Silicagel-supported $H_6P_2W_{18}O_{62}.24H_2O$: a reusable catalyst to prepare diphenylmethyl (DPM) ethers

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Abstract
In this work, we report an efficient and facile preparation of diphenylmethylethers (benzydryl ethers, DPM-ethers) from benzhydrol and alcohols or phenols. Wells-Dawson heteropolyacid ($H_6P_2W_{18}O_{62}.24H_2O$), bulk or supported on silica showed catalytic activity for DPM-ethers preparation in toluene, at 60-80°C, in 0.5-1.5h. In these conditions twelve diphenylmethylethers of alcohols and phenol were obtained which excellent yields (78-96%). The heterogeneous reaction conditions provided a very simple, environmentally friendly, clean, economical and selective protocol, for the preparation of unsymmetrical ethers. The catalyst is easily recycled and reused without loss of the catalytic activity.

Keywords: $H_6P_2W_{18}O_{62}.24H_2O$, silicagel-supported catalyst, DPM-ethers, protecting groups, alcohols, phenols

Introduction

The use of heteropolyacids (HPAs) as catalysts for organic chemistry synthetic processes has been developed for important industries related to fine chemicals, such as flavor, pharmaceutical and food industries. Heteropolyacids are more active catalysts than conventional mineral acids. They have many advantages over liquid acid catalysts: higher acid strengths and thermal stabilities; they are noncorrosive, environmentally benign, cheap and reusable and require less waste disposal.[1]

We have recently studied the catalytic activity for the heteropolyacid $H_6P_2W_{18}O_{62}.24H_2O$ with Wells-Dawson structure. We have already used this catalyst for performing the tetrahydropyranylation of alcohols and phenols and their detetrahydropyranylation,[2] cleavage of MOM–ethers of phenols,[3] preparation of acylals,[4] and coumarin synthesis via the Pechmann reaction.[5]

On the other hand, the correct choice of an efficient protecting group is often decisive for successfully synthesizing a complex molecule.[6] Protection of the hydroxy functional group is an important procedure[7,8,9] in multistep organic synthesis. The preparation of DPM ethers is one of the popular methods in view of their low cost and high stability towards a variety of reagents. Additionally, DPM ethers and DPM groups are found as part of the structure of pharmacological active compounds.[10]

A wide variety of reagents are available for the preparation of DPM ethers such as diphenylmethyl chloride or bromide in the presence of a base,[11] diphenylmethanol in the presence of concentrated sulfuric[12] or p-toluenesulfonic[13] acids, xenon difluoride,[14] diphenylmethyldiazomethane,[15] diphenylmethylphosphate-trifluoroacetic acid,[16] ytterbium triflate-ferric chloride[17] and other ferric or ferrous salts.[10a] More recently Varma has described a suitable method using Nafion-H as a reusable catalyst.[18]

In continuation of our work on the catalytic properties of Wells-Dawson heteropolyacids, herein we report the use of bulk or silica-supported Wells-Dawson acid as a reusable, heterogeneous catalyst for an efficient DPM-ether preparation over a wide variety of alcohols and phenols.

Results and Discussion

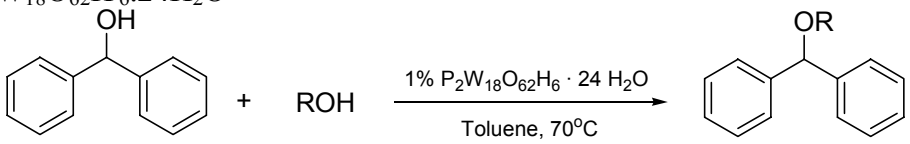
The catalytic activity of the bulk Wells-Dawson acid (WD) and that of Wells-Dawson acid containing 40% by weight of the acid (WD_{40}/SiO_2) was tested in the preparation of DPM-ethers (Scheme in Table 1). The protection reaction was studied using different alcohols and phenols as substrates, and diphenylmethanol for introducing the DPM group. In all cases, toluene was used as solvent.

Initially we conducted blank experiments without the presence of WD. No product was detected when 1 mmol of methanol and 1 mmol of benzhydrol were warmed at 60°C for 5 h. When the mixture of methanol and benzhydrol was warmed under identical conditions but in the presence of silica (support), benzhydrol was the only product detected by TLC.

The preparation of DPM-ethers starting from methanol and benzydrol was tested under a variety of conditions (temperature and solvent), using the bulk catalyst. The reaction gives higher yields in toluene solution compared to the use of chloroform. The reaction was complete in 1 h at 60°C and in 4 h at 40°C, affording DPM ether in 93% (entry 1), and 78% (entry 2), respectively. No reaction was detected at room temperature (entry 3). Similarly benzhydrol and

n-butanol were warmed in toluene at 70°C for 1 h with a catalytic amount of WD to give 83% of the DPM-ether (entry 5).

