

A Mild Procedure for the Regiospecific Benzoylation and Allylation of Polyhydroxy-compounds *via* their Stannylene Derivatives in Non-polar Solvents

By Serge David,* Annie Thieffry, and Alain Veyrières, Laboratoire de Chimie Organique Multifonctionnelle, Université de Paris-Sud, 91405 Orsay Cédex, France

The reactions of benzyl and allyl bromides on the stannylene derivatives of polyhydroxy-compounds, which normally proceed only at insignificant speed in refluxing benzene solution, are greatly accelerated in the presence of quaternary ammonium halides. These conditions were tested on benzyl β -D-galactopyranoside (1) and ten derivatives, (2)—(11), which were benzylated, allylated, or acetalated. In such a collection may be found all the possible arrangements, except one, of two, three, or four hydroxy-groups on a β -D-galactopyranoside ring. Regiospecific substitution in good yield was observed on nine of the starting polyols. Benzoylation in this way of benzyl 2,3-di-*O*-benzyl- α -D-glucopyranoside only gave the 6-*O*-benzyl ether in 80% yield, a great improvement over the reaction in *NN*-dimethylformamide, which has no preparative value. The same new method allows a smooth preparation of the monomethoxymethyl ethers of glycols. The preparations and synthetic uses of the stannylene derivatives of γ - and ε -glycols are reported for the first time.

ONE of us has recently reported¹ that the course of the reaction of allyl bromide with tributylstannylated benzyl β -D-mannopyranoside could be much improved, in terms of speed, yield, and general convenience, by working in the presence of quaternary ammonium halides in toluene solution. Such conditions are probably among the mildest ever reported for etherification. We had found already² that the treatment of stannylenes with benzoyl chloride at room temperature, *without added base*, gave the monobenzoates of the parent diols, in a quantitative reaction which was generally rapid and regiospecific.† By contrast, benzoylation and allylation were not possible in these conditions and had to be conducted in *NN*-dimethylformamide solution at higher temperatures.³ In such polar solvents, conceivably, stannylenes may build co-ordinated monomers, while there is strong evidence that they exist as fairly stable dimers in solvents of low polarity. In the solid state and in chloroform solution, the dibutylstannylene of methyl 4,6-*O*-benzylidene- α -D-glucopyranoside was shown to be dimeric with a Sn₂O₂ parallelogram unit.⁴ Moreover the ¹¹⁹Sn chemical shifts in the n.m.r. spectra of deuteriochloroform solutions of the carbohydrate stannylenes considered in ref. 2 were found⁵ in the range characteristic of pentaco-ordinated tin.⁶ In view of our permanent interest in dimeric stannylenes, we decided to investigate their substitutions with reactive halides in the conditions described by Alais and Veyrières,¹ since they used solvents where the dimeric structures presumably would be stable. The method was first tested on a difficult case: benzoylation of the stannylene of benzyl 2,3-di-*O*-benzyl- α -D-glucopyranoside (28) in *NN*-dimethylformamide was reported² to give the 6-*O*-benzyl ether (29) only as a minor component in an untractable mixture. On the other hand, the new technique gave regiospecifically the 6-*O*-benzyl ether in

80% yield. This led us to test it on a wide range of benzyl β -D-galactopyranoside derivatives (1)—(11). The galactose configuration was selected because of its prime importance in glycoprotein and glycolipid research, and benzyl and allyl ethers were used throughout as protected derivatives because of their usefulness in oligosaccharide synthesis.

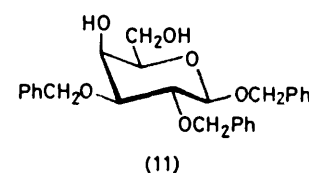
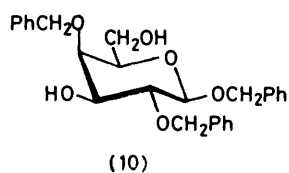
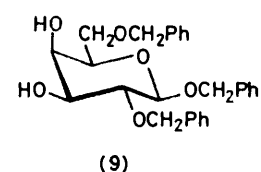
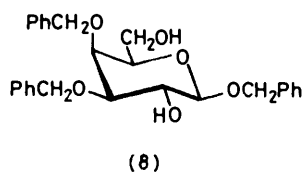
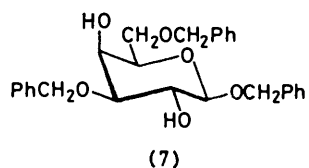
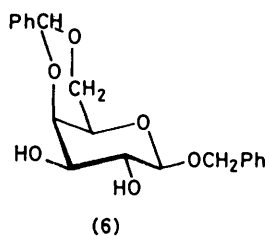
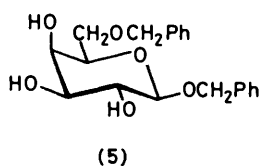
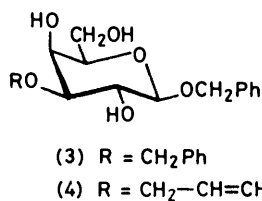
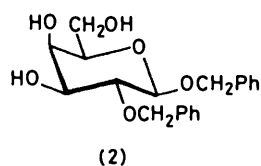
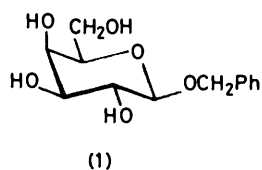
RESULTS AND DISCUSSION

