Synthesis of Heterocyclic Compounds with Saccharidic Component

[a]J. KOZÁK, [a]S. KUČÁR, [a]M. MATULOVÁ, and [b]E. JEDLOVSKÁ

[a]*Institute of Chemistry, Slovak Academy of Sciences, CS-842 38 Bratislava*

[b]*Department of Organic Chemistry, Faculty of Chemical Technology, Slovak Technical University, CS-812 37 Bratislava*

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Dedicated to the memory of Professor Adolf Jurášek, DrSc.

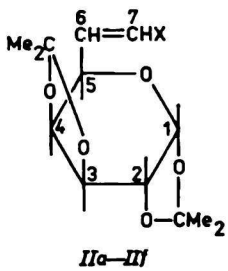
A series of eighteen *E*- and *Z*-isomers of heterocyclic compounds with saccharidic component was prepared by Wittig reaction of 6-phosphoranes of D-tagatose, D-glucose, and D-galactose with 2-furaldehyde and its derivatives. 6-Phosphoranes of saccharides were generated by deprotonization of phosphonium salts with ethereal solution of n-butyllithium in the mixture of tetrahydrofuran (THF) and hexamethylphosphoric triamide (HMPTA) (φ_r = 2 1) at − 50 °C.

Wittig reaction [1], discovered in 1953, is the most suitable method for the preparation of unsaturated compounds. A wide variety of products can be achieved by different type of the used phosphorane. In the chemistry of saccharides, this reaction was applied for the first time by *Kuhn* in 1962 [2] when reaction of glyceraldehyde with nonsaccharidic phosphorane was described. As a beginning of systematic investigation of Wittig reaction in the chemistry of saccharides, the works by *Zhdanov*, *Kochetkov*, and *Dmitriev* [3—5] can be considered. As an example of Wittig reaction where carbonyl component is represented by saccharide, works by *Tronchet* [6—9] can be mentioned. Interesting case of Wittig reaction represents application of saccharidic phosphoranes. Synthesis of the first carbohydrate phosphorane was published by *Zhdanov* and *Polenov* [10] who prepared resonance-stabilized phosphorane from 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-(triphenylphosphonio)-α-D-*xylo*-5-hexulofuranose bromide. In the papers [11, 12], the preparation of unstabilized phosphoranes is described.

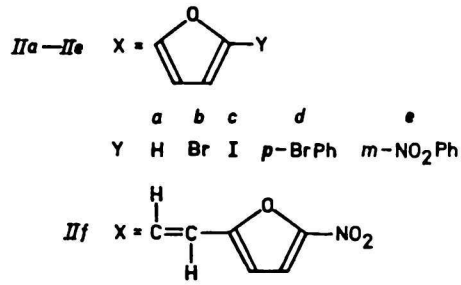
Our work, having preparation of heterocyclic compounds with saccharidic component as a target, starts from the preparation of phosphonium salts of D-glucose, D-galactose, and D-tagatose by the reaction of corresponding 6-deoxy-6-iodo derivatives with triphenylphosphine in tetrahydrothiophene 1,1-dioxide (sulfolane). By deprotonization of these phosphonium salts with n-butyllithium, corresponding phosphoranes were prepared. With regard to their instability, the unstabilized phosphoranes were brought into reaction with six aldehydes of furan type without isolation. These aldehydes were selected with respect to their synthetic prominence as well as anticipated antimicrobial activity of products of Wittig reaction.

