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SUBSTITUENT EFFECTS ON CARBOHYDRATE COUPLING REACTIONS PROMOTED BY INSOLUBLE SILVER SALTS.

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Abstract

Coupling reactions were performed in the α-D-glucopyranosyl bromide series (i.e. compounds 1 a-c, 2 a, b, 3 and 4) and the α-D-mannopyranosyl bromide series (i.e. compounds 7 a-c, 8 a, b, 9) with aglycons 5 or 10 in the presence of insoluble silver salt promotors (i.e. silver silicate and silver zeolite). The insoluble silver salt promotes the formation of the β-glycosidic linkage, while a non-participating group is present at C-2 of the glycon. It was found that in both series 4-O-acyl functions increase the β/α ratio of the glycosidic bond formation relative to 4-O-alkyl functions, whereas 3-O and 6-O-acyl functions decrease this ratio.
We assume that inductive effects are responsible for the influence exerted by 3-O-substituents, but that through-bond interactions are essential for the effects exerted by 4-O and 6-O substituents.
Another unexpected finding was that coupling of α-D-mannopyranosyl bromide derivatives gave much higher β / α ratios than the corresponding reactions of α-D-glucopyranosyl bromides.

Introduction

The main challenge in the synthesis of oligosaccharides is the stereoselective formation of the glycosidic linkage between an activated anomeric centre of a glycon and the hydroxyl function of a suitably protected aglycon derivative.[1,2] It is well recognized that protecting groups on the glycon as well as on the aglycon may exert tremendous influence on the rate and stereochemical outcome of carbohydrate coupling reactions. In particular, the hydroxyl protecting group at C-2 of a glycon is known to be of high importance in directing the formation of the glycosidic bond. For example, 2-O-acyl substituents on fully protected α-D-glycopyranosyl halides direct the formation of 1,2-trans-glycopyranosidic bonds, because of neighbouring-group participation of the ester function at C-2. On the other hand, the presence of a non-participating group (e.g. benzyl or azido groups) at C-2 of a glycon is a prerequisite for the synthesis of virtually all 1,2-cis-glycopyranosidic linkages. Thus, the introduction of a 1,2-cis-glycosidic bond in the gluco-galacto-and fucopyranosyl series can readily be performed in the presence of a soluble promotor, under conditions where a rapid *in situ* anomerization of an α-tight ion-pair into a β-tight ion-pair occurs.[1-3]
Because the β-ion-pair has a much greater reactivity relative to the α-ion-pair, mainly an α-glycosidic linkage (1,2-cis bond) will be formed. However, a convenient introduction of a 1,2-cis-glycosidic bond in the manno-and rhamnopyranosyl series is impossible under *in situ* anomerization conditions. Nevertheless, it is possible to promote the conversion of a suitably

protected α-D-manno(rhamno)pyranosyl halide into a 1,2-cis-(β)glycoside by utilizing an insoluble or immobilized silver salt.[4-10]

In addition to the firmly established influence of C-2 substituents on coupling reactions, some information is also available on the effects exerted by substituents at the C-3, C-4 and C-6 sites of a glycon.[1,2] In general, O-allyl-and O-benzyl-protected glycons appear to be more reactive than O-acetylated derivatives which in turn are more reactive than O-trichloroacetyl protected glycons.[1] However, up to now no profound investigations have been performed to elucidate the differences in the stereochemical outcome of a coupling reaction, when a given protective group is positioned at either the C-3, C-4 or C-6 site of the glycon.

In this paper we wish to discuss in which way hydroxyl protecting groups, at the 3,4 and 6 positions of α-D-gluco-and α-D-mannopyranosyl bromides affect the formation of the β-glycosidic bond in coupling reactions promoted by insoluble silver salts. This particular reaction was chosen, because its mechanism is less complex than that of reactions conducted in the presence of soluble silver or mercury salts, which give rise to the formation of many intermediate ion-pairs.[1]

More precise information obtained, about substituent effects on coupling reactions, may be highly important for the selection of appropriate carbohydrate protecting groups.

Results and discussion

Koenigs and Knorr have described the use of insoluble silver salts (i.e. Ag_2O and Ag_2CO_3) as promotors for the synthesis of β-glycosides starting from a 2,3,4,6-tetra-O-acetyl-α-D-glycopyranosyl halide and an alcohol.[11]

The drawback of the insoluble silver reagents Ag_2O and Ag_2CO_3 turned out to be the formation of water during the reaction, leading to hydrolysis of the starting materials.

