# *Notes*

## A Single Step Conversion of Tetrahydropyranyl Ethers to Acetates†

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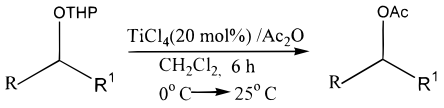
The acetylation of alcohols is a useful transformation, as the resulting acetate group serves as an effective blocking group that is stable to acidic conditions.[1] Also, acetates of natural products show biological profiles different from those of the parent compounds (morphine to heroin and salicylic acid to aspirin serve as excellent examples). With its importance in mind, several useful methods have been reported[2] for the conversion of alcohols to acetates, under both acidic and basic conditions. Development of new methods for the direct conversion of one protective group to an other has been gaining importance in recent times. Methods are now available for the one-step conversion of silyl ethers to acetates,[3] tetrahydropyranyl ethers to silyl-protected alcohols,[4] *p*-methoxy benzyl ethers to *p*-methoxymethyl ethers,[5] or benzyl ethers to acetates.[6] Surprisingly however, there is only one report that deals with the direct conversion of a tetrahydropyranyl (OTHP) ether to an acetate (AcOH/AcCl).[7] These conditions, being harsh, have not found wide applicability. While working toward the synthesis of pheromone components of *Aproaerema modicella* [8] and *Spodoptera litura*,[9] we desired a direct method for this transformation to improve the overall synthetic efficiency. Toward this goal, herein we report a mild method for direct conversion of THP ethers to acetates (Scheme 1). After screening various Lewis acid catalysts, it was concluded that 20 mol % of $TiCl_4$ and 1.2 equiv of $Ac_2O$ were effective for this transformation. Importantly, this protocol installs a base-labile protective group in place of an acid-labile protective group in one step.

Representative examples of direct conversions of THP ethers to acetates are shown in Table 1. In the first

**Scheme 1**




instance, the THP ether of 3-phenyl-1-propanol **1a** (entry 1) was treated with 20 mol % of $TiCl_4$ and $Ac_2O$ in anhydrous $CH_2Cl_2$ at ambient temperature for 6 h to obtain the corresponding acetate **1b** in 78% yield. This prompted us to study the conversion of the THP ether of benzyl alcohol **2a** (entry 2) and 2-phenylethanol **3a** (entry 3), which proceeded efficiently with 80% and 85% yields, respectively. The bis THP ether derivative **4a** (entry 4) also underwent smooth conversion; however, the isopropylidine group was also displaced to yield tetra acetate derivative **4b** in 80% yield. Another bis OTHP ether **5a** was converted to the diacetate derivative **5b** in 90% yield. The terpenyl derivative having an allyl alcohol **6a** (entry 6), the steroidal derivative **9a** (entry 9), and the bromo THP ether **10a** (entry 10) were also effectively converted to corresponding acetates. The tricyclic sertraline intermediate[10] **8a** (entry 8), enyne derivative **12a** (entry 12, pheromone components of *Spodoptera litura*), and the 7-ene derivative **14a** (entry 14, pheromone component of *Aproaerema modicella*) are other representative examples studied having biological importance. Entry 13 describes the mildness of the protocol, wherein silyl ether stability is demonstrated.

In conclusion, an efficient one-step conversion of THP ethers to acetates is described that has direct applications in the total synthesis of biologically active natural product derivatives and pheromones.

### Experimental Section

**General Methods.** Crude products were purified by column chromatography on silica gel of 60−120 mesh. $^1H$ NMR spectra are obtained in $CDCl_3$ at 200 MHz. Chemical shifts are given in ppm with respect to internal TMS, and *J* values are quoted in Hz. Infrared spectra were obtained neat, and only the most significant absorptions are indicated, in $cm^{-1}$. Dichloromethane was distilled over $CaH_2$ prior to use. All reactions were carried out under an atmosphere of nitrogen using dry glassware. $TiCl_4$ (1 M in $CH_2Cl_2$) was obtained from Aldrich Chemical Co. and was used as received.

