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Preyssler heteropolyacid $H_{14}[NaP_5W_{29}MoO_{110}]$: A heterogeneous, green and recyclable catalyst used for the protection of functional groups in organic synthesis

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ABSTRACT

Efficient protection of alcohols, phenols, amines, thiols and aldehydes has been carried out under catalysis by the highly active Preyssler heteropolyacid $H_{14}[NaP_5W_{29}MoO_{110}]$ ($H_{14}PMo$). In this paper we report the catalytic activity of bulk $H_{14}PMo$ in each procedure to form: 2-tetrahydropyranyl acetals of alcohols and phenols, working at room temperature and using toluene as solvent; aldehyde 1,1-diacetates (acylals), a solvent-free preparation using Ac_2O at room temperature; alcohol acetates, phenols, amines and thiols, working at room temperature, using toluene as solvent and Ac_2O as acetylating agent; benzhydryl-ethers from the reaction of alcohols or phenols and diphenylmethanol, in toluene at 60–80 °C; and silylation of phenol and alcohols with hexamethyldisilazane as silylating agent in toluene at 85 °C.

All the described procedures provide useful alternatives for performing the protection of different functional groups, which are general, rapid, selective and inexpensive, and have a low environmental impact. The catalyst was easily recovered and reusable in all of the described procedures, without loss of its catalytic activity.

1. Introduction

The use of protecting groups is highly significant in organic synthesis and is often the key to the success of many synthetic enterprises. Protection and deprotection of functional groups are often necessary during the course of a synthetic sequence, especially in the construction of polyfunctional compounds such as nucleosides, carbohydrates, steroids, and other natural products [1]. There are various procedures for carrying out these transformations [2,3].

Transformations of phenols and alcohols into their mixed acetals, ketals, ethers or esters, have been recognized as useful methods for performing the hydroxyl group protection. Tetrahydropyranyl acetal is one of the most common and useful derivatives for this protection, because of its easy formation, relatively easy removal, stability of the to various nonacidic reaction conditions, resistance to oxidizing and reducing agents and also because of the reagent is of low cost.

Introduction of a protecting group to on oxygen is usually carried out using a mineral acid [4] as catalyst, either in liquid phase or adsorbed on a solid support [5]. THP-ethers can be prepared from the corresponding hydroxyl compound and 3,4-dihydro-2*H*-pyran (DHP). A number of catalysts have been used for performing the tetrahydropyranylation. The reaction has been carried out in the presence of soluble acids such as protic [6] and Lewis acids [7,8]. Besides, tetrahydropyranylation has been carried out using some recoverable heterogeneous catalysts, for example, ion exchange resins [9], zinc chloride on alumina, natural kaolinite clay and sulfuric acid adsorbed on silica [5], heteropolyoxometalates [10], heteropolyacids (HPAs) [11–13], $AlCl_3$ supported on polystyrene [14], and sulfonic acids supported on silica [14].

Acylals are interesting as an alternative to acetals for the protection of aldehydes because of their stability to non-nucleophilic bases and neutral media, and some 1,1-diacetates have been used for the synthesis of dienes for Diels–Alder reactions [15]. Preparation of acylals (1,1-diacetates) from aldehydes and acetic anhydride generally involves the use of strong protic acids such as sulfuric, methanesulfonic or phosphoric acids [16–18], or Lewis acids such as $FeCl_3$ [19], $ZnCl_2$ [15], PCl_3[15], and LiOTf [19]. Nafion-H also has been used [20]. In some cases, these methods are not entirely satisfactory because of low yields, long reaction times and some environmental problems. Several suitable catalysts have been employed more recently, for example, iodine

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[21], expansive graphite [22], bulk and supported heteropolyacids [23–25], Fe^{3+} on montmorillonite [26], and PVC-$FeCl_3$ complex [27].

Acetylation is another general method for the protection of the hydroxyl group; thiols and amines can also be protected. Different procedures can be applied [2], involving an acid chloride or acid anhydride with a base or an acid anhydride in the presence of an acid catalyst [28–31]. Currently used as homogeneous catalysts for this purpose are *p*-toluenesulfonic acid and sulfamic acid [32], and a variety of Lewis acids including simple salts [33–36], various triflates [32,37] and heteropolycompounds [38–40]. Besides, NBS [41], $Sc(NTf_2)_3$ [42], and PPh_3/CBr_4 [43] for achieving alcohol acetylation and formylation have been employed as catalysts. Amines and thiols are acylated using Lewis acids as catalysts, for example LiCl $Mg(ClO_4)_2$ or $InCl_3$ [44]. In spite of their efficiency, the above mentioned soluble catalysts have some disadvantages: the industrial use of mineral acids leads to hard environmental problems due to highly acidic waste streams. Lewis acids are efficient as catalysts but most of them are wasteful because they are usually hydrolyzed during the isolation, and triflates are generally expensive. Bases lead to the formation of their salts, having one of the lowest economics of reaction.

