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ORIGINAL PAPER

Saccharinsulfonic acid: an efficient and recyclable catalyst for acetylation of alcohols, phenols, and amines

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Abstract Saccharinsulfonic acid is an efficient catalyst of the protection of alcohols, phenols, and amines with acetic anhydride. All reactions were performed under mild and completely heterogeneous reaction conditions. with excellent yields.

Keywords Saccharinsulfonic acid · Acetylation · Alcohols · Acetic anhydride · Heterogeneous reaction conditions

Introduction

Acetylation is one of the most important methods widely used for protection of the alcoholic hydroxyl group. This method is important because of the ease of introduction of the acetyl group, the stability of the product to acidic conditions, and ease of removal of the protecting group by alkaline hydrolysis [1]. In general, acetylation takes place by treatment of the alcohols with acid anhydrides or acid chlorides in the presence of tertiary amines such as triethylamine and pyridine [2]. 4-(Dimethylamino)pyridine [3, 4], *p*-toluenesulfonic acid [5], sulfamic acid [6], scandium triflate [7], indium triflate [8], copper triflate [9], bismuth triflate [10], Me_3SiOTf [11], electron-deficient tin(IV) porphyrin [12], silica gel supported sodium hydrogen sulfate [13], potassium dodecatungstocobaltate trihydrate [14], NBS [15], alumina-supported MoO_3 [16], $Gd(OTf)_3$ [17], $NbCl_5$ [18], HBF_4-SiO_2 [19], manganese(III) bis(2-hydroxyanil)acetylacetonato complex [20], fluorous distannoxane [21], 3-nitrobenzene boronic acid [22], bis(cyclopentadienyl)zirconium dichloride [23], polymer-supported gadolinium triflate [24], *N,N*-dibromo-4-methylbenzenesulfonimide [25], *N,N*-dichloro-4-methylbenzenesulfonimide [26], $Al(OTf)_3$ [27], silica sulfuric acid [28], $Al(HSO_4)_3$ [29], $V(HSO_4)_3$ [30], and *o*-benzenedisulfonimide [31] have also been used as catalysts for acetylation of alcohols. However, some of these methods suffer from one or more of the following disadvantages: long reaction times, harsh reaction conditions, tedious work-up procedure, use of reagents with unpleasant odors, use of highly flammable and expensive reagents, formation of by-products, and low yields of the desired products. Therefore, introduction of new methods and catalysts for the preparation of acetates is still in demand.

Results and discussion

We recently reported the preparation of saccharinsulfonic acid (SaSA) as a stable derivative of saccharin, and its application in acceleration of the chemoselective trimethylsilylation of alcohols with hexamethyldisilazane [32]. In continuation of this study we have observed that this reagent is also a highly effective catalyst of acetylation of alcohols with acetic anhydride. All reactions were performed in CH_2Cl_2 under reflux, with good to high yields (Scheme 1; Table 1).

A wide variety of alcohols, including benzylic, primary, secondary, and tertiary aliphatic alcohols underwent acetylation with acetic anhydride in the presence of catalytic amounts of SaSA in CH_2Cl_2 under reflux in good to high

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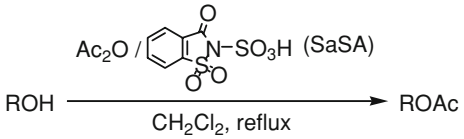
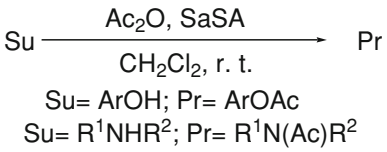


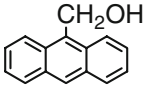
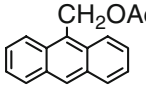
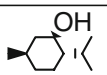
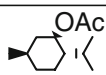
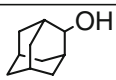
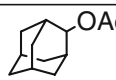
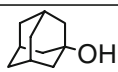
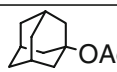
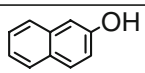
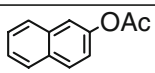
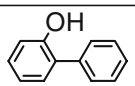
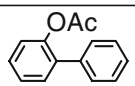
Scheme 1



Scheme 2

yields. Primary benzylic, including electron-donating or withdrawing groups, and aliphatic alcohols were acetylated with excellent yields (Table 1, entries 1–11, 13–16). The protection of benzylic, cyclic, and linear secondary alcohols was also achieved satisfactorily (Table 1, entries 12, 17, 18). It is in general known that diaryl carbinols can easily dimerize or dismutate in the presence of a Lewis acid catalyst [33]. However, benzhydrol itself, as model compound, was acetylated in 85% yield using Ac_2O in the presence of SaSA without any dimerisation (Table 1, entry