The benzyl β -D-galactopyranoside derivatives (2)—(11) are numbered in the order of increasing substitution. Some were known compounds and some were prepared in the present study by the stannylene procedure. The starting derivatives (2), (5), (8), (9), and (10) were synthesized as follows: monomolecular benzoylation of benzyl 3,4-*O*-isopropylidene- β -D-galactopyranoside with benzyl bromide and sodium hydride in *NN*-dimethylformamide gave a mixture of the 2,6-di-*O*-benzyl (13), the 6-*O*-benzyl (14), and the 2-*O*-benzyl ether (16), which were separated by column chromatography. A downfield shift of the signal of 2-H was observed in the ¹H n.m.r. spectrum of the acetate (15) of compound (14). This proved that the parent alcohol (14) had a free hydroxy-group at C-2. Conversely, a downfield shift of the signal of the 6-H, 6'-H protons was observed after acetylation of compound (16). Mild, acidic hydrolysis of the isopropylidene acetal function in compounds (13), (14), and (16) gave the polyols (9), (5), and (2).

Conventional allylation of (12) gave in 80% yield the 2,6-di-*O*-allyl ether (18), which was hydrolysed in dilute acid to the diol (19). Conventional benzoylation then gave the fully protected galactoside (20) (88%). Selective removal of the allyl ether function then gave the diol (8). Finally, the perbenzoylation of the 3,6-di-*O*-allyl ether (21) gave another fully protected galactoside (22) which was hydrolysed to the diol (10) in the same way as above.

For the description of the etherification of the stannylenes of derivatives (1)—(11) in the presence of quaternary ammonium halides (Table), we shall begin with the

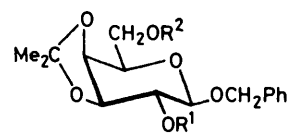
† The small-scale preparation of benzyl 4,6-*O*-benzylidene-3-*O*-benzoyl- β -D-galactopyranoside could be repeated without difficulty on the 5-g scale without molecular sieves, and in quantitative yield.



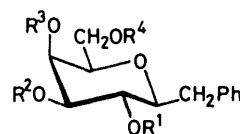
presumably less complex reactions of compounds with only two hydroxy-groups. Benzylation of the stannylene of the 2,3-diol (6) gave a 5.5 : 1 mixture of the 3-*O*- and 2-*O*-benzyl ethers, (23) and (24), from which the main component (23) could be easily separated. The sites of etherification were ascertained as above, by inspection of the chemical shifts of 2-H and 3-H after acetylation. Benzylation of the 3,4-diol (9) was regiospecific, to give only the 3-*O*-benzyl ether (27) in 87% yield. The same benzylations were much less satisfactory in dimethylformamide solution without catalyst: while the first diol (6) gave an intractable mixture, the reaction was regiospecific with the second one (9) but only in 66% yield.

The preparation and benzylation of stannylenes with the tin atom spanning the 4,6 oxygen atoms of a pyranoside has been already reported.² Although a six-membered-ring stannylene appears a little less strained than a five-membered one, these derivatives are also dimeric.⁵ Under our conditions, benzylation of the

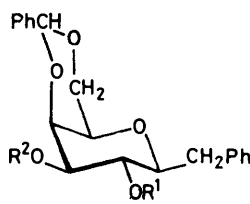
stannylene of the β -glycol (11) gave regiospecifically the 6-*O*-benzyl ether (27) in 60% yield. The case of the other β -glycol (7), which failed to give a stannylene, will be considered in more detail below in the general discussion.



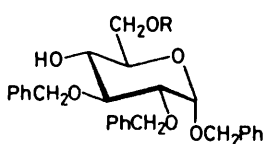
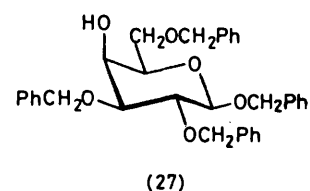
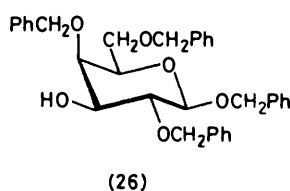
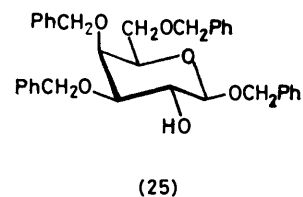
- (12) R¹ = R² = H
 (13) R¹ = R² = CH₂Ph
 (14) R¹ = H, R² = CH₂Ph
 (15) R¹ = Ac, R² = CH₂Ph
 (16) R¹ = CH₂Ph, R² = H
 (17) R¹ = CH₂Ph, R² = Ac
 (18) R¹ = R² = CH₂-CH=CH₂



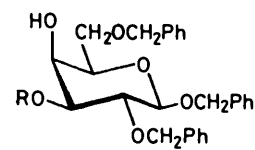
- (19) R¹ = R⁴ = CH₂-CH=CH₂, R² = R³ = H
 (20) R¹ = R⁴ = CH₂-CH=CH₂, R² = R³ = CH₂Ph
 (21) R¹ = R³ = H, R² = R⁴ = CH₂-CH=CH₂
 (22) R¹ = R³ = CH₂Ph, R² = R⁴ = CH₂-CH=CH₂