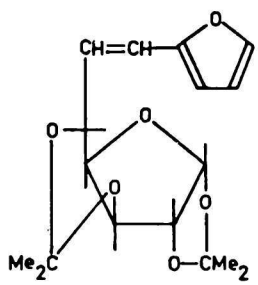
EXPERIMENTAL

Optical rotation [α](D, 20 °C, ρ = 10 g dm^{-3}, $CHCl_3$) was determined on a Perkin—Elmer, Model 141, polarimeter. Preparative chromatography was performed using column chromatography on silica gel with 100—250 μm grain size using 1500 mm × 25 mm or 1500 mm × 45 mm glass columns. Thin-layer chromatography (TLC) for reaction course observation was performed on Silufol plates (Kavalier, Votice). For detection, spraying with 5 % solution of sulfuric acid in ethanol followed by heating to 105 °C, was used. ^{1}H and ^{13}C NMR spectra (Tables 1—6) were measured on a Bruker AM-300 spectrometer at 298 K. For water-soluble derivatives, D_2O was used as a solvent with TSP (sodium 3-(trimethylsilyl)propionate, δ = 0), respectively methanol (δ = 50.15) as an internal standard. The other derivatives were measured in $CDCl_3$ solution with TMS (tetramethylsilane, δ = 0) as an internal standard. ^{1}H NMR spectra (300.13 MHz) were measured in 5 mm proton probe with digital resolution 0.12 resp. 0.16 Hz per point. For the assignment of signals in the spectra, 1D-COSY and 1D-relayed experiment with relaxation time of 2.5 s was used. Fixed intervals for transport of magnetization were optimized from the known values of coupling constants. The time of soft Gaussian pulse took 40 ms. The signals in ^{13}C NMR spectra (75.46 MHz) were unambiguously assigned using semiselective INEPT technique with the following parameters: digital resolution 1.9 Hz/point, relaxa-

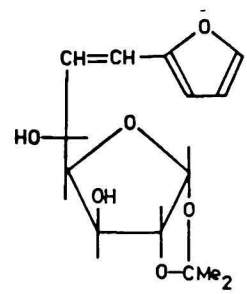


IIa—IIf

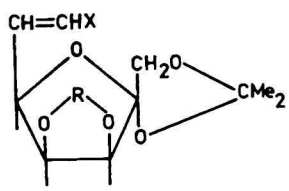




Va



Vb



VIIIa, VIIIf (X as at *II*; R = CMe_2)

tion interval 2.5 s, time of semiselective pulse for magnetization transport τ_{90} 9.5 ms. The time intervals in pulse sequence were optimized on the long-range coupling constant $^{n}J_{C,H}$ = 7 Hz.

General Procedure for the Preparation of Ylides and Their Condensation with Heterocyclic Aldehydes

In a two-necked flask equipped with a drying tube and capillary for nitrogen inlet, a solution of phosphonium salt (2 mmol) in a mixture of HMPTA—THF (φ_r = 1 2, 12 cm^3) was cooled to −50 °C. Ethereal solution of n-butyllithium (2 mmol) was added. Owing to this addition of organometallic base, deprotonation of phosphonium salt and formation of ylide takes place and reddish-brown colouring of the solution is observed. Furaldehyde (3 mmol) is added without solvent, the other aldehydes are added dissolved in THF (5—10 cm^3). Reaction mixture is warmed up to −5 to −10 °C. According to TLC in the corresponding system, reaction is finished after 90 min. A mixture of petroleum ether—ether (φ_r = 1 1, 100 cm^3) is added into reaction mixture, precipitated triphenylphosphine oxide is filtered off and washed with the above mixture. Filtrate is saturated under diminished pressure and the residue is dissolved in a mixture of petroleum ether—ether (φ_r = 1 : 1). This solution is washed with water (3 × 50 cm^3), saturated solution of $NaHSO_3$ (2 × 50 cm^3), again with water and organic layer is dried over anhydrous sodium sulfate. After evaporation of solvents, crude mixture is obtained from which products of Wittig reaction are isolated by column chromatography on silica gel using appropriate elution system.

(*E*)- and (*Z*)-6,7-Dideoxy-1,2:3,4-di-*O*-isopropylidene-7-(5-Y-2-furyl)-α-D-*galacto*-6-heptenopyranose *IIa—IIe*

For their preparation 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-(triphenylphosphonio)-α-D-galactopyranose iodide (*I*) [12] (1.264 g, 2 mmol), ethereal solution of n-butyllithium (ρ = 49.1 g dm^{-3}, 2.6 cm^3, 2 mmol), and the corresponding 2-furaldehyde [13—

16] (3 mmol) were used. *E*- and *Z*-isomers of *IIa*—*IIe* from the reaction mixture were separated on a column of silica gel with: *a*) benzene—ethyl acetate (φ_r = 80 2); *b* and *c*) benzene—ethyl acetate (φ_r = 97 : 3); *d*) cyclohexane—ethyl acetate (φ_r = 40 : 3.7); *e*) cyclohexane—ethyl acetate (φ_r = 40 4.5).

Isomer (*E*)-*IIa*: Yield 0.1768 g (27.44 %), m.p. = 108—110 °C (96 % ethanol), [α] = −177.1°. For $C_{17}H_{22}O_6$ (M_r = 322.45) w_i(calc.): 63.34 % C, 6.88 % H; w_i(found): 63.15 % C, 6.82 % H.

