International Journal of Chemistry and Applications.
ISSN 0974-3111 Volume 6, Number 1 (2014), pp. 47-53
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Copper Sulphate as an Efficient Catalyst for Protection of Hydroxyl Groups Using Acetyl Chloride

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Abstract

Acetylation of hydroxyl groups is the most commonly used transformation method in organic chemistry. Acetyl group is most popular among the various protecting groups due to its easy introduction, stability towards acidic reaction condition, easy removal etc. We have developed a protocol using acetyl chloride as acetylating agent and copper sulphate ($CuSO_4$) as a catalyst without using a solvent at ambient temperature. It has been found to be a very good catalyst for acetylation of varieties of alcohols. The yields were excellent with shorter time period.

$$\mathrm{ROH} \xrightarrow[\text{2. } \mathrm{CuSO_4} \text{ (10 mol\%)}]{\text{1. AcCl (2 equiv.)}} \mathrm{ROAc}$$

Keywords: Acetylation, $CuSO_4$, acetyl chloride, acetic acid

Introduction

Acetylation groups is the most commonly used transformation method in organic chemistry as it is an efficient and inexpensive means for protecting hydroxyl groups. Actyl group is most popular among the various protecting groups due to its easy introduction, stability towards acidic reaction condition, easy removal etc.

Review of literature

Wide varieties of methods have been developed for this purpose. Acetylation is usually carried out by treatment of an alcohol with acetyl chloride or acetic anhydride in a suitable organic solvent, although acetic anhydride is the most commonly used.[i]To increase the rate of acetylation, the reaction is carried out under an acid catalyzed condition or under base catalysed condition. In this respect Heteropoly acids, [ii, iii, iv]yttria–zirconia-based Lewis acid, [v]sulfamic acid, [vi]Perchloric acid, [vii]*p*-toluene sulfonicacid, [viii]etc acidic catalysts were used. Many of such reactions were reported using homogeneous basic catalyst such as amine[ix]DMAP, [x] tri-butyl phosphine[xi]etc. Some other common base catalysts are 1, 4-diazobicyclo[2.2.2]-octane (DABCO), [xii]and *N, N, N, N*-tetramethylethylenediamine (TMEDA).[xiii]

Besides these other reagents like various metal salts such as, $ZnCl_2$, [xiv]$COCl_2$, [xv]VanadylSulfate ($VOSO_4.3H_2O$), [xvi]$RuCl_3$, [xvii]$TiCl_4$-$AgClO_4$, [xviii]$TaCl_5$, $TaCl_5$-SiO_2, [xix]Sn (IV) porphyrine, [xx]Flourous-distannoxane, [xxi]Distannoxane**,** [xxii]$AlPW_{12}O_{40}$, [xxiii]Zr $(HSO_4)_4$, [xxiv]$ZrCl_4$, [xxv] Cu $(BF_4)_2.6H_2O$, [xxvi]$LiClO_4$, [xxvii]$ZrOCl_2.8H_2O$, [xxviii]$CeCl_3$, [xxix]$BiOClO_4.XH_2O$, [xxx]$MgBr_2$, [xxxi]LiCl, [xxxii] La $(NO_3)_3.6H_2O$, [xxxiii] some metal triflates such as Sc $(OTf)_3$[xxxiv]MeSiOTf, [xxxv]Ce (III) triflate, [xxxvi] In $(OTf)_3$, [xxxvii] Cu $(OTf)_2$, [xxxviii] Bi $(OTf)_3$, [xxxix]LiOTf, [xl]Gd $(Otf)_3$[xli] and other reagents like bis (cyclopentadienyl) zirconium dichloride, [xlii]I_2, [xliii]Titanium-modified MCM-41, [xliv]1, 3-dibromo-5, 5-dimethylhydentoin or trichloroisocyanuric acid, [xlv]Lanthanide (III) Tosylates, [xlvi]NBS, [xlvii] metal triflates in ionic liquids, [xlviii] twisted amides, [xlix] solid supported reagents, [l] Lipase enzymes, [li]KF–Al_2O_3, [lii]$A1PO_4$-$A1_2O_3$, [liii] 1-Methyl imidazole, [liv]$InCl_3$/montmorillonite K-10[lv] catalysts, Al $(HSO_4)_3$, [lvi] Graphite Bisulphate, [lvii]Chiral Phosphines[lviii]etc have been investigated to meet the demand for more efficient and selective methods. Now a days some green chemical methods, like use of Chlorofer rate (III) Ionic Liquid, [lix] ultrasound promoted acetylation, [lx] solvent and catalyst free acetylation[lxi] etc. are also used in this purpose.

