SYNTHESIS OF PYRAZOLE *C*-GLYCOSIDES BY 1,3-DIPOLAR CYCLOADDITION OF NITRILIMINES FORMED BY LEAD TETRAACETATE OXIDATION OF *p*-NITROPHENYLHYDRAZONES OF ALDEHYDO SUGARS

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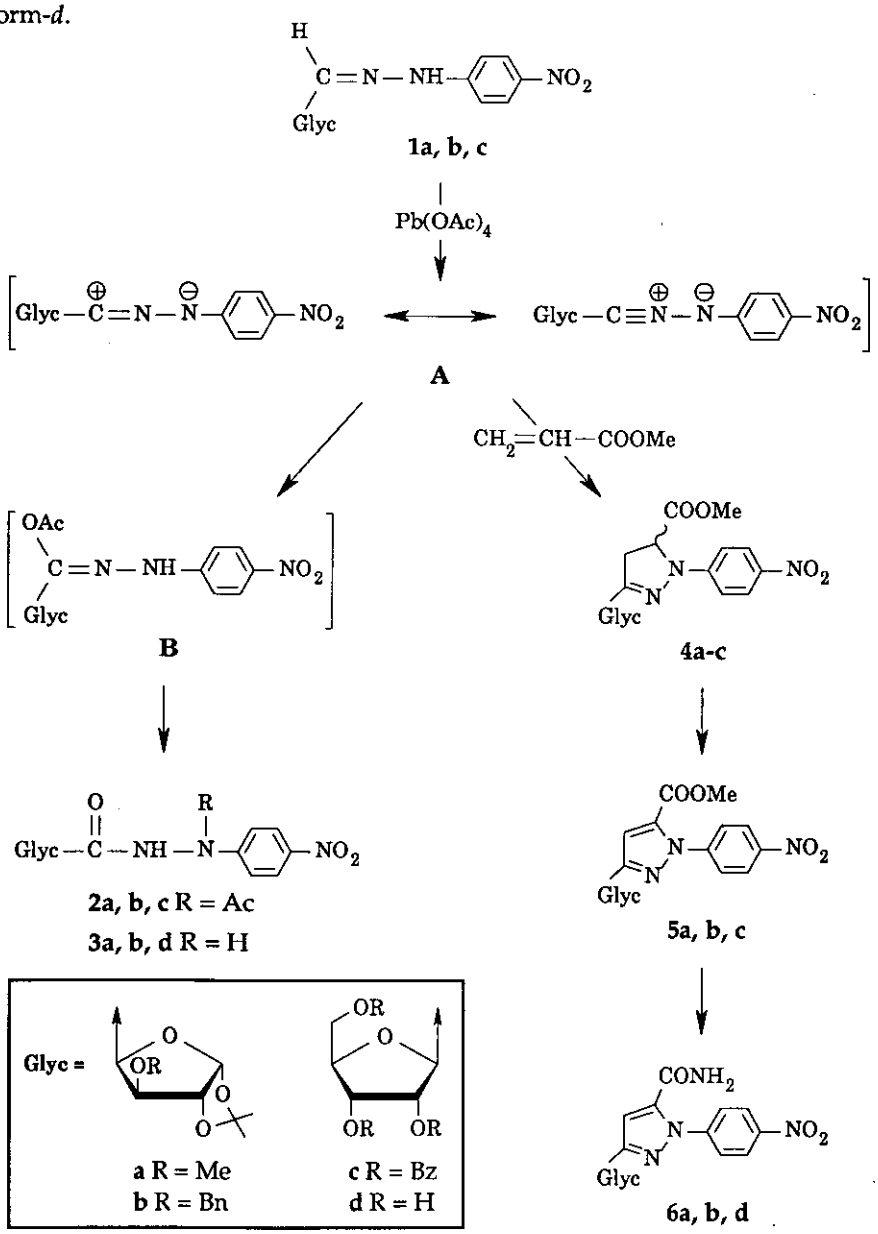
Abstract - Aldehydo sugars *p*-nitrophenylhydrazones upon treatment with lead tetraacetate in the presence of an excess of methyl acrylate afforded, besides *N'*-acetylhydrazide derivatives, methyl 3-glycosyl-1-*p*-nitrophenylpyrazoline-5-carboxylates which were readily oxidized to the corresponding pyrazoles. The methyl pyrazole-5-carboxylates were converted to 5-carboxamides.

