

Ammonium Decatungstocerate(IV): An Efficient Catalyst for the Protection and Deprotection of Tetrahydropyranyl Ethers

D. Karimian, B. Yadollahi* and V. Mirkhani

*Department of Chemistry, University of Isfahan, Isfahan 81746-73441, Iran**(Received 27 April 2014, Accepted 13 May 2016)*

In multi-step organic syntheses, the protection and deprotection of tetrahydropyranyl (THP) ethers is one of the most frequently used methods. Over the years, different methods have been used from various catalytic systems for the protection of hydroxyl groups as THP ethers and their deprotection. Herein we have reported that various alcohols and phenols have been efficiently converted to the corresponding THP ethers in high to excellent yields using catalytic amounts of ammonium decatungstocerate(IV) at room temperature. In the presence of this catalyst, various THP ethers have also been deprotected to the parent alcoholic or phenolic compounds. Mild reaction conditions, high to excellent yields, easy handling, compatibility with the other protecting groups and heterogeneous, non-toxic and cost-effective catalyst are some of the major advantages of this procedure. Because of its operational simplicity, generality, and efficacy, this method could be used for the conversion of various hydroxyl compounds to the corresponding THP ethers and vice-versa.

Keywords: Catalysis, Polyoxometalate, Protection, Deprotection, Tetrahydropyranyl ethers

INTRODUCTION

The protection-deprotection of hydroxyl compounds as THP ethers is one of the most frequently employed transformations in multi-step organic syntheses [1] because of their low cost, ease of preparation, stability towards basic media and ease of removal of protecting groups at a later stage. Over the years, numerous methods have been developed for the protection of hydroxyl groups as THP ethers and their deprotection. Catalysts such as *p*-TsOH [2], pyridinium *p*-toluenesulfonate (PPTS) [3], (TMSO)₂SO₂ [4], Nafion-H [5], K-10 montmorillonite [6], Ph₃P·HBr [7], H-Y zeolite [8], ZnCl₂ on alumina [9], heteropoly acids [10], CuCl [11], LiClO₄ in diethyl ether [12], LiBr in CH₂Cl₂ [13], VO(OAc)₂ [14], K₃CoW₁₂O₄₀·3H₂O [15], In(OTf)₃ [16], InCl₃ immobilized in ionic liquids [17,18], N,N'-dibromo-N,N'-1,2-ethanedylbis(benzene sulfonamide) [19], silica triflate [20], Fe(HSO₄)₃ [21], copper(II) chloride-acetic acid [22], copper *p*-toluenesulfonate [23],

Cu(NO₃)₂·3H₂O/HOAc [24], and SiO₂-*p*-TSA [25] have been used for this aim. However, some of the reported procedures have drawbacks, such as requiring higher reaction temperatures, much longer reaction times, use of volatile organic solvents, being incompatible with other acid-sensitive functional groups, and involving expensive catalysts. Thus, in spite of a number of existing methods for the formation of THP ethers, the development of new methods, which utilize highly catalytic, versatile and easy to handle reagents is desirable.

Polyoxometalates (POMs) as anionic transition-metal oxide clusters have received much attention not only for their unmatched structural diversity [26] but also for their potential applications in quite diverse disciplines including catalysis [27,28] and materials science [29]. There are numerous applications of POMs as acid and oxidation catalysts, including several large-scale industrial processes, both in heterogeneous and homogeneous conditions [30-32]. In the last two decades, the broad utilities of POMs have been demonstrated in a wide variety of synthetically useful selective transformations of organic substrates [33,34]. Due

*Corresponding author. E-mail: yadollahi@chem.ui.ac.ir



Scheme 1. Tetrahydropyranylation-depyranylation of benzyl alcohol in the presence of $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$.

to our continued interest in POMs, especially in cerium containing ones [35-39], and need for using a new and efficient method for protection and deprotection of the hydroxy group as THP ether, we investigated the use of ammonium decatungstocerate(IV) as a catalyst for the conversion of alcohols and phenols to the corresponding THP ethers as well as their subsequent deprotection. Herein, for the first time we want to report a simple and convenient synthetic protocol for tetrahydropyranylation of alcohols and phenols by catalytic amount of $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$ under mild reaction conditions, and their depyranylation to the corresponding parent compounds using the same catalyst in CH_3CN (Scheme 1).

