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Zinc Triflate: A Mild and Efficient Catalyst for Deprotection of Tetrahydropyranyl Ethers[1]

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Abstract—Treatment of tetrahydropyranyl (THP) ethers with zinc triflate in methanol provides a simple and efficient process for deprotection of these ethers and the parent alcohols are obtained in excellent yields.

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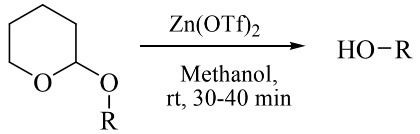
INTRODUCTION

Success of any protective group largely depends on its stability to acidic or non-acidic reagents, and on the fact that it can be easily installed and deprotected. The tetrahydropyranyl (THP) group is widely used as a hydroxyl protecting group, because it can easily be introduced and is stable under a variety of reaction conditions, including strongly basic conditions like treatment with Grignard reagent, lithium alkyls, alkylating, acylating reagents and reactions involving oxidation and reduction by inorganic hydrides [1]. In recent years, a number of different methods have been reported for the deprotection of THP groups by using protic acids, Lewis acids, ion exchange resins [2], heteropolyacids, *p*-toluenesulfonic acid [3] and different catalysts like silica sulfuric acid [4], copper(II) chloride [5], ceric ammonium nitrate [6], 3-carboxypyridinium chlorochromate (CPCC) [7], decaborane [8], poly(4-vinylpyridinium) *p*-toluenesulfonate [9], cerium(III) chloride heptahydrate [10], *N*-bromosuccinimide (NBS) [11], 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) [12], $PdCl_2(CH_3CN)_2$ [13], ($K_5CoW_{12}O_{40}\cdot 3H_2O$) [14], tetrabutylammonium tribromide (TBAB) [15], acetyl chloride [16], aluminum chloridehexahydrate [17], indium triflate [18], bismuth triflate [19], acetonyltriphenylphosphoniumbromide (ATPB) and poly-*p*-styryldiphenylacetonylphosphonium bromide [20], lithium bromide [21], zirconium tetrachloride [22], $MgBr_2$ [23], dimethylaluminum chloride [24], $NaHSO_4$–SiO_2 [25]. Although these methods are suitable for many synthetic conditions, many of these are associated with several drawbacks, which include long reaction time, reflux conditions, the use of catalysts which may affect other functionalities present, severe and acidic conditions, poor selectivity, formation of polymeric byproducts of the dihydropyran, and isomerization. In addition, some of these catalysts require a work-up of the reaction mixture. Thus, there is still a need for mild selective methods for this purpose.

Zinc(II) trifluoromethanesulfonate (zinc triflate) has recently been shown to be a versatile reagent for organic synthesis and it is used as a mild Lewis acid catalyst for wide range of organic transformations [26–28]. Zinc triflate is commercially available or it may be prepared by reacting trifluoromethanesulfonic acid with zinc carbonate in methanol [29]. Herein, we report a simple and efficient zinc(II) triflate (10 mol %) catalyzed deprotection of tetrahydropyranyl ethers (see scheme).



R = aryl, alkyl.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on 400 MHz Varian FT-NMR spectrometer with tetramethylsilane (TMS) as the internal reference. The solvent $CDCl_3$ was used for NMR analysis. The mass spectra were recorded on a Waters ZQ-4000 equipped with ESI and API mass detector. The carbon, hydrogen

