SHORT PAPER

J. Chem. Research (S), 2003, 412–414

Silica gel-supported phosphotungstic acid (PTA) catalysed acylation of alcohols and phenols with acetic anhydride under mild reaction conditions†

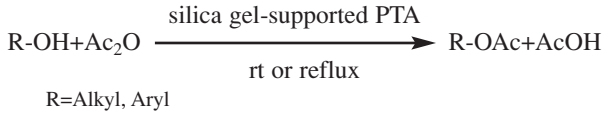
Tong-Shou Jin,* Jin-Chong Xiao, Zhen-Hua Wang and Tong-Shuang Li

Department of Chemistry, Hebei University, Baoding 071002, Hebei Province, P. R. China

Phosphotungstic acid, which is commercially available, practically and efficiently catalyses the acylation of a series of alcohols and phenols with acetic anhydride at room temperature or at refluxing temperature.

Keywords: acetylation, phosphotungstic acid, alcohol, phenol

The hydroxyl group is nucleophilic and easily oxidised by a wide range of reagents. Because it can participate in a great number of transformations under mild conditions, it is important in organic synthesis to ensure that a specific hydroxyl function in a multifunctional molecule is protected from unwanted reactions. Ester groups are the most common protective groups in organic synthesis.[1] The acylation of alcohols and phenols by acetic anhydride or acetyl chloride is routinely carried out in the presence of tertiary amines such as triethylamine and pyridine. [2] It is well known that 4-(dimethylamino) pyridine (DMAP) and 4-pyrrolidinopyridine (PPY) can be used to catalyse the reaction and to increase the rate of acylation of alcohols.[3] Tributylphosphine[4] and iodine[5] have also been introduced as acetyl transfer catalysts. In addition, protonic acids such as *p*-toluenesulfonic acid,[6] sulfamic acid[7] and Lewis acids such as zinc chloride,[8] cobalt chloride,[9] magnesium bromide,[10] $Cu(OTf)_2$,[11] TMSOTf,[12] thallium chloride,[13] scandium trifluoromethanesulfonate,[14] lithium chloride[15] and lithium perchlorate[16] are also known to catalyse the acylation of alcohols and phenols. Each of the methods has its merits and some shortcomings. Most of these methods cannot be entirely satisfactory; for example, triethylamine and pyridine have unpleasant odours, DMAP is not easily obtained and expensive, and tributylphosphine is irritant, highly flammable and expensive. Therefore, several solid catalysts such as montmorillonite K10, KSF,[17-18] expansive graphite,[19] cobalt polyoxometalate[20] have been used recently for the acetylation of alcohols and phenols. Even though a wide range of catalysts has been reported for the protection of the hydroxyl of alcohols and phenols, there is still a demand for efficient acid catalysts to generate esters. In this paper we wish to report a novel method for the acylation of alcohols and phenols with acetic anhydride catalysed by **s**ilica gel-supported phosphotungstic acid.



Scheme 1

In recent years, PTA, a kind of heteropoly acid (HPA), has been proved to be a practical and useful catalyst in a variety of organic reactions.[21] HPA is superior to common inorganic acids due to its high reactivity, lack of odour, non-volatility and excellent stability. Reactions catalysed by phosphotungstic acid are usually carried out under mild conditions in excellent yield due to its strong acidity. The work-up of the reactions is also very simple, involving only removal of the catalyst by filtration and of the solvent by evaporation.

As shown in Table 1, a series of alcohols and phenols are treated with acetic anhydride in the presence of **s**ilica gel-supported PTA in $CHCl_2$, $CHCl_3$, cyclohexane or solvent-free at room temperature or at refluxing temperature. Primary (**1**, **2**, **3**, **4** and **5**) and secondary (**6**, **7**, **8** and **9**) alcohols can be easily acetylated at room temperature. However, the hindered tertiary alcohol shows the lowest activity. For example, triphenylmethanol (**10**) was treated with acetic anhydride in the presence of **s**ilica gel-supported phosphotungstic acid at higher temperature (refluxing cyclohexane) and longer reaction time (3h), but it remains unchanged. Therefore primary and secondary alcohols can be acetylated more easily than tertiary alcohols.

