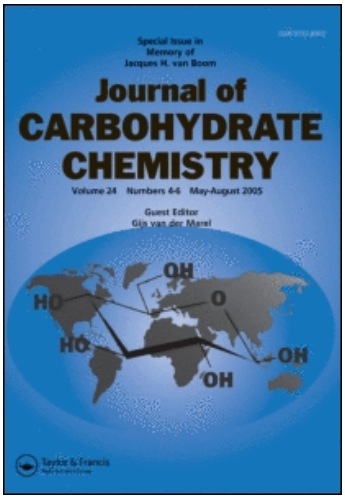

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MECHANISM OF REGIOSELECTIVE MITSUNOBU THIOFUNCTIONALIZATION OF PENTOFURANOSES

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ABSTRACT

Triphenylphosphine and diethyl azodicarboxylate react with 1,2-*O*-isopropylidene-α-D-xylo- (**1**) and ribofuranose (**2**) to give six-membered-ring phosphoranes. Xylofuranose **1** undergoes cyclodehydration to produce oxetane **17** in 85% yield, but ribofuranose **2** gives a pyrazolidine derivative **19** in 80% yield. In the presence of 2-mercaptobenzothiazole, the desired 5-*S*-(benzothiazol-2-yl)-5-thio derivatives **3** and **4** were isolated in 80% yield. ^{31}P NMR examination of this Mitsunobu thiofunctionalization reveals the presence of an alkoxytriphenylphosphonium species as the most stable intermediate which reacts with the thio-nucleophile via S_N2 in a rate limiting step.

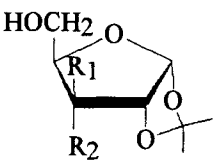
INTRODUCTION

Sulfur-containing saccharides have become frequently used as chiral synthons. A recent paper[1] has introduced new heterocycle/thiosugar hybrids which can be readily prepared using miscellaneous thio-nucleophiles in the Mitsunobu reaction.[2] These

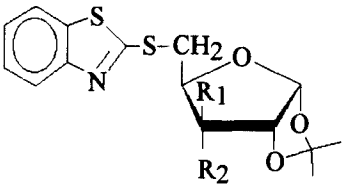
uncommon thiosugars can easily be transformed into the corresponding deoxy sugars,[3] chiral vinyl sulfones,[4] or can promote C-alkylation.[5] Exceptionally mild and convenient conditions of the regioselective thiofunctionalization of the primary hydroxyl function of hexosides[1,3] associated with reasonably high yields prompted us to focus on the unexplored case of partially protected pentofuranoses.

RESULTS AND DISCUSSION

The readily available[6] 1,2-*O*-isopropylidene-α-D-xylofuranose (**1**) and 1,2-*O*-isopropylidene-α-D-ribofuranose (**2**) were chosen as model compounds and after reaction with 2-mercaptobenzothiazole (HetSH), crystalline products **3** and **4** were isolated in ca. 80% yield. During optimization, it was found that the reaction rate could be affected by the order of addition of reagents, so we decided to investigate the mechanism of the title reaction using ^{31}P NMR.

