ORIGINAL PAPER



Reusable and efficient polyvinylpolypyrrolidone-supported triflic acid catalyst for acylation of alcohols, phenols, amines, and thiols under solvent-free conditions

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Received: 19 February 2015/Accepted: 24 December 2016 © Springer-Verlag Wien 2017

Abstract A triflic acid-functionalized polyvinylpolypyrrolidone was prepared and fully characterized by FT-IR, TGA, and SEM. This super acidic solid catalyst shows high catalytic activity for selective acylation of alcohols, phenols, amines, and thiols with anhydrides under solvent-free conditions at room temperature. In addition, this method features an easy to handle solid super acid catalyst and an operationally simple procedure, affording the desired acylated products in excellent yields.

Graphical abstract



Keywords Acylation · Reusable · Solid acid · Solvent free · Thiols

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Introduction

Acyl transfer is at the heart of functional group transfers utilized both in nature and in the chemical laboratory. Acylations are part of the natural assembly machinery for the generation of complex molecules and for energy transport in biological systems. In contrast to nature, chemists utilize acylation reactions as a practical way for stereoselection and functional group protection. Commercial availability of the typical acylation reagents such as anhydrides, acyl halides, and carboxylic acids made the acyl group transfer one of the most common, successful and preparatively relevant enantioselective organocatalytic transformations [1-3]. The protection of alcohols, phenols, thiols, and amines is often necessary during the various transformations in a synthetic sequence, especially in the preparation of polyfunctional molecules, such as nucleosides, carbohydrates, steroids, and natural products [4-6]. In general, traditional methods for performing such a process involve the use of acid anhydride or acyl halide in the presence of a base like triethylamine or pyridine [7, 8]. In recent years, several synthetic methods have been reported for acylation reactions with acetic acid or acetic anhydride [9-12] showing varying degrees of successes as well as limitations including low yields, long reaction times, high cost of catalysts, use of hazardous materials, air or moisture sensitivity, elevated temperature, tedious workup, and requirement of anhydrous organic solvents. Therefore, there is still a need to develop a convenient catalytic system for the acylation reactions in terms of operational simplicity, reusability, economic viability, and greater selectivity.

Trifluoromethanesulfonic acid (triflic acid, CF₃SO₃H, TfOH) is a well-known strong acid which is used in many organic reactions including Friedel–Crafts reactions, polymerization, and Koch carbonylation [13, 14].





However, the recovery of the triflic acid from the reaction mixture results in the formation of large amounts of waste. The design of acid-catalyzed reactions over solids has found a pronounced need for further research in this area and supported triflic acid or materials with $-CF_2SO_3H$ group are becoming now available to replace homogeneous acid solutions [15].

Cross-linked polyvinylpolypyrrolidone (C-PVPP) is a cheap amphiphilic high molecular weight polymer bearing polar amine and carbonyl groups, which is insoluble in water, odorless, non-toxic, and recyclable [16–18]. These features make the C-PVPP a susceptible candidate for supporting the reactive center such as mineral acids.

Although the use of triflic acid supported on silica has been extensively studied [19–22], the study of triflic acid supported on polyvinylpolypyrrolidone is still very rare. Recently, we have investigated the immobilization of triflic acid (TfOH) onto polyvinylpolypyrrolidone (PVPP.OTf) and used it as an efficient catalyst in the synthesis of *bis*indolylmethanes [23], quinoxaline derivatives [24], and benzoxanthenes [25]. In continuation of our research work on the use of solid organocatalysts in organic transformations [26–28], we disclose the application of the immobilized super acid (PVPP.OTf; 4.3 mmol TfOH/g) as an efficient heterogeneous catalyst for the acylation of alcohols, phenols, amines, and thiols with anhydrides under solvent-free conditions at ambient temperature.

Results and discussion

The characterization of the Brønsted acid sites present in the polymer was performed by recording the FT-IR spectrum of PVPP.OTf, which shows a strong broad absorption at 3400 cm⁻¹ for the O–H bond and a moderate absorption at 1648 cm⁻¹ corresponding to the internal imine groups present in the pendant rings of the polymer (Fig. 1). The bands at 1225 and 1174 cm⁻¹ were assigned to the S=O asymmetric and symmetric stretching vibrations of $-SO_3^$ group, respectively [29].