There are several methods to prepare benzhydryl ethers of phenols and alcohols. DMP-ethers are commonly used in organic synthesis because they are relatively inexpensive to prepare and stable towards a variety of reagents; benzhydryl ethers are also found as a structural moiety of several pharmacologically active compounds. There are literature reports on several reagents for the preparation of DMP-ethers, such as diphenylmethanol in the presence of concentrated sulfuric [45] or *p*-toluenesulfonic acids [46], $Y(OTf)_3$-$FeCl_3$ [47], iron salts [48], or diphenylmethyl chloride or bromide in the presence of a base [49]. More recently, Nafion-H and silica supported Wells Dawson heteropolyacid were used as efficient and reusable catalysts [50,51].

The trimethylsilyl group is one of the most important and is widely used for protecting the hydroxyl function; besides, it is often used to prepare silyl ethers as volatile derivatives of alcohols and phenols [52]. Silyl ethers have a general stability in most nonacidic reagents and also a high solubility in nonpolar solvents [53]. Several methods have been reported for silylating the hydroxyl group, including the reaction of an alcohol with a trimethylsilyl halide in the presence of the stoichiometric amount of a base, such as imidazole [54], or 4-(*N*,*N*-dimethylamino)pyridine [55]; with trimethylsilyl triflate, which is more reactive than chloride; or allylsilanes in the presence of a catalytic amount of *p*-toluenesulfonic acid, iodine, trifluoromethane sulfonic acid, and $Sc(OTf)_3$ [52]. However, some of these methods have frequently suffered from drawbacks such as lack of reactivity or the difficulty in removing the amine salt derived from the reactions of by-produced acid and co-bases during the silylation reaction [56]. In this way, hexamethyldisilazane (HMDS) is a cheap, commercially available, and stable compound that can be used for the preparation of trimethylsilyl ethers from hydroxyl compounds [57]. Its handling does not require special precautions, and the workup is not time-consuming, because the only by-product of the reaction is ammonia, which is easily removed from the reaction medium [53]. Even though the handling of this reagent is easy, the low silylating power of HMDS is the main drawback to its application; therefore, there is a variety of catalysts for performing the activation of this reagent [58], such as amines, $(CH_3)_3SiCl$ [59], phosphomolybdic acid [60], H-β-zeolite [61], alumina/KF [62], metal triflates [63], perchloric acid supported on silica gel [58], and sulfonic acid-functionalized ordered nanoporous silica [53]. Recently Mojtahedi et al. reported an efficient solvent-free method for the preparation of silyl ethers in the presence of no additive using ultrasound to promote the protection reactions [57].

In recent years great interest has developed in the reactions performed under heterogeneous catalysis, because of the possibility of recovering and recycling the acid catalyst, reducing the environmental impact to a large extent. A diversity of noncorrosive materials has been used as heterogeneous catalysts. Some of them are zeolite HSZ-360 [64], Nafion-H [65], $ZrOCl_2{\cdot}8H_2O$ in solvent-free conditions [66], and solid- supported reagents (SSRs) under microwave irradiation [67]. In general, the reactions proved to be simpler and cleaner, having excellent yields.

The environmental problems mainly associated with the handling and disposal of the inorganic acids, and their potential hazards, have attracted the chemists attention to the development of alternative processes using novel catalysts. Among them, heteropolycompounds are useful and versatile to a number of transformations because of their redox and superacidic properties [68].

Heravi's research group has studied the Preyssler heteropolyacids as green and recyclable catalysts. They are most active and selective than Wells Dawson and Keggin heteropolyacids. Some advantages described by Heravi are high stability (pH 0–12), and high thermal stability, having a large number of acidic protons [69]. An important number of sustainable organic transformations have been reported using the Preyssler tungsten heteropolyacid $H_{14}[NaP_5W_{30}O_{110}]$, for example, alkylation of phenol with 1-octene [70], acetylation reactions [71], synthesis of heterocycles [72–74], and oxidation of benzylic, allylic, and aliphatic alcohols [75]. Most recently, Heravi himself has describes the use of most active Preyssler heteropolyacid doped with molybdenum ($H_{14}[NaP_5W_{29}MoO_{110}]$, $H_{14}PMo$) in the following sustainable reactions: synthesis of lactones [76], oxidation of primary aromatic amines [69], and esterification of phtalic anhydride with 1-butanol and 2-ethylhexanol [77].

