Highly chemoselective acetalization of carbonyl compounds catalyzed by a novel recyclable ammonium triflate-functionalized silica

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Abstract

A novel ammonium triflate-functionalized silica ($NH_4^+OTf^-@SiO_2$, ATFS) has been prepared and characterized by simple operation from commercially available and relatively cheap starting materials. Various types of aldehydes as well as cyclic ketones were selectively converted to the corresponding 1,3-dioxanes in the presence of ethyl orthoformate, 1,3-propanediol and a catalytic amount of ATFS catalyst via an *in situ* acetal-exchange process. The catalyst can be recovered and reused for at least six reaction cycles without considerable loss of its reactivity.
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1. Introduction

The protection of carbonyl compounds or diols as acetals is of paramount importance in organic synthesis, as shown by a large number of methods that have been developed for this key transformation [1–19]. Moreover, chiral acetals are particularly important precursor for the preparation of enantiomerically pure compounds [20]. The versatility of acetals requires the development of new improved and mild acetalization procedures, especially based on new selective acid catalysts [21–24]. On the other hand, many of the acid catalysts which have been explored for this transformation present limitations such as toxicity, corrosiveness, and tedious work-up procedure. However, ever-increasing environmental pressures have resulted in much attention being recently directed toward the development of environmentally friendly solid acid catalysts for clean processes in many of the fine chemical industries. Hence, various types of solid acids are receiving increased attention for various types of organic transformations due to their operational simplicity, selectivity coupled with the possibility of reusability [25–27]. A particularly interesting feature in this area is to design purely Lewis or purely Brønsted solid acids as well as those that have both characteristics and variable strength of acidity. Thus, a number of the silica-based solid acids such as HMS-supported zinc triflate [28], HMS-sulfonic acid [29], SBA-15-sulfonic acids [30], solid version of $AlCl_3$, BF_3, and SbF_3 [28], and MCM-type sulfonic acid [31] have been prepared. However, despite the importance and attractiveness of these solid acids less attention has been paid to the widespread application of these materials and also design and preparation of milder version of solid acids. Along the line of our studies in design and application of new solid catalysts in chemical transformation [32–42], we wish to introduce a new version of ammonium triflate-functionalized silica (ATFS) as a mild and recyclable Brønsted solid acid for chemoselective acetalization of carbonyl compounds.

2. Experimental

2.1. General remarks

Chemicals were either prepared in our laboratories or purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products unless otherwise stated. The products were characterized by comparison of their physical data with those of known samples or by their spectral data. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 500 MHz spectrometer in $CDCl_3$ as the solvent and TMS as internal standard. Most

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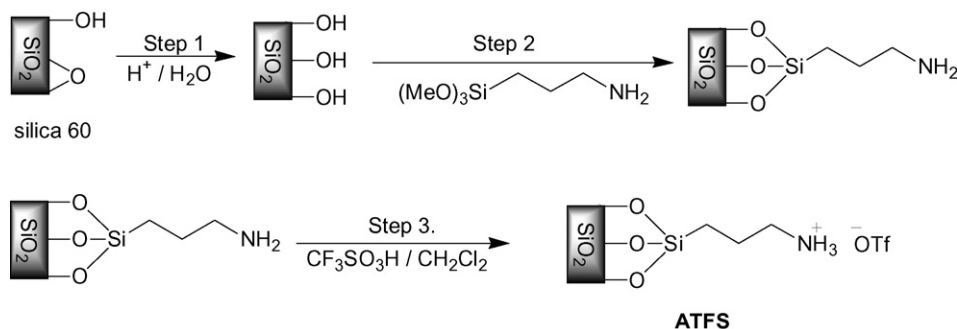
Scheme 1.

of the products are known and all of the isolated products gave satisfactory IR and NMR spectra.

