxy-5-*C*-phosphinyl-D-xylo-, -D-gluco-, and -L-idopyranoses (e.g., **3**). As for the furanoid analogues, apparently owing to the difficulties in preparing their appropriate precursors, only two examples have been reported so far: namely, 2,3,4-trideoxy-4-*C*-(phenylphosphinyl)pentofuranoses[9] (**6**) and 4,5-dideoxy-4-*C*-(phenylphosphinyl)-D-ribo- and -L-lyxofuranoses[10,11] (**8**) via precursors **5** and **7**, respectively. In

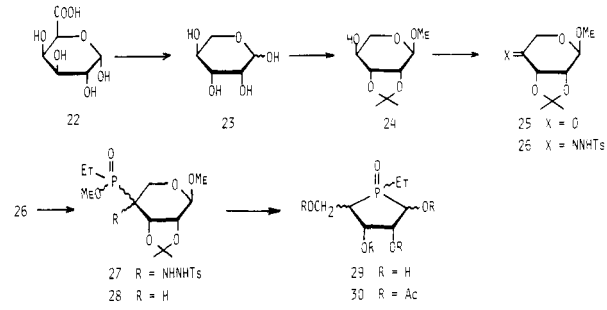
(1) (a) Okayama University. (b) Shizuoka University. (c) The University of Alberta.
(2) Inouye, S.; Tsuruoka, T.; Ito, T.; Niida, T. *Tetrahedron* **1968**, *24*, 2125 and references cited therein.
(3) Whistler, R. L.; Lake, W. C. *Biochem. J.* **1970**, *130*, 919. Chen, M.; Whistler, R. L. *Arch. Biochem. Biophys.* **1975**, *169*, 392 and references cited therein. Kim, J. H.; Kim, S. H.; Hahn, E. W. *Science* **1978**, *200*, 206. Song, C. W.; Guertin, D. P.; Levitt, S. H. *Int. J. Radiat. Oncol., Biol. Phys.* **1979**, *5*, 965.
(4) Anisuzzman, A. K. M.; Whistler, R. L. *Carbohydr. Res.* **1977**, *55*, 205 and references cited therein.
(5) For reviews, see: Paulsen, H.; Todt, K. *Adv. Carbohydr. Chem.* **1968**, *23*, 115. Horton, D.; Hutson, D. H. *Ibid.* **1963**, *18*, 123.
(6) For a review, see: Yamamoto, H.; Inokawa, S. *Adv. Carbohydr. Chem. Biochem.*, in press.
(7) Yamamoto H.; Yamamoto, K.; Inokawa, S.; Yamashita, M.; Armour, M.-A.; Nakashima, T. T. *J. Org. Chem.* **1983**, *48*, 435 and references cited therein.
(8) Yamamoto, H.; Hanaya, T.; Inokawa, S.; Seo, K.; Armour, M.-A.; Nakashima, T. T. *Carbohydr. Res.* **1983**, *114*, 83. Yamamoto, H.; Hanaya, T.; Inokawa, S.; Armour, M.-A. *Ibid.* **1983**, *124*, 195.
(9) Yamashita, M.; Yoshikane, M.; Ogata, T.; Inokawa, S. *Tetrahedron* **1979**, *35*, 741.
(10) Yamamoto, H.; Nakamura, Y.; Kawamoto, H.; Inokawa, S.; Yamashita, M.; Armour, M.-A.; Nakashima, T. T. *Carbohydr. Res.* **1982**, *102*, 185.

0022-3263/84/1949-1364$01.50/0

Scheme I. Preparation of 4-Deoxy-4-*C*-phosphinyl-D-*erythro*-pentose 1′,3′-Dimethyl-1′,3′-propanediyl Acetals



Scheme II. Preparation of 4-Deoxy-4-*C*-(ethylphosphinyl)-D-ribo- and -L-lyxofuranoses



this paper we wish to describe a new convenient route for the predominant preparation of 4-deoxy-4-*C*-(ethylphosphinyl)-D-ribofuranoses, starting from D-galacturonic acid.[12]

First, we attempted to prepare an open-chain precursor (e.g., **15**) analogous to the D-*erythro*-pentose **7** which had been employed[10] for the synthesis of **8**. Thus, 2,3,5-tri-*O*-benzyl-β-D-ribofuranose (**9**), readily prepared[13] from D-ribose in three steps in an overall yield of 80%, was treated with various diol reagents to effect the ring opening of **9** (utilizing an equilibrium shift), to lead to the 4-OH free, open-chain derivative (Scheme I). After many trials, 2,4-pentanediol was found to be the most effective reagent to provide the acetal **10** (66% yield). The same reaction using other diols such as ethylene glycol or 2,2-dimethyl-1,3-propanediol (or their cyclohexanone acetals), resulted in the formation of very low yields of the acetals analogous to **10**; in these reactions, the main products were furanosides of **9** bearing the diol reagent linearly at C-1 (see Experimental Section).

Having confirmed a smooth cleavage of the protecting group of **10** (to regenerate **9**) by treating with 6 M hydrochloric acid–acetic acid (1:7) at 65 °C, we proceeded to the oxidation of the 4-hydroxyl group of **10** with dimethyl sulfoxide–oxalyl chloride–triethylamine[14] in dichloromethane at −70 °C, affording 2,3,5-tri-*O*-benzyl-D-*erythro*-pent-4-ulose 1′,3′-dimethyl-1′,3′-propanediyl (**11**) quantitatively. Following the similar scheme employed previously,[7] **11** was converted into the (*p*-tolylsulfonyl)-hydrazone **12**, which was then treated with methyl phenyl- and ethylphosphinate in the presence of trifluoromethanesulfonic acid. However, the anticipated addition products were produced in extremely low yields: **13** (~0%) and **14** (10% yield). Moreover, the subsequent reductive removal of the (*p*-tolylsulfonyl)hydrazino group from **14** with sodium borohydride failed to produce the desired precursor **15** (Scheme I).

Since such a poor yield of the addition products **13** and **14** had seemed to be attributed to the relatively large steric hindrance caused by the three benzyloxyl groups on C-2, 3, and 5 of **12**, compound **11** was thus catalytically hydrogenated to triol **16**, which was then peracetylated to provide the tri-*O*-acetate **17**. This was similarly converted into the hydrazone **18**. The following addition reaction of various phosphinates to **18** proceeded more smoothly than to the tri-*O*-benzyl compound **12**, giving the adducts **19** (68% yield), **20** (26%), and **21** (78%). However, the subsequent reductive removal of the (*p*-tolylsulfonyl)hydrazino group from **19**–**21** to obtain the desired precursors analogous to **15** (Scheme I) remained unsuccessful despite many trails under various conditions.

Therefore, we turned our attention to another approach to the preparation of the target compounds: namely, an application of the ring contraction of a pentopyranoid precursor to a pentofuranose, which had been previously employed[9] in the conversion of **5** into **6**. Methyl 2,3-*O*-isopropylidene-α-L-lyxopranoside (**24**), conveniently prepared[15] from D-galacturonic acid (**22**) via L-lyxopyranose (**23**) in 38% overall yield, served as the starting material for this synthesis (Scheme II). Compound **24** was likewise oxidized with the aforementioned reagent [Me_2SO–$(COCl)_2$–Et_3N] to give methyl 2,3-*O*-isopropylidene-β-D-*erythro*-pentopyranosid-4-ulose (**25**: 74% yield), which was then converted into the (*p*-tolylsulfonyl)hydrazone (**26**; 91% yield). The addition of methyl ethylphosphinate to **26** in the presence of trifluoromethanesulfonic acid, afforded the product **27**, which, on reduction with sodium borohydride in oxolane, gave the phosphinate **28** in 42% overall yield from **26**.