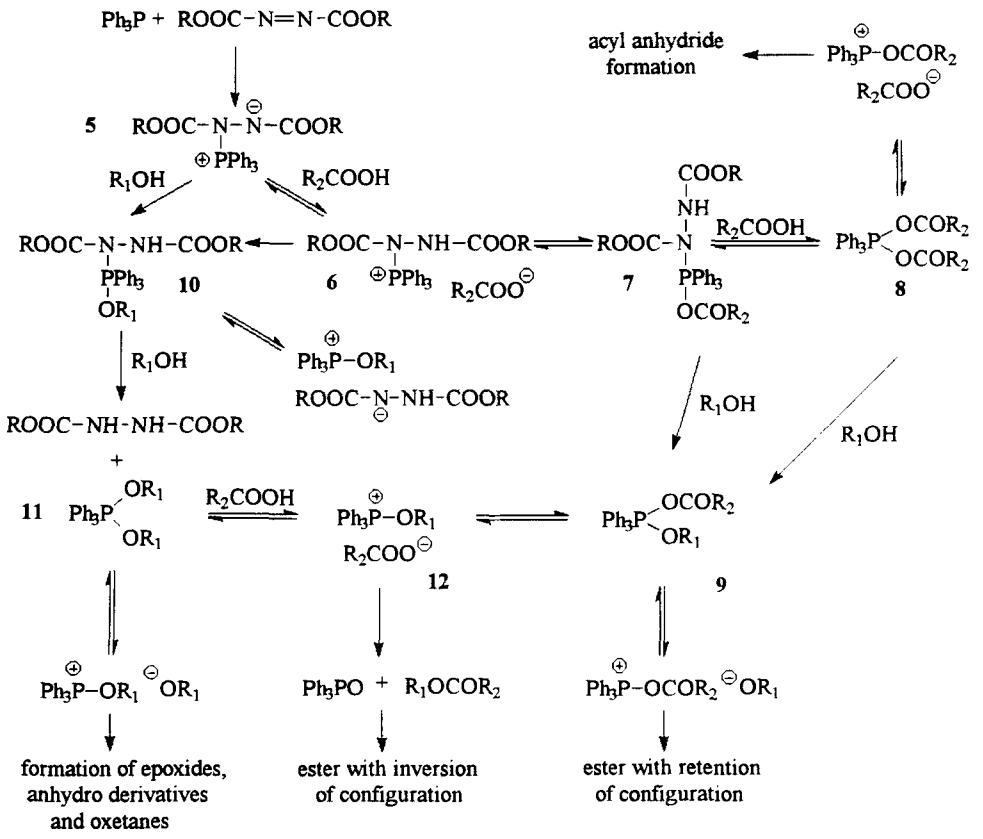


1 R_1 = OH, R_2 = H
2 R_1 = H, R_2 = OH



3 R_1 = OH, R_2 = H
4 R_1 = H, R_2 = OH

The mechanism of the Mitsunobu esterification,[2] employing a mixture of triphenylphosphine and a dialkyl azodicarboxylate, has been well documented[7-18] and Scheme 1 shows many of the possible intermediates generated during this reaction and the effects produced by adding acids or alcohols to the transient betaine **5**. This betaine is formed through an irreversible[19] nucleophilic attack of the phosphine on a nitrogen atom under a standard mode of addition (e.g. adding the azodicarboxylate to a solution of triphenylphosphine (TPP), the alcohol and the carboxylic acid in tetrahydrofuran). However, when the acid is added last, or when a large excess of azodicarboxylate and TPP is present, a radical chain mechanism can also be envisaged.[20] The attack of the carboxylate



Scheme 1

on the triphenylphosphonium group of **5** yielding mono- and diacylated hydrazides was also observed.[21] If the carboxylic acid was replaced by hydrazoic acid in the azido modification of the Mitsunobu reaction other relatively stable intermediates of type **7** and **8** with an azido group attached were involved.[22] The complexity of these intermediates and the possibility of radical side reactions depended strongly on the order of addition of reagents, thus it may influence the outcome of the Mitsunobu reaction in some cases.

The key role was attributed to an equilibrium between the dioxatriphenylphosphorane **11** and the oxyphosphonium ion pair **12** which can be affected by changes in the concentration or the pK_a of the acid, and changes in the solvent polarity.

Treatment of TPP (1.1 equiv) and diethyl azodicarboxylate (DEAD, 1 equiv) in pyridine at 10 °C under argon resulted in the immediate appearance of a dominant signal at

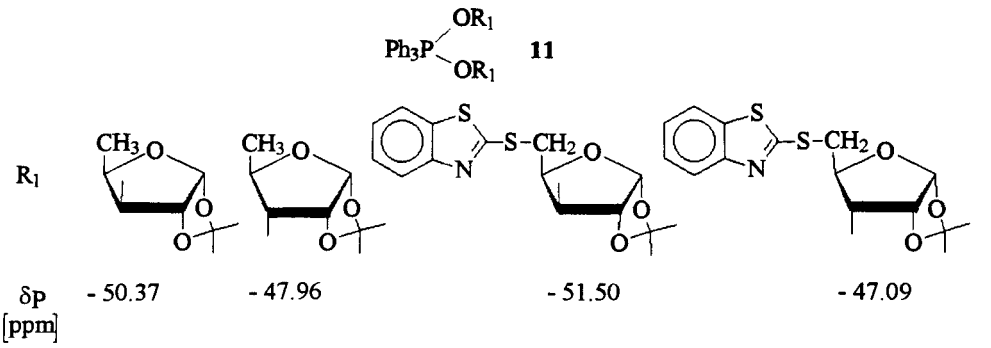
Table 1. Relative abundance of phosphorane intermediates derived from furanoses 1 and 2

Xylofuranose 1[a], δ_P [ppm]				
Time [min]	-50.29	-51.96	-55.04	-56.24
0	73	14	10	3
20	75	11	14	0
40	79	5	16	0
60	80	0	20	0

Ribofuranose 2[b], δ_P [ppm]					
Time [min]	-51.24	-54.85	-56.68	-56.89	sum of minor
0	19	16	0	65	0
20	20	10	15	48	7
40	40	6	22	20	12

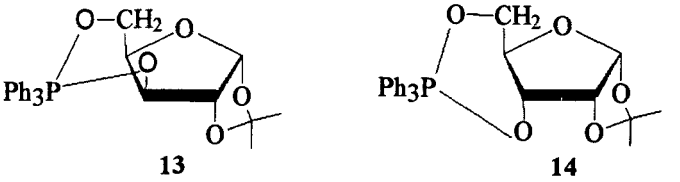
a. chloroform, 10 °C, molar ratio **1** : **5** = 1 : 1; b. pyridine, 10 °C, molar ratio **2** : **5** = 1 : 2.

