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$Mg(HSO_4)_2$ AS A MILD AND EFFICIENT REAGENT FOR ACETYLATION OF ALCOHOLS

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ABSTRACT

A variety of alcohols were acetylated in good to high yields with acetic anhydride, in the presence of $Mg(HSO_4)_2$ in CH_2Cl_2 under mild and heterogeneous conditions.

Key words: $Mg(HSO_4)_2$, Acetic anhydride, Acetylation, Heterogeneous conditions.

INTRODUCTION

The acetylation of the hydroxyl group is one of the most widely used transformations in organic synthesis.[1,2] A direct esterification of alcohols with carboxylic acids is generally avoided because the equilibrium that is established between the reagents and the products requires the use of excess reagents or elimination of water form the reaction mixture to drive the process to completion. Many useful methods for esterification have been reported in the literature.[3–5] Some of the recently developed methods involve the use of organic [6–8] inorganic[9] and organometallic reagents.[10] However, most of these methods suffer from one or more of the following disadvantages: long reaction times, vigorous reaction conditions, the occurrence of side reactions and unavailability of the reagents, as well as poor yields of the desired product in many cases.

Acetylation is normally performed by using acetic anhydride or acetyl chloride in the presence of a base such as trimethylamine or pyridine. Further, the rate of acetylation is known to be increased considerably if 4–dimethylaminopyridine is used as a co–catalyst.[2] *p*–Toluenesulfonic acid [11] (a protic acid) and Lewis acids such as $TiCl_4$/ $AgClO_4$,[12] $Cu(OTf)_2$,[13] $TaCl_5$,[14] $FeCl_3$,[15] $Cu(NO_3)_2.3H_2O$[16], $NaHSO_4.H_2O$[17] have been used to acetylate alcohols. Apart from these catalysts, TMSOTf,[18] and TMSCl[19] have also been used as efficient catalysts for acetylation of alcohols.

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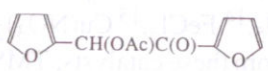
EXPERIMENTAL

General procedure for acetylation of alcohols using acetic anhydride: To a solution of alcohol (1 mmol) and acetic anhydride (1.5 mmol) in dichloromethane (5 mL) $Mg(HSO_4)_2$ (0.5 mmol) was added and the mixture was refluxed until complete disappearance of the starting material (The reaction was monitored by TLC). After completion, the reaction mixture was quenched with water (20 mL), and the mixture was extracted by CH_2Cl_2 (30 mL). The organic layer was separated , and washed with saturated $NaHCO_3$ (25 mL) and water (15 mL) and dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding acetates from good to high yields.

In continuation of our studies in the applications of $Mg(HSO_4)_2$ in organic chemistry,[20,21,22] we wish to report the applicability of $Mg(HSO_4)_2$ for efficient acetylation of alcohols. All reactions were performed under mild and heterogeneous conditions (Table, Scheme). The actual role of $Mg(HSO_4)_2$ is not clear. However, we can consider two plausible explanations, which are: a) activation of acyl moiety by coordination, b) smooth adsorption of the generated water. This methodology is not useful for the acetylation of allylic alcohols (Table 1, entry 11).

Table 1. Acetylation and formylation of alcohols in the presence of $Mg(HSO_4)_2$

Entry	Substrate	Ac_2O/AcOH/ HCO_2H	Product	Time (hr)	Yield %[a,b]
1	$C_6H_5CH_2OH$	Ac_2O	$C_6H_5CH_2OAc$	0.17	92
2	$2\text{–}BrC_6H_4CH_2OH$	Ac_2O	$2\text{–}BrC_6H_4CH_2OAc$	0.50	90
3	$2\text{–}MeC_6H_4CH_2OH$	Ac_2O	$2\text{–}MeC_6H_4CH_2OAc$	0.17	85
4	$4\text{–}ClC_6H_4CH_2OH$	Ac_2O	$4\text{–}ClC_6H_4CH_2OAc$	0.25	82
5	$2\text{–}NO_2C_6H_4CH_2OH$	Ac_2O	$2\text{–}NO_2C_6H_4CH_2OAc$	2.00	60
6	$C_6H_5CH_2CH_2CH_2OH$	Ac_2O	$C_6H_5CH_2CH_2CH_2OAc$	0.50	90
7	$C_6H_5CH_2CH(OH)CH_3$	Ac_2O	$H_5CH_2CH(OAc)CH_3$	0.50	93
8	Cyclohexyl–OH	Ac_2O	Cyclohexyl–OAc	1.50	87
9	$C_6H_5CH(OH)C(O)C_6H_5$	Ac_2O	$C_6H_5CH(OAc)C(O)C_6H_5$	1.00	80
10		Ac_2O		0.17	50
11	$C_6H_5CH{=}CHCH_2$ OH	Ac_2O	$C_6H_5CH{=}CHCH_2OAc$	0.17	–[c]