Compound **28** was reduced with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA), and then, without isolation, the product was refluxed with ethanolic 0.5 M HCl, affording 4-deoxy-4-*C*-[(*RS*)-ethylphosphinyl]-D-ribo- and -L-lyxofuranoses (**29**), which were characterized by conversion into the peracetates (**30**) with acetic anhydride in pyridine. Purification in a column of silica gel with benzene–ethyl acetate (and then with ethyl acetate–ethanol) as the eluant gave **30** (in 46% overall yield from **28**) as a syrup which consisted of at least seven components (by TLC). By rechromatography with the same eluant, the crude product was separated into five major fractions, which will be referred to as A, B, C, D, and E according to their decreasing R_f values (0.45, 0.40–0.36, 0.32, 0.27, and 0.25–0.16 with 5% ethanol–ethyl acetate).

The fastest eluting fraction A (R_f 0.45) gave a single compound as a colorless syrup. The molecular composition of this product was elucidated by the EI and CI (NH_3) mass spectra, which clearly gave the M + 1 ion at m/z 379,

(11) Luger, P.; Yamamoto, H.; Inokawa, S. *Carbohydr. Res.* **1982**, *110*, 187.

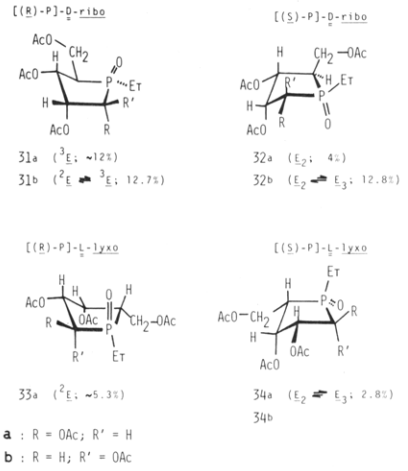
(12) A part of the results has been reported as a preliminary communication: Yamamoto, H.; Nakamura, Y.; Inokawa, S.; Yamashita, M.; Armour, M.-A.; Nakashima, T. T. *Carbohydr. Res.* **1983**, *118*, C7.

(13) Barker, R.; Fletcher, Jr., H. G. *J. Org. Chem.* **1961**, *26*, 4605.

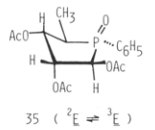
(14) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1970**, *43*, 2480.

(15) Bobek, M.; Whistler, R. L. *Methods Carbohydr. Chem.* **1972**, *6*, 292, and references cited therein, we followed essentially the procedures of the references but, by subjecting the crude intermediates to the subsequent steps, we obtained slightly better yields of the products than those described in the references.

Chart I. Structures of 1,2,3,5-Tetra-*O*-acetyl-4-deoxy-4-*C*-(ethylphosphinyl)pentofuranoses (and their probable conformations; yields)



corresponding to $C_{15}H_{24}O_9P$; detailed analysis of the EI mass spectrum is described later. The precise structure, 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-*C*-[(*R*)-ethylphosphinyl]-β-D-ribofuranose (**31b**; Chart I), for this product was established on the evidence of the 400 MHz ^1H NMR spectrum (see Figure 1), which closely resembled that of the structurally similar peracetate[10] **35** of **8**. The



H-1 signal of **31b** consisted of a triple doublet with intermediate $J_{1,2}$ (6.0 Hz), small $J_{1,P}$ (2.5 Hz), and an extremely small $J_{1,4}$ (~0.5 Hz, long-range coupling) values. As both H-1 and H-4 signals appeared at relatively high field and the absolute configurations of H-2 and H-3 were known, these values led to the 4-*C*-[(*R*)-phosphinyl]-β-D-ribofuranose structure for this product **31b**; assignments of all signals, along with the data of **35** for comparison, are summarized in Table I. That $J_{2,P}$ (10.5 Hz) and $J_{3,P}$ (13.5 Hz) have almost the same magnitude suggests an average conformation of ^2E and ^3E (~1:1), wherein the two dihedral angles of P–C-1–C-2–H and P–C-4–C-3–H become close;[16] this is in conformity with the Karplus rule to the relationship between $^3J_{H,P}$ values and the dihedral angles in P(V) heterocyclic systems.[17] Apparently, the relatively low-energy barrier between these two forms[16] would result in rapidly interconverting conformations in solution.

Fraction B was found to consist of mainly the α-anomer (**31a**; R_f 0.40) of **31b** but contained an inseparable minor component (**33a**; R_f 0.36). The structure of **31a** was derived by the similar NMR spectral analysis, and the parameters of the spectrum are shown in Table I. The remarkable difference in the magnitudes of $J_{2,P}$ (26.5 Hz) and $J_{3,P}$ (1.0 Hz) of **31a** is strongly indicative of an unsymmetrical conformation of the molecule, particularly with respect to H-2 and H-3; the product most likely exists in the ^3E conformation, wherein the dihedral angles P–C-1–C-2–H and P–C-4–C-3–H are ~150° and 90°, respectively (Chart I). Such a shape would allow minimization of nonbonded interactions due to the substituents on the adjacent atoms, as had been confirmed[11] by X-ray crystallographic analysis

Table I. ^1H NMR (400 MHz) Parameters for Peracetylated 4-Deoxy-4-*C*-(ethylphosphinyl)-D-ribo- and -L-lyxofuranoses in $CDCl_3$[a]

compd	chemical shift														
	H-1	H-2	H-3	H-4	H-5	H-5′	AcO-1,2,3,5[b]	P-CH–Me	P-CH′–Me	P-C-CH_3
31a	5.45	5.78	5.39	2.58	4.46	4.37	2.17, 2.13, 2.12, 2.08	2.1[c]	1.92	1.39
31b	4.97	5.66	5.54	2.62	4.53	4.30	2.23, 2.13, 2.12, 2.10	2.28	2.01	1.35
35[d]	5.15	5.72	5.46	2.67	1.39[e]		2.23, 2.14, 2.12	7.90, 7.58, 7.62[f]		
32a	4.97	5.75	5.00	3.12	4.47	4.34	2.22, 2.19, 2.11, 2.09	2.08	2.05	1.30
32b	5.43	5.36	5.20	2.95	4.43	4.34	2.19, 2.18, 2.14, 2.11	2.00	1.94	1.29
33a	4.98	5.50	5.68	2.88	4.45[c]	4.30	2.22, 2.17, 2.13, 2.09	2.04[c]	1.83	1.23
34a	5.92	4.80	5.8[c]	2.48	4.29	4.20	2.20, 2.16, 2.13, 2.02	1.74	1.69	1.21