- (24) R¹ = CH₂Ph, R² = H



- (29) R = CH₂Ph
 (30) R = CH₂OMe



- (32) R = CH₂OMe

TABLE
Substitution of stannylenes

Starting glycoside	Time (h)	Chromatography eluant	Product	Yield (%)
<i>(a) Benzylation^a</i>				
(1)	2	Chloroform-ethyl acetate (3 : 2)	(3)	67
(2)	4	Chloroform-methanol (98 : 2)	(11)	68
(3)	24	Chloroform-methanol (97 : 3)	(7)	72
(5)	24	Ether-light petroleum (1 : 1)	(27)	35
(6)	5	Chloroform-acetone (95 : 5)	(7)	28.5
			(23)	55
			(24)	10
(8)	30	Ether-light petroleum (1 : 1)	(25)	49
(9)	6	Ether-light petroleum (1 : 1)	(27)	87
(10)	48	Ether-light petroleum (2 : 1)	(26)	48
(11)	28	Ether-light petroleum (1 : 1)	(27)	60
(28)	16	Chloroform-acetone (99 : 1)	(29)	80
<i>(b) Allylation^b</i>				
(1)	8	Chloroform-methanol (95 : 5)	(4)	85
(4)	24	Chloroform-methanol (99 : 1)	(21)	60
<i>(c) Methoxymethylation^c</i>				
(28)	3.5	Chloroform-acetone (98 : 2)	(30)	87
(31)	3.5	Chloroform-acetone (95 : 5)	(32)	92

^a General procedure; a mixture of the glycoside (1 mmol) and dibutyltin oxide (1 mmol) in benzene was refluxed for 16 h with azeotropic removal of water. The solution was evaporated to ca. 25 ml, tetrabutylammonium iodide (1 mmol) and benzyl bromide (0.25 ml) were added, and the mixture was refluxed. Evaporation to dryness gave a residue which was processed by column chromatography on silica gel. Toluene was used instead of benzene for the reactions of the galactosides (8) and (10). ^b The procedure was the same as above except that the substitution was carried out with allyl bromide (0.5 ml) at 60 °C. ^c The procedure was the same as above except that the substitution was carried out at room temperature for methoxymethyl chloride (1.1 mol) in the presence of molecular sieves (4 A, 1 g).

The preparation of stannylene derivative of carbohydrate-derived γ -glycols has so far not been reported. We have found that the reaction of dibutyltin oxide with but-2-ene-1,4-diol is very rapid; the co-ordination of tin in the derivative is more than four.⁵ On the other hand, a 48-h reflux in toluene was necessary to prepare the stannylene of the γ -glycol (10), and there were still traces of the hydroxy-derivative in the preparation as judged from its i.r. absorption. This high activation energy probably reflects the necessity for the galactoside (10) to adopt the unfavourable D^4C_1 conformation. The seven-membered-ring stannylene built on such a conformation does not appear to suffer more angular strain than one with a five- or six-membered ring. Benzylolation occurred exclusively at the primary position, in acceptable yield (48%).

An eight-membered-ring δ -glycol stannylene built on the 2- and 6-positions of the diol (8) (perhaps in a boat-like conformation) would appear to be an extremely congested structure. In any case, after a 30-h reflux in toluene, the i.r. absorption near 3 500 cm^{-1} was greatly diminished, and benzylolation with the present procedure gave a 49% yield of the 6-*O*-benzyl ether.

We now come to the triol derivatives. It may be recalled in this respect that the first stannylenes used as intermediates for substitution at oxygen were those of the common nucleosides, *i.e.* triols.⁷ Benzyl 2-*O*-benzyl- β -D-galactopyranoside (2) gave only the 3-*O*-benzyl ether

in good yield, while benzyl 3-*O*-benzyl- β -D-galactopyranoside (3) and the analogous allyl ether (4) were specifically substituted at the primary position to give, respectively, the 6-*O*-benzyl and 6-*O*-allyl ethers, (7) and (21). Surprisingly, benzylolation of the stannylene of the 6-*O*-benzyl ether (5) gave a relatively large proportion of a di-substitution product (27), together with a comparable amount of the expected 3-*O*-benzyl derivative.

Finally, treatment of benzyl β -D-galactopyranoside itself (1), that is, a pyranoside with four free hydroxy-groups, was completely regiospecific, to give excellent yields of either the 3-*O*-benzyl (3) or the 3-*O*-allyl ether (4). We have seen above that ether (4) can be easily converted to the benzyl 3,6-di-*O*-allyl- β -D-galactopyranoside (21), with two temporary⁸ protecting groups, and hence to benzyl 2,4-di-*O*-benzyl- β -D-galactopyranoside (10). This affords a new, efficient synthesis of this useful protected sugar.⁹

The method was also tested on other configurations. We have mentioned above the efficient benzylolation of benzyl 2,3-di-*O*-benzyl- α -D-glucopyranoside at the primary position. On the other hand, we have not been able to improve on the yield reported¹⁰ in the allylation of methyl α -D-mannoside in *NN*-dimethylformamide. The reaction under our conditions gave a quantitative recovery of starting material. Likewise, allylation of benzyl 6-*O*-trityl- α -D-mannopyranoside gave only a 45% yield of the 3-*O*-allyl ether, so the tributylstannylation procedure is still the best method of preparation of benzyl 3-*O*-allyl-6-*O*-trityl- α -D-mannopyranoside (62% yield).¹

