Synthesis of *p*-Methoxybenzyl D-Galacturonate

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The reaction of *p*-methoxybenzyl alcohol with 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronic acid gave preferentially the corresponding *p*-methoxybenzyl D-galactopyranuronate. *N*,*N*-Dimethylformamide dineopentyl acetal was used as the reagent for esterification.

In connection with the study of properties of the bonds between lignin and polysaccharides in plant materials [1], model compounds representing various types of linkages have been synthesized [2—5]. Only little information is available about the properties of the ester lignin—carbohydrate bond from studies using model compounds [6—8]. *Eschenmoser et al.* [9] described a detailed, conclusive study of the reaction of formamide acetals with carboxylic acids and noted that the reaction was a facile means for the preparation of esters. The conversion of carboxylic acids to benzyl esters with *N*,*N*-dimethylformamide dibenzyl acetal in high yields under mild conditions has been reported [10]. The objective of this paper was to prepare benzyl and *p*-methoxybenzyl D-galactopyranuronates as model compounds for the ester lignin—carbohydrate linkage using the above-mentioned method.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage. Optical rotations were measured using a Perkin—Elmer automatic polarimeter, model 141. ^{1}H NMR spectra for solutions in chloroform-*d* were recorded with a Bruker AM-300 spectrometer. Thin-layer chromatography on silica gel (Merck PF_{254}) coated glass slides was carried out using the systems A (dichloromethane—methanol, $\varphi_r = 6:1$), B (ethyl acetate—acetic acid—water, $\varphi_r = 10:1:1$), and column chromatography on columns of dry packed silica gel (product No. 9385, Merck) was carried out using the systems C (chloroform—methanol, $\varphi_r = 10:1$) and D (ethyl acetate—n-heptane, $\varphi_r = 5:1$) as eluents. Detection was performed by charring with 5 % sulfuric acid in ethanol. *N*,*N*-Dimethylformamide dibenzyl acetal and *N*,*N*-dimethylformamide dineopentyl acetal were commercial products (Fluka).

Benzyl 1,2;3,4-Di-*O*-isopropylidene-α-D-galactopyranuronate (*II*)

Method A

1,2;3,4-Di-*O*-isopropylidene-α-D-galactopyranuronic acid (*I* [11, 12]) (2.73 g; 10 mmol) was dissolved in anhydrous dichloromethane (50 cm^3) and *N*,*N*-dimethylformamide dibenzyl acetal (4.08 g; 15 mmol) was added. The solution was kept at room temperature for 48 h with the exclusion of moisture. T.l.c. (system A) showed then that most of the starting material was consumed. The mixture was diluted with 50 cm^3 of chloroform and washed (2 × 50 cm^3) with cold water. The organic layer was dried over anhydrous sodium sulfonate, the solution was concentrated and crystallization from n-heptane gave pure *II* (2.18 g; 68 %).

Method B

A solution of *I* (2.73 g; 10 mmol) in a mixture of dichloromethane (50 cm^3) and benzyl alcohol (1.3 g; 12 mmol) was treated with *N*,*N*-dimethylformamide dineopentyl acetal (2.8 g; 12 mmol) as described in method *A*. Yield of *II* was 62 % (2.25 g).

p-Methoxybenzyl 1,2;3,4-Di-*O*-isopropylidene-α-D-galactopyranuronate (*III*)

A solution of *I* (2.73 g; 10 mmol) and *p*-methoxybenzyl alcohol (1.66 g; 12 mmol) in 50 cm^3 of dichloromethane was treated with *N*,*N*-dimethylformamide dineopentyl acetal (2.8 g; 12 mmol) as described for the preparation of *II*. The crude product was purified by column chromatography (system C), yielding 64 % (2.52 g) of sirupy *III*.

