Carbohydrate Research, 44 (1975) 205–214

A SIDE-REACTION IN THE METHYLATION OF GALACTURONATE DERIVATIVES WITH DIAZOMETHANE–BORON TRIFLUORIDE ETHERATE*

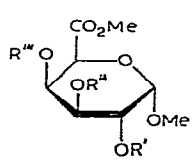
PAVOL KOVÁČ, RADOSLAV PALOVČÍK, VLADIMÍR KOVÁČIK, AND JÁN HIRSCH
Institute of Chemistry, Slovak Academy of Sciences, 809 33 Bratislava (Czechoslovakia)
(Received May 27th, 1975; accepted for publication, June 30th, 1975)

ABSTRACT

Partial *p*-nitrobenzoylation of methyl (methyl 2-*O*-methyl-α-D-galacto-pyranosid)uronate (**1**) gave the 3-*p*-nitrobenzoate **2** in good yield. Treatment of **2** or methyl (methyl 2,3-di-*O*-benzoyl-α-D-galactopyranosid)uronate (**11**) with diazo-methane–BF_3-etherate gave, in addition to the expected 4-methyl ethers, by-products resulting from lengthening of the carbon chain. The by-products were formulated as derivatives of methyl 4,7-anhydro-α-D-*galacto*-heptopyranosid-6-ulose dimethyl acetal on the basis of p.m.r. and i.r. spectral data, by analysis of their mass-spectral fragmentation pattern, and by chemical transformations.

INTRODUCTION

In connection with synthetic work in this laboratory, the need arose for a large amount of methyl (methyl 2,4-di-*O*-methyl-α-D-galactopyranosid)uronate (**6**). Although we have previously[2] obtained **6** in a sixteen-step synthesis (starting from D-galactose), a shorter synthesis was desirable. The starting point in the new synthesis was crystalline[3] methyl (methyl 2-*O*-methyl-α-D-galactopyranosid)uronate (**1**) which is readily accessible *via* the quasi one-step preparation of the intermediate 1,2:3,4-di-*O*-isopropylidene-D-galacturonic acid[4]. We now report a more-facile synthesis of **6** (8 steps from D-galactose) and present evidence for the structure of compounds **7** and **12** formed by side-reactions in the methylation of the esters **2** and **11** with diazo-methane–BF_3–etherate.



	R′	R″	R‴		R′	R″	R‴
1	Me	H	H	5	Me	NBz	Me
2	Me	NBz	H	6	Me	H	Me
3	Me	NBz	NBz	11	Bz	Bz	H
4	Me	H	NBz	15	H	H	Me

NBz = *p*-nitrobenzoyl

*Synthesis and reactions of uronic acid derivatives: Part VII[1].

RESULTS AND DISCUSSION

The synthesis of **6** was accomplished by taking advantage of the lower reactivity of the axial HO-4 in **1** as compared with the equatorial HO-3. Accordingly, **1** was treated with *p*-nitrobenzoyl chloride in pyridine under controlled conditions and, in addition to small proportions of **3** and **4**, crystalline methyl (methyl 2-*O*-methyl-3-*O*-*p*-nitrobenzoyl-α-D-galactopyranosid)uronate (**2**) was isolated in 67% yield. The location of the *p*-nitrobenzoyl groups in **2** and **4** was based on p.m.r. spectral data (Table I) which clearly showed the downfield position of the signal for the proton in the HCONBz group.

