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STEREOSELECTIVE SYNTHESIS OF S-(2-DEOXY-α-D-GLYCOSYL)-PHOSPHORODITHIOATES[1] AND OF THEIR (2R)-2-DEOXY-2-DEUTERIO-ANALOGUES. NOVEL ROUTE TO C-2 DEUTERIUM LABELED 2-DEOXY-MONOSACCHARIDES

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Abstract - Addition of O,C-dialkylphosphorodithioic acids to fully protected 1,2-unsaturated hexo- and pentopyranoses gives S-(2-deoxy-glycosyl)-phosphorodithioates in quantitative yield and high stereoselectivity with respect to the α-isomer. The stereochemistry of this reaction is "cis" as demonstrated by the addition of deuterated O,O-dialkylphosphorodithioic acids to 3,4,6-tri-O-acetyl-D-glucal which gives exclusively the α-dithiophosphates of (2R)-2-deoxy-2-deuterio-D-arabinohexopyranose. This result provides an efficient and fully stereoselective method of labeling of the deoxy function in 2-deoxy monosaccharides and their glycosylic derivatives.

This paper is a part of our studies on new glycosylating reagents in the 2-deoxy sugar series and deals with the addition reaction of O,C-dialkyl-phosphorodithioic H and ^{2}H acids to 1,2-unsaturated hexo- and pentopyranoses.

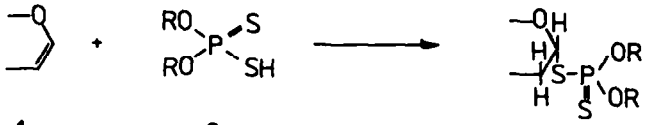
Addition reactions to 1,2-unsaturated sugars are of interest as a way to a variety of 2-deoxy sugar derivatives in particular to glycosylating reagents. 1,2-Unsaturated sugars having a double bond between C-1 and C-2 are vinyl ethers and consequently take part in a variety of selective addition reactions. The mesomeric influence of the ring oxygen ensures that the electrophile enters at position C-2. The consecutive attack of the nucleophilic reagent is directed on the resonance stabilized C-1 carbonium ion. Addition of X-H nucleophiles depends on the structure of X, of their acidity and reaction conditions. For instance, when hydrogen halides are added to 1,2-unsaturated sugars generally 2-deoxyglycosyl halides are obtained.[2] In many cases, however, secondary products such as 1-halogeno-2,3-unsaturated and 2,3-dideoxy-1,3-dihalogeno sugars are formed thus diminishing the yield of the desired 2-deoxyglycosyl-X compound.[3,4] A similar complex reaction course takes place in acid catalyzed additions of water,[5] hydrogen halides,[6] alcohols,[7,8] phenols,[9] carboxylic acids,[10,11] mercaptanes[12] and monothiocarboxylic acids[13] to 1,2-unsaturated sugars. These reactions when

performed in the presence of acids are accompanied by anomerisation leading to thermodynamically controlled final products, usually of α-configuration.

RESULTS AND DISCUSSION

O,O-Dimethyl-, O,O-dineopentyl- phosphorodithioic acids 2a,b[14] and 2-mercapto-2-thiono-5,5-dimethyl-1,3,2-dioxaphosphorinane 2c[15] used in these investigations are readily available, either commercially or from the reaction of the corresponding alcohols with P_4S_{10}. 3,4,6-Tri-O-acetyl-D-glucal 1a[16], 3,4,6-tri-O-acetyl-D-galactal 1b[17], 3,4-di-O-acetyl-D-xylal 1c[18] and 3,4-di-O-acetyl-D-arabinal 1d[19] were employed as representative 1,2-unsaturated sugars.