C-Glycosides and particularly C-glycosyl nucleosides constitute an interesting class of compounds which often possess useful biological properties.[1] We have previously studied the preparation of pyrazole glycosides by 1,3-dipolar cycloaddition reactions of sugar nitrilimines generated by dehydrohalogenation of hydrazonoyl bromides prepared from sugar phenylhydrazones.[2] In continuation of our studies on the reactivity of phenylhydrazones of sugars with lead tetraacetate,[3] we investigated the behavior of *p*-nitrophenylhydrazones of aldehydo sugars towards lead tetraacetate oxidation. Some of our results have already been presented in a preliminary form.[4]

Hydrazones (**1a**) and (**1b**) were known[5] whereas **1c** was obtained in 89% yield as a mixture of *E* and Z isomers which were separated and crystallized. Properties of *(Z)*-**1c** and *(E)*-**1c** are collected in Table 1.

E and *Z* configurations were assigned on the basis of the chemical shifts of H-1 (more deshielded for the *E*-isomer[6]) and H-2 (more deshielded for the *Z*-isomer[6]). Lead tetraacetate oxidation of hydrazones (**1a-c**) afforded the corresponding *N*-acetylhydrazides (**2a-c**) which were easily deacetylated to the hydrazides (**3a,b,d**) respectively (Scheme 1). The ^{1}H-nmr data of compounds (**2**) and (**3**), collected in Table 2, confirmed their structures. In particular, a small $^3J_{NH,NH}$ coupling (*ca* 2 Hz) was noted for spectra of **3** in chloroform-*d*.



Scheme 1

Table 1. Some Properties of Hydrazones *(E)*-**1c** and *(Z)*-**1c**.

	Properties	*(E)*-**1c**	*(Z)*-**1c**
	mp (°C)	72.6-73.8	151.6-152.4
	R_F[a]	0.2	0.75
	ir (cm^{-1})	3300 (NH), 1725 (CO), 1600-1330 (NO_2)	3260 (NH), 1715 (CO), 1590-1330 (NO_2)
^{1}H-nmr chemical shifts (δ, ppm)	H-1	7.19 *d*	6.67 *d*
	H-2	4.95 *t*	5.17 *dd*
	H-3	5.90 *q*	5.64 *dd*
	H-4	5.87 *td*	5.56 *dd*
	H-5	4.69 *q*	4.82 *q*
	H-6a	4.54 *dd*	4.61 *dd*
	H-6b	4.82 *dd*	4.91 *dd*
	pNO_2Ph	7.00 *m*, 8.14 *m*	7.23 *m*, 8.18 *m*
	Bz	7.31-7.65 *m*, 7.90-8.15 *m*	7.36-7.69 *m*, 7.98-8.12 *m*
	NH	10.5	10.12
Coupling constants (Hz)	$J_{1,2}$	6.0	4.5
	$J_{2,3}$	6.0	1.2
	$J_{3,4}$	6.0	5.0
	$J_{4,5}$	4.0	7.0
	$J_{6a,6b}$	8.5	12.0
	$J_{5,6a}$	4.0	3.2
	$J_{5,6b}$	4.0	3.2

a. 4:3 Et_2O/hexane.

The fact that lead tetraacetate oxidation of hydrazones takes place *via* nitrilimine intermediates **A** (then hydrazinoyl acetates **B**)[7] was confirmed by the formation of cycloadducts (**4a-c**) when the oxidation of **1a-c** was performed in the presence of the 1,3-dipole scavenger methyl acrylate. Depending on the reaction conditions, the pyrazolines (**4**) were either isolable from the reaction medium (**4a,c**) or directly oxidized to the corresponding pyrazole (**4b** --> **5b**). A certain amount of the *N*-acetylhydrazide was also formed. For example, *N'*-acetyl-2-*O*-benzyl-*N'*-*p*-nitrophenyl-α-D-xylofuranuronohydrazide (**2b**) was isolated and characterized after the cycloaddition reaction. Upon reacting sugar nitrilimines - obtained by dehydrobromation of the corresponding hydrazonoyl bromides - with methyl propiolate, the formation of a nitrilimine dimer, a tetrazine, had been previously observed.[8] This was not the case here. Pyrazoline (**4a**) was obtained as a 1:1 resolvable mixture of the *(5S)* and *(5R)* epimers [^{1}H-nmr

Table 2. ^{1}H-nmr Data (δ/ppm, *J* /Hz) for Compounds **2-3**.