δ_P +45.64 ppm,[23] corresponding[8,9] to the formation of **5**. Addition of half an equivalent of xylofuranose **1** gave rise to a single sharp peak (δ_P -50.00 ppm) in the phosphorane **11** (Scheme 1) region[11,12] of the ^{31}P NMR spectrum, while addition of ribofuranose **2** produced at least four sharp peaks, the relative proportions of which were time-dependent (Table 1). The highest-field (δ_P -56.89 ppm) phosphorane was the least stable among them. The same results were obtained in THF and chloroform. As expected the peak due to remaining betaine **5** was still present.[23] When this experiment was repeated with one equivalent of xylofuranose **1**, the mixture of four phosphoranes was also formed (Table 1). These observations agree surprisingly well with the results for acyclic α,ω-diols described previously.[11,12] Under similar conditions, α,ω-diols react with the betaine **5** to give cyclic dioxatriphenylphosphoranes which appear to be oligomeric.[11] Such phosphoranes undergo exchange reactions with one another to give mixed species. According to the chemical shift assignments in the case of propane-1,3-diol,[11] the lowest-field signals (for **1**: -50.3 ppm, for **2**: -51.2 ppm) can be readily assigned to six-membered-ring cyclic phosphoranes **13** and **14**, respectively. The formation of analogous cyclic phosphoranes was also reported[11] for conformationally restricted 1,3-diols such as methyl 2,3-di-*O*-benzoyl-α-D-glucopyranoside

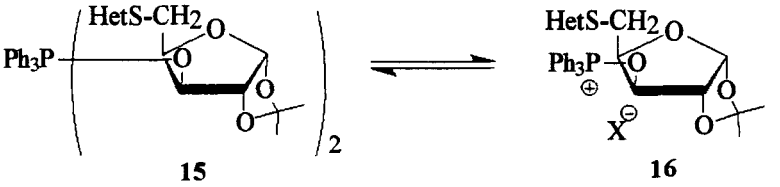


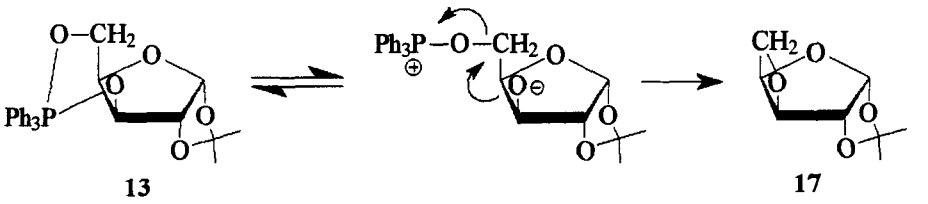
Scheme 2

(δ_P -51.7 ppm) and methyl 2,3-di-*O*-(*p*-tolylsulfonyl)-α-D-galactopyranoside (δ_P -52.9 ppm). The ^{31}P chemical shifts of phosphoranes originated from 1,2-*O*-isopropylidene-α-D-



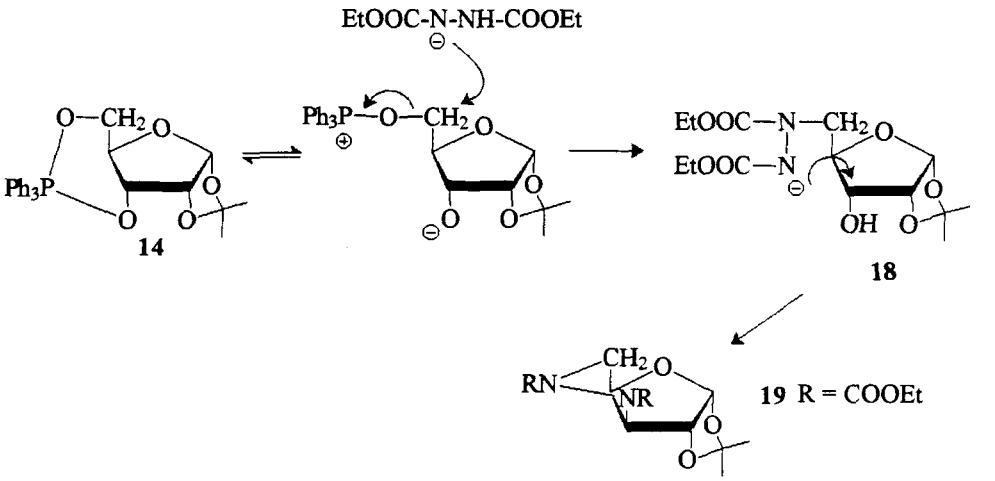
-pentofuranose derivatives with only one free secondary hydroxyl group were also measured (Scheme 2). Their structures can be attributed to acyclic *O,O*-phosphoranes of type **11** on the secondary *O*-sites according to known type-11-phosphoranes (R = Et: δ_P -54 ppm,[17] R = *i*Pr: δ_P - 49.6 ppm,[17] R = 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl: δ_P -57.5 ppm,[9,15] R = neopentyl: δ_P -57.5 ppm[16]). Interestingly, the phosphorane **15** was in equilibrium with the alkoxyphosphonium salt **16** (δ_P +66.32 ppm) even in the absence of added acid. The direct observation of this equilibrium had not been described previously.