2.1.1. Preparation of ammonium triflate-functionalized silica (ATFS) catalyst

Mesoporous silica gel (average pore diameter 60 Å) was activated by refluxing in concentrated hydrochloric acid (6 M) and then washed thoroughly with the deionized water and dried before undergoing chemical surface modification. Refluxing the activated silica gel (10 g) with 3-aminopropyltrimethoxysilane (3.3 mmol) in dry toluene for 18 h. The solid material was then filtered off and washed with hot toluene for 12 h in a continuous extraction apparatus (Soxhlet) and then dried in oven at 110 °C overnight to give the surface bound amine (AMPS) group at a loading *ca.* 0.31 mmol g^{-1} (by elemental analysis and back titration). The resulting AMPS were allowed to react with twofold excess of CF_3SO_3H in dry CH_2Cl_2 for 8 h and then filtered and washed successively with CH_2Cl_2, EtOH and Et_2O and then dried in a vacuum desiccator at 40 °C overnight to afford ATFS.

2.1.2. General experimental procedure

To a solution of the carbonyl compound (2 mmol), 1,3-propanediol (6–10 mmol) and $(EtO)_3CH$ (2.2 mmol), in anhydrous CH_2Cl_2 (50 mL), ATFS (0.08 mmol, 0.258 g) was added, and the resulting mixture was stirred at room temperature. After completion of the reaction (TLC or GC), the reaction mixture was filtered to a cold aqueous solution of NaOH (10%, 25 mL) and the filter cake was washed with CH_2Cl_2 and the catalyst was recovered. The organic phase was separated and washed with water (2 × 15 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure gave almost pure product(s). The organic solvent (CH_2Cl_2) was collected, distilled and used in the other experiments. Further purifica-
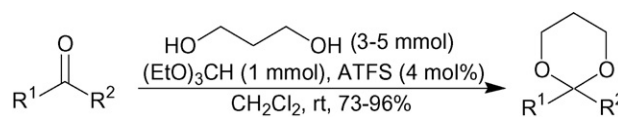
Scheme 2.

Table 1
Chemoselective acetalization of carbonyl compounds under mild conditions using ATFS in the presence of triethyl orthoformate (TEO) and 1,3-propanediol

| Entry	R^1	R^2	Subst./diol/TEO/ATFS	Time (h)	Yield[a] (%)
1	Ph	H	1:3:1.1:0.04	12	89
2	$4\text{-}(Cl)C_6H_4$	H	1:3:1.1:0.04	16	90
3	$4\text{-}(MeO)C_6H_4$	H	1:3:1.1:0.04	8	90
4	$4\text{-}(i\text{-}Pr)C_6H_4$	H	1:3:1.1:0.04	5	89
5	$4\text{-}(NO_2)C_6H_4$	H	1:3:1.1:0.04	24	95
6	Citral (mixture)		1:5:1.1:0.04	24	90[b]
7	$n\text{-}C_3H_7$	H	1:3:1.1:0.04	15	84
8	$n\text{-}C_6H_{13}$	H	1:3:1.1:0.04	11	95
9	Ph—cyclohexanone		1:5:1.1:0.04	10	73
10	cyclododecanone		1:5:1.1:0.04	14	75
11	C_6H_4	CH_3	1:5:1.1:0.04	48	–[c]
12	$PhCH_2CH_2$	CH_3	1:5:1.1:0.04	48	–[c]
13	$CH_3CH{=}CH$	CH_3	1:5:1.1:0.04	48	–[c]
14	Cyclohexenone		1:5:1.1:0.04	48	–[d]

[a] Isolated yields.
[b] GC conversion.
[c] No reaction.
[d] Less than 25% conversion.
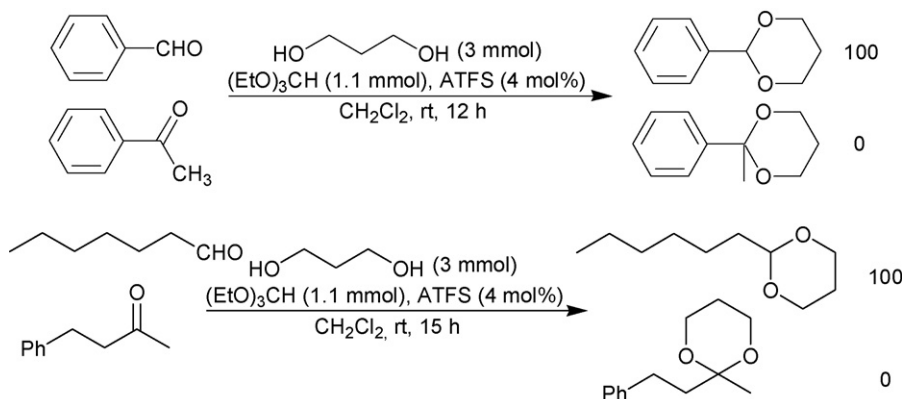
Scheme 3.
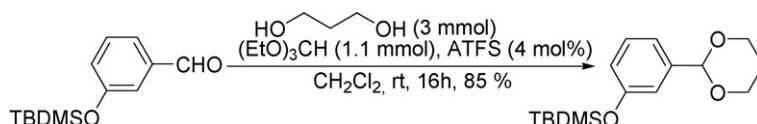
Scheme 4.