As part of a program of "Green Chemistry Catalysts" we have recently used a Wells Dawson heteropolyacid ($P_2W_{18}O_{62}H_6{\cdot}24H_2O$) for performing tetrahydropyranylation of alcohols and phenols [11], preparation of 1,1-diacetates from aldehydes [78], synthesis of coumarins by the von Pechmann reaction [79] and preparation of flavones and chromones [80]. Besides, some of us have explored the use of supported Keggin heteropolyacid ($H_3PMo_{12}O_{40}$ and $H_3PW_{12}O_{40}$) catalysts in the tetrahydropyranylation reaction [12] and flavone preparation [81].

In the present paper, we report several catalytic procedures using the most active Preyssler heteropolyacid, $H_{14}PMo$, in bulk form for performing:

- Tetrahydropyranylation of phenol using different heteropolycompounds to show the most active catalyst.
- Tetrahydropyranylation of alcohols and phenols with DHP at room temperature in toluene.
- Preparation of 1,1-diacetates from aldehydes and Ac_2O at room temperature in solvent-free conditions.
- Acetylation of primary and secondary alcohols, phenols, amines and thiols with Ac_2O at room temperature in toluene.
- Preparation of DMP-ethers from alcohols or phenols and benzhydrol at 60–80 °C in toluene.
- O-Trimethylsilylation of a wide variety of phenols and alcohols using readily available hexamethyldisilazane (HMDS), in toluene at 80–90 °C.

2. Experimental

2.1. General procedures

All the yields were calculated from pure products. All the products were identified by comparison of analytical data (mp, TLC, NMR) with those reported or with authentic samples prepared by the conventional methods using sulfuric acid as catalyst. Melting points of the compounds were determined in sealed capillary tubes and are uncorrected. ^{13}C NMR and ^{1}H NMR spectra were recorded at room temperature on Bruker AC-250 and Bruker Avance DPX-400 spectrometers using TMS as internal standard. Low resolution mass spectra were recorded on a PerkinElmer Q-mass 910. Spectral data agree with the expected values.

2.2. *Catalyst preparation*

The Mo-doped Preyssler heteropolyacid ($H_{14}[NaP_5W_{29}MoO_{110}]$, H_{14}PMo) was prepared following a literature method [77]. In a typical experiment, 56 g (0.169 mol) $Na_2WO_4\cdot2H_2O$ and 2 g (0.008 mol) $Na_2MoO_4\cdot2H_2O$ were dissolved in 70 ml of water, and then mixed at 60 °C for 30 min. The solution was cooled to room temperature (r.t.) and 45 ml of concentrated phosphoric acid was added. The resulting yellow solution was refluxed for 48 h. The color turned to dark green at the end of reaction (^{31}P NMR at −11,533 ppm). The solution was brought to r.t., diluted with 30 ml water and then 20 g potassium chloride was added with stirring. The mixture was stirred for 30 min and then heated up to dryness; a greenish solid was obtained. This raw product was dissolved in 70 ml of warm water and upon cooling to r.t. yellow crystals formed, which were collected and recrystallized from boiling water (yield, 18%). The molybdenum-substituted heteropolyanion, $K_{14}[NaP_5W_{29}MoO_{110}]$ was converted to its corresponding acid by passing it through a column filled with Dowex-50W-X8 ion exchange resin.

2.3. *General procedure for the tetrahydropyranylation of phenols and alcohols*

To a mixture of phenol or alcohol (0.5 mmol) and DHP (1 mmol) in toluene (2 ml), H_{14}PMo catalyst (1% mmol) was added and stirred at room temperature for 2 h. The reaction mixture was filtered, washed (1 M NaOH and then H_2O but only for phenol substrates) and the solution was dried over anhydrous Na_2SO_4. Filtration and concentration followed by flash column chromatography on silica (hexane–toluene) afforded THP-acetals.

2.4. *General procedure for the preparation of acylals*

A mixture of aldehyde (1 mmol), acetic anhydride (1 ml) and H_{14}PMo catalyst (1% mmol) was stirred at room temperature for 30 min and then ethyl acetate (3× 5 ml) was added to the reaction mixture. The resulting solution was successively washed with 1 M NaOH and water, dried over anhydrous Na_2SO_4, and filtered. The solution was then concentrated, and the solid crude product was recrystallized from petroleum ether yielding each of the pure acylals.