However most of these methods still have limitations such as harsh reaction conditions, long periods of reaction, use of large amount of organic solvents as the reaction medium and air sensitive nature of catalysts, tedious work up procedure, difficult product isolation process of high boiling solvents, formation of by-products etc. Nowadays, the reactions are carried out under catalyst and solvent-free conditions which are considerably safe, nontoxic, environmentally friendly and inexpensive. Therefore searching of new procedures is still going on.

Results and discussion

Recently, $CuSO_4.5H_2O$ has been used as a Lewis acid catalyst for various organic transformations as an inexpensive, available and safe reagent.[lxii]Heravi et al described a procedure for acetylation of alcohols and phenols under solvent-free conditions in the presence of a catalytic amount of Copper (II) sulfate pentahyd rate with acetic anhydride at room temperature.[lxiii] However, in case of alcohols, the reactions are completed in 24 hrs. Phenols also took 1-2 hrs. for completion of the reaction. Such a long time period is a great disadvantage for a reaction.

Therefore, we thought that changing of acetylating agent may affect the time period of the reaction. We have used acetyl chloride as acetylating agent and copper sulphate ($CuSO_4$) as a catalyst in the acetylation reaction (Scheme 1).

$$\mathrm{ROH} \xrightarrow[\text{2. } \mathrm{CuSO_4} \text{ (10 mol\%)}]{\text{1. AcCl (2 equiv.)}} \mathrm{ROAc}$$

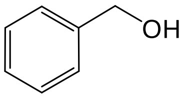
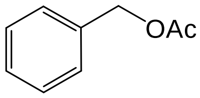
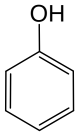
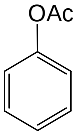
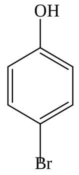
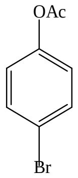
Scheme-1

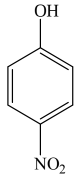
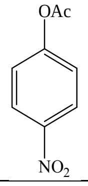
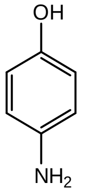
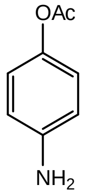
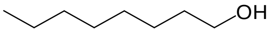
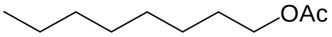
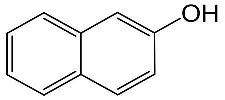
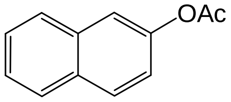
Our study began with the reaction of benzyl alcohol as test reaction. No solvents were used and it was carried out at ambient temperature. It has been found that the reaction with benzyl alcohol took place within 8 minutes as expected. The formation of the product was confirmed by monitoring TLC. After usual work up the benzyl acetate was found with excellent yield. At first the reaction was carried out using 1 equivalent of benzyl alcohol, 1 equivalent of acetyl chloride using 10 mol % of $CuSO_4$. However, reaction time decreases only to 6 hrs. When 2 equivalent of acetyl chloride was used the reaction took place within 8 minutes. The reaction was further studied using different alcohols ranging from aromatic to aliphatic alcohols under the same reaction conditions (Table 1).

General Procedure

Substrate 1mmol, and acetyl chloride (2 mmol, 2.5mmol[a]) were added to $CuSO_4.5H_2O$ (10 mol%, 20 mol%[a]) in a 50 ml round bottomed flask. The mixture was stirred at room temperature and progress of the reaction was monitored by TLC. The mixture was diluted with 10% sodium bicarbonate (15 ml) and extracted with dichloromethane. Combined organic layers were dried over Na_2SO_4. The solvent was distilled off under reduced pressure to get the pure acetylated product.