		2a	**2b**	**3a**	**3b**
Chemical shifts	H-1	6.02 *d*	6.11 *d*	6.07 *d*	6.09 *d*
	H-2	4.67 *d*	4.74 *d*	4.68 *d*	4.70 *d*
	H-3	4.17 *d*	4.48 *d*	4.15 *d*	4.49 *d*
	H-4	4.90 *d*	4.96 *d*	4.87 *d*	4.89 *d*
	p-NO_2Ph	7.22 *m*, 8.12 *m*	7.40 *m*, 7.50 *m*	6.90 *m*, 8.12 *m*	6.70 *m*, 7.72 *m*
	NH	8.90 *s*	8.76 *s*	6.25 *d*, 8.20 *d*	6.38 *d*, 8.17 *d*
	$COCH_3$	2.30 *s*	2.20 *s*		
	$C(CH_3)_2$	1.37 *s*, 1.52 *s*	1.39 *s*, 1.54 *s*	1.37 *s*,1.52 *s*	1.34 *s*, 1.51 *s*
	Others	OCH_3 3.42 *s*	CH_2Ph 4.56 *d*, 4.70 *d* Ph 7.16-7.40 *m*	OCH_3 3.45 *s*	CH_2Ph 4.58 *d*, 4.71 *d* Ph 7.20-7.40 *m*
Coupling constants	$J_{1,2}$	3.8	3.8	3.9	3.5
	$J_{2,3}$	0	0	0	0
	$J_{3,4}$	3.6	3.5	3.8	3.5
	$J_{NH,NH}$	-	-	2.2	2.0
	Others		CH_2Ph 11.0		CH_2Ph 11.0

		2c[a]	**3d**[b]
Chemical shifts	H-2	4.92 *d*	4.26 *d*
	H-3	5.97 *td*	4.08 *m*
	H-4	5.80 *td*	3.97 *m*
	H-5	4.66-4.87 *m*	3.82 *dt*
	p-NO_2Ph	7.49 *m*, 7.97 *m*	6.13 *m*, 8.05 *m*
	NH	9.87 *s*	9.50 *bs* 10.02 *bs*
	$COCH_3$	2.18 *s*	-
	H_2-C_6	4.66-4.87 *m*	3.51 *bdd*, 3.70 *ddd*
	Others	COPh 7.30-7.66 *m* 7.85-8.10 *m*	OH 5.00 *d*, 5.15 *bs*, 5.36*d*
Coupling constants	$J_{2,3}$	5.0	2.5
	$J_{3,4}$	5.0	4.5
	$J_{4,5}$	5.0	7.0
	$J_{NH,NH}$	-	-
	Others		$J_{3,OH}$ = 5, $J_{4,OH}$ = 5, $J_{6a,6b}$ = 12.5, $J_{5,6a}$ = $J_{5,6b}$ = 2.5, $J_{6b,OH}$ ~ 5

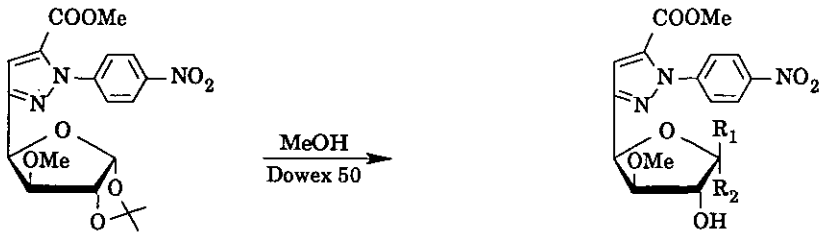
a. At 60 °C. b. In DMSO-d_6

data: δ 3.30 (1 H, *dd*, $J_{4a,5}$ = 5.8 Hz, $J_{4a,4b}$ = 14 Hz, Ha-4), 3.51 (1 H, *dd*, $J_{4b,5}$ = 12.5 Hz, Hb-4), 4.80 (1 H, *dd*, H-5) for one isomer and δ 3.25 (1 H, *dd*, $J_{4a,5}$ = 6 Hz, $J_{4a,4b}$ = 18 Hz, Ha-4), 3.51 (1 H, *dd*, $J_{4b,5}$ = 13 Hz, Hb-4), 4.78 (1 H, *dd*, H-5) for the other] whereas in the case of **4c** the *ca* 1:1 mixture could not be resolved. In neither case, could the configuration at C5 be established, differences in the nmr data of epimers being too small to allow reliable assignments. When isolated, **4** readily oxidized to **5**, structures of which were established mainly from the nmr data (Table 3). As 5-carbamoylpyrazol-3-yl glycosides like pyrazomycin[9]

Table 3. ^{1}H-nmr Data (δ/ppm, *J*/Hz) for Compounds **5-6**.