2.5. *General procedure for the acylation of alcohols, phenols, amines and thiols*

A mixture of alcohol, phenol, amine or thiol (1 mmol), toluene (1 ml), acetic anhydride (1.5 mmol) and the H_{14}PMo catalyst (1% mmol) was stirred at room temperature for the stated time (see Table 4). The catalyst was removed by filtration and then washed with a few toluene (2× 1 mL). The solution was concentrated and the residue was generally subjected to column chromatography on silica to give the desired alkyl acetates, aryl carboxylates, amides or thiol esters.

2.6. *General procedure for the preparation of benzhydryl (DMP) ethers from alcohols and phenols*

A mixture of alcohol or phenols (1 mmol), diphenylmethanol (1 mmol) and 1% mmol of H_{14}PMo catalyst in toluene (3 ml) was stirred at 60–80 °C for 1–2 h. The reaction mixture was filtered, washed (1 M NaOH and then H_2O but only for the phenol substrates), and the solution was dried over anhydrous Na_2SO_4. Filtration and concentration followed by flash column chromatography on silica (hexane–toluene) afforded pure DMP-ethers.

2.7. *General procedure for the trimethylsilylation of phenols and alcohols*

To a mixture of the substrate (1 mmol) and H_{14}PMo (1% mmol) in toluene (3 ml), HMDS (0.7 mmol) was added dropwise within 2 min with stirring at 85 °C. The reaction was monitored by TLC. After completion of the reaction, the catalyst was filtered off and washed twice with toluene (3 ml). The filtrate and the washing liquids were combined and the obtained phase was washed with 1 M NaOH solution (5 ml). Then it was dried over anhydrous sodium sulfate, filtered and concentrated in vacuum. The residue was subjected to a short flash chromatography column, eluting the product with 1:1 hexane–toluene mixtures.

2.8. *NMR spectra of representative compounds*

2.8.1. *Benzyl tetrahydropyranyl ether*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (m, 5H), 4.80 (d, 1H, J = 12 Hz), 4.70 (m, 1H), 4.40 (d, 1H, J = 12 Hz), 3.79 (m, 1H), 3.50 (m, 1H), 1.48–1.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 25.9, 31.0, 62.4, 69.1, 97.9, 127.7, 118.0, 128.5, 138.5.

2.8.2. *Benzaldehyde 1,1-diacetate*

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.38 (d, 2H, J = 8 Hz), 7.42 (dd, 1 H, J = 1.6, J = 8 Hz), 7.28 (d, 2H, J = 8 Hz), 2.10 (s, 6H). EIMS: m/z (%) 208 (M^+, 2), 201 (12), 199 (40), 139 (90), 111 (30), 77 (30) and 43 (100).

2.8.3. *Acetanilide*

^{1}H NMR (200 MHz, $CDCl_3$): δ 8.5 (s, 1H), 7.5 (d, 2H, J = 8 Hz), 7.35 (dd, 1H, J = 8 Hz, J = 2 Hz), 7.22 (dd, 2H, J = 8 Hz, J = 2 Hz), 2.1 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 24.1, 124.1, 128.7, 120.4, 138.2, 169.5.

2.8.4. *Benzhydryl phenyl ether*

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.12–7.38 (m, 12H), 6.93 (m, 3H), 5.50 (s, 1H); EIMS: m/z (%) 260 (M^+, 85), 183 (65), 181 (100), 165 (80), 112 (28), 115 (15).

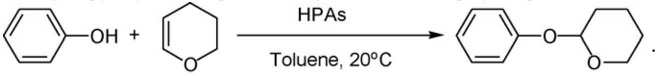
2.8.5. *Trimethylphenoxy silane*

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.30 (t, 2H, J = 8 Hz), (7.04 t, 1H, J = 7.2 Hz), 6.92 (d, 2H, J = 7.8 Hz), 0.35 (s, 9H).

3. Results and discussion

The results of the tetrahydropyranylation of phenol with dihydropyran using a variety of heteropolycompounds as catalysts in toluene at room temperature (20 °C) are shown in Table 1. Comparison of $H_3PMo_{12}O_{40}$, $H_3PW_{12}O_{40}$, $Cs_{3.8}H_{0.2}SiW_{12}O_{40}$, $H_6P_2W_{18}O_{62}\cdot24H_2O$, $H_{14}[NaP_5W_{30}O_{110}]$, and $H_{14}[NaP_5W_{29}MoO_{110}]$ showed that the highest catalytic performance and selectivity are achieved using molybdenum-doped heteropolyacid ($H_{14}[NaP_5W_{29}MoO_{110}]$) (Table 1).