Although some carbohydrate chemists tried to overcome this problem by performing the reaction in the presence of a drying agent (e.g. Drierite), the attention was turned to the use of soluble mercury and silver salts.[2,12,13]

Recently, the use of insoluble silver salts has been advocated again for the synthesis of β-glycosidic bonds. However, the insoluble silver salts are now applied mainly for the synthesis of β-D-mannopyranoside and β-L-rhamnopyranoside derivatives, containing non-participating groups at the 2-O position of the glycon.[4-10]

The mechanism we propose for this reaction is outlined in Fig.1. It can be seen that an α-D-mannopyranosyl bromide and an aglycon XOH react with each other in the presence of an insoluble promotor.

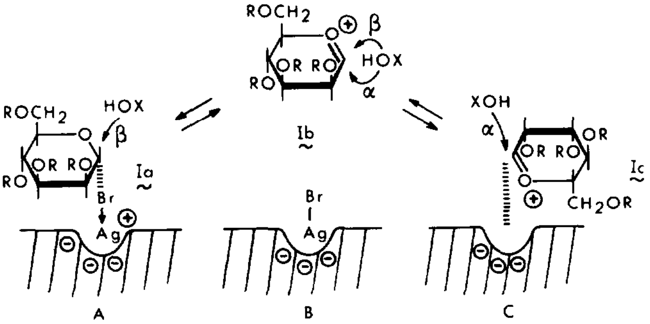
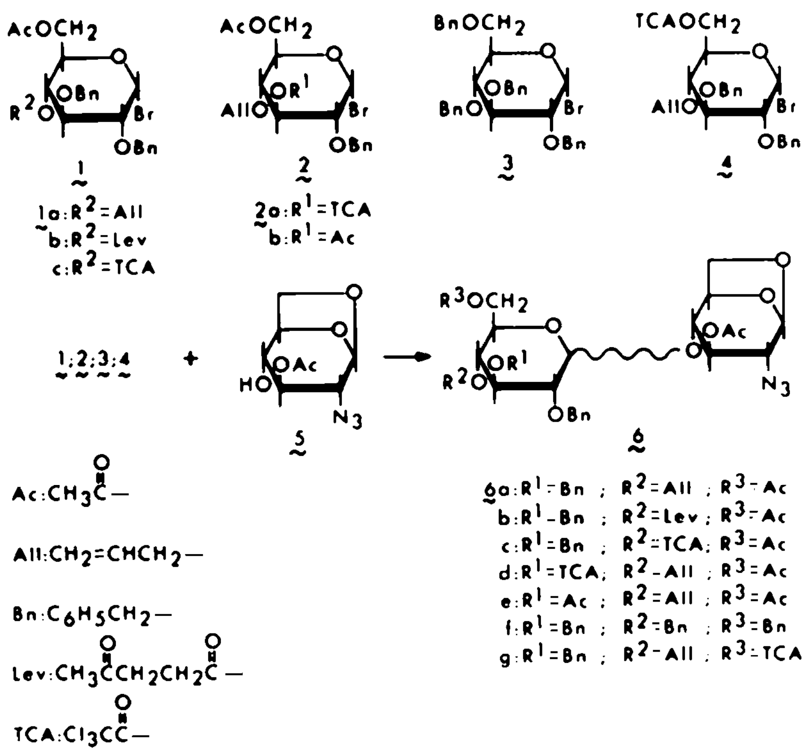


FIGURE 1



1a: R^2=All
b: R^2=Lev
c: R^2=TCA

2a: R^1=TCA
b: R^1=Ac

1;2;3;4 + 5 → 6

6a: R^1=Bn ; R^2=All ; R^3=Ac
b: R^1=Bn ; R^2=Lev ; R^3=Ac
c: R^1=Bn ; R^2=TCA ; R^3=Ac
d: R^1=TCA ; R^2=All ; R^3=Ac
e: R^1=Ac ; R^2=All ; R^3=Ac
f: R^1=Bn ; R^2=Bn ; R^3=Bn
g: R^1=Bn ; R^2=All ; R^3=TCA