compd	coupling constants[g]														
	$J_{1,2}$	$J_{1,P}$	$J_{1,4}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,5'}$	$J_{4,P}$	$J_{5,5'}$	$J_{5,P}$	$J_{5',P}$	$^2J_{H,P}$	$^2J_{H',P}$	$^2J_{H,H}$	$^3J_{H,P}$	$^3J_{H,H}$
31a	4.5	12.5	~0	3.0	26.5	11.2	1.0	8.5	5.8	8.7	11.2	12.0	17.0	15.0	9.0	15.0	18.5	7.8
31b	6.0	2.5	~0.5	3.6	10.5	6.0	13.5	7.3	7.5	6.5	12.0	9.2	12.2	15.0	11.5	15.0	17.0	7.5
35[d]	5.7	1.4	~0.5	3.8	11.7	7.0	13.5	7.5		6.0		14.2						
32a	4.8	2.6	~0	3.0	24.6	12.0	1.0	4.8	7.0	22.0	12.0	14.8	17.0	c	c	c	17.0	7.5
32b	3.6	7.8	~0.5	3.8	15.1	10.0	5.5	5.2	6.8	21.2	11.8	14.8	16.0	15.0	10.5	15.0	17.0	7.5
33a	10.0	0.5	~0	~1.0	~3.5	4.0	~25	9.5	6.0	20.5	12	c	c	c	c	c	17.0	7.5
34a	8.6	10.2		3.0	15.2	1.8	~31	11.5	5.2	12.0	11.5	c	c	c	c	c	16.5	7.5

[a] Chemical shifts (δ shifts) are parts per million from Me_4Si. [b] Assignments may have to be interchanged. [c] Values are approximate (or uncertain) because of overlapping with other signals. [d] Reference 10. [e] CH_3. [f] P-C_6H_5 (*o,p,m*). [g] Coupling constants (*J*, Hz) were confirmed by double resonance.

(16) For pseudorotation for furanose sugars, see, e.g.: Hall, L. D.; Steiner, P. R.; Pedersen, C. *Can. J. Chem.* **1970**, *48*, 1155.

(17) Awebouch, O.; Kashman, Y. *Tetrahedron* **1975**, *31*, 33. Chan, T. H.; Nwe, K. T. *Ibid* **1975**, *31*, 2537.

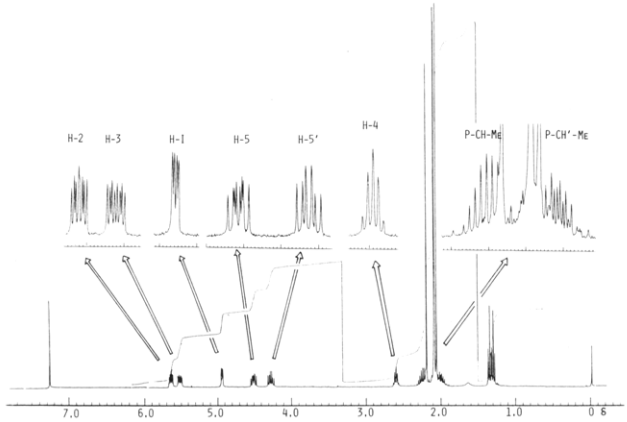


Figure 1. ^{1}H NMR (400 MHz) spectrum of compound **31b** in $CDCl_3$.

of a per-*O*-acetate of **8**. The structure of the [(*R*)-ethylphosphinyl]-α-L-lyxofuranoid form in a ^2E conformation for **33a** was also assigned on the basis of the splitting patterns of its clearly recognizable H-1, H-4, and H-5′ signals and also by analogy with the NMR spectrum of the structurally similar per-*O*-acetyl-4,5-dideoxy-4-*C*-[(*S*)-phenylphosphinyl]-α-lyxopyranose derived from **8**;[10,18] see assignments of the spectrum of **33a** recorded in Table I.

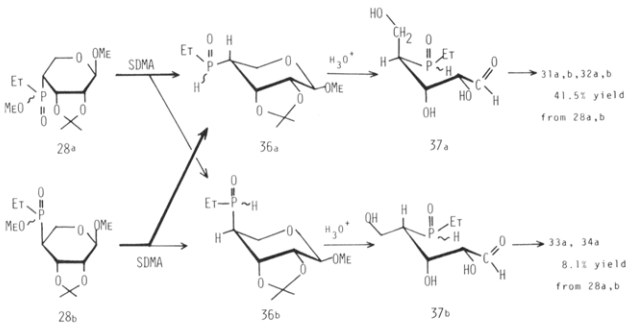
Fraction C (R_f 0.32) contained an almost single product, to which the [(*S*)-ethylphosphinyl]-β-D-ribofuranose structure **32b** was unequivocally assignable by the analysis of its ^{1}H NMR spectral parameters (see Table I); the splitting patterns of **32b** closely resembled those of the structurally similar 1,2,3-tri-*O*-acetyl-4,5-dideoxy-4-*C*-[(*R*)-phenylphosphinyl]-β-D-ribofuranose,[10] which had been considered to exist in an average conformation of E_2 and E_3, wherein the former was the more favored, considering the relative magnitude of $J_{2,P}$ and $J_{3,P}$ values. The EI high-resolution mass spectrum of **32b**, which showed a very similar fragmentation pattern to that of **31b**, supported the molecular composition.

Fraction D (R_f 0.25) gave a single compound of mp 145–146 °C as colorless needles. The EI mass spectrum of this crystalline product gave almost indentical fragmentations with those of **31b** and **32b**, confirming the same molecular composition. A similar analysis of the 400 MHz ^{1}H NMR spectrum established the α-anomeric structure **32a** for the product; the large values of $J_{4,P}$ and $J_{2,P}$ for **32a** should be noted in view of its conformational assignment E_2; see assignments shown in Table I.

The slowest eluting fraction (E) contained mainly one product (R_f 0.27), which was assigned to be 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-*C*-[(*S*)-ethylphosphinyl]-α-D-lyxofuranose (**34a**) in an average conformation of E_3 and E_2, wherein the former is more favored on the basis of $J_{2,P}$ and $J_{3,P}$ values. The NMR signals of other minor product (R_f 0.16) in this fraction was not completely clear, although it was presumed to be due to the other diastereomer **34b** (on the basis of the low R_f value as in the case of the similar analogue[10] obtained from **8**).

The preponderant formation of β-anomers for the D-ribofuranoses and α-anomers for L-lyxofuranoses, compared with the other anomers (see the yields shown in Scheme III), can be rationalized in terms of the more favorable formation of the corresponding anomers of the precursors **29**. The ratio of the combined yields of the D-ribofuranoses (**31a**, **31b**, **32a**, and **32b**) to the L-lyxofuranoses (**33a** and **34a**) is ~5:1, whereas that of *R* and *S* isomers of the ring phosphorus atom is ~3:2. A possible explanation for the predominant formation of the D-ribofuranoses (**31**, **32**) over the L-lyxofuranoses (**33**, **34**) is that thermodynamically favorable intermediate **36a** (compared with **36b**) is probably produced in a larger proportion from both epimers **28a** and **28b** by reduction with strongly basic SDMA, because the rates of the subsequent ring closures of the open-chain phosphinyl intermediates **37a** and **37b** do not seem to differ appreciably, as illustrated in Scheme III. This is in striking contrast to the formation of almost the same ratio of the peracetyl derivatives of D-ribo- and -L-lyxofuranoses (**8**) from the precursor **7**, which had been presumed to be due to an equimolar equilibration by SDMA during the reduction.[10]

