Partial Hydrolysis of Acyl Derivatives of Saccharides III. Methanolysis and Hydrazinolysis of Acyl Derivatives of α- and β-D-Xylopyranosides

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Dedicated to Dr. Ing. Š. Bauer, DrSc., in honour of his 70th birthday

The course of partial hydrolysis of *O*-acyl derivatives of methyl α- and β-D-xylopyranosides as well as of 4-methylumbelliferyl β-D-xylopyranoside has been followed in dependence on the reaction medium (methanolysis, hydrazinolysis), anomeric arrangement on C-1, and type of the acyl groups (acetyl, benzoyl). The obtained results have shown that the course of hydrolysis is influenced mainly by anomeric arrangement on C-1 and by the reaction medium. Eighteen mono- and di-*O*-acyl derivatives of methyl α- and β-D-xylopyranosides and nine mono- and di-*O*-acyl derivatives of 4-methylumbelliferyl β-D-xylopyranoside have been prepared.

In our previous works [1, 2] we dealt with partial methanolysis and hydrazinolysis of some acyl derivatives (acetyl, benzoyl, butyryl, palmitoyl) of 1,6-anhydro-β-D-glucopyranose. It was found that the course of hydrolysis was influenced not only by spatial arrangement of the 1,6-anhydro-β-D-glucopyranose molecule but also by reaction conditions (acetyl group on C-3 was the most stable in methanolysis and most labile in hydrazinolysis). One of the aims of the present work was to verify this finding with other model compounds. Since 1,6-anhydro-β-D-glucopyranose may be taken for an internal glycoside, methyl α- and β-D-xylopyranosides with three secondary hydroxyl groups were chosen as model compounds.

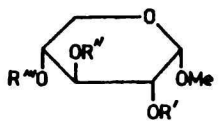
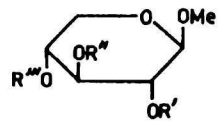
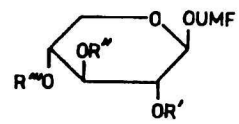
Partially acylated derivatives of xylosides are important intermediates in synthetic sugar chemistry. In the literature, there are described preparations of partially benzoylated derivatives of methyl α- and β-D-xylopyranosides by direct benzoylation [3], hydrazinolysis of methyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside [4], or by multi-step synthesis of partially acetylated derivatives of methyl α- and β-D-xylopyranosides [5].

Another aim of this work was to utilize the obtained knowledge in partial hydrolyses of fully acylated methyl α- and β-D-xylopyranosides for preparation of the so far not described partially acylated derivatives of 4-methylumbelliferyl β-D-xylopyranoside, which are important intermediates in preparation of the respective 4-methylumbelliferyl β-D-xylobiosides, potential fluorogenic substrates for β-xylosidases and β-xylanases.

EXPERIMENTAL

In the experiments the following derivatives were used as starting compounds: Methyl α- and β-D-xylopyranosides were commercial products (Serva), methyl 2,3,4-tri-*O*-acetyl-α- and -β-D-xylopyranosides were prepared according to [5], 2,3,4-tri-*O*-benzoyl derivatives of methyl α- and β-D-xylopyranosides after [3], 4-methylumbelliferyl β-D-xylopyranoside and its 2,3,4-tri-*O*-acetyl derivative according to [6].

The values of optical rotation and melting points of the obtained partially acylated (acetyl, benzoyl) derivatives of methyl α- and β-D-xylopyranosides are in accordance with the literature data [3—11]. The studied compounds are reviewed schematically. Table 1 presents the values of optical rotation and melting points of acyl derivatives of 4-methylumbelliferyl β-D-xylopyranoside, not described in the literature so far. Their structures were confirmed by NMR spectroscopy, the data are presented in Table 2. The melting points were determined on a Kofler block, optical rotations were measured with a Perkin—Elmer 141 polarimeter, ^{1}H NMR spectra with a Bruker AM-300 spectrometer in $CDCl_3$ solutions with TMS as