The method was also tested with another active halide, methoxymethyl chloride. There was only an insignificant conversion of the stannylene derivative from diol (31) in benzene after 1.5 h, while the reaction in the presence of 1 equiv. of tetrabutylammonium iodide at room temperature gave in the same length of time a quantitative yield of the monomethoxymethyl ether (32). The hydroxy-function 4-OH is the free one in this product on the basis of the n.m.r. spectrum of the acetylated product, in which the 4-H doublet has moved to lower fields. A similar treatment of the stannylene from compound (28) gave an 87% yield of the methoxymethyl ether (30) of the primary hydroxy-function of the parent diol, together with a small amount of disubstituted product. Again the position of etherification in the main product was ascertained by acetylation, which caused a downfield shift of the pseudo-triplet of 4-H in the n.m.r. spectrum. Ethers (32) and (30) are alkali-stable protected derivatives of one hydroxy-function in the diols (31) and (28). The methoxymethyl ether (32), dissolved in trifluoroacetic acid-water (9 : 1), was quantitatively hydrolysed back to diol (31) in <1 h at room temperature. Presumably other α -chloro-ethers, such as 2-chlorotetrahydropyran or 2-chlorotetrahydrofuran, would also react with stannylenes under the same conditions to give useful, protected derivatives of sugars.

Inspection of the Table permits some general comments. Substitution at position 4 was never observed, and substitution at position 2 was never regiospecific.

Position 3 was highly favoured when there was at least one hydroxy-group vicinal to it in the starting polyol. Regiospecific substitution at the primary position occurred in all other cases. The simplest interpretation of these facts seems to be the following one: substitution of a stannylene involving the primary position always occurs at that position. However, the building of such rings, which are at least six-membered ones, does not occur when a five-membered ring is possible. Such a ring may span the 3- and 4-positions, and in this case, substitution will occur on oxygen 3-O, for the known unreactivity of a free hydroxy-group at position 4 on a pyranose derivative appears to be still prevalent in stannylenes involving that position. The other possible five-membered ring stannylene spans the 2- and 3-positions, and then the outcome of the reaction may be more complex.

Non-regiospecific substitutions may be explained in several ways. From any glycol system two isomeric dimers may be built with alternate activation of the oxygen atoms. This may be the case for the benzylidene-galactoside (6). The behaviour of compound (5) is more complex in that there is polysubstitution. The crude stannylene preparation probably was a mixture of derivatives spanning the 2-, 3-, and 3-, 4-positions. Disubstitution of the first one may well be a consequence of the extended time necessary for the reaction. Indeed, disubstitution by prolonged heating in the presence of the more reactive acid chlorides is the basis of a recently reported method¹¹ for macrocyclic lactone synthesis.* On comparing the behaviour of compound (5) with the clean substitution of benzyl β -D-galactopyranoside, it is obvious that the protection of the primary position, although seemingly not involved, has drastically altered the course of the reaction. This suggests that the favourable outcome of the substitution of benzyl β -D-galactopyranoside is mediated at some step by hydrogen-bonding, probably with the oxygen atom at position 4.

The failure of diol (7) to give a stannylene is a consequence of the 1,3-*trans* disposition of its two free hydroxy-groups. The distance between the corresponding oxygen atoms is more than twice the length of the covalent Sn-O bond (2.1 Å). In connection with this, the chelation, once considered, between tin and the anomeric oxygen in the stannylene of methyl 4,6-O-benzylidene- α -D-glucopyranoside,¹² could have been rejected *a priori*, for this means bridging by tin the *trans* oxygen atoms on C-1 and C-3, and the length of even the apical Sn-O bond is of the order of 2.3 Å.

The mechanism of the effect of the quaternary ammonium iodide cannot simply be the replacement of bromine by iodine in the active halide, for quaternary bromides are also efficient catalysts. Although the reaction needs more time for completion, it is still preparatory useful for the yields are the same. Indeed its use has been demonstrated in a case where some side-

* In this paper, and the following ones from the same group, the authors use a structure for the stannylene dimer which is no longer considered as valid.⁶ However, this does not change our argument.

reaction caused the discharge of iodine.¹ Besides, we have observed in this laboratory that sluggish reactions of stannylenes with acid anhydrides may be enormously accelerated by quaternary halides, when no exchange of halide may be involved. We suggest that the coordination of the halide anion to the tin enhances the nucleophilicity of one of the bound oxygen atoms. Activation in *NN*-dimethylformamide solution may have a similar origin.

EXPERIMENTAL

General Methods.—Hydrogen-1 n.m.r. spectra were recorded at 250 MHz in deuteriochloroform with tetramethylsilane as internal reference. The course of the reaction was followed by t.l.c., using the same mobile phases as in the subsequent column chromatography. Acetylations were carried out with acetic anhydride-pyridine.

Benzyl 2,6-Di-O-benzyl-3,4-O-isopropylidene- β -D-galactopyranoside (13), Benzyl 6-O-Benzyl-3,4-O-isopropylidene- β -D-galactopyranoside (14), and Benzyl 2-O-Benzyl-3,4-O-isopropylidene- β -D-galactopyranoside (16).—A solution of benzyl-3,4-O-isopropylidene- β -D-galactopyranoside¹³ (3.1 g) in *NN*-dimethylformamide (100 ml) was stirred for 2 h at room temperature in the presence of sodium hydride (0.32 g) and then cooled to 0 °C. Benzyl bromide (1.3 ml) was added dropwise. The mixture was stirred for 4 h at room temperature, diluted with water, and extracted with ether. Chromatography of the extract (ether-light petroleum, 1 : 1) first gave the ether (13) as a syrup (0.72 g, 15%), transparent in the vicinity of 3 500 cm⁻¹; δ 1.32, 1.38 (2 \times 3 H, 2 s, Me₂C), 4.4 (1 H, d, $J_{1,2}$ 8 Hz, 1-H), and 7.31 (15 H, m, 3 Ph).