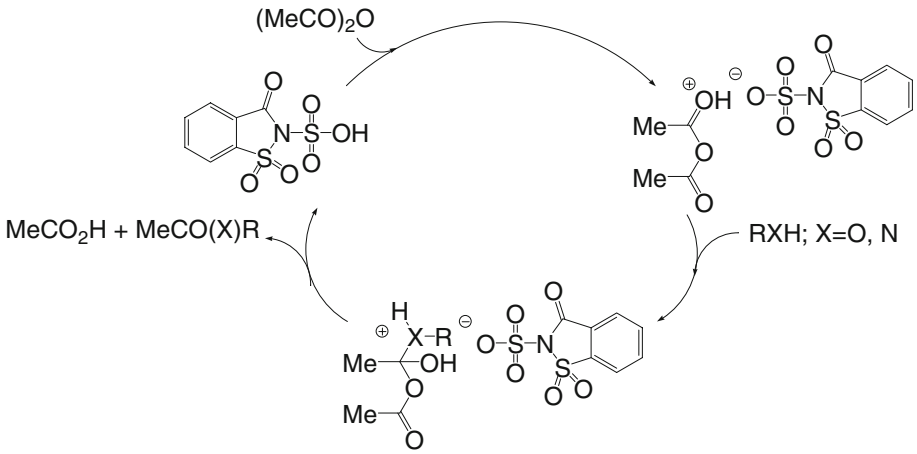
Table 1 Acetylation of alcohols, phenols, and amines catalyzed by SaSA

Entry	Substrate	Product	Time (h)	Yield (%)
1	2-$ClC_6H_4CH_2OH$	2-$ClC_6H_4CH_2OAc$	2	95
2	4-$ClC_6H_4CH_2OH$	4-$ClC_6H_4CH_2OAc$	2	92
3	2-$BrC_6H_4CH_2OH$	2-$BrC_6H_4CH_2OAc$	1.5	90
4	2-$MeC_6H_4CH_2OH$	2-$MeC_6H_4CH_2OAc$	1.5	92
5	2-$MeOC_6H_4CH_2OH$	2-$MeOC_6H_4CH_2OAc$	1	92
6	3-$MeOC_6H_4CH_2OH$	3-$MeOC_6H_4CH_2OAc$	1	92
7	2-$NO_2C_6H_4CH_2OH$	2-$NO_2C_6H_4CH_2OAc$	5.8	90
8	3-$NO_2C_6H_4CH_2OH$	3-$NO_2C_6H_4CH_2OAc$	4.5	85
9	4-$NO_2C_6H_4CH_2OH$	4-$NO_2C_6H_4CH_2OAc$	4	90
10	Ph_2CHOH	Ph_2CHOAc	2	85
11			0.5	92
12	$PhCH_2CH_2OH$	$PhCH_2CH_2OAc$	2	90
13	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CH_2OAc$	2	87
14	$PhCH(Me)CH_2OH$	$PhCH(Me)CH_2OAc$	1.5	90
15			1.5	92
16			1.5	90
17	$PhCH_2C(OH)Me_2$	$PhCH_2C(OAc)Me_2$	1	92
18			1.5	89
19	Ph_3COH	Ph_3COAc	2	85
20	2- $(CH_2{=}CH)C_6H_4OH$	2- $(CH_2{=}CH)C_6H_4OAc$	0.5	90
21			0.8	92
22			0.5	90
23			3	90[a]
24	$PhNH_2$	PhNHAc	1	92
25	4-$MeC_6H_4NH_2$	4-MeC_6H_4NHAc	1	90
26	PhNHMe	PhN(Ac)Me	0.25	85

Products were characterized by their physical constants, comparison with authentic samples, IR and NMR spectroscopy [12, 13, 16, 17, 20, 23, 24, 26, 30, 34, 35], isolated yield, phenols and amines are acetylated at room temperature

[a] Reaction was performed using 2.4 mmol of acetic anhydride

Scheme 3



12). It is noteworthy that in the case of optically active alcohols the reaction proceeded well with complete retention of configuration (Table 1, entry 17). Interestingly, hindered tertiary alcohols such as 1-phenyl-2-methyl-2-propanol, 1-adamantanol, and triphenyl carbinol, as models for acetylation of tertiary alcohols, were also converted to the corresponding acetates in CH_2Cl_2 under reflux in good to excellent yields (Table 1, entries 19–21). Our investigation showed that SaSA is also able to catalyze the acetylation of phenols and amines in CH_2Cl_2 at room temperature in good to high yields (Scheme 2; Table 1, entries 22–33).

We have found that SaSA is a reusable catalyst and even after three runs for the acetylation of the substrates with acetic anhydride the catalytic activity of SaSA was almost the same as that of the freshly used catalyst. Although the actual role of SaSA is not clear, the mechanism shown in Scheme 3 is selected as highly probable.

In conclusion, the acetylation of alcohols, phenols, and amines with Ac_2O is efficiently catalyzed in the presence of SaSA, a newly prepared melamine-based reagent. High yields of the products, relatively short reaction times, ease of the preparation, stability and reusability of the reagent, heterogeneous reaction conditions, and easy work-up are among the other advantages of this new method which make this procedure a useful and attractive addition to the methods available.

Experimental

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. All yields refer to the isolated products. Determination of the purity of the substrate and monitoring of the reaction were accomplished by thin-layer chromatography (TLC) on a silica-gel polygram SILG/UV 254 plates.

General procedure

A mixture of 1 mmol substrate, 0.12 cm^3 acetic anhydride (1.2 mmol), and 13 mg SaSA (0.05 mmol) in 3 cm^3 CH_2Cl_2 was stirred at room temperature or heated at reflux. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid residue was washed with 5 cm^3 CH_2Cl_2 and then dried. The recovered catalyst can be used for two further reactions. The organic layer was washed with 2 × 5 cm^3 saturated $NaHCO_3$ and 10 cm^3 water and dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on silica gel afforded the pure acetate.

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