Isomer (*Z*)-*IIa*: Yield 0.3166 g (49.14 %), oil, [α] = −92.8°, w_i(found): 63.20 % C, 6.81 % H.

Unseparated fractions of *E*- and *Z*-isomers: Yield 0.0375 g (5.82 %). Total yield of *IIa* is 0.5309 g (82.4 %).

Isomer (*Z*)-*IIb*: Yield 0.1825 g (22.75 %), oil, [α] = −72.1°. For $C_{17}H_{21}BrO_6$ (M_r = 401.38) w_i(calc.): 50.88 % C, 5.28 % H; w_i(found): 50.85 % C, 5.23 % H.

Isomer (*E*)-*IIb*: Yield 0.4105 g (51.18 %), oil, [α] = −92.8°, w_i(found): 50.75 % C, 5.22 % H.

Unseparated fraction of *E*- and *Z*-isomers: Yield 0.031 g (3.86 %). Total yield of *IIb* is 0.624 g (77.8 %).

Isomer (*Z*)-*IIc*: Yield 0.2125 g (23.71 %), oil, [α] = −85.7°. For $C_{17}H_{21}IO_6$ (M_r = 448.38) w_i(calc.): 45.56 % C, 4.72 % H; w_i(found): 45.45 % C, 4.69 % H.

Isomer (*E*)-*IIc*: Yield 0.4237 g (23.71 %), oil, [α] = −115.2°, w_i(found): 45.50 % C, 4.65 % H.

Unseparated fraction of *E*- and *Z*-isomers: Yield 0.0394 g (4.39 %). Total yield of *IIc* is 0.6756 g (75.4 %).

Isomer (*Z*)-*IId*: Yield 0.4024 g (42.16 %), oil, [α] = +61°. For $C_{23}H_{25}BrO_6$ (M_r = 477.49) w_i(calc.): 57.87 % C, 5.28 % H; w_i(found): 57.45 % C, 5.22 % H.

Isomer (*E*)-*IId*: Yield 0.2468 g (25.86 %), m.p. = 138—140 °C (96 % ethanol), [α] = −143.7°, w_i(found): 57.55 % C, 5.23 % H.

Unseparated fraction of *E*- and *Z*-isomers: Yield 0.0752 g (7.88 %). Total yield of *IId* is 0.7244 g (75.9 %).

Isomer (*E*)-*IIe*: Yield 0.2758 g (31.13 %), oil, [α] = −46.8°. For $C_{23}H_{25}NO_8$ (M_r = 443.58) w_i(calc.): 62.29 % C, 5.68 % H, 3.16 % N; w_i(found): 62.15 % C, 5.63 % H, 3.15 % N.

A mixture of *Z*- and *E*-isomers (the amount of substance ratio 2 : 3 — determined on the basis of NMR data): Yield 0.4394 g. Total yield of *IIe* is 0.7152 g (80.72 %).

Table 1. ^{1}H NMR Data of Products from Wittig Reaction of D-Galactose and D-Glucose

Compound	Chemical shift δ																				
	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8	H-9	H-10	H-11	H-12	H-13	H-14	H-15	H-16	H-17	CH_3 Isoprop.			
IIa c	5.52	4.30	4.59	4.28	5.20	5.58	6.28	–	*d*	*d*	7.40	–	–	–	–	–	–	1.50	1.42	1.28	1.27
t	5.61	4.34	4.64	4.28	4.43	6.23	6.52	–	6.25	6.34	7.32	–	–	–	–	–	–	1.59	1.48	1.38	1.37
IIb c	5.53	4.29	4.61	4.31	5.09	5.58	6.15	–	6.24*	6.27*	–	–	–	–	–	–	–	1.55	1.42	1.28	1.27
t	5.52	4.27	4.57	4.19	4.34	6.14	6.35	–	6.18*	6.11*	–	–	–	–	–	–	–	1.47	1.40	1.29	1.29
IId c	5.63	4.41	4.73	4.61	5.39	5.68	6.30	–	6.41*	6.67*	–	–	*e*	*e*	–	*e*	*e*	1.52	1.44	1.37	1.33
t	5.63	4.35	4.66	4.30	4.47	6.32	6.54	–	6.31*	6.61*	–	–	*e*	*e*	–	*e*	*e*	1.52	1.42	1.40	1.35
IIe c	5.62	4.42	4.84	4.63	5.35	5.78	6.37	–	6.52*	6.86*	–	–	7.94	7.54	8.09	–	8.42	1.52	1.37	1.34	1.27
t	5.64	4.37	4.68	4.34	4.51	6.40	6.58	–	6.35*	6.78*	–	–	7.94	7.54	8.06	–	8.47	1.52	1.50	1.36	1.35
IIf c,c,t	5.62	4.38	4.68	4.24	4.83	5.97	6.37	7.40	6.39	–	6.46*	7.31*	–	–	–	–	–	1.57	1.46	1.38	1.37
t,c,t	5.60	4.35	4.64	4.26	4.43	6.09	6.49	7.06	6.34	–	6.45*	7.31*	–	–	–	–	–	1.75	1.50	1.42	1.39
Va c	5.99	4.53	4.38	4.10	5.49	5.75	6.33	–	6.31	6.40	7.40	–	–	–	–	–	–	1.55	1.45	1.43	1.31
Vb c	6.07	4.64	4.50	4.22	4.49	5.80	6.37											1.43	1.32	–	–