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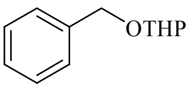
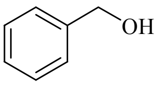
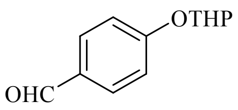
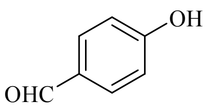
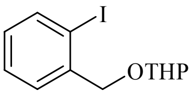
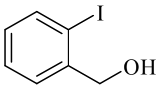
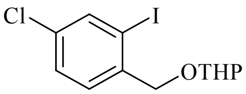
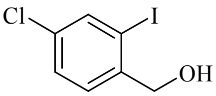
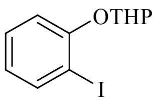
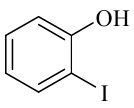
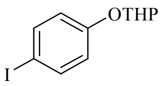
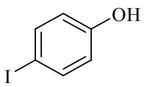
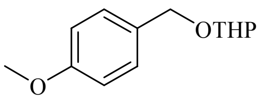
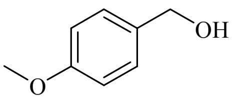
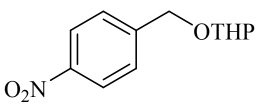
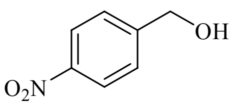
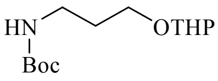
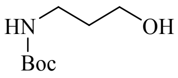
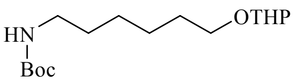
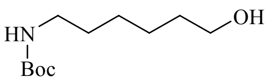
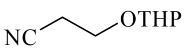
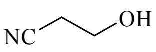
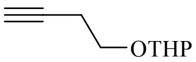
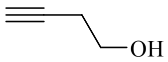
[1] The text was submitted by the authors in English.

Deprotection of THP ethers by using zinc triflate in methanol at room temperature[a]

Entry	Substrate	Product	Time, min	Yield, %
a			30	96
b			30	95
c			30	96
d			35	95
e			30	96
f			30	92
g			35	95
h			35	90
i			35	88
j			35	89
k			40	81
l			35	87

[a] The structures of the products were confirmed by direct comparison of their spectral data with published spectra.

and nitrogen (CHN) analysis was done on Perkin-Elmer PE 2400 Series II analyzer. The thin layer chromatography (TLC) was performed either using the Merck precoated TLC plates or on ACME's silica gel with 13% calcium sulfate ($CaSO_4$) as binder and the components were visualized in iodine chamber or by

UV exposure or by the potassium permanganate ($KMNO_4$) spray technique. Flash column chromatography was performed using Merck silica gel (100–200 mesh). The chemicals and solvents were purchased from commercial suppliers either from Aldrich, Spectrochem, and Sisco research laboratories (SRL), and they were used without purification prior to use. The structures of generated alcohols were established by direct comparison of their spectral (^{1}H NMR, 400 MHz) data with those of the authentic alcohols.

General procedure for deprotection reactions. A solution of THP Ether (1.0 mmol) in methanol (10 mL) was treated with $Zn(OTf)_2$ (0.1 mmol) and stirred at room temperature for 30–40 min. After the completion of reaction (TLC analysis), the solvent was removed under reduced pressure and the obtained residue was treated with EtOAc (20 mL). The organic layer was washed with water (10 mL), brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure to give the crude product. It was purified by flash column chromatography (100–200 mesh silica gel, EtOAc–petroleum ether) to furnish the desired alcohols or phenols in 81–96% yields.

2-(4-Chloro-2-iodobenzyloxy)tetrahydro-2*H*-pyran (see table, entry **d**). Light pale yellow gummy compound. ^{1}H NMR ($CDCl_3$), δ, ppm: 7.82 s (11H), 7.41–7.33 m (2H), 4.77–4.75 m (1H) 4.71 d (*J* = 13.2 Hz, 1H), 4.44 d (*J* = 13.6 Hz, 1H), 3.93–3.87 m (1H), 3.59-3.53 m (1H), 1.92–1.53 m (6H); ^{13}C NMR ($CDCl_3$, 400 MHz), δ, ppm: 19.26, 25.35, 30.42, 62.22, 72.23, 97.26, 98.42, 128.28, 129.20, 133.51, 138.25, 139.37. Calculated, %: C 40.88; H 4.00; Cl 10.05; I 35.99; O 9.08. $C_{12}H_{14}ClIO_2$. Found, %: C 40.95; H 4.15. (LC-MS) *m/z:* 350.9 [*M* – H].

(4-Chloro-2-iodophenyl)methanol (see table, entry **d**). Off-white solid; mp 114–116°C. ^{1}H NMR ($CDCl_3$), δ, ppm: 7.87 (s, 1H), 7.48–7.44 m (2H), 5.52 t (*J* = 5.6 Hz, 1H), 4.38 d (*J* = 5.6 Hz, 2H). (LC-MS) *m/z:* 266.9 [*M* – H].