	R′	R″	R‴		R′	R″	R‴		R′	R″	R‴
I	H	H	H	*IX*	H	H	H	*XXIV*	H	H	H
II	Ac	H	H	*X*	Ac	H	H	*XXV*	Ac	H	H
III	H	Ac	H	*XI*	H	Ac	H	*XXVI*	H	Ac	H
IV	H	H	Ac	*XII*	H	H	Ac	*XXVII*	H	H	Ac
V	Ac	H	Ac	*XIII*	Ac	H	Ac	*XXVIII*	Ac	H	Ac
VI	Ac	Ac	H	*XIV*	Ac	Ac	H	*XXIX*	Ac	Ac	H
VII	H	Ac	Ac	*XV*	H	Ac	Ac	*XXX*	H	Ac	Ac
VIII	Ac	Ac	Ac	*XVI*	Ac	Ac	Ac	*XXXI*	Ac	Ac	Ac
				XVII	Bz	H	H	*XXXII*	Bz	H	Bz
				XVIII	H	Bz	H	*XXXIII*	Bz	Bz	H
				XIX	H	H	Bz	*XXXIV*	H	Bz	Bz
				XX	Bz	H	Bz	*XXXV*	Bz	Bz	Bz
				XXI	Bz	Bz	H				
				XXII	H	Bz	Bz				
				XXIII	Bz	Bz	Bz				

Ac = acetyl
Bz = benzoyl
UMF = 4-methylumbelliferyl

internal standard at 0.154 Hz per point digital resolution. The compounds *XXV*—*XXVII* were measured in methanol-d_4. Signal assignment was made by using homocorrelated spectroscopy (COSY-45).

The course of hydrolysis was monitored on silufol plates (Kavalier, Votice), the spots being visualized by spraying with 5 % H_2SO_4 in ethanol and heating the plates at 105 °C. Preparative separation of the hydrolysis products was performed on silica gel L-100/250 (Lachema, Brno) columns of dimensions of 2.5 cm x 90 cm (for derivatives of methyl xylopyranosides) and 4 cm x 180 cm (for derivatives of 4-methylumbelliferyl β-D-xylopyranoside) using the following elution systems: *A*, benzene—ethyl acetate ($\varphi_r = 7 : 3$); *B*, ethyl acetate—benzene—2-propanol ($\varphi_r = 8 : 4 : 1$); *C*, ethyl acetate—hexane ($\varphi_r = 4 : 1$); *D*, benzene—hexane—ethyl ether ($\varphi_r = 1 : 2 : 30$); *E*, ethyl acetate—benzene—hexane ($\varphi_r = 3 : 1 : 1$).

Table 1. Analytical Data an Physicochemical Properties of 4-Methylumbelliferyl *O*-Acyl-β-D-xylopyranosides

Compound	Formula	w_i(calc.)/% w_i(found)/% C	H	[α](D)/° Solvent	M.p./°C Solvent
XXV	$C_{17}H_{18}O_8$	58.28	5.17	−73	187—188
		58.26	5.18	Methanol	Ethyl acetate
XXVI	$C_{17}H_{18}O_8$	58.28	5.17	−14	189—190
		58.35	5.25	Methanol	Benzene
XXVII	$C_{17}H_{18}O_8$	58.28	5.17	+12	164—166
		58.30	5.21	Methanol	Benzene
XXVIII	$C_{19}H_{20}O_9$	58.16	5.13	−34	
		58.25	5.18	Chloroform	Sirup
XXIX	$C_{19}H_{20}O_9$	58.16	5.13	−15	107—110
		58.28	5.20	Chloroform	Methanol
XXX	$C_{19}H_{20}O_9$	58.16	5.13	−62	197—198
		58.24	5.25	Chloroform	Methanol
XXXII	$C_{29}H_{24}O_9$	67.43	4.68	−11	80—81
		67.40	4.75	Chloroform	Methanol
XXXIII	$C_{29}H_{24}O_9$	67.43	4.68	+75	232—235
		67.51	4.74	Chloroform	Methanol
XXXIV	$C_{29}H_{24}O_9$	67.43	4.68	−50	207—208
		67.54	4.70	Chloroform	Methanol
XXXV	$C_{36}H_{28}O_{10}$	69.65	4.54	+6	172—173
		69.70	4.62	Chloroform	Methanol