Addition of O,O-dimethylphosphorodithioic acid 2a to 3,4,6-tri-O-acetyl--D-glucal 1a proceeds smoothly in benzene at 20°C yielding O,O-dimethyl-S-(2-deoxy-3,4,6-tri-O-acetyl-α-D-arabinohexopyranosyl)phosphorodithioate 3a in quantitative yield. The reaction monitored by ^{31}P-NMR spectroscopy and tlc was completed within 48 h. No traces of the alternative β-isomer were observed. Recrystallization of the crude reaction product gave analytically pure 3a in 93% yield. Addition of the O,O-dineopentylphosphorodithioic acid 2b to 3,4,6-tri-O-acetyl-D-glucal 1a performed under the same conditions gave the α-adduct 3b in quantitative yield. The reaction was completed within 72 h. The prolonged reaction time required was presumably the consequence of steric hindrance caused by the bulky neopentyl groups. Similarly, we observed the exclusive formation of the α-adduct 3c when the unsaturated sugar 1a was allowed to react with the acid 2c in methylene chloride solution at -20°C. This stereoselective addition is relatively slow and requires up to 5 days. The same reaction, however, in benzene at room temperature was completed within 48 h but its stereoselectivity was distinctly lower. A mixture of α- and β-isomers was formed in 85:15 ratio. The α-isomer 3c was isolated by simple crystallization. The reaction between the acid 2c and 3,4,6-tri-O-acetyl-D-galactal 1b proceeds in similar manner to that between the acid 2c and the unsaturated sugar 1a. The addition performed in benzene at ambient temperature was completed within 48 h giving a mixture of α- and β-isomers in 85:15 ratio with quantitative overall yield. The α-isomer isolated by crystallization was obtained with 80% yield. The stereoselectivity of addition reaction of the acid 2c to 3,4-di-O-acetyl-D-xylal 1c depends even more on the conditions applied. When 2c and 1c were allowed to react in methylene chloride solution at -12°C the observed α/β ratio was 92:8, respectively. Interestingly, the same reaction performed in benzene at 20°C lead to a mixture of α and β isomers in 52:48 ratio. The addition reactions of the acids 2a and 2c to 3,4-di-O-acetyl-D-arabinal 1d performed in benzene at ambient temperature lead to predominant formation of



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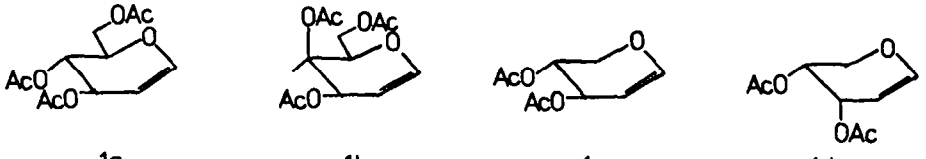
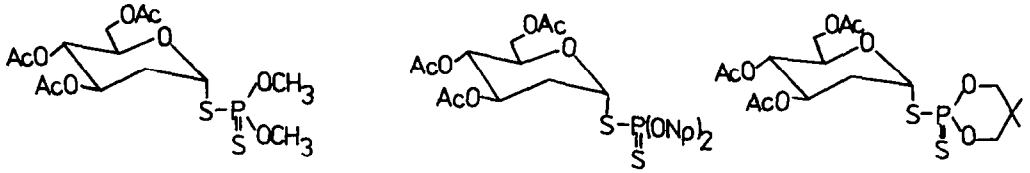
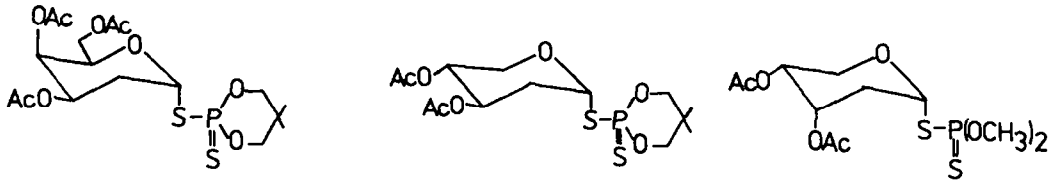