Table: 1 Acetylation of alcohols using acetyl chloride as acetylating agent

	Entry	Substrate	Product	Yield	Time (min)
	1			75	8
	2			80	8
	3			83	10

	4			78	10
	5			78	5
	6[a]			78	15
	7			81	5

Reaction condition: Substrate 1mmol, acetyl chloride 2 mmol, catalyst 10 mol%
[a]Reaction condition: Substrate 1mmol, acetylating agent 2.5mmol, catalyst 20 mol%

Both aromatic as well as aliphatic alcohols gave very good results. In all cases yields were very good and especially time periods were very short. After getting the products, these are characterized by IR and NMR spectral analysis.

Conclusion

Therefore, in conclusion, a better protocol has been developed using acetyl chloride as acetylating agent and Copper sulphate ($CuSO_4$) as a catalyst without using a solvent in lesser time period.

Supporting informations

1. Benzyl acetate: IR (KBr, cm^{-1}) ν: 2956, 2364, 1740, 1598, 1456, 1362, 1232, 1028, 832, 748, 698, 612, 502; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.24-7.20 (m, 5H), 4.98 (s, 2H), 1.97 (s, 3H).
2. Phenyl acetate: ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.29-7.29 (m, 2H), 7.28-7.12 (m, 1H), 7.03-7.00 (m, 2H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 169.6, 150.6, 129.4, 125.8, 121.5, 21.1

Acknowledgement

We thank the Director, Sikkim Manipal Institute of Technology, Majitar, Sikkim-737136 for providing research facilities.

References

[1] (*a*) Greene, T. W.; Wuts, P. G. M.; *Protective Groups in Organic Synthesis*, Wiley, New York, 3rd edn., **1999**, 150; (b) Pearson, A. L.; Roush, W. J.; *Handbook of Reagents for Organic Synthesis: Acetylating Agents and Protecting Groups*, John Wiley, Chichester, **1999**

[2] Heravi, M. M.; Behbahani, F. K.; Bamoharram, F. F.; *ARKIVOC*, **2007**, (xvi), 123-131

[3] Romanelli, G. P.; Bennardi, D. O.; Autino, J. C.; Baronetti, G. T.; Thomas, H. J.; *E-J. Chem.*, **2008**, *5*, 641.

[4] Heravi, M, M.; Bakhtiari, K.; Javadi, N. M.; Oskooie, H. A.; Bamoharram, F. F.; *Monatsh.Chem*. **2007**, *138*, 445.

[5] Kumar, P.; Pandey, R. K.; Bodas, M. S.; Dagade, S. P.; Dongare, M. K.; Ramaswamy, A. V.; *J. Mol. Catal. A: Chem*., **2002,** *181*, 207.

[6] Jin, T.-S.; Ma, Y.-R.; Zhang Z.-H.; Li, T.-S., *Synth. Commun*, **1998**, 28, 17, 3173-3177

[7] Fritz, J. S.; Schenk, G. H.; Anal. Chem., **1959**, *31*, 1808.

[8] Cope, A.; Herrick, E. C.; *Org. Synth.,* **1963**, *4*, 304.

[9] Zhdanov, R. I.; Zhenodarova, S. M.; *Synthesis*, **1975**, *4***,** 222.

[10] (a) Hofle, G., Steglich, V., Vorbruggen, H., *Angew. Chem. Int. Ed.*1978, **17**, 569. (b) Scriven, E. F. V., *Chem. Soc. Rev.***1983**, *12***,** 129.

[11] Vedejs, E., Diver, S. T., *J. Am. Chem. Soc.***1993**, *115***,** 3358.

[12] (a) Ishihara, K.; Kurihara, H.; Yamamoto, H.; *J.Org. Chem.,* **1993**, *58***,** 3791. (b) Hajipour, A. R.; Mazloumi, G.; *Synth. Commun.,* **2002**, *32***,** 23.

[13] Sano, T.; Ohashi, K.; Oriyama, T.; *Synthesis,* **1999**, *7***,** 1141.

[14] Gupta, R.; Kumar, V.; Gupta, M.; Paul, S.; Gupta, R. *Ind. J. Chem.*, **2008**, *47B*, 1739.

