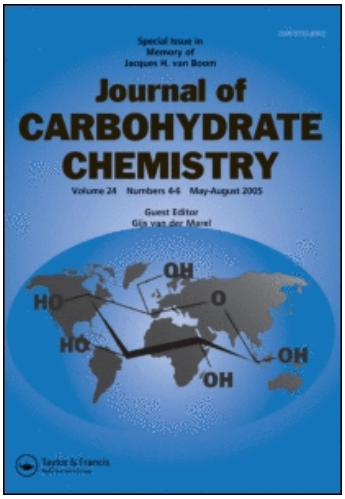

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The Allyl Group for Protection in Carbohydrate Chemistry. 13. The N-Allylbenzylamino Group for Protection in the Amino-Sugar Series

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Communication

THE ALLYL GROUP FOR PROTECTION IN CARBOHYDRATE CHEMISTRY, PART 13.[1] THE N-ALLYLBENZYLAMINO GROUP FOR PROTECTION IN THE AMINO-SUGAR SERIES.

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Derivatives of 2-benzamido-2-deoxy-D-glucose can be converted[2] in good yield, into the 2-N-allylbenzylamino derivatives *via* the 2-N-allylbenzamido derivatives. The N-allylbenzylamino group is a protected amino function which can be readily converted[2] into the benzylamino and acylamino functions and we now show other uses for this protecting group in the chemistry of the amino-sugars.

Hydrolysis of the benzylidene group from the benzylidene derivatives 1[2] and 2[2] gave the diols 3 and 13 and isomerisation of the allyl groups in these compounds with potassium *t*-butoxide in dimethyl sulphoxide gave the N-(prop-1-enyl) benzylamino derivatives 4 and 18 which hydrolysed spontaneously[2] in air to give the benzylamino derivatives 5 {m.p. 116-118°, $\{\alpha\}_D^{28}$ -20°(*c*1,$CHCl_3$)} and 19 {m.p. 103-105°, $\{\alpha\}_D^{26}$ -3°(*c*1,$CHCl_3$)}. Benzylation of the diols 3 and 13 with benzyl bromide and sodium hydride in N,N-dimethylformamide

at 20° gave the fully benzylated derivatives 6 and 14 without problems of quaternisation of the amino function. Isomerisation of the allyl groups in 6 and 14, as above, gave the prop-1-enyl derivatives 7 and 20 from which the N-(prop-1-enyl) groups hydrolysed spontaneously in the air to give the benzylamino derivatives 8 {m.p. 72-74°, $\{\alpha\}_D^{28}$-6° (*c*1,$CHCl_3$)} and 21 {m.p. 66-68°, $\{\alpha\}_D^{25}$+13° (*c*1,$CHCl_3$)}.

Tritylation of the diols 3 and 13 gave the trityl ethers 9 and 15 which were benzylated, as above, to give 10 and 16. Acidic hydrolysis of the trityl groups from 10 and 16 gave the alcohols 11 and 17 and isomerisation of the allyl groups in these, as above, and subsequent spontaneous hydrolysis of the N-(prop-1-enyl) groups gave the benzylamino derivatives 12 {m.p. 113-115°, $\{\alpha\}_D^{26}$-13° (*c*1, $CHCl_3$)} and 22 {m.p. 127-129°, $\{\alpha\}_D^{26}$-2° (*c*1,$CHCl_3$)}.

Thus the N-allylbenzylamino group is a suitable form of protection for the amino function to allow vigorous O-alkylation conditions to be used. O-Alkylation of amino-sugars in the form of the acylamino derivatives must be carried out under selective conditions[3] to prevent N- or O- alkylation of the amido-group. The N-benzylacetamido group which is readily available from the benzylamino derivatives is also[2] a suitably protected form of the acetamido group for O-alkylation under the above vigorous conditions.