1a 1b 1c 1d

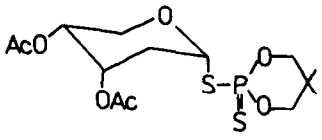
2a R=CH_3 2b R=$CH_2C(CH_3)_3$ 2c R=



3a 3b 3c



3d 3e 3f



3g

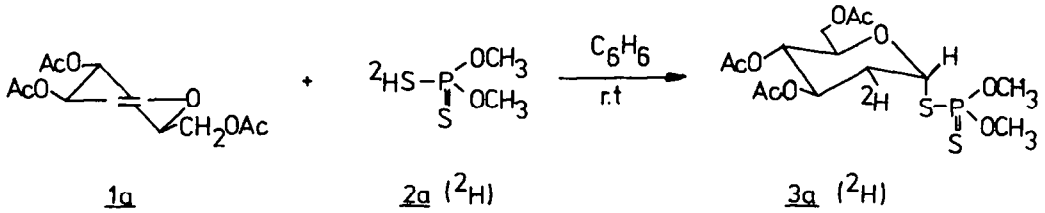
Scheme I

the α-adducts. The observed α/β ratio was 89:11 and 92:8, respectively. Also in these cases isolation of the α-isomers 3f and 3g was readily accomplished by crystallization.

The structure of the adducts 3a-g obtained in these investigations was assigned on the basis of the following data. The chemical shift for the resonance of the anomeric proton in the ^{1}H-NMR spectrum (5.78-6.40 ppm), its splitting pattern (ddd) and spin-spin coupling constants ($^3J_{1,2a}$ 4.5 Hz; $^3J_{1,2e}$ 1.5 Hz; $^3J_{1,F}$ 10 Hz) were indicative of the α-configuration of the dithiophosphoryl group. The presence of the deoxy function at C-2 was shown by the chemical shift, multiplicity of the two CH_2 protons(axial 1.9-2.1 (ddd); equatorial 2.2-2.5 (ddd)) in the ^{1}H-NMR spectrum and confirmed by the chemical shift and spin-spin coupling between ^{31}P and ^{13}C-2 nuclea (32.8-36.6 ppm; $^3J_{P,C-2}$ 7 Hz) in the ^{13}C-NMR spectrum. The sugar ring protons and carbons as well as those of the alkoxy groups attached to phosphorus exhibited resonances at the expected values (cf. Table 1 and Table 2). An additional indication of the α-configuration was the high positive rotation value characteristic of the α-anomers in the D-glucose series.

We want to emphasize that the addition reactions of phosphorodithioic acids 2a-2c to 1,2-unsaturated sugars 1a-1d are not only fully regio- and highly or fully stereoselective but they are free of side products observed in the case of hydrogen halides, carboxylic acids, mercaptanes and thioacetic acid additions to 1,2-enosugars. All obtained adducts are crystalline compounds. Their most valuable property is the anomeric stability and solubility in aprotic solvents. In moisture-free atmosphere these compounds can be stored for months without decomposition. It was demonstrated in our laboratory that the 2-deoxy-1-dithiophosphates obtained by addition reaction are efficient glycosyl donors.[20,21]

It was of interest to elucidate the question of stereochemical course of the addition reaction of phosphorodithioic acids to 1,2-unsaturated pento- and hexo-pyranoses. To solve this problem S-deuterio-O,O-dimethyl- and S-deuterio-O,O-di-neopentylphosphorodithioic acids 2a (^{2}H) and 2b (^{2}H) were prepared by isotopic exchange with CH_3O^2H using the procedure described by Dyer and Hall.[22,23] The isotopic purity of acids 2a (^{2}H) and 2b (^{2}H) evaluated by ^{1}H-NMR spectroscopy was 95%. These acids in undeuterated form add to 3,4,6-tri-O-acetyl-D-glucal 1a with exclusive formation of the α-adduct. The addition reactionsof the deuterated acids to 1a were performed under analogous conditions as with undeuterated species.



