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Preliminary communication

The ferric chloride-catalyzed glycosylation of alcohols by 2-acylamido-2-deoxy-β-D-glucopyranose 1-acetates

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Interest in glycosylating agents related to 2-acetamido-2-deoxy-D-glucose and other *N*-acylated hexosamines stimulated recent work in our laboratory[1] and others[2,3], on *O*-benzylated derivatives (**1**, R^{3-6} = Bn; R^{3-6} = 2 Bn + 1 Ac) of 2-methyl-(1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline. As a continuation of this work, we undertook the preparation of oxazolines having electronegative substituents at position 2. These compounds proved to be somewhat elusive, but in the course of our investigation we developed a new, convenient and apparently general procedure for the synthesis of alkyl β-glycosides of 2-acylamido-2-deoxyglucopyranoses (and, presumably, of 2-acylamido-2-deoxygalactopyranoses). Our results are presented here, and application of the method to oligosaccharide synthesis is described in an accompanying communication[4].

The preparation of the oxazoline **1**, (R^{3-6} = Ac) by treatment of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**2**) with ferric chloride in dichloromethane solution was described by Matta and Bahl[5]**. We found that, when an alcohol was included in the mixture, the product obtained was the corresponding β-glycoside, rather than the oxazoline. The reaction was conducted by adding 4 mL of dichloromethane (dried over molecular sieves) and 200 mg of anhydrous calcium sulfate to 125 mg of anhydrous ferric chloride, and stirring the mixture for 5–10 min. The β-acetate **2** (200 mg) and the alcohol (2–10 molar portions) were then added, and in some cases ~60 μL of *N,N,N′,N′*-tetramethylurea***. Stirring was continued overnight at room temperature, and then the mixture was poured into ice-cold, aqueous sodium hydrogencarbonate. After the addition of a little chloroform, the two liquid phases were stirred together until the organic phase became colorless. The product was isolated conventionally from the organic phase and crystallized from ethanol. As may be seen in Table I, the yields of glycosides were excellent with allyl, benzyl, and isopropyl alcohols as glycosyl acceptors, but only modest with *tert*-butyl alcohol.

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**The procedure is attributed to F. Bach and H. G. Fletcher, Jr.
***Later experience[4] has demonstrated that the tetramethylurea is needed only when the glycosyl acceptor is acid labile.

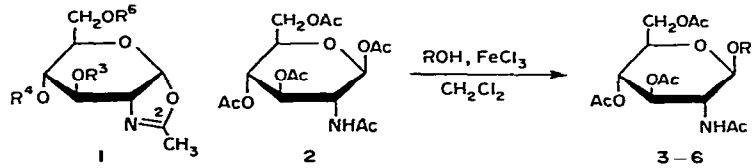

TABLE I

ALKYL 2-ACETAMIDO-3,4,6-TRI-*O*-ACETYL-2-DEOXY-β-D-GLUCOPYRANOSIDES FROM THE 1-ACETATE

Compound no.	*R*	*Yield (isolated) (%)*	*M.p. (°C)*[a]	$[\alpha]_D^{25}$ *(°)*[a,b]	$[\alpha]_{436}^{25}$ *(°)*[b]	*Lit. ref.*
3	allyl	82	164–167	–14.4	–32.4	6
4	benzyl	80	164–165	–54.4 –41 (MeOH)	–108 –85 (MeOH	7
5	isopropyl	85	174–175	–6.4[c]	–10.8	8
6	*tert*-butyl	55	206–207	+2	+6.4	9

[a] Melting points and $[\alpha]_D$ values agree satisfactorily with those recorded in the literature, except as noted. [b] Specific rotations determined in chloroform, $c = 0.5$, except as noted. [c] Differs from the value given in the literature (23 ± 2°), but is consistent with the values shown by the other members of the series.

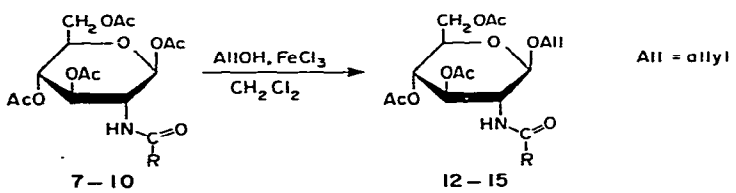

TABLE II

ALLYL 3,4,6-TRI-*O*-ACETYL-2-ACYLAMIDO-2-DEOXY-β-D-GLYCOPYRANOSIDES

N-Acyl group	*Precursor formula no.*	*Glycoside formula no.*	*Yield (isolated) (%)*	*M.p. (°C)*	$[\alpha]_D^{25}$ *(°)*[a]	$[\alpha]_{435}^{25}$ *(°)*[a]
Benzoyl	7	12	85	240 (dec.)	+22.2	+46
Phenoxyacetyl	8[b]	13	78	160–161	+18.6	+40.6
Methoxyacetyl	9[c]	14	80	176–177	–11	–19
Chloroacetyl	10	15	83	166–167	–9	–17.4
Phthaloyl	11	16	86	109–110	+36.8	+91.2

[a] Optical rotations determined in chloroform, $c = 0.5$. [b] New compound, m.p. 208–209°, $[\alpha]_D^{25}$ +29.2°. [c] New compound, m.p. 187–188°, $[\alpha]_D^{25}$ +5.4°.

The same procedure, applied to the 1,3,4,6-tetra-*O*-acetyl-2-acylamido-2-deoxy-β-D-glucopyranoses **7**—**10**, with allyl alcohol as the acceptor, gave high yields of the glycosides **12**—**15** (Table II). Similarly, an *N*-phthaloyl derivative, 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose (**11**), gave the corresponding allyl glycoside (**16**, Table II) in 86% yield.

When the preformed oxazoline **1** (R^{3-6} = Ac) was used as the starting material instead of **2**, we observed a rapid (~3 h) glycosylation of allyl alcohol. Thus, oxazolines may be intermediates in the "direct" conversion of β-1-acetates to glycosides described here.

The β-acetate **2** and β-acetates **7**—**11** were made by *N*-acylation of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose, prepared[10] and stored as the hydrochloride. The new compounds of this series (**8**, **9**) and the allyl glycosides **12**—**16** gave elemental analyses in satisfactory accord with theory. The β-anomeric configuration of the glycosides was established from their ^{1}H-n.m.r. spectra, taken at 270 MHz.

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