		5a	**5b**	**6a**	**6b**	**5c**	**5d**[a]
Chemical shifts (δ, ppm)	H-1'	6.07 *d*	6.11 *d*	5.98 *d*	6.11 *d*	5.46 *d*	4.68 *d*
	H-2'	4.77 *d*	4.76 *d*	4.67 *d*	4.77 *d*	5.94 *t*	4.02 *t*
	H-3'	3.92 *d*	4.14 *d*	3.85 *d*	4.15 *d*	5.90 *t*	4.91 *m*
	H-4'	5.39 *d*	5.42 *d*	5.31 *d*	5.43 *d*	4.76 *m*	3.82 *m*
	p-NO_2Ph	7.62 *m* 8.35 *m*	7.62 *m* 8.35 *m*	7.60 *m* 8.10 *m*	7.64 *m* 8.32 *m*	7.57 *m* 8.28 *m*	7.68 *m* 8.32 *m*
	$C(CH_3)_2$	1.37 *s* 1.56 *s*	1.36 *s* 1.52 *s*	1.30 *s* 1.50 *s*	1.38 *s* 1.58 *s*	- -	- -
	H-4	7.22 *s*	7.24 *s*	6.87 *s*	6.94 *s*	7.12 *s*	7.02
	$COOCH_3$	3.85 *s*	3.85 *s*	-	-	3.77 *s*	-
	$CONH_2$	-	-	5.98 *bs*	5.65 *bs* 5.94 *bs*	-	7.55 *s* 8.22 *s*
	Others	OCH_3 3.32 *s*	CH_2-Ph 4.42*d* , 4.57 *d* Ph 7.10-7.40 *m*	OCH_3 2.23*s*	CH_2-Ph 4.37 *d* 4.60 *d* Ph 7.12- 7.28 *m*	COPh 7.30-7.50 *m* 7.86-8.14 *m* H-5'a 4.60 *dd* H-5'b 4.87 *dd*	4.95 *t* $C_{5'}$-OH 4.95 *d* $C_{3'}$-OH 5.09 *d* $C_{2'}$-OH
Coupling constants (Hz)	$J_{1',2'}$	3.9	4.1	3.9	3.8	5.0	6.0
	$J_{3',4'}$	3.5	3.6	3.0	3.2	5.0	4.0
	Others		CH_2Ph 12.0		CH_2Ph 11.8	$J_{5'a,5'b}$ = 12.0 $J_{5'a,4'}$ = 4.2 $J_{5'b,4'}$ = 3.5	$J_{5',OH}$ = 5.0 $J_{3',OH}$ = 6.0 $J_{2',OH}$ = 6.0 $J_{5'a,5'b}$ = 11.5 $J_{5'a,4'}$ = 4.8 $J_{5'b,4'}$ = 4.0

a. In DMSO-d_6



5a

7 $R_1 = H, R_2 = OMe$

8 $R_1 = OMe, R_2 = H$

Scheme 2

exhibit interesting biological activities, pyrazoles (**5a-c**) were converted to the amides (**6a,b,d**). On the other hand, **5c** was methanolized to the resolvable epimeric mixture of **7** and **8** (Scheme 2).

ACKNOWLEDGEMENTS

The authors express their appreciation for the skillful technical assistance of Miss Nadine Feldmann. They thank Prof. A. Buchs and Dr F. Gulaçar for the ms and the Swiss National Science Foundation for grants # 20-26460.89 and 20-31259.91.

EXPERIMENTAL

General methods. - Solutions were concentrated under diminished pressure at <40 °C. Melting points are uncorrected and were obtained with a Mettler FP 52 melting-point microscope. Tlc was performed on silica gel HF_{254} (Merck) with detection by uv light or with phosphomolybdic-sulfuric acid.[10] Dry column chromatography[11] was conducted with silica gel 60 F_{254} (Merck) and flash chromatography[12] on silica gel Merck 60 (0.04-0.063 mm). Ir spectra were recorded with a Perkin-Elmer Model 357 spectrophotometer and uv spectra with an Unicam SP 800 spectrophotometer. Nmr spectra were recorded at 35 or 20°C for solutions in $CDCl_3$ (internal Me_4Si) using a Bruker WP 200 Sy spectrometer. Optical rotations were measured on solutions in chloroform with a Schmidt-Haensch polarimeter. Microanalyses have been performed by Dr H. Eder from this Laboratory. Results for compounds **1-8** are collected in Table 4.

***(E)*- and *(Z)*-2,5-Anhydro-3,4,6-tri-*O*-benzoyl-1-deoxy-1-*p*-nitrophenylhydrazono-D-allitol (1c).** - To 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allose[13] (1.42 g, 2.99 mmol) in ethanol (50 ml), *p*-nitrophenylhydrazine (460 mg, 2.99 mmol) was added. After 1 h at 78 °C, the solution was evaporated until the volume was reduced to 20 ml and the precipitate was collected by filtration to give **1c** (1.62 g, 89%) as a mixture of *Z* and *E* isomers which could be separated by column chromatography (4:1 ether/hexane). For their properties, see Table 1.