Ac: $CH_3C(=O)-$
All: $CH_2=CHCH_2-$
Bn: $C_6H_5CH_2-$
Lev: $CH_3C(=O)CH_2CH_2C(=O)-$
TCA: $Cl_3CC(=O)-$

FIGURE 2

In Fig. 1A it is shown that a surface- bound α-D-mannopyranosyl bromide (i.e. Ia) is replaced by the hydroxyl function of an aglycon (XOH) in an S_N2-reaction, leading to inversion of configuration so that the required β-glycosidic linkage is obtained. Analogously, it should be possible to introduce a β-glycosidic linkage in the gluco- and galactopyranosyl series without the assistance of an acyl substituent at the 2-O position.[1]

In this reaction the undesired α-linkage can only be formed via a glycosyloxocarbonium ion (i.e. Ib in Fig.1B), which originates after dissociation of the β-intimate ion-pair Ia. Because the attack of the aglycon XOH on the highly reactive glycosyloxocarbonium ion Ib does not proceed stereoselectively, a mixture of α and β glycosides results.

Alternatively, the oxocarbonium ion Ib may combine again with the negatively charged surface to give α or β intimate ion-pairs (i.e. Ia and Ic respectively). Reaction of the β-intimate ion-pair Ic with the aglycon XOH gives also the undesired α-glycosidic linkage. Thus, in order to minimize the formation of the α-glycosidic linkage, the formation of the free glycosyloxocarbonium ion Ib has to be suppressed. Consequently, the reactions should be performed in apolar solvents such as dichloromethane or toluene.

Furthermore, reactions with reactive hydroxyl groups as well as application of an excess of the aglycon should facilitate the formation of the β-glycosidic linkage considerably. Other factors that influence this reaction are the temperature, the type of insoluble silver salt and the protective groups at the glycon.

Recently, new insoluble silver salts have been introduced for the coupling reactions mentioned above. Paulsen et al. developed highly reactive silver silicate immobilized on alumina or silica,[7-10] and Garegg et al. recommended the application of silver zeolite for the synthesis of β-D-manno- and β-L-rhamnoglycosidic derivatives.

Paulsen et al.[1,7,8,9,10] also discussed the influence of glycon protecting groups, and stated that protective groups should be selected that afford an α-glycopyranosyl halide of the highest possible reactivity. This means that allyl and benzyl groups are preferred over desactivating acyl protective groups. In agreement with this, coupling reactions of 3-O-allyl-or benzyl protected α-D-mannopyranosylbromide derivatives, with an aglycon in the presence of silversilicate afford disaccharides with a higher β/α ratio than obtained by coupling of the corresponding 3-O-acetyl protected glycons.[10]

However, in the course of a study directed at the synthesis of $\beta 1 \rightarrow 4$ glycosidic bonds we were confronted with unexpected results, which indicated that the influence of carbohydrate protecting groups on coupling reactions is more complex than stated by Paulsen et al.

For instance, when the 4-O-levulinoyl derivative 1b (see Fig.2) was reacted with aglycon 5 in the presence of silver zeolite, disaccharide 6b was obtained with a β/α ratio of 2.0/1 (Table 1, entry 3), whereas a similar coupling with the corresponding 4-O-allyl derivative 1a afforded disaccharide 6a with a low β/α ratio of 1/2.2 (Table, entry 1).

Thus, contrary to expectations, a desactivating protective group (i.e. 4-O-levulinoyl) instead of an activating protective group (i.e. 4-O-allyl) facilitates the formation of the β-glycosidic linkage.

In principle this phenomenon might be explained by participation of the remote 4-O-levulinoyl group as depicted in Figure 3. If this explanation is correct coupling of a corresponding glycon, containing a poor participating and strongly electron-withdrawing group (e.g. trichloroacetyl [14]) at the 4-O position (i.e. compound 1c), is expected to give more α-glycosidic linked product than coupling of the 4-O-allyl protected glycon 1a. However, reaction of the 4-O-trichloroacetyl protected glucopyranosyl bromide 1c with aglycon 5 in the presence of silver silicate on silica (Table 1, entry 4) gave an anomeric mixture of disaccharide 6c with an unexpected high β/α ratio again (β/α=1.5/1). Therefore, it is unlikely that the increased β/α ratio has to be ascribed to participation of a 4-O-acyl function.