Table 1. Preparation of DPM-ethers from alcohols and phenols using both bulk and silica-supported $P_2W_{18}O_{62}H_6.24H_2O$



Alcohol	Entry	Time (h)	Yield (%) WD	Entry	Time (h)	Yield (%) WD_{40}/SiO_2
Methanol	**1**[a]	1	93	**15**[a]	1	94(94,93)[d]
	2[b]	4	78			
	3[c]	10	-			
Isopropanol	**4**[a]	1	91	**16**[a]	1	85
n-Butanol	**5**	1	83	**17**	1	85
Tert-Butanol	**6**	1.5	87	**18**	1.5	86
Allylic Alcohol	**7**	1	89	**19**	1.5	89
Benzyl alcohol	**8**	0.5	84	**20**	0.5	83
2-Phenethyl alcohol	**9**	1	81	**21**	1	81
Benzhydrol	**10**	1	95	**22**	0.5	96
Phenol	**11**	1	84	**23**	1	84(85,85)[d]
4-Methyl-phenol	**12**	1	85	**24**	1	85
3- Methyl-phenol	**13**	1	83	**25**	1	84
4-Nitro-phenol	**14**	1	81	**26**	1	80

[a] 60°C, [b]40°C, [c]20°C

[d] In parentheses, yields obtained in the first and second reuse of the catalyst.

Other primary, secondary, tertiary, allylic, and benzylic alcohols were also protected in the same way in short reaction times, the yields of DPM-ethers being higher than 81% (entries 4-10). The reactivity trend of this reaction for different alcohols was found to be benzylic > allylic = primary = secondary > tertiary.

Primary and secondary alcohols give good to very good yields of DPM ethers (see Table 1, entries 1, 5, 9 and 4, 10). Likely, benzyl, allyl, and *tert*-butyl alcohols (entries 8, 7, 6) gave good yields, although the reaction times were somewhat different, between 0.5 and 1.5 h under the selected experimental conditions.

We applied similar reaction conditions for the protection of substituted phenols. The reactions proceeded efficiently with good yields and the nature of the substituents seems to have no effects on the conversion rates (see Table 1, entries 11-14).

In view of the obtained results when the bulk catalyst was employed, we used WD_{40}/SiO_2 for comparative purposes; very similar yields were obtained in comparable reaction times (entries 15-24). Furthermore, use of the supported catalyst allows an easy separation and recovery for its immediate reutilization.

Recycling of the catalyst was studied for the reaction between methanol and benzydrol using WD_{40}/SiO_2. The procedure was repeated twice without any significant loss of activity, as the catalyst remained active even after the third cycle (93% yield, entry 15). Similar results were obtained for DPM-ether of phenol (85% yield, entry 23).

Experimental Section

General Procedures. Commercially available alcohols and phenols Aldrich or Fluka were distilled or recrystallized before use. Melting points of the compounds were determined in open capillary tubes and are uncorrected. Boiling points were read from a thermometer in the microdistillation head and are reported uncorrected. ^{1}H-RMN spectra ($CDCl_3$) were recorded on Bruker 200 MHz spectrometer using TMS as internal standard. Low-resolution mass spectra were recorded on a Perkin Elmer GC-MS model (Q-MASS 910). Spectral data agree with the expected values. Elemental microanalyses were performed in F & M instrument. The purity determination of the products was accomplished by GC analysis on a Perkin Elmer instrument and TLC on silica gel 60 F_{254} plates, for co-injection with authentic samples prepared by known methods. The purity established by GLC, was better than 97% in all the cases.

Catalyst preparations

The Dawson acid ($H_6P_2W_{18}O_{62}.24H_2O$.) was prepared by the Drechsel method[19, 20] from a α/β $K_6P_2W_{18}O_{62}.10H_2O$ isomer mixture. This Dawson-type salt was prepared according to the technique reported by Lyon et al.[21]. Concentrated H_3PO_4 in a 4:1 acid/salt ratio was added to a boiling aqueous solution of $Na_2WO_4.2H_2O$, and the mixture was kept boiling in a reflux system for 8 h. The salt was precipitated by adding KCl, then purified by recrystallization and cooled overnight to 278 K. The product, which is a mixture of the α and β isomers, was filtered, washed and then vacuum-dried for 8 h.