Scheme III. Possible Pathway for the Formation of 4-Deoxy-4-*C*-(ethylphosphinyl)-D-ribo- and -L-lyxofuranoses 31–34 from Precursors 28



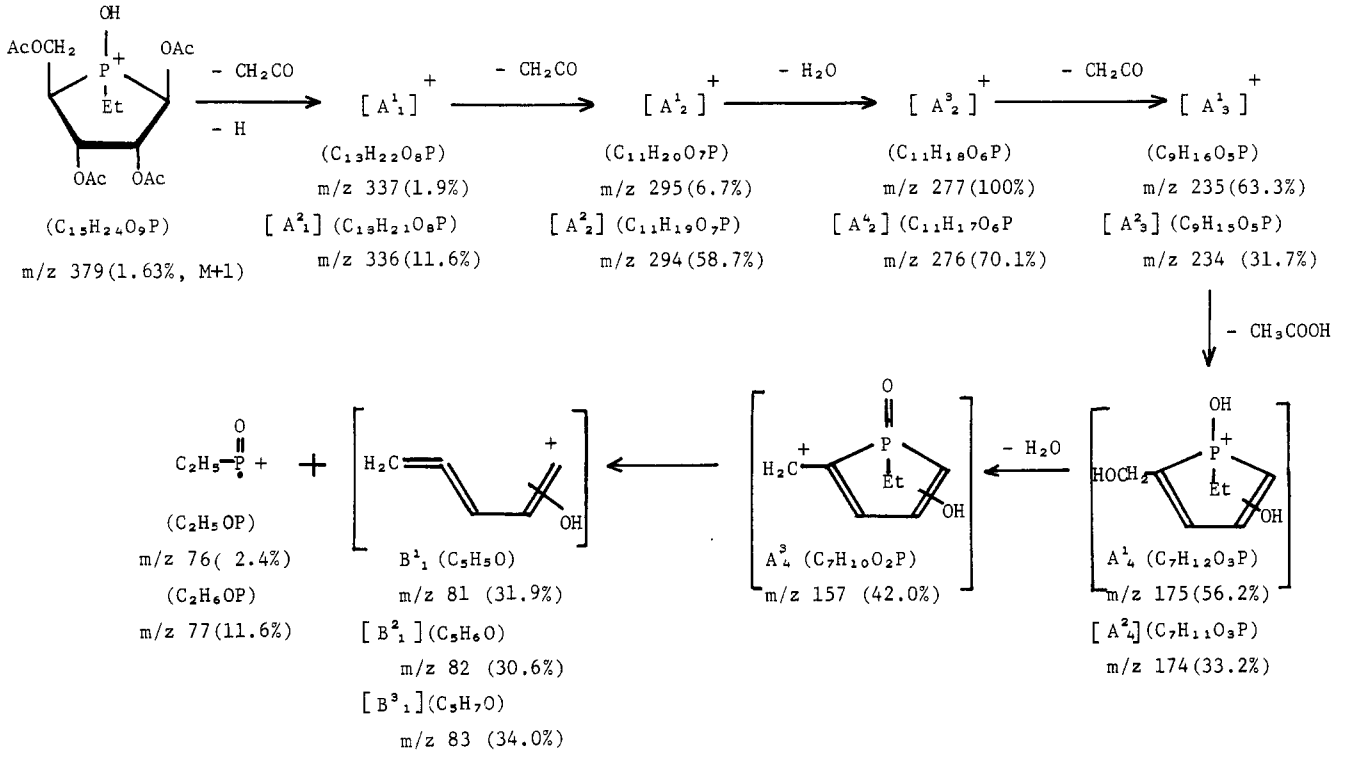
Mass Spectra of Per-*O*-acetylated 5-Deoxy-5-*C*-(ethylphosphinyl)-D-ribofuranoses. There has been reported[19] a systematic analysis of the mass spectra of per-*O*-acetylated derivatives of 5-deoxy-5-*C*-(ethylphosphinyl)-D-glucopyranoses (**3**), 5-deoxy-5-*C*-phosphinyl-D-xylopyranoses, and 4,5-dideoxy-4-*C*-(phenylphosphinyl)-L-lyxofuranoses. Detailed analysis of the EI mass spectrum of compound **31b** is presented here as the first example of the per-*O*-acetylated 4-deoxy-4-*C*-phosphinyl-D-ribofuranoses.

The molecular ion of **31b** is detected as the resonance-stabilized hydroxyphosphonium ion (M + 1) at *m*/*z* 379, similarly to those of other analogues having phosphorus in the hemiacetal ring.[19] Although the relative intensity of the M + 1 ion is rather weak (1.63%) in the EI mass spectrum, the CI–MS (NH_3) of **31b** shows the molecular ion as the base peak (100%) at *m*/*z* 379. As illustrated in Scheme IV, **31b** then gives rise to the major fragmentation of the first series A (according to nomenclature used by Chizhov and Kochetkov[20]), producing ions A_1–A_4 of the λ^5-phosphorole oxide structure, although the position of the hydroxyl group on this ring remained unestablished. It is noteworthy that these species show relatively intense peaks, suggesting the high stability of the phosphorus-containing ring system; this is in contrast to the spectra of per-*O*-acetylated monosaccharides of the oxygenated ring, where the intensities of oxygen containing rings are generally much lower than those of ring-ruptured fragment ions.[21] As in the case of tri-*O*-acetyl-4,5-dideoxy-4-(phenylphosphinyl)-L-lyxofuranoses, the subsequent ring-opening fragmentation seems to take place by the exclusive removal of the ethylphosphine oxide, producing the phosphorus-free fragments B_1. In addition to these ions,

(18) The assignemnt of the signals at δ 5.75 (ddd; *J* = 27, 4.5, and 3.0 Hz) and 5.71, which had been incorrectly made[10] for H-2 and H-3, respectively, should have been reversed.

(19) Yamamoto, H.; Inokawa, S. *Phosphorus and Sulfur* **1983**, *16*, 135.
(20) Kochetkov, N. K.; Chizhov, O. S. *Adv. Carbohydr. Chem.* **1966**, *21*, 39.
(21) Biemann, K.; DeJongh, D. C.; Schnoes, H. K. *J. Am. Chem. Soc.* **1963**, *85*, 1763. DeJongh, D. C.; Biemann, K. *Ibid.* **1963**, *85*, 2289.

Scheme IV. Major Fragmentation of Mass Spectrum of 31b and Probable Structures of the Intermediate Fragments



there existed two, phosphorus-containing fragments of appreciable intensities corresponding to $C_6H_{13}O_4P$ (m/z 180, 60.7%) and $C_4H_{10}O_2P$ (m/z 121, 64.0%); structures of these species, however, could not be identified.

Mass spectra of other diastereomers **32a** and **32b** showed fragmentation patterns similar to that of **31b**. The presence of such a characteristic set of fragmentations in turn conveniently serves to differenciate the mass spectra of the furanoid compounds from those[19] of pyranoid compounds (such as **3**).

Although a more precise mechanistic study with regard to this intricate ring contraction (**28** → **29**), as well as improvement of the yields of some steps, remains to be done, the present work demonstrates a novel way for the preparation particularly of 4-deoxy-4-*C*-phosphinyl-D-ribofuranoses which are considered to be of great value in view of, for example, derivatization to the nucleotide analogues having potential biological activities. This work also establishes the effective use of ^{1}H NMR spectra for determining the configuration and conformation of the D-ribo- and -L-lyxofuranoses containing a phosphorus atom in the ring.