EXPERIMENTAL

All materials were purchased from Merck and Fluka chemical companies and used without further purification. All products were identified by comparison of their physical and spectral data with those of authentic samples, and yields referred to isolated products. GC analysis was performed on a Shimadzu GC-16A instrument with a flame-ionization detector using silicon DC 200 or carbowax 20-M columns. Infrared spectra were recorded on a Nicolet impact 400D spectrophotometer. ^1H NMR spectra were recorded on a Bruker-AC 500 MHz spectrometer. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX. The chemical purity of all THP ethers was checked by gas chromatography and confirmed to be higher than 98%.

Preparation of the Catalyst

The ammonium decatungstocerate(IV) icosahydrate was prepared according to the literature [40]. $\text{Na}_2\text{WO}_4\cdot 2\text{H}_2\text{O}$ (25 g, 75 mmol) was dissolved in 100 ml of water, and the pH was adjusted to 7.2 by addition of acetic acid. After heating at 90 °C with stirring, an aqueous solution containing

$(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_2\cdot 2\text{H}_2\text{O}$ (2.5 g, 7.5 mmol) in 1 equiv. HNO_3 solution was added to make CeW_{10} precipitation in the solution. Cerium containing POM was obtained after filtration and used as catalyst. The structure of the catalyst was confirmed by IR, NMR, thermal gravimetric analysis (TGA) and elemental analysis. Thermal gravimetric analysis was performed on the catalyst, and the results indicated that the hydration numbers are between 18 and 21.

General Procedure for Protection of Alcohols into THP Ethers at Room Temperature

To a solution of alcohol (1 mmol), and 3,4-dihydro-2H-pyran (DHP) (2 mmol) in CH_3CN (3 ml), the catalyst (0.002 mmol) was added. The mixture was stirred at room temperature for a few minutes and progress of the reaction was monitored by GC. Filtration was carried out after completion of the reaction and the catalyst, because of its insolubility, was easily removed from the mixture. The pure product was separated by column chromatography, using ethylacetate/n-hexane (1:4) as the eluent. Evaporation of the solvent under reduced pressure gave the pure product (Table 1).

General Procedure for Deprotection of THP Ethers

To a solution of THP ether (1 mmol) in acetonitrile (3 ml), ammonium decatungstocerate(IV) (0.02 mmol) was added and the mixture was stirred for an appropriate time at room temperature. Progress of the reaction was monitored by GC and after completion of the reaction, the mixture was filtered. Evaporation of the solvent followed by chromatography on a short column of silica gel, gave the pure products (Table 2).

RESULTS AND DISCUSSION

In the first consideration, the focus was on the role of

Table 1. Catalytic Conversion of Alcohols to THP Ethers in the Presence of $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$ in $\text{CH}_3\text{CN}^{\text{a}}$

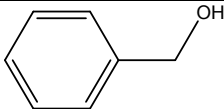
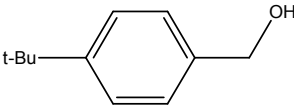
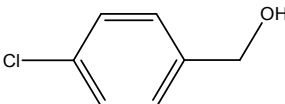
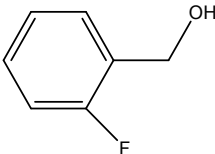
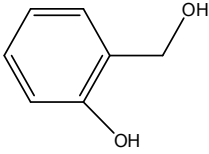
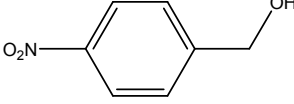
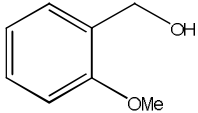
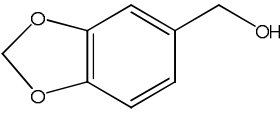
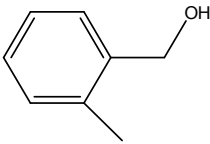
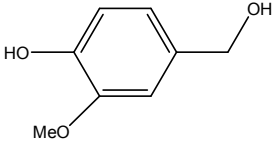
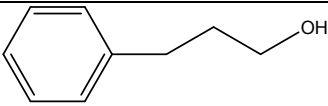
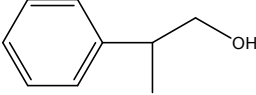
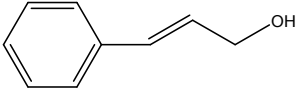
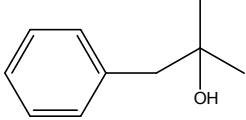
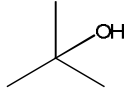
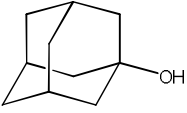
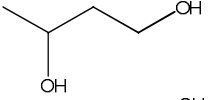
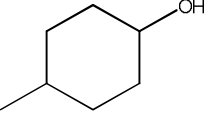
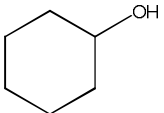
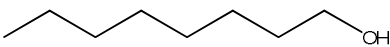
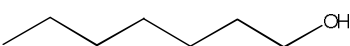
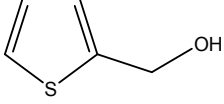
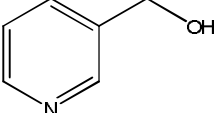
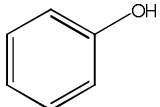
| Entry | Alcohol | Time (min) | Yield (%) ^b |
|-------|---|------------|------------------------|
| 1 |  | 1 | 96 |
| 2 |  | 3 | 90 |
| 3 |  | 2 | 85 |
| 4 |  | 2 | 80 |
| 5 |  | 1 | 96 |
| 6 |  | 4 | 60 |
| 7 |  | 1 | 90 |
| 8 |  | 1 | 92 |
| 9 |  | 2 | 86 |
| 10 |  | 4 | 73 |