	Coupling constants J/Hz																
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{9,10}$	$J_{10,11}$	$J_{11,12}$	$J_{12,13}$	$J_{13,14}$	$J_{14,15}$	$J_{15,16}$	$J_{16,17}$	$^4J_{5,7}$
IIa c	5.1	2.6	8.2	2.0	8.2	12.3	–	–	3.3	1.8	–	–	–	–	–	–	–
t	5.0	2.4	7.9	2.1	6.2	15.9	–	–	3.3	1.8	–	–	–	–	–	–	1.3
IIb c	5.4	2.6	7.7	2.0	8.2	12.0	–	–	3.3	–	–	–	–	–	–	–	1.0
t	5.1	2.6	7.8	2.0	5.6	15.9	–	–	3.3	–	–	–	–	–	–	–	1.2
IId c	5.2	2.6	8.0	1.8	7.4	12.1	–	–	3.3	–	–	–	**	–	–	**	1.2
t	5.2	2.6	8.0	1.8	5.9	15.9	–	–	3.3	–	–	–	**	–	–	**	1.3
IIe c	5.1	2.5	7.9	1.8	7.6	12.0	–	–	3.3	–	–	–		–	–		1.5
t	5.1	2.3	7.8	1.9	5.6	15.6	–	–	3.3	–	–	–		–	–		1.4
IIf c,c,t	5.1	2.6	7.7	2.0	8.2	10.3	11.5	15.6	–	–	3.8	–	–	–	–	–	1.2
t,c,t	4.9	2.3	8.0	2.0	5.9	15.1	11.0	15.6	–	–	3.8	–	–	–	–	–	1.5
Va c	3.8	1.0	2.3	2.0	8.5	12.0	–	–	3.3	1.8	–	–	–	–	–	–	1.0
Vb c	3.6	1.0	2.3	1.2	8.5	12.0	–	–	**	**	–	–	–	–	–	–	**

c - *cis*-orientation of protons of the side chain; t - *trans*-orientation of protons of the side chain; *e* - signals form multiplet of higher order at δ = 7.50; *d* - signals overlapped in the range of δ = 6.20—6.30. * Signals are mutually exchangeable; ** coupling constants unassigned or undistinguished.

(*Z,Z,E*)- and (*E,Z,E*)-1,2:3,4-di-*O*-isopropylidene-9-(5-nitro-2-furyl)-α-D-*galacto*-6,8-nonadienopyranose (*IIf*)

For its preparation *I* (1.0 g, 1.58 mmol), ethereal solution of n-butyllithium (ρ = 49.1 g dm^{-3}, 2.2 cm^3, 1.58 mmol), 3-(5-nitro-2-furyl)propenal [17] (0.396 g, 2.37 mmol) were used. Reaction mixture of *Z,Z,E*- and *E,Z,E*-isomers of compound *IIf* was separated using chromatography with cyclohexane—ethyl acetate (φ_r = 45 : 8) as an eluent.

Isomer (*Z,Z,E*)-*IIf*: Yield 0.148 g (23.8 %), oil, [α] = − 69°. For $C_{19}H_{23}NO_8$ (M_r = 393.50) w_i(calc.): 58.00 % C, 5.89 % H, 3.56 % N; w_i(found): 57.95 % C, 5.84 % H, 3.54 % N.