Phenols carrying either electron-donating or electron-withdrawing substituents can afford high yields of products at room temperature in a short time (**11**, **12**, **13**, **14**, **16**, **17**, **18**, **19**, **23** and **24**). When 2-nitrophenol (**15**) was treated with acetic anhydride in the presence of **s**ilica gel-supported PTA, conversion into 2-nitrophenyl acetate requires 3 hours at room temperature, but only 3 minutes in refluxing cyclohexane on catalysis by **s**ilica gel-supported PTA. The explanation for this result may be the presence of the intramolecular hydrogen bond in 2-nitrophenol which would reduce the activity of the molecular at room temperature, whereas heating overcomes this deactivation. Furthermore, we also find that sterically hindered phenols can give the corresponding acetate in a quantitative yield (**26**, **27** and **28**). The temperature is quite crucial to the success of the acylation. The acetylation of 2,6-ditertbutyl-4-methyl phenol (**26**) requires 30 minutes at room temperature while only 5 minutes at refluxing $CHCl_3$. 2,4,6-Tritertbutylphenol (**28**) hardly reacts at room temperature in 1 hour while the reaction would be successfully performed in refluxing $CHCl_3$ in equal time. Polyhydroxy compounds could be transformed into the corresponding polyacetates (**20**, **21** and **22**).

In conclusion, the catalysis by **s**ilica gel-supported phosphotungstic acid is good for the acetylation of alcohols, phenols and polyhydroxy compounds. This method offers several advantages including mild reaction conditions, cleaner reactions, high yields of products as well as simple experimental and isolation procedures which makes it a useful and attractive process for acetylation.

Experimental

Melting points and boiling points were uncorrected. The melting points were determined on a Kofler hot stage. The products were characterised by IR spectra, ^{1}H NMR spectra, Mass spectra and by comparison of their melting or boiling points with literature values. IR spectra were recorded on a PE-983G spectrometer. ^{1}H NMR

* To receive any correspondence. E-mail: orgsyn@mail.hbu.edu.cn

† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Acetylation of alcohols and phenols catalysed by silica gel-supported phosphotungstic acid

