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$ZrCl_4$ as a mild and efficient catalyst for the one-pot conversion of TBS and THP ethers to acetates

Ch. Sanjeeva Reddy,[a,]* G. Smitha[a] and S. Chandrasekhar[b]

[a]*Department of Chemistry, Kakatiya University, Warangal-506009, India*
[b]*Indian Institute of Chemical Technology, Hyderabad-500007, India*

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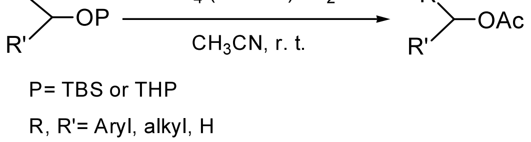
Abstract—A mild, efficient and chemoselective method has been developed for the direct transformation of *tert*-butyldimethylsilyl and tetrahydropyranyl protected alcohols into the corresponding acetates with acetic anhydride and zirconium(IV) chloride as the catalyst in acetonitrile, in a one-pot reaction with high yields and short reaction times. This method has been applied to a variety of substrates.

Selective protection and deprotection of functional groups is a commonly used process in multistep organic synthesis and the interconversion of one protecting group into another is also an important transformation in synthetic organic chemistry. Thus, development of new methods for such interconversions in one-step avoiding the intermediate step of going back to the parent functionality has gained importance in recent times.[1] Amongst protecting groups for alcohols, *tert*-butyldimethylsilyl (TBS) and tetrahydropyranyl (THP) ethers are most frequently used due to their reasonable stability and compatibility to various reaction conditions and reagents such as strongly basic media, alkyl lithiums, metal hydrides, and catalytic hydrogenation.[2] However, they are not stable under strongly acidic conditions. On the other hand, acetates serve as effective hydroxyl blocking groups, which are stable to acidic conditions. Thus the conversion of TBS and THP ethers to the corresponding acetates is an important transformation in organic synthesis. The methods available for this transformation are limited and include $AcCl/ZnCl_2$,[3] $AcBr/SnBr_2$,[4] $FeCl_3/Ac_2O$[5] or AcOH[6] and $Cu(OTf)_2/Ac_2O$[7] (for the conversion of TBS and THP ethers to acetates), AcOH/AcCl,[8] $TiCl_4/Ac_2O$,[9] In/I_2–EtOAc[10] and recently $In(OTf)_3/Ac_2O$[11] (for the conversion of THP ethers to acetates). However, these procedures suffer from some disadvantages such as elevated reaction temperatures, long reaction times, and incompatibility with other protecting groups.[12] Despite all these methods, an efficient and practical method for this transformation is desired. Toward this goal, our experience in protecting group interconversion[9,13] prompted us to explore new methods for this useful transformation. We found that the zirconium(IV) chloride (5 mol%) and acetic anhydride reagent system converts TBS and THP ethers to the corresponding acetates under mild conditions, in one-pot and in short reaction times (Scheme 1).

A wide range of structurally diverse TBS and THP ethers were subjected to this protocol to produce the corresponding acetates. The results are summarized in Table 1. In the first case, 3-phenyl-1-propanol TBS ether was treated with catalytic $ZrCl_4$ (5 mol%) and acetic anhydride in CH_3CN at room temperature to give the corresponding acetate in 94% yield within 5 min (entry 1).[14] Primary and secondary benzylic alcohol TBS ethers also gave the corresponding acetates in short reaction times, in 93 and 90% yields, respectively (entries 2 and 3). Entries 4 and 5 clearly demonstrate that the TBS ethers of aliphatic alcohols can be selectively converted to acetates in the presence of phenolic TBS and TIPS (triisopropylsilyl) ethers. This conversion is also effective in the presence of an acid labile



Scheme 1.

Keywords: zirconium(IV) chloride; one-pot reaction.