**General Procedure for the One-Step Conversion of Tetrahydropyranyl Ethers to Acetates As Described for 1a.** First, 20 mol % of $TiCl_4$ (1 M in $CH_2Cl_2$, 84 mg, 0.45 mmol) was added dropwise to a solution of 2-(3-phenylpropoxy) tetrahydro-2*H*-pyran **1a** (0.5 g, 2.27 mmol) and acetic anhydride (0.27 mL, 2.72 mmol) in dichloromethane(10 mL) at 0 °C under a nitrogen atmosphere. The resulting mixture was stirred at ambient temperature for 6 h, and the mixture was diluted with water, extracted with dichloromethane, and washed with brine solution. Evaporation of the volatiles followed by chromatography furnished 0.31 g of corresponding acetate (**1b**, 78%).

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(3) Oriyama, T.; Oda, M.; Gono, J.; Koga, G. *Tetrahedron Lett.* **1994**, 35, 2027.
(4) Oriyama, T.; Yatabe, K.; Sugawara, S.; Machiguchi, Y.; Koga, G. *Syn Lett.* **1996**, 523.
(5) Oriyama, T.; Kimura, M.; Koga, G. *Bull. Chem. Soc. Jpn.* **1994**, 67, 885.
(6) Yang, G.; Ding, X.; Kong, F. *Tetrahedron Lett.* **1997**, 37, 6725. (b) Ganem, B.; Small, V. R., Jr. *J. Org. Chem.* **1974**, *39*, 3728−3730.
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(9) Bestman, H. J.; Sub, J.; Vostrowsky, O. *Liebigs Ann. Chemie* **1981**, 2117.
(10) Qualich, G. J.; Woodall, T. M. *Tetrahedron* **1992**, 48, 10239. (b) Lautens, M.; Rovis, T. *J. Org. Chem.* **1997**, 62, 5246. (c) Chandrasekhar, S.; Reddy, M. V. *Tetrahedron* **2000**, 56, 1111−1114.
(11) Entries 2 and 9 were comparable with literature values, *J. Org. Chem.* **1992**, 57, 2001.

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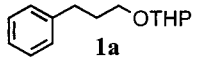
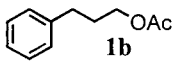
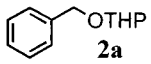
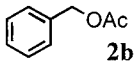
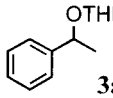
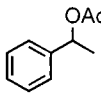
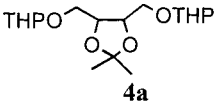
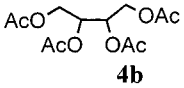
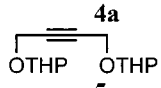
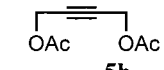
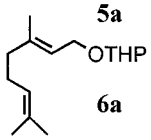
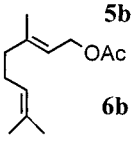
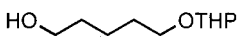
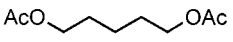
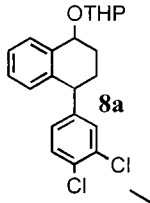
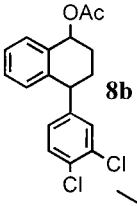
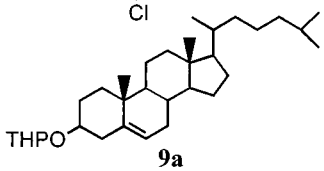
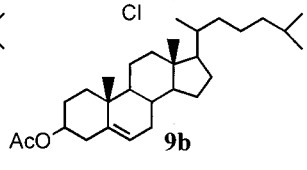
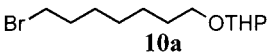
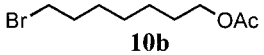
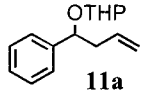
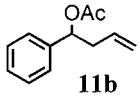
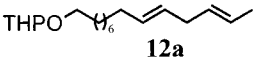
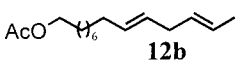
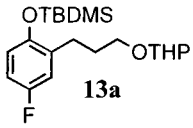
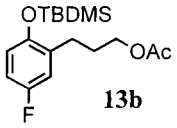
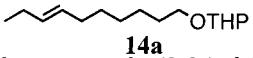
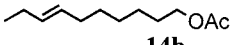
**Table 1. One-Step Conversion of Tetrahydropyranyl Ethers to Acetates**