Further elution (ether-hexane, 2 : 1) then gave the benzyl ether (14) (0.82 g, 20%); ν_{\max} 3 500 cm⁻¹ (OH); δ 2.67 (1 H, OH), 3.59 (1 H, pseudo-t, $J_{1,2}$ 8, $J_{2,3}$ 7 Hz, 2-H), 4.01 (1 H, dd, $J_{3,4}$ 5 Hz, 3-H), and 4.23 (1 H, d, 1-H).

The more polar component was the benzyl ether (16) (0.9 g, 23%); ν_{\max} 3 500 cm⁻¹ (OH); δ 2.12 (1 H, OH), 3.46 (1 H, dd, $J_{1,2}$ 8, $J_{2,3}$ 7 Hz, 2-H), 4.10 (1 H, pseudo-t, 3-H), and 4.41 (1 H, d, 1-H).

Acetylation of compound (14) gave benzyl 2-O-acetyl-6-O-benzyl-3,4-O-isopropylidene- β -D-galactopyranoside (15); δ 4.10 (1 H, dd, $J_{2,3}$ 7, $J_{3,4}$ 5 Hz, 3-H), 4.34 (1 H, d, $J_{1,2}$ 8 Hz, 1-H), and 5.06 (1 H, pseudo-t, 2-H). Acetylation of compound (16) gave benzyl 6-O-acetyl-2-O-benzyl-3,4-O-isopropylidene- β -D-galactopyranoside (17); δ 3.46 (1 H, dd, $J_{1,2}$ 8, $J_{2,3}$ 7 Hz, 2-H), 4.16 (1 H, pseudo-t, 3-H), and 4.38 (3 H, m, 1-H, 6-H, 6'-H).

Benzyl 2,6-Di-O-benzyl- β -D-galactopyranoside (9).—A solution of the acetal (13) (0.72 g) in 50% aqueous acetic acid was heated at 80 °C for 2 h, and then evaporated to dryness. The residue was co-evaporated several times with toluene to give the benzyl ether (9) (0.65 g), m.p. 107 °C (ether-light petroleum), $[\alpha]_D^{20}$ -14.4° (*c* 1.8 in CH₂Cl₂) (Found: C, 71.8; H, 6.65; O, 21.1. C₂₇H₃₀O₆ requires C, 72.0; H, 6.8; O, 21.3%).

Benzyl 6-O-Benzyl- β -D-galactopyranoside (5).—The above method, starting from acetal (14) (0.81 g), gave the benzyl ether (5) as a syrup (0.72 g), $[\alpha]_D^{20}$ -28.3° (*c* 3.8 in CH₂Cl₂) (Found: C, 66.7; H, 6.7; O, 26.6. C₂₀H₂₁O₆ requires C, 66.65; H, 6.7; O, 26.6%).

Benzyl 2-O-Benzyl- β -D-galactopyranoside (2).—Hydrolysis as above of the acetal (16) (0.90 g) gave the known benzyl

ether (2) (0.77 g), m.p. 137 °C (ethyl acetate–light petroleum) [lit.,¹³ m.p. 138–139 °C (benzene–hexane)].

Benzyl 2,6-Di-O-allyl-3,4-O-isopropylidene-β-D-galactopyranoside (18).—A solution of the protected galactoside (12) (1.6 g, 5.1 mmol) in *NN*-dimethylformamide (100 ml) was stirred for 1 h at room temperature in the presence of sodium hydride (0.37 g, 15.3 mmol), and then cooled to 0 °C. Benzyl bromide (1.76 ml, 20.4 mmol) was added, the mixture was kept for 20 h at room temperature and evaporated to dryness after destruction of excess of sodium hydride with methanol. The residue was extracted with dichloromethane. Evaporation to dryness of the washed, organic layer gave the *allyl ether* (18) as a syrup (1.60 g, 80.5%), $[\alpha]_D^{20} 0^\circ$ (*c* 1.0 in CH₂Cl₂) (Found: C, 67.7; H, 7.8; O, 24.4. C₂₂H₃₀O₆ requires C, 67.7; H, 7.4; O, 24.6%).

Benzyl 2,6-Di-O-allyl-β-D-galactopyranoside (19).—A solution of the acetal (18) (1.5 g) in 50% aqueous acetic acid (100 ml) was heated at 80 °C for 2 h, and then evaporated to dryness. The residue was purified by co-evaporation with toluene to give finally the *allyl ether* (19) as a syrup (1.15 g; 86%), $[\alpha]_D^{20} -28.5^\circ$ (*c* 2.0 in CH₂Cl₂) (Found: C, 65.1; H, 7.4; O, 27.7. C₁₉H₂₆O₆ requires C, 65.1; H, 7.5; O, 27.4%).

Benzyl 2,6-Di-O-allyl-3,4-di-O-benzyl-β-D-galactopyranoside (20).—Benzyl bromide (1 ml) and sodium hydride (0.25 g) were added in succession to a solution of compound (19) (1.035 g, 3 mmol) in dry tetrahydrofuran (100 ml). The mixture was refluxed for 7 h, diluted with methanol, and evaporated to dryness. Extraction of the residue with dichloromethane gave *compound* (20) (1.4 g, 88%), m.p. 81 °C (light petroleum), $[\alpha]_D^{20} -14.8^\circ$ (*c* 2.0 in CH₂Cl₂) (Found: C, 74.8; H, 7.2; O, 17.7. C₃₃H₃₈O₆ requires C, 74.7; H, 7.2; O, 18.0%).