The shape and surface morphology of the sample was investigated by SEM analysis. As shown in Fig. 2, the particle size of the polymer-supported triflic acid is similar to that of the polymer, which demonstrates that the particles of polymer had a good mechanical stability during the immobilization step. However, it is apparent from the SEM images that the surface of the PVPP is very slick (Fig. 2a), whereas the surface of PVPP.OTf catalyst (Fig. 2b) is greatly plain. This finding could demonstrate that the surface of PVPP is bonded to triflic acid, forming a compact and thin surface layer.

The stability of PVPP.OTf was determined by thermogravimetric analysis (Fig. 3). Thermal gravimetric analysis (TGA) was conducted over a temperature range from 30 to 650 °C at a heating rate of 10 °C min⁻¹ under N₂ atmosphere for the PVPP and compared with the parentsupported sample, PVPP.OTf. A weight loss below 110 °C is observed for the PVPP.OTf, which is due to the adsorbed water from the surface of the grafted polymer. This adsorbed water could be related to the high water-absorbing property of sulfonate moieties in spite of the strictly reduced pressure drying. The decomposition of the PVPP.OTf is characterized by two general steps, one in the region of 260-320 °C and the other over 400 °C. The former transitional weight loss involves the oxidation and degradation of sulfonic acid groups which probably begin near 250 °C. The decomposition of cross-linked polymer begins near 400 °C, a tendency that is consistent with that



Fig. 2 SEM images of PVPP (a) and PVPP.OTf (b)





Table 1 Effect of PVPP.OTf
loading and solvents in the
model reaction

Entry	PVPP.OTf loading/g (mol%)	Solvent	Time/min	Yield/% ^a
1	0	Solvent free	180	Trace
2	0.005 (2.2)	Solvent free	30	70
3	0.008 (3.4)	Solvent free	7	96
4	0.008 (3.4)	Toluene	60	50
5	0.008 (3.4)	CH_2Cl_2	120	30
6	0.008 (3.4)	THF	60	40
7	0.008 (3.4)	CH ₃ CN	60	50
8	0.008 (3.4)	Diethyl ether	120	20
9	0.01 (3.4)	Solvent free	7	98

Reaction conditions: benzyl alcohol (1 mmol), acetic anhydride (1 mmol), 2 cm³ solvent, r.t.

^a Isolated yield

of the PVPP. Thermal gravimetric analysis results reveals that the PVPP.OTf is thermally stable up to 260 °C under nitrogen flow atmosphere. The loading capacity of the reagent was determined by titration and found to be 4.3 mmol/g.

To investigate the catalytic activity of PVPP.OTf, the acylation of benzyl alcohol with acetic anhydride was chosen as a model reaction under different conditions and the results are given in Table 1. The best result was obtained with 1.0:1.0 molar ratios of benzyl alcohol and acetic anhydride in the presence of polyvinylpolypyrrolidonium triflate (3.4 mol%, 0.008 g) under solvent-free conditions at room temperature. The reaction is completed in 7 min with 96% yield (entry 3). Increasing either the amounts of catalyst and/or prolonging the reaction time does not improve the yield significantly (entry 9), while reducing the catalyst loading leads to a lower yield (entry 2).

 Table 2
 PVPP.OTf catalyzed the acetylation of alcohols and phenols under solvent-free conditions

Entry	R-OH	Time /min	Product	Yield /% ^b
1	ОН	7	3a	96
2	Н3СО ОН	5	3b	96
3	Н3СО ОН	6	3c	90
4	Вг	4	3d	91
5	ОН	7	3e	90
6	СІСІОН	8	3f	90
7	O2N OH	9	3g	95
8	Отон	12	3h	95
9	ОН	7	3i	90
10	ОН	7	3j	92
11	OH	22	3k	89
12	ОН	23	31	90
12	OH	14	2	05
15	ОН	14	2-	95
14	CI	16	3n	97
15	CI CI	13	30	97
16	Br	13	3р	96
17	O ₂ N	28	3q	86
18	UH	12	3r	92
19	OH	11	3s	92
	ОН	10	24	05
20	ОН	18	31	95
21	$\bigcirc \bigcirc \bigcirc$	40	3u	80
22	OH OH	8	3v	95
23	OH	13	3w	95
24	OH	14	3x	84
25	Уон	7	3у	95

Reaction conditions: alcohols (1 mmol), acetic anhydride (1 mmol), 0.008 g catalyst (3.4 mol%), solvent free, r.t.