Table 1
Tetrahydropyranylation of phenol using different heteropolycompounds (HPAs) as catalysts[a].



Entry	Catalyst	Yield (%)[b]	Reference
1	$H_3PMo_{12}O_{40}$	90	Ref. [12][c]
3	$H_4SiMo_{12}O_{40}$	87	This work
4	$Cs_{3.8}H_{0.2}SiW_{12}O_{40}$	89	Ref. [81]
5	$H_6P_2W_{18}O_{62}\cdot 24H_2O$	98	Ref. [11]
6	$H_{14}[NaP_5W_{30}O_{110}]$	96	This work
7	$H_{14}[NaP_5W_{29}MoO_{110}]$	99	This work

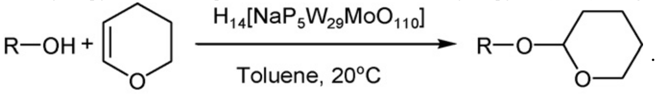
[a] *Reaction conditions*: 1 mmol of phenol, 2 mmol of dihydropyran, 3 ml of toluene, 1% mmol of HPA, 20 °C, stir, 2 h.
[b] Isolated yield.
[c] Using the heteropolyacid supported on silica.

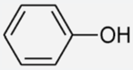
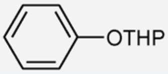
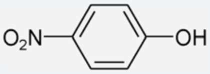
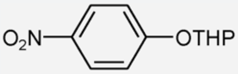
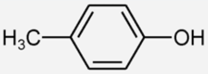
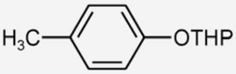
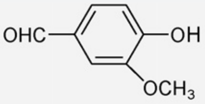
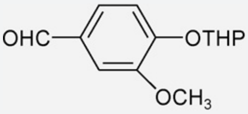
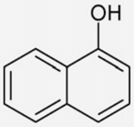
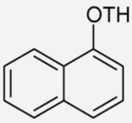
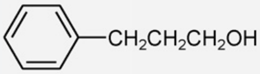
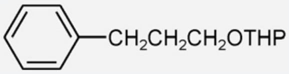
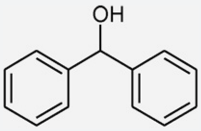
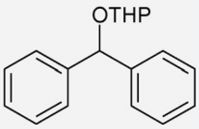
3.1. Tetrahydropyranylation of phenol and alcohols with dihydropyran

The reaction of dihydropyran (DHP) and alcohols or phenols is one of the most practical routes to the protection of the hydroxyl group. Investigation of the application of H_{14}PMo as a highly active catalyst is of practical importance.

In order to optimize the reaction conditions, the protection was studied using phenols and alcohols. Different reaction conditions were checked: temperature, time, and concentration of the solutions. The reaction was carried out using a bulk catalyst. The results indicate that the best reaction conditions are: room temperature (20 °C), in toluene as solvent, using 1% (mmol) of Mo-doped Preyssler acid and reaction time of 2 h. Under these conditions, phenol gives the corresponding THP-ether in 99% yield (Table 2, entry 1). The catalyst was washed with hot toluene and reused without appreciable loss of the catalytic activity (96% yield after first reuse, and 96% yield after second reuse – Table 2, entry 1).

Table 2
Tetrahydropyranilation of phenols and alcohols with dihydropyran (DHP) using $H_{14}[NaP_5W_{29}MoO_{110}]$ as catalyst[a].



Entry	Hydroxyl Compounds	Product	Yield[b] (%)
1			99 (96, 96)[c]
2			62
3			95
4			78
5			98
6			98
7			95

[a] *Reaction conditions*: 1 mmol of phenol or alcohol, 2 mmol of dihydropyran, 3 ml of toluene, 1% mmol of $H_{14}[NaP_5W_{29}MoO_{110}]$, 20 °C, stir.
[b] Isolated yield.
[c] Yields after first and second reuse.

When there is a nitro group at the phenyl ring, moderate yields are obtained, unmodified by prolonged reaction times; however, yields are at least good in the presence of other electron withdrawing groups. Compound structure and reaction conditions are shown in Table 2.