***tert*-Butyl 3-(tetrahydro-2*H*-pyran-2-yloxy)propylcarbamate** (see table, entry **i**). Colourless gummy compound. ^{1}H NMR ($CDCl_3$), δ, ppm: 4.92 s (11H), 4.57–4.56 m (1H), 3.85–3.78 m (2H), 3.51–3.43 m (2H), 3.25–3.24 m (2H), 1.84–1.46 m (8H), 1.43 s (19H); ^{13}C NMR ($CDCl_3$, 400 MHz), δ, ppm: 19.40, 25.34, 28.35, 29.57, 30.55, 38.61, 62.20, 65.70, 78.82, 98.81, 155.95. Calculated, %: C 60.21; H 9.72; N, 5.40; O 24.68. $C_{13}H_{25}NO_4$. Found, %: C 60.44; H 9.98; N 5.45.

***tert*-Butyl 3-hydroxypropylcarbamate** (see table, entry **i**). Colourless gummy compound. ^{1}H NMR ($CDCl_3$), δ, ppm: 4.77 s (11H), 3.64–3.68 m (2H), 3.27–3.31 m (2H), 3.01 t (*J* = 6Hz, 1H), 1.66–1.69 m (2H), 1.44 s (19H).

***tert*-Butyl 6-(tetrahydro-2*H*-pyran-2-yloxy)hexylcarbamate** (see table, entry **j**). Colourless gummy compound. ^{1}H NMR ($CDCl_3$), δ, ppm: 4.57–4.55 m (1H), 4.51 s (11H), 3.89–3.87 m (1H), 3.76–3.70 m (1H), 3.52–3.50 m (1H), 3.39–3.36 m (1H), 3.13–3.08 m (2H), 1.85–1.64 m (3H), 1.61–1.33 m (11H), 1.44 s (19H); ^{13}C NMR ($CDCl_3$, 400 MHz), δ, ppm: 19.63, 25.40, 25.87, 26.55,28.35, 29.57, 29.94, 30.69, 40.45, 62.30, 67.40, 78.89, 98.80, 155.91; IR (DCM film, cm^{-1}): 3355, 2936, 2865, 1702, 1523, 1365, 1251,1169,1033, 868. Calculated, %: C 63.75; H 10.37; N, 4.65; O 21.33. $C_{16}H_{31}NO_4$. Found C 64.01; H 10.45; N, 4.72. (LC-MS) *m/z:* 302.1 $[M + H]^+$.

***tert*-Butyl 6-hydroxyhexylcarbamate** (see table, entry **j**). Colourless gummy compound. ^{1}H NMR ($CDCl_3$), δ, ppm: 4.49 s (1H), 3.62–3.65 m (2H), 3.10–3.12 m (2H), 1.33–1.56 m (9H), 1.44 s (19H).

RESULT AND DISCUSSION

A variety of THP ethers with different structures were prepared according to standard procedures [30]. THP ethers were subjected to deprotection with 10 mol % of $Zn(OTf)_2$ in methanol at room temperature for 30–40 min (see scheme). Under such conditions all the THP groups investigated in our study were cleanly and completely removed within a short time and the corresponding alcohols and phenols were isolated in good yields. The solvent plays an important role in the deprotection reactions. It was found that methanol is the best one among the solvents tested with THP ether of 2-iodo phenol. Methanol gave the best results compared to other solvents like ethanol, isopropyl alcohol, acetone, acetonitrile, and THF.

CONCLUSIONS

In conclusion, we have developed a simple, inexpensive, and efficient protocol for deprotection of THP ethers using $Zn(OTf)_2$ at room temperature. The reaction completed within 30–40 min. Experimental simplicity, utilization of cheap, commercially available catalyst and excellent yields are the main advantages of the present procedure. Further, it was shown that substrates such as Aldehyde, Boc, nitro, and methoxy groups are also unaffected by the present reagent system.