13 17

Scheme 3



14 18 19 R = COOEt

Scheme 4

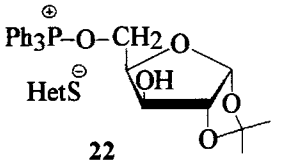
Furthermore, both phosphoranes **13** and **14** were unstable under the Mitsunobu conditions. Treatment of **1** with DEAD and TPP at 80 °C for 45 min gave 3,5-anhydro-1,2-*O*-isopropylidene-α-D-xylofuranose (**17**) in 85% yield as the result of attack of an internal nucleophile (Scheme 3). In contrast, the *ribo*-epimer **2** reacted[14] predominantly with the conjugated base of diethyl *N,N'*-hydrazinodicarboxylate and the transient species **18** underwent S_N2 cyclisation to afford the pyrazolidine derivative **19** (Scheme 4), which was subsequently isolated by chromatography in 80% yield and its structure confirmed in the usual way (^{1}H NMR, ^{13}C NMR, MS).

Addition of one equivalent of HetSH to the solution of phosphorane **13** generated from one equivalent of TPP and DEAD, and half an equivalent of **1** (pyridine, 10 °C, **5**: δ_P +45.64 ppm, **13**: δ_P -50.00 ppm) caused the immediate disappearance of the betaine **5** and

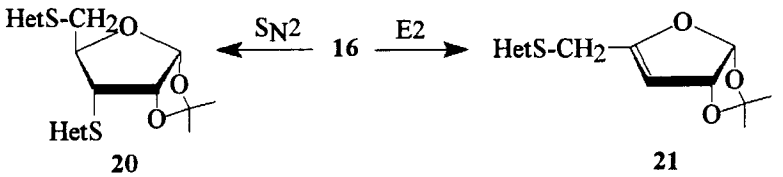
Table 2. Relative abundance of alkoxyphosphonium intermediates obtained from furanoses **1** and **2** in the Mitsunobu reaction with HetSH.

Time [min]	Xylofuranose **1**, δ_P [ppm]				Ribofuranose **2**, δ_P [ppm]	
	+64.12	+64.98	+66.38	+66.72	+64.40	+65.14
20	100	0	0	0	100	0
40	74	6	14	6	79	21
60	50	5	38	7	60	40
next day	0	0	100	0	0	100

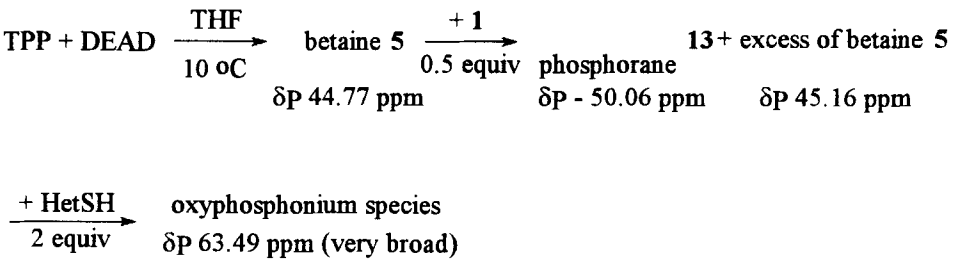
phosphorane **13** peaks and gave rise[23] to several new peaks in the ^{31}P NMR. Two signals at δ_P +53.17 ppm and 51.97 ppm in a ratio 20 : 1 and a downfield-shifted peak at δ_P +64.12 ppm appeared. At this moment, no product **3** was formed according to TLC therefore the signal at δ_P +64.12 ppm indicative[15,16] of a phosphonium ion represents the primary oxyphosphonium intermediate **22**. The intensity of its signal decreased with a time-rate following the appearance of additional signals in this ^{31}P NMR region (Table 2). As the intensity of the most stable alkoxyphosphonium salt (δ_P +66.38 ppm) increased, product **3** was formed until it was the only signal present and no starting material **1** could be detected on TLC anymore. Clearly, the structure of this alkoxyphosphonium species must involve one molecule **3** and therefore, the descriptive formula **16** seems to be the most probable. The presence of **16** in the reaction mixture was also confirmed by a preparative experiment in which the minor fraction of less polar products consisted in compounds **20** and **21** resulting from its subsequent S_N2 and E2 reaction, respectively. The formation of related compounds has previously been reported[3] in the reaction of methyl D-hexopyranosides.



