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Cerium Polyoxometalate as a Reusable Catalyst for Acetylation and Formylation of Alcohols

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Summary. Efficient esterification of primary and sterically-hindered secondary or tertiary alcohols with acetic anhydride was achieved in the presence of ammonium decatungestocerate(IV) icosahydrate, $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$, as catalyst in high yields. Primary and secondary alcohols were also converted to their corresponding acetates and formates with acetic acid and ethyl formate in the presence of this catalyst. Easy work-up, non-toxicity, reusability, and stability of the catalyst are noteworthy advantages of this method.

Keywords. Cerium polyoxometalate; Acetylation; Formylation; Alcohol.

Introduction

Developing efficient and mild methods for the protection of hydroxyl groups of alcohols is of importance in synthetic organic chemistry. One of the most common methods for the protection of these compounds is the formation of acetyl derivatives [1].

The protection of such functional groups is often necessary during the course of various transformations in a synthesis sequence, in particular in the construction of polyfunctional molecules such as nucleosides, carbohydrates, steroids, and natural products. A number of methods and reagents such as 4-(dimethylamino)pyridine, 4-pyrrolidinopyridine [2], *N*,*N*,*N*′,*N*′-tetramethylethylenediamine [3], tributylphosphine [4], iodine [5], *p*-toluenesulfonic acid [6], alumina [7], zinc chloride [8], cobalt chloride [9], montmorillonite K-10 and KSF [10], zeolite HSZ-360 [11], zirconium sulfophenyl phosphonate [12], scan-

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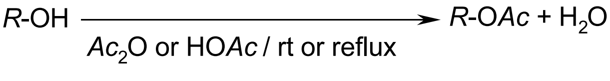
dium trifluoromethanesulfonate $[\mathrm{Sc(O}\mathit{Tf})_3]$ [13], $TaCl_5$ [14], trimethylsilyl trifluoromethanesulfonate [15], copper trifluoromethanesulfonate [16], indium trifluoromethanesulfonate [17], magnesium bromide [18], bismuth(III) salts [19], ferric perchlorate adsorbed on silica-gel [20], and tin(IV) tetraphenylporphyrin perchlorate [21] have been reported for the acetylation of alcohols. Formylation is also a very important process and several catalysts, such as bismuth(III) salts [22], $Cu(NO_3)_2 \cdot 3H_2O$ [23], and $\mathrm{Ce(O}\mathit{Tf})_4$ [24] have been used for this transformation. Due to the instability of the anhydride and the acid chloride of formic acid, formylation of alcohols by ethyl formate is an important synthetic reaction.

However, some of the reported methods for the acetylation and formylation of alcohols suffer from one or more of the following disadvantages, such as high temperature and drastic reaction conditions, formation of undesirable or toxic byproducts, expensive reagents, hygroscopicity and thermal instability of the reagents, long reaction times, low yields of the desired products and bulk requirement of solid bed. Therefore, introduction of new methods and catalysts for the preparation of esters is still in demand.

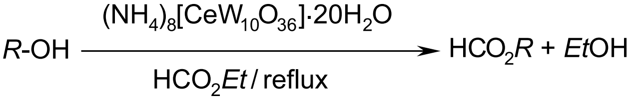
In recent years there has been a tremendous upsurge of interest in various chemical transformations performed under heterogeneous catalysis [25]. Moreover, using inexpensive and none corrosive heterogeneous catalysts, chemical transformations occur with better efficiency, higher purity of products, and easier work-up, with evident economic and ecological advantages especially for industrial processes.

Polyoxometalates have been proven to be good catalysts in various oxidations. They are applied in bulk or in supported forms, and both homogenous and heterogeneous catalysis are possible. Due to their acidic and redox properties, heteropoly compounds are useful and versatile catalysts in a number of transformations [26]. In continuation of our research on the application of polyoxometalates in organic synthesis [27–32], we wish to report a simple, efficient, and selective method for the acetylation of alcohols with acetic anhydride and acetic acid (Scheme 1) and formylation of alcohols with ethyl formate (Scheme 2) using $(NH_4)_8[CeW_{10}O_{36}] \cdot 20H_2O$ as a heterogeneous, reusable, and stable catalyst at room temperature or under reflux conditions.



$$\mathit{R}\text{-OH} \xrightarrow[\mathit{Ac}_2\text{O or HO}\mathit{Ac}\text{ / rt or reflux}]{(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O} \mathit{R}\text{-O}\mathit{Ac} + H_2O$$

Scheme 1



$$\mathit{R}\text{-OH} \xrightarrow[\text{HCO}_2\mathit{Et}\text{ / reflux}]{(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O} \text{HCO}_2\mathit{R} + \mathit{Et}\text{OH}$$

Scheme 2

Results and Discussion

Acetylation of Alcohols with Acetic Anhydride and Acetic Acid Catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$

Initially, benzyl alcohol was chosen as a model substrate for the acylation reactions. The reaction of this alcohol with acetic anhydride ($2\,cm^3$) in the presence of 0.04 molar equivalents of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ at room temperature was completed in 30 min and the corresponding acetate was obtained in 96% yield. In the absence of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ as catalyst, Ac_2O was much less efficient for the conversion of alcohols to esters (5–12%).