tion was proceeded by vacuum distillation or recrystalization in appropriate solvent to afford pure acetals (Table 1).

3. Results and discussion

The catalyst precursor aminopropyl silica (AMPS) was prepared according to the literature procedure [43]. The preparation of the silica-supported ammonium triflate is summarized in Scheme 1. Typically, surface bound ammonium triflate at a loading *ca.* $0.31 \, \text{mmol} \, \text{g}^{-1}$ (by TGA analysis) was obtained.

In continuation, we hypothesized that this solid version of ammonium triflate might be a suitable and mild acid catalyst for acetalization of carbonyl compounds. In this regard, we have observed that 1,3-dioxanes of various types of aldehydes could be prepared using 1,3-propanediol (3–5 mmol) in the presence of $(\text{EtO})_3\text{CH}$ (1.1 mmol, as dehydrating agent) and a catalytic amounts of ATFS (4 mol%) in dry CH_2Cl_2 at room temperature (Scheme 2, Table 1, entries 1–8).

In two separate blank experiments we found that no considerable acetalization was observed under similar reaction conditions in the absence of ATFS or in the presence of silica, respectively. Cyclic ketones were also converted into their acetals in satisfactory yields under the same reaction conditions to afford the corresponding 1,3-dioxane in good yields (Table 1, entries 9, 10).

Interestingly, under the described reaction conditions other types of ketones including open-chain aliphatic ketones and aromatic ketones and α,β-unsaturated ketones survived intact under the presented reaction conditions even after prolonged reaction time (Table 1, entries 11, 14). Therefore, it might be possible to utilize this protocol for the chemoselective acetalization of aldehydes in the presence of ketones. Based on reactivity difference between aldehydes and ketones, we have also monitored chemoselective acetalization of aldehydes in the presence of ketones. We found that benzaldehyde and heptanal were con-

verted to their acetals in the presence of acetophenone and benzylacetone, respectively, with high degree of chemoselectivity (Scheme 3).

An interesting challenging problem during many syntheses of reasonable complexity is how to protect a carbonyl group in the presence of a wide variety of sensitive functional groups. Along this line, we have found that the presented method even tolerates highly acid sensitive TBDMS ethers (Scheme 4). This observation clearly shows that the present ATFS could be safely utilized for chemoselective acetalization of molecules comprising acid-sensitive functional groups.

When using a supported catalyst the most important points are the deactivation and reusability of the catalyst. Our preliminary examination shows that ATFS is reusable. Thus, after the successful acetalization of 4-iso-propylbenzaldehyde in first run, which gave the corresponding 1,3-dioxane in 89% isolated yield (Table 1, entry 2), the ATFS catalyst was subjected to a second acetalization reaction from which it gave the acetal in 86% yield; the average chemical yield for five consecutive runs was 85%, which clearly demonstrates the practical recyclability of this catalyst.

4. Conclusion

In conclusion, a novel ammonium triflate-functionalized silica (ATFS), which can be prepared by simple operation from commercially available and relatively cheap starting materials, efficiently catalyzes the chemoselective acetalization of a variety of aldehydes and cyclic ketones. It can also be recovered and reused for several reaction cycles without considerable loss of reactivity. Further investigations on the development of organic transformations using this new heterogeneous Brønsted acid are ongoing in our laboratories.