Benzyl 3,4-Di-O-benzyl-β-D-galactopyranoside (8).—A solution of the di-*O*-allyl ether (20) (1.03 g, 2 mmol), tris(triphenylphosphine)rhodium chloride (75 mg), and 1,4-diazabicyclo[2.2.2]octane (450 mg) in ethanol–benzene–water (8 : 3 : 1) was refluxed for 4 h, then evaporated to dryness and extracted with dichloromethane. The extract was dissolved in acetone (15 ml) and 1M aqueous hydrochloric acid (2 ml), and refluxed for 15 min. The solution was neutralized with sodium hydrogencarbonate, evaporated to dryness, and extracted with dichloromethane. Chromatography of the extract gave the *di-O-benzyl ether* (8) (0.82 g, 91%), $[\alpha]_D^{20} -17.4^\circ$ (*c* 0.9 in CH₂Cl₂) (Found: C, 72.2; H, 7.0; O, 19.7. C₂₇H₃₀O₆ requires C, 72.0; H, 6.8; O, 21.3%).

Benzyl 3,6-Di-O-allyl-2,4-di-O-benzyl-β-D-galactopyranoside (22).—Benzyl bromide (1.4 ml) and sodium hydride (0.27 g) were added to a solution of galactoside (21) in dry tetrahydrofuran (100 ml). The mixture was refluxed for 6 h, then evaporated to dryness. Dichloromethane extraction gave the fully protected galactoside (22) as a syrup (1.2 g; 63%), $[\alpha]_D^{20} -12^\circ$ (*c* 2.0 in CH₂Cl₂) (Found: C, 74.2; H, 7.2; O, 17.8. C₃₃H₃₈O₆ requires C, 74.7; H, 7.2; O, 18.1%).

Benzyl 2,4-di-O-benzyl-β-D-galactopyranoside (10).—Compound (22) was de-allylated as above, to give the di-*O*-benzyl ether (10) (85%), m.p. 111.5–113.5 °C (benzene) (lit.,⁹ m.p. 111–113 °C).

General Procedures for the Substitutions of Stannylenes.—These are given as footnotes to the Table. The characterization of the products is reported below.

Benzyl 3-O-benzyl-β-D-galactopyranoside (3). Crystals, m.p. 105 °C (ether), $[\alpha]_D^{20} -20^\circ$ (*c* 2.0 in CH₂Cl₂); δ 4.40 (1 H, d, *J*_{1,2} 8 Hz, 1-H), and 4.85 (2 H, dd, *J*_{2,2'} 12 Hz, PhCH₂)

(Found: C, 66.1; H, 6.76; O, 26.2. C₂₀H₂₄O₆ requires C, 66.6; H, 6.7; O, 26.6%).

Benzyl 3-O-allyl-β-D-galactopyranoside (4). Syrup, $[\alpha]_D^{20} 0^\circ$ (*c* 2.0 in CH₂Cl₂); δ 3.37 (1 H, dd, *J*_{2,3} 10 Hz, *J*_{3,4} 3.5 Hz, 3-H), 3.47 (1 H, pseudo-t, *J*_{5,6} 6 Hz, 5-H), 3.55, 3.85 (m, OH), 4.09 (1 H, d, 4-H), 4.37 (1 H, d, *J*_{1,2} 8 Hz, 1-H), 4.55, 4.80 (each 1 H, 2 d, *J*_{gem} 12 Hz, PhCH₂), 5.13 (2 H, m, allyl-CH₂), 5.75 (1 H, m, –CH=), and 7.2 (5 H, m, Ph). The 2,4,6-triacetate; δ 2.03, 2.07, 2.12 (each 3 H, 3 s, 3 Ac), 3.46 (1 H, dd, *J*_{2,3} 10, *J*_{3,4} 3.5 Hz, 3-H), 3.76 (1 H, pseudo-t, *J*_{5,6} = *J*_{5,6'} = 6 Hz, 5-H), 4.15 (2 H, d, 6-H, 6'-H), 4.40 (1 H, d, *J*_{1,2} 8 Hz, 1-H), 4.55, 4.85 (2 H, 2 d, PhCH₂), 5.12 (1 H, dd, 2-H), 5.37 (1 H, d, 4-H), 5.70 (1 H, m, –CH=), and 7.30 (5 H, m, Ph).

Benzyl 3,6-di-O-benzyl-β-D-galactopyranoside (7). Syrup, $[\alpha]_D^{20} -25^\circ$ (*c* 1.3 in CH₂Cl₂); δ 2.5 (2 H, OH), 3.38 (1 H, dd, *J*_{2,3} 10, *J*_{3,4} 3.5 Hz, 3-H), 3.68 (1 H, m, 5-H), 3.79 (3 H, m, 2-H, 6-H, 6'-H), 4.00 (1 H, d, 4-H), 4.30 (1 H, d, *J*_{1,2} 8 Hz, 1-H), and 7.32 (15 H, 3 Ph) (Found: C, 71.7; H, 6.8; O, 21.1. C₂₇H₃₀O₆ requires C, 72.0; H, 6.8; O, 21.3%). The 2,4-diacetate; δ 1.98, 2.10 (each 3 H, 2 s, 2 MeCO), 3.48 (1 H, dd, *J*_{2,3} 10, *J*_{3,4} 3.5 Hz, 3-H), 3.60 (2 H, m, 6-H, 6'-H), 3.71 (1 H, m, 5-H), 4.39 (1 H, d, *J*_{1,2} 8 Hz, 1-H), 5.17 (1 H, dd, 2-H), and 5.59 (1 H, d, 4-H).