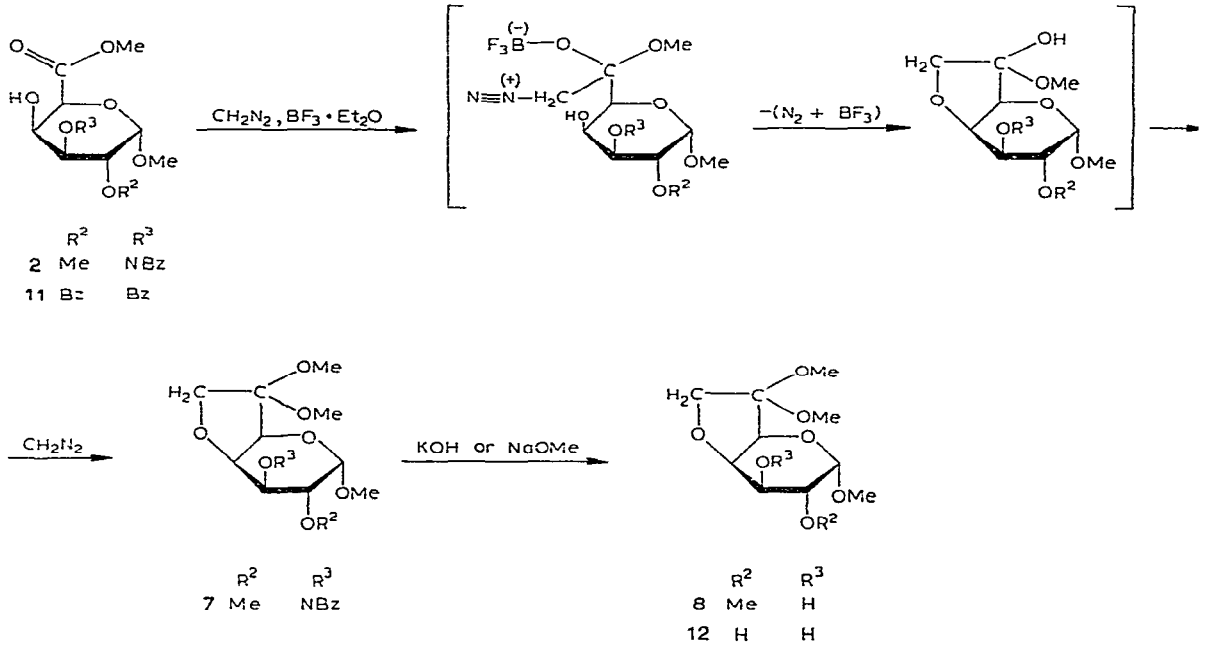
Methylation of **2** under conditions which do not cause migration of the base-labile substituents[5] afforded the corresponding di-*O*-methyl derivative **5**, which was de-*p*-nitrobenzoylated with aqueous sodium hydroxide to give, after esterification with ethereal diazomethane, crystalline **6**. Compound **6** gave a mass spectrum containing all features characteristic[6] of the fragmentation of methyl (methyl 2,4-di-*O*-methylhexopyranosid)uronates, and was in all respects identical with the previously[2] described substance.

Although **5** was obtained in good yield, the conversion **2**→**5**, as shown by t.l.c., was accompanied by a side reaction which yielded the crystalline tetrahydrofurone derivative **7**. A similar cyclization reaction was observed in the methylation of **11** under identical conditions, and the debenzoylated product **12** was also isolated crystalline.

The formulation of the structure of the tetrahydrofurone dimethyl acetals **7**, **8**, and **12**, and a mechanism for their formation are given in Scheme 1, which is based on p.m.r., mass, and i.r. spectral data, and chemical evidence.

The integrated p.m.r. spectra of **7**, **8**, and **12** showed the presence of 19, 20, and 18 aliphatic protons, respectively, which, together with the elemental analysis, suggested that the cyclization reaction involved 1 mol. of the starting esters **2** and **11** and 2 mol. of diazomethane. The p.m.r. spectra of **7**, **8**, and **12**, together with the i.r. spectra of **8** and **12**, revealed the absence of an ester group, and proved that, under the conditions of methylation, a modification of the methoxycarbonyl groups in **2** and **11** had occurred. While the signals for the COOMe groups in the esters **1**–**6** appear downfield (δ 3.70–3.85) as a result of the deshielding effect of the carbonyl group and are well-separated from those (δ 3.43–3.60) of the other methyl groups in the molecule, all signals for the methyl groups of **7**, **8**, and **12** appear at upfield positions (δ 3.27–3.52), indicating that the methyl groups are not linked to a carbonyl group. Further evidence for the structures of **7**, **8**, and **12** was derived from the chemical shift (δ 3.84–4.06) for H-5 of these substances, as compared to that (δ 4.40–4.85) for H-5 of the esters **1**–**6**, showing again that in **7**, **8**, and **12** C-5 is not adjacent to an alkoxycarbonyl group.

The p.m.r. spectra of the dimethyl acetals show 2-proton AB quartets, the chemical shifts of which (Table I) are consistent with a methylene group linked to an oxygen. The value of the geminal coupling constants (9.1–9.7 Hz) observed for the



SCHEME 1

methylene protons in **7**, **8**, and **12** agreed with that normally observed for a tetrahydrofuran structure[7] and excluded the presence of an epoxide (*J* usually[7] 4–6.3 Hz). The fact that the methylene protons of these substances were uncoupled with other protons of the molecule showed that they were probably located more than 3 bonds distant from carbon atoms bearing protons.

