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SAC-13 silica nanocomposite solid acid catalyst in organic synthesis

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Abstract

Nafion-H SAC-13 solid superacid is shown to exhibit outstanding properties as catalyst in the formation of various protective groups. These include the formation of tetrahydropyranyl ethers of alcohols and the removal of this protective group, acetalization of carbonyl compounds with ethane-1,2-diol and propane-1,3-diol, and the transformation of aldehydes to 1,1-diacetates. Products are isolated in good to excellent yields and the catalyst can be reused with practically no loss of activity.

Keywords: Nafion-H SAC-13; Tetrahydropyranylation; Acetalization; Aldehyde 1,1-diacetates; Catalyst recycling

1. Introduction

The use of solid (heterogeneous) catalysts in organic synthesis and in the industrial manufacture of chemicals is of increasing importance since they provide green alternatives to homogeneous catalysts. This is particularly important in acid catalysis where solid acids can be the safe alternatives of such hazardous and corrosive materials as HF, sulfuric acid and nitric acid [1–3]. Heterogeneous catalysts are used extensively in protection/deprotection processes in organic synthesis [4].

Nafion resins, that is perfluorinated resinsulfonic acid based ion-exchanged polymers, have been widely used in organic synthesis [5,6]. They exhibit an acidic character comparable to that of 100% sulfuric acid. Thermal stability, chemical resistance, and possible regeneration make Nafion a safe and valued solid acid catalyst. However, because of the very low surface area ($\sim 0.02\ m^2\ g^{-1}$) and the inaccessibility of most of the active sites Nafion has low specific activity.

The preparation of Nafion-H silica nanocomposites, that is, the immobilization of Nafion into a silica matrix reported by Harmer and coworkers [7,8] overcomes this problem. It was shown that these nanocomposites have large surface area ($150–500\ m^2\ g^{-1}$) and contain small (<100 nm) Nafion particles entrapped in a porous silica framework [7]. Outstanding catalytic performance was found in further studies [7–12] and demonstrated recently with a commercially available catalyst sample called Nafion-H SAC-13 [13–15], although it proved to be less efficient than a polymer-bound super Brønsted acid [16].

We have previously demonstrated the excellent catalytic performance of SAC-13 solid superacid in the formation of mixed acetals using dialkoxymethanes [15]. As a continuation of this work we now present data with respect to the use of SAC-13 in forming various protective groups.

2. Experimental

All compounds and the SAC-13 catalyst were purchased from Aldrich and were of appropriate purity to be used without further purification.

Reactions were performed under magnetic stirring at room temperature or under reflux in appropriate solvents or under solvent free conditions. Tetrahydropyranylation: 20 mmol of alcohol, 30 mmol of 3,4-dihydro-2*H*-pyrane, 100 mg of SAC-13 catalyst, 30 ml of dichloromethane, room temperature. Deprotection of THP ethers: 7 mmol of THP ether, 3.5 ml of methanol, 200 mg of SAC-13 catalyst, room temperature. Formation of cyclic acetals: 1 mmol of

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carbonyl compound, 2 mmol of diol, 100 mg of SAC-13 catalyst, 6 ml of dichloromethane, reflux. Formation of 1, 1-diacetates: 1 mmol of carbonyl compound, 50 mmol of acetic anhydride and 100 mg of SAC-13 catalyst, room temperature (aliphatic aldehydes) or 90 °C (aromatic aldehydes). In recycling studies, the catalyst was recovered by filtration after completion of reaction, washed with ethanol, dried and reused.

The progress of the reactions was monitored by gas chromatography (HP 5890 GC, 50 m × 0.32 mm × 1.05 μm HP-1 column, flame ionization detector) and TLC. Product identification was performed by means of GC–MS (HP 5890 GC coupled with a HP 5970 mass selective detector) and by NMR spectroscopy (Bruker DRX 500 spectrometer at 500 MHz, $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal reference). All products are known compounds and gave satisfactory spectral data.

3. Results and discussion

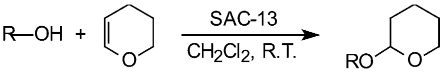
3.1. Tetrahydropyranylation of alcohols and phenols

The early work with Nafion H [17], our study using heteropoly acids [18], as well as recent examples applying ITQ-2 delaminated zeolite [19], silica chloride [20], zirconia catalysts [21,22], and supported heteropoly acids [23] show the effective use of solid acids in the protection of alcohols and phenols as tetrahydropyranyl ethers (THP ethers).

