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Note

$KHSO_4$-SiO_2-MeOH An efficient selective solid-supported system for deprotection of alcohols from esters

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$KHSO_4$-SiO_2 can efficiently deprotect alcohols from esters through transesterification in methanol under mild condition. Esters of aromatic alcohols are easily transesterified at room temperature compared to the corresponding aliphatic or alicyclic alcohol. *N*-Acetyl compounds and ethers are resistant to the reagent under the above condition. The method is very useful for preparation of bio-diesel methyl ricinoleate from castor oil.

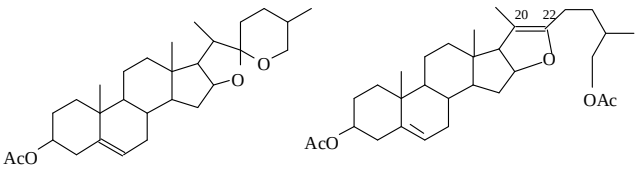
Keywords: Transesterification, diosgenin acetate, furostadiene, castor oil, methyl ricinoleate

Ester hydrolysis is an important fundamental reaction for deprotection of alcohols generally carried out either by chemical or biochemical methods. Chemical methods involve hydrolytic[1] or non-hydrolytic[2] methods using homogeneous or heterogeneous reagents. Because of the advantages of recycling and easy separability from the reaction-mixture solid-supported heterogeneous catalysts[3] are attractive from the economic and environmental point of view. Solid-supports such as alumina[3b], zeolite[3c], acid resin[4], etc that are generally in use suffer from certain limitations such as requirement in large volume, pore size dependency, substrate specificity, etc.

Recently selective cleavage of only prenyl esters using silica-supported sodium hydrogen sulphate in a nonprotic solvent was reported[5]. In this system groups other than the prenyl are resistant to deprotection. The deprotection was carried out in a non-protic solvent dichloromethane. In this system the proton required for the reaction is supplied by the prenyl part which subsequently releases 2-methyl-1,3-butadiene. But in a chance discovery we came across the $KHSO_4$-SiO_2-MeOH system where the alcohol system is not affected.

Results and Discussion

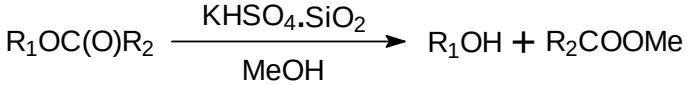
In continuation of the work on steroidal drug intermediates[6a,b] efforts have been carried out to develop a non-acetic anhydride route[7-9] to convert diosgenin acetate **1** to furostadiene derivative **2** using ethyl acetate[10]. The presence of spiro ethers in **1** is tempted to use mild acidic reagent $KHSO_4$ for this purpose that has found application in dehydration of alcohols[11], several acid catalyzed reactions[12a,b,c] such as deprotection of TBDMS ethers, Diels–Alder reactions and preparation of *bis*-indolyl methanes, etc.



1 **2**

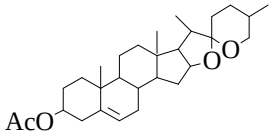
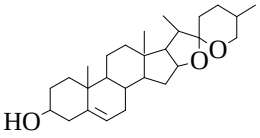
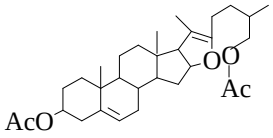
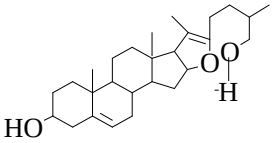
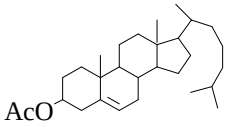
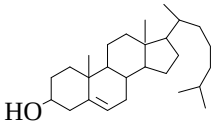
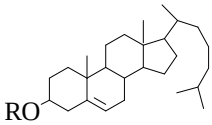
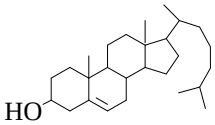
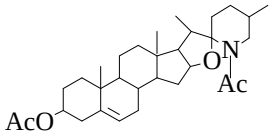
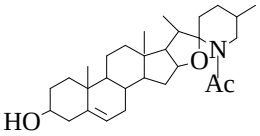
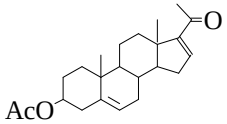
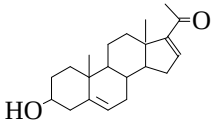
We carried out the reaction of diosgenin monoacetate **1** by refluxing in ethyl acetate in presence of $KHSO_4$ for 5 hr. The reaction did not proceed as expected. However, a mixture of ethyl acetate and methanol (1:1) produced deacetylated product diosgenin with 50% yield on refluxing for 20 hr. The conversion reduced to 30% when water was added (water EtOAc : MeOH, 1:1:1). From this it was clear that methanol, a protic solvent alone was responsible for the deprotection. In order to study the reaction a solid-supported $KHSO_4$ –SiO_2 was prepared to examine its activity against esters. It was observed that diosgenin acetate **1** was converted to its corresponding alcohol diosgenin on refluxing in methanol in presence of $KHSO_4$ – SiO_2 (**Scheme I**).