The absence of an oxirane arrangement or a methoxycarbonyl group in **7** was further proved when treatment with methanolic sodium methoxide and with aqueous sodium hydroxide (Scheme 2) caused only de-*p*-nitrobenzoylation, giving a high yield of **8**. The losses were manipulative. Had a methoxycarbonyl group been present in **7**, treatment with aqueous sodium hydroxide would have resulted in the saponification of this group with the formation of the sodium salt of the uronic acid derivative. On the other hand, treatment with methanolic sodium methoxide of an esterified uronic acid derivative would have resulted, at least partially, in *β*-elimination of the C-4 substituent with the formation of olefinic products[1,3,8–10]. The formation of salts of uronic acids and unsaturated products is exceptionally easy to monitor by t.l.c. on silica gel, but the presence of such products was not observed. The conditions of de-*p*-nitrobenzoylation would also have been sufficient to open an epoxide ring. The same conclusions can be drawn from the mode of isolation of **12**.

The structures of **7** and **8** are consistent with their mass-spectral fragmentation, the interpretation of which was based on the differences between the observed fragmentation and that known to occur with methyl derivatives of uronic acids[6]. The

TABLE I

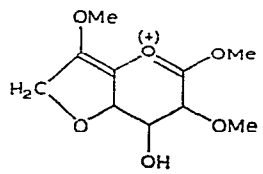
FIRST-ORDER CHEMICAL SHIFTS AND COUPLING CONSTANTS ($CDCl_3$)[a]

Compound	*Chemical shifts*[b] (δ)											*Coupling constants (Hz)*				
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-7*[c]	*H-7'*[c]	*OMe*	*COOMe*	*Aromatic*	*OH*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{7,7'}$
1	5.05d	3.58q	4.00q	4.33q	4.40d	—	—	3.46;3.50	3.82	—	3.02	3.4	10.2	3.2	1.4	—
2	5.10d	3.97q	5.40q	4.57q	4.42d	—	—	3.50[d]	3.76	8.31s	3.13	3.4	10.3	3.2	1.4	—
3	5.28d	3.97q	5.73q	6.17q	4.85d	—	—	3.52;3.60	3.71	7.93–8.43m[e]	—	3.6	10.5	3.3	1.4	—
4	5.20d	3.67q	4.33q	5.92q	4.66d	—	—	3.51;3.53	3.70	8.30s	3.40	3.5	10.7	3.2	1.3	—
5	5.14d	3.98q	5.54q	4.28q	4.55d	—	—	3.43;3.49;3.51	3.85	8.31s	—	3.6	10.4	3.0	1.6	—
6	5.05d	3.58o[f]	4.05q	4.02m	4.40d	—	—	3.44;3.50;3.52	3.84	—	2.66	3.5	11.0	3.2	1.4	—
7	5.07d	3.87q	3.58q	4.61q	4.06d	4.01d	3.82d	3.27;3.38;3.48;3.52	—	8.23s	—	3.4	10.1	3.7	2.1	−9.5
8	4.98d	3.45q	4.05q	4.37q	3.97d	4.02d	3.76d	3.28;3.37;3.47;3.52	—	—	2.68	3.4	10.0	3.7	2.3	−9.7
9	4.93d	3.52q	4.21q	4.31bq[g]	3.87bd[g]	4.31bd[g]	3.90bd[g]	3.46;3.53	—	—	3.1	3.2	10.0	3.7	2.5	−17.2
12[h]	4.67d	3.55q	3.77q	4.13q	3.84d	3.87d	3.57d	3.21;3.26;3.36;3.42	—	—	—	3.0	9.9	3.5	2.2	−9.1
13	5.03d	3.97q	5.65q	4.62bq[g]	4.00bd[g]	3.88bd[g]	4.33bd[g]	3.53;3.55	—	8.31s	—	3.5	9.8	2.8	2.5	−17.2

[a]Data obtained from spectra recorded at a sweep width of 100 Hz. [b]Observed multiplicities: d, doublet; q, quartet; o, octet; m, multiplet; b, broadened. [c]The C-7 proton resonating at lower field is designated H-7, and that resonating at higher field is designated H-7'. [d]6-Proton singlet. [e]8-Proton multiplet. [f]The large coupling of H-3 with H-4, and their small difference in chemical shift, cause further splitting of the H-2 signal through "virtual coupling" (1.5 Hz). [g]The broadening of the signals is due to the small ^4J long-range couplings between H-7,7' and H-4 and H-5. [h]Measured in Me_2SO:$CDCl_3$ (~3:1) containing a drop of D_2O.

molecular weight of **7** was confirmed by the presence of the large molecular-ion peak at *m/e* 413 (5% of the intensity of the base peak for $NO_2C_6H_4C{=}O^+$ ions at *m/e* 150). The presence of a molecular ion peak is not characteristic of the fragmentation of common methyl derivatives of uronic acids, and supports the proposed bicyclic structure of **7** and related substances described herein.