22



20 **21**



Scheme 5

The analogous experiment with ribofuranose **2** led to the mixture of two oxyphosphonium species (Table 2) : the signal at δ_P +64.40 ppm can be attributed to a *ribo* analog of **22** and this one at δ_P +65.14 ppm to an oxyphosphonium cation of the product **4**. Practically the same course of the reaction was found in THF as the solvent (Scheme 5) with the exception that the interconversion of phosphonium species was not detectable due to the signal broadening. This is in accordance with the expectation that polar solvents should favor ion-pair formation.[16,17]

Changing the order of addition of the reagents to the betaine **5** solution gave similar but not identical results. Thus, addition of HetSH (1 equiv) to the betaine **5** (δ_P +45.14 ppm; 1 equiv) in pyridine at 10 °C afforded two signals at 53.21 ppm and 52.06 ppm in a ratio 20 : 1. When half an equivalent of **1** was introduced, the intensity of these peaks decreased and a new signal at δ_P +64.10 ppm appeared. After addition of ribofuranose **2** into the solution containing TPP, DEAD, and HetSH, the oxyphosphonium salt at δ_P +64.40 ppm appeared immediately as well. The further course of both reactions monitored by ^{31}P NMR and TLC was the same as discussed in the previous experiment. No sign of the formation of dialkoxyphosphoranes[24] was observed and therefore it appears that in the presence of HetSH, oxyphosphonium species are stable in solution with respect to any possible phosphoranes.

Finally, the generally accepted mode[2] of the Mitsunobu reaction was tested. The solution of TPP, HetSH and xylofuranose **1** was prepared first (pyridine, 10 °C, molar ratio 1.1 : 1 : 0.5) and only the TPP signal was observed (δ_P -4.51 ppm). One equivalent of DEAD was then introduced directly into solution and the ^{31}P NMR spectrum was recorded after 5 min. Surprisingly, two approximately equal phosphorus signals were present besides

Table 3. The ^{31}P NMR chemical shifts[a] of betaine **5** and protonated betaine **6** depending on experimental conditions

5 δ_P [ppm]	**6** δ_P [ppm]	Acid	Solvent	Temperature	References
44.8	51.5	fluoroboric	-	-30	25
44.8			$CHCl_3$	0	9
44.7			THF	0	9
44.9	52.3	hydrazoic	$CHCl_3$	-	22
43.7			THF	0	17
44	51	benzoic	THF	-78	17
43.7	51.3	trifluoroacetic	THF	-	13
44.9	53.1	fluoroboric	THF	-	8
43.9			benzene	-	8
44.7			$CHCl_3$	-	8
45.4			DMF	-	8
43.0			THF	-	19
44.0	50.0	benzoic	THF	0	15

a. relative to external 85% phosphoric acid ($\delta_P = 0$)

the smallest one (17 % rel) corresponding to TPP. The peak at δ_P +27.39 ppm (44 % rel) was attributed to TPPO and the downfield-shifted peak at δ_P +64.17 ppm (39 % rel) was assumed to be **22**. The composition of the solution changed very slowly during several hours (TPP - 17 %, TPPO - 51 %, and **22** - 32 % after 3 hours) liberating the TPPO and the conversion was estimated to be 10 - 20 % according to TLC. The reason why this reaction is extremely slow is not yet clear and will be the object of further investigations.

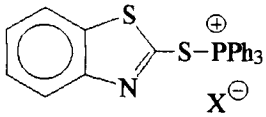
Further experiments were centered on a reaction of HetSH with betaine **5** giving two signals in ^{31}P NMR spectrum at δ_P +53.17 ppm and δ_P +51.97 ppm in an approximately 20 : 1 ratio. As has been demonstrated by previous studies on the Mitsunobu reaction, the betaine **5** reacts with acids to produce a protonated betaine **6** (Scheme 1, Table 3) and therefore the reaction of betaine **5** with benzoic acid was examined at first (pyridine, 10 °C). If only half an equivalent of benzoic acid was introduced, the signals of **5** and **6** were

Table 4. Relative abundance of phosphonium species derived from 2-mercaptobenzothiazole

		5 - HetSH (2 : 1)[a]			
δ_P [ppm]	54.40	53.38	52.30	51.24	50.52
rel %	5	70	2	18	5
		5 - benzoic acid - HetSH (2 : 1 : 2)[a]			
δ_P [ppm]	54.70	53.64	52.63		
rel %	14	84	2		
		5 - benzoic acid - HetSH (2 : 2 : 2)[a]			
δ_P [ppm]	54.68	53.59	52.77		
rel %	20	78	2		

a. a molar ratio

unresolved corresponding to a rapid chemical exchange.[17] On adding one equivalent of benzoic acid, the signal of **6** was shifted to lower field (δ_P +51.69 ppm) and when HetSH (1 equiv) was introduced subsequently it disappeared at once. Two new signals were formed at δ_P +53.22 ppm and δ_P +52.06, respectively, the former being predominant.[26] The temperature was then lowered at -60 °C and pyridine was replaced by THF. The rate of equilibrium **5** $\rightleftharpoons$ **6** efficiently decreased and the signals of **5** and **6** were resolved (**5**: δ_P +46.53 ppm, **6**: δ_P +51.87 ppm). On adding HetSH to a solution of **5**, **6** or a mixture of **5** and **6**, several peaks - which were not visible at higher temperature - rose in the phosphonium region (Table 4). The major signal could be asigned to a protonated betaine **6** probably associated with $HetS^-$ as a counterion but the remaining signals are difficult to identify. The data extracted from literature (Table 3) do not seem to be useful enough because any correlation between the chemical shifts of **5** or **6** and solvent, temperature, or acid used can hardly be discovered. Nevertheless, it seems that the formation of the thiophosphonium species **23** can be admitted. Especially the peaks at δ_P +54.70 ppm and



23

$X^{\ominus}$ = $HetS^{\ominus}$ or $EtOOC\text{-}\overset{\ominus}{N}\text{-}NH\text{-}COOE$ or $C_6H_5COO^{\ominus}$

δ_P +51.24 ppm are of interest, the content of the first one increased with concentration of protonated betaine **6** originally present and the latter was found only in reaction with the betaine **5** (Table 4).

