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THE SELECTIVE ACETYLATION OF PRIMARY ALCOHOLS IN THE PRESENCE OF SECONDARY ALCOHOLS IN CARBOHYDRATES

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Abstract: Treatment of primary-secondary sugar diols with ethyl acetate in the presence of Woelm neutral alumina produced selectively the corresponding primary monoacetates in good yield. No di-acetate was formed in a detectable amount.

Selective acetylation of hydroxyl groups in carbohydrates, in addition to being of theoretical interest, has great practical utility. Among the various methods developed for this purpose[1-4], the use of N-acetylimidazole[4] seems to be attractive for the preparation of desired product in good yields. In another approach, for the introduction of an acetyl group particularly at the primary hydroxyl group, the sugar alcohol is per(trimethylsilyl)ated[5] to get the fully protected trimethylsilyl (Me_3Si) derivative which on treatment with pyridine-acetic anhydride-acetic acid[6], followed by removal of Me_3Si groups at the secondary positions, provides the corresponding monoacetate. In the present report, we describe a convenient and extremely simple method for the selective acetylation of primary hydroxyl group, which involves the use of neutral alumina in presence of ethylacetate.

According to Posner et al.[7], treatment of primary alcohols in ethyl acetate solvent over commercially available Woelm. neutral, chromatographic alumina very conveniently produces the corresponding acetates. We have extended the use of this simple procedure for selective acetylation of various sugar diols, as shown in Table 1.

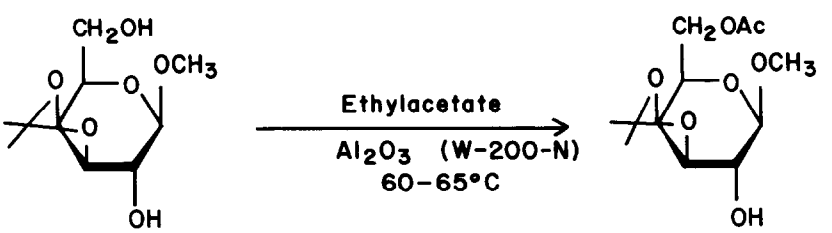
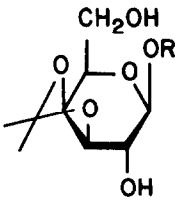
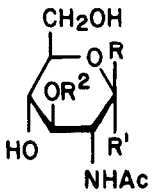
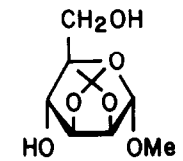
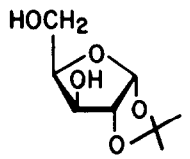


TABLE I

SELECTIVE ACETYLATION OF THE PRIMARY HYDROXYL GROUP OF PRIMARY-SECONDARY DIOLS

	Diol	Reaction Time (h)	% Yield of Primary Monoacetate[a]	m.p. °C	$[\alpha]_D^b$
					
1.	R = CH_3	40	62.7	125-126[c]	+19.2° (c 1.3)
2.	R = $C_6H_4NO_2$-p	40	55	138-139[c]	-39.4° (c 1.3)
3.	R = 2,3:5,6-Di-O-isopropylidene-D-glucose dimethyl acetal	48	46	-	+39.8° (c 1.2) (lit.[8] +41°)
					
4.	R = H, R' = OMe; $R^2 = CH_2Ph$	40	54.5	165-166[c]	+84.2° (c 1.2)
5.	R = OCH_2Ph, R^1 = H, R^2 = 2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl	48	37	104-106[c]	-15.6° (c 1.6)
6.		20	72.5	-	+1.33° (c 1.9)
7.		20	22	96-97° (lit[9] 100-105°)	+20.5° (c 1.3) (lit.[9] +23°)

a. After crystallization or purification by silica gel column chromatography.
b. In chloroform at room temperature.
c. Crystallized from Acetone-Hexane or Acetone-Ether-Hexane.
d. Physical constants of the isolated products were in agreement with those of the authentic samples.

In a typical experiment, a solution of the diol methyl 3,4-O-isopropylidene-β-D-galactopyranoside (1, 1 mmol) in anhydrous ethylacetate (100 ml), was stirred at 60-65° for 40 h in the presence of neutral alumina (10 g). The contents were filtered and the solid residue was washed with ethylacetate. The combined filtrate was evaporated to get methyl 6-O-acetyl-3,4-O-isopropylidene-β-D-galactopyranoside which was found to be quite pure and was further purified by crystallization from acetone-hexane.

Our comments on the use of this procedure are as follows: (1) The given alcohol should be fairly soluble in ethylacetate; (2) we didn't observe the formation of any di-O-acetate; (3) virtually all the monosaccharide diols gave the expected monoacetates which were isolated in pure form via direct crystallization, and column chromatography was not required; (4) in case of disaccharides, chromatographic purification was essential step for the separation of monoacetate from the starting material; (5) at room temperature, the yield of the product was low; (6) in case of aliphatic sugar alcohols such as 3-O-benzyl-1,2-propanediol and batyl alcohol, the reaction didn't proceed well; (7) in case of 1,2-O-isopropylidene-α-D-xylofuranose, yield of monoacetate was only 22% and we couldn't recover any starting material from the reaction mixture.

In conclusion, the present procedure provides a simple method for the preparation of suitable intermediates for oligosaccharide synthesis.

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