At this point it should be noted that the latter reaction was performed with silver silicate as promotor instead of less reactive silver zeolite, since the trichloroacetyl group desactivates glycopyranosyl bromide 1c considerably. That the unexpectedly high β/α ratio can not to be attributed to the use of silver silicate was confirmed by the silver silicate promoted reaction of 1a with 5, which gave a similar unfavourable β/α ratio of 1/2.0 (Table 1, entry 2).

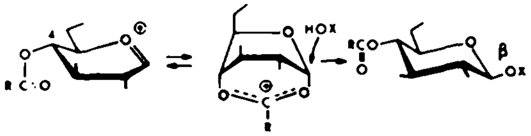


FIGURE 3

Having established that, in the case of 4-O-acyl protection , the enhancement of β-glycosidic bond formation, can hardly be ascribed to participation of the acyl group, we turned our attention to 3-O-acyl-protected derivatives.

In order to avoid a possible participation, it was decided first to investigate a coupling reaction with the 3-O-trichloroacetyl protected glycon 2a (see Fig.2). The coupling of compound 2a with aglycon 5 was performed with silver silicate as activating agent (Table 1, entry 5) to afford disaccharide 6d as an anomeric mixture with a β/α ratio of 1/9. Coupling of the 3-O-acetyl protected derivative 2b with 5 gave disaccharide 6e with an equally unfavourable β/α ratio of 1/9 (Table 1, entry 6).

These examples clearly demonstrate the great difference in stereochemical outcome if an electron withdrawing group is placed at either the 3-O function (Table 1, entries 5 and 6) or the 4-O function (Table 1, entries 3 and 4).

As mentioned already, it was found that a 3-O-acetyl substituent at a mannopyranosyl bromide has a deleterious effect on the β-coupling reaction. Thus, coupling of the 3-O-acetyl protected α-D-mannopyranosylbromide derivative 7a with aglycon 10 (see Fig.4) resulted into the formation of disaccharide 11a with a β/α ratio of 1/1 (Table 1, entry 9). On the other hand, a similar reaction performed with the 3-O-benzyl protected α-D-mannopyranosyl bromide derivative 7b provided disaccharide 11b with a β/α ratio of 6/1 (Table 1, entry 10).

In view of our observations in the gluco-series it was expected that a coupling of aglycon 10 with the 4-O-acetyl-α-D-mannopyranosyl bromide derivative 8a would give more of the β-coupled product than by using 3-O-acetylated derivative 7a (see Fig.4). In agreement with this expectation, the reaction of compound 8a with aglycon 10, performed under the conditions described by Paulsen,[10] yielded disaccharide 11c with a high β/α ratio of 9/1 (Table 1, entry 12).

Table 1

entry	glycon	aglycon	product	β/α ratio	yield[a)]	reaction conditions
1:	1a	5	6a	1/2.2	59%	silver zeolite ; r.t. ; 3 days
2:	1a	5	6a	1/2	64%	silver silicate ; -40° ; 3 hrs
3:	1b	5	6b	2/1	46%	silver zeolite ; r.t. ; 3 days
4:	1c	5	6c	1.5/1	40%	silver silicate ; 0°-r.t. ; 16 hrs
5:	2a	5	6d	1/9	68%	silver silicate ; 0°-r.t. ; 16 hrs
6:	2b	5	6e	1/9	68%	silver silicate ; 0°-r.t. ; 16 hrs
7:	3	5	6f	2.8/1	50%	silver zeolite ; -78°-r.t. ; 3 days
8:	4	5	6g	1/3.6	56%	silver zeolite ; r.t. ; 2 days
9:	7a	10	11a	1/1[b)]	80%[b)]	silver silicate ; r.t. ; 3.5 hrs
10:	7b	10	11b	6/1[b)]	76%[b)]	silver silicate ; r.t. ; 3 hrs
11:	7c	10	11d	1/1.2	40%	silver silicate ; r.t. ; 16 hrs
12:	8a	10	11c	9/1	45%	silver silicate ; r.t. ; 16 hrs
13:	8b	10	11e	>10/1	20%	silver silicate ; r.t. ; 16 hrs
14:	9	5	12	5.1/1	67%	silver silicate ; -50°-r.t ; 7 hrs

a) Yield based on glycon b) See reference 10

Furthermore, coupling of the 3-O and 4-O trichloroacetyl protected α-D-mannopyranosyl bromides 7c and 8b respectively, with aglycon 10 gave results similar to the coupling reactions of the corresponding acetylated derivatives mentioned above (Table 1, entries 11 and 13 respectively). Therefore, it can be concluded that, both in the gluco- and the mannopyranosyl series, a 4-O-acyl function increases the β/α ratio, whereas a 3-O-acyl substituent decreases this ratio.