[15] Iqbal, J.; Srivastava, R. R.; *J. Org.Chem.*, 1992, **57,** 2001.

[16] Oskooie, H. A.; Baghernezhad, B.; Heravi, M. M.; Beheshtiha, Y. S. *J. Chin.Chem.Soc.*, **2008**, *55*, 713.

[17] Xi, Z.; Hao, W.; Wang, P.; Cai, M.; *Molecules,* **2009**, *14*, 3528.

[18] Cope, A. C.; Herrich, E. C.; *Organic Synthesis Coll, Vol. IV*, Wiley: New York, **1963.**

[19] Chandrasekhar, S.; Chander, T. R.; Takhi, M.; *TetrahedronLett.,* **1998**, *39*, 3263.

[20] Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; MohammadpourBaltrork, I.; Shabani, R.; *J. Mol. Catal.,* **2004**, *219*, 73.

[21] Peng, Z.; Orita, A.; An, D.; Otera, J.; *TetrahedronLett*., 2005, *46*, 3187.

[22] Orita, A.; Mitsutome, A.; Otera, J.; *J. Org. Chem.,* **1998,** *63*, 2420.

[23] Firouzabadi, H.; IranPoor, N.; Amani, K.; *Chem. Commun*., **2003**, *6*, 764.

[24] Shirini, F.; Zolfigol, M. A.; Safari, A. *Ind. J. Chem.,* **2005,** *44 (B)*, 201.

[25] Chakraborti, A.K.; Gulhane, R.; *Synlett,* **2004**, *4*, 627

[26] Chakraborti, A.K.; Gulhane, R.; Shivani, R.G.; *Synthesis,* **2004**, *1*, 111.

[27] Lu, K.-C.; Hsieh, S.-Y.; Patkar, L. N.; Chen, C.-T. Lin, C.-C. *Tetrahedron*, **2004**, *60*, 8967.

[28] Ghosh, R.; Swarupananda, M.; Chakraborty, A.; *Tetrahedron Lett.***2005**, *46*, 177.

[29] Torregiani, E.; Gianfranco, S.; Minassi, A.; Appendino, G.; *Tetrahedron Lett.*, **2005**, *46*, 2193.

[30] Chakraborti, A.K.; Shivani, R.G.; *Synlett,* **2003**, *12*, 1805.

[31] Pansare, S.; Malusare, M.G.; Rai, A.N.; *Synth. Commun.*, **2000**, *30*, 2587.

[32] Sabitha, G.; Reddy, B.V.S.; Srividya, R.; Yadav, J.S.; *Synth.Commun.*, **1999**, *29*, 2311.

[33] Akhlaghinia, B.; Seyyedlary, Z. P.; *J. Iran.Chem. Res.*, **2009**, *2*, 31.

[34] Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H.; *J. Org. Chem.* **1996**, *61*, 4560. (b) Zhao, H.; Pendri, A.; Greenwald, R. B. *J. Org. Chem.* **1998,** *63*, 7559-7562

[35] Procopiou, P. A.; Baugh, S. P. D.; Flack, S. S, Inglis, G. G. A.; *J. Org. Chem.*, **1998**, *63*, 2342.

[36] Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Procopiou, P. A.; Nardi, M.; Bartoli, G.; Romeo, R.; *Tetrahedron Lett.*, **2003**, *44*, 5621.

[37] Chauhan, K. K.; Frost, C.G.; Love, I.; Waite, D., *Synlett,* **1999**, 1743.

[38] Chandra, D.; Saravanan, P.; Singh, R. K.; Singh, V. K.; *Tetrahedron,* **2002**, *58*, 1369.

[39] Orita, A.; Tañáis, G.; Kakuda, A.; *J. Angew.Chem. Int. Ed.*, **2000**, 39, 2877.

[40] Karimi, B.; Maleki, J. *J. Org. Chem.* **2003**, *68*, 4951.

[41] Yoon, H.-J.; Lee, S.-M.; Kim, J.-H.; Cho, H.-J.; Lee, Y.-S. Appl. Chem., **2007**, *11*, 425.

[42] Kantam, M. L.; Aziz, K.; Likhar, P. R. *Catal.Commun.***2006**, *7*, 484.