Experimental Section

Melting points were measured with a Yanagimoto MP-S3 instrument and are uncorrected. Column chromatography was performed with Wako C-200 silica gel or, when necessary, by using a Merck Lobar silica gel prepacked column (Size A). TLC was conducted on plates precoated with silica gel 60F (0.25 mm, Merck). ^{1}H NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) with a Hitachi R-20A (60 MHz) or a Bruker WH-400 cryospectrometer (400 MHz, for **31**–**34**) at 27 °C. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0) as the internal standard. Mass spectra were measured with an AEI MS 50 ultrahigh-resolution instrument (for the accurate mass measurement) and an AEI MS 12 apparatus (for chemical ionization with NH_3) and are given in terms of m/z (relative intensity) compared with the base peak. All molecular formulas shown in Scheme IV were supported by the accurate mass of the fragment ions, derivation of which is normally within a range of ±3 ppm error from the calculated values. Optical rotation was determined with a Nohonbunko DIP-4 polarimeter.

2,3,5-Tri-*O*-benzyl-D-ribose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (10). 2,3,5-Tri-*O*-benzyl-β-D-ribofuranose (**9**) was prepared from D-ribose in three steps (80% overall yield) according to the procedures of Barker and Fletcher.[13] A solution of **9** (60 mg, 0.143 mmol), 2,4-pentanediol (0.06 mL, 0.45 mmol), and *p*-toluenesulfonic acid (3 mg) in dry benzene (10 mL) was refluxed for 16 h and then neutralized with solid $NaHCO_3$. After filtration, the solvent was evaporated in vacuo and the residue was purified by silica gel TLC with ethyl acetate–hexane (1:1) as the eluant, giving **10** as a colorless syrup: 48 mg (66%); R_f 0.60 (AcOEt–hexane, 1:2); $[\alpha]^{26}_D$ +34.8 (c 1.04, $CHCl_3$); IR 3400 (OH) cm^{-1}; ^{1}H NMR 1.19, 1.21 (3 H each, d, J = 6.0 Hz, 2 CH_3-1′,3′), 1.1–1.7 (2 H, m, 2 H-2′), 3.05 (1 H, br d, J = 4.5 Hz, OH, exchangeable with D_2O), 3.58 (2 H, d, J = 4.5 Hz, H-5), 3.7–4.2 (5 H, m, H-2,3,4,1′,3′), 4.46–4.80 (6 H, m, O–CH_2–Ph-2,3,5), 4.80 (1 H, d, J = 4.8 Hz, H-1), 7.24, 7.29 (15 H, both s, O–C–C_6H_5-2,3,5). Anal. Calcd for $C_{31}H_{38}O_6$: C, 73.49; H, 7.56. Found: C, 73.75; H, 7.80.

The similar treatment of **9** with 2,2-dimethyl-1,3-propanediol(3 equiv mol) gave 2,3,5-tri-*O*-benzyl-D-ribose 2′,2′-dimethyl-1′,3′-propanediyl acetal [colorless syrup; 13% yield; R_f 0.50 (AcOEt–hexane, 1:2); ^{1}H NMR 0.70, 1.22 (3 H each, s, 2 CH_3-2′), 2.87 (1 H, m, OH), 3.29–4.29 (9 H, m, H-2,3,4,5,1′,3′), 4.47, 4.55 (6 H, s, O–CH_2–Ph-2,3,5), 4.69 (1 H, d, J = 2.7 Hz, H-1), 7.27, 7.31 (15 H, s, O–C–C_6H_5-2,3,5)] and 2′,2′-dimethyl-3′-hydroxylpropyl 2,3,5-tri-*O*-benzyl-β-D-ribofuranoside [colorless syrup; 29% yield; R_f 0.37 (AcOEt–hexane, 1:2); ^{1}H NMR 0.83 (6 H, s, 2 CH_3-2′), 2.96–4.26 (9 H, m, H-2,3,4,5, 4 H-1′,3′), 3.28 (1 H, m, OH), 4.46, 4.50, 4.60 (2 H each, s, O–CH_2–Ph-2,3,5), 4.94 (1 H, s, H-1), 7.33, 7.35 (15 H, s, O–C–C_6H_5-2,3,5)].

Compound **10** was recovered almost quantitatively by refluxing with 0.5 M HCl–MeOH (1:2) for 16 h. However, the treatment of **10** with 6 M HCl–AcOH (1:7) at 65 °C for 1.3 h yielded **9** quantitatively.

2,3,5-Tri-*O*-benzyl-D-*erythro*-pentos-4-ulose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (11). According to the procedures of Mancuso et al.[14] dimethyl sulfoxide (1.03 mL, 9.2 mmol) dissolved in CH_2Cl_2 (3 mL) was added dropwise at −70 °C to a solution of oxalyl chloride (0.61 mL, 9.2 mmol) in CH_2Cl_2 (15 mL). Then a mixture of **10** (4.23 g, 8.35 mmol) and CH_2Cl_2 (6 mL) was slowly added, followed by stirring for 20 min at −70 °C. After addition of triethylamine (4.2 mL), the reaction temperature was allowed to rise gradually to room temperature and then cold water was added. The resultant mixture was extracted with CH_2Cl_2,

and the combined organic layer was successively washed with brine, 1% aqueous HCl, 5% aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and evaporated in vacuo to give **11** as a pale yellow syrup: 4.16 g (99%); R_f 0.63 (AcOEt–hexane, 1:2); $[\alpha]^{26}_D$ +14.2 (*c* 1.10, $CHCl_3$); IR 1720 (C=O) cm^{-1}; ^1H NMR 1.13, 1.23 (3 H each, d, J = 6.0 Hz, 2 CH_3-1′,3′), 1.2–1.5 (2 H, m, 2 H-2′), 3.5–4.0 (2 H, m, H-1′,3′), 4.2–4.85 (11 H, m, H-1,2,3,5, O–CH_2–Ph-2,3,5), 7.30 (15 H, s, O–C–C_6H_5-2,3,5).

2,3,5-Tri-*O*-benzyl-D-*erythro*-pentos-4-ulose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (*E,Z*)-4-[(*p*-Tolylsulfono)hydrazide] (12). To a mixture of finely powdered molecular sieves (3 Å, 2.66 g) and methanol (7 mL) was added *p*-toluenesulfonylhydrazide (735 mg, 3.94 mmol) under stirring, and then **11** (992 mg, 1.97 mmol) was added, followed by stirring at 40 °C for 40 h. The molecular sieves were filtered off and the filtrate was evaporated in vacuo. The residue was diluted with CH_2Cl_2 and washed with dilute HCl, aqueous $NaHCO_3$, and then with water. The organic layer was dried (Na_2SO_4) and evaporated in vacuo to give **12** as a pale yellow syrup: 1.30 g (98%); R_f 0.27 (AcOEt–hexane, 1:4); ^1H NMR δ 1.11, 1.15, 1.22 (6 H, all d, J = 6.0 Hz, 2 CH_3-1′,3′), 1.2–1.5 (2 H, m, 2 H-2′), 2.31 (3 H, s, S–C_6–CH_3), 3.23–3.74 (4 H, m, H-5,1′,3′), 4.13 (1 H, m, H-2), 4.15, 4.20, 4.26 (2 H each, s, O–CH_2–Ph-2,3,5), 4.38 (1 H, br d, J = 4.7 Hz, H-3), 4.64 (1 H, d, J = 4.7 Hz, H-1), 6.83 (1 H, m, NH), 7.20, 7.70 (2 H each, AA′BB′ quartet, $J_{A,B}$ = 8.3 Hz, S–C_6H_4–Me), 7.30 (15 H, s, O–C–C_6H_5-2,3,5). Anal. Calcd for $C_{38}H_{44}N_2O_7S$: C, 67.83; H, 6.59; N, 4.16. Found: C, 67.95; H, 6.81; N, 3.84.