Entry	Substrate	Solvent /Temp/°C /T min	Yield/%[a]	Product	B.p. / torr or M.p. / °C	
					Found	Reported
1	Heptan-1-ol **1**	$CHCl_3$/rt/3	96	Heptyl acetate	96–98/20	191–192/760[23]
2	Octan-1-ol **2**	$CHCl_3$/rt/2	95	Octyl acetate	88–90/20	211.5/760[23]
3	Benzyl alcohol **3**	$CHCl_3$/rt/7	96	Benzyl acetate	102–104/20	134/102[23]
4	2-Phenylethanol **4**	$CHCl_3$/rt/4	97	2-Phenylethyl acetate	122–124/20	232/760[23]
5	Octadecan-1-ol **5**	$CHCl_3$/rt/2	98	Octadecyl acetate	32–33	33[23]
6	Benzoin **6**	$CHCl_3$/rt/5	97	Benzoin acetate	82–83	83[23]
7	Cyclohexanol **7**	$CHCl_3$/rt/3	95	Cyclohexyl acetate	80–82/25	175/760[23]
8	Cholesterol **8**	$CHCl_3$/rt/1	97	Cholesteryl acetate	113–114	114–115[23]
9	Diphenylmethanol **9**	$CHCl_3$/rt/1	98	Diphenylmethyl acetate	41–42	41–42[23]
10	Triphenylmethanol **10**	Cyclohexane /81/180		No reaction		
11	Phenol **11**	CH_2Cl_2/rt/2	89	Phenyl acetate	95–96/20	196/760[23]
12	4-Methoxyphenol **12**	CH_2Cl_2/rt/1	98	4-Methoxyphenyl acetate	31–32	32[22]
13	3-Methylphenol **13**	None/rt/3	94	3-Methylphenyl acetate	102–104/20	212/760[23]
14	4-Methylphenol **14**	CH_2Cl_2/rt/2	94	4-Methylphenyl acetate	102–104/20	212–213/760[23]
15	2-Nitrophenol **15**	Cyclohexane /81/3	88	2-Nitrophenyl acetate	39–40	40–41[23]
16	3-Nitrophenol **16**	CH_2Cl_2/rt/3	96	3-Nitrophenyl acetate	55–56	55–56[23]
17	4-Nitrophenol **17**	CH_2Cl_2/rt/1	97	4-Nitrophenyl acetate	80–82	81–82[23]
18	4-Chlorophenol **18**	CH_2Cl_2/rt/1	94	4-Chlorophenyl acetate	106–108/20	226–228/760[23]
19	2,4-Dichlorophenol **19**	CH_2Cl_2/rt/5	95	2,4-Dichlorophenyl acetate	124–126/20	244–245/760[23]
20	Catechol **20**	None/rt/1	92	Benzene-1,2-diyl diacetate	62–63	63.5[23]
21	Resorcinol **21**	None/rt/1	84	Benzene-1,3-diyl diacetate	158–160/20	278/760[23]
22	Hydroquinone **22**	$CHCl_3$/rt/1	95	Benzene-1,4-diyl diacetate	121–122	123–124[23]
23	1-Naphthol **23**	$CHCl_3$/rt/2	90	1-Naphthyl acetate	48–49	48–49[23]
24	2-Naphthol **24**	CH_2Cl_2/rt/1	98	2-Naphthyl acetate	69–70	70[23]
25	4-Hydroxybenzoic acid **25**	$CHCl_3$/62/9	95	4-Acetoxybenzoic acid	186–187	187–188[23]
26	2,6-Ditertbutyl-4-methylphenol **26**	$CHCl_3$/rt/30	98	2,6 -Di-tertbutyl-4-methyl phenyl acetate[b]	64–65	
27	2,6-Ditertbutyl-4-methylphenol **27**	$CHCl_3$/62/5	98	2,6 -Di-tertbutyl-4-methyl phenyl acetate[b]	64–65	
28	2,4,6-Tritertbutylphenol **28**	$CHCl_3$/62/60	95	2,4,6-Tritertbutylphenyl acetate [b]	109–110	

[a]Yields refer to isolated products.
[b]The structural assignment here must formally be regarded as tentative in the absence of literature or full characterisation data.

spectra were determined on Bruker 300(300MHz), using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal reference. Mass spectra were measured on a VG-7070E spectrometer (EI, 70eV). All used chemicals were obtained commercially.

The preparation of catalyst: PTA (10g) was dissolved in diethyl ether (50ml), and silica gel (10g) was added to the solution. After the mixture had been stirred for 1 h, the solvent was removed under reduced pressure. The mixture was dried at 110°C for 2 h, and finally stored in a desiccator until use.

General procedure for the acetylation of alcohols and phenols: A mixture of the alcohol or phenol (10mmol), acetic anhydride (2 equivalent to each hydroxyl group in the alcohols or phenols), silica gel-supported PTA (300mg) and solvent (CH_2Cl_2, $CHCl_3$ or cyclohexane) was stirred at room temperature or refluxing temperature for the length of time indicated in the Table 1. The progress of the reactions was monitored by thin layer chromatography (TLC). After completion of the reaction, the solvent was evaporated and diethyl ether (15ml) added to the mixture. The catalyst was removed by filtration and washed with diethyl ether (2×10ml). The filtrate was washed with 5% HCl (20ml), 5% $NaHCO_3$ (20ml) and brine (2×10ml) successively. After drying with anhydrous sodium sulfate, the solvent was evaporated under reduced pressure and the crude product was purified by recrystallisation from 95% ethanol or by column chromatography on silica gel using petroleum ether and diethyl ether to get the pure product.