Methanolysis of *VIII*

2,3,4-Tri-*O*-acetyl derivative *VIII* (1.5 g) was dissolved in anhydrous methanol (45 cm^3) and 4 % hydrogen chloride in methanol (3 cm^3) was added. After 24 h the reaction mixture was made neutral with Amberlite IRA-402 (HCO_3^-). Then the ion exchanger was filtered off, the filtrate was concentrated to sirup and separated on a silica gel column using system *A* and, after elution of the di-*O*-acetyl derivatives, system *B*. The obtained fractions contained the following compounds: *VIII* (150 mg; 10 %), *VII* (297 mg; 23.1 %), a mixture of *VII* and *V* (mass ratio = 1 : 1; 104 mg; 8.1 %), *V* (72 mg; 5.6 %), *III* (170 mg; 15.9 %), a mixture of *III* and *II* (mass ratio = 4 : 1; 100 mg; 9.4 %), a mixture of *II* and *IV* (mass ratio = 1 : 3; 120 mg; 11.2 %), *IV* (65 mg; 6.1 %), and *I* (150 mg; 14 %).

Table 2. ^{1}H NMR Data of 4-Methylumbelliferyl O-Acyl-β-D-xylopyranosides

Compound	Chemical shift δ						Coupling constants J/Hz					
	H-1	H-2	H-3	H-4	H-5	H-5′	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$
XXV	5.15	4.91	3.58	3.61	3.94	3.43	7.5	9.8	9.7	5.3	10.3	11.8
XXVI	5.06	3.56	4.96	3.69	3.95	3.49	7.5	9.4	9.2	5.1	10.3	11.6
XXVII	5.02	3.53	3.67	4.74	4.01	3.47	7.5	9.5	9.5	5.2	10.4	11.8
XXVIII	5.25	5.17	3.97	4.98	4.24	3.57	6.2	7.7	8.2	5.2	8.1	12.6
XXIX	5.24	5.18	5.10	3.95	4.18	3.59	6.2	7.9	7.9	5.4	7.9	12.6
XXX	5.17	3.89	5.20	5.02	4.17	3.54	6.2	7.9	7.9	5.2	7.9	12.6
XXXII	5.58	5.44	4.33	5.24	4.43	3.82	4.6	6.2	5.6	3.8	5.4	12.6
XXXIII	5.50	5.61	5.41	4.10	4.35	3.74	5.6	7.7	7.2	4.6	7.2	12.3
XXXIV	5.34	4.12	5.64	5.39	4.41	3.78	5.6	7.7	7.2	4.5	7.3	12.1
XXXV	5.68	5.57	5.61	5.35	4.53	3.96	3.6	5.4	5.5	3.3	4.6	12.8

Hydrazinolysis of *VIII*

2,3,4-Tri-*O*-acetyl derivative *VIII* (1 g) was dissolved in pyridine (25 cm^3) and hydrazine hydrate (0.5 cm^3) was added. After 2 h acetone (10 cm^3) was added and the reaction mixture was concentrated and separated on a silica gel column in system *A* to give the following derivatives: *VIII* (210 mg; 21 %), a mixture of *VI* and *VII* (mass ratio = 0.75 : 1; 300 mg; 35 %), and *V* (40 mg; 4.6 %). Mono-*O*-acetyl derivatives were isolated together with the hydrazine derivatives. Rechromatography of this mixture in system *B* resulted in *III* (35 mg; 5 %), *II* (66 mg; 8 %), and *IV* (106 mg; 15 %). Similarly, rechromatography of the mixture of di-*O*-acetyl derivatives *VI* and *VII* gave *VII* (150 mg; 17.5 %) and *VI* (100 mg; 11.6 %).