Apart from this discovery we met another remarkable phenomenon when comparing coupling reactions in the mannose series with the glucose series.

Thus, it was found that coupling of α-D-glucopyranosyl bromide derivative 1a with 5 in the presence of silver silicate was achieved with a β/α ratio of 1/2, (Table 1, entry 2) whereas a similar coupling performed with the mannose analogue 9 resulted into the formation of disaccharide 12 (see Fig.4) with a β/α ratio of 5.1/1 (Table 1, entry 14). It is most unusual that a coupling reaction of a mannopyranosyl bromide derivative proceeds with a higher β/α ratio than a similar coupling with the corresponding glucopyranosyl derivative, because it is generally accepted that the

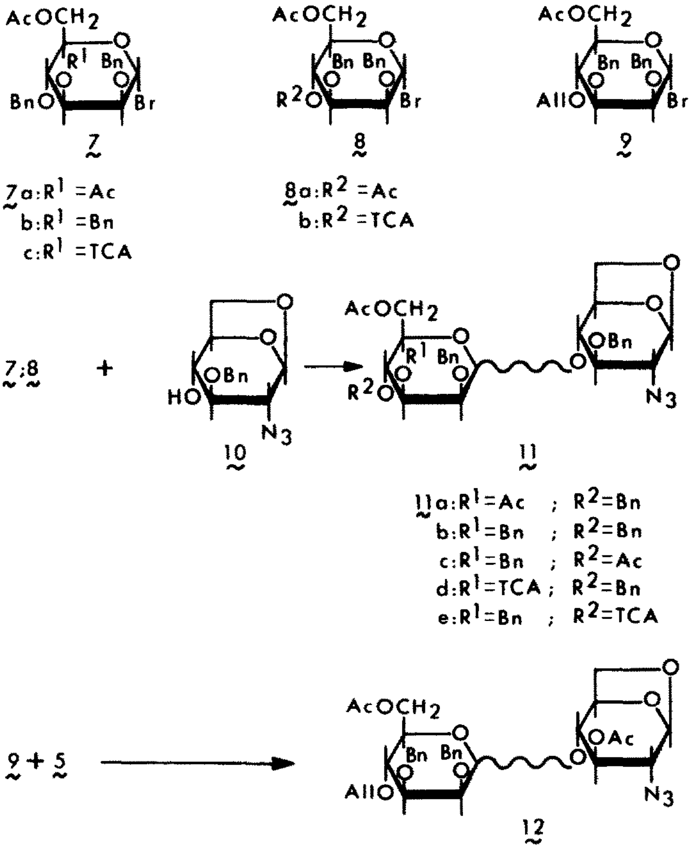


FIGURE 4

axial C-2 substituent of mannose facilitates the formation of the α-glycosidic linkage.[1,15,16] Apparently, in the presence of an insoluble promotor an S_N2 reaction such as outlined in Fig. 1A is more favoured for fully protected mannopyranosyl bromide derivatives than for their glucopyranosyl analogues.

It remains to be investigated where this phenomenon should be attributed to.[17] Possibly, in a apolar solvent the hydroxyl function of the aglycon can become hydrogen bonded to the axial oxygen atom at C-2 of mannose and in this way the β-attack is facilitated. In addition, the presence of an axial C-2 substituent at a mannopyranosyl derivative leads to flattening of the pyranose ring, which in turn lowers the S_N2 transition state.

However, it should be emphasized that the latter argument does not hold completely, because flattening of the pyranose ring should also facilitate the formation of the free glycosyloxocarbonium ion <u>Ib</u> (Fig.1B).[15,16]

Finally, we were anxious to find out the influence of 6-O-protecting groups on coupling reactions performed with insoluble promotors. In order to establish the effect of 6-O-alkyl substituents 2,3,4,6-tetra-O-benzyl α-D-glucopyranosyl bromide <u>3</u> was coupled with <u>5</u> in the presence of silver zeolite. This reaction leads to the formation of disaccharide <u>6f</u> with a β/α ratio of 2.8/1 (Table 1, entry 7), which is substantially higher than found for the corresponding coupling reaction of the 6-O-acetyl derivative <u>1a</u> with <u>5</u> (β/α = 1/2.2). In the latter coupling reaction, participation of the 6-O-acetyl group in principle may account for the adverse β/α ratio. However, in this reaction also participation of a 6-O-acetyl function is very unlikely, because coupling of the 6-O-trichloroacetyl derivative <u>4</u> with aglycon <u>5</u> leads to the formation of <u>6g</u>, with an unfavourable β/α ratio again (see Table 1, entry 8, β/α = 1/3.6).