Table 4. Microanalytical Data for Compounds (**1-8**).

Compd	Formula	Elementary analyses					
		Calcd			Found		
		C	H	N	C	H	N
***(E)*-1c**	$C_{33}H_{27}N_3O_9$	65.02	4.46	6.89	65.12	4.46	6.99
***(Z)*-1c**	$C_{33}H_{27}N_3O_9$	65.02	4.46	6.89	64.99	4.52	6.87
2a	$C_{17}H_{21}N_3O_8$	51.64	5.35	10.63	51.73	5.32	10.71
2b	$C_{23}H_{25}N_3O_8$	58.59	5.34	8.91	58.31	5.36	8.71
2c	$C_{35}H_{29}N_3O_{11}$	62.97	4.38	6.29	63.25	4.66	6.01
3a	$C_{15}H_{19}N_3O_7$	50.99	5.42	11.89	51.25	5.48	11.99
3b	$C_{21}H_{23}N_3O_7$	58.74	5.40	9.79	58.62	5.32	9.80
3d	$C_{12}H_{15}N_3O_7$	46.01	4.83	13.41	45.92	4.80	13.23
4a	$C_{19}H_{23}N_3O_8$	54.15	5.50	9.97	54.25	5.58	10.19
4c	$C_{37}H_{31}N_3O_{11}$	64.07	4.50	6.06	63.93	4.49	6.06
5a	$C_{19}H_{21}N_3O_8$	54.41	5.05	10.02	54.53	5.20	10.06
5b	$C_{25}H_{25}N_3O_8$	60.60	5.09	8.48	60.83	5.29	8.20
5c	$C_{37}H_{29}N_3O_{11}$	64.25	4.23	6.08	63.99	4.34	5.84
6a	$C_{18}H_{20}N_4O_7$	53.46	4.99	13.85	53.72	5.19	13.61
6b	$C_{24}H_{24}N_4O_7$	60.00	5.03	11.66	59.71	5.00	11.50
6d	$C_{15}H_{16}N_4O_7$	49.45	4.43	15.38	49.41	4.36	15.24
7	$C_{17}H_{19}N_3O_8$	51.91	4.87	10.68	51.86	4.86	10.62
8	$C_{17}H_{19}N_3O_8$	51.91	4.87	10.68	51.88	4.86	10.65

Preparation of *N'*-acetyl-*p*-nitrophenylhydrazides (2a-c) (Tables 2 and 5).

Procedure A. - Preparation of *N'*-acetyl-1,2-*O*-isopropylidene-3-*O*-methyl-*N'*-*p*-nitrophenyl-α-D-xylofuranuronohydrazide (2a). - To a solution of 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose 5-(*p*-nitrophenylhydrazone)[5] (100 mg, 0.29 mmol) in a mixture of THF (1 ml) and benzene (5 ml) at 0 °C,[14] lead tetraacetate (257 mg, 0.58 mmol) was added. After 1.5 h, ethylene glycol (1 ml) and H_2O (10 ml) were added. The organic layer was decanted, dried ($MgSO_4$) and the solvents were removed by evaporation. **2a** was purified by recrystallization (ether/hexane).

Procedure B. Preparation of *N'*-acetyl-2,5-anhydro-3,4,6-tri-*O*-benzoyl-*N'*-*p*-nitrophenyl-D-

allonohydrazide (2c). - A solution of **1c** (230 mg, 0.37 mmol) in dichloromethane (20 ml) was slowly dropped into a solution of lead tetraacetate (164 mg, 0.37 mmol) in dichloromethane (10 ml) at 0 °C. After 1.5 h, the mixture was treated as described in procedure A and purified by column chromatography (4:1 ether/hexane).

Procedure C. - Compounds (**2a-c**) were obtained as by-products during preparation of compounds (**4a-c, 5a-c**). They were isolated by column chromatography (*vide infra*).

Preparation of 1,2-*O*-isopropylidene-3-*O*-methyl-*N'*-*p*-nitrophenyl-α-D-xylofuranuronohydrazide (3a); 3-*O*-benzyl-1,2-*O*-isopropylidene-*N'*-*p*-nitrophenyl-α-D-xylofuranuronohydrazide (3b) and 2,5-anhydro-*N'*-*p*-nitrophenyl-D-allonohydrazide (3d).