(4*RS*)-2,3,5-Tri-*O*-benzyl-4-deoxy-4-*C*-[(*RS*)-methoxyethylphosphinyl]-4-*C*-[(*p*-tolylsulfono)hydrazino]-D-*erythro*-pentose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (14). To a mixture of methyl ethylphosphinate[22] (0.25 mL, 3.9 mmol) and **12** (215 mg, 0.32 mmol) was added trifluoromethanesulfonic acid (0.019 mL) at 0 °C under argon, followed by stirring at 20 °C for 70 h. The mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and then with water, dried (Na_2SO_4), and evaporated in vauo. The residure was purified by silica gel TLC with ethyl acetate–hexane (4:1) as the eluant, giving, besides recovered **12** (83 mg), **14** as a pale yellow syrup: 25 mg (10%); R_f 0.75 and 0.65 (EtOH–AcOEt, 1:19); ^1H NMR δ 0.83–2.14 (13 H, m, P–Et, 2 CH_3-1′,3′, 2 H-2′), 2.44 (3 H, s, S–C_6–CH_3), 3.41–3.70 (5 H, m, H-5,1′,3′, NH-4), 3.69, 3.76 (3 H, both d, J = 10.5 Hz, P–OMe), 4.23–4.63 (2 H, m, H-2,3), 4.70–5.03 (6 H, m, O–CH_2–Ph-2,3,5), 5.18 (1 H, d, J = 3.0 Hz, H-1), 7.33, 7.39, 7.44 (5 H each, s, O–C–C_6H_5-2,3,5), 7.29, 7.79 (2 H each, AA′BB′ quartet, J = 8.3 Hz, S–C_6H_4–Me), 7.65 (1 H, br s, NH).

When methyl phenylphosphinate was used for the above addition reaction, no expected product **13** was obtained; the starting material **12** was mostly recovered.

Reduction of **14** with sodium borohydride in THF[7,9] was found to give no desired product **15**, but most of **14** was recovered.

2,3,5-Tri-*O*-acetyl-D-*erythro*-pentos-4-ulose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (17). A solution of **11** (927 mg) in ethanol (6 mL) was hydrogenated over 10% Pd/C (200 mg) at 20 °C for 42 h. After filtration of the catalyst, the filtrate was evaporated in vacuo, and the residue, dissolved in acetic acid (5 mL), was again hydrogenated over 10% Pd/C (1.06 g) at 20 °C for 7 h. The mixture was poured into cold aqueous $NaHCO_3$, and the catalyst was filtered off. The filtrate was evaporated in vacuo, and the residue was diluted with EtOH–ethyl acetate (1:5) and filtered through an active carbon bed to remove the resultant sodium acetate. The filtrate was evaporated in vacuo, giving crude D-*erythro*-pentos-4-ulose 1′,3′-dimethyl-1′,3′-propanediyl acetal (**16**) as a colorless syrup [739 mg; R_f 0.07 (AcOEt–hexane, 1:2); ^1H NMR (D_2O/DSS) δ 1.1, 1.2 (3 H each, s, 2 CH_3-1′,3′), 1.4–1.6 (2 H, m, 2 H-2′), 3.55–4.0 (3 H, m, OH), 4.2–4.5 (4 H, m, H-2,3,5), 5.2 (1 H, d, J = 3.0 Hz, H-1).

A mixture of the above product **16**, pyridine (5.6 mL), and acetic anhydride (2.3 mL) was stirred at 0 °C for 10 min and then at 20 °C for 18 h. The mixture was concentrated in vacuo (by pump) and the residue was diluted with CH_2Cl_2 and washed successively with dilute HCl, $NaHCO_3$, and water. After drying (Na_2SO_4), the organic layer was evaporated in vacuo, giving **17** as a pale yellow syrup: 504 mg (76% overall yield from **11**); R_f 0.41 (AcOEt–hexane, 1:2); IR 1820 (C=O), 1740 (ester) cm^{-1}; ^1H NMR 1.18, 1.25 (3 H each, s, 2 CH_3-1′,3′), 1.40–1.80 (2 H, m, 2 H-2′), 2.10, 2.20, 2.24 (3 H each, s, AcO-2,3,5), 3.60–4.02 (2 H, m, H-1′,3′), 4.90 (2 H, s, 2 H-5), 5.34 (2 H, br s, H-2,3), 5.70 (1 H, d, J = 3.0 Hz, H-1).

2,3,5-Tri-*O*-acetyl-D-*erythro*-pentos-4-ulose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (*E,Z*)-4-[(*p*-Tolylsulfono)hydrazide] (18). A solution of **17** (504 mg, 1.40 mmol) and *p*-toluenesulfonylhydrazide (261 mg, 1.40 mmol) in absolute methanol (2.5 mL) was stirred at 20 °C for 22 h and then evaporated in vacuo. The residue was diluted with CH_2Cl_2, washed successively with cold dilute aqueous HCl, $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed in a column of silica gel with ethyl acetate–benzene (1:2) as the eluant, giving **18** as a yellow syrup: 588 mg (80% yield); R_f 0.48 (AcOEt–hexane, 1:2); IR 1740 (ester), 1695 (C=N) cm^{-1}; ^1H NMR 1.08, 1.20 (3 H each, s, 2 CH_3-1′,3′), 1.30–1.57 (2 H, m, 2 H-2′), 1.95–2.08 (9 H, m, AcO-2,3,5), 2.43 (3 H, s, S–C_6–CH_3), 3.43–3.80 (2 H, m, H-1′,3′), 4.63 (2 H, s, 2 H-5), 4.65 (1 H, d, J = 5.1 Hz, H-3), 5.20 (1 H, t, J = 5.1 Hz, H-2), 5.59 (1 H, d, J = 5.1 Hz, H-1), 7.33, 7.83 (2 H each, AA′BB′ quartet, J = 8.3 Hz, S–C_6H_4–Me), 9.40 (1 H, br s, NH).