As shown in Table 1 a series of primary alcohols (including aliphatic and aromatic alcohols) and secondary alcohols were acetylated with Ac_2O in the presence of 0.04 mol% of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ at room temperature or under reflux conditions. Tertiary alcohols such as 1-adamantanol and triphenylmethanol were also acetylated in good yields (entries 17 and 18). In contrast with the data reported with other heterogeneous catalysts such as montmorillonite clay [10],

Table 1. Acetylation of alcohols with Ac_2O and $HOAc$ catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ at reflux[a]

Entry	Alcohol	Product[b]	Acetic anhydride		Acetic acid	
			Time /min	Yield /%[c]	Time /h	Yield /%[c]
1	$PhCH_2OH$	$PhCH_2OAc$	30	96	8	90
2	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CH_2OAc$	5	100	8	87
3	$4\text{-}CH_3OC_6H_4CH_2OH$	$4\text{-}CH_3OC_6H_4CH_2OAc$	15	96	6	94
4	$3\text{-}CH_3OC_6H_4CH_2OH$	$3\text{-}CH_3OC_6H_4CH_2OAc$	30	90	6	78
5	$2\text{-}NO_2C_6H_4CH_2OH$	$2\text{-}NO_2C_6H_4CH_2OAc$	90	97	8	36
6	$PhC_6H_4CH_2OH$	$PhC_6H_4CH_2OAc$	90	80	8	82
7	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CH_2OAc$	15	100	4	90
8	*n*-Pentanol	*n*-Pentyl acetate	15	97	5	95
9	*n*-Heptanol	*n*-Heptyl acetate	15	99	8	91
10	*n*-Octanol	*n*-Octyl acetate	15	99	8	93
11	2-Ethylhexanol	2-Ethylhexyl acetate	15	97	4	96
12	Cyclohexanol	Cyclohexyl acetate	90	92	6	40
13	Menthol	Menthyl acetate	90	88	6	30
14	$PhCH(OH)CH_3$	$PhCH(OAc)CH_3$	15	98	6	60
15	α-Tetralol	α-Tetralyl acetate	90	80	4	33
16	Phenyl-2-pyridylmethanol	Phenyl-2-pyridylmethyl acetate	90	98	6	50
17	1-Adamantanol	1-Adamantyl acetate	180	92	8	0
18	Triphenylmethanol	Triphenylmethyl acetate	180	72	8	0

[a] In entries 1 and 3 alcohols reacted in acetylation with Ac_2O at room temperature; [b] all products were identified by comparison of their physical and spectral data with those of authentic samples; [c] isolated yields

zeolite HSZ-360 [11], and zirconium sulfophenyl phosphonate [12], these results clearly indicate that $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ is an excellent catalyst for the acetylation of tertiary alcohols.

We extended the scope of this process by performing the reaction in acetic acid. The results, which are summarized in Table 1, show that $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ could catalyze the acetylation of primary and secondary alcohols in refluxing acetic acid with good yields. Tertiary alcohols, such as 1-adamantanol and triphenylmethanol (entries 17 and 18), remained unchanged under this reaction condition.

Formylation of Alcohols with Ethyl Formate Catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$

The formylation of alcohols in refluxing ethyl formate was also investigated in the presence of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$. The experimental results show that primary and secondary alcohols are converted to their corresponding formates in the presence of 0.04 mol% of the catalyst in good yields (Table 2), whereas under this condition tertiary alcohols such as 1-adamantanol and triphenylmethanol (entries 17 and 18) remained unchanged in the reaction mixture. It is worth mentioning that cerium polyoxometalate $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ can be used as a recyclable

Table 2. Formylation of alcohols with ethyl formate catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ at reflux

Entry	Alcohol	Product[a]	Time/h	Yield/%[b]
1	$Ph\mathrm{CH_2OH}$	$Ph\mathrm{CH_2OCOH}$	5	60
2	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CH_2OCOH$	7	58
3	$4\text{-}CH_3OC_6H_4CH_2OH$	$4\text{-}CH_3OC_6H_4CH_2OCOH$	3	95
4	$3\text{-}CH_3OC_6H_4CH_2OH$	$3\text{-}CH_3OC_6H_4CH_2OCOH$	9	85
5	$2\text{-}NO_2C_6H_4CH_2OH$	$2\text{-}NO_2C_6H_4CH_2OCOH$	5	50
6	$Ph\mathrm{C_6H_4CH_2OH}$	$Ph\mathrm{C_6H_4CH_2OCOH}$	5	73
7	$Ph\mathrm{CH_2CH_2CH_2OH}$	$Ph\mathrm{CH_2CH_2CH_2OCOH}$	5	86
8	*n*-Pentanol	*n*-Pentyl formate	5	85
9	*n*-Heptanol	*n*-Heptyl formate	6	84
10	*n*-Octanol	*n*-Octyl formate	6	83
11	2-Ethylhexanol	2-Ethylhexyl formate	6	70
12	Cyclohexanol	Cyclohexyl formate	5	44
13	Menthol	Menthyl formate	7	35
14	$Ph\mathrm{CH(OH)CH_3}$	$Ph\mathrm{CH(OCOH)CH_3}$	5	47
15	α-Tetralol	α-Tetralyl formate	5	11
16	Phenyl-2-pyridylmethanol	Phenyl-2-pyridylmethyl formate	5	40
17	1-Adamantanol	1-Adamantyl formate	5	0
18	Triphenylmethanol	Triphenylmethyl formate	5	0

