Triethylborane Induced Selective 1,4-Reduction of α,β-Unsaturated Carbonyl Compounds with Triphenyltin Hydride or Tributyltin Hydride

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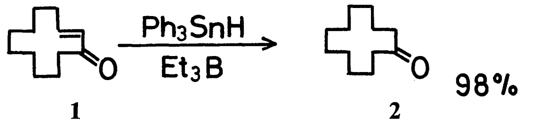
Synopsis. Reduction of α,β-unsaturated ketones and esters with triphenyltin hydride or tributyltin hydride in the presence of triethylborane has been studied. Whereas the reaction of α,β-unsaturated ketones ($R^1CH{=}CHCOR^2$) with triphenyltin hydride provided the corresponding saturated ketones ($R^1CH_2CH_2COR^2$), treatment of α,β-unsaturated ester ($PhCH{=}CHCOOMe$ or $CH_3CH{=}CHCOO\text{-}n\text{-}C_6H_{13}$) afforded an adduct ($PhCH_2CH(SnPh_3)COOMe$ or $CH_3CH(SnPh_3)CH_2COO\text{-}n\text{-}C_6H_{13}$).

1,4-Selective reduction of α,β-unsaturated carbonyl compounds has been achieved by triphenyltin hydride in refluxing toluene.[1] Recently we have reported that triethylborane induced a facile addition of triphenyltin hydride to an acetylenic bond to give alkenylstannane effectively.[2] The reaction proceeded at low temperature compared with the conventional method which uses azobisisobutyronitrile or peroxide as a radical initiator. Taking this advantage, we applied our method to the title reaction and found that selective reduction of α,β-unsaturated carbonyl compounds to saturated carbonyl compounds proceeded efficiently by treatment with triphenyltin hydride or tributyltin hydride in benzene at 25 °C.

Treatment of a benzene solution of 2-cyclododecenone **1** and Ph_3SnH with Et_3B at 25 °C for 6 h provided cyclododecanone **2** in 98% yield (Scheme 1). The other representative results are shown in Table 1.

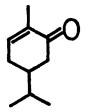
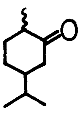
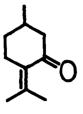
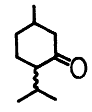
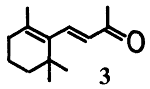
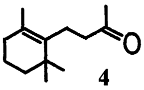
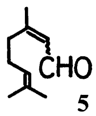
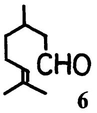


Scheme 1.

The reduction of β-ionone (**3**) provided α,β-unsaturated ketone **4** in 88% yield selectively and no 1,6-reduction product was observed in the reaction mixture (Entry 7 in Table 1). α,β-Unsaturated aldehyde was converted into saturated aldehyde in good yield which was exemplified by the reduction of citral (**5**) (Entry 8 in Table 1). Over-reduction of 3,7-dimethyl-6-octenal (**6**) into alcohol (3,7-dimethyl-6-octen-1-ol) was not observed because of the mildness of the reaction conditions.[3] An alkynone such as 3-octyn-2-one was reduced to 2-octanone in 50% yield with 4 equivalents of Ph_3SnH.

The use of less than 2 equivalents of triphenyltin hydride resulted in an incompletion of the reduction. However, the amount of triethylborane could be reduced to catalytic amount without decrease of the

Table 1. 1,4-Reduction of α,β-Unsaturated Ketones with $Ph_3SnH^{a)}$

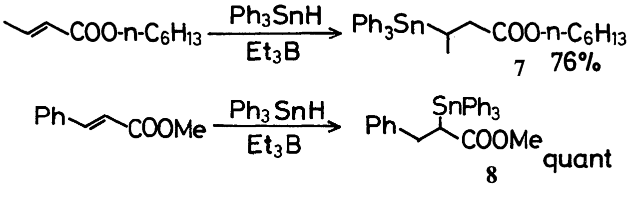
Entry	Unsaturated ketone	Reaction time/h	Product	Yield/%
1	3-Dodecen-2-one	12	2-Dodecanone	86
2	2-Dodecen-4-one	12	4-Dodecanone	85
3	2-Cyclohexenone	3	Cyclohexanone	$74^{b)}$
4	4-Methyl-2-cyclohexenone	3	4-Methylcyclohexanone	$98^{b)}$
5		5		84
6		7		80
7	 **3**	12	 **4**	88
8	 **5**	12	 **6**	80
9	$n\text{-}C_4H_9C{\equiv}CCO\text{-}n\text{-}C_6H_{13}$	12	$n\text{-}C_4H_9CH_2CH_2CO\text{-}n\text{-}C_6H_{13}$	$50^{c)}$

a) Triethylborane (2.2 mol), triphenyltin hydride (2.2 mol), and α,β-unsaturated ketones (1.0 mol) were empolyed. b) GLPC yields. c) Triphenyltin hydride (4.0 mol) was employed.

yield of saturated ketones. For instance, an addition of catalytic amount of triethylborane (0.1 mmol) to a solution of 2-cyclohexenone (1.0 mmol) and triphenyltin hydride (2.2 mmol) provided cyclohexanone in 77% yield after stirring for 3 h at 25 °C. Tributyltin hydride could be used instead of triphenyltin hydride and the reaction of 2-cyclododecenone with tributyltin hydride in the presence of triethylborane gave cyclododecanone in 98% yield after 7 h at 25 °C.