Methanolysis of *XVI*

2,3,4-Tri-*O*-acetyl derivative *XVI* (1.5 g) was dissolved in anhydrous methanol (100 cm^3) and 4 % hydrogen chloride in methanol (10 cm^3) was added. After 3 h the reaction mixture was neutralized with Amberlite IRA-402 (HCO_3^-). According to TLC (elution repeated thrice) in system *D*, the mixture consisted of about 40 % of the starting derivative, 50 % of di-*O*-acetyl derivative, and 10 % of mono-*O*-acetyl derivative. Preparative separation was performed on a column in the same system to give *XVI* (615 mg; 41 %), *XV* (188 mg; 14.7 %), *XIV* (150 mg; 11.7 %), *XIII* (49 mg; 3.8 %), a mixture of *XIV* and *XIII* (mass ratio = 2 : 1; 195 mg; 15.2 %), *XI* (81 mg; 7.6 %), and a mixture of *X* and *XII* (mass ratio = 1 : 1; 55 mg; 5.2 %).

Hydrazinolysis of *XVI*

2,3,4-Tri-*O*-acetyl derivative *XVI* (1.5 g) was dissolved in pyridine (35 cm^3) and hydrazine hydrate (0.75 cm^3) was added. After 6 h the reaction was terminated by addition of acetone (15 cm^3). Column separation of the reaction mixture in system *D* gave *XVI* (76 mg; 5.1 %), *XV* (189 mg; 14.8 %), a mixture of *XIV* and *XIII* (mass ratio = 1.5 : 1; 537 mg; 42 %), *XI* (161 mg; 15.1 %), and a mixture of *X* and *XII* (mass ratio = 1 : 1; 317 mg; 29.8 %).

Hydrazinolysis of *XXIII*

2,3,4-Tri-*O*-benzoyl derivative *XXIII* (2.5 g) was dissolved in pyridine (25 cm^3) and hydrazine hydrate (1 cm^3) was added. After 2 h the reaction was terminated by addition of acetone (15 cm^3). Column separation of the concentrated reaction mixture in system *D* afforded *XXIII* (0.7 g; 28 %), a mixture of *XX* and *XXII* (mass ratio = 1 : 1; 414 mg; 21.2 %), *XXII* (211 mg; 10.8 %), *XXI* (382 mg; 19.7 %), *XVIII* (176 mg; 12.5 %), *XIX* (80 mg; 5.7 %), and *XVII* (83 mg; 5.9 %). Rechromatography of the mixture of *XX* and *XXII* in system *A* provided *XX* (172 mg; 8.8 %) and *XXII* (165 mg; 8.5 %).

Methanolysis of *XXXI*

2,3,4-Tri-*O*-acetyl derivative *XXXI* (2.5 g) was dissolved in anhydrous methanol (250 cm^3) and 4 % hydrogen chloride in methanol (6 cm^3) was added. After 24 h the reaction mixture was neutralized with Amberlite IRA-402 (HCO_3^-) and separated by column chromatography in system *E* to give *XXXI* (1050 mg; 42 %), *XXX* (300 mg; 13.3 %), *XXIX* (330 mg; 14.6 %), *XXVIII* (250 mg; 11.1 %), *XXVI* (150 mg; 7.5 %), *XXVII* (50 mg; 2.5 %), and *XXV* (100 mg; 5 %).