3.2. *Solvent-free preparation of aldehyde 1,1-diacetates*

A rapid preparation of aldehyde 1,1-diacetates was tested using $H_{14}PMo$ as a homogeneous catalyst. The protection reaction (Table 3) was studied using various aldehydes as substrates. We have previously reported the optimization of the reaction conditions using benzaldehyde as substrate. The selected experiments were carried out at 20 °C in 1 M solution and varying the reaction time and the amount of catalyst used. When 1% (mmol) $H_{14}PMo$ was added, the higher yield of 1,1-diacetates was attained in 30 min.of reaction at room temperature; shorter and longer times giving lower yields. Aldehydes gave excellent yields of the corresponding acylals. For example 3-chlorobenzaldehyde gave 3-chlorophenylmethanediol diacetate (Table 3, entry 2) in 95% and 3-nitrobenzaldehyde gave 3-nitrophenylmethanediol diacetate in 92% (same Table, entry 2). About reutilization of the catalyst in the benzaldehyde 1,1-diacetate preparation, the yield after the first reuse was 95%; after the second reuse the yield was 93% (Table 3, entry 1).

The nature of the constituent on the aromatic ring seems to have no relevant effect on the reaction, see for example Table 3, entries 1–5; but hydroxyaldehydes gave the corresponding triacetates (same Table, entries 4 and 5). Aliphatic aldehydes were also protected with very good yields (Table 3, entries 6 and 7). Some aliphatic and aromatic ketones were also checked for the reaction: acetone and acetophenone did not read under the described experimental conditions. Structure and results are shown in Table 3.

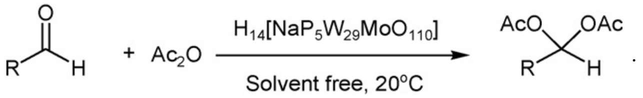
3.3. *Acetylation of alcohols, phenols, amines and thiols with Ac_2O*

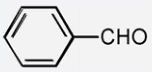
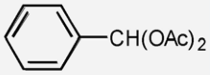
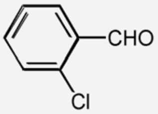
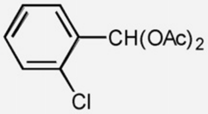
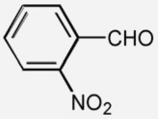
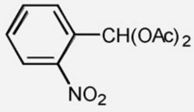
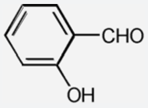
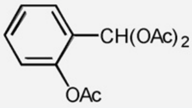
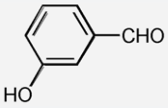
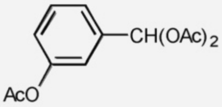
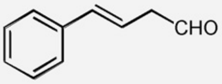
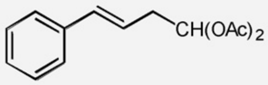
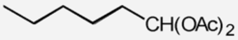
We report here a catalytic procedure for the easy acetylation of alcohols, phenols, amines and thiols with Ac_2O at room temperature in toluene, under heterogeneous catalysis by bulk $H_{14}PMo$.

Reaction conditions were optimized by varying temperature, anhydride:substrate and $H_{14}PMo$:substrate ratios, amount of catalyst and reaction time. Experiments for checking the reutilization of the catalyst showed almost no lowering of the yields over two successive batches. In these experiments the catalyst was washed with toluene and then was reused in subsequent reactions.

Table 3

Conversion of aldehydes in 1,1-diacetates (acylals) with Ac_2O using $H_{14}[NaP_5W_{29}MoO_{110}]$ as catalyst[a].



Entry	Aldehyde	1,1-Diacetate	Yields[b] (%)
1			96 (95, 93)[c]
2			95
3			90
4			94
5[d]			95
6			97
7			91

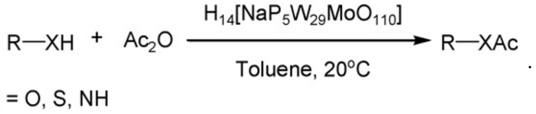
[a] *Reaction conditions*: 1 mmol of aldehyde, 1 ml of acetic anhydride, 1% mmol $H_{14}[NaP_5W_{29}MoO_{110}]$, 20 °C, stir, 30 min.

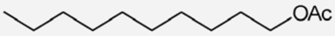
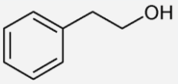
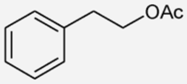
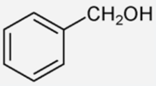
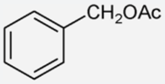
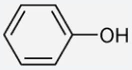
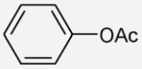
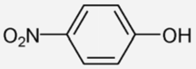
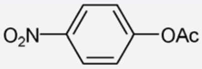
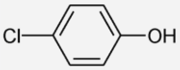
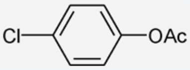
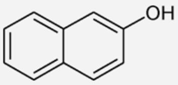
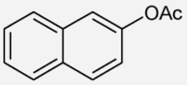
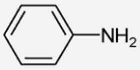
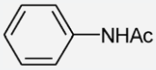
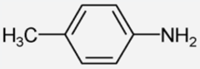
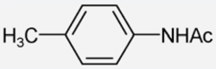
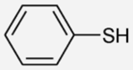
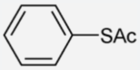
[b] Yields are expressed from crystallized products.