Octyl acetate **:** δ_H 0.88(3H, t, –C**H**$_3$), 1.20–1.43(10H, m, CH_3(C**H**$_2$)$_5$–), 1.78(2H, m, –C**H**$_2$$CH_2OOC$ CH_3), 2.04(3H, s, –OCOC**H**$_3$), 4.05(2H, t, –C**H**$_2$OCOCH_3).

Benzyl acetate **:** δ_H 2.07(3H, s, –OCOC**H**$_3$), 5.09(2H, s, ArC**H**$_2$–), 7.26-7.36(5H, m, –C$_6$**H**$_5$).

*2-Phenylethyl acetate***:** δ_H 2.06(3H, s, –OCOC**H**$_3$), 2.32(2H, t, ArC**H**$_2$–), 4.83(2H, t, –C**H**$_2$–), 7.15-7.38 (5H, m, –C$_6$**H**$_5$).

*1-Octadecyl acetate***:** δ_H 0.89(3H, t, –C**H**$_3$), 1.27(30H, m, CH_3(C**H**$_2$)$_{15}$–), 1.80(2H, m, –C**H**$_2$$CH_2OOC$ CH_3), 4.34(2H, t, –C**H**$_2$OCOCH_3), 2.02(3H, s, –OCOC**H**$_3$).

*Benzoin acetate***:** δ_H 7.30–8.01(10H, m, Ar–**H**), 5.82(1H, s, –C**H**), 2.03(3H, s, –OCOC**H**$_3$).

*Cyclohexyl acetate***:** δ_H1.25–1.60(10H, m, –C$_6$**H**$_{11}$), 3.02(1H, m, –C**H**OOCCH_3), 2.00(3H, s, –OCOC**H**$_3$).

*Cholesteryl acetate***:** δ_H5.30(1H, d, 6-**H**), 3.51(1H, m, 3α-**H**), 1.18(3H, s,19-C**H**$_3$), 0.95(3H, d, 21-C**H**$_3$), 0.88(6H, d, 26, 27-C**H**$_3$), 0.65(3H, s, 18-C**H**$_3$), 2.01(3H, s, –OCOC**H**$_3$).

*4-Methylphenyl acetate***:** δ_H2.01(3H, s, –OCOC**H**$_3$), 2.25(3H, s, –Ar–C**H**$_3$), 6.92(2H, d, 2',6'–Ar–**H**), 7.04(2H, d, 3',5'–Ar–**H**).

*4-Chlorophenyl acetate***:** δ_H1.98(3H, s, –OCOC**H**$_3$), 6.98(2H, d, 2',6'–Ar–**H**), 7.25(2H, d, 3',5'–Ar–**H**).

*2,6-Ditertbutyl-4-methyl phenyl acetate***:** IR ν_{max} (KBr): 2955, 1760, 1600, 1470, 1380, 1100, 870 cm^{-1} ; δ_H1.34(18H, s, –C(C**H**$_3$)$_3$), 2.32(3H, s, –C**H**$_3$), 2.36(3H, s, –OCOC**H**$_3$), 7.11(2H, s, 3,5-Ar-**H**); *m*/*z*(EI): 262(3%, M$^+$), 43(100), 57(65), 77(10), 91(15), 105(14), 145(10), 161(8), 205(88), 220(60).

*2,4,6-Tritertbutylphenyl acetate***:** IR ν_{max}(KBr): 2960, 1750, 1600, 1460, 1370, 1110, 900 cm^{-1};δ_H1.33(9H, s, -4-C(C**H**$_3$)$_3$), 1.37(18H, s, -2,6-C(C**H**$_3$)$_3$), 2.35(3H, s, –OCOC**H**$_3$), 7.34(2H, s, –C$_6$**H**$_2$); *m*/*z*(EI): 304(2%, M$^+$), 41(55), 43(82), 57(100), 77(5), 91(9), 105(6), 145(2), 231(7), 246(50), 261(30).