Transformation of alcohols to the corresponding THP ethers through the reaction with dihydropyrane occurs with ease in the presence of SAC-13 (Table 1). Good to high yields (81–100%) were obtained in very short reaction times in most cases. All types of alcohols including primary, secondary, tertiary, benzylic, and allylic alcohols can be conveniently converted. Mixed results were found for various phenols studied. Lower reactivity of phenol as compared to alcohols, is attributed to the decreased nucleophilic character of the phenolic oxygen. *p*-Methylphenol, in contrast, bearing the activating methyl group, shows high reactivity. In addition, solubility problems also contribute to unsatisfactory results. *p*-Nitrophenol, for example, is not soluble in dichloromethane and a reaction in diethyl ether furnished the corresponding THP ether in very low yield.

In turn, deprotection of THP ethers, in general, requires prolonged reaction times. A possible explanation is that the crude reaction mixtures obtained in the formation of THP ethers were directly used in deprotection reactions. Minor byproducts formed in the first reaction may cause some deactivation of the catalyst in the second reaction. Moreover, the catalyst is not effective in two cases: tetrahydrofurfuryl alcohol and 2-methyl-2-butanol could be recovered only in very low yields. These two alcohols are known to rather sensitive under acidic conditions easily undergoing dehydration and various rearrangements. It appears that these side reactions taking place during the prolonged reaction necessary in the deprotection process are responsible for the phenomenon observed.

Table 1
Transformation of alcohols to THP ethers and removal of the protective group



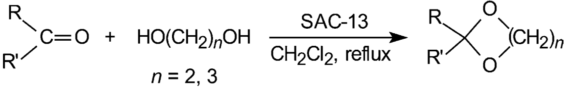
Alcohol	Protection		Deprotection	
	Time	Yield (%)	Time	Yield (%)
1-Octanol	30 min	100	30 min	97
Benzyl alcohol	30 min	90	3 h	94
Isobutyl alcohol	30 min	96	2 h	95
Tetrahydrofurfuryl alcohol	2 h	86		Low
Allyl alcohol	30 min	95	6 h	81
2-Octanol	30 min	84	5 h	91
Cyclopentanol	30 min	81	6 h	94
Cyclohexanol	30 min	98	6 h	85
2-Methyl-2-butanol	4 h	76		Low
Phenol	30 min	55		
p-Methylphenol	30 min	91		

3.2. Protection of carbonyl compounds as cyclic acetals

Our own work with Envirocat reagents [24] and recent literature procedures applying Ti-montmorillonite [25], metallic sulfates supported on silica gel [26], zirconium sulphenyl phosphonate [27], and a Pt–Mo/ZrO_2 catalyst [28] are prime examples for the easy and effective utilization of solid acids in the formation of cyclic acetals as protective groups for carbonyl compounds.

Data collected in Table 2 indicate that SAC-13 shows high activity and selectivity in the formation of cyclic acetals in most of the cases studied. Various types of aldehydes and

Table 2
Transformation of carbonyl compounds to cyclic acetals



Carbonyl compound	Ethane-1,2-diol		Propane-1,3-diol	
	Time	Yield (%)	Time	Yield (%)
Pentanal	60 min	100	15 min	98
Octanal	60 min	92	2 h	96
Cyclohexanecarbaldehyde	45 min	98	60 min	100
Benzaldehyde	2.5 h	94	30 min	99
p-Nitrobenzaldehyde	2 h	90	7 h	31
p-Anisaldehyde	6 h	90	30 min	87
Cinnamic aldehyde	3.5 h	92	60 min	98
Heptan-4-one	2 h	76	2 h	34
Cyclopentanone	2 h	64	2 h	70
Cyclohexanone	30 min	95	40 min	70
Acetophenone	3 h	78	4 h	57

ketones (open chain and cyclic, aliphatic and aromatic, α,β-unsaturated) undergo facile transformation with ethane-1,2-diol and propane-1,3-diol to form, respectively, 1,3-dioxolanes and 1,3-dioxanes in good to high yields. Whereas yields with the two diols are practically identical for aldehydes, ketones give better yields in the reaction with ethane-1,2-diol. This can be accounted for by steric reasons. One of the substituents at C(2) in 1,3-dioxanes formed in the reaction between ketones and propane-1,3-diol is necessarily in the axial position, which results in unfavorable steric interactions. Steric strain in the highly flexible 1,3-dioxolane ring, in turn, is less severe.

