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Preliminary communication

A new reaction of the 1-propenyl glycosides of 2-acetamido-2-deoxy-β-D-glucopyranose· direct conversion into oxazolines*

MINA A NASHED, CHARLES W SLIFE, MAKOTO KISO, and LAURENS ANDERSON†

Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin–Madison Madison Wisconsin 53706 (U S A)

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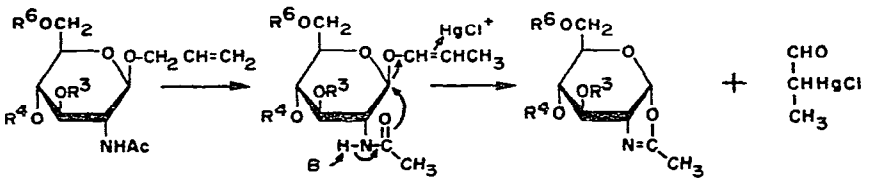
The use of oxazoline derivatives, primarily **3a** and its disaccharide congeners, is a well-established method for introducing 2-acetamido-2-deoxy-β-D-glucopyranosyl ('*N*-acetyl-D-glucosamine") groups into synthetic oligosaccharides[1] However, the method has been little used in sequential syntheses, where partial deprotection of the incorporated amino sugar group and extension of the oligosaccharide chain is involved To bring such syntheses within the scope of the method, it appeared desirable to create oxazolines carrying combinations of temporary and persistent blocking groups, such as the 3,4-di-*O*-acetyl-6-*O*-chloroacetyl analog of **3a** recently described by Matta and Barlow[2], or the *O*-acetyldi-*O*-benzyl analogs **3b** and **3c** We undertook the synthesis of **3b** and **3c**, and the fully benzylated analog **3d**, and in the course of the work developed a facile procedure for closing the oxazoline ring The procedure is presented in this communication



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Bn = benzyl
Ac = acetyl

	R^3	R^4	R^6	
2a	Ac	Ac	Ac	**3a**
2b	Ac	Bn	Bn	**3b**
2c	Bn	Ac	Bn	**3c**
2d	Bn	Bn	Bn	**3d**

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†Please address correspondence to this author

To prepare **3b–d**, the partial or complete benzylation of allyl 2-acetamido-2-deoxy-β-D-glucopyranoside[3] (**1**, R^{3-6} = H) was first effected by appropriate sequences of reactions* The allyl glycosides were then isomerized[4] to the 1-propenyl glycosides, and unsubstituted hydroxyl groups were acetylated. Further elaboration to the oxazolines by previously known chemistry would have required several steps, including hydrolysis of the 1-propenyl glycosides to the free sugars, and the conversion of these into the glycosyl chlorides[5], or the β-glycosyl acetates[6] In the hope of shortening the procedure, we considered the possibility of a direct, mercuric ion-catalyzed cyclization by the mechanism shown in the formula chart

Experimental test showed that all of the 1-propenyl glycosides **2a–d** are efficiently transformed into oxazolines by treatment with mercuric chloride and mercuric oxide in acetonitrile Thus, a mixture of 1-propenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**2a**, 0 25 g, 0 65 mmol), mercuric chloride (0 25 g, 0 92 mmol), and mercuric oxide (0 25 g, 1 15 mmol) in dry acetonitrile (5 ml) was stirred and heated for 1 h under reflux, with exclusion of atmospheric moisture The mixture was then filtered through Celite, the filter cake was washed with a little acetonitrile, and the combined filtrates were evaporated under diminished pressure The syrupy residue was taken up in dichloromethane, the solution was washed twice with saturated aqueous potassium iodide and twice with water, and dried Evaporation of the dichloromethane gave a product having the spectral and chemical properties recorded[7] for the known 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano) [2′,1′ 4,5]-2-oxazoline (**3a**), it was chromatographically identical with an authentic sample The p m r spectrum ($CDCl_3$) of **3a**, which is completely resolved at 270 MHz, indicates a marked deviation from the $^4C_1$ (D) conformation of the parent glycoside Particularly diagnostic for the oxazoline structure are the chemical shift (δ 5 97) and coupling constant ($J_{1,2}$ 7 4 Hz) of the anomeric proton, and the signal for the protons of the 2-methyl group at δ 2 09 The latter gives a doublet as a result of long-range coupling (J 1 8 Hz) to H-2 of the sugar

The *O*-benzylated oxazolines **3b–d** were prepared by the procedure just described, except that the duration and temperature of the reaction were changed for **3c** and **3d** Details are given in Table I In all cases, equal weights of 1-propenyl glycoside, mercuric chloride, and mercuric oxide were used The effect, on the reaction rates, of varying the proportions of mercury salts has not yet been tested According to t l c analysis, the conversions were essentially quantitative, and thus the lowering to 80–90% of the yields of purified oxazolines must arise from losses during isolation

The characterization of the products as oxazolines rests not only on the p m r data given in Table I, but also on the resistance of the compounds to hydrolysis by mercuric chloride in aqueous acetone (distinction from 1-propenyl glycosides), and on their i r spectra recorded in chloroform or dichloromethane We found the most useful i r-spectroscopic indicator of oxazoline formation to be the disappearance of the bands for N-H at 1510 and 3420 cm^{-1} shown by the acetamido group of the precursors Pure samples, as judged by t l c , of all oxazolines could be obtained by chromatography on columns of

*The details will be given in full papers describing this work

TABLE I

OXAZOLINES FROM 1-PROPENYL GLYCOSIDES

Compound no	*Reaction time (h)*	*Reaction temp (°)*	*Isolated yield (%)*	$[\alpha]_D^{25}$ *(CHCl₃)* *(°)*	*δ, H-1* [a] *(p p m.)*	*δ, CH₃ of oxazoline* [a] *(p p m.)*
3a	1	~80	83	+7 2	5 97	2 09
3b	1	~80	89	+52 3	5 99	2 06
3c	5	40–50	86	+17 1	6 01	2 05
3d	0 5	~25	79	+29 7	6 01	2 03

[a] P m r spectra in $CDCl_3$ $J_{1,2}$ ranged from 7 35 to 7 4 Hz, J_{2,CH_3} from 1 5 to 1 8 Hz

silica gel Compound **3c** purified in this way gave a correct elemental analysis, but for **3b** and **3d**, the values for carbon were low, perhaps as a result of partial hydrolysis during transit to the analytical laboratory

In support of a concerted mechanism for the 1-propenyl glycoside → oxazoline transformation, we found that the α anomers of **2a** and **2d** fail to give oxazolines when heated with mercuric chloride and mercuric oxide in dry acetonitrile

The simplicity and high yield of the mercuric ion-catalyzed cyclization reported here make it an attractive method for the preparation of substituted oxazolines of 2-acetamido-2-deoxyglucopyranose whenever the requisite 1-propenyl β-glycosides are available It seems likely that the method will be applicable to a variety of other 1-propenyl 2-acylamido-2-deoxyglycosides having a 1,2-*trans* configuration

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