a: Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy, b: Isolated yields, c: Mixture of products

$$Ac_2O + ROH \xrightarrow[CH_2Cl_2,\ reflux]{Mg(HSO_4)_2} CH_3COOR$$

Scheme

In conclusion, we have shown that $Mg(HSO_4)_2$ is a good reagent for acetylation of a variety of alcohols under mild reaction conditions. The reactions are clean and the products yields are good to high and the procedure is easy. Further investigation on the new applications of $Mg(HSO_4)_2$ is ongoing in our laboratories.

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REFERENCES

1. T. W. Greene and P. G. Wuts, "Protective Groups in Organic Synthesis", 3rd ed.; John Wiley & Sons, NY (1991).
2. (a) G. Hofle, V. Steglich and H. Vorbruggen, Angew. Chem. Int. Ed. Engl., **17**, 569 (1978). (b) E.F.V. Scriven, Chem. Soc. Rev.,**12**, 129 (1983).
3. E. Haslam, Tetrahedron, **36**, 2409 (1980).
4. R. B. Wagner and D. H. Zook, "Synthetic Organic Chemistry", Wiley; NY (1953) p 479.
5. H. Henecka, Method Org. Chem., **8**, 541 (1953).
6. B. Kumar, K. R. Verma and H. Singh, Indian J. Chem., Sect. B, 692 (1986).
7. P. H. Wassel, T. Iverson and D. R. J. Bundle, J. Chem. Soc., Perkin Trans. 1, 2247 (1985).
8. K. Wakasugi, A. Nakamura and Y. Tanabe, Tetrahedron Lett., **42**, 7424 (2001).
9. B. Karimi and H. Seraj, Synlett., **4**, 519 (2001).
10. Y. Ishii, M. Takeno, Y. Kawasaki, A. Muromachi, Y. Nishiyama and S. Sakaguchi, J. Org. Chem., **61**, 3088 (1996).
11. A. C. Cope and E. C. Herrick, Org. Synth. Coll., Vol 4, 304 (1963).
12. M. Miyashita, I. Shiina, S. Miyoshi and T. Mukaiyama, Bull. Chem. Soc. Jpn., **66**,1516 (1993).
13. P. Saravanan and V. K. Singh, Tetrahedron Lett., **40**, 2611 (1999).
14. S. Chandrasekahar, T. Ramachander and M. Takhi, Tetrahedron Lett., **39**, 6081 (1998).
15. G. V. M. Sharma, A. K. Mahalingam, M. Nagarajan, A. Ilangovan and P. Radhakrishna, Synlett, **8**, 1200 (1999).

16. N. Iranpoor, H. Firouzabadi and M. A. Zolfigol, Synth. Commun., **28**, 1923 (1998).
17. Y. Q. Li, Synth. Commun., **29**, 3901 (1999).
18. P. A. Procopion, S. P. D. Bangh, S. S. Flack and G. G. A. Inglis, *Chem. Com*mun., 2625 (1996).
19. R. Kumareswaran, A.Gupta and Y.D. Vankar, Synth. Commun., **27**, 277 (1997).
20. F. Shirini, M. A. Zolfigol, B. Mallakpour, S. E. Mallakpour and A. R. Hajipour, Aust. J. Chem., **54**, 405 (2001).
21. F. Shirini, M. A. Zolfigol, B. Mallakpour, S.E.Mallakpour, A. R. Hajipour and I. Mohammadpour –Baltork, Tetrahedron Lett., **43**, 1555 (2002).
22. F. Shirini, M. A. Zolfigol, B. Mallakpour, I. Mohammadpour–Baltork, S.E. Mallakpour and A. R. Hajipour, J. Chem. Res (S), accepted for publication.

GRAPHICAL ABSTRACT

$Mg(HSO_4)_2$ as a mild and efficient reagent for acetylation and formylation of alcohols $Mg(HSO_4)_2$

$$Ac_2O + ROH \xrightarrow[CH_2Cl_2,\ reflux]{Mg(HSO_4)_2} CH_3COOR$$

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