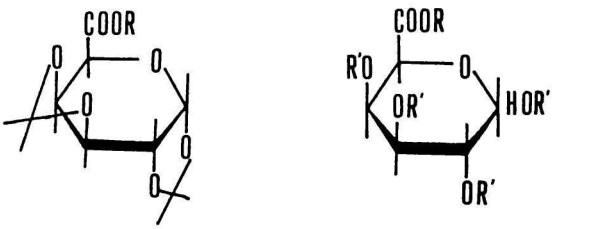
p-Methoxybenzyl D-Galactopyranuronate (*IV*), resp. Benzyl D-Galactopyranuronate (*VI*)

Table 1. Characterization of the Prepared Compounds

Compound	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	M.p./°C	[α](D, 20 °C, ϱ = 10 g dm^{-3}, $CHCl_3$)/°
II	$C_{19}H_{24}O_7$	62.63	6.64	94—95	−82.2
	364.4	62.4	6.6		
III	$C_{20}H_{26}O_8$	60.90	6.65	sirup	−76.3
	394.43	61.0	6.6		
IV	$C_{14}H_{18}O_8$	53.50	5.77	sirup	+22.4 → +14.3*
	314.29	53.5	5.7		
V	$C_{22}H_{26}O_{12}$	54.77	5.43	sirup	+42.8
	482.45	54.8	5.5		
VI	$C_{13}H_{16}O_7$	54.93	5.67	128—129	+28.4 → +18.2*
	284.27	54.5	5.5		
VII	$C_{21}H_{24}O_{11}$	55.75	5.35	sirup	+61.4
	452.42	55.7	5.4		

* ϱ = 10 g dm^{-3}, H_2O.

A suspension of *III* (1.97 g; 5 mmol), resp. *II* in trifluoroacetic acid (98 %, 20 cm^3), and water (2 cm^3) was shaken for 30 min at room temperature. T.l.c. (system C) showed complete conversion of the starting material. The reaction mixture was concentrated under diminished pressure and the residual acid was removed by co-distillation with the mixture of toluene and methanol (50 cm^3, φ_r = 5:1). The crude product was purified by chromatography (system B) to give pure sirupy substance *IV* in 36 % (0.56 g) yield, resp. crystallization from ethanol gave 94 % of compound *VI*.



R		R	R′
I	H	*IV*	H
II	$PhCH_2$	*V*	Ac
III	p-OCH_3PhCH_2	*VI*	H
		VII	Ac

Formula 1

p-Methoxybenzyl 1,2;3,4-Tetra-*O*-acetyl-α/β-D-galactopyranuronate (*V*), resp. Benzyl 1,2;3,4-Tetra-*O*-acetyl-α/β-D-galactopyranuronate (*VII*)

Method A

Compound *III* (1.97 g; 5 mmol) was treated with a mixture of acetic anhydride (20 cm^3) and perchloric acid (0.1 cm^3, 70 %) for 3 h at 4 °C [12]. Chromatography (system D) gave sirupy *V* in 62 % (1.50 g) yield. The same treatment of *II* (1.42 g; 5 mmol) gave pure *VII* in 60 % (1.25 g) yield.

Method B

Conventional esterification of *IV* and *VI* with a mixture of acetic anhydride and pyridine resulted in crude products which were purified in the same manner to give *V* and *VII* in 72 % and 75 % yield, respectively.

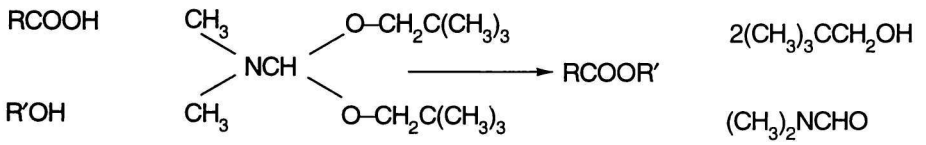
RESULTS AND DISCUSSION

1,2;3,4-Di-*O*-isopropylidene-α-D-galactopyranuronic acid (*I*) used as a starting material was prepared by permanganate oxidation of 1,2;3,4-di-*O*-isopropylidene-β-D-galactopyranose [11] using the phase-transfer catalysis [12]. Subsequent treatment of *I* with *N*,*N*-dimethylformamide dibenzyl acetal in dichloromethane at room temperature (method *A*) yielded benzyl 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronate *II* (68 %) (Formula 1, Table 1).