Procedure D. - To a solution of **2** (~ 1 mmol) in anhydrous methanol (30 ml) sodium methanolate (3 mg, 0.05 mmol) was added. The mixture was heated to reflux for 0.5 h. To the cooled solution Dowex 50 (H^+, in methanol) was added until neutralization. Filtration and evaporation of methanol afforded crystalline **3** which were recrystallized (see Table 5).

Methyl 3-(1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-tetro-1,4-furanos-4-yl)-1-*p*-nitrophenylpyrazoline-5-carboxylate (4a) and methyl 3-(1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-tetro-1,4-furanos-4-yl)-1-*p*-nitrophenylpyrazole-5-carboxylate (5a) (Tables 3 and 5).

Procedure E1. - To a solution of **1a** (600 mg, 1.78 mmol) and methyl acrylate (6 ml, 66 mmol) in dichloromethane (15 ml) at -30 °C, under nitrogen, a solution of lead tetraacetate (1.57 g, 3.56 mmol) in dichloromethane (45 ml) was added dropwise. The reaction mixture was allowed to warm to room temperature. After 48 h, filtration under celite and evaporation of the solvent gave a mixture of **2a, 4a,** and **5a**. Separation by flash column chromatography (ether) afforded **2a** (140 mg, 35.4%), **4a** (330 mg, 44%), and **5a** (70 mg, 9%).

Procedure F. - As described for the procedure E1, except that after 48 h, a second portion of lead tetraacetate (1.57 g, 3.56 mmol) in dichloromethane (45 ml) was added in the reaction mixture in order to oxidize **4a** in **5a**. The reaction was followed by thin layer chromatography (4:1 ether/hexane) and after 24 h, treated as described in procedure E1. Separation by flash column chromatography (ether) gave **2a** (140 mg, 35.4%) and **5a** (380 mg, 50.9%).

Procedure G. - As described in the procedure E1, a solution of **1a** (1.8 g, 5.34 mmol) and methyl acrylate (18 ml, 200 mmol) in dichloromethane (25 ml) was treated with lead tetraacetate (4.7 g, 10.7 mmol) in dichloromethane (50 ml). After 12 h, filtration under celite and evaporation of the solvent gave a

Table 5. Methods of Preparation and Some Properties of Compounds (**2-8**).

Compd	Method	Yield (%)	mp (solvent) °C	$[\alpha]_D$ (t, c)[a]	R_F (solvent)[b]
2a	A	61	196.2-196.4 (Et_2O/hexane)	-40.2° (24, 0.8)	0.08[1)]
	C	35.4			
2b	C	28	164.9-166.3 (Et_2O/hexane)	+97.7° (24.5, 0.8)	0.20[1)]
2c	B	68	non crystalline solid	-8.2° (22.0, 0.8)	0.30[2)]
	C	18.7			
3a	D	62	136.8-138.2 (AcOEt/hexane)	-6.87° (23, 0.9)	0.48[3)]
3b	D	77	180.4-180.8 (AcOEt/hexane)	+34.3° (24, 1.2)	0.55[2)]
3d	D	72	177.3-179.4 ($CHCl_3$, EtOH)	0° (22, 1.4)[c]	0.40[4)]
4a	E1	44	167.5-168.2 (Et_2O/hexane)[d]	+11.7° (22, 0.1)[d]	0.72[5)]
4c	E2	27			0.48[1)]
5a	E1	9	142.1-143.2 (Et_2O/hexane)	-81.2° (23, 1.2)	0.48[1)]
	F	50.9			
	G	60			
5b	F	66	51.4-52.1 (Et_2O/hexane)	-73.3° (23, 0.8)	0.68[1)]
5c	E2	18	non crystalline solid	-133° (26, 1.1)	0.63[1)]
	H	70	non crystalline solid		
6a	see text	85	109.1-109.5 (Et_2O/hexane)	-61.9° (28, 1.0)	0.42[3)]
6b	see text	70	143.4-144.7 (Et_2O/hexane)	-89.9° (20, 1.0)	0.32[5)]
6d	see text	51	206.0-208.0 (methanol)	-35.4° (22, 0.4)[e]	0.36[4)]
7	see text	42[f]	128.5-129.2 (methanol)	+46° (22, 0.6)	0.48[6)]
8	see text	21[f]	123.7-124.1 (methanol)	-78° (22, 1.0)	0.30[6)]

a. In $CHCl_3$. b. Solvents: 1) 4:1 Et_2O/hexane; 2) Et_2O; 3) 4:1 AcOEt/hexane; 4) 5:1 AcOEt/MeOH; 5) 1:1 AcOEt/hexane; 6) 9:1 $CHCl_3$/Acetone. c. In EtOH. d. One isomer e. In pyridine. f. 98% yield for the *ca* 1:1 mixture of **7** and **8**.