Isomer (*E,Z,E*)-*IIf*: Yield 0.285 g (45.8 %), m.p. = 120—123 °C (96 % ethanol), [α] = − 175°, w_i(found): 57.97 % C, 5.83 % H, 3.54 % N.

Unseparated fraction of *Z,Z,E*- and *E,Z,E*-isomers: Yield 0.0548 g (8.81 %). Total yield of *IIf* is 0.4878 g (78.42 %).

6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-(triphenylphosphonio)-α-D-glucofuranose Iodide (*IV*)

A solution of 6-deoxy-6-iodo-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (*III*) [18] (5.8 g, 15.6 mmol) and triphenylphosphine (5.0 g, 19 mmol) in 7.3 cm^3 of sulfolane was heated at 105—110 °C for 24 h. After this time, only traces of starting compound *III* were observed by TLC. Reaction mixture was worked up analogically as in the case of compound *I* [12]. Totally, 9.7 g (97.72 %) of product was obtained, m.p. = 175—178 °C, crystallization from ethyl acetate—methanol (φ_r = 10 : 1), [α] = + 10°. For $C_{30}H_{34}IO_5P$ (M_r = 632.65) w_i(calc.): 56.97 % C, 5.42 % H; w_i(found): 56.65 % C, 5.41 % H.

(*Z*)-6,7-Dideoxy-1,2:3,5-di-*O*-isopropylidene-(*Va*) and (*Z*)-6,7-Dideoxy-1,2-*O*-isopropylidene-7-(2-furyl)-α-D-*gluco*-6-heptenofuranose (*Vb*)

Phosphonium salt (*IV*) (1.264 g, 2 mmol), ethereal solution of n-butyllithium (ρ = 49.1 g dm^{-3}, 2.2 cm^3, 1.58 mmol), and 2-furaldehyde (0.288 g, 3 mmol) were used. *Z*-Isomer of *Va* and *Vb* was obtained analogically as in case of compound *IIb*.

Isomer *Va*: Yield 0.1585 g (24.6 %), oil, [α] = + 49°. For $C_{17}H_{22}O_6$ (M_r = 322.45) w_i(calc.): 63.34 % C, 6.88 % H; w_i(found): 63.15 % C, 6.81 % H.

Isomer *Vb*: Yield 0.0373 g (6.6 %), oil, [α] = + 29°. For $C_{14}H_{18}O_6$ (M_r = 282.37) w_i(calc.): 59.57 % C, 6.42 % H; w_i(found): 59.51 % C, 6.36 % H.

Mixture of isomers *Va* and *Vb*: Yield 0.0285 g (4.7 %). Total yield of *Va* and *Vb* was 0.224 g (35.9 %).

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-(triphenylphosphonio)-α-D-tagatofuranose Iodide (*VII*)

6-Deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-tagatofuranose (*VI*) [19] (1.4 g, 3.8 mmol) and tri-

Table 2. ^{13}C NMR Data of Products from Wittig Reaction of D-Galactose and D-Glucose