^a Isolated yield

 Table 3 PVPP.OTf-catalyzed acylation of benzyl alcohol with different carboxylic anhydrides

Entry	Acylating reagent	Time/min	Yield/% ^b
1	Ac ₂ O	7	96
2	(EtCO) ₂ O	16	90
3	(iso-PrCO) ₂ O	20	87
4	(tert-BuCO) ₂ O	35	80
5	(PhCO) ₂ O ^a	40	80

Reaction conditions: benzyl alcohol (1 mmol), carboxylic anhydrides (1 mmol), 0.008 g catalyst (3.4 mol%), solvent free, r.t.

^a 2 equivalents of (PhCO)₂O was used

^b Isolated yield

With the established optimal conditions, the scope of the reaction was examined as highlighted in Table 2. A wide range of substrate combinations, such as *tert*-butanol, structurally modified secondary and primary benzylic alcohols, and different anhydrides (Tables 2, 3), were studied. In all cases, the reactions were clean and high yielding.

Structurally and electronically different benzylic and aliphatic alcohols underwent reaction with acetic anhydride at room temperature to afford the corresponding esters in high yields (Table 2, entries 1-8 and 20-22). It is important to note that in acylation of both primary and secondary alcohols, no by-product was observed (e.g., entries 9 and 23). Interestingly, hindered tertiary alcohols such as tertbutanol and triphenylmethanol, also gave the corresponding acylated products in high yields (Table 2, entries 21 and 25). The reaction also works well with primary and secondary allylic alcohols, affording the acetylation products in good yields and with complete stereoselectivity without isomerization or formation of undesired by-products (Table 2, entries 10 and 24). Moreover, activated, deactivated, and sterically hindered phenols were all acetylated smoothly (Table 2, entries 11–17). α - and β naphthols were also acetylated to afford the corresponding acetates in high yields (Table 2, entries 18 and 19). The results of Table 2 reveal that PVPP.OTf enables the acylation of various alcohols at room temperature.

To show the generality of this system, the reaction of benzyl alcohol was conducted with different carboxylic anhydrides under optimal reaction conditions (Table 3). For acylation with benzoic anhydride, two equivalents of $(PhCO)_2O$ were required (Table 3, entry 5). The results in Table 3 clearly show the highest activity of the Ac₂O compared with other anhydrides (comparing entry 1 with entries 2–5).

The competitive acetylation of 2-phenylethanol and phenol with one equivalent of acetic anhydride in the presence of PVPP.OTf (3.4 mol%, 0.008 g) was



 Table 4
 PVPP.OTf-catalyzed acetylation of amines and thiols under solvent-free conditions

Entry	R-XH	Time /min	Product	Yield /% ^D
1	NH ₂	4	4a	97
2	NH ₂	5	4b	97
3	H ₃ CO NH ₂	3	4c	98
4	CI NH2	3	4d	97
5	Br NH ₂	3	4e	97
6	O ₂ N NH ₂	9	4f	90
7	N NH2	7	4g	89
8	SH	19	4h	93
9	SH	15	4i	95
10	SH	20	4j	91

Reaction conditions: amines or thiols (1 mmol), acetic anhydride (1 mmol), 0.008 g catalyst (3.4 mol%), solvent free, r.t. ^a Isolated yield

carried out at room temperature under solvent-free conditions. After 7 min, only 2-phenylethyl acetate was formed, and phenol remained almost unaffected (Scheme 1).