This method [12] has not been used for preparing *p*-methoxybenzyl 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranuronate *III*, apparently because *N*,*N*-dimethylformamide di(*p*-methoxybenzyl) acetal is not easy to obtain [9]. It has been reported [9, 13, 14] that while *N*,*N*-dimethylformamide dineopentyl acetal does not esterify acids, it readily undergoes acetal exchange reaction with alcohols. The resulting mixed acetals thus obtained can be used as reagents for esterification of an acid by any alcohol (Scheme 1).

The above method has been used for the esterification (90 %) of cephalosporin with *p*-methoxybenzyl alcohol [15]. Accordingly, compound *III* was prepared in 60 % yield by treatment of a solution of *I* in CH_2Cl_2 with *p*-methoxybenzyl alcohol and *N*,*N*-dimethylformamide dineopentyl acetal at room temperature. The same method, when applied for the preparation of *II* (method *B*), gave the desired substance in essentially the same yield.

The simultaneous removal of both isopropylidene

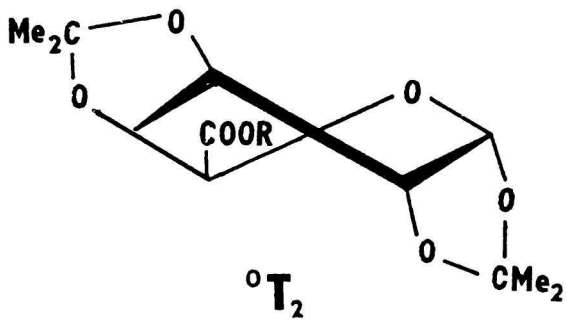


Scheme 1

Table 2. Chemical Shifts and Coupling Constants of Some Compounds Prepared

Compound	δ											$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
	H-1	H-2	H-3	H-4	H-5	Me			OMe	Ph—CH_2	Ph	Hz	Hz	Hz	Hz
II	5.67 d 1H	4.38 dd 1H	4.66 dd 1H	4.58 dd 1H	4.48 d 1H	1.33 s 6H	1.45 s 3H	1.52 s 3H		5.27 dd 2H	7.3—7.4 5H	5.1	2.6	7.8	2.2
III	5.65 d 1H	4.36 dd 1H	4.67 dd 1H	4.57 d 1H	4.45 d 1H	1.31 s 6H	1.42 s 3H	1.50 s 3H	3.78 s 3H	5.21 dd 2H	6.91 d 7.31 dd 2H 2H	5.1	2.6	7.8	2.2
V	6.5 d 1H	5.32 t 2H		5.76 dd 1H	4.72 d 1H	1.82—2.12 4 s 4×3H Ac			3.72 s 3H	5.12 dd 2H	6.96 d 7.30 dd 2H 2H	1.6		2.9	1.5
VII	6.51 d 1H	5.36 t 2H		5.81 dd 1H	4.76 d 1H	1.85—2.16 4 s 4×3H Ac				5.17 dd 2H	7.35 m 5H	1.6		2.9	1.5

* Coupling constants were not observed.



Formula 2

groups from *II* and *III* by their treatment with aqueous trifluoroacetic acid at room temperature yielded compounds *IV* and *VI*, respectively. This is in agreement with the behaviour of diisopropylidene derivatives of D-galactose [12]. The conformation of such substances was described in detail [16—18]. ^{1}H NMR analysis of the spectra of *II* and *III* showed that the signals for saccharide protons were located similarly as those in the spectra of derivatives of 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose. Differences were found only for the aromatic substituents at O-6 of the saccharide (Table 2). The coupling constants were found to be the same for both derivatives, and a change of the substituent at C-6 had no influence on the conformation of the pyranoside ring. Based on the results obtained, a $^OT_2$ conformation can be suggested for both *II* and *III*, in agreement with the observation of *Jarosz* [19] and *Vogel* [12].

Tetra-*O*-acetyl-α/β-D-galactopyranuronates *V* and *VII* were prepared by acetolysis of di-*O*-isopropylidene-α-D-galactopyranuronates *II* and *III*, using trifluoroacetic acid and acetic anhydride (method *A*) [12]. The same derivatives were obtained by conventional acetylation of *IV* and *VI* with acetic anhydride—pyridine.

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