Compound	Chemical shift δ																			
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	CH_3 isoprop.	$C_{isoprop.}$	
IIa c	96.5	70.1	70.9	73.5	65.4	110.8	118.3	152.2	125.0	111.2	142.2	–	–	–	–	–	–	25.9	25.7	109.0
																		25.0	24.3	108.5
t	96.5	70.5	70.9	73.3	68.3	108.2	120.6	152.3	123.5	111.1	141.9	–	–	–	–	–	–	26.1	25.9	109.3
																		24.9	24.3	108.5
IIb c	96.5	70.1	71.0	73.3	65.6	126.2	117.3	154.3	128.2*	117.3	143.3	–	–	–	–	–	–	26.3	26.0	109.2
																		25.0	24.4	108.7
t	96.4	70.4	70.8	73.1	68.0	110.4	119.4	154.3	121.4	112.9	124.2	–	–	–	–	–	–	26.1	26.0	109.3
																		24.9	24.2	108.5
IId c	96.6	70.5	71.2	73.4	66.5	126.7	117.1	152.3	107.4	113.0	129.1	152.9	131.9	125.3	121.3	125.3	131.9	26.5	26.0	109.3
																		25.0	24.4	108.8
t	96.5	70.6	70.9	73.3	68.3	124.0	120.3	152.2*	107.4	110.7	129.5	152.1*	131.7	125.2	121.0	125.2	131.7	26.9	26.2	109.3
																		24.9	24.3	108.5
IIe c	96.6	70.1	70.4	73.5	66.3	127.6	117.4	152.8	109.2	113.1	129.8		129.2*		127.6*	121.8*	118.5*	26.5	26.1	109.2
																		25.2	24.5	108.7
t	96.5	70.6	70.9	73.2	68.2	125.1	119.9	153.1	109.1	110.7	139.6	150.6	132.1*	129.6*	129.1*	121.5*	118.5*	26.5	26.3	109.4
																		24.9	24.3	108.6
IIf c,c,t	96.7	70.1	70.7	72.9	63.7	131.4	129.5	131.1	119.4	151.4	113.8*	111.1	149.1	–	–	–	–	29.7	29.6	109.4
																		19.6	19.1	108.6
t,c,t	96.3	70.3	70.7	73.0	68.0	134.5	130.6	134.3	117.6	155.8	114.0*	110.2*		–	–	–	–	26.1	25.9	109.4
																		24.8	24.3	108.6
Va c	105.1	73.7*	73.4*	84.1	66.3	125.1	119.4	152.5	128.6*	126.6*	145.2	–	–	–	–	–	–	29.7	29.4	111.3
																		26.7	26.2	111.2
Vb c	105.2	79.1	74.2	82.9	73.9	123.8	119.3	151.8	**	**	142.6	–	–	–	–	–	–	26.4	26.0	111.7

c, *t* as in Table 1. * Signals can be mutually exchanged; ** unassigned signals.

Table 3. ^{1}H NMR Data of Phosphonium Salts of D-Galactose, D-Glucose, and D-Tagatose

Compound	Chemical shift δ											
	H-1	H-1′	H-2	H-3	H-4	H-5	H-6	H-6′	$CH_{3\ isoprop.}$			
I	5.13	–	4.19	4.52	4.73	3.70	4.89	4.35	1.40	1.27	0.8	
IV	5.90	–	4.50	4.34	4.83	3.68	4.79	3.60	1.52	1.28	1.24	0.5
VII	4.15	3.51	–	4.56	5.20	4.67	*e*	*d*	1.41	1.31	1.26	0.9

	Coupling constants J/Hz							
	$J_{1,1'}$	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
I	–	5.0	2.0	7.0	1.0	3.3	10.8	15.6
IV	–	3.6	0.2	3.9	6.6	**	**	**
VII	9.9	–	–	5.8	3.1	3.6	10.7	15.2

e – two signals at δ = 5.07 and 5.11; *d* – signals are overlapped in the range of δ = 3.45—3.62. ** Unassigned or undistinguished. Signals of benzene rings are in the range of δ = 7.60—7.90 for all three compounds.

phenylphosphine (1.2 g, 4.56 mmol) in sulfolane (1.8 cm^3) were heated at 80 °C. TLC in the system ethyl acetate—benzene (φ_r = 20 1) revealed that reaction was over after 72 h. Reaction mixture was worked up as in the case of compound *I* [12]. M.p. = 207—209 °C, [α] = +89°. For $C_{30}H_{34}IO_5P$ (M_r = 632.65) w_i(calc.): 56.92 % C, 5.42 % H; w_i(found): 56.85 % C, 5.40 % H.

(*E*)- and (*Z*)-6,7-Dideoxy-1,2:3,4-di-*O*-isopropylidene-7-(2-furyl)-α-D-*lyxo*-6-hepten-2-ulofuranose (*VIIIa*)

For its preparation phosphonium salt (*VII*) (1.0 g, 1.58 mmol), ethereal solution of n-butyllithium (ρ = 49.1 g dm^{-3}, 2.2 cm^3, 1.58 mmol), and 2-furaldehyde (0.23 g, 2.37 mmol) were used. Sepa-

Table 4. ^{13}C NMR Data of Phosphonium Salts of D-Galactose, D-Glucose, and D-Tagatose

Compound	Chemical shift δ										
	C-1	C-2	C-3	C-4	C-5	C-6	$CH_{3\ isoprop.}$				$C_{isoprop.}$
I	95.6	69.6	70.2	71.4	83.1	25.1	25.8	25.5	24.3	23.9	108.8
				71.3	83.0						108.4
IV	106.0	74.6	82.3	83.7	67.3	29.9	27.2	27.1	24.0	23.9	112.6
			82.1			29.1					
VII	68.6	111.5	73.0	80.0	84.6	23.8	26.0	25.7	25.5	24.3	112.3
			73.1	79.9		23.0					111.7

Signals of benzene rings carbon atoms are registered in the range of δ = 117—135. Owing to the bulky substituent at C-6 atom, some signals are doubled in the ^{13}C as well as ^{1}H NMR spectra of compounds *I*, *IV*, and *VII*.