(4*RS*)-2,3,5-Tri-*O*-acetyl-4-deoxy-4-*C*-[(*RS*)-methoxyphenylphosphinyl]-4-*C*-[(*p*-tolylsulfono)hydrazino]-D-*erythro*-pentose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (19). Procedures similar to those for the preparation of **14** were used. From **18** (174 mg), methyl phenylphosphinate (0.42 mL), and trifluoromethanesulfonic acid (0.023 mL) was obtained **19** as a yellow syrup: 72 mg (68%); R_f 0.52 (AcOE); ^1H NMR 1.15, 1.23 (3 H each, s, 2 CH_3-1′,3′), 1.35–1.62 (2 H, m, 2 H-2′), 1.78–2.03 (9 H, m, Ac-2,3,5), 2.92 (3 H, s, S–C_6–CH_3), 3.53–3.76 (4 H, m, H-5,1′,3′), 3.78 (3 H, d, $^3J_{H,P}$ = 10.5 Hz, P–OMe), 4.05–4.79 (3 H, m, H-2,3, NH-4), 5.54 (1 H, m, H-1), 7.24–7.98 (10 H, m, S–C_6H_4–Me, P–C_5H_6, NH).

(4*RS*)-2,3,5-Tri-*O*-acetyl-4-deoxy-4-*C*-[(*RS*)-methoxyethylphosphinyl]-4-*C*-[(*p*-tolylsulfono)hydrazino]-D-*erythro*-pentose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (20). Similar procedures as above were followed. After stirring a mixture of **14** (169 mg), methyl ethylphosphinate (0.29 mL), and trifluoromethanesulfonic acid (0.016 mL) at 20 °C for 72 h, the crude product was separated by silica gel TLC with ethyl acetate–hexane (4:1) as the eluant, giving 36 mg (18%) of **20** as a pale yellow syrup [and 53 mg (31%) of unreacted **14**]: R_f 0.55 (AcOEt); ^1H NMR 0.90–1.89 (13 H, m, P–Et, 2 CH_3-1′,3′, 2 H-2′), 1.97, 2.02, 2.07 (3 H each, s, AcO-2,3,5), 2.43 (3 H, br s, S–C_6–CH_3), 3.45–4.00 (4 H, m, H-5,1′,3′), 3.75 (3 H, d, $^3J_{H,P}$ = 11.0 Hz, P–OMe), 4.17–4.83 (3 H, H-2,3, NH-4), 5.55 (1 H, m, H-1), 7.31, 7.81 (2 H each, AA′BB′ q, J = 8.3 Hz, S–C_6H_4–Me), 7.65 (1 H, br s, NH).

(4*RS*)-2,3,5-Tri-*O*-acetyl-4-deoxy-4-*C*-[(*RS*)-dimethoxyphosphinyl]-4-*C*-[(*p*-tolylsulfono)hydrazino]-D-*erythro*-pentose 1′,3′-Dimethyl-1′,3′-propanediyl Acetal (21). The same procedures as above were followed. From **14** (171 mg), dimethyl phosphonate (0.30 mL), and trifluoromethanesulfonic acid (0.016 mL) was obtained **21** as a pale amber syrup: 161 mg (78%); R_f 0.48 (5% EtOH–AcOEt); ^1H NMR 1.06–1.41 (8 H, m, 2 CH_3-1′,3′, 2 H-2′), 2.03–2.18 (9 H, m, AcO-2,3,5), 2.43 (3 H, s, S–C_6–CH_3), 3.74–4.04 (4 H, m, H-5,1′,3′), 3.79 (6 H, d, $^3J_{H,P}$ = 11.3 Hz, P–OMe), 4.18–4.46 (2 H, m, H-2,3), 4.7 (1 H, br s, NH), 5.55 (1 H, m, H-1), 7.36, 7.86 (2 H each, AA′BB′ q, J = 7.8 Hz, S–C_6H_4–Me), 7.88 (1 H, m, NH).

Methyl 2,3-*O*-Isopropylidene-β-D-*erythro*-pentopyranosid-4-ulose (25). Methyl 2,3-*O*-isopropylidene-α-L-lyxopyranoside (**24**) was prepared from D-galacturonic acid (**22**) via L-galactono-1,4-lactone (100%), α-L-lyxopyraose (**23**; 58%), and methyl α-L-lyxopyranoside (85%) in an overall yield of 38% according to the known procedures.[15] Compound **24** (2.79 g) was oxidized with dimethyl sulfoxide (1.14 mL)–oxalyl chloride (1.34 mL)–triethylamine (9.5 mL) in CH_2Cl_2 (60 mL) at −70 °C by the produres described earlier (for **11**), giving **25** as a pale yellow syrup: 2.06 g (74%); R_f 0.58 (AcOEt–hexane, 1:2); ^1H NMR 1.35, 1.50 (3 H each, s, CMe_2), 3.47 (3 H, s, MeO-1), 4.14 (2 H, s, 2 H-5), 4.40 (2 H, br s, H-2,3), 4.76 (1 H, br s, H-1).

Methyl 2,3-*O*-Isopropylidene-β-D-*erythro*-pentopyranosid-4-ulose (*E,Z*)-4-[(*p*-Tolylsulfono)hydrazide] (26). Compound **25** (2.06 g) was treated with *p*-toluenesulfonylhydrazide

(22) Petrov, K. A.; Bliznyuk, N. K.; Studnev, Yu. N.; Kolomiets, A. F. *Zh. Obshch. Khim.* **1961**, *31*, 179.

(1.90 g) in absolute methanol (18 mL) at 20 °C for 48 h in the same manner as **12**, and the crude product was purified by column chromatography with ethyl acetate–benzene (1:2), giving **26** as a pale yellow syrup: 3.43 g (91%); R_f 0.43 (**26a**), 0.34 (**26b**) (1:1) (AcOEt–hexane, 1:2); IR 3200 (NH), 1600 (C=N) cm^{-1}; ^1H NMR for **26a** (*Z*), 1.06, 1.32 (3 H each, s, CMe_2), 2.40 (3 H, s, S–C_6–CH_3), 3.41 (3 H, s, MeO-1), 4.10 (3 H, m, H-2,5), 4.82 (1 H, d, J = 6 Hz, H-3), 4.85 (1 H, br s, H-1), 7.30, 7.80 (2 H each, AA'BB' q, J = 8.3 H, S–C_6H_4–Me), 9.20 (1 H, s, NH); for **26b** (*E*), 1.30, 1.43 (3 H each, s, CMe_2), 2.43 (3 H, s, S–C_6–CH_3), 3.34 (3 H, s, MeO-1), 4.14 (1 H, d, $J_{2,3}$ = 7.5 Hz, H-2), 4.26 (2 H, s, 2 H-5), 4.52 (1 H, br s, H-1), 4.66 (1 H, d, J = 7.5 Hz, H-3), 7.33, 7.83 (2 H each, AA'BB'q, J = 8.3 Hz, S–C_6H_4–Me), 8.0 (1 H, m, NH) (for the reasoning behind the assignments of *Z* and *E* isomers to **26a** and **26b**, see ref 23).

