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ORGANIC REACTIONS AT ALUMINA SURFACES. AN EXTREMELY SIMPLE, CONVENIENT AND SELECTIVE METHOD FOR ACETYLATING PRIMARY ALCOHOLS IN THE PRESENCE OF SECONDARY ALCOHOLS.

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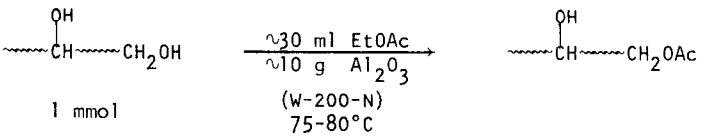
Summary. Stirring primary-secondary diols in ethyl acetate solvent over Woelm alumina leads to the corresponding primary monoacetates simply, conveniently, and in good yields. In this way, primary hydroxyalkylphenols are converted into acetoxyalkylphenols, and primary arylamines are transformed into the corresponding acetamides.

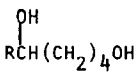
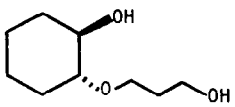
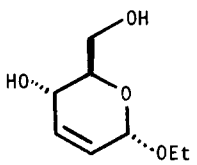
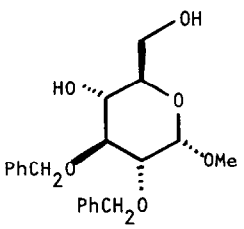
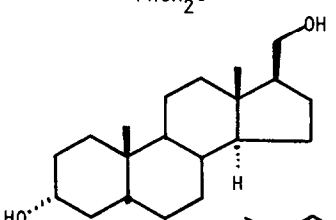
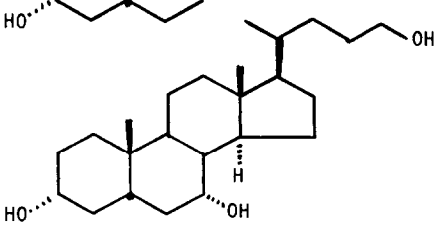
Acylation of alcohols is one of the most fundamental transformations in organic chemistry. Often chemoselective acylation of the primary hydroxyl group of a primary-secondary diol is required, and several sophisticated and relatively expensive reagents have been developed for this purpose; some of the most useful examples include triphenylphosphine-diethyl azodicarboxylate,[1] 2,2'-bipyridyl carboxylates-cesium fluoride,[2] iodotrimethylsilane,[3] and N-acetylimidazole.[4]

We have claimed recently that stirring a wide variety of primary alcohols in ethyl acetate solvent over commercially available Woelm, neutral, chromatographic alumina very conveniently produces the corresponding acetates.[5] We report here that this simple and convenient heterogeneous procedure also allows chemospecific acetylation of the primary hydroxyl group in a series of structurally diverse primary-secondary diols, according to eq. 1. Filtration, evaporation of the ethyl acetate solvent, and column chromatography or preparative tlc provided pure primary monoacetates, as shown in Table I.



(1)

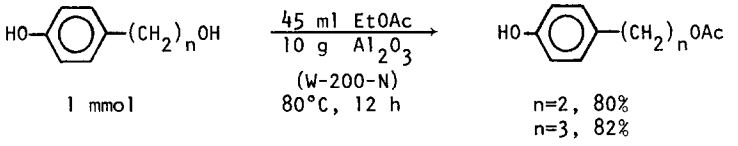
Table 1. Selective Acetylation of the Primary Hydroxyl Group of Primary-Secondary Diols According to eq. 1.

Diol	Reaction Time (h)	% Yield of Primary Monoacetate[a]
		
R = Me	2.0	71 (85)[b]
R = n-Bu	1.5	71
R = Ph	1.0	69 (92)[b]
	47	71[c]
	24	45 (69)[b,c]
	24	58 (97)[b]
	16	55 (86)[b,c]
	19	63 (92)[b,c]

a. After preparative tlc or column chromatography to separate product monoacetate from reactant diol.
b. Yield based on recovered reactant alcohol.
c. All new compounds gave satisfactory spectral and analytical data.

Several features of the results shown in Table I deserve comment, as follows: (1) virtually no diacetates were observed in the crude reaction products; (2) some unsaturated and polyether carbohydrates were effectively monoacetylated without disturbing the sugar structure or the ether linkages,[6] and (3) despite their large size and therefore their inability to fit inside the narrow pores of the most porous solids, some steroidal diols and a triol were conveniently monoacetylated. Control experiments using each of several of the diols shown in Table I and one equivalent of acetyl chloride in pyridine gave a mixture of diol, monoacetate, and diacetate. 1,2-Diols and 1,3-diols were not acetylated chemoselectively using this alumina procedure.

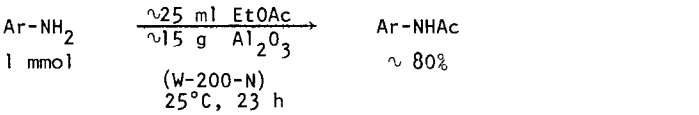
In contrast to Mukaiyama's procedure,[2] phenols were not acetylated; chemospecific acetylation of the aliphatic hydroxyl group of primary hydroxyalkylphenols is therefore possi as illustrated by eq. 2.



(2)

Ethyl acetate is not the only acetate ester which works effectively in this heterogeneous procedure. Methyl acetate and, in somewhat slower reactions, n-butyl acetate and phenyl acetate worked also in acetylating primary alcohols. Likewise it is possible, using ethyl priopionate or methyl benzoate as solvents, to convert a primary (e.g. oleyl) alcohol into the corresponding propionate (42%) or benzoate (58%). Furthermore, using dimethylcarbonate as solvent, several primary (e.g. oleyl, geranyl) alcohols were converted conveniently and in good yield into the corresponding methyl carbonates.

Although aliphatic primary amines were not effectively acetylated by ethyl acetate over alumina, aromatic primary amines (e.g. aniline, p-bromoaniline) were conveniently acetylated according to eq. 3.



(3)

The ability of alumina to direct a chemical reaction at one site of a polyfunctional molecule is probably due to the different rates and/or extents of functional group adsorption to the solid surface.[7] We have used this preferential binding previously in alumina-promoted isopropyl alcohol chemoselective reduction of the relatively unhindered carbonyl group in some ketoaldehydes and diketones[8] and alumina-promoted chemoselective elimination of the sulfonate group from some sulfonate and carboxylate diesters of diols.[9] The methodology reported here represents yet another example of alumina-promoted chemoselectivity in polyfunctional molecules as well as an extremely simple, cheap, and convenient laboratory method for converting (1) primary-secondary diols selectively into the corresponding primary monoacetates, (2) primary hydroxyalkylphenols selectively into the corresponding acetoxyalkylphenols, and (3) primary aromatic amines into the corresponding acetamides.

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