The debenzoylation product **8** was studied by low- and high-resolution mass spectrometry. The molecular ion at *m/e* 264 (1.5%) has the elemental composition $C_{11}H_{20}O_7$. Fragmentation occurs mainly in the pyranoid part of the molecule. The loss of the glycosidic methoxyl group gives the A_1 ion (according to the nomenclature of Kochetkov *et al.*[11]) at *m/e* 233 (1.4%) which loses water from C-3 to give the ion A_2 at *m/e* 215 (2%). Elimination of methanol from the A_1 ion yields the ion at *m/e* 201 (11.4%). Since it has been established[12] that, in the fragmentation of uronic acid derivatives, MeO-2 is involved to a negligible extent in the elimination of methanol from the A_1 ion to give the A_2 ion, the high intensity of $[M-OMe-MeOH]^+$ ions can be explained by the participation of one of the acetal methoxyl groups in the formation of the stable, highly conjugated ions of the following type:



This type of elimination is supported by the fact that the ion $[M-OMe-MeOH]^+$ was not present in the mass spectrum of the ketone **9**.

The intense ion of the elemental composition of $C_8H_{12}O_4$ at *m/e* 172 (35.8%) arises by a similar elimination of methanol from the C_1 ion[11] at *m/e* 204 (1.1%) which is produced by the elimination of methyl formate from the molecular ion. The pronounced elimination of methanol from the C_1 species can again be attributed to the participation of one of the acetal methoxyl groups to give a stable, conjugated ion. This phenomenon does not occur in the fragmentation of the ketones **9** and **10**.

The substituents at C-1,2,3 are confirmed by the presence of H_1 ions[11] at *m/e* 88 (100%) and 74 (79%). The absence of intense peaks of the F_1 species at *m/e* 101, the formation of which would be analogous to the fragmentation of methyl 2,4-di-*O*-methylhexopyranosides[13] and the corresponding methyl uronates[6], proves the absence of a methyl group at C-4, and the absence of the peaks of the ions $[M-59]^+$ and $[M-73]^+$ in the spectra of **7** and **8** constitute a further proof of the absence of a methoxycarbonyl group or a longer exocyclic residue at C-5. The same fragmentation pathway was observed in the spectra of **12**.

Further evidence for the structures **7** and **8** was provided by hydrolysis of **8** with dilute, aqueous mineral acid which gave (t.l.c.) first the ketone **9** (ν_{max} 1780 cm^{-1}) and then **10** as a minor product.

The mass spectrum of **9** was interpreted with the aid of the spectrum of a

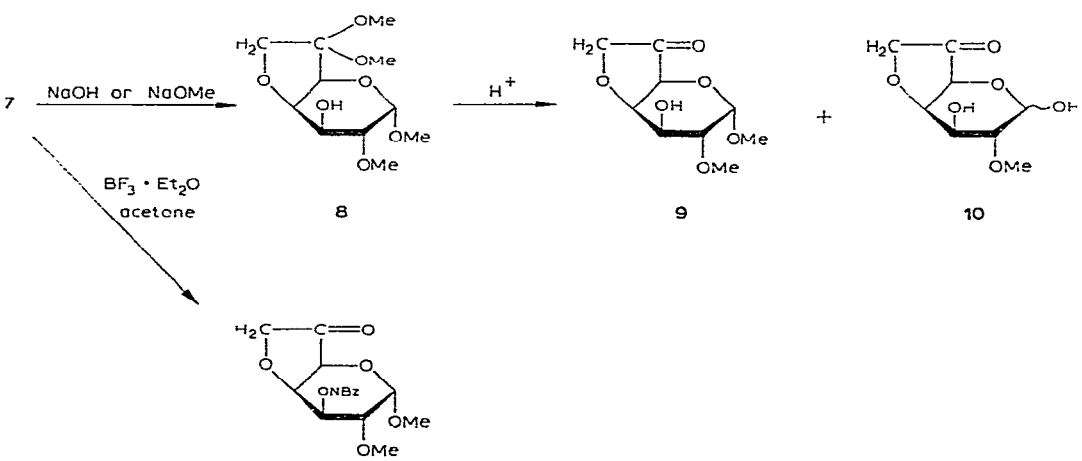
deuterated analogue. A weak, molecular ion peak was present at *m/e* 218 (219 after deuteration). The A_1 ion, formed by loss of the glycosidic methoxyl group, was represented by the peak at *m/e* 187 (188) (0.2% of the base peak at *m/e* 74). An intense peak for the C_1 ion occurred at *m/e* 158 (159, 20.8%). This ion, compared to the C_1 ion formed in the fragmentation of **8**, is stabilized by cyclization with the keto group of the furone derivative, and is not fragmented further.