We are tempted to assume following reaction mechanism: (1) Triphenyltin hydride or tributyltin hydride adds to α,β-unsaturated ketones ($R^1CH{=}CHCOR^2$) in 1,4-fashion to give $R^1CH_2CH{=}CR^2$ ($OSnR_3$) ($R{=}Ph$ or n-Bu) and (2) subsequent hydrogenolysis with second triphenyltin hydride or tributyltin hydride to provide saturated ketones and $R_3Sn{-}SnR_3$ ($R{=}Ph$ or n-Bu).

Treatment of α,β-unsaturated ester with triphenyltin hydride in the presence of triethylborane gave β-triphenylstannyl or α-triphenylstannyl carboxylic ester (**7** or **8**) in contrast to the reaction of α,β-unsaturated ketones (Scheme 2). Triphenylstannyl radical attacked β-carbon of hexyl crotonate to give a carbon radical $Ph_3SnCH(Me)\dot{C}HCOO$-n-C_6H_{13} which abstracted hydrogen from Ph_3SnH to form the product. In contrast, triphenylstannyl radical attacked α-carbon of methyl cinnamate to provide a carbon radical $Ph\dot{C}HCH(SnPh_3)COOMe$ because phenyl group stabilizes an adjacent carbon radical more effectively than carboalkoxy group.[5] The reaction of tributyltin hydride in place of triphenyltin hydride with α,β-unsaturated ester was sluggish and resulted in an incompletion.[6–8] Treatment of $PhCH{=}CHCOOMe$ with tributyltin hydride in the presence of triethylborane provided $PhCH_2CH(Sn$-n-$Bu_3)COOMe$ in 50% yield along with recovered starting material (10%) and saturated ester, $PhCH_2CH_2COOMe$ (10%). The reaction of $CH_3CH{=}CHCOO$-n-C_6H_{13} with tributyltin hydride gave β-tributylstannylated ester, $CH_3CH(Sn$-n-$Bu_3)CH_2COO$-n-C_6H_{13} in 15% yield along with starting ester (47%).



Scheme 2.

In conclusion, the coexistence of triethylborane facilitate the reduction of α,β-unsaturated ketones into saturated ketones with triphenyltin hydride or tributyltin hydride. The reduction proceeded under mild conditions (25 °C) compared with the conventional methods which require high reaction temperature (100—150 °C).

Experimental

Analytical gas chromatography (GLPC) was performed with a Shimadzu gas chromatograph, Model GC-8A using thermal conductivity detector and helium as carrier gas. ^1H NMR and ^{13}C NMR spectra were taken on a Varian XL-200 spectrometer, $CDCl_3$ was used as solvent and chemical shifts were given in δ with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO IR-810 spectrometer. The elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

General Procedure for the Reduction of α,β-Unsaturated Ketones with Triphenyltin Hydride. The reduction of 2-cyclododecenone is representative. A hexane solution of triethylborane[4] (1.0 M, 1 M=1 mol dm^{-3}, 2.2 ml, 2.2 mmol) was added to a solution of 2-cyclododecenone (0.18 g, 1.0 mmol) and triphenyltin hydride (0.77 g, 2.2 mmol) in benzene (10 ml) at 25 °C under argon atmosphere. After stirring for 6 h at 25 °C, the reaction mixture was concentrated and the residue was submitted to silica-gel column chromatography using hexane–ethyl acetate (10 : 1) as an eluant to give cyclododecanone (0.18 g) in 98% yield

Reduction of 2-Cyclohexenone with Triphenyltin Hydride. A hexane solution of triethylborane (1.0 M, 2.2 ml, 2.2 mmol) was added to a solution of 2-cyclohexenone (96 mg, 1.0 mmol) and triphenyltin hydride (0.77 g, 2.2 mmol) in benzene (10 ml) at 25 °C under argon atmosphere. After stirring for 3 h at 25 °C, nonane (90 mg, 0.85 mmol) was added to the resulting mixture. The yield of cyclohexanone was determined by GLPC (OV-1 2% on Chromosorb W AW DMCS 60—80 mesh, 2 m, 65 °C, cyclohexanone: $t_r{=}2.54$ min, nonane: $t_r{=}3.35$ min).