mixture of **2a** and **4a** which were separated by flash chromatography (ether) giving **2a** (560 mg, 26%) and **4a** (1.40 g, 3.32 mmol, 62%). **4a** was immediately dissolved in dichloromethane (20 ml) and treated with a solution of lead tetraacetate (1.7 g, 3.8 mmol) in dichloromethane (20 ml) at 0 °C, under nitrogen. After 24 h, ethylene glycol (1 ml) then ice-cold water (20 ml) were added in the reaction mixture. The organic layer was separated, dried ($MgSO_4$) and evaporated. Purification by flash chromatography

(ether) gave **5a** (1.36 g, 60% from **2a**).

Methyl 3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetro-1,4-furanos-4-yl)-1-(*p*-nitrophenyl)pyrazole-5-carboxylate (5b). - According to procedure F, **1b** (900 mg, 2.18 mmol) and methyl acrylate (6 ml, 66.6 mmol) in dichloromethane (30 ml) were treated with lead tetraacetate (2x2.4 g, 2x5.51 mmol) in dichloromethane (20 ml). Treatment of the reaction mixture as described in procedure E1 and flash chromatography (4:1 ether/hexane) gave **5b** (720 mg, 66%) and **2b** (287 mg, 28%).

Methyl 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1-(*p*-nitrophenyl)pyrazoline-5-carboxylate (4c) and methyl 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-(1-*p*-nitrophenyl)pyrazole-5-carboxylate (5c).

Procedure E2. - As described in procedure E1 but **1c** (200 mg, 0.32 mmol) was dissolved in 1:5 THF/benzene (24 ml) at 0 °C and treated with methyl acrylate (2 ml, 22 mmol) and lead tetraacetate (285 mg, 0.64 mmol) in 1:5 THF/benzene (24 ml). After 24 h, filtration under celite and evaporation of the solvent gave a mixture of **2c**, **4c**, and **5c**. Separation by flash chromatography (4:1 ether/hexane) gave **5c** (40 mg, 18%), **4c** (60 mg, 27%) and **2c** (40 mg, 18.7%).

Procedure H. - To a solution of **1c** (500 mg, 0.82 mmol) and methyl acrylate (3 ml, 33 mmol) in 1:5 THF/benzene (30 ml) at 0 °C, under nitrogen, a solution of lead tetraacetate (727 mg, 1.64 mmol) in 1:5 THF/benzene (30 ml) was added dropwise. The reaction mixture was allowed to warm to room temperature. After 12 h, filtration under celite and evaporation of the solvents yielded a mixture of **2c** and **4c**. Separation by flash chromatography (4:1 ether/hexane) gave **2c** (101 mg, 18%) and **4c** (450 mg, 79%). **4c** was dissolved in 1:5 THF/benzene (20 ml) and oxidized with a solution of lead tetraacetate (443 mg, 1 mmol) in 1:5 THF/benzene (20 ml). After 24 h, ethylene glycol (1 ml) and ice-cold water (20 ml) were added, and the organic layer was separated and dried ($MgSO_4$). Evaporation of the solvent gave **5c** (400 mg, 70%).

3-(1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-*xylo*-tetro-1,4-furanos-4-yl)-1-*p*-nitrophenylpyrazole-5-carboxamide (6a). - To a solution of **5a** (300 mg, 0.72 mmol) in dioxane (15 ml) concentrated ammonia (25 ml) was added and the solution was stirred for 24 h at room temperature. After distillation of the solvents, the residue was dissolved in dichloromethane (20 ml) and the organic phase was washed with H_2O (15 ml), dried ($MgSO_4$), and was evaporated to give crystalline **6a** (250 mg, 85%) (Table 5). Ir: 3420, 3360 (NH_2), 1692 (C=O), 1532, and 1355 (NO_2) cm^{-1}; uv: 203 nm (ε 15000), 218 (12300), and 302 (10700); ms *m/z* (%): 404 (1, $M^{\cdot+}$), 389 (5, $M^{\cdot+}$ - Me), 346 (2.2), 319 (4), 288 (2.5), 261 (53), 244 (24), 142 (4.8), 85 (100), 68 (15), and 59 (65). ^{1}H-nmr, see Table 3.