[c] Yields after first and second reuse.

[d] Compound in entry 5 was triacetylated.

Table 4
Acetylation of alcohols, phenols, amines and thiols with Ac_2O using $H_{14}[NaP_5W_{29}MoO_{110}]$ as catalyst[a].



Entry	Substrate	Product	Time (min)	Yields[b] (%)
1			60	93
2			60	99
3			45	94
4			60	97
5			300	89
6			60	98
7			30	98
8			20	95
9			20	98
10			60	95
11	$n\text{-}C_{16}H_{33}SH$	$n\text{-}C_{16}H_{33}Sac$	60	92

[a] *Reaction conditions*: 1 mmol of substrate, 1.5 mmol of acetic anhydride, 1% mmol $H_{14}[NaP_5W_{29}MoO_{110}]$, 20 °C, stir.
[b] Isolated yield.

Alcohols acetylate with excellent yields (Table 4, entries 1–3). The best yield of 1-decyl acetate (93%) was attained at almost 1 h of reaction at room temperature. Shorter and longer times gave somewhat lower yields.

Phenols gave their acetates in very good to excellent yields (Table 4, entries 4–7). Different reaction times are required according to the nature of their substituents; *p*-nitrophenol requires a higher reaction time, as well as a higher catalyst: substrate ratio than the other examples. Experiments for recovering and recycling of the catalyst were performed using phenol as the substrate (Table 4, entry 4).

Aromatic and aliphatic representative thiols were assayed for their acetylation (Table 4, entries 10 and 11). In both cases the reaction completes in about 1 h at room temperature, no progress was observed by extending the reaction time. Besides, some aromatic amines were assayed for the reaction, requiring a lower reaction time than phenol or thiophenol to obtain very good yields of the corresponding amides (Table 4, entries 8 and 9).

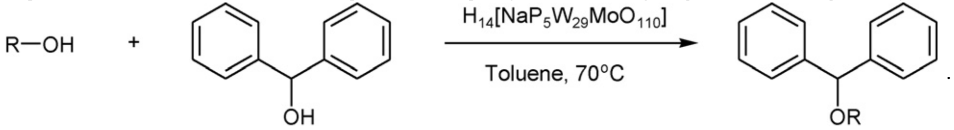
3.4. Preparation of benzhydryl ethers

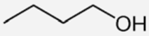
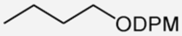
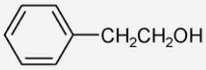
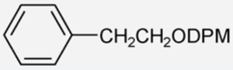
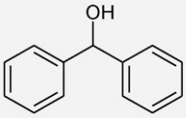
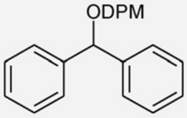
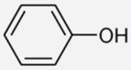
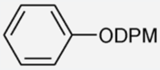
We report here a catalytic preparation of benzhydryl ethers (DMP-ethers) from benzhydrol (diphenylmethanol) and alcohols or phenol, using $H_{14}PMo$ as catalyst. Bulk $H_{14}PMo$ showed catalytic activity for DMP-ether preparation at 60–80 °C in toluene (heterogeneous phase) with a low formation of by-products. Reaction conditions were optimized by varying temperature, benzhydrol:substrate and catalyst:substrate ratios, the amount of catalyst and the reaction time. Experiments for checking reutilization of the catalyst showed almost no lowering of the yields over two successive batches. In these experiments the catalyst was washed with toluene and then reused in subsequent reaction. Structure and reaction conditions are shown in Table 5.

3.5. Trimethylsilylation of phenols and alcohols

Primarily as model reaction, silylation of phenol with hexamethyldisilazane (HMDS) was performed in the presence of $H_{14}PMo$,

Table 5
Preparation of DPM-ethers of alcohols and phenol with diphenylmethanol using $H_{14}[NaP_5W_{29}MoO_{110}]$ as catalyst[a].