Table 5. ^{1}H NMR Data of Products from Wittig Reaction of D-Tagatose

Compound		Chemical shift δ											
		H-1	H-1′	H-2	H-3	H-4	H-5	H-6	H-7	H-8	H-9	H-10	H-11	H-12
VIIIa	*c*	4.33	4.10	–	4.69	4.95	5.27	5.67	6.41	–	6.36	6.38	7.41	–
	t	4.32	4.09	–	4.64	4.73	4.51	6.24	6.53	–	**	**	**	–
VIIIf	*c,c,t*	4.33	4.11	–	4.69	4.83	4.95	5.91	6.39	7.32	6.40	–		**
	t,c,t	4.31	4.09	–	4.65	4.78	4.51	6.11	6.49	7.08	6.37	–		

		Coupling constants J/Hz									
		$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{9,10}$	$J_{10,11}$	$J_{11,12}$	$^4J_{5,7}$
VIIIa	*c*	9.7	5.7	3.8	8.0	12.0	–	–	3.3	1.7	–	1.1
	t	9.7	5.7	3.7	7.6	15.9	–	–	**	**	–	0.9
VIIIf	*c,c,t*	9.8	5.7	3.7	7.9	10.9	11.5	15.4	–	–	**	1.1
	t,c,t	9.8	5.8	3.8	7.2	15.4	11.1	15.6	–	–		0.9

c, *t* as in Table 1. ** Unassigned or undistinguished. Chemical shifts of protons of methyl group for *c*-*VIIIa* and *t*-*VIIIa* are registered in the range of δ = 0.8—1.6.

Table 6. ^{13}C NMR Data of Products from Wittig Reaction of D-Tagatose

Compound	Chemical shift δ																	
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	$CH_{3\ isoprop.}$				$C_{isoprop.}$
VIIIa c	69.2	112.4	85.5	81.7	76.6	111.2	115.7	152.0	123.2	110.9	142.5	–	–	26.4	26.3	26.0	24.9	112.6 111.6
t	69.2		81.6	80.0	76.6	**		**		**	**	–	–	29.6	29.0	26.2		**
VIIIf c,c,t	**		**	**	**			**	**	**	**	**	**	**				
t,c,t	69.2	111.7	85.4	81.7	79.6	132.7	118.1	133.9	132.1*	151.3	113.9*	110.5*	155.6	26.9	26.3	26.0	25.0	113.9 111.7

c, *t* as in Table 1. * Signals are mutually exchangeable; ** unassigned signals.

ration of the reaction mixture using chromatography on a column of silica gel was unsuccessful. The ratio of isomers $n(Z)$: $n(E)$ = 10 1 was determined on the basis of NMR spectral data. For $C_{17}H_{22}O_6$ (M_r = 322.45) w_i(calc.): 63.34 % C, 6.88 % H; w_i(found): 63.15 % C, 6.80 % H. Total yield of *VIIIa* was 0.3982 g (78.15 %).

(*Z,Z,E*)- and (*E,Z,E*)-1,2:3,4-di-*O*-isopropylidene-9-(5-nitro-2-furyl)-α-D-*lyxo*-6,8-nonadien-2-ulofuranose (*VIIIf*)

For its preparation phosphonium salt (*VII*) (1.0 g, 1.58 mmol), ethereal solution of n-butyllithium (ρ = 49.1 g dm^{-3}, 2.2 cm^3, 1.58 mmol), (5-nitro-2-furyl)-acrolein (0.396 g, 2.37 mmol) were used. Reaction mixture of *Z,Z,E*- and *E,Z,E*-isomers of compound *VIIIf* was separated using chromatography with cyclohexane—ethyl acetate (φ_r = 40 : 8).