The acid was obtained from an aqueous solution of α/β $K_6P_2W_{18}O_{62}.10H_2O$ salt, which was treated with ether and concentrated HCl (37%) solution. The Dawson acid so released formed an addition compound with the ether, which allows it to be separated from the solution. After obtaining the ether solution with the acid, the ether was eliminated by flowing dry air and the remaining solution was placed in a vacuum-desiccator until crystallization.

Silica-supported Wells-Dawson acids (WD_{40}/SiO_2) was prepared by wet impregnation Grace Davison silica (Grade 59, specific area= 250 m^2/g) with an aqueous solution of the synthesized WD acid. A catalyst containing 40 wt% of WD was prepared. After impregnation, samples were dried at room temperature in a vacuum-dessicator for 8 h.

Typical procedure for the preparation of DPM-ethers of alcohols

A mixture of alcohol (1 mmol), diphenylmethanol (1 mmol), and $P_2W_{18}O_{62}H_6 \cdot 24H_2O$ (1% mmol, approx. 40 mg of bulk catalyst, or 100 mg of the silica-supported one) was stirred at the indicated temperature and time (see Table 1), in toluene (5 mL). The reaction mixture was diluted with toluene (15 mL), and the catalyst was filtered off, then the solution was washed with water (2 x 10 mL), dried with anhydrous Na_2SO_4, the solvent was evaporated, and the residue was purified by column chromatography (silicagel, ethyl acetate:hexanes) to afford pure DPM-ethers.

Benzhydryl methyl ether. Colorless oil (94%); bp: 150-151°C (20 Torr) (lit bp: 147-148°C (17 Torr)[22]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 3.49 (3H, s), 5.37 (1H, s) 7.30-7.41 (10H, m); MS (EI), 70 eV, m/z (rel. intensity): 198 (65) [M^+], 167 (97), 152 (22), 121 (100), 105 (70); Anal Calcd. For $C_{14}H_{14}O$: C 84.81, H 7.12; Found: C 84.78, H 7.08.

Benzhydryl isopropyl ether. Colorless oil **(**91%); bp: 160-162°C (20 Torr) (lit. bp: 156-159.5°C (15 Torr)[16]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 1.20 (6H, d, J=6Hz), 3.67 (1H, sp, J=6Hz), 5.30 (s, 1H), 7.15-7.25 (10H, m); Anal Calcd. For $C_{16}H_{18}O$: C 84.92, H 8.02; Found: C 84.90, H 8.02.

Benzhydryl n-butyl ether. Colorless oil (85%); bp: 165-166 °C (10 Torr) (lit. bp: 166-167.5°C (10 Torr)[16]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 0.92 (t, 3H, 6Hz), 1.30-160 (m, 4H), 3.45 (t, 2H, 6Hz), 5.34 (s, 1H), 7.10-7.30 (m, 10H); MS (EI), 70 eV, m/z (rel. intensity): 240 (10) [M^+], 183 (5), 167 (100), 153 (21), 107 (37), 105 (28); Anal Calcd. For $C_{17}H_{20}O$: C 84.96, H 8.39; Found: C 84.92, H 8.40.

Benzhydryl *t*-butyl ether. White needles (87%); mp: 50-51°C (Methanol) (lit. mp: 50°C (Methanol)[24]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 1,20 (s, 9H), 5.34 (s, 1H), 7.11-7.31 (m, 10H); MS (EI), 70 eV, m/z (rel. intensity): 240 (1) [M^+], 222 (66), 207 (70), 178 (25), 165 (29), 91 (60); Anal Calcd. For $C_{17}H_{20}O$: C 84.96, H 8.39; Found: C 84.93, H 8.42.

Benzhydryl allyl ether. Colorless oil (89%); bp: 125-126 °C (1 Torr) (lit. bp: 120°C (0.2 Torr)[23]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 3.81 (d, 2H, J=3Hz), 5.20 (m, 2H), 5.42 (s, 1H), 6.01 (m, 1H), 7.15-722 (m, 10H); MS (EI), 70 eV, m/z (rel. intensity): 224 (5) [M^+], 182 (49), 168 (58), 167 (100), 166 (56), 105 (85); Anal Calcd. For $C_{16}H_{16}O$: C 85.68, H 7.18 ; Found: C, 85.66 H 7.22.

Benzhydryl benzhyl ether. White needles (84%); mp: 49-51°C (Ethanol) (lit. mp: 51°C (Ethanol)[24]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 4.50 (s, 2H), 5.40 (s, 1H) 7.10-7.35 (m, 15H); MS (EI), 70 eV, m/z (rel. intensity): 274 (1) [M^+], 183 (91), 167 (98), 152 (25), 105 (72), 91 (100); Anal Calcd. For $C_{20}H_{18}O$: C 87.56, H 6.61 ; Found: C, 87.59 H 6.64.