* Corresponding author. Tel./fax: +91-870-243-8833; e-mail: chsrkuc@yahoo.co.in

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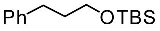
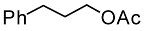
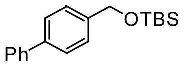
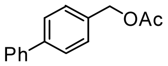
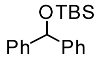
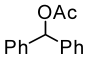
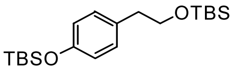
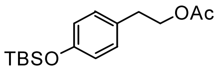
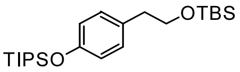
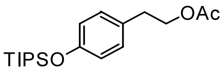
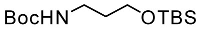
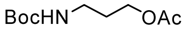
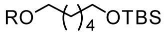
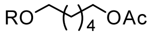
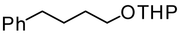
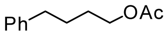
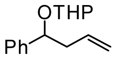
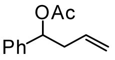
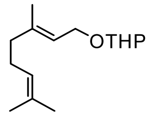
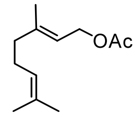
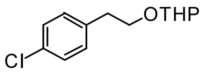
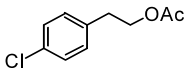
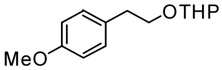
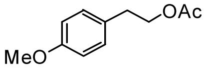
Table 1. Conversion of TBS and THP ethers to acetates

entry	substrate	time (min.)	product	yield (%)[a]
1		5		94
2		8		93
3		10		90
4		8		88
5		8		86
6		30		78
7	 R= TBDPS	6	 R= TBDPS	88
8	R= Bn	8	R= Bn	89
9	R= allyl	10	R= allyl	87
10	R= Ts	10	R= Ts	90
11	R= H	6	R= Ac	92
12	R= TIPS	10	R= Ac	85
13	R= THP	5	R= Ac	80
14		5		88
15		12		84
16		10		83
17		10		86
18		10		85

[a] All the yields refer to pure isolated products characterized by ^{1}H NMR and mass spectroscopy.

N-^{t}butyl carbamate group within 30 min (entry 6). To check the compatibility and prove the mildness of the reagent system, we have studied a series of 1,6-hexane diol diether substrates having a TBS ether at one end and a hydroxyl-protecting group at the other end. Interestingly, the TBS ether was selectively converted to acetate even though a TBDPS ether was located at the other end (entry 7). Furthermore, the benzyl and allyl ethers and tosylates were stable to the present protocol (entries 8, 9 and 10). However, aliphatic TIPS (entry 12) and THP (entry 13) ethers were not stable, being smoothly converted to the corresponding acetates. A brief literature search showed that, there was no report presenting the conversion of THP ethers to acetates with $ZrCl_4$.[15] This result has encouraged us to extend the generality of the direct conversion of THP ethers to acetates to a few other substrates. Accordingly, the primary and secondary alcohol THP ethers (entries 14–18) were prepared and subjected to the $ZrCl_4$–Ac_2O system to afford the corresponding acetates rapidly and in good yields. During this study, olefinic (entries 15 and 16), halo (entry 17) and methyl ether (entry 18) functionalities were also found to be unaffected under the present reaction conditions.

In summary, we have developed a rapid and efficient method for the one-pot conversion of TBS and THP ethers to the corresponding acetates in the presence of a catalytic amount of $ZrCl_4$. The advantages of this protocol such as mild reaction conditions, chemoselectivity, shorter reaction times and high yields of the desired products are worthy of mention and make this method an attractive and useful contribution to present methodologies.

General experimental procedure: To a stirred solution of the substrate (1 mmol) in CH_3CN (10 mL), Ac_2O (1 mmol)[16] followed by $ZrCl_4$ (5 mol%) was added and the reaction mixture was stirred at room temperature for the given time (see Table 1). After completion of the reaction, the solvent was evaporated in vacuo, extracted with EtOAc, washed with 10% $NaHCO_3$ solution. The combined organic layers were dried (Na_2SO_4) and evaporated to give the corresponding acetate[17] which was purified by column chromatography.