Thiols are known to react with TPP and DEAD producing disulfides[27] and in the case of *t*-butyl mercaptan, isobutene and triphenylphosphine sulfide were identified as by-products arising from rapid β-elimination in the corresponding thiophosphonium salt. Similarly, the presence of triphenylphosphine sulfide in a reaction between *O,O*-diethyl phosphorodithioic acid and ethanol under the Mitsunobu conditions was explained[25] through the intermediacy of an unstable thiophosphonium salt. In addition, the chemical shift of phosphorus in *p*-tolylthiophosphonium perchlorate was[28] +46.5 ppm. Under the conditions used, no trace of triphenylphosphine sulfide was found, so the reaction of **23** with furanose **1** must be faster than the disulfide formation. No evidence for thiophosphoranes was apparent as well.

Conclusion. Under the Mitsunobu conditions (DEAD, TPP), the phosphoranes of variable stability are produced from the partially protected pentofuranoses. Their subsequent reaction with an external nucleophile can be complicated by a competitive reaction with an internal nucleophile or with diethyl *N,N'*-hydrazinodicarboxylate anion. In the presence of HetSH, the formation of the oxyphosphonium ion is favored over the phosphoranes and a rate limiting step is then the S_N2 displacement of the primary oxyphosphonium intermediate. The reaction of HetSH with both betaine **5** and protonated betaine **6** gives several phosphonium species therefore the presence of an unstable thiophosphonium salt cannot be excluded. The mechanism of the thiofunctionalization studied is analogous to this one reported for the Mitsunobu esterification. The reaction rate and the yield of the title reaction is not affected by the order of the reagents if the solution of betaine **5** is made first. Keeping the classic route with the adding of DEAD last of all, the reaction is slow and leads to a low yield of the desired products.

EXPERIMENTAL

General Methods. Diethyl azodicarboxylate, triphenylphosphine and 2-mercaptobenzothiazole were purchased from Aldrich. 1,2-*O*-Isopropylidene-α-D-

xylofuranose (1) was synthesized from D-xylose via a one-pot procedure[6] and 1,2-*O*-isopropylidene-α-D-ribofuranose (2) was prepared in 70% yield from 1 by pyridinium dichromate oxidation[29] followed by reduction with sodium borohydride.[30] All solvents were dried prior to distillation and stored over molecular sieves. Solvents were removed under diminished pressure below 45 °C. Column chromatography was performed on Silica Gel Lachema (Brno, Czech Republic), 100 - 160 μm, and TLC on Silica Gel G according to Stahl, 10 - 40 μm (Merck, Darmstadt, Germany). Compounds on TLC plates were visualized by spraying with 1 % cerium(IV)sulfate in 10 % sulfuric acid and subsequent mineralization. Melting points were determined with a Kofler hot block and are uncorrected. Optical rotations were measured on an Opton Photoelectric Precision Polarimeter 0.005. NMR data were extracted from spectra measured in solution of $CDCl_3$ (TMS as an internal standard) with a BRUKER AM-400 spectrometer. Carbon-signal shifts were made by HETCOR experiment and proton-signal shifts were obtained by first order analysis of the spectra using COSY experiment and a selective decoupling. Mass spectra were recorded on a JEOL DX 303 instrument using an EI technique at 70 eV.

General Procedure for ^{31}P NMR Experiments. A solution of TPP (47 mg, 0.179 mmol) in pyridine or THF (1.5 mL) was cooled at 10 °C or -60 °C in a 10 mm NMR tube with rubber seal. DEAD (26 μL, 0.166 mmol) was inserted into this solution under argon in one portion. The mixture was shaken and after 5 min the ^{31}P NMR spectrum was recorded. Changing the order of compounds a volume 50 μL (a molar ration of betaine **5** to an agent 2 : 1) or 100 μL (a ratio 1 : 1) of 1.6 M solutions of each **1**, **2**, HetSH, and benzoic acid was quickly added under argon. The mixture was shaken and the spectrum was recorded again. All stock solutions were kept under argon. This technique gave better results than those obtained by dropwise addition of solution or by inserting the solid compounds. Nevertheless, the content of TPPO in betaine **5** solution was about 20 % of all phosphorus signals detected. The ^{31}P NMR chemical shifts were measured with external 85% phosphoric acid as a reference. The signal of TPP was used as an internal reference at -60 °C and its value was set at -4.58 ppm.