Table 1. Continued

| | | | |
|----|---|-----|----|
| 11 |  | 2 | 96 |
| 12 |  | 1 | 96 |
| 13 |  | 3 | 67 |
| 14 |  | 3 | 96 |
| 15 |  | 2 | 90 |
| 16 |  | 2 | 92 |
| 17 |  | 2 | 96 |
| 18 |  | 1 | 96 |
| 19 |  | 1 | 96 |
| 20 |  | 2 | 95 |
| 21 |  | 2 | 90 |
| 22 |  | 2 | 96 |
| 23 |  | 2 | 96 |
| 24 |  | 120 | 60 |

^aAll products were identified by comparison of their physical and spectral data with those of authentic samples [14-25]. ^bIsolated yield.

Table 2. Catalytic Conversion of THP Ethers into Parent Alcohols by $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}] \cdot 20\text{H}_2\text{O}$ in CH_3CN^a

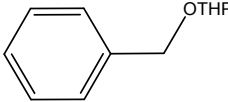
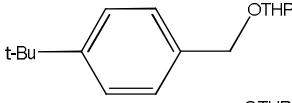
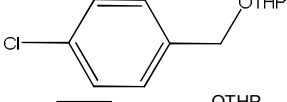
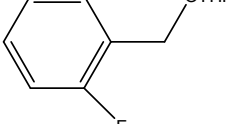
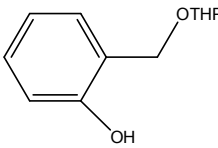
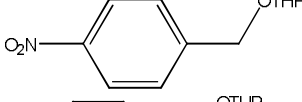
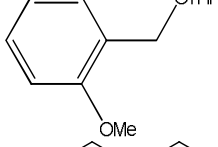
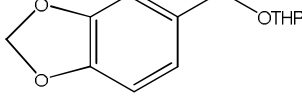
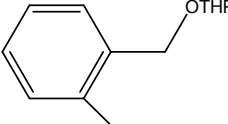
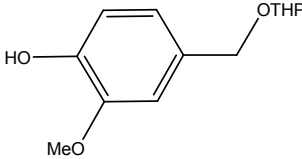
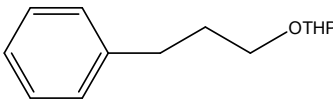
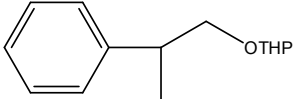
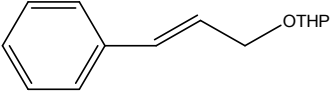
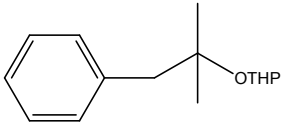
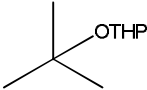
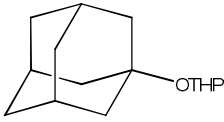
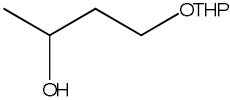
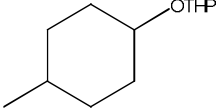
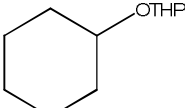
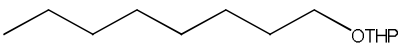
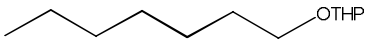
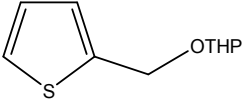
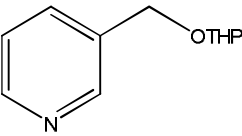
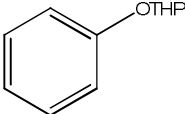
| Entry | Ether | Time (min) | Yield (%) ^b |
|-------|---|------------|------------------------|
| 1 |  | 30 | 96 |
| 2 |  | 120 | 83 |
| 3 |  | 120 | 72 |
| 4 |  | 120 | 80 |
| 5 |  | 120 | 75 |
| 6 |  | 180 | 60 |
| 7 |  | 120 | 70 |
| 8 |  | 60 | 67 |
| 9 |  | 180 | 62 |
| 10 |  | 120 | 70 |
| 11 |  | 30 | 80 |