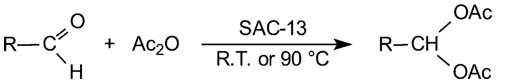
Benzophenone, in turn, showed very low reactivity with either reagent (data not shown) under the reaction conditions applied. Surprisingly, butan-2-one exhibited similar characteristics. The difference in reactivities observed for cyclic ketones (cyclopentanone and cyclohexanone) is due to the I strain [29].

3.3. Formation of 1,1-diacetates

Nafion-H [30] and a number of solid acids have been applied to transform aldehydes to 1,1-diacetates (acylals) [4]. $FeCl_3$-PVC [31], Zn montmorillonite [32], zirconium sulphenyl phosphonate [33], a Wells-Dawson heteropoly acid [34], Amberlyst-15 [35], and Al[$PW_{12}O_{40}$] [36] were recently found to be effective. In addition, EPZ10 catalyst [37] and $FeCl_3/SiO_2$ [38] are also useful under microwave irradiation.

SAC-13 exhibits high activity in the transformation of aliphatic aldehydes to 1,1-diacetates under solvent free conditions (Table 3). The reaction takes place almost instantaneously to yield 1,1-diacetates in 100% yield. Aromatic aldehydes, in turn, show mixed reactivity. Benzaldehyde exhibits low conversion at room temperature and requires long reaction time at increased temperature to give satisfactory yield. Deactivated aldehydes such as *p*-anisaldehyde as well as cinnamic aldehyde do not react, which is in sharp contrast to the high reactivity of *p*-nitrobenzaldehyde.

Table 3
Transformation of aldehydes to 1,1-diacetates



Carbonyl compound	Time	Yield (%)
Pentanal	5 min[a]	100
Octanal	5 min[a]	100
Cyclohexanecarbaldehyde	5 min[a]	100
Benzaldehyde	5 min[a]	65
	10 h[b]	87
p-Nitrobenzaldehyde	30 min[b]	84
p-Anisaldehyde	10 h[b]	No reaction
Cinnamic aldehyde	10 h[b]	No reaction
Cyclohexanecarbaldehyde + acetophenone	10 min[a]	96[c] + 0[d]

[a] Room temperature.
[b] 90 °C.
[c] Yield of cyclohexanecarbaldehyde 1,1-diacetate.
[d] Acetophenone was recovered unreacted.

Table 4
Catalyst recycling in *O*-protection reactions

Reaction	Reactant	Yields (%) first run	5th run
Tetrahydropyranylation	1-Octanol	100	100
	Allyl alcohol	95	96
	Cyclohexanol	98	99
Formation of cyclic acetal[a]	Pentanal	100	90
	Benzaldehyde	94	95
Formation of 1,1-diacetate	Octanal	100	100
	Cyclohexanecarbaldehyde	97	96

[a] Reagent: ethane-1,2-diol.

Such differences in reactivities are brought about by the differing electrophilicity of the carbonyl carbon. Electron donating substituents on the aromatic ring, such as a methoxy group (*p*-anisaldehyde), help the delocalization of the partial positive charge of the carbonyl carbon through conjugation. This results in a decrease in electrophilicity and, consequently, the reactivity towards nucleophiles decreases. Electron withdrawing groups, such as nitro (*p*-nitrobenzaldehyde), in turn, increase electrophilicity, thereby increasing reactivity.

The chemoselectivity of the method can be demonstrated by running competitive reactions of aldehyde–ketone pairs: a mixture of cyclohexanecarbaldehyde and acetophenone yields exclusively the 1,1-diacetate of the aldehyde.

3.4. Catalyst recycling

Data collected in Table 4 demonstrate that SAC-13 can be used effectively in successive runs in all *O*-protection reactions studied. After a simple washing with ethanol and drying high activity can be maintained with practically no loss of activity.

4. Conclusions

SAC-13 solid superacid with highly dispersed Nafion-H as the active component is found to be a highly effective catalyst in various *O*-protection reactions. Good to high yields were obtained in the selective formation of THP ethers of alcohols and in the protection of carbonyl compounds as cyclic acetals. The catalyst exhibits lower activity in the deprotection of THP ethers. Aliphatic aldehydes undergo chemoselective transformation almost instantaneously to yield 1,1-diacetates.

SAC-13 can be reused in five successive runs with no considerable activity loss requiring only very simple regeneration (washing with ethanol and drying).

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