5-*S*-(Benzothiazol-2-yl)-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose (3). TPP (2.9 g, 10.8 mmol) and **1** (1.0 g, 5.4 mmol) were dissolved in pyridine (30 mL) and DEAD (1.7 mL, 10.8 mmol) was introduced in one portion under nitrogen. After standing for 5 min, HetSH (1.8 g, 10.8 mmol) was added and the mixture was heated at 80 °C under

nitrogen for 15 min. After evaporation of pyridine, the residue was purified by chromatography (150 g silica gel, petroleum ether/AcOEt from 8 : 1 to 6 : 1). The first eluated fraction of non polar products (166 mg) contained two compounds in a ratio 2 : 1 identified by NMR as 3,5-di-*S*-(benzothiazol-2-yl)-1,2-*O*-isopropylidene-3,5-dithio-α-D-ribofuranose (**20**) and 5-*S*-(benzothiazol-2-yl)-3-deoxy-1,2-*O*-isopropylidene-5-thio-α-D-*erythro*-pent-3-enofuranose (**21**) which could not be separated. ^{1}H NMR δ [ppm], **20**: 1.35 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.81 (dd, 1H, $J_{4,5a}$ = 4.4 Hz, $J_{5a,5b}$ =14.4 Hz, H-5a), 3.95 (dd, 1H, $J_{4,5b}$ = 3.6 Hz, H-5b), 4.55 (m, 1H, H-4), 4.66 (dd, 1H, $J_{3,4}$ = 10.2 Hz, $J_{2,3}$ = 4.6 Hz, H-3), 4.97 (dd, 1H, H-2), 5.95 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 7.1 - 7.9 (m, arom H). **21**: 1.41 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 4.11 (s, 2H, 2 x H-5), 5.28 (d, 1H, H-2), 6.09 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1), 7.1 - 7.9 (m, arom H, H-3).

Further elution afforded product **3** (1.62 g, 88.5 %) which was recrystallized from ether-petroleum ether (1.04 g, 56 %), mp. 149 - 150 °C, $[\alpha]_D^{20}$ +276 (*c* 1.4, $CHCl_3$). Chromatography of the mother liquor gave a further fraction of 420 mg, the overall yield of **3** being 1.46 g (80 %). ^{1}H NMR δ [ppm]: 1.32 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.30 (dd, 1H, $J_{4,5a}$ = 3.2 Hz, $J_{5a,5b}$ =14.7 Hz, H-5a), 3.95 (dd, 1H, $J_{4,5b}$ = 11.3 Hz, H-5b), 4.15 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,OH}$ = 2.5 Hz, H-3), 4.36 (ddd, 1H, H-4), 4.63 (d, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ ≅ 0 Hz, H-2), 5.97 (d, 1H, H-1), 6.16 (d, 1H, OH-3), 7.34 (ddd, 1H, aromH-6), 7.45 (ddd, 1H, aromH-5), 7.75 (d, 1H, aromH-7), 7.82 (d, 1H, aromH-4). ^{13}C NMR δ [ppm]: 26.15 and 26.86 (2 x CH_3), 29.31 (C-5), 73.39 (C-3), 81.90 (C-4), 84.96 (C-2), 104.94 (C-1), 111.70 (*tert*C), 120.77 (aromC-4), 121.19 (aromC-7), 124.96 (aromC-6), 126.55 (aromC-5), 134.75 (aryl-C-S), 151.60 (aryl-C-N), 168.53 (C-S).

Anal.Calcd for $C_{15}H_{17}NO_4S_2$ (339.42): C, 53.06; H, 5.01; N, 4.12; S, 18.89. Found: C, 53.21; H, 5.15; N, 4.01; S, 18.67.

5-*S*-(Benzothiazol-2-yl)-1,2-*O*-isopropylidene-5-thio-α-D-ribofuranose (4). Starting from **2** (890 mg, 4.7 mmol) the same experiment as described above afforded product **4** (1.32 g, 84.3 %). After crystallization and chromatography of the mother liquor, 1.1 g of pure **4** (70 %) was obtained, mp. 119 - 120 °C, $[\alpha]_D^{20}$ -102 (*c* 1.4, $CHCl_3$). ^{1}H NMR δ [ppm]: 1.35 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 3.87 (dd, 1H, $J_{4,5a}$ = 3.1 Hz, $J_{5a,5b}$ =14.9 Hz, H-5a), 3.87 (dd, 1H, $J_{4,5b}$ = 3.7 Hz, H-5b), 3.95 (dd, 1H, $J_{2,3}$ = 4.3 Hz, $J_{3,4}$ = 8.7 Hz, $J_{3,OH}$ ≅ 0 Hz, H-3), 4.35 (m, 1H, H-4), 4.40 (bs,1H, OH-3), 4.64 (dd, 1H, H-2), 5.78 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 7.33 (dd, 1H, aromH-6), 7.43 (dd, 1H, aromH-5), 7.76 (d, 1H,

aromH-7), 7.80 (d, 1H, aromH-4). ^{13}C NMR δ [ppm]: 26.35 and 26.60 (2 x CH_3), 34.56 (C-5), 73.63 (C-3), 77.85 (C-4), 79.02 (C-2), 103.84 (C-1), 113.03 (*tert*C), 121.13 (aromC-4), 121.17 (aromC-7), 124.70 (aromC-6), 126.37 (aromC-5), 135.20 (aryl-C-S), 152.49 (aryl-C-N), 168.45 (C-S).