Benzyl 2,3-di-O-benzyl-β-D-galactopyranoside (11). Crystals, m.p. 116.5 °C (ether–light petroleum) (lit.,¹⁴ m.p. 117 °C).

Benzyl 3,6-di-O-allyl-β-D-galactopyranoside (1). Syrup, $[\alpha]_D^{20} -27^\circ$ (*c* 4.0 in CH₂Cl₂) (Found: C, 64.3; H, 7.5; O, 27.2. C₁₉H₂₆O₆ requires C, 65.1; H, 7.5; O, 27.4%).

Benzyl 3-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (23). Crystals, m.p. 167 °C (ethanol), $[\alpha]_D^{20} 0^\circ$ (*c* 1.0 in CHCl₃); ν_{\max} (Nujol) 3 500 cm⁻¹ (OH); δ 2.58 (1 H, s, OH), 3.46 (1 H, dd, *J*_{2,3} 9.5, *J*_{3,4} 3.5 Hz, 3-H), 4.38 (1 H, d, *J*_{1,2} 8 Hz, 1-H), 4.64 (1 H, d, *J*_{gem} 12 Hz, PhCHH), and 4.96 (1 H, d, PhCHH) (Found: C, 71.2; H, 6.3; O, 22.3. C₂₇H₂₈O₆ requires C, 71.5; H, 6.5; O, 22.0%). The 2-acetate had m.p. 173 °C (ethanol), $[\alpha]_D^{20} +8.8^\circ$ (*c* 1.0 in CHCl₃); δ 2.04 (3 H, s, Ac), 3.58 (1 H, dd, *J*_{2,3} 9.5, *J*_{3,4} 3 Hz, 3-H), 4.68 (1 H, d, *J*_{1,2} 8 Hz, 1-H), and 3.7 (1 H, 2-H) (Found: C, 70.9; H, 6.1; O, 23.0. C₂₉H₃₀O₇ requires C, 71.0; H, 6.2; O, 22.8%).

Benzyl 2-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (24). This was obtained as the more polar component in the benzylation of compound (6). Crystals, m.p. 143–145 °C (ethanol), $[\alpha]_D^{20} -11.6^\circ$ (*c* 1.0 in CHCl₃); ν_{\max} (Nujol) 3 500 cm⁻¹ (OH); δ 2.54 (1 H, s, OH) and 4.50 (1 H, d, *J*_{1,2} 8 Hz, 1-H) (Found: C, 71.8; H, 6.2; O, 21.5. C₂₇H₂₈O₆ requires C, 71.5; H, 6.5; O, 22.0%) {lit.,¹³ m.p. 144 °C (ethanol); $[\alpha]_D^{20} -10.4^\circ$ (*c* 0.7 in CHCl₃)}. The 3-acetate was a syrup, $[\alpha]_D^{20} +42.4^\circ$ (*c* 1.7 in CHCl₃); δ 2.06 (3 H, s, Ac), 3.92 (1 H, dd, *J*_{1,2} 8 Hz, *J*_{2,3} 10 Hz, 2-H), 4.60 (1 H, d, 1-H), and 4.92 (1 H, dd, *J*_{3,4} 3.5 Hz, 3-H) (Found: C, 71.2; H, 6.4; O, 22.6. C₂₉H₃₀O₇ requires C, 71.0; H, 6.2; O, 22.8%).

Benzyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (25). Syrup, $[\alpha]_D^{20} -34.2^\circ$ (*c* 1.5 in CH₂Cl₂); δ 2.5 (1 H, s, OH), 3.41 (1 H, dd, *J*_{2,3} 10, *J*_{3,4} 2.5 Hz, 3-H), 3.91 (1 H, d, 4-H), 4.01 (1 H, dd, *J*_{1,2} 8 Hz, 2-H), and 4.32 (1 H, d, 1-H). The 2-acetate; ¹⁵ δ 1.98 (3 H, s, MeCO), 3.48 (1 H, dd, *J*_{2,3} 10, *J*_{3,4} 2.5 Hz, 3-H), 3.94 (1 H, d, 4-H), 4.39 (1 H, d, *J*_{1,2} 8 Hz, 1-H), and 5.44 (1 H, dd, 2-H).

Benzyl 2,4,6-tri-O-benzyl-β-D-galactopyranoside (26). Crystals, m.p. 61 °C (ethanol) (lit.,¹³ m.p. 60–63 °C). The 3-acetate; δ 1.88 (3 H, s, MeCO), 3.83 (1 H, dd, *J*_{1,2} 8, *J*_{2,3}

10 Hz, 2-H), 3.95 (1 H, d, $J_{3,4}$ 2.5 Hz, 4-H), 4.52 (1 H, d, 1-H), and 4.88 (1 H, dd, 3-H).

Benzyl 2,3,6-tri-O-benzyl-β-D-galactopyranoside (28). Syrup, $[\alpha]_D^{20} -15^\circ$ (c 2.0 in CH_2Cl_2) {lit.,¹⁶ $[\alpha]_D^{20} -14^\circ$ (CHCl_3)}. The 4-acetate; δ 2.04 (3 H, s, Ac), 3.50 (1 H, dd, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, 3-H), 4.46 (1 H, d, $J_{1,2}$ 8 Hz, 1-H), 5.56 (1 H, d, 4-H), and 7.3 (20 H, m, Ph).

Benzyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside (29). Syrup; δ 2.48 (1 H, OH), 3.52 (1 H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 9 Hz, 2-H), 3.62 (2 H, m, 6-H, 6'-H), 3.78 (1 H, m, 5-H), 3.86 (1 H, t, $J_{3,4}$ 9 Hz, 3-H), 4.84 (1 H, d, 1-H), and 7.3 (20 H, m, 4 Ph). This spectrum was identical with that of the known compound.^{2,17}

Benzyl 2,3-di-O-benzyl-6-O-methoxymethyl-α-D-glucopyranoside (30). Tetrabutylammonium iodide was added (0.4 mmol). Chromatography gave first the 4,6-di-O-methoxymethyl ether (61 mg, 6%), no OH absorption in the i.r., and then the mono-ether (30) as a syrup (960 mg, 87%), $[\alpha]_D^{20} +64^\circ$ (c 2.0 in CHCl_3); ν_{max} (film) 3 500 cm^{-1} (OH); δ 2.54 (1 H, s, OH), 3.52 (3 H, s, OMe), 4.84 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), and 5.00 (2 H, d, J_{gem} 12 Hz, PhCH_2) (Found: C, 70.5; H, 6.9; O, 22.7. $\text{C}_{29}\text{H}_{34}\text{O}_7$ requires C, 70.4; H, 6.9; O, 22.6%). The 4-acetate was a syrup, $[\alpha]_D^{20} +48^\circ$ (c 4.5 in CHCl_3); δ 1.92 (3 H, s, Ac), 3.32 (3 H, s, OMe), 4.84 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), and 5.04 (1 H, pseudo-t, $J_{3,4} = J_{4,5} = 9.5$ Hz, 4-H) (Found: C, 69.1; H, 6.7; O, 24.0. $\text{C}_{31}\text{H}_{36}\text{O}_8$ requires C, 69.4; H, 6.8; O, 23.8%).

Benzyl 2,6-di-O-benzyl-3-O-methoxymethyl-α-D-galactopyranoside (32). Syrup (907 mg, 92%); $[\alpha]_D^{20} -66.5^\circ$ (c 2.6 in CHCl_3); ν_{max} (film) 3 500 cm^{-1} (OH); δ 2.92 (1 H, br s, OH), 3.38 (3 H, s, OMe), 4.86 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), and 4.88 (1 H, d, $J_{3,4}$ 3 Hz, 4-H) (Found: C, 70.4; H, 6.5;

O, 23.1. $\text{C}_{29}\text{H}_{34}\text{O}_7$ requires C, 70.4; H, 6.9; O, 22.7%). The 4-acetate was a syrup, $[\alpha]_D^{20} +78.5^\circ$ (c 2.0 in CHCl_3); δ 2.06 (3 H, s, Ac), 3.38 (3 H, s, OMe), 4.86 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), and 5.46 (1 H, d, $J_{3,4}$ 3 Hz, 4-H) (Found: C, 69.6; H, 7.0; O, 24.0. $\text{C}_{31}\text{H}_{36}\text{O}_8$ requires C, 69.4; H, 6.8; O, 23.9%).

[0/1839 Received, 1st December, 1980]

REFERENCES

- 1 J. Alais and A. Veyrières, *J. Chem. Soc., Perkin Trans. 1*, 1981, 377.
- 2 S. David and A. Thieffry, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1568.
- 3 C. Augé, S. David, and A. Veyrières, *J. Chem. Soc., Chem. Commun.*, 1976, 375.
- 4 S. David, C. Pascard, and M. Cesario, *Nouveau J. Chim.*, 1979, **3**, 63.
- 5 S. David, A. Forchioni, and A. Thieffry, unpublished data.
- 6 P. J. Smith, R. F. M. White, and L. Smith, *J. Organomet. Chem.*, 1972, **40**, 341.
- 7 D. Wagner, J. Verheyden, and J. G. Moffatt, *J. Org. Chem.*, 1974, **39**, 24.
- 8 See R. Gigg, *J. Chem. Soc., Perkin Trans. 1*, 1980, 738, and references therein.
- 9 S. David, C. A. Johnson, and A. Veyrières, *Carbohydr. Res.*, 1973, **28**, 121.
- 10 V. K. Srivastava and C. Schuerch, *Tetrahedron Lett.*, 1979, 3269.
- 11 A. Schanzer and N. Mayer-Schochet, *J. Chem. Soc., Chem. Commun.*, 1980, 176.
- 12 R. Munavu and H. Szmant, *J. Org. Chem.*, 1976, **41**, 1832.
- 13 A. Stoffyn and P. Stoffyn, *J. Org. Chem.*, 1967, **32**, 4001.
- 14 J. R. Turvey and T. P. Williams, *J. Chem. Soc.*, 1962, 2119.
- 15 J. C. Jacquinet and P. Sinaÿ, *Tetrahedron*, 1976, **32**, 1693.
- 16 A. Liptak, *Tetrahedron Lett.*, 1976, **39**, 3551.
- 17 A. Lubineau, A. Thieffry, and A. Veyrières, *Carbohydr. Res.*, 1976, **46**, 143.