Table 2. Continued

| | | | |
|----|---|-----|----|
| 12 |  | 30 | 96 |
| 13 |  | 100 | 60 |
| 14 |  | 180 | 75 |
| 15 |  | 180 | 75 |
| 16 |  | 120 | 80 |
| 17 |  | 120 | 65 |
| 18 |  | 60 | 96 |
| 19 |  | 120 | 94 |
| 20 |  | 200 | 70 |
| 21 |  | 200 | 73 |
| 22 |  | 120 | 70 |
| 23 |  | 120 | 86 |
| 24 |  | 60 | 92 |

^aAll products were identified by comparison of their physical and spectral data with those of authentic samples [14-25]. ^bIsolated yield.

Table 3. Comparison of Results between some of the Recently Reported Catalysts and $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$ for the Protection of Benzyl Alcohol by DHP

| Entry | Catalyst | Catalyst (mol%) | Time (min) | Yield (%) | Ref. |
|-------|--|-----------------|------------|-----------|------|
| 1 | $\text{VO}(\text{OAc})_2$ | 0.270 | 60 | 95 | [14] |
| 2 | $\text{K}_5\text{CoW}_{12}\text{O}_{40}\cdot 3\text{H}_2\text{O}$ | 0.010 | 5 | 97 | [15] |
| 3 | $\text{In}(\text{OTf})_3$ | 0.005 | 30 | 85 | [16] |
| 4 | N,N'-Dibromo-N,N'-1,2-ethanediylbis benzene sulfonamide | 0.010 | 110 | 89 | [19] |
| 5 | $\text{CuCl}_2\cdot 2\text{H}_2\text{O}/\text{HOAc}$ | 0.600 | 60 | 86 | [22] |
| 6 | $\text{Cu}(p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_3)_2\cdot 6\text{H}_2\text{O}/\text{HOAc}$ | 0.045 | 30 | 95 | [23] |
| 7 | $\text{Cu}(\text{NO}_3)_2\cdot 3\text{H}_2\text{O}/\text{HOAc}$ | 0.600 | 6 | 93 | [24] |
| 8 | Solid silica-based sulfonic acid | 0.020 | 15 | 92 | [41] |
| 9 | Bromodimethylsulfonium bromide $(\text{CH}_3)_2\text{S}^+\text{Br}^-$ | 0.010 | 5 | 85 | [42] |
| 10 | $(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$ | 0.002 | 1 | 96 | - |

$(\text{NH}_4)_8[\text{CeW}_{10}\text{O}_{36}]\cdot 20\text{H}_2\text{O}$ as a heterogeneous catalyst in the protection of alcohols to the corresponding THP ethers. To find the optimized reaction conditions, benzyl alcohol was chosen as a model substrate. At first, the catalytic amount of ammonium decatungstocerate(IV) was optimized and the best results were obtained using 0.002 equivalents of the catalyst in acetonitrile. The optimized amount of protecting group (DHP) was investigated in the second step and our data showed that the 2 mmol is the best. In the next step, we focused on choosing the best solvent. As we didn't observe the acceptable results from running the reaction in the presence of CH_2Cl_2 , CHCl_3 , THF and C_6H_6 , the CH_3CN was selected as the best solvent because of remarkable outcomes. According to these conditions, the conversion of benzyl alcohol to corresponding THP ether was carried out in high yield. In order to show the role of the catalyst, two distinct reactions in the presence and absence of ammonium decatungstocerate(IV) was performed. The observed data showed that in the absence of the catalyst, the reaction did not take place and the alcohol remained intact.