Isomer (*E,Z,E*)-*VIIIf*: Yield 0.3867 g (62.15 %), oil, [α] = – 114.5°. For $C_{19}H_{23}NO_8$ (M_r = 393.50) w_i(calc.): 58.01 % C, 5.89 % H, 3.56 % N; w_i(found): 57.95 % C, 5.84 % H, 3.57 % N.

Mixture of *E,Z,E*- and *Z,Z,E*-isomers: Yield 0.0973 g, oil. The ratio of isomers $n(Z,Z,E)$ $n(E,Z,E)$ = 3 4 was determined on the basis of NMR spectroscopy.

DISCUSSION

Application of Wittig reaction in the chemistry of saccharides with regard to their chemical properties is connected with some troubles. The question is mainly instability of saccharides in alkaline medium which is involved in the processing of phosphonium salts. The course of reaction of saccharidic phosphonio ylides is unambiguous only in the case when protected aldoses or ketoses are used. In the other case, alkaline degradation of saccharide can have priority over Wittig reaction. Therefore, preparation of suitable derivative of phosphonium salt is one of the problems. Preparation of isopropylidene derivatives represents one of the possibilities for protection of hydroxyl groups in the saccharide.

In this work, we have prepared phosphonium salts of D-galactose, D-glucose, and D-tagatose. Corresponding 6-phosphoranes were generated from phosphonium salts by using n-butyllithium. For the preparation of the mentioned phosphoranes, it is necessary to use corresponding 6-deoxy-6-iodo derivatives and more drastic reaction conditions than for the preparation of stabilized phosphorane according to *Zhdanov* [10]. This fact is a consequence of lower reactivity of the corresponding phosphonium salt owing to the absence of carbonyl group in α-position to the reactive C-6 carbon atom.

An interesting case was observation of temperature of conversion of the corresponding 6-deoxy-6-iodo derivative to phosphonium salt. Preparation of phosphonium salt of D-galactose requires 105—110 °C for 36—42 h, for phosphonium salt of D-glucose 85—90 °C is sufficient during 36—42 h while no destruction of molecule takes place at higher temperature but in the case of D-tagatose, destruction of 6-deoxy-6-iodo derivative takes place at 105 °C. In this case, temperature optimum is 80—85 °C during 72 h. Because it was a question of preparation of unstabilized phosphoranes, their isolation is impossible, generation of ylide from phosphonium salt and subsequent Wittig reaction is performed in the same reaction pot. It is necessary to use inert atmosphere at very low temperature (– 50 to – 60 °C) promoting reactivity by the use of highly polar solvent — hexamethylphosphoric triamide (dipole moment p = 14.38 × 10^{-30} C m).

Stereoselectivity of Wittig reaction is low, *i.e.* a mixture of geometric isomers is formed. Phosphonium salts of D-tagatose and D-galactose afford majority of *E*-isomer by the reaction with the derivatives of 2-furaldehyde excepting 2-furaldehyde and 5-(4-bromophenyl)-2-furaldehyde. By the Wittig reaction of phosphonium salts of D-tagatose and D-galactose with 2-furaldehyde, *cis*-isomer is formed predominantly, in the case of D-tagatose the amount of substance ratio of *Z,Z,E*-

and *E,Z,E*-isomers is even 10 1. Interesting result was observed in the case of reaction of phosphonium salt derived from D-glucose with 2-furaldehyde. Wittig reaction afforded only *Z*-isomer in about 36 % yield and we have isolated its monoisopropylidene and diisopropylidene derivative. In the case of compound *Vb*, only signals of two methyls of isopropylidene group are present in the ^{1}H and ^{13}C NMR spectra. Chemical shifts values as well as coupling constants in the ^{1}H and ^{13}C NMR spectra indicate the presence of derivative with *cis*-orientation of protons at C-6 and C-7 carbon atoms and with one isopropylidene group attached to C-1 and C-2 carbon atoms. Possible explanation is given regarding the lower stability of isopropylidene group in the position C-3 and C-5. In consequence of that fact, this group was split off in the stage of ylide formation changing so the structure of phosphorane, which influenced stereoselectivity of reaction. In comparison with the other cases, the reaction yield is half due to instability of phosphonium salt in alkaline medium. Instability of heterocyclic component was observed in the case of 5-bromo- and 5-iodo-2-furyl derivatives of D-galactose. Decomposition of products *IIb* and *IIc* under formation of black resinous material resulted in the case of these derivatives. For that reason, characterization of *IIc* derivative using NMR spectroscopy was impossible.

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