[a] All products were identified by comparison of their physical and spectral data with those of authentic samples; [b] isolated yields

catalyst for the acetylation of alcohols without loss of catalytic activity (see experimental section).

In conclusion, we have demonstrated that $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ is an efficient, reusable, and heterogeneous catalyst for the acetylation and formylation of alcohols. The advantage of this system is that even hindered substrates can be acetylated with acetic anhydride in high yields. In addition, short reaction times, simple work-up, stability, non-toxicity, and ease of preparation of the catalyst make this method a useful addition to the present methodologies.

Experimental

All products were characterized by comparison of their spectral and physical data with those of authentic samples. ^1H NMR spectra was recorded in $CHCl_3$ as solvent on a Bruker AM 80 MHz spectrometer using *TMS* as an internal standard. Infrared spectra were run on a Philips PU9716 or Shimadzu IR-435 spectrophotometer. All GC analyses were performed on a Shimadzu GC-16A instrument with a flame ionization detector using silicon DC-200 or Carbowax 20-M columns. The catalyst was characterized by UV-vis, IR spectroscopy, magnetic susceptibility, thermal gravimetric analysis (TGA), and elemental analysis. Chemicals were purchased from Fluka and Merck chemical companies.

Preparation of the Catalyst

Ammonium decatungestocerate icosahydrate was prepared according to Peacok [33]. $Na_2WO_4\cdot 2H_2O$ (25 g, 75 mmol) was dissolved in 100 cm^3 of ion-exchanged H_2O, the *pH* of which was adjusted to 7.2 by addition of acetic acid. After heating to 90°C with stirring, an aqueous solution containing $(NH_4)_4Ce(SO_4)_2\cdot 2H_2O$ (4.75 g, 7.5 mmol) and 1 equiv of H_2SO_4 were added to make CeW_{10} form in the solution. This solution was obtained after filtration and used as catalyst. The structure of the catalyst was confirmed by IR, UV-vis, magnetic susceptibility, thermal gravimetric analysis (TGA), and elemental analysis.

General Procedure for Acetylation of Alcohols with Acetic Anhydride Catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$

In a round-bottom flask (25 cm^3) equipped with a magnetic stirrer, a solution of 1 mmol of alcohol in 2 cm^3 of Ac_2O was prepared. To this solution 0.04 mmol of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ were added and the reaction mixture was stirred at room temperature or under reflux conditions. The reaction progress was monitored by GLC. After completion of the reaction, the suspension was filtered and washed with 10 cm^3 of CH_2Cl_2. Evaporation of the solvent followed by chromatography on a short column of silica-gel gave the pure product.

General Procedure for Acetylation of Alcohols with Acetic Acid Catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$

To a solution of 1 mmol of alcohol in 3 cm^3 of acetic acid were added 0.04 mmol of catalyst and the reaction mixture was stirred under reflux. The progress of the reaction was monitored by GLC. Acetic acid was removed under reduced pressure and 20 cm^3 of ether were added. The reaction mixture was washed with 5% $NaHCO_3$ solution, then with H_2O, and dried ($MgSO_4$). Evaporation of the solvent followed by silica-gel chromatography provided the pure acetate.

General Procedure for Formylation of Alcohols with Ethyl Formate Catalyzed by $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$

Alcohol (1 mmol) and 0.04 mmol of catalyst were mixed together in 3 cm^3 of ethyl formate. The reaction mixture was stirred under reflux. The progress of the reaction was monitored by GLC. The solution was evaporated under reduced pressure and 20 cm^3 of ether were added. The reaction mixture was washed with H_2O and dried (Na_2SO_4). Evaporation of the solvent followed by chromatography on a short column of silica-gel gave the pure formate.

Catalyst Reuse and Stability

The stability of $(NH_4)_8[CeW_{10}O_{36}]\cdot 20H_2O$ was studied in repeated acetylation reactions. The acetylation of 1-heptanol with Ac_2O was chosen as a model substrate for studying of catalyst's reuse and stability. The reaction was carried out as described above. At the end of each reaction, the catalyst was removed by filtration, washed with H_2O and acetone, and reused. After the use of catalyst for four consecutive cycles, the yield of 1-heptyl acetate produced from the reaction of 1-heptanol with acetic anhydride was 99% and after six times was 86%.

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