3-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-1-*p*-nitrophenylpyrazole-5-carboxamide (6b). - According to the procedure described for the preparation of **6a**, **6b** was synthesized from **5b** (570 mg, 1.15 mmol). Purification by column chromatography (1:1 AcOEt/hexane) afforded **6b** (390 mg, 70%) (Table 5). Ir: 3420, 3340 (NH_2), 1690 (C=O), and 1535-1350 (NO_2) cm^{-1}; uv: 205 nm (ε 23000) and 303 (12500); ms *m/z* (%): 480 (5, $M^{\cdot+}$), 465 (6, $M^{\cdot+}$ - Me), 345 (18), 316 (33), 287 (64), 261 (28), 230 (13), 162 (23), 129 (32), and 91 (100). ^{1}H-nmr, see Table 3.

1-*p*-Nitrophenyl-3-(β-D-ribofuranosyl)pyrazole-5-carboxamide (6d). - To a solution of **5c** (450 mg, 0.65 mmol) in dioxane (10 ml) concentrated ammonia (20 ml) was added and the mixture was stirred for 4 days at room temperature. Removal of the solvents, then flash chromatography (5:1 ethyl acetate/methanol) afforded **6d** (121.5 mg, 51%) (Table 5). Ir: 3466, 3355, 3300, 3244 (NH_2, OH), 1689 (C=O), 1511 and 1350 (NO_2) cm^{-1}; uv: 202 nm (ε 3834), 217 (2799), and 302 (2376); ms (*m/z* %): 364 (5, $M^{\cdot+}$), 334 (9), 275 (78), 261 (100), 245 (18), 215 (10), 199 (4), 142 (4), 73 (14), and 57 (11). ^{1}H-nmr, see Table 3.

Methyl 3-(methyl 3-*O*-methyl-α- and β-D-*xylo*-tetro-1,4-furanosid-4-yl)-1-*p*-nitrophenylpyrazole-5-carboxylate (7) and (8). - To a solution of **5a** (500 mg, 1.2 mmol) in anhydrous methanol (50 ml) Dowex 50 (H^+ in anhydrous methanol ~ 1.5 ml) was added. After 20 h at 65 °C, the reaction mixture was filtered, the solvent was distilled and the residue, submitted to chromatography (9:1 chloroform/acetone), afforded pure **7** (200 mg, 42%), pure **8** (100 mg, 21%) and a fraction containing both anomers (167 mg, cumulated yield 98%) (Table 5). **7**. - Ir: 3280 (OH), 1720 (C=O), 1515, and 1345 (NO_2) cm^{-1}; uv: 226 nm (ε 8952), and 299 (10674). ^{1}H-nmr: δ 2.86 (1 H, *d*, $J_{2',OH}$ = 6.8 Hz, OH-2'), 3.32, 3.54, and 3.82 (3x3 H, 3 *s*, 3 OMe), 3.94 (1 H, *dd*, $J_{2',3'}$ = 3.8 Hz, $J_{3',4'}$ = 6, H-3'), 4.35 (1 H, *ddd*, $J_{1',2'}$ = 6.8 Hz, $J_{2',OH}$ = 6.8 Hz, $J_{2',3'}$ = 3.8 Hz, H-2'), 5.12 (1 H, *d*, H-1'), 5.39 (1 H, *d*, H-4'), 7.14 (1 H, *s*, H-4), 7.64 and 8.31 (2x2 H, 2 *m*, Ph); ms (*m/z* %): 363 (0.5), 362 (2.5), 304 (26.8), 301 (5.3), 276 (24.6), 259 (9.2), 258 (4.2), 118 (7.6), 117 (6.2), 103 (13.2), 101 (31.5), and 87 (100).

8. - Ir: 3280 (OH), 1720 (C=O), 1515, and 1345 (NO_2) cm^{-1}; uv: 220 nm (ε 12456), and 301 (11320). ^{1}H-nmr: δ 2.32 (1 H, *bs*, OH-2'), 3.20, 3.58, and 3.83 (3x3 H, 3 *s*, 3 OMe), 3.93 (1 H, *dd*, $J_{2',3'}$ = 3 Hz, $J_{3',4'}$ = 5.5 Hz, H-3'), 4.37 (1 H, *dd*, $J_{1',2'}$ = 1.75 Hz, $J_{2',3'}$ = 3 Hz, H-2'), 4.97 (1 H, *d*, $J_{1',2'}$ = 1.75 Hz, H-1'), 5.52 (1 H, *d*, $J_{3',4'}$ = 5.5 Hz, H-4'), 7.23 (1 H, *s*, H-4), 7.64 and 8.32 (2x2 H, 2 *m*, Ph); ms (*m/z* %): 362 (1.69), 304 (19.2), 276 (25.4), 259 (10.9), 258 (3.1), 228 (2.9), 118 (8.3), 117 (6.9), 103 (14.4), 88 (11.9), and 87 (100).

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Received, 28th September, 1992