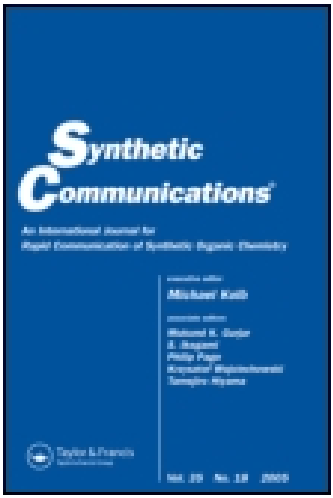

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# Tributyltin Hydride-Induced Free Radical Deoxygenation of the Cyclic Thionocarbonates of Threo-2,3-Dihydroxy Esters and Ketones

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SYNTHETIC COMMUNICATIONS, 27(22), 3887-3893 (1997)

# TRIBUTYLTIN HYDRIDE-INDUCED FREE RADICAL DEOXYGENATION OF THE CYCLIC THIONOCARBONATES OF *THREO*-2,3-DIHYDROXY ESTERS AND KETONES

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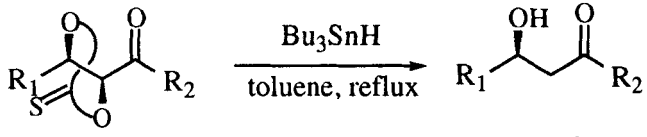
**Abstract:** A practical and enantiospecific method for the synthesis of optically pure β-hydroxy esters and ketones is described. The key reaction is free radical deoxygenation of the cyclic thionocarbonates of *threo*-2,3-dihydroxy esters and ketones with tributyltin hydride.

Optically pure β-hydroxy esters and ketones are useful chiral synthons in the synthesis of natural products. Several synthetic methods for their preparation have been reported which include enantioselective microbial reduction of β-keto esters[1] and β-diketones,[2] from the biopolymer PHB,[3] or Ru-(*R*)- or (*S*)-BINAP catalyzed asymmetric hydrogenation[4] of β-keto esters, aldol reaction utilizing enantiomerically pure β-keto dioxolane sulfoxide,[5] reductive cleavage of epoxy esters and ketones mediated by tributyltin hydride,[6] $SmI_2$,[7] and others.[8] Here we wish to report a method for the preparation of optically active β-hydroxy esters

and ketones based on the free radical deoxygenation of cyclic thionocarbonates[9] by using tributyltin hydride in toluene (Scheme 1).

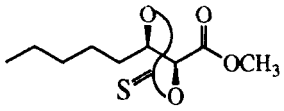
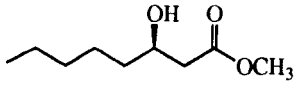
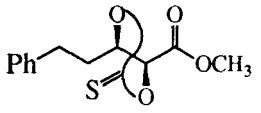
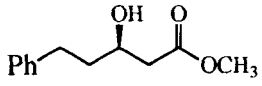
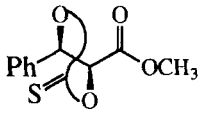
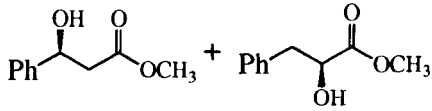
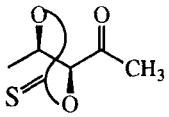
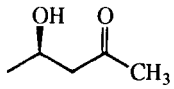
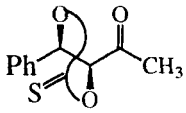
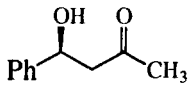



$R_2 = OCH_3$, $CH_3$ (1) → $R_2 = OCH_3$, $CH_3$ (2)

**Scheme 1**

The results of deoxygenation of cyclic thionocarbonates are summarized in Table 1. Optically active *threo*-2,3-dihydroxy esters and ketones can be readily prepared from the corresponding (*E*)-alkenes by Sharpless asymmetric dihydroxylation.[10] The diols were transformed to the cyclic thionocarbonates by treating with thiophosgene. The cyclic thionocarbonate **1a** was reacted with tributyltin hydride (2 equiv.) in refluxing toluene for 30 min to afford methyl (*R*)-3-hydroxy octanoate (**2a**)[1c, 4b] in 85% yield (entry 1 in Table 1). For the cyclic thionocarbonate **1b**, β-hydroxy ester **2b**[4c] was obtained as the sole product (entry 2). Regioselectivity can be explained by the stability of deoxygenated radical intermediate. The radical of C(α) position is more stable than that of C(β) positon. However, treatment of the cyclic thionocarbonate **1c** with tributyltin hydride in toluene afforded β-hydroxy ester **2c**[1b] and α-hydroxy ester **3**[11] in the ratio of 4 : 1 (entry 3). This apparantly indicates that phenyl group acted as stabilizing substituent of the radical intermediate. The ratio of regioisomer was confirmed by 300 MHz $^1$H NMR. This method was applied to the cyclic thionocarbonate derived from *threo*-2,3-dihydroxy ketones. When the cyclic thionocarbonate **1d** was reacted in

Table 1. Tributyltin hydride-induced deoxygenation of the cyclic thionocarbonate of *threo*-2,3-dihydroxy esters and ketones [a]

| Entry | Substrate | time (min) | Product[b] | Yield(%)[c] |
|---|---|---|---|---|
| 1 |  **1a** | 30 |  **2a** | 85 |
| 2 |  **1b** | 50 |  **2b** | 87 |
| 3 |  **1c** | 35 |  **2c** (4 : 1) **3** | 90 |
| 4 |  **1d** | 30 |  **2d** | 70 |
| 5 |  **1e** | 40 |  **2e** | 75 |

[a]All the reactions were run with tributyltin hydride (2 equiv.) in refluxing toluene.
[b]The specific rotations, $[\alpha]^{25}_{D}$ values; **2a**: -20.2 (*c*, 0.12, $CHCl_3$), **2b**: +2.4 (*c*, 0.15 , $CH_2Cl_2$), **2d**: -57.5 (*c*, 0.10, $CHCl_3$), **2e**: -67.8 (*c*, 0.14, $CHCl_3$).
[c]The yields are isolated ones.

the same condition, (*4R*)-hydroxy-2-pentanone (**2d**)[2b] was obtained as the sole product (entry 4). Finally, the cyclic thionocarbonate **1e** with tributyltin hydride produced β-hydroxy ketone **2e**,[8a] where deoxygenation had occured exclusively at position C(α) (entry 5).