The Reaction of α,β-Unsaturated Ester with Triphenyltin Hydride. The reaction of hexyl crotonate with triphenyltin hydride is a typical example. A hexane solution of triethylborane (1.0 M, 2.2 ml, 2.2 mmol) was added to a solution of hexyl crotonate (0.17 g, 1.0 mmol) and triphenyltin hydride (0.77 g, 2.2 mmol) in benzene (10 ml) at 25 °C under argon atmosphere. The reaction mixture was stirred for 3 h at 25 °C and concentrated in vacuo. The residual oil was submitted to silica-gel column chromatography to give hexyl 3-triphenylstannylbutanoate (**7**, 0.39 g) in 76% yield as a colorless oil: IR (neat) 3062, 2954, 2926, 2856, 1725, 1481, 1459, 1428, 1351, 1294, 1190, 1147, 1074, 909, 727, 698 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta{=}0.87$ (t, $J{=}6.6$ Hz, 3H), 1.05—1.70 (m, 8H), 1.42 (d, $J{=}7.4$ Hz, 3H), 2.32 (m, 1H), 2.67 (dd, $J{=}12.0$, 7.0 Hz, 1H), 2.73 (dd, $J{=}16.0$, 7.0 Hz, 1H), 3.88 (t, $J{=}6.7$ Hz, 2H), 7.35—7.56 (m, 9H), 7.56—7.83 (m, 6H); ^{13}C NMR ($CDCl_3$) $\delta{=}13.99$, 18.27, 19.04, 22.50, 25.50, 28.43, 31.38, 39.97, 64.68, 128.4, 128.7, 137.3, 138.8, 173.9. Found: C, 64.79; H, 6.70%. Calcd for $C_{28}H_{34}O_2Sn$: C; 64.52; H, 6.57%.

Methyl 3-Phenyl-2-triphenylstannylpropanoate (8): Mp 94.5—95.5 °C; IR (KBr) 3055, 2948, 1720, 1425, 1303, 1202, 1145, 1078, 1040, 995, 830, 765, 740, 720, 698 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta{=}3.03$ (dd, $J{=}13.8$, 4.7 Hz, 1H), 3.27 (s, 3H), 3.31 (dd, $J{=}9.8$, 4.7 Hz, 1H), 3.49 (dd, $J{=}13.8$, 9.8 Hz, 1H), 7.05—7.70 (m, 20H); ^{13}C NMR ($CDCl_3$) $\delta{=}34.15$, 36.33, 50.85, 126.2, 128.4, 128.6, 129.4, 136.7, 137.1, 137.4, 141.6. Found: C, 65.25; H, 5.16%. Calcd for $C_{28}H_{26}O_2Sn$: C, 65.53; H, 5.11%.

Reduction of Methyl Cinnamate with Tributyltin Hydride. A hexane solution of triethylborane (1.0 M, 2.2 ml, 2.2 mmol) was added to a solution of methyl cinnamate (0.16 g, 1.0 mmol) and tributyltin hydride (0.64 g, 2.2 mmol) in benzene (10 ml) at 25 °C under argon atmosphere. After stirring for 15 h at 25 °C, the resulting mixture was concentrated in vacuo. The residual oil was submitted to silica-gel column chromatography using hexane–ethyl acetate (10 : 1) as an eluant to give methyl 3-phenyl-2-tributylstannylpropanoate (0.23 g, 50%) and methyl 3-phenylpropanoate (16 mg, 10%) along with recovered methyl cinnamate (16 mg, 10%). Following the literature,[8] a solution of 3-phenyl-2-tributylstannylpropanoate (0.23 g, 0.5 mmol) and benzoic acid (0.12 g, 1.0 mmol) was heated at reflux for 3 h to give methyl 3-phenylpropanoate (65 mg, 80%).

Reduction of Hexyl Crotonate with Tributyltin Hydride. A hexane solution of triethylborane (1.0 M, 2.2 ml, 2.2 mmol) was added to a solution of hexyl crotonate (0.17 g, 1.0 mmol) and tributyltin hydride (0.64 g, 2.2 mmol) in benzene (10 ml) at 25 °C under argon atmosphere. After stirring for 15 h at 25 °C, the resulting mixture was concentrated. The residual oil was submitted to silica-gel column chromatography to give hexyl 3-tributylstannylbutanoate (68 mg, 15% yield) along with recovered hexyl crotonate (80 mg, 47%). Hexyl 3-tributylstannylbutanoate: Bp 110—120 °C (2 Torr, 1 Torr=133.322 Pa, bath temp); IR (neat) 2954, 2924, 2854, 1732, 1459, 1377, 1288, 1185, 1134, 1072 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.77—0.91 (m, 18H), 1.16—1.65 (m, 24H), 2.41—2.50 (m, 2H), 4.05 (t, J=6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ=8.33, 13.69, 13.98, 14.95, 18.68, 22.52, 25.60, 27.54, 28.63, 29.23, 31.42, 40.37, 64.43, 174.3. Found: C, 57.14; H, 10.27%. Calcd for $C_{22}H_{46}O_2Sn$: C, 57.28; H, 10.05%.

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