References

1. (a) Yang, G.; Ding, X.; Kong, F. *Tetrahedron Lett.* **1997**, *38*, 6725; (b) Oriyama, T.; Yatabe, K.; Sugauttra, S.; Machiguchi, Y.; Koga, G. *Synlett* **1996**, 523; (c) Oriyama, T.; Kimura, M.; Koga, G. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 885.
2. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999; (b) Kocienski, P. J. *Protective Groups*; Georg Thieme: Stuttgart, 1994.
3. Kim, S.; Lee, W. J. *Synth. Commun.* **1986**, *16*, 659.
4. Oriyama, T.; Oda, M.; Gono, J.; Koga, G. *Tetrahedron Lett.* **1994**, *35*, 2027.
5. Ganem, B.; Small, V. R. *J. Org. Chem.* **1974**, *39*, 3728.
6. Sharma, G. V. M.; Mahalingam, A. K.; Nagarajan, M.; Ilangoan, A.; Radhakrishna, P. *Synlett* **1999**, 1200.
7. Chandra, K. L.; Saravanan, P.; Singh, V. K. *Tetrahedron Lett.* **2001**, *42*, 5309.
8. Schwarz, M.; Waters, R. M. *Synthesis* **1972**, 567.
9. Chandrasekhar, S.; Ramachander, T.; Reddy, M. V.; Takhi, M. *J. Org. Chem.* **2000**, *65*, 4729.
10. Ranu, B. C.; Hajra, A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 355.
11. Mineno, T. *Tetrahedron Lett.* **2002**, *43*, 7975.
12. (a) Benzyl ethers were cleaved under AcBr/$SnBr_2$ conditions; (b) Benzyl and methyl ethers are also cleaved with the $FeCl_3$/Ac_2O reagent system.
13. (a) Chandrasekhar, S.; Babu, B. N.; Reddy, Ch. R. *Tetrahedron Lett.* **2003**, *44*, 2057 (for NBn, NDPM and NTr to NHBoc) (for NHCbz to NHBoc); (b) Chandrasekhar, S.; Chandraiah, L.; Reddy, Ch. R.; Reddy, M. V. *Chem. Lett.* **2000**, 780.
14. The same reaction was tested with $ZrCl_4$ (5 mol%) in the absence of Ac_2O, wherein we observed that TBS ether cleavage occurred in 10 h.

15. There is one method reported for THP deprotection with $ZrCl_4$ in MeOH, where the reaction time was 2–6 h. See: Rezai, N.; Alsadat, M.; Salehi, P. *Synth. Commun.* **2000**, *30*, 1799.
16. For entries 11–13, 2 equiv. of Ac_2O were used.
17. Spectroscopic data for selected products: Entry 4: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.1 (d, $J=7.6$ Hz, 2H), 6.8 (d, $J=8$ Hz, 2H), 4.25 (t, $J=6.8$ Hz, 2H), 2.88 (t, $J=2.8$ Hz, 2H), 2.06 (s, 3H), 1.0 (s, 9H), 0.2 (s, 6H); EIMS (*m*/*z*): 294 (M^+). Entry 5: ^{1}H NMR ($CDCl_3$): δ 7.07 (d, $J=8$ Hz, 2H), 6.83 (d, $J=8$ Hz, 2H), 4.25 (t, $J=7.2$ Hz, 2H), 2.88 (t, $J=7.2$ Hz, 2H), 2.05 (s, 3H), 1.31–1.21 (m, 3H), 1.1 (d, $J=7.2$ Hz, 18H); EIMS (*m*/*z*): 336 (M^+). Entry 6: ^{1}H NMR ($CDCl_3$): δ 4.14 (t, $J=6$ Hz, 2H), 3.2 (t, $J=5.6$ Hz, 2H), 2.07 (s, 3H), 1.84–1.8 (m, 2H), 1.45 (s, 9H); EIMS (*m*/*z*): 116 (M^+-101). Entry 8: ^{1}H NMR ($CDCl_3$): δ 7.36–7.24 (m, 5H), 4.5 (s, 2H), 4.06 (t, $J=3.2$ Hz, 2H), 3.46 (t, $J=6.8$ Hz, 2H), 2.04 (s, 3H), 1.68–1.58 (m, 4H), 1.45–1.35 (m, 4H); EIMS (*m*/*z*): 250 (M^+).