The absence of the peaks of the A_1 ion $(M-OMe]^+$ in the spectrum of **10** showed that the compound was the product of further hydrolysis of **9**. Elimination of formic acid gives rise to the ion C_1 at *m/e* 158 (9.2% of the base peak of the H_1 ion at *m/e* 74), identical with the C_1 ion observed in the fragmentation of **9**.

The conclusive evidence for the sequence of atoms in the tetrahydrofurone arrangement was provided by the p.m.r. spectra of the ketones **9** and **13**, the latter being obtained by treatment of **7** with acetone and BF_3-etherate (acetal exchange).

In the p.m.r. spectra of **9** and **13**, there was a considerable change of the geminal coupling constant $J_{7,7'}$ as compared to that for the acetals **7** and **8**. The absolute value of the geminal coupling constant (Table I) for the methylene protons is increased markedly by the presence of the carbonyl group in the system (carbonyl effect), as is often observed in similar systems[14]. A long-range coupling (<0.4 Hz, *i.e.*, the resolving power of the spectrometer) between the methylene protons and H-4 and H-5 was manifested by line broadening in the spectra of **9** and **13**. The values $J_{7,5}+J_{7,4}$ 1.5 Hz, and $J_{7',5}+J_{7',4}$ 1.2 Hz, respectively, were obtained by comparison of the H-7,H-7' line-widths at half-height (W_H) in the spectra of **9** and **13** with W_H of tetramethylsilane. The carbonyl-induced, long-range interaction across four single bonds found in the ketones **9** and **13** was not observed in the spectra of the acetals **7**, **8**, and **12**, and confirms the sequence of atoms in the five-membered ring.

It may be argued that, for the ketones **9** and **13**, as with the esters **1–6**, the downfield position of the H-5 signals should be observed due to the neighbouring



carbonyl group. However, the observed chemical shifts (δ 3.87 and 4.0, respectively) were comparable to those of the acetals. Measurements on Dreiding models, constructed on the basis of the values observed for the $J_{1,2}$–$J_{4,5}$ coupling constants, showed that the $^4C_1$(D) conformation of the tetrahydropyran ring is not affected by the attachment of the 5-membered ring, and that the orientation of the carbonyl group with respect to H-5 in **9** and **13** is such that its deshielding effect on H-5, calculated as recommended[15], is negligible, thus explaining the similarity of the chemical shift found for H-5 in the ketones and the acetals.

The reaction of diazomethane with esterified sugar acids described herein is analogous to the diazomethane synthesis, a method widely used in carbohydrate chemistry for lengthening the carbon chain. In the presence of boron trifluoride, the electron deficiency on the methoxycarbonyl carbon atom becomes more pronounced, which facilitates nucleophilic attack by the carbon atom of diazomethane. In the examples reported herein, the substrates contain an axial HO-4 group that undergoes methylation only with difficulty, and the reaction does not proceed in the usual manner[16]. In contrast to the reaction of diazomethane with aldoses, ketoses, and poly-*O*-acylaldonyl chlorides, after the loss of nitrogen from the intermediate complex, the system is stabilized by cyclization to give a product with a stable 5-membered ring. In the presence of an excess of the methylating agent, the intermediate hemiacetal is methylated to give the tetrahydrofurone dimethyl acetal derivative (Scheme 1).

EXPERIMENTAL

M.p.s. were determined on a Kofler hot-stage. Optical rotations were measured with a Perkin–Elmer automatic polarimeter Model 141. P.m.r. spectra were measured at 80 MHz (internal Me_4Si) with a Tesla BS-487-B spectrometer; for solvents, see Table I. Proton-signal assignments were made by the INDOR technique. Mass spectra were obtained at 70 eV, using an MCh-1306 spectrometer (U.S.S.R.), and exact mass measurements were made with an MS-902S spectrometer (resolving power 20,000). The temperature at the site of evaporation was 30–100°. I.r. spectra were obtained for 5% solutions in chloroform with a Perkin–Elmer spectrometer, Model 457. T.l.c. was performed on Silica Gel G, and column chromatography on dry-packed silica gel (0.1–0.15 mm), with *A*, benzene–acetone (4:1); *B*, dichloromethane–acetone (13:1); *C*, tetrachloromethane–acetone (7:1); *D*, chloroform–acetone (4:1); *E*, benzene–acetone (10:1); and *F*, chloroform–methanol (15:1). Prior to packing, the silica gel was equilibrated with 40% (v/w) of the mobile phase, instead of the recommended[17] 10%. Detection was effected by charring with 5% sulphuric acid in ethanol. *p*-Nitrobenzoyl chloride and boron trifluoride etherate were freshly purified[18]. Solutions were concentrated under diminished pressure at <40°.