All products gave satisfactory IR spectra. Some representative NMR data are as follows:

2-(4-Chlorophenyl)-1,3-dioxane: ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C, TMS): $(=7.40$–7.49 (d, $J=8.0$ Hz, 2H), $(=7.30$–7.34 (d, $J=8.0$ Hz, 2H), $(=5.44$ (s, 1H), $(=4.20$–4.26 (dd, $J=5.0$ Hz, $J=11.3$ Hz, 2H), $(=3.88$–3.98 (*pseudo*-t, $J=11.3$ Hz, 2H), $(=2.14$–2.23 (tq, $J=5$ Hz, $J=13.2$ Hz, 1H), $(=1.37$–1.43 (quind, $J=1.2$ Hz, $J=13.2$ Hz 1H); ^{13}C NMR(63 MHz, CDCl$_3$, 25 °C, TMS): $(=137.70$, 134.95, 128.81, 127.91, 101.19, 67.78, 26.09.

2-(4-Nitrophenyl)-1,3-dioxane: ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C, TMS): $(=7.98$–8.28 (d, $J=9.0$ Hz, 2H), $(=7.62$–7.73 (d, $J=9.0$ Hz, 2H), 5.54 (s, 1H), $(=4.24$–4.51 (dd, $J=5$ Hz, $J=13.8$ Hz, 2H), $(=3.94$–4.05 (*pseudo*-t, $J=13.8$ Hz, 2H), $(=2.13$–2.25 (tq, $J=5$ Hz, $J=13.3$ Hz, 1H), $(=1.43$–1.50 (quind, $J=1.1$ Hz, $J=13.3$ Hz, 1H); ^{13}C NMR(63 MHz, CDCl$_3$, 25 °C, TMS): $(=154.5$, 147.05, 132.33, 127.50, 102.52, 67.80, 34.5.

1,5-Dioxa-spiro[5.11]heptadecane: ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C, TMS): $(=3.57$–3.79 (m, 4H), $(=1.59$–1.66 (m, 6H), $(=1.16$–1.26 (m,broad, 18H), ^{13}C NMR(63 MHz, CDCl$_3$, 25 °C, TMS): $(=100.77$, 60.28, 60.03, 40.30 (two peak), 36.50, 30.29 (7 peak), 19.25 (two peak).

9-Phenyl-1,5-dioxa-spiro[5.5]undecane: ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C, TMS): $(=7.29$–7.32 (m, 2H), 7.24–7.26 (m, 2H), 7.18–7.22 (tt, $J=1.4$ Hz, $J=7.2$ Hz, 5H), 3.97–4.00 (t, $J=5.7$ Hz, 2H), 3.93–3.95 (t, $J=5.7$ Hz, 2H), 2.56–2.60 (tt, $J=4.4$ Hz, $J=11.7$ Hz, 1H), 2.40–2.45 (m, 2H), 1.74–1.80 (m, 6H), 1.47–1.54 (m, 2H); ^{13}C NMR(125 MHz, CDCl$_3$, 25 °C, TMS): $(=154.93$, 128.23, 126.57, 98.36, 55.01, 66.81, 33.73, 29.76, 28.36, 28.35.

***tert*-Butyl-(3-[1,3-dioxane-2-yl-phenoxy)-dimethylsilane**: ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C, TMS): $(=7.22$–7.25 (t, $J=7.9$ Hz, 1H), 7.02–7.11 (d, $J=7.9$ Hz, 1H), 7.01 (t, $J=2.0$ Hz, 1H), 6.82–6.84 (dd, $J=7.9$ Hz, $J=2.0$ Hz, 2H), 5.46 (s, 1H), 4.24–4.28 (dd, $J=11.0$ Hz, $J=5.0$ Hz, 2H), 3.93–3.99 (*pseudo*-t, $J=11.0$ Hz, 2H), 2.17–2.26 (tq, $J=5$ Hz, $J=12.4$ Hz), 1.39–1.44 (quind, $J=2.4$ Hz, $J=12.4$ Hz, 1H), 1.02 (s, 9H), 0.23 (s, 6H). ^{13}C NMR(125 MHz, CDCl$_3$, 25 °C, TMS): $(=155.62$, 140.40, 129.21, 120.22, 119.02, 117.94, 101.38, 67.35, 25.82, 25.76, 18.20, -4.35.

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