With the optimized conditions in hand, varieties of

alcohols, such as benzylic and aliphatic, were used for preparation of corresponding THP ethers. In all cases the clean reactions with high to excellent yields have been observed (Table 1). Accordingly, in the case of aliphatic alcohols (Table 1, entries 11-13, 20, 21), the reactions were fast and high yields were observed. Interestingly, this method can be used for protection of multifunctional compounds containing benzylic and phenolic hydroxyl groups, in which both of the groups will be protected (Table 1, entry 5). This method was also used for protection of secondary and tertiary alcohols (Table 1, entries 14-19) and excellent yields were observed.

In the second consideration, the suitable reaction conditions for deprotection of THP ethers into the corresponding hydroxyl compounds were found. At the beginning, different catalytic amounts of ammonium decatungstocerte(IV) were used, and the 0.02 equivalent of the catalyst was chosen as the best. Afterwards, optimization of the solvent was carried out. We observed that using CH_3CN presented better results than other solvents such as $(\text{CH}_3\text{CH}_2)_2\text{O}$, CH_2Cl_2 , CHCl_3 , THF and

C₆H₆. For further attempt, the deprotection reaction was conducted in the absence of the catalyst. In these conditions, the reaction progressed only 5% and showed that the presence of the catalyst is crucial for the conversion of THP ethers. Wide varieties of benzylic and aliphatic THP ethers were deprotected under the above-mentioned conditions at room temperature and mild reaction conditions, to afford the corresponding alcohols in high to excellent yields (Table 2). As shown in Table 2, using this procedure, besides the benzylic (Table 2, entry 1-10) and aliphatic (Table 2, entry 11-17 and 20, 21) THP ethers, the phenolic and cyclic ethers have also been converted to parent alcohols in high yields (Table 2, entry 18, 19 and 24).

Some of the recently reported methods, about the preparation of benzyl alcohol THP ether in the presence of various catalysts, have been compared with the present results. As you see in Table 3, (NH₄)₈[CeW₁₀O₃₆].20H₂O shows better applicability and efficiency to most of the previously reported catalysts.

CONCLUSIONS

In summary, we have successfully demonstrated a simple and convenient method for preparation of THP ethers from the corresponding alcohols under room temperature and ambient conditions. Deprotection to the parent hydroxyl compounds using the same catalyst by tuning the amount of catalyst and the reaction conditions was also successful. In addition, this method is very simple and mild, easy to handle, and compatible with the presence of a large number of other protecting groups. Because of its operational simplicity, generality, and efficacy, this method is expected to have wide applicability for the conversion of various hydroxyl compounds to the corresponding THP ethers and vice-versa.

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REFERENCES

[1] T.W. Greene, P.G.M. Wuts, Protective Groups in

Organic Synthesis, 3rd ed., John Wiley & Sons, New York, 1999.