The potential application of PVPP.OTf as a catalyst for acetylation of various amines and thiols was also investigated (Table 4). Excellent results were obtained at room temperature with one equivalent of acetic anhydride in the presence of PVPP.OTf (3.4 mol%, 0.008 g). The experimental procedure is very efficient, convenient, rapid, and has the ability to tolerate a variety of other functional groups, such as alkyl, methoxy, nitro, and halides under the optimal reaction conditions (Table 4, entries 1–10).

Recyclability of the catalyst was also examined in a model reaction. The catalyst was simply recovered from the reaction mixture by adding ethyl acetate after completion of the reaction, followed by filtration. The collected catalyst was dried under reduced pressure and was reused successively for the next four cycles (Table 5). As it is clear, the catalyst shows good catalytic activity even after the fourth run. The stability of the catalyst was further confirmed by determining the acid content of the used catalyst after the fourth run by the acid–base titration method (4.1 mmol/g H^+ sites).

In conclusion, we have developed a simple and highly efficient method for the acylation of various nucleophiles with acid anhydrides under mild conditions using PVPP.OTf as an efficient catalyst. The catalyst is easily prepared from commercially available polyvinylpolypyrrolidone and triflic acid. Short reaction times, mild reaction conditions, high yielding procedure, reusability of the catalyst, generality, and selectivity between alcohols and phenols together with compliance with the green chemistry protocol make this method a good alternative to the other existing methods.

Experimental

Chemical materials were purchased from Merck and Fluka Chemical Companies. All products are known compounds and their structures were identified by comparison of physical properties and spectral data with the authentic

Table 5 The r	ecyclability of
the catalyst in	the acetylation of
benzyl alcohol	

Cycle	1	2	3	4	5
Time/min	7	10	12	12	14
Yield/% ^a	96	94	92	90	90

Reaction conditions: benzyl alcohol (1 mmol), acetic anhydride (1 mmol), 0.008 g catalyst, solvent free, r.t.

^a Isolated yields

samples. Cross-linked polyvinylpolypyrrolidone (Divergan[®] RS) with average molecular weight more than 1,000,000 was purchased from Fluka. The progress of the reaction was monitored by thin-layer chromatography, TLC plates (silica gel 60 F₂₅₄). FT-IR spectra were recorded on a Bruker Tensor 27 spectrometer, using KBr pellets for solids. ¹H, ¹³C NMR spectra were recorded on a Bruker DRX-400 AVANCE instrument (400.1 MHz for ¹H, 100.6 MHz for ¹³C). Chemical shifts were on the δ scale, relative to internal Me₄Si. Thermogravimetric analysis (TGA) was conducted with TGA-50 analyzer in the temperature range of 30–650 °C at 10 °C/min under N₂. Scanning electron microscope (SEM) pictures were obtained using the VEGA//TESCAN KYKY-EM3200 microscope (acceleration voltage 26 kV).

Preparation of the polyvinylpolypyrrolidonium triflate (PVPP.OTf)

To a suspension of 3.0 g polyvinylpolypyrrolidone in 35 cm^3 toluene, 2.0 g TfOH (13 mmol) was added. The mixture was stirred magnetically for 60 min at r.t. The solvent was removed under reduced pressure and the residue was dried at 110 °C for 2 h to afford PVPP.OTf as a white powder. The number of H⁺ sites of PVPP.OTf was determined by acid–base titration to be 4.3 mmol/g.

General experimental procedure

To a mixture of substrate (1.0 mmol) and acetic anhydride (1.0 mmol), 0.008 g PVPP.OTf (3.4 mol%) was added. The mixture was stirred at room temperature for the time indicated in Tables 2, 3 and 4. The progress of the reaction was followed by TLC or GC for aliphatic alcohols. After completion of the reaction, ethyl acetate ($2 \times 10 \text{ cm}^3$) was added, and the catalyst was separated by filtration. The filtrate was washed with an aqueous solution of NaHCO₃ (10%, $2 \times 10 \text{ cm}^3$) and water ($2 \times 10 \text{ cm}^3$) and dried with Na₂SO₄. The solvent was evaporated under reduced pressure to afford the expected product. All the products are known and their structures were identified by comparison of the physical properties and spectral data with the authentic samples or literature data.

Acknowledgements We are grateful to the University of Mazandaran for supporting our research.

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