In summary, free radical deoxygenation of the cyclic thionocarbonates of optically active *threo*-2,3-dihydroxy esters and ketones afforded β-hydroxy esters and ketones with highly regioselectivity, which are useful chiral synthons in organic synthesis.

## Experimental Section

### Typical Procedure

### Methyl (*R*)-3-hydroxy octanoate (2a)

To a stirred solution of the cyclic thionocarbonate **1a** (200 mg, 0.86 mmol) in toluene (4ml) under nitrogen atmosphere was added $Bu_3SnH$ (500 mg, 1.72 mmol) and the reaction mixture was heated at reflux for 30 min. The mixture was quenched with saturated $NH_4Cl$ solution (10ml) and then extracted with $CH_2Cl_2$ (2X20mL). The organic layer was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*. The crude product was separated by $SiO_2$ column chromatography (EtOAc/hexanes 1 : 1, $R_f$ = 0.48) to give **2a** (128 mg, 85%). $[\alpha]^{25}_D$ -20.2 ( *c* 0.12, $CHCl_3$). IR(neat) 3451, 2929, 1732 $cm^{-1}$. $^1H$ NMR($CDCl_3$, 300 MHz) δ 4.01(m, 1H), 3.70(s, 3H), 2.87(bs, 1H), 2.47(dd, 1H, *J* = 16.5, 3.3 Hz), 2.36(dd, 1H, *J* = 16.5, 8.7 Hz), 1.22 ~ 1.63(m, 8H), 0.93(t, 3H, *J* = 6.6 Hz). MS(m/e) 174($M^+$), 156, 103(base peak), 71, 43.

**Methyl (*R*)-3-hydroxy-5-phenyl pentanoate (2b)**

TLC, $SiO_2$, EtOAc/hexanes 1 : 1, $R_f$ = 0.57. $[\alpha]^{25}_D$ +2.4 ( *c* 0.15, $CH_2Cl_2$). IR(neat) 3450, 3010, 1730 $cm^{-1}$. $^1H$ NMR($CDCl_3$, 300 MHz) δ 7.21(m, 5H), 4.02(m, 1H), 3.62(s, 3H), 3.01(bs, 1H), 2.81(m, 1H), 2.73(m, 1H), 2.52(dd, 1H, *J* = 16.5, 3.6 Hz), 2.48(dd, 1H, *J* = 16.5, 8.4 Hz), 1.80(m, 2H). MS(m/e) 208($M^+$), 190, 130(base peak), 117, 91.

**Methyl (*S*)-3-hydroxy-3-phenyl propanoate (2c) and Methyl (*S*)-2-hydroxy-3-phenyl propanoate (3)**

**2c** (major): TLC, $SiO_2$, EtOAc/hexanes 1 : 1, $R_f$ = 0.35. IR(neat) 3453, 3012, 1735 $cm^{-1}$. $^1H$ NMR($CDCl_3$, 300 MHz) δ 7.19(m, 5H), 5.16(m, 1H), 3.65(s, 3H), 3.24(bs, 1H), 2.75(m, 2H). MS(m/e) 180($M^+$), 107(base peak), 79.

**3** (minor): $^1H$ NMR($CDCl_3$, 300 MHz) δ 7.19(m, 5H), 4.42(m, 1H), 3.68(s, 3H), 3.16(dd, 1H, *J* = 13.8, 4.2 Hz), 3.00(dd, 1H, *J* = 13.8, 6.6 Hz), 2.76(bs, 1H). MS(m/e) 180($M^+$), 162, 91(base peak).

**(*4R*)-Hydroxy-2-pentanone (2d)**

TLC, $SiO_2$, EtOAc/hexanes 1 : 1, $R_f$ = 0.42. $[\alpha]^{25}_D$ -57.5 ( *c* 0.10, $CHCl_3$). IR(neat) 3460, 1712 $cm^{-1}$. $^1H$ NMR($CDCl_3$, 300 MHz) δ 4.12(m, 1H), 2.94(bs, 1H), 2.56(dd, 1H, *J* = 17.8, 2.9 Hz), 2.51(dd, 1H, *J* = 17.8, 9.1 Hz), 2.21(s, 3H), 0.97(t, 3H, *J* = 6.5 Hz). MS(m/e) 102($M^+$), 84, 43(base peak).

**(*4S*)-Hydroxy-4-phenyl-2-butanone (2e)**

TLC, $SiO_2$, EtOAc/hexanes 1 : 1, $R_f$ = 0.56. $[\alpha]^{25}_D$ -67.8 ( *c* 0.14, $CHCl_3$). IR(neat) 3458, 3015, 1709 $cm^{-1}$. $^1H$ NMR($CDCl_3$, 300 MHz) δ 7.25(m, 5H), 5.15(m, 1H),

3.27(bs, 1H), 2.90(dd, 1H, $J$ = 17.4, 8.4 Hz), 2.83(dd, 1H, $J$ = 17.4, 3.6 Hz), 2.18(s, 3H). MS(m/e) 164($M^+$), 107(base peak), 79.

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