*Methyl (methyl 2-*O*-methyl-3-*O*-*p*-nitrobenzoyl-* (**2**) *and -4-*O*-*p*-nitrobenzoyl-α-*D*-galactopyranosid)uronate* (**4**). — To a cold (−20°) solution of **1** (5 g, 21 mmol) in dry pyridine (125 ml), a solution of *p*-nitrobenzoyl chloride (4.45 g, 24 mmol) in dry pyridine (60 ml) was added dropwise with stirring and exclusion of moisture. The

mixture was kept at room temperature for 2 h, and t.l.c. (solvent *A*) then showed that the reaction mixture still contained an appreciable amount of the starting material. More *p*-nitrobenzoyl chloride (2.3 g, 13.5 mmol) in pyridine (30 ml) was then added in the same manner. After 30 min at room temperature, the reaction mixture, which contained 3 products (R_F 0.35, 0.4, and 0.6), was worked-up in the usual manner. The crude product solidified after trituration with methanol, and crystallization from chloroform–ether (twice) gave the major product **2** (4 g) in a chromatographically pure state (R_F 0.4), m.p. 203–205° (sintering at 195°), $[\alpha]_D^{24}$ +161° (*c* 1, chloroform). T.l.c. of the melt revealed two components (R_F 0.35 and 0.4) in the ratio ~1:1, showing that, as with similar derivatives of methyl β-L-arabinopyranoside[18], partial migration of NBzO-3 to HO-4 occurred on heating, and was responsible for the unsharp melting-point observed (Found: C, 49.98; H, 4.88; N, 3.69. $C_{16}H_{19}NO_{10}$ calc.: C, 49.87; H, 4.97; N, 3.64%).

The product in the mother liquor was chromatographed with solvent *B* to give the di-*p*-nitrobenzoate **3** (0.9 g, 8%), m.p. 144–146° (from chloroform–methanol, twice), $[\alpha]_D^{24}$ +226° (*c* 1, chloroform) (Found: C, 51.60; H, 4.11; N, 5.13. $C_{23}H_{22}N_2O_{13}$ calc.: C, 51.69; H, 4.15; N, 5.24%).

Subsequently eluted were the 3-*p*-nitrobenzoate **2** (1.5 g; total yield, 67.4%), and the 4-*p*-nitrobenzoate **4** (1.15 g, 14%), $[\alpha]_D^{24}$ +100° (*c* 1, chloroform), which could not be crystallized (Found: C, 49.63; H, 5.0; N, 3.45%).

*Methyl (methyl 2,4-di-*O*-methyl-3-*O*-p-nitrobenzoyl-α-*D*-galactopyranosid)-uronate* (**5**). — Compound **2** (3.2 g) was dissolved in dichloromethane (32 ml), and boron trifluoride etherate (10 μl) was added with stirring at −20° and exclusion of moisture. An ~1% solution of diazomethane in dichloromethane was then added slowly until a yellow colour persisted, the temperature of the reaction mixture being kept below −15°. The addition of the reagents was repeated several times, and when t.l.c. showed ~90% conversion of the starting material, the mixture containing two products (R_F 0.4 and 0.5, solvent *C*) was processed in the usual manner. Elution of the crude product from a silica gel column gave first the tetrahydrofurone derivative **7** (405 mg, 11.8%), m.p. 183–185° (from methanol, thrice), $[\alpha]_D^{24}$ +150° (*c* 1, chloroform) (Found: C, 52.35; H, 5.58; N, 3.24; OMe, 30.28. $C_{18}H_{23}NO_{10}$ calc.: C, 52.30; H, 5.60; N, 3.39; OMe, 30.03%).

Eluted next was the ester **5** (2.4 g, 72.3%) which, when crystallized from methanol (twice), had m.p. 131.5–132.5°, $[\alpha]_D^{24}$ +140.5° (*c* 1, chloroform) (Found: C, 51.00; H, 5.15; N, 3.53. $C_{17}H_{21}NO_{10}$ calc.: C, 51.13; H, 5.30; N, 3.51%).

