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Chemoselective Conversion of Thioesters to Aldehydes: Palladium-Catalyzed Reduction of (Z)-1,3-Bis(arylthio)-2-alken-1-ones with *n*-Bu$_3$SnH

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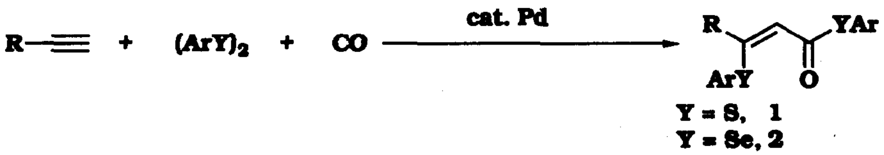
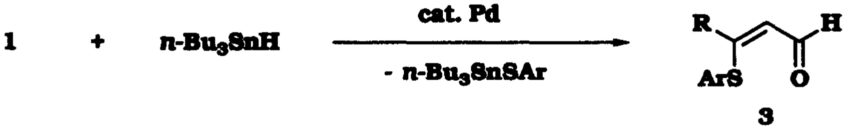
Key Words: thioester; palladium catalyst; chemoselective and site-selective reduction; tin hydride; thioformylation

Abstract: (Z)-1,3-Bis(arylthio)-2-alken-1-ones (1) are chemoselectively reduced to the corresponding aldehydes (3) by n-Bu$_3$SnH with the aid of palladium catalysts under the very mild reaction conditions.

The investigations of transition-metal-catalyzed reactions with chalcogen compounds have been limited, partly because chalcogen compounds have been widely accepted as poisons for transition-metal catalysts. On the contrary, we have recently opened up a new field of transition-metal-catalyzed reaction systems using organic sulfides and selenides: stereoselective double thiolation and double selenation of terminal acetylenes;[1] regio- and stereoselective carbonylative double thiolation and selenation of terminal acetylenes (eq 1);[1] regioselective hydrothiolation[2] and hydroselenation[3] of acetylenes. These reactions clearly demonstrate that the transition-metal catalysts are indeed available for the synthetic reactions of organic sulfides and selenides. In this paper, we wish to report a new entry based on the same concept, namely, palladium-catalyzed chemoselective and site-selective reduction of (Z)-1,3-bis(arylthio)-2-alken-1-ones (1) (which can be easily prepared according to eq 1, Y = S) with *n*-Bu$_3$SnH to give the (Z)-3-(arylthio)-2-alkenals (3) in good yields under moderate reaction conditions (eq 2).[4]



(1)

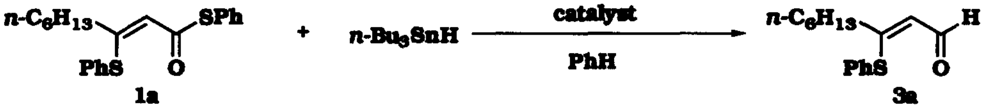


(2)

Because the examples of reduction of thioesters have been limited,[5] the present n-Bu_3SnH/Pd catalyst reduction system[6,7] would be expected to provide a general access to aldehydes from thioesters.

Table 1 summarizes the effects of catalysts on the reaction of (*Z*)-1,3-bis(phenylthio)-2-nonen-1-one (**1a**) with n-Bu_3SnH. Among the catalysts examined, $Pd(PPh_3)_4$ (0.4 mol% for **1a**) gave the best result (entry 1).[8] Further decrease in the amount of $Pd(PPh_3)_4$ caused the palladium-promoted decomposition of n-Bu_3SnH into hexabutyldistannane and gaseous hydrogen (entry 2). The overreduction from **3a** hardly occurred, even if the reaction was carried out with excess amount of n-Bu_3SnH (entry 3).[9] $Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2$ also exhibited the catalytic activities (entries 4 and 5), while $Ni(PPh_3)_2Cl_2$, $Pt(PPh_3)_4$, and $Rh(PPh_3)_3Cl$ did not catalyze this reduction. The reaction of **1a** with Et_3SiH in the presence of Pd on carbon[5b] or $Pd(PPh_3)_4$ failed (entries 6 and 7). For the reductions of acid chlorides and selenoesters with n-Bu_3SnH, AIBN-initiated radical reactions have already been reported.[10,11] However, AIBN- and Et_3B-initiated reactions[12] resulted in the double bond isomerization from (*Z*)-**1a** to (*E*)-**1a** (entries 8 and 9).

Table 1. Reduction of 1a with n-Bu_3SnH in the Presence of Several Catalysts[a]

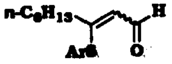
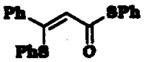