1a 2a (^{2}H) 3a (^{2}H)

Scheme 2

Table 1. Proton NMR chemical shifts of the suger moiety (C_6D_6) in 3a-3g (chemical shifts in ppm)

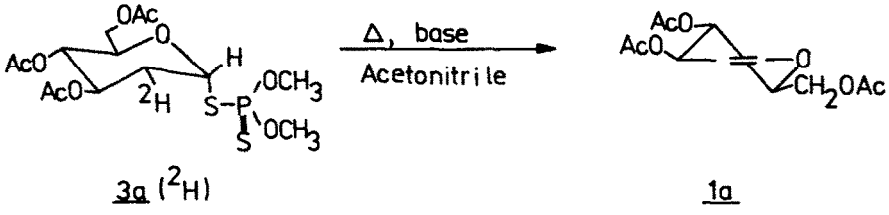
Compound	H-1	H-2a	H-2e	H-3	H-4	H-5	H-6 and H-6'	$^3J_{1,P}$	$^3J_{1,2a}$	$^3J_{1,2e}$
3a	5.84 ddd	1.90 m	2.15 m	5.62 m	5.02 m	3.83 ———	4.60 m	10.0 Hz	5.0 Hz	1.5 Hz
3a ^2H	5.85 dd	1.95 m	-	4.90 ———	5.50 m	3.80 ———	4.50 m	12.0 Hz	5.5 Hz	-
3b	6.05 ddd	2.12 m	2.49 m	5.10 ———	5.63 m	3.63 ———	4.63 m	10.0 Hz	5.0 Hz	1.5 Hz
3b ^2H	6.10 dd	2.16 m	-	5.10 ———	5.50 m	4.10 ———	4.55 m	12.5 Hz	5.3 Hz	-
3c	6.32 ddd	1.98 m	2.25 m	5.60 ———	5.32 m	4.12 ———	4.56 m	10.0 Hz	5.0 Hz	1.5 Hz
3d	6.40 ddd	2.06 m	2.45 m	5.21 dd	5.46 m	4.20 m	3.80 m	10.5 Hz	4.7 Hz	1.0 Hz
3e	5.78 ddd	2.13 m	2.33 ddd	5.08 ddd	4.77 ddd	3.75 dd (H-5ax)		10.6 Hz	4.5 Hz	1.0 Hz
						4.01 dd (H-5eq)				
3f	5.93 ddd	1.86 m	2.34 m	5.19 m	5.12 dd	3.61 dd (H-5ax)		11.4 Hz	3.9 Hz	2.4 Hz
						3.78 dd (H-5eq)				
3g	6.04 ddd	2.05 m	2.50 m	5.15 m	5.10 m	3.85 dd (H-5ax)		10.8 Hz	4.0 Hz	2.8 Hz
						3.99 dd (H-5eq)				

Table 2. Carbon-13 NMR chemical shifts of adducts 3a-3g (25.2 MHz, $CDCl_3$) and C-P coupling constants (chemical shifts in ppm)

Compound	C-1	C-2	C-3	C-4	C-5	C-6	R
3a	84.8 d $^2J_{P-C}$ 2.9 Hz	36.5 d $^3J_{P-C}$ 7.3 Hz	69.3[a]	70.5[a]	71.3[a]	62.3	54.2 (t[b], 2xCH_3, $^2J_{P-C}$ 5.9 Hz)
3c	84.4 $^2J_{P-C}$ < 1 Hz	36.6 d $^3J_{P-C}$ 7.5 Hz	69.2[a]	70.9[a]	75.7[a]	61.8	22.1 (CH_3ax) 20.7 (CH_3 eq) 32.4 (d, $\underline{C}(CH_3)_2$, $^3J_{P-C}$ 5.7 Hz)
3d	85.2 $^2J_{P-C}$ < 1 Hz	31.7 d $^3J_{P-C}$ 7.5 Hz	69.3[a]	66.7[a]	65.8[a]	61.4	22.1 (CH_3 ax) 20.7 (CH_3 eq) 31.7 (d, $\underline{C}(CH_3)_2$, $^3J_{P-C}$ 7.6 Hz)
3e	83.6 $^2J_{P-C}$ < 1 Hz	35.5 d $^3J_{P-C}$ 9.0 Hz	68.1[a]	67.9[a]	63.6	-	21.9 (CH_3 ax) 20.7 (CH_3 eq) 32.3 (d, $\underline{C}(CH_3)_2$, $^3J_{P-C}$ 7.0 Hz) 77.4 (dd, CH_2)
3f	85.4 $^2J_{P-C}$ < 1 Hz	32.9 d $^3J_{P-C}$ 11.3 Hz	67.04[a]	66.1[a]	63.5	-	54.0 (d, 2xCH_3, $^2J_{P-C}$ 7.5 Hz)
3g	85.3 $^2J_{P-C}$ < 1 Hz	32.8 d $^3J_{P-C}$ 9.0 Hz	66.8[a]	66.1[a]	63.7	-	21.9 (CH_3 ax) 20.7 (CH_3 eq) 32.3 (d, $\underline{C}(CH_3)_2$, $^3J_{P-C}$ 6.0 Hz) 77.3 (dd, CH_2)