The hydrogenolysis of 4,6-O-benzylidene groups of carbohydrates with lithium aluminium hydride-aluminium chloride has been successfully developed[4] for the synthesis of the corresponding monobenzylated diols but we are aware of only one example where this reaction has been applied to amino-sugars. 4,6-O-Benzylidene derivatives of 2-(benzyloxycarbonyl)amino-2-deoxy-D-glucose and galactose were hydrogenolysed[5] under these conditions to give the monobenzylated diols in moderate yields. There was no indication of attack on the (benzyloxycarbonyl)amino group although lithium aluminium hydride is known[6] to convert this function into the methylamino group.

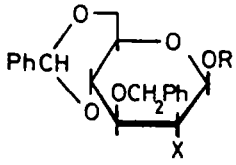
Compounds 1 and 2 are stable to lithium aluminium hydride at 20° as used in their preparation,[2] but since a previous report[7] had indicated that 2-dialkylaminotetrahydropyrans were ring-opened by lithium aluminium hydride, compound 2 was treated with lithium aluminium hydride in tetrahydrofuran under reflux for 2h. but no reaction was observed. The reaction of the benzylidene derivatives 1 and 2 with lithium aluminium hydride-aluminium chloride was therefore investigated.

With an excess of the reagent there was a rapid reaction at 20° to give two major products in approximately equal proportions. The less polar products were shown to be the 4-O-benzyl derivatives 11 and 17 since on isomerisation of the allyl groups, as above, and subsequent spontaneous hydrolysis of the N-(prop-1-enyl) groups, the crystalline benzylamino derivatives 12 and 22, indentical with the materials prepared as described above, were obtained. The more polar products gave O-isopropylidene derivatives in acidified acetone indicating that they were probably the acyclic derivatives 23 and 24. The acyclic structure of compound 23 was confirmed by the experiments reported below.

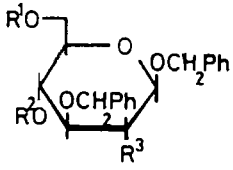
After leaving the reaction mixture of 1 for 4h. most of the 4-O-benzyl derivative 11 was consumed and the major product was the acyclic derivative 23 together with a more polar product which was shown to be the corresponding benzylamino derivative 26, produced by N-deallylation of 23 by the reagents.

Ring-opening reactions during hydrogenolysis with lithium aluminium hydride-aluminium chloride are unusual in the carbohydrate series and have only recently been reported[8] to occur with 3,5-O-benzylidene derivatives of methyl D-xylofuranosides to give 5-O-benzyl-1-O-methyl-xylitol derivatives, although the hydrogenolysis of 2-alkoxytetrahydrofurans and pyrans under these conditions resulted in ring cleavage.[9]

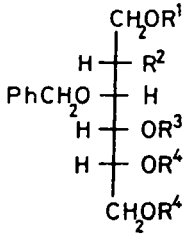
We have recently reported[10] a ring-opening reaction of 4,6-O-benzylidene derivatives of O-protected glycosides of 2-benzamido-2-deoxy-D-glucose under the action of trimethylsilyl chloride-



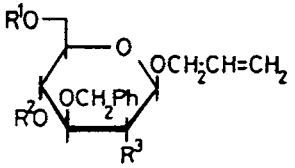
(1) R = CH_2Ph
(2) R = $CH_2CH{=}CH_2$



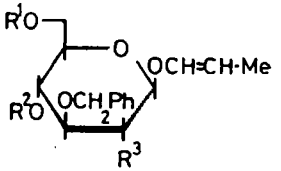
(3) $R^1 = R^2 = H$; $R^3 = X$
(4) $R^1 = R^2 = H$; $R^3 = Y$
(5) $R^1 = R^2 = H$; $R^3 = NHCH_2Ph$
(6) $R^1 = R^2 = CH_2Ph$; $R^3 = X$
(7) $R^1 = R^2 = CH_2Ph$; $R^3 = Y$
(8) $R^1 = R^2 = CH_2Ph$; $R^3 = NHCH_2Ph$
(9) $R^1 = CPh_3$; $R^2 = H$; $R^3 = X$
(10) $R^1 = CPh_3$; $R^2 = CH_2Ph$; $R^3 = X$
(11) $R^1 = H$; $R^2 = CH_2Ph$; $R^3 = X$
(12) $R^1 = H$; $R^2 = CH_2Ph$; $R^3 = NHCH_2Ph$