This project is supported by NSFC (29872011 and 29572039). Educational Ministry of China, Educational Department of Hebei Province (990104), Science and Technology Commission of Hebei Province.

Received 18 December 2002, accepted 28 March 2003
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References

1 (a) T. W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 2nd edn (John Wiley and Sons Inc, New York), 1991, p 87–118; 162-170; (b) T.S. Li, Y.L.Li and X.T. Liang, *Steroids*, 1990, **55,** 263; (c) C.B. Reese, *Protective Groups in Organic Chemistry*; J.F.W. McOmie, ed.; Plenum: London, 1973, 109; (d) P.J. Kocienski, *Protective Groups*; Thieme: New York, 1994, 22; (e) R.C. Larock, *Comprehensive Organic Transformations*, 2nd edn Wiley-VCH: New York, 1999, 1995.

2 (a) R.I. Zhdanov and S.M. Zhenodarova, *Synthesis*, 1975, 222; (b) D. Horton, *Org. Synth*., 1973, **5,** 1.
3 (a) G. Holfe, V. Steglich and H. Vorbruggen, *Angew. Chem.,Int. ed Engl*., 1978, **17**, 569; (b) E.F.V. Scriven, *Chem . Soc. Rev*, 1983, **12**, 129.
4 E. Vedejs, N.S. Bennett, L.M. Conn, S.T. Diver, M. Gingras, S. Lin, P.A. Oliver and M.J. Peterson, *J. Org. Chem*., 1993, **58**, 7286.
5 R. Borah, N. Deka and J.C. Sarma, *J. Chem. Res(S)*., 1997, 110.
6 A.C. Cope and E.C. Herrich, *Org. Synth*., 1963, **4**, 304.
7 T.S. Jin, Y.R. Ma A.H. Zhang and T.S. Li, *Synth. Commun*., 1998, **28**, 3173.
8 R.H. Baker and F.G. Bordwell, *Org. Synth*., 1955, **3**, 141.
9 J. Iqbal and R.R. Srivastava, *J. Org. Chem*., 1992, **57**, 2001.
10 S.V. Pansare, M.G. Malusare and A.N. Rai, *Synth. Commun*., 2000, **30**, 2587.
11 P. Saravanan and V.K. Singh, *Tetrahedron Lett*., 1999, **40**, 2215.
12 P.A. Procopiou, S.P.D. Baugh, S.S. Flack and G.G.A. Inglis, *Chem. Commun*., 1996, 2625.
13 S. Chandrasekhar, T. Ramachander and M. Takhi, *Tetrahedron Lett*., 1998, **39**, 3263.
14 K. Ishihara, M. Kubota, H. Kurihara and H. Yamamoto, *J. Org. Chem*., 1996, **61**, 4560.
15 G. Sabitha, B.V.S. Reddy, R. Srividya and J. S. Yadav, *Synth. Commun*., 1999, **29**, 2311.
16 Y. Yasuyuki, I. Kusaki and T. Sato, *Synlett*., 2001, **10**, 1584.
17 A.X. Li, T.S. Li and T.H. Ding, *Chem. Commun*., 1997, 1389.
18 T.S. Li and A.X. Li, *J. Chem. Soc. Perkin.Trans1*., 1998, 1913.
19 T.S. Jin, Y.R. Ma and T.S. Li, *Ind. J. Chem*., 1999, **38**, 109.
20 M.H. Habibi, S. Tangestaninejad, V. Mirkhani and B. Yadollahi, *Synth. Commun*., 2002, **32**, 863.
21 (a) Y.X. Lu, Journal of *Zhengzhou Institute of Light Industry*, 1999, **14**, 60; (b) I. V. Kozhevnikov, S. M. Kulikov and N.G. Chukaeve, *et al. React Kinet, Catal. Lett*., 1992, **47**, 59.
22 L. Syper and L.S. Mlochowski, *Tetrahedron*, 1987, **43**, 212.
23 J. Buckingham, F. Macdonald, *Dictionary of Organic Compounds*. 1996, 6th edn., Chapman and Hall, New York.