Methyl (4*RS*)-4-Deoxy-2,3-*O*-isopropylidene-4-*C*-[(*RS*)-methoxyethylphosphinyl]-4-*C*-[(*p*-tolylsulfono)-hydrazino)-β-D-*erythro*-pentopyranoside (27). Compound **26** (3.28 g) was treated with methyl ethylphosphinate (5.2 mL) in the presence of trifluoromethanesulfonic acid (0.28 mL) as described earlier (for **14**), and the crude product was chromatographed in a column of silica gel with ethyl acetate–benzene (1:1) (which was gradually changed to 1:4 MeOH–ethyl acetate), giving, besides recovered **26** (0.84 g, 24%), **27** as a pale yellow syrup: 2.76 g (65%); R_f 0.52, 0.40, 0.29 (EtOH–AcOEt, 1:19); ^1H NMR 0.80–2.25 (5 H, m, P–Et), 1.15, 1.35, 1.28, 1.50 (6 H, all s, CMe_2), 2.35, 2.43 (3 H, both s, S–C_6–CH_3), 3.40, 3.48 (3 H, both s, MeO-1), 3.70, 3.72 (3 H, both d, $^3J_{H,P}$ = 12.8 Hz, P–OMe), 3.68–4.18 (3 H, m, 2 H-5, NH-4), 4.3–4.7 (2 H, m, H-2,3), 4.78–4.95 (1 H, m, H-1), 7.30, 7.80 (2 H each, AA'BB' q, J = 7.8 Hz, S–C_6H_4–Me), 8.10 (1 H, m, S–NH).

Methyl (4*RS*)-4-Deoxy-2,3-*O*-isopropylidene-4-*C*-[(*RS*)-methoxyethylphosphinyl]-β-D-ribo- and -α-L-lyxopyranoside (28). Sodium borohydride (3.29 g, 89 mmol) was added at 5 °C to a solution of **27** (2.09 g, 4.36 mmol) in dry THF (70 mL). The mixture was stirred at 20 °C for 2 days (then at 50 °C for 1 day) and then brought to pH 4 with 50% aqueous acetic acid at 0 °C. After solvent evaporation in vacuo, the residue was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ and then with water, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on a silica gel column with ethyl acetate–hexane (1:1) (which was gradually changed to 1:5 ethanol–ethyl acetate) thus giving **28** as a mixture of diastereomers: 0.62 (48%); pale yellow syrup; R_f 0.48 (EtOH–AcOEt, 1:19); ^1H NMR 0.88–2.13 (5 H, m, P–Et), 1.28, 1.38, 1.53 (6 H, all s, CMe_2), 3.38, 3.49 (3 H, both s, MeO-1), 3.58–4.04 (3 H, m, H-2,5), 3.78, 3.80 (3 H, both d, $^3J_{H,P}$ = 9.5 Hz, P–OMe), 4.35–4.75 (2 H, m, H-1,3).

1,2,3,5-Tetra-*O*-acetyl-4-deoxy-4-*C*-[(*R*)-ethylphosphinyl]-α-D-ribopyranose (31a), Its β-Anomer 31b, the 5-*C*-((*S*)-Phosphinyl)-α,β-D-ribofuranoses 32a,b, and the 5-*C*-[(*RS*)-Phosphinyl]-α-L-lyxofuranoses (33a and 34a). A solution of SDMA (70% in benzene, 0.52 mL, 1.0 equiv) was slowly added at 0 °C to a stirred solution of **28** (613 mg) in dry benzene (5 mL) under argon, followed by stirring at 5 °C for ca. 1 h (until the starting material disappeared). Then water (1 mL) was added at 0 °C, and the mixture was stirred for 30 min and centrifuged to remove aluminum hydroxide; the precipitate was extracted with several portions of benzene. The organic layers were combined and evaporated in vacuo, giving methyl (4*RS*)-4-deoxy-2,3-*O*-isopropylidene-4-*C*-[(*RS*)-ethylphosphinyl]-β-D-ribo- and α-L-lyxopyranoside as a pale yellow syrup.

Oxygen free 0.5 M hydrochloric acid (17 mL) was added immediately to the above product which had been diluted with ethanol (1.5 mL), and the mixture was refluxed for 24 h under argon. After cooling, the acid was neutralized by passing through a column of Amberlite IRA-45 anion exchange resin (weakly basic), which was washed with methanol. The eluant and washings were combined and evaporated in vacuo, to give (4*RS*)-4-deoxy-4-*C*-[(*RS*)-ethylphosphinyl]-D-ribo- and -L-lyxofuranoses (**29**) as a pale yellow syrup.

This product was acetylated with acetic anhydride (2.5 mL) and pyridine (6.5 mL) at 20 °C for 23 h in the usual manner, and the crude product was chromatographed on a silica gel column with ethyl acetate–benzene (2:1) (which was gradually changed to ethyl acetate and then to 10% ethanol/ethyl acetate) as the eluant. The fraction having R_f 0.45–0.16 (EtOH–AcOEt, 1:19) was collected and concentrated in vacuo, giving the per-*O*-acetates **30** as a diastereomeric mixture: pale yellow syrup; 405 mg (46% from **28**). This was then separated by rechromatography using a Merck Lobar silica gel column with the same eluant as above into five fractions, A–E.

Fraction A (R_f 0.45) gave **31b** as a colorless syrup: 76 mg (12.7% from **28**); $[\alpha]^{26}_D$ –0.20 (*c* 3.1, $CHCl_3$); ^1H NMR (400 MHz), see Table I; CI (NH_3) MS, *m/z* 379 (100, M + 1), 277 (7.6), 43 (22.0); EI MS, see Scheme IV; exact mass calcd for $C_{15}H_{24}O_9P$, [(M + 1)$^+$] 379.1158; found, 379.1159.

Fraction B gave a colorless syrup (93 mg) which was mainly **31a** (R_f 0.40, ~12% from **28**) but contained a minor amount of **33a** (R_f 0.36, ~5.3% from **28**, the ratio being estimated by NMR); ^1H NMR (400 MHz), see Table I.

Fraction C (R_f 0.32) gave **32b** as a colorless syrup: 77 mg (12.8% from **28**); $[\alpha]^{26}_D$ –0.38 (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz), see Table I; CI (NH_3) MS, *m/z* 379 (100, M + 1), 319 (22.5), 235 (26.5), 73 (42.7), 43 (29.9); EI MS, *m/z* 379 (1.52), 336 (15.7), 294 (77.0), 277 (82.2), 276 (76.5), 235 (72.9), 234 (50.8), 180 (100), 175 (84.6), 174 (72.6), 157 (64.6), 121 (96.9), 83 (33.4), 82 (36.8), 81 (44.0), 77 (18.0); exact mass calcd for $C_{15}H_{24}O_9P$, (M + 1) 379.1158; found, 379.1145.

Fraction D (R_f 0.27) gave **32a** as colorless needles: mp 145–146 °C (from ethyl acetate–hexane); 24 mg (4.0% from **28**); ^1H NMR (400 MHz), see Table I; CI (NH_3) MS, *m/z* 379 (100, M + 1), 319 (17.3), 43 (24.8); EI MS, *m/z* 379 (3.21), 336 (18.3), 294 (65.7), 277 (100), 276 (66.9), 235 (70.9), 234 (48.4), 180 (79.9), 175 (77.0), 157 (59.6), 121 (81.1), 83 (43.3), 82 (34.7), 81 (43.4), 77 (14.1); exact mass calcd for $C_{15}H_{24}O_9P$, (M + 1) 379.1158; found, 379.1158.

Fraction E gave a colorless syrup (17 mg) which consisted mainly of **34a** (2.8% from **28**, R_f 0.27) but contained a small amount of an unidentified product (R_f 0.16), although it was speculated to be the β-anomer **34b** from the low R_f value.

(23) Yamamoto, H.; Hosoyamada, C.; Kawamoto, H.; Inokawa, S.; Yamashita, M.; Armour, M.-A.; Nakashima, T. T. *Carbohydr. Res.* **1982**, *102*, 159.