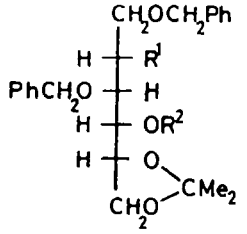
(23) $R^1 = R^3 = CH_2Ph$; $R^2 = X$; $R^4 = H$
(24) $R^1 = CH_2CH{=}CH_2$; $R^2 = X$; $R^3 = CH_2Ph$; $R^4 = H$
(25) $R^1 = R^3 = CH_2Ph$; $R^2 = N(CH_2Ph)Ac$; $R^4 = Ac$
(26) $R^1 = R^3 = CH_2Ph$; $R^2 = NHCH_2Ph$; $R^4 = H$



(13) $R^1 = R^2 = H$; $R^3 = X$
(14) $R^1 = R^2 = CH_2Ph$; $R^3 = X$
(15) $R^1 = CPh_3$; $R^2 = H$; $R^3 = X$
(16) $R^1 = CPh_3$; $R^2 = CH_2Ph$; $R^3 = X$
(17) $R^1 = H$; $R^2 = CH_2Ph$; $R^3 = X$



(18) $R^1 = R^2 = H$; $R^3 = Y$
(19) $R^1 = R^2 = H$; $R^3 = NHCH_2Ph$
(20) $R^1 = R^2 = CH_2Ph$; $R^3 = Y$
(21) $R^1 = R^2 = CH_2Ph$; $R^3 = NHCH_2Ph$
(22) $R^1 = H$; $R^2 = CH_2Ph$; $R^3 = NHCH_2Ph$



(27) $R^1 = NHCH_2Ph$; $R^2 = H$
(28) $R^1 = N(CH_2Ph)Ac$; $R^2 = CH_2Ph$
(29) $R^1 = X$; $R^2 = CH_2Ph$
(30) $R^1 = NHCH_2Ph$; $R^2 = CH_2Ph$

X = $N(CH_2Ph)CH_2CH{=}CH_2$
Y = $N(CH_2Ph)CH{=}CH\text{-}Me$

sodium hydride and subsequent lithium aluminium hydride reduction which gave 4,6-O-benzylidene-2-benzylamino-2-deoxy-D-glucitol derivatives in high yield. A similar reaction was observed[10] with benzyl 3-O-benzyl-2-benzamido-2-deoxy-5,6-O-isopropylidene-β-D-glucofuranoside under these conditions which gave the isopropylidene derivative 27 which is related to the presumed product 23 obtained above.

Compounds 23 and 27 were shown to be related as follows: N-Acetylation of 27 and subsequent O-benzylation gave 28. Acetonation of 23 gave 29 and removal of the N-allyl group gave 30 which on acetylation also gave 28 {syrup, $\{\alpha\}_D^{25}+10^\circ$ ($c2,CHCl_3$)}. Compound 30 was also converted into 2-amino-2-deoxy-D-glucitol hydrochloride[11] by catalytic hydrogenolysis and subsequent acidic hydrolysis. Deacetonation of compound 28, obtained by both routes, and acetylation gave samples of 25 {syrup, $\{\alpha\}_D^{25}+11^\circ$ ($c2,CHCl_3$)} which were identical by TLC, IR and NMR.

These acyclic derivatives prepared by the route described in this paper and by the route described previously[10] should be useful intermediates for synthetic studies on the sphingosine bases and ceramides by methods described previously.[12]

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