*Methyl (methyl 2,4-di-*O*-methyl-α-*D*-galactopyranosid)uronate* (**6**). — Water (10 ml) was added to a solution of **5** (2 g) in 1,2-dimethoxyethane (20 ml), the solution was cooled in ice, and 10% aqueous sodium hydroxide (5 ml) was added slowly with stirring. Another portion of 10% sodium hydroxide (5 ml) was added after 10 min, and the solution was kept at 50° for 1 h. After dilution with water (100 ml) and cooling in ice, the solution was deionized with Dowex-50W(H^+) resin, filtered, and cocentrated to remove the organic solvent. The aqueous solution was extracted with ether to remove *p*-nitrobenzoic acid. The residue obtained on evaporation was dis-

solved in methanol and ethereal diazomethane was added. Concentration and chromatography gave **6** (1.1 g, 87.7%), m.p. 118.5–119° (from methyl acetate–ether), $[\alpha]_D^{22}$ +133° (*c* 1, chloroform); lit.[2] m.p. 118.5–119°, $[\alpha]_D$ +131°.

*Methyl 4,7-anhydro-2-*O*-methyl-α-*D*-galacto-heptopyranosid-6-ulose dimethyl acetal* (**8**). — (*a*) To a solution of **7** (250 mg) in dry methanol (10 ml) a few drops of methanolic M sodium methoxide were added, and the solution was kept at room temperature for 30 min. T.l.c. (solvent *C*) then showed that no starting material remained and a single product (R_F 0.4, solvent *D*) was detected. The solution was deionized with Dowex-50W(H^+) resin and concentrated, and the residue was chromatographed to remove methyl *p*-nitrobenzoate. Compound **8** (132 mg, 82.5%) was obtained as an oil having $[\alpha]_D^{24}$ +151° (*c* 1, chloroform), and no i.r. carbonyl absorption (Found: 49.77; H, 7.99. $C_{11}H_{20}O_7$ calc.: C, 49.99; H, 7.63%).

(*b*) Compound **7** (150 mg) was treated as described for the conversion of **5** into **6**, and the product (72 mg, 75%) was identical with **8** described in (*a*).

*Methyl 4,7-anhydro-2-*O*-methyl-α-*D*-galacto-heptopyranosid-6-ulose* (**9**). — A solution of **8** (50 mg) in 0.5M sulphuric acid (2 ml) was heated at 90°. Monitoring of the reaction by t.l.c. (solvent *C*) showed gradual disappearance of the starting material (R_F 0.4) and the formation of a product having R_F 0.25. After 2 h, a second product (R_F 0.1) was detected, but some of the starting material was still present. The reaction was terminated by addition of barium carbonate, and the mixture was worked-up in the usual manner. Elution of the product from a small column of silica gel afforded the faster-moving component **9** (23 mg, 55.8%), $[\alpha]_D^{22}$ +166° (*c* 1, chloroform) (Found: C, 49.21; H, 6.40. $C_9H_{14}O_6$ calc.: 49.54; H, 6.47%). The slower-moving substance **10** was obtained in an amount sufficient only for m.s. analysis.

*Methyl 4,7-anhydro-α-*D*-galacto-heptopyranosid-6-ulose dimethyl acetal* (**12**). — Methyl (methyl 2,3-di-*O*-benzoyl-α-D-galactopyranosid)uronate[19] (**11**, 3 g) was methylated by the method described in the preparation of **5**, and t.l.c. showed that two products (R_F 0.5 and 0.55, solvent *E*) were formed. After processing of the reaction mixture as described above, a solution of the crude product in 1,2-dimethoxyethane (20 ml) was diluted with water (5 ml), and debenzoylated with 10% aqueous sodium hydroxide by heating at 60° for 1 h. The solution was diluted with water, deionized with Dowex-50W(H^+) resin, filtered, concentrated to ~2 ml, and eluted from a small column of Amberlite IRA-410(HO^-) resin with water. Concentration of the eluate gave a chromatographically homogeneous, yellow oil (R_F 0.3, t.l.c., solvent *F*), which crystallized on standing to give **12** (136 mg, 7.8%). After recrystallization from methyl acetate (twice), the product had m.p. 166–167°, $[\alpha]_D^{22}$ +160° (*c* 0.94, chloroform), and no i.r. carbonyl absorption (Found: C, 48.12; H, 7.27. $C_{10}H_{18}O_7$ calc.: C, 47.99; H, 7.25%).