Benzhydryl phenethyl ether. Colorless oil (81%); bp: 135-136 °C (1 Torr) (lit. no data)[25]. ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 2.71 (t, 2H, 6Hz), 3.50 (t, 2H, 6Hz), 5.42 (s, 1H), 7.12-7.35 (m, 15H); MS (EI), 70 eV, m/z (rel. intensity): 288 (9) [M^+], 183 (18), 167 (100), 152 (15), 105 (18), 91 (10); Anal Calcd. For $C_{21}H_{20}O$: C 87.46, H 6.99 ; Found: C, 87.47 H 6.97.

Dibenzhydril ether. White needles (96%); mp: 106-107°C (Benzene) (lit. mp: 107-107.5°C (Ethanol)[19]; ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 5.40 (s, 2H), 7.20-7.39 (m, 20H); Anal Calcd. For $C_{26}H_{22}O$: C 89.11, H 6.32 ; Found: C, 89.12 H 6.32.

Typical procedure for the preparation of DPM-ethers of phenols

A mixture of phenol (1 mmol), diphenylmethanol (1 mmol), and $P_2W_{18}O_{62}H_6{\cdot}24H_2O$ (1% mmol, approx. 40 mg, bulk or 100 mg supported on silica) was stirred at the indicated temperature and time (see Table 1), in toluene (5 mL). The reaction mixture was diluted with toluene (15 mL), the catalyst was filtered off, and then the solution was washed with 1 M NaOH (10 mL) and water (2 x 10 mL), dried with anhydrous Na_2SO_4, solvent was evaporated, and the residue purified by column chromatography (silicagel, ethyl acetate:hexanes) to afford pure DPM-ethers.

Benzhydryl phenyl ether. White needles (85%); mp: 53-54 °C (Methanol) (lit. mp: 52-54°C)[26]. ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 5.50 (s, 1H), 6.93 (m, 3H), 7.12-7.38 (m, 12H); MS (EI), 70 eV, m/z (rel. intensity): 260 (85) [M^+], 183 (65), 181 (100), 165 (80), 152 (28), 115 (15); Anal Calcd. For $C_{19}H_{16}O$: C 87.65, H 6.19; Found: C, 87.63, H 6.17.

Benzhydryl 4-methylphenyl ether. White needles (85%); mp: 74-75 °C (Methanol) (lit. mp: 74.5-75.5°C)[27]. ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 2.20 (s, 3H), 5.50 (s, 1H), 6.71 (d, 2H, J=8Hz), 6.97 (d, 2H, J=8Hz), 7.17-7.36 (m, 10H); MS (EI), 70 eV, m/z (rel. intensity): 274 (10) [M^+], 260 (5), 196 (40), 152 (25), 115 (15), 51 (100); Anal Calcd. For $C_{20}H_{18}O$: C 87.56, H 6.61; Found: C, 87.53, H 6.59.

Benzhydryl 3-methylphenyl ether. White needles (84%); mp: 121-122°C (Methanol) (lit. mp: 124°C)[28]. ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 2.20 (s, 3H), 5.50 (s, 1H), 6.91 (m, 3H), 7.15-7.36 (m, 11H); MS (EI), 70 eV, m/z (rel. intensity): 274 (10) [M^+], 260 (15), 196 (50), 181 (51) 165 (30), 152(20), 115 (15), 51 (100); Anal Calcd. For $C_{20}H_{18}O$: C 87.56, H 6.61; Found: C, 87.52, H 6.60.

Benzhydryl 4-nitrophenyl ether. Yellow needles (81%); mp 117-118°C (Methanol) (lit mp: no data)[29]. ^{1}H-NMR δ_H (200 MHz, $CDCl_3$, TMS): 5.50 (s, 1H), 6.91 (d, 2H, J=8Hz), 7.15-7.36 (m, 10H), 8.2 (d, 2H, J=8Hz); Anal Calcd. For $C_{19}H_{15}O$: C 74.74, H 4.95, N 4.59; Found: C, 74.76, H 4.93, N 4.58.

Recycling of the catalyst. The filtered catalyst was washed with toluene (2 x 5 mL), dried under vacuum and then reused.

Conclusions

The present method describes an efficient and simple alternative for the preparation of DPM-ethers of alcohols and phenols. This method has the advantages of simplicity in operation and mild reaction conditions, low cost, very good yields, and environment friendliness compared to homogeneous catalysis procedures. Moreover, this procedure introduces a practical and viable technology for the synthesis of DPM-ethers.

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