If we compare the stereochemical outcome of the coupling reactions (see Table 1), it may be concluded that electron withdrawing groups, at the 3-O and 6-O positions of both mannose-and glucopyranosyl bromide derivatives, adversely affect the formation of the β-glycosidic linkage, whereas such substituents at the 4-O position facilitate the formation of the β-glycosidic bond.

In our opinion, these differences can not be ascribed to participation or to inductive effects only.

Taking into consideration inductive effects we refer to studies of Paulsen et al.[18], in which was shown that S_N2 reactions at 2-azido-2-deoxy-α-D-glucopyranosyl bromide derivatives are retarded by acetyl substituents.

Consequently, it should be expected[1] that acetyl and trichloroacetyl substituents, at the 3-O, 4-O or 6-O positions of gluco-and mannopyranosyl bromide derivatives, hinder the formation of the β-glycosidic bond, since this bond is formed <u>via</u> an S_N2 reaction. However, in this paper we have demonstrated that acyl groups at 4-O facilitate the formation of the β-glycosidic bond. Apparently, an electron-withdrawing substituent at 4-O suppresses the formation of a glycosyloxocarbonium ion (formation of <u>Ib</u> and <u>Ic</u> in Fig.1) more than it does the S_N2 reaction, whereas the opposite is the case for electron-withdrawing substituents at the 3-O and 6-O positions, in accordance with the predictions of Paulsen.

Moreover, it is surprisingly that the effects exerted by 4-O and 6-O substituents are reversed, since the substituents are separated by the same number of single bonds from the anomeric centre and inductive effects are supposed to be similar.

In order to explain the contradicting effects brought about by substituents at 3-O, 4-O and 6-O, we propose that through-bond interactions[19-23] should also be taken into account.[24]

In carbohydrate chemistry the interactions of oxygen lone pair orbitals have been discussed particularly in connection with the anomeric effect.[25] Recently, Box discussed the importance of lone pair interactions in the chemistry of monosaccharides.[26,27] In these publications it has been assumed that lone pairs interact through space and are therefore mostly pronounced when they are close together.

However, it has been recently shown that distant orbitals may also be coupled through-bonds via σ orbitals of the same symmetry.[19-23] It has been predicted that such interactions most readily apply to molecules having isolated or lone pair (n) orbitals, which couple with each other through trans arrangements of bonds.

Taking into account that through-bond interactions will be significant only when a succession of "trans bridges" is available, it can be deduced that lone pairs of the 3-O oxygen of a gluco- or mannopyranosyl derivative can neither be coupled with the ring oxygen lone pairs, nor with the $-C=O^{+}-$ π bond of the intermediate oxocarbonium ion Ib. Therefore we assume that the influence of 3-O-electron-withdrawing substituents on coupling reactions will be attributed mainly to inductive effects, which hinder the S_N2 reaction more than the formation of Ib and Ic.

On the other hand, a lone pair of the oxygen atom at C-4 (i.e. n_a in Fig.5) can be coupled with the equatorial lone pair (i.e. n_1 in Fig.5) of the ring oxygen, but not with the $-C=O^{+}-$ π bond of Ib.

While the ring oxygen lone pairs n_1 and n_2 can be described in terms of a pair of canonical orbitals with p and sp symmetry, the remote 4-O substituent also interacts through-bond with the p(O) orbital of the ring oxygen, which stabilizes the anomeric carbonium ion carbon of Ib. Taking into account this through-bond interaction, it may be understood that a distant electron-withdrawing substituent at 4-O suppresses the formation of glycosyloxocarbonium ion Ib stronger than expected on the basis of inductive effects only.