Hydrazinolysis of *XXXI*

2,3,4-Tri-*O*-acetyl derivative *XXXI* (2.5 g) was dissolved in pyridine (60 cm^3) and hydrazine hy-

drate (1.25 cm^3) was added. After 2 h acetone (20 cm^3) was added and the reaction mixture was concentrated to a sirup. Column separation of this residue in system *E* afforded the following products: *XXXI* (950 mg; 38 %), *XXX* (560 mg; 25.2 %), *XXIX* (460 mg; 20.4 %), and *XXVIII* (240 mg; 10.9 %).

Acetylation of *XXIV*

4-Methylumbelliferyl β-D-xylopyranoside *XXIV* (1.5 g) was dissolved in pyridine (15 cm^3) and acetic anhydride (2.3 cm^3) was added. After 18 h methanol (10 cm^3) was added and the reaction mixture was concentrated. Pyridine was removed by repeated evaporation with toluene and ethanol. The obtained sirup was separated by column chromatography in system *E* to give the following products: *XXXI* (170 mg; 8.1 %), *XXX* (130 mg; 6.9 %), *XXIX* (120 mg; 6.5 %), *XXVIII* (410 mg; 21.8 %), *XXVI* (240 mg; 14.4 %), *XXVII* (230 mg; 13.9 %), and *XXV* (250 mg; 15.1 %).

Hydrazinolysis of *XXXV*

2,3,4-Tri-*O*-benzoyl derivative *XXXV* (3 g) was dissolved in pyridine (30 cm^3) and hydrazine hydrate (0.5 cm^3) was added. After 24 h when the reaction mixture contained, according to TLC in system *A*, about 25 % of the starting derivative *XXXV*, 60 % of di-*O*-benzoyl and 15 % of mono-*O*-benzoyl derivatives, hydrazinolysis was terminated by addition of acetone (20 cm^3). The concentrated reaction mixture was separated by column chromatography in system *A*. The following products were obtained: *XXXV* (760 mg; 25.6 %), a mixture of *XXXII* and *XXXIV* (mass ratio = 1 : 2; 880 mg; 35.2 %), and *XXXIII* (610 mg; 24.4 %). Pure mono-*O*-benzoyl derivatives were not isolated due to contamination with hydrazine derivatives.

Preparation of Di-*O*-benzoyl Derivatives of *XXIV*

Mono-*O*-acetyl derivatives *XXV*, *XXVI*, and *XXVII*, respectively (0.35 g) were dissolved in pyridine (5 cm^3) and benzoyl chloride (0.5 cm^3) was added. After 24 h $NaHCO_3$ solution was added to the reaction mixture and the product was extracted with chloroform. The concentrated residue was dissolved in anhydrous methanol (15 cm^3) and 4 % hydrogen chloride in methanol (2 cm^3) was added. After 24 h the reaction mixture was neutralized with Amberlite IRA-402 (HCO_3^-), concentrated, and crystallized from methanol to give *XXXII* (0.46 g), *XXXIII* (0.45 g), and *XXXIV* (0.44 g).

DISCUSSION

Partial deacylations (methanolysis, hydrazinolysis) were studied with the following substrates: methyl α-D-xylopyranoside *I*, methyl β-D-xylopyranoside *IX*, and 4-methylumbelliferyl β-D-xylopyranoside *XXIV* and their acyl derivatives (acetyl, benzoyl), respectively. Methanolysis and hydrazinolysis were monitored by TLC. The reaction time was chosen so that optimum amounts of di-*O*-acyl derivatives were present in the reaction mixture. Methanolysis of *VIII* afforded a mixture composed of two di-*O*-acetyl derivatives only, namely 3,4-di-*O*-Ac *VII* and 2,4-di-*O*-Ac *V* in the mass ratio of about 5 : 1, and three mono-*O*-acetyl derivatives, *i.e.* 3-*O*-Ac, 2-*O*-Ac, and 4-*O*-Ac in the mass ratio of 5 : 1 : 3. Hydrazinolysis of *VIII* afforded a mixture of compounds as well. However, in this case all three di-*O*-Ac derivatives were formed and the relative representation of both di-*O*-Ac and mono-*O*-Ac derivatives was different.