Entry	Substrate	Product	Time (min)	Yields[b] (%)
1[c]	CH_3OH	CH_3ODPM	60	94
2			60	85
3			60	86
4			30	93
5			60	85

[a] *Reaction conditions*: 1 mmol of alcohol or phenol, 1 mmol of diphenylmethanol, 1% mmol of $H_{14}[NaP_5W_{29}MoO_{110}]$, 70 °C, stir.
[b] Isolated yield.
[c] The reaction was performed to 60 °C.

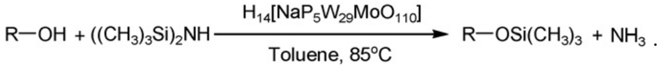
in toluene at 85 °C. The reaction yields showed very low conversions in the absence of a catalyst (15% for 120 min), but when an HPA is added, the times are reduced considerably and the conversion increases to values close to 100%. When $H_{14}PMo$ is used, a yield of 95% is observed at 120 min of reaction (Table 6, entry 1).

Due to the need to obtain catalysts for green processes, the use of recycled catalysts is required for reducing the catalytic cost. When the reaction was completed, the catalyst (insoluble) was filtered, dried under vacuum (20 °C) and reused, without appreciable loss of the catalytic activity.

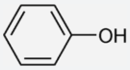
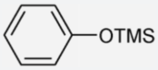
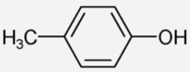
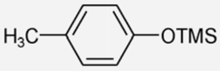
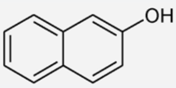
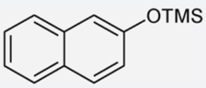
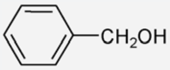
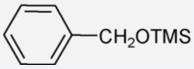
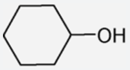
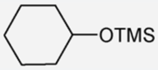
In order to evaluate the possible solubilisation of catalysts in the cases in which solvent was required, an additional test was performed. A $H_{14}PMo$ sample was refluxed in toluene for 5 h, filtered and dried in vacuum till constant weight. The activity of treated catalyst was the same as that of fresh catalyst (97% yield) on tetrahydropyranilation of phenols. The refluxed toluene was used as solvent for attempting the reaction without adding the catalyst. After 5 h products were not detected and the starting materials were quantitatively recovered.

Being the reaction conditions optimized for the selective silylation of phenol, the reaction was extended to other starting phenols

Table 6
Trimethylsilylation of alcohols and phenol with HMDS using $H_{14}[NaP_5W_{29}MoO_{110}]$ as catalyst[a].



$$R{-}OH + ((CH_3)_3Si)_2NH \xrightarrow[\text{Toluene, 85°C}]{H_{14}[NaP_5W_{29}MoO_{110}]} R{-}OSi(CH_3)_3 + NH_3 .$$

Entry	Substrate	Product	Time (min)	Yields (%)[b]
1			1	95
2			1	92
3			2	95
4			1	96
5			2	98

[a] *Reaction conditions*: 1 mmol of alcohol or phenol, 0.7 mmol of HMDS, 3 ml of toluene, 1% mmol of $H_{14}[NaP_5W_{29}MoO_{110}]$, 85 °C, stir.
[b] Isolated yield.

and alcohols. Table 6 shows the results for the above-mentioned compounds. In all the reactions that we studied, evolution of ammonia gas was observed. We were also able to isolate all the catalyst from the reaction mixture and reuse it in similar reactions, without any observable loss of its catalytic activity.

Structure and reaction conditions are shown in Table 6.

4. Conclusions

These procedures provide a useful alternative for performing the preparation of tetrahydropyranil ethers from alcohols and phenols; preparation of 1,1-diacetates from aldehydes; and preparation of benzhydryl ethers, acylation of alcohols, phenols, amines and thiols; and trimethylsilylation of phenols and alcohols.

Heteropolyacids are effective solid acid catalysts for all these transformations. The molybdenum-doped Preyssler heteropolyacid shows higher activity than Keggin or Wells Dawson heteropolyacids due to its higher number of acidic protons. Also, molybdenum-substituted Preyssler-type heteropolyacid exhibits higher activity than that of the unsubstituted HPA, which is attributable to the reduction of Mo (VI) to Mo (V).

The advantages of this methodology are: operational simplicity, noncorrosive and reusable catalyst, mild reaction conditions, short reaction times and excellent yields. The use the solid catalysts allow replacement of the usual soluble inorganic acids, contributing to the reduction of waste.

Further investigation about the use of this heterogeneous catalyst, $H_{14}[NaP_5W_{29}MoO_{110}]$, for the synthesis of heterocyclic compounds is in progress in our laboratory.

Acknowledgements

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