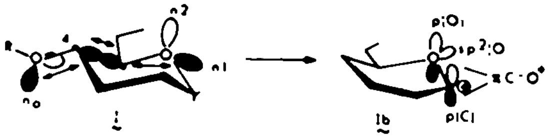


FIGURE 5

Alternatively, the effect of the 4-O substituent may also be explained by through-bond interactions via "ribbon orbitals", which have been proposed for six-membered rings.[28] For instance Zefirov[29] used frontier orbital interactions of "ribbon orbitals" to explain that equatorially[30] positioned electron-withdrawing groups at C-4 of cyclohexane hinder the generation of a positive charge at C-1 considerably. According to both explanations, electron-withdrawing groups at 4-O strongly suppress the formation of the glycosyloxocarbonium ion Ib. Therefore the β-coupled product will be formed predominantly.

Although the β/α ratio is effected similarly by 3-O and 6-O-substituents, the cause is probably different. As described earlier no through-bond interactions are possible between the 3-O function and the anomeric region. However, 6-O lone pairs may interact through-bond. The through-bond interaction is depicted in Fig. 6A, in which it can be seen that the lone pair n_a, borne by the oxygen atom at C-6, interacts through-bond with the $-C=O^{+}-$π bond of intermediate Ib, but not with the equatorial lone pair of the ring oxygen. The energy level of the 6-O lone pair n_a is lowered by electron-withdrawing groups (R) to give energy level n_a-w and raised by electron donating groups (R) to give energy level n_a-d (see fig.6B). The interaction of n_a-w and n_a-d with the $-C=O^{+}-$π orbital is shown by a molecular-orbital diagram.

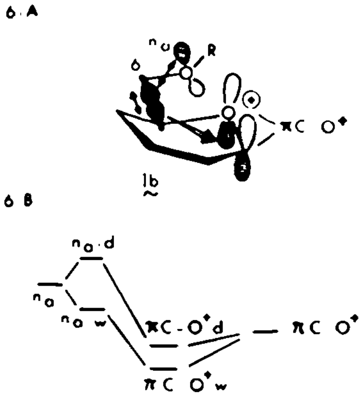


FIGURE 6

It can be seen that the $-C = O^+-\pi$ orbital will be stabilized more by a 6-O electron-withdrawing group. If through-bond interactions outweigh inductive effects, it will be found that 6-O-acyl protected glycosylcarbonium ions are more stabilized than their corresponding 6-O-alkyl derivatives. The consequence is that 6-O-acyl functions decrease the β/α ratio of the coupling product. The curious phenomenon that 6-O-acyl-substituents stabilize the glycosyloxocarbonium ion (in contrast with 3-O-acyl substituted derivatives) finds support in the observation of Schuerch et al.,[31] who performed kinetic measurements on carbohydrates.

They established that the solvolysis of 1-O-tosyl-2,3,4-tri-O-benzyl-6-O-(N-phenylcarbamoyl)-D-glucopyranoside proceeds faster than the solvolysis of the corresponding 6-O-benzyl protected derivative.

In conclusion, the stereochemical outcome of coupling reactions promoted by insoluble silver salts, is strongly dependent on the type of protective group that is used and its place of substitution at the glycon. Thus, with respect to O-alkyl protected derivatives, 4-O-acyl functions increase the β/α ratio, whereas 3-O and 6-O acyl functions decrease this ratio. It remains to be investigated whether this influence is similar for other carbohydrate coupling reactions performed with other solvents and different promotors.

Experimental Part.

'Methods and Materials'

Silver zeolite and silver silicate on silica were prepared as described in references 6, 7, and 10 respectively. Toluene was distilled from P_2O_5 and stored over sodium wire.

Molecular sieves 4A were activated under reduced pressure (50 mm Hg) at 200°C. TLC analysis was performed on Merck-Fertigplatten (Kieselgel 60, F254, 5 x 10 cm). The solvent system used was dichloromethane/acetone (95/5, v/v).

Compounds were visualized by spraying with sulphuric acid/ethanol (1/9, v/v) and charring at 140°C for a few minutes. Column-chromatography was performed on Merck Lobar Fertigsäulen B(310-25), Lichroprep Si60 (40-63 um).

^{1}H-NMR and ^{13}C-NMR spectra were measured with a Bruker WM-360 spectrometer, equipped with an ASPECT 3000 computer, operating in the Fourier transform mode. Chemical shifts are given in ppm (δ) relative to TMS as internal reference.