The mass ratio of 3,4-di-*O*-Ac : 2,3-di-*O*-Ac : 2,4-di-*O*-Ac was 8 : 6 : 1, while that of 4-*O*-Ac : 2-*O*-Ac : 3-*O*-Ac was 3 : 2 : 1. The results show that the most labile acetyl group both in methanolysis and hydrazinolysis was that in position O-2. Methanolysis and hydrazinolysis [2] proceeded differently as to the acetyl groups in positions O-3 and O-4. While in methanolysis the acetyl group on O-3 was released faster, in hydrazinolysis it was the acetyl group at O-4. Moreover, in methanolysis the release of the acetyl group at O-2 against that at O-3 was more preferable than in hydrazinolysis against that at O-4 (5 : 1 and 4 : 3, respectively). The results of hydrazinolysis of *VIII* are in agreement with those of hydrazinolysis of 2,3,4-tri-*O*-benzoyl derivative of methyl α-D-xylopyranoside, obtained by *Ishido et al.* [4].

Methanolysis as well as hydrazinolysis of *XVI* afforded a mixture of all di-*O*-acetyl derivatives. Since separation of *XIV* and *XV* was difficult, the quantitative composition of the mixture was determined by NMR spectroscopy. From the mass ratios of the formed di-*O*-acetyl derivatives in methanolysis (2,3-di-*O*-Ac : 3,4-di-*O*-Ac : 2,4-di-*O*-Ac = 3 : 2 : 1) and in hydrazinolysis (1.5 : 1 : 1) it can be seen that the stability of the individual acetyl groups was approximately the same, except the acetyl group on O-4 in methanolysis. The course of hydrazinolysis of 2,3,4-tri-*O*-benzoyl derivative *XXIII* was similar. The mass ratio of the formed 2,3-, 3,4-, and 2,4-di-*O*-benzoyl de-

rivatives was about 2 : 1 : 1, which indicated that the influence of the benzoyl group was essentially the same as that of the acetyl group. The derivatives *XXXI* and *XXXV* have on the anomeric centre a bulky 4-methylumbelliferyl group. Methanolysis and hydrazinolysis of these compounds, similarly as of *XVI* and *XXIII*, provided a mixture of all three di-*O*-acyl derivatives. In methanolysis of *XXXI* the mass ratio of the formed 2,3-di-*O*-Ac : 3,4-di-*O*-Ac : 2,4-di-*O*-Ac was 1.3 : 1.2 : 1, in hydrazinolysis it was 1.9 : 2.3 : 1. Hydrazinolysis of *XXXV* afforded di-*O*-benzoyl derivatives (2,3-, 3,4-, and 2,4-) in the mass ratio of 2 : 2 : 1. From these results it is evident that in methanolysis and in hydrazinolysis the relative stability of the acyl group on O-3 is higher than on O-2 and O-4. However, in partial acetylation the mass ratio of the formed di-*O*-acetyl derivatives (2,4-, 2,3-, and 3,4-) 3.3 : 1 : 1 was shifted significantly in favour of the 2,4-di-*O*-acetyl derivative *XXVIII*. This recognition may be utilized in preparative preparation of this derivative.

As in hydrazinolysis of *XXXV* isolation of pure derivatives *XXXII* and *XXXIV* from the reaction mixture was unsuccessful, these were prepared from mono-*O*-acetyl derivatives of 4-methylumbelliferyl β-D-xylopyranoside by benzoylation and subsequent methanolysis of the acetyl groups. In conclusion it can be stated that the reactivities of the individual hydroxyl groups in the used substrates, except the hydroxyl group on C-2 of derivative *I*, do not differ substantially. Consequently, a diverse mixture of compounds is formed both in methanolysis and hydrazinolysis of the respective acyl derivatives. However, preferable formation of some derivatives may be achieved by choosing suitable reaction conditions (methanolysis, hydrazinolysis, acylation).

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