[43] Bosco, J. W. J.; Agrahari, A.; Saikia, A. K. *Tetrahedron Lett.***2006**, *47*, 4065.

[44] Angeles-Beltrán, D.; Negrón-Silva, G.; Lomas-Romero, L.; Iglesias-Arteaga, M. A.; Santos-Aires, F. J. C.*J. Mex. Chem. Soc.* **2008**, *52*, 175.

[45] Zolfigol, M. A.; Khazaei, A.; Choghamarani, A.G.; Rostami, A.; Hajjami, M. *Catal.Commun.***2006**, *7*, 399.

[46] Parac-Vogt, T. N.; Deleersnyder, K.; Binnemans, K. *Eur. J. Org. Chem.* **2005**, 1810.

[47] (a) Kartha, K.P.R.; Field, R.A.; *Tetrahedron,* **1997**, *53*, 8129. (b) Karimi, B.; Seradj, H.; *Synlett,* **2001**, 4, 519.

[48] Orita, A.; Tanahashi, C., Kakuda, A.; Otera, J.; *Angew.Chem. Int. Ed.***2000**, *39*, 2877.

[49] S. Yamada, T. Sugaki, K. Matsuzaki, *J. Org. Chem.***1996**, 61, 5932

[50] (a) Ballini, R.; Bosica, G.; Carloni, S.; Ciaralli, L.; Maggi, R.; Sartori, G.; *Tetrahedron Lett.* **1998**, *39*, 6049. (b) Li, A.-X.; Li, T.-S.; Ding, T.-H.; *Chem. Commun.***1997**, *14*, 1389. (c) Bhaskar, P.M., Loganathan, D.; *Tetrahedron Lett.***1998**, *39*, 2215. (d) Reddy, C.R., Iyengar, P.; Nagendrappa, G.; Jai Prakash, B.S.; *J. Mol. Catal. A: Chem.* **2005**, *229*, 31.

[51] Berger, B.; Rabiller, C.G.; Konigsberger, K.; Faber, K.; Griengl, H.; *Tetrahedron: Asymmetry,* **1990**, *1*, 541.

[52] Yadav, V.K.; Babu, K.G.; Mittal, M.; *Tetrahedron,* **2001**, *57*, 7047.

[53] Costa, A.; Riego, J. M.; *Can. J. Chem.*, **1987**, *65*, 2327.

[54] Qin-pei, W.; Hua, L.; Hai-xia, L.; Xi, C.; Hao, W.; Qing-shan, Z.; Yun-zheng, L.; *Chem. Res. Chin. Univ.*, **2010**, *26*, 55.

[55] Choudhary, V. R.; Patil, K. Y.; Jana, S. K.; *J. Chem. Sci.*, **2004**, *116*, 175.

[56] Shirini, F**.;** Zolfigol, M. A.; Abedini, M.; Salehi**, P.;** *Bull. Korean Chem. Soc.*, **2003**, *24*, 1683.

[57] Seçen, H.; Kalpar, A. H. ; *Turk J Chem.*, **1999**, *23*, 27.

[58] Vedejs, E.; Daugulis, O.; Diver, S. T.; *J. Org. Chem.*, **1996,** *61*, 430.

[59] Wang, D.-S.; Li, G.-Y.; Yan-Qing Peng, Y.-Q.; *J. Chin. Chem. Soc.*, **2009**, *56*, 834.

[60] Gholap, A. R.; Venkatesan, K.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V**.;** *Green Chem.*, **2003**, *5*, 693.

[61] Ranu, B. C.; Dey, S. S.; Hajra, A.; *Green Chem.*, **2003**, *5*, 44.

[62] (a)Khan, A. T.; Choudhury, L., H.; Ghosh, S.; *TetrahedronLett.*, **2004**, *45*, 7891. (b) Akhlaghinia, B.; Tavakoli, S.; *Synthesis* **2005**, 11. (c) Gohain, M.; Prajapati, D.; Sandhu, J. S.; *Synlett*, **2004**, 235.

[63] Heravi, M.M.; Behbahani, F. K.; Zadsirjan, V.; Oskooie, H. A.; *J. Braz. Chem. Soc.*, **2006**, *17*, 1045.