- [2] J.H. Van Boom, J.D.M. Herschied, C.B. Reese, *Synthesis* (1973) 169.
- [3] M. Miyashita, A. Yoshikoshi, P.A. Grieco, *J. Org. Chem.* 42 (1977) 3772.
- [4] Y. Morizawa, I. Mori, T. Hiyama, H. Nozaki, *Synthesis* (1981) 899.
- [5] G.A. Olah, A. Husain, B.P. Singh, *Synthesis* (1983) 892.
- [6] S. Hoyer, P. Laszlo, M. Orlovic, E. Polla, *E. Synthesis* (1986) 655.
- [7] V. Bolitt, C. Mioskowski, D.S. Shin, J.R. Falck, *Tetrahedron Lett.* 29 (1988) 4583.
- [8] P. Kumar, C.U. Dinesh, R.S. Reddy, B. Pandey, *Synthesis* (1993) 1069.
- [9] B.C. Ranu, M. Saha, *J. Org. Chem.* 59 (1994) 8269.
- [10] A. Molnar, T. Beregszaszi, *Tetrahedron Lett.* 37 (1996) 8597.
- [11] U.T. Bhalerao, K.J. Davis, B.V. Rao, *Synth. Commun.* 26 (1996) 3081.
- [12] B.S. Babu, K.K. Balasubramanian, *Tetrahedron Lett.* 39 (1998) 9287.
- [13] A.M. Reddy, R.L. Reddy, N. Bhanumathi, R.K. Rao, *Synth. Commun.* 30 (2000) 4323.
- [14] B.M. Choudary, V. Neeraja, M.L. Kantam, *J. Mol. Catal. A: Chem.* 175 (2001) 169.
- [15] M.H. Habibi, S. Tangestaninejad, I. Mohammadpoor-Baltork, V. Mirkhani, B. Yadollahi, *Tetrahedron Lett.* 42 (2001) 2851.
- [16] T. Mineno, *Tetrahedron Lett.* 43 (2002) 7975.
- [17] J.S. Yadav, B.V.S. Reddy, D. Gnaneshwar, *New J. Chem.* 27 (2003) 202.
- [18] Y.J. Kim, R.S. Varma, *Tetrahedron Lett.* 46 (2005) 1467.
- [19] A. Khazaei, A. Rostami, M. Mahboubifar, *Catal. Commun.* 8 (2007) 383.
- [20] F. Shirini, K. Marjani, H.T. Nahzomi, *Phosphorus Sulfur Silicon Relat. Elem.* 182 (2007) 2235.
- [21] F. Shirini, M.A. Zolfigol, A.R. Abri, *Chin. Chem. Lett.* 18 (2007) 803.
- [22] M. Wang, Z.G. Song, H. Jiang, H. Gong, *Monatsh. Chem.* 138 (2007) 599.
- [23] M. Wang, Z.G. Song, H. Jiang, H. Gong, *Monatsh.*

- Chem. 139 (2008) 601.
- [24] M. Wang, Z.G. Song, H. Jiang, H. Gong, *Monatsh. Chem.* 140 (2009) 177.
- [25] A.A. Dos Santos, A.A. Brito, M.V.L. Archilha, T.G.A. Bele, G.P. Dos Santos, M.B.M. De Mello, *J. Braz. Chem. Soc.* 20 (2009) 42.
- [26] D. Long, E. Burkholder, L. Cronin, *Chem. Soc. Rev.* 36 (2007) 105.
- [27] N. Mizuno, K. Yamaguchi, K. Kamata, *Coord. Chem. Rev.* 249 (2005) 1944.
- [28] C.L. Hill, *J. Mol. Catal. A: Chem.* 262 (2007) 2.
- [29] A. Müller, S. Roy, *Coord. Chem. Rev.* 245 (2003) 153.
- [30] M.T. Pope, T. Yamase, *Polyoxometalate Chemistry for Nanocomposite Design*, Kluwer, Dordrecht, 2002.
- [31] N. Mizuno, M. Misono, *Chem. Rev.* 98 (1998) 199.
- [32] I.V. Kozhevnikov, *J. Mol. Catal. A: Chem.* 262 (2007) 86.
- [33] T. Okuhara, N. Mizuno, M. Misono, *Adv. Catal.* 41 (1996) 113.
- [34] Y. Izumi, K. Urabe, M. Onaka, *Zeolite, Clay and Heteropoly Acid in Organic Reactions* Kodansha/VCH, Tokyo, 1992.
- [35] V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, *Tetrahedron* 59 (2003) 8213.
- [36] V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, *Catal. Lett.* 91 (2003) 129.
- [37] V. Mirkhani, S. Tangestaninejad, L. Alipanah, *Synth. Commun.* 32 (2002) 621.
- [38] V. Mirkhani, S. Tangestaninejad, M. Moghadam, B. Yadollahi, L. Alipanah, *Monatsh. Chem.* 135 (2004) 1257.
- [39] V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, *Catal. Lett.* 101 (2005) 93.
- [40] a) R.D. Peacock, T.J.R. Weakley, *J. Chem. Soc. A*, (1971) 1836; b) R. Shiozaki, H. Goto, Y. Kera, *Bull. Chem. Soc. Jpn.* 66 (1993) 2790.
- [41] B. Karimi, M. Khalkhali, *J. Mol. Catal. A: Chem.* 232 (2005) 113.
- [42] A. Khan, E. Mondal, B. Borah, S. Ghosh, *Eur. J. Org. Chem.* (2003) 4113.