The α-D-glycopyranosyl bromide derivatives 1 a, c; 2 a, b; 7 a, b, c; 8 a, b and 9 were prepared by $TiBr_4$ treatment[32] of the corresponding 1-O-acetyl derivatives.[33]

The α-D-glucopyranosyl bromide derivatives 1b and 3 were prepared by reaction of the corresponding 1-hydroxy derivatives with oxalyl bromide in dichloromethane/N,N-dimethylformamide [34] (20/1, v/v).

In a typical reaction, the aglycon 5 [35] or 10 [32] (0.8 mmole) was dissolved in dry toluene (1.5 ml). Silver zeolite (1.2 gr.) or silver silicate on silica (700 mg) as well as activated molecular sieves 4A (300 mg) were added to this solution.

The mixture was stirred under nitrogen for one hour at the appropriate temperature (see Table 1) and then the α-D-glucopyranosyl bromide derivative, dissolved in dry toluene (1 ml), was added dropwise. When TLC analysis (dichloromethane/acetone: 95/5, v/v) revealed that the reaction was complete (see Table 1), the reaction mixture was

	^{13}C - resonance (δ)				^{1}H - resonance (δ)				Rf$^{a)}$	
disaccharide	$C_1(\alpha)$	$C'_1(\alpha)$	$C_1(\beta)$	$C'_1(\beta)$	$H_1(\alpha)$	$H_1'(\alpha)$	$H_1(\beta)$	$H_1'(\beta)$	α	β
6 a	100.5	98.7	100.4	103.8	5.59	5.05$^{e)}$	5.49	4.59$^{g)}$	0.41	0.31
6 b	100.4	99.1	100.3	103.6	5.59	-	5.49	4.54$^{g)}$	0.17	0.10
6 c	100.5	99.0	100.3	104.0	5.58	5.05$^{e)}$	5.48	4.72$^{g)}$	0.53	0.47
6 d	100.3	98.3	100.1	103.5	5.55	4.98$^{e)}$	5.49	4.69$^{g)}$	0.45	0.37
6 e	100.2	98.1	100.1	103.7	5.53	5.05$^{e)}$	5.49	4.65$^{g)}$	0.17	0.11
6 f	100.4	98.6	100.1	103.5	5.55	5.08$^{e)}$	5.49	4.58$^{g)}$	0.60	0.50
6 g	100.3	98.2	100.2	103.6	5.56	5.04	5.48	4.65$^{g)}$	0.66	0.56
11 a$^{b)}$	-	-	-	-	5.48	4.83$^{f)}$	5	4.80$^{g)}$	-	-
11 b$^{b)}$	-	-	100.5	98.9$^{c)}$	-	-	5.41	4.72	0.57	0.51
11 c	100.8	99.3$^{c)}$	100.7	98.7$^{d)}$	5.55	4.81$^{f)}$	5.51	4.70	0.45	0.37
11 d	100.7	98.8$^{c)}$	100.4	98.4$^{d)}$	5.51	4.80$^{f)}$	5.49	-	0.65	0.61
11 e	-	-	100.7	98.6$^{d)}$	5.55	4.79$^{f)}$	5.53	4.76	0.64	0.60
12	100.3	98.5$^{c)}$	100.1	98.4$^{d)}$	5.52	4.79$^{f)}$	5.47	4.69	0.38	0.31

a: dichloromethane/acetone : 95/5, v/v. b: see reference 10. c: $^{1}J_{C-H}$ = 170 - 172 Hz. d: $^{1}J_{C-H}$ = 155 Hz. e: $^{3}J_{H_1-H_2}$ = 3.5 - 3.8 Hz. f: $^{3}J_{H_1-H_2}$ = 2.2 Hz. g: $^{3}J_{H_1-H_2}$ = 7.6 - 7.9 Hz.

Table 2.

diluted with dichloromethane (25 ml) and then filtered through Celite to remove the insoluble promotor. The filtrate was evaporated under reduced pressure and the residue was applied to a column of silicagel suspended in dichloromethane. Elution with dichloromethane/acetone (99:1--->97:3, v/v) and evaporation of the appropriate fractions gave the desired β and α disaccharides. The identity of all disaccharides (β&α) was established by ^{1}H-NMR and ^{13}C-NMR spectroscopy. Some characteristic resonances are presented in Table 2.

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