a - may be interchanged b - pseudotriplet (two diastereotopic CH_3 groups)

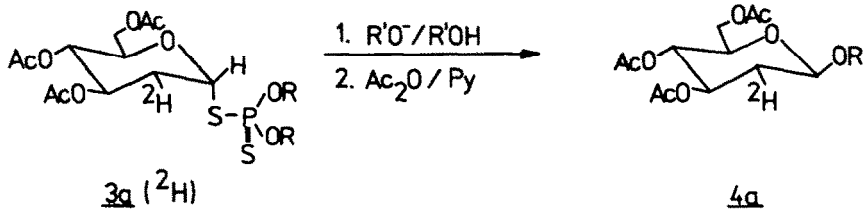
The reaction was fully stereoselective at both reaction centres: C-1 and C-2 and occurred with quantitative formation of O,O-dialkyl-S-(3,4,6-tri-O-acetyl-D-arabino-pyranosyl(phosphorodithioates 3a (^{2}H) and 3b (^{2}H). The structure of the products 3a (^{2}H) and 3b (^{2}H) was unambigously prooved by the ^{1}H-NMR spectrum. The splitting pattern of the anomeric proton distinctly shows only two coupling constants: first - between the C-1 proton and phosphorus ($^3J_{1,P}$ = 12 Hz) and second - between the H-1 proton and H-2 proton (J = 5.4 Hz). The observed values are characteristic of equatorial-axial proton coupling. These facts clearly indicate that the stereo-chemistry of the addition reaction is "cis". Compounds 3a (^{2}H) and 3b (^{2}H) when refluxed in acetonitrile or toluene and in the presence of base (e.g. $Hg(CN)_2$, K_2CO_3 or amines), gave undeuterated 3,4,6-tri-O-acetyl-D-glucal 1a and the corresponding salts of deuteriophosphorodithioic acids. These eliminations were shown to be "cis" as well.



3a (^{2}H) 1a

Scheme 3

The reaction with the deuterated phosphorodithioic acids was useful not only for elucidation of the stereochemistry of the addition reaction. In the view of our recent discovery that the dithiophosphoryl groups in α-dithiophosphates of 2-deoxysugars undergo easy nucleophilic displacement by a variety of nucleophiles, this reaction created a novel, stereoselective route to deuterium-labeled (2R)-2-deoxysugar derivatives. Following the procedure elaborated for the synthesis of β-alkyl-2-deoxy glycosides[20], we obtained the C-2 deuterium labeled methyl- and isopropyl (2R)-2-deoxy-2-deuterio-β-D-arabinohexopyranosides 4a and 4b in high yield and high isotopic purity.



3a (^{2}H) 4a

Scheme 4

We believe that the procedure employed for the introduction of deuterium can easily be extended to the synthesis of tritium - labeled 2-deoxy sugars useful in biological essays.