Anal.Calcd for $C_{15}H_{17}NO_4S_2$ (339.42): C, 53.06; H, 5.01; N, 4.12; S, 18.89. Found: C, 53.28; H, 5.05; N, 4.20; S, 18.60.

3,5-Anhydro-1,2-*O*-isopropylidene-α-D-xylofuranose (17). TPP (1.4 g, 5.4 mmol) was dissolved in pyridine (15 mL) and DEAD (0.83 mL, 5.4 mmol) was added in one portion under nitrogen. Solid **1** (513 mg, 2.7 mmol) was introduced after 5 min and the mixture was heated at 80 °C for 30 min. After concentration, a residue was separated on silica gel (100 g) with petroleum ether - ethyl acetate from 6 : 1 to 6 : 2 (v/v). Product **17** was obtained (340 mg) in 85 % yield, $[\alpha]_D^{20}$ +11 (*c* 1.0, $CHCl_3$), ref.[31] $[\alpha]_D^{24}$ = +11.9 (*c* 0.75, $CHCl_3$). ^{1}H NMR, δ [ppm]: 1.38 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 4.27 (dd, 1H, $J_{4,5a}$ = 2.3 Hz, $J_{5a,5b}$ = 8.0 Hz, long range coupling 0.5 Hz, H-5a), 4.74 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-2), 4.76 (dd, 1H, $J_{4,5b}$ = 4.2 Hz, H-5b), 5.13 (dt, 1H, H-4), 5.22 (d, 1H, $J_{3,4}$ = 4.0 Hz, H-3), 6.31 (d, 1H, H-1) agrees with those[31] reported.

Diethyl 6,6-dimethyl-4aH-(3a*S*,4a*R*,7a*S*,7b*R*)-[1,3]-dioxolo-[4,5]furo[3,2-c] pyrazolidin-1,2-dicarboxylate (19). Starting from **2** (513 mg, 2.7 mmol) and using the same procedure as for **17** product **19** was isolated as a syrup in yield 80 % (700 mg), $[\alpha]_D^{20}$ -15 (*c* 0.7, $CHCl_3$), ^{1}H NMR, δ [ppm]: 1.31 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.28 (q, 6H, 2 x CH_3), 3.17 (dd, 1H, $J_{4,5a}$ = 2.2 Hz, $J_{5a,5b}$ =12.7 Hz, H-5a), 4.20 (m, 5H, CH_2, H-5b), 4.53 (d, 1H, $J_{3,4}$ = 4.5 Hz, $J_{2,3} \cong 0$ Hz, H-3), 4.85 (bs, d at 50 °C, 1H, H-2), 5.03 (dd, 1H, $J_{4,5b} \cong 0$ Hz, H-4), 5.76 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1). ^{13}C NMR δ [ppm]: 14.39 and 14.55 (2 x CH_3), 27.42 and 26.69 (2 x CH_3), 55.10 (broad, C-5), 62.96 and 62.73 (2 x OCH_2), 67.96 (broad, C-3), 82.77 (C-4), 84.14 (C-2), 106.69 (C-1), 112.89 (*tert*C), 152.66 and 152.66 (2 x CO). MS (*m/z*): 330(14) (M^+), 315(11) (M^+-CH_3), 285(4) (M^+-OCH_2CH_3), 258(70) (M^+-CH_2CH_2, -CO_2), 69(100) ($C_3H_5N_2^+$), 97(80) ($C_4H_5N_2O^+$), 29(74), 141(55) ($C_6H_9N_2O_2^+$), 117(45) ($C_5H_9O_3^+$), 185(37) ($C_8H_{13}N_2O_3^+$), 59(41) ($C_2H_3O_2^+$).

Anal.Calcd for $C_{14}H_{22}N_2O_7$ (330.34): C, 50.90; H, 6.71; N, 8.48. Found: C, 50.81; H, 6.65; N, 8.11.

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23. Two minor peaks were also observed : the one at - 4.30 ppm corresponded to a slight excess of TPP and the second at + 27.32 ppm was the signal of TPPO.
24. When the reaction of protonated betaine **6** with **1** was examined by low-temperature ^{31}P NMR, the phosphorane **13** was observed as a broad signal at +51.30 ppm even if benzoic acid was added first, in agreement with the observations of Evans.[17]
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26. If furanose **1** was treated with a mixture of Ph_3P, DEAD, benzoic acid, and HetSH, the formation of oxetane **17** besides product **3** was detected on TLC.
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