Similarly cholesteryl acetate was deacetylated in 8 hr (Entry **3**). The reaction did not proceed in ethyl



Scheme 1

Table I — Deprotection of alcohols using $KHSO_4$-SiO_2-MeOH System

No	Substrate	Temp (^oC)	Time (hr)	Product[a] (Alcohol)A	Product[b] (Ester)B	Yield (%)	m.p. /b.p. (^oC)(Lit)	Sp.Rot. $[\alpha]^{25}_{259}$ =(1,$CHCl_3$)
1		65	5		AcOMe	A=90	A=202(204)	A=128[b] (-129)
2		65	2		AcOMe	A=95	A=100(101)	A=-45 (-47)
3		65	8		AcOMe	A=85	A=146 (148)	A=-33(-35)
4		65	10		ROMe	A=91 B=71	A=146 (148) B=216 (218)	A=-6(-9)
5		65	10		AcOMe	A=81	A=147 (150)	A=-66 (-66)
6		65	5		AcOMe	A=87	A=160 (161)	
7	C_6H_5OAc	RT	1	C_6H_5OH	AcOMe	A=95	A=179 (182)	
8	3-Ac-C_6H_4OAc	RT	1	3-Ac-C_6H_4OH	AcOMe	A=94	A=95(97)	
9	4-Ac-C_6H_4OAc	RT	1	4-Ac-C_6H_4OH	AcOMe	A=95	A=108 (109)	
10	$Me(CH_2)_3OAc$	65	5	$Me(CH_2)_3OH$	AcOMe	A=92	A=115 (117)	
11	$C_6H_5CH_2OAc$	65	5	$C_6H_5CH_2OH$	AcOMe	A=89	A=202 (205)	
12	$C_6H_{12}OAc$	65	5	$C_6H_{11}OH$	AcOMe	A=85	A=159 (160)	
13	$C_6H_5CH(OAc)CH_3$	65	2	$C_6H_5CH(OH)CH_3$	AcOMe	A=93	A=87(88)	
14	$(CH_2OR_1)_2CHOR_1$	65	5	$(CH_2OH)_2CHOH$	R_1OMe	A=58 B=94	A=179(182)B =225(225)	

RT = Room temperature. a = Characterized from spectroscopic, sp. rotation and m.p. data that matched with the reported values[4,14-19], $R=CH_3(CH_2)_7CH=CH(CH_2)_7CO$-, $R_1=CH_3(CH_2)_5CH(OH)CH_2CH=CH(CH_2)_7CO$-

acetate or acetonitrile alone. Castor oil can be very easily transformed into bio-diesel methyl ricinoleate[13]. Presence of water (5%) inhibited the reaction. *N*-Acetyl compounds and ethers were resistant to the reagent. Aromatic esters were easily transesterified (Entry **7-9**). The reagent could be recycled 4 times. The surface of silica gel probably formed a reaction field where reagents and substrates were accumulated by absorption and bound the reactants in close proximity for the reaction to occur[7]. In conclusion, a novel method has been developed for hydrolysis of esters using solid-supported heterogeneous catalyst.

Experimental Section

Chemicals

All the chemicals were of AR grade and needed no further purification. Potassium hydrogen sulfate, silica gel (6—120 mesh) and methanol were obtained from Merck India Ltd. All the alcohols used were from Sigma-Aldrich and Merck India Ltd.

Catalyst preparation

$KHSO_4$ (10 g, 72 mmole) was dissolved in 100 mL distilled water to have clear saturated solution. The solution was soaked completely in silica gel (25 g, 60-120 mesh). The soaked mixture was thoroughly mixed and dried in a hot oven at 150°C. for 24 hr to have free flowing powdery solid. The dried solid mixture was then kept in vacuum desicator to use as stock solid support in different reactions.

General procedure for deprotection of alcohols

A solution of ester (0.21mmole) in methanol (10 mL) was added cautiously to $KHSO_4$-SiO_2 solid support (0.2 g) from the stock that contains 0.057 g (0.42 mmole) of $KHSO_4$ and 0.14 g (2.33 mmoles) of silica gel keeping the molar ratio of the substrate to $KHSO_4$ in 1:2. Stirred the entire mixture for about an hr and refluxed for 1-10 hr. Then the solvent was removed under reduced pressure. Water (10 mL) was added to the concentrated mass and the aqueous layer in ethyl acetate (3 × 20 mL) was extracted and dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to get pure alcohol.The alcohols and methyl esters isolated were identified from their characteristic spectroscopic data and comparing with their reported values in the literature.

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