| entry | substrate | product | yield[a] (%) |
|---|---|---|---|
| 1 |  **1a** |  **1b** | 78 |
| 2 |  **2a** |  **2b** | 80[11] |
| 3 |  **3a** |  **3b** | 85 |
| 4 |  **4a** |  **4b** | 80[b] |
| 5 |  **5a** |  **5b** | 90[b] |
| 6 |  **6a** |  **6b** | 80 |
| 7 |  **7a** |  **7b** | 85[b] |
| 8 |  **8a** |  **8b** | 75 |
| 9 |  **9a** |  **9b** | 75[11] |
| 10 |  **10a** |  **10b** | 72 |
| 11 |  **11a** |  **11b** | 75 |
| 12 |  **12a** |  **12b** | 78 |
| 13 |  **13a** |  **13b** | 85 |
| 14 |  **14a** |  **14b** | 80 |

[a] Yields calculated after column chromatography ($SiO_2$) of the products. [b] In these cases, $Ac_2O$ and $TiCl_4$ were increased proportionately.

**3-Phenylpropyl acetate (1b):** $^1$H NMR ($CDCl_3$) $\delta$ 7.3−7.1 (m, 5H), 4.1 (t, 2H, $J$ = 6 Hz), 2.7 (t, 2H, $J$ = 6.25 Hz), 2.05 (s, 3H), 1.95 (t, 2H, $J$ = 7.2 Hz); IR (neat) 845, 1737 cm$^{-1}$; MS ($M^+$) 178. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.07; H, 7.95.

**Phenylethyl acetate (3b):** $^1$H NMR ($CDCl_3$) $\delta$ 7.35−7.25 (m, 5H), 5.85 (q, 1H, $J$ = 6.8 Hz, 11.3 Hz), 2.05 (s, 3H), 1.55 (d, 3H, $J$ = 6.8 Hz); IR (neat) 847, 1740 cm$^{-1}$; MS 164 ($M^+$). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.11; H, 7.34.

**2,3-Di(methylcarbonyloxy)-1-methylcarbonyloxymethylpropyl acetate (4b):** $^1$H NMR ($CDCl_3$) $\delta$ 4.35 (dd, 2H, $J$ = 4.45, 13.3 Hz), 4.05 (dd, 2H, $J$ = 6.67, 11.2 Hz), 3.6 (dd, 2H, $J$ = 2.2 Hz), 2.15 (s, 6H), 2.1 (s, 3H), 2.05 (s, 3H); IR (neat) 1740 cm$^{-1}$; MS ($M^+$ − 43) 247. Anal. Calcd for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25. Found: C, 49.70; H, 6.50.

**4-Methylcarbonyloxy-2-butynyl acetate (5b):** $^1$H NMR ($CDCl_3$) $\delta$ 4.6 (s, 4H), 2.05 (s, 6H); IR (neat) 1740 cm$^{-1}$; MS 127 ($M^+$ − 43). Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.40, H, 5.88.

**3,7-Dimethyl-(2*E*)-2,6-octadienyl acetate (6b):** $^1$H NMR ($CDCl_3$) $\delta$ 5.3 (bt, 1H), 5.05 (bt, 1H), 4.55 (d, 2H, $J$ = 6.6 Hz), 2.05 (m, 4H), 2.0 (s, 3H), 1.7 (s, 3H), 1.65 (s, 3H), 1.6 (s, 3H); IR (neat) 1740 cm$^{-1}$; MS 153 ($M^+$ − 43). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.38; H, 10.22.