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REFERENCES

1. Greene, T.W. and Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed., John Wiley and Sons, New York, 1999, p. 102.
2. Bongini, A., Cardillo, G., Orena, M., and Sandri, S., *Synthesis*., 1979, vol. 8, pp. 618–620.
3. Miyashita, M., Yoshikoshi, A., and Grieco, P.A., *J. Org. Chem*., 1977, vol. 42, pp. 3772–3774.
4. Hajipour, A.R., Zarei, A., Khazdooz, L., Pourmousavi, S.A., Zahmatkesh, S., and Ruoho, A.E. *Indian. J. Chem. B*, 2006, no. 45, pp. 305–308.
5. Wang, J., Zhang, C., Qu, Z., Hou, Y., Chan, B., and Wu, P., *J. Chem. Research (S)*, 1999, pp. 294–295.
6. Gupta, A.D., Singh, R.S., and Singh, V.K., *Synlett*., 1996, no. 1, pp. 69–71.
7. Baltork, I.M. and Pouranshirvani, S., *Synthesis*., 1997, no. 7, pp. 756–758.
8. Jung, Y.J., Park, E.S., Lee, J.H., and Yoom, C.M., *Bull. Korean Chem. Soc*., 2002, vol. 23, pp. 791–792.
9. Li, Z. and Ganesan, A., *Synth. Commun*., 1998, vol. 28, pp. 3209–3212.
10. Reddy, G.S., Neelakantan, P., and Iyengar, D.S. *Synth. Commun*., 2000, vol. 30, pp. 4107–4111.
11. Narendar, M., Reddy, M.S., and Rao, K.R., *Synthesis*. 2004, vol. 11, pp. 1741–1743.
12. Raina, S.,and Singh, V.K., *Synth. Commun*., 1995, vol. 25, pp. 2395–2400.
13. Wang, Y.G., Wu, X.X., and Jiang, Z.Y., *Tetrahedron Lett*., 2004, vol. 45, pp. 2973–2976.
14. Habibi, M.H., Tangestaninejad, S., Baltork, I.M., Mirkhani, V., and Yadollahi, B., *Tetrahedron Lett*., 2001, vol. 42, pp. 2851–2853.
15. Naik, S., Gopinath, R., and Patel, B.K., *Tetrahedron Lett*. 2001, vol. 42, pp. 7679–7681.
16. Yeom, C.E., Shin, Y.J., and Kim, B.M., *Bull. Korean. Chem. Soc*., 2007, vol. 28, pp. 103–107.
17. Namboodiri, V.V. and Varma, R.S., *Tetrahedron Lett*., 2002, vol. 43, pp. 1143–1146.
18. Mineno, T., *Tetrahedron Lett*., 2002, vol. 43, pp. 7975–7978.
19. Stephens, J.R., Butler, P.R., Clow, C.H., Oswald, M.C., Smith, R.C., and Mohan, R S., *Eur. J. Org. Chem.,* 2003, vol. 19, pp. 3827–3831.
20. Hon, Y.S., Lee, C.F., Chen, R.J., and Szu, P.H., *Tetrahedron*. 2001, vol. 57, pp. 5991–6001.
21. Reddy, M.A., Reddy, L.R., Bhanumathi, N., and Rao, K.R., *Synth. Commun.,* 2000, vol. 30, pp. 4323–4328.
22. Rezai, N., Meybodi, F.A., and Salahi, P., *Synth. Commun*., 2000, vol. 30, pp. 1799–1805.
23. Kim, S. and Park, J.H., *Tetrahedron Lett*., 1987, vol. 28, pp. 439–440.
24. Ogawa, Y. and Shibasaki, M., *Tetrahedron Lett*., 1984, vol. 25, pp. 663–664.
25. Ravi Kumar, K., Satyanarayana, P.V.V., and Reddy, B.S., *Chin. J. Chem*., 2012, vol. 30, pp. 1189–1191.
26. Lekhok, K.C., Bhuyan, D., Prajapati, D., and Boruah, R.C., *Mol. Divers*., 2010, vol. 14, pp. 841–846.
27. Kumar, V.N., Sridhar, G., Laxminarayana, E., Mallaiah, B., and Giri, T., *J. Drug. Chem. (IJPI)*, 2012, no. 2, p. 10.
28. Atukuri, D., Ravindra, R.K., and Pramod, P.K., *Lett. Org. Chem*., 2013, no. 10, pp. 510–517.
29. Corey, E. J., and Shimoji, K. *Tetrahedron Lett*., 1983, vol. 24, 169–172.
30. Miyashita, M., Yoshikoshi, A., and Grieco, P.A., *J. Org. Chem*., 1977, vol. 42, p. 3772.