EXPERIMENTAL

Melting points were determined with Boetius PHMKC 5 apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of the Centre of Molecular and Macromolecular Studies of the Polish Academy of Sciences, Lodz. ^{1}H-NMR spectra were determined in C_6D_6 (Varian 60 MHz, Bruker 90 MHz, Bruker 300 MHz, Bruker 400 MHz). ^{13}C-NMR spectra were determined in $CDCl_3$ (Tesla BS 567A, 25.2 MHz). ^{31}P-NMR spectra were determined in $CDCl_3$ with H_3PO_4 as internal standard (Jeol 60 MHz FT operating at 24.3 MHz). Specific rotations were determined with Polamat A polarimeter. Tlc was carried out on silica gel plates (Kieselgel 60 F_{254} Merck) with benzene-chloroform-acetone 3:1:1 as developing solvent. Detection was effected by exposure to iodine vapours and, in parellel, by phosphate reagent.

General method of the addition reaction of O,O-dialkylphosphorodithioic acids to acetylated 1,2-unsaturated hexo- and pentopyranoses

A solution of equimolar amounts of O,O-dialkylphosphorodithioic acid 2a-2c and of the acetylated 1,2-unsaturated sugar (1a-1d) in minimum amount of benzene or methylene chloride was kept at room temperature and the reaction was monitored by ^{31}P-NMR and tlc. The mixture was washed with water, dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was checked by ^{31}P-NMR spectroscopic method. Repeated crystallization from diethyl ether gave the analytically pure α-adducts (3a-3g). Analogous procedure was applied to the synthesis of the deuterated adducts.

General method of deuteration of the O,O-dialkylphosphorodithioic acids

Deuteration of the acids 2a and 2b was accomplished by repeated exchange with CH_3OD and subsequent evaporation of the solvent (5 x 5 ml). The isotopic purity of the deuterated products was checked by ^{1}H-NMR. The reactions of the deuterated acids 2a and 2b with the unsaturated sugar 1a were performed in dry solvents (previously exchanged with D_2O) and well protected from moisture.

O,O-Dimethyl-S-(3,4,6-tri-O-acetyl-2-deoxy-α-D-arabino-hexopyranosyl)phosphorodithioate (3a). Unsaturated sugar 1a (1.36 g, 5 mmol) and acid 2a (0.79 g, 5 mmol) in benzene (5 ml); 20°C; 48 h; ^{31}P-NMR (crude product): δ 96.04. Data for 3a: colourless crystals, m.p. 94-95°, $[\alpha]_{578}^{20}$ +222 (c = 1.8, $CHCl_3$). Yield: 2 g, 90%; ^{31}P-NMR: δ 96.04; ^{1}H-NMR (90 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{14}H_{23}O_9S_2P$: C, 39.07; H, 5.34; P, 7.20. Found: C, 38.98; H, 5.48; P, 7.50.

O,O-Dimethyl-S-(3,4,6-tri-O-acetyl-2(R)-2-deoxy-2-deuterio-α-D-arabinohexopyranosyl)phosphorodithioate 3a(^{2}H). Unsaturated sugar 1a (0.68 g, 2.5 mmol) and deuterioacid 2a(^{2}H) (0.43 g, 2.75 mmol) in benzene (10 ml); 20°C, 72 h. Data for 3a(^{2}H): colourless crystals, m.p. 92-93° (diethyl ether-pentane), $[\alpha]_{578}^{23}$ +218 (c = 1.5, $CHCl_3$). Yield: 0.83 g, 75%; ^{31}P-NMR: δ 96.1; ^{1}H-NMR (60 MHz, C_6D_6): cf Table 1.

O,O-Dineopentyl-S-(3,4,6-tri-O-acetyl-2-deoxy-α-D-arabino-hexopyranosyl) phosphorodithioate (3b). Unsaturated sugar 1a (0.68 g, 2.5 mmol) and acid 2b (0.67 g, 2.5 mmol) in benzene (5 ml); 20°C; 72 h; ^{31}P-NMR (crude product): δ 91.20. Data for 3b: colourless crystals, m.p. 75-77°, $[\alpha]_{578}^{19}$ +206 (c = 1.5, $CHCl_3$). Yield: 1.3 g, 92%; ^{31}P-NMR: δ 91.20; ^{1}H-NMR (60 MHz, C_6D_6): cf Table 1;

^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{22}H_{39}O_9S_2P$: C, 48.70; H, 7.19; P, 5.71. Found: C, 48.70; H, 7.33; P, 5.68.