**5-Methylcarbonyloxy pentyl acetate (7b):** $^1$H NMR ($CDCl_3$) $\delta$ 4.05 (bt, 4H), 2.0 (s, 6H), 1.65 (m, 4H); IR (neat) 1740 cm$^{-1}$; MS 145 ($M^+$ − 43). Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.55; H, 9.02.

**4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenyl acetate (8b):** $^1$H NMR ($CDCl_3$) $\delta$ 7.4−71 (m, 5H), 6.95

(d, 1H), 6.8 (m, 1H), 6.05 (distd. t, 1H), 4.20 (distd. t, 1H), 2.45−2.20 (m, 1H), 2.15−2.0 (m, 1H), 2.1 (s, 3H), 1.9−1.85 (m, 2H); IR (neat) 850, 1735 $cm^{-1}$; MS ($M^+ - 43$) 292. Anal. Calcd for $C_{18}H_{16}C_{l2}O_2$: C, 64.49; H, 4.81. Found: C, 64.46; H, 4.78.

**7-Bromoheptyl acetate (10b):** $^1$H NMR ($CDCl_3$) $\delta$ 4.05 (t, 3H, $J$ = 4.5 Hz), 3.4 (t, 3H, $J$ = 5.6 Hz), 2.05 (s, 3H), 1.7−1.2 (m, 12H); IR (neat) 1735 $cm^{-1}$; MS 194 ($M^+$-43). Anal. Calcd for $C_9H_{17}O_2Br$: C, 45.49; H, 7.23. Found: C, 46.10; H, 7.30.

**4-Phenyl-3-butenyl acetate (11b):** $^1$H NMR ($CDCl_3$) $\delta$ 7.21−7.51 (m, 5H), 5.67 (t, 1H, $J$ = 7.01 Hz), 5.62−5.71 (m, 1H), 5.15−5.21 (m, 2H), 2.45−2.51 (m, 2H), 2.05 (s, 3H); IR (neat) 845, 1737 $cm^{-1}$; MS 190 ($M^+$).; Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76, H, 7.41. Found: C, 75.36; H, 7.28.

**9*Z*,12*E*-Tetradecadienyl acetate (12b):** $^1$HNMR ($CDCl_3$) $\delta$ 5.35 (m, 4H), 4.0 (t, 2H), 2.7 (t, 2H), 2.05 (s, 3H), 1.95−2.0 (m, 5H), 1.3−1.7 (m, 12H); IR (neat) 1735 cm $^{-1}$; MS 209 ($M^+ - 43$). Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 75.88; H, 11.12.

**3-(5-Fluoro-2-*O*-*tert*-butyldimethylsilanyloxyphenyl)-propyl acetate (13b):** $^1$H NMR ($CDCl_3$) $\delta$ 6.95−6.75 (m, 3H), 4.15 (t, 2H, $J$ = 4.8 Hz), 2.70 (t, 2H, $J$ = 6 Hz), 2.12 (s, 3H), 2.05−1.95 (m, 2H), 1.10 (s, 9H), 0.3 (s, 6H); IR (neat) 848, 1738 $cm^{-1}$; MS ($M^+$) 282 ($M^+ - 43$). Anal. Calcd for $C_{17}H_{27}O_3SiF$: C, 62.54; H, 8.34. Found: C, 62.65; H, 8.20.

**(*E*)-7-Decenyl acetate (14b):** $^1$HNMR ($CDCl_3$) $\delta$ 5.35 (m, 2H), 4.05 (t, 2H, $J$ = 4.4 Hz), 2.1 (s, 3H), 1.95−2.0 (m, 4H), 1.3 (m, 8H), 1.2 (t, 3H, $J$ = 6.5 Hz); IR (neat) 1737 $cm^{-1}$; MS 155 ($M^+ - 43$). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.55; H, 10.98.

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