Elution of the resin with methanol–acetic acid–water (45:45:10) gave the uronic acid components. The eluate was concentrated, with co-distillation of water to remove acetic acid, and the residue in methanol was treated with excess of ethereal diazomethane. T.l.c. comparison with authentic samples[19] showed the presence of methyl

(methyl α-D-galactopyranosid)uronate, resulting from the incomplete methylation of **11**, and of methyl (methyl 4-*O*-methyl-α-D-galactopyranosid)uronate (**15**). The solution was concentrated, and chromatographed with solvent *F* to give **15** (465 mg, 28%), m.p. 140–142° (from acetone); lit.[19] m.p. 140–141°.

*Methyl 4,7-anhydro-2-O-methyl-3-*O-p-*nitrobenzoyl-α-*D-galacto-*heptopyranosid-6-ulose* (**13**). — A solution of **7** (75 mg) and BF_3-etherate (0.25 ml) in dry acetone (15 ml) was heated under reflux with the exclusion of moisture for 24 h. T.l.c. (solvent *F*) then showed that only traces of the starting material (R_F 0.5) were present. The major reaction product (R_F 0.3) was isolated from the concentrated solution by elution from a silica gel column to give **13** (46.2 mg, 69%), $[\alpha]_D^{21}$ +106° (*c* 1.2, chloroform) (Found: C, 52.40; H, 4.80; N, 3.72. $C_{16}H_{17}NO_9$ calc.: C, 52.32; H, 4.67; N, 3.81%).

ACKNOWLEDGMENTS

The authors thank J. Alföldi for i.r. spectroscopy, B. Leščáková and O. Juríková for the microanalyses, and G. Košický for measurements of optical rotation.

REFERENCES

1 Part VI: J. HIRSCH, P. KOVÁČ, AND V. KOVÁČIK, *J. Carbohyd. Nucleosides Nucleotides*, 1 (1974) 433–448.
2 P. KOVÁČ AND R. BREŽNÝ, *Chem. Zvesti*, in press.
3 P. KOVÁČ, J. HIRSCH, AND V. KOVÁČIK, *Carbohyd. Res.*, 32 (1974) 360–365.
4 P. KOVÁČ, *J. Carbohyd. Nucleosides Nucleotides*, 1 (1974) 183–186.
5 J. O. DEFERRARI, E. G. GROS, AND I. M. THIEL, *Methods Carbohyd. Chem.*, 6 (1972) 365–367.
6 V. KOVÁČIK AND P. KOVÁČ, *Org. Mass Spectrom.*, 10 (1975) 376–383.
7 H. BOOTH, in J. W. EMSLEY, J. FEENEY, AND L. H. SUTCLIFFE (Eds.), *Progress in Nuclear Magnetic Resonance Spectroscopy*, Pergamon, 1969, pp. 149–381.
8 J. N. BEMILLER AND G. V. KUMARI, *Carbohyd. Res.*, 25 (1972) 419–428.
9 P. HEIM AND H. NEUKOM, *Helv. Chim. Acta*, 45 (1962) 1735–1738.
10 G. O. ASPINALL AND P. E. BARRON, *Can. J. Chem.*, 50 (1972) 2203–2210.
11 N. K. KOCHETKOV, N. S. WULFSON, O. S. CHIZHOV, AND B. M. ZOLOTAREV, *Tetrahedron*, 19 (1963) 2209; N. K. KOCHETKOV AND O. S. CHIZHOV, *Advan. Carbohyd. Chem.*, 21 (1966) 39–93.
12 V. KOVÁČIK AND P. KOVÁČ, *Org. Mass Spectrom*, 9 (1974) 172–180.
13 V. KOVÁČIK AND P. KOVÁČ, *Chem. Zvesti*, 27 (1973) 662–667.
14 T. TAKAHASHI, *Tetrahedron Lett.*, (1964) 565–572.
15 L. M. JACKMAN AND S. STERNHELL, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon, 1969, pp. 61–114.
16 L. HOUGH AND A. C. RICHARDSON, in W. PIGMAN AND D. HORTON (Eds.), *The Carbohydrates*, Vol. IA, Academic Press, New York and London, 1972, pp. 113–163.
17 B. LOEV AND M. M. GOODMAN, *Chem. Ind. (London)*, (1967) 2026–2032.
18 P. KOVÁČ AND R. PALOVČÍK, *Carbohyd. Res.*, 36 (1974) 379–384.
19 J. HIRSCH, P. KOVÁČ, AND V. KOVÁČIK, *Chem. Zvesti*, 28 (1974) 833–839.