O,O-Dineopentyl-S-(3,4,6-tri-O-acetyl-2(R)-2-deoxy-2-deuterio-α-D-arabino-hexopyranosyl)phosphorodithioate 3b(^{2}H). Unsaturated sugar 1a (0.68 g, 2.5 mmol) and deuterioacid 2a(^{2}H) (0.75 g, 2.75 mmol) in benzene (5 ml); 20°C; 72 h. Data for 3b(^{2}H): colourless crystals, m.p. 75-76° (diethyl ether-pentane); $[\alpha]_{578}^{20}$ +210 (c = 1.5, $CHCl_3$). Yield: 0.53 g, 75%; ^{31}P-NMR: δ 91.3; ^{1}H-NMR (60 MHz, C_6D_6): cf Table 1.

5,5-Dimethyl-2-tioxo-2-(3,4,6-tri-O-acetyl-2-deoxy-α-D-arabino-hexopyranosylthio)-1,3,2-dioxaphosphorinane (3c). A. Unsaturated sugar 1a (0.68 g, 2.5 mmol) and acid 2c (0.48 g, 2.5 mmol) in benzene (5 ml): 20°C; 48 h; ^{31}P-NMR (crude product): δ 82.42 and δ 82.82 (85:15). Data for 3c: colourless crystals, m.p. 126-127°, $[\alpha]_{578}^{18}$ +182 (c = 1.9, $CHCl_3$). Yield: 0.9 g, 76%; ^{31}P-NMR: δ 82.42; ^{1}H-NMR (90 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{17}H_{27}O_9S_2P$: C, 43.41; H, 5.77; P, 6.59; S, 13.63. Found: C, 43.43; H, 5.87; P, 6.78; S, 13.72.

B. Unsaturated sugar 1a (0.68 g, 2.5 mmol) and acid 2c (0.48 g, 2.5 mmol) in CH_2Cl_2 (5 ml); -20°C; 5 days; ^{31}P-NMR (crude product): δ 82.42. No traces of the β-isomer were detected.

5,5-Dimethyl-2-tioxo-2-(3,4,6-tri-O-acetyl-2-deoxy-α-D-lyxo-hexopyranosylthio)-1,3,2-dioxaphosphorinane (3d). Unsaturated sugar 1b (1.36 g, 5 mmol) and acid 2c (0.96 g, 5 mmol) in benzene (5 ml); 20°C; 48 h; ^{31}P-NMR (crude product): δ 83.15 and δ 83.31 (85:15). Data for 3d: colourless crystals, m.p. 120-121°, $[\alpha]_{578}^{18}$ +193 (c = 1.3, $CHCl_3$). Yield: 1.9 g, 80%; ^{31}P-NMR: δ 83.23; ^{1}H-NMR (90 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{17}H_{27}O_9S_2P$: C, 43.41; H, 5.77; P, 6.59; S, 13.63. Found: C, 43.80; H, 5.95; P, 7.00; S, 13.94.

5,5-Dimethyl-2-tioxo-2-(3,4-di-O-acetyl-2-deoxy-α-D-threo-pentopyranosylthio)-1,3,2-dioxaphosphorinane (3e). A. Unsaturated sugar 1c (0.60 g, 3 mmol) and acid 2c (0.6 g, 3 mmol) in CH_2Cl_2 (8 ml); -12°C; 9 days; ^{31}P-NMR (crude product): δ 84.08 and δ 86.86 (92:8). Data for 3e: colourless crystals, m.p. 145-146°, $[\alpha]_{578}^{19}$ +79 (c = 1.1, $CHCl_3$). Yield: 0.5 g, 41%; ^{31}P-NMR: δ 84.79: ^{1}H-NMR (400 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{14}H_{23}O_7S_2P$: C, 42.21; H, 5.77; P, 7.78; S, 16.09. Found: C, 42.20; H, 6.02; P, 7.80; S, 15.83.

B. Unsaturated sugar 1c (0.6 g, 3 mmol) and acid 2c (0.6 g, 3 mmol) in benzene (5 ml); 20°C; 48 h; ^{31}P-NMR (crude product): δ 84.29 and δ 85.91 (52:48).

O,O-Dimethyl-S-(3,4-di-O-acetyl-2-deoxy-α-D-erythro-pentopyranosyl)phosphorodithioate (3f). Unsaturated sugar 1d (1.20 g, 6 mmol) and acid 2a (0.95 g, 6 mmol) in benzene (5 ml); 20°C; 48 h; ^{31}P-NMR (crude product): δ 96.48 and δ 97.09 (89:11). Data for 3f: colourless crystals, m.p. 58-60°, $[\alpha]_{578}^{20}$ -256 (c = 2.0, $CHCl_3$). Yield: 0.85 g, 41%; ^{31}P-NMR: δ 96.50; ^{1}H-NMR (300 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{11}H_{19}O_7S_2P$: C, 36.86; H, 5.34; S, 17.89; P, 8.64. Found: C, 36.84; H, 5.43; S, 17.81; P, 8.66.

5,5-Dimethyl-2-tioxo-2-(3,4-di-O-acetyl-2-deoxy-α-D-erythro-pentopyranosylthio)-1,3,2-dioxaphosphorinane (3g). Unsaturated sugar 1d (0.60 g, 3 mmol) and acid 2c (0.60 g, 3 mmol) in benzene (5 ml); 20°C; 20 min.; ^{31}P-NMR (crude product): δ 84.30 and δ 83.69 (92:8). Data for 3g: colourless crystals, m.p. 107-108°, $[\alpha]_{578}^{20}$ -207 (c = 1.7, $CHCl_3$). Yield: 0.75 g, 69%; ^{31}P-NMR: δ 84.09; ^{1}H-NMR (400 MHz, C_6D_6): cf Table 1; ^{13}C-NMR ($CDCl_3$): cf Table 2. Calc for $C_{14}H_{23}O_7S_2P$: C, 42.21; H, 5.77; P, 7.78; S, 16.09. Found: C, 42.32; H, 6.02; P, 7.75; S, 15.80.

O-Methyl- and O-isopropyl 3,4,6-tri-O-acetyl-2(R)-2-deoxy-2-deuterio-β-D-arabino-hexopyranosides 4a and 4b[20]. Adduct 3a(^{2}H) (0.6 g, 1.3 mmol) was added to 50 ml of the appropriate alcohol containing 0.13 g (5.6 mmol) of sodium at -15°C. The mixture was kept 2 h at -15°C then 1 h at 20° and concentrated. The residual syrup was acetylated (Ac_2O, Py) under standard conditions. The acetylated glycosides were crystallized from diethyl ether and pentane. Yield 70%. Data for 4a: m.p. 98-99°, $[\alpha]_{578}^{20}$ -29.4 (c = 2, $CHCl_3$); ^{1}H-NMR: δ H-1 4.5(d); $J_{1,2a}$ 9.5 Hz; Data for 4b: m.p. 64-66°, $[\alpha]_{578}^{19}$ -46.5 (c = 3, $CHCl_3$); ^{1}H-NMR δ H-1 4.6(d); $J_{1,2a}$ 10 Hz.

Elimination reaction of O,O-dimethyldithiophosphoric acid 2a(^{2}H) from the deuterio-adduct 3a(^{2}H). The deuterated adduct 3a(^{2}H) (1 g) and K_2CO_3 (1 g) in toluene (10 ml) were refluxed for 3 h. The precipitate was filtered off, the solvent removed under vaccuo and the residual product (1a) subject to ^{1}H-NMR analysis (δ H-1 6.45(d); $J_{1,2}$ 6.5 Hz). Analogous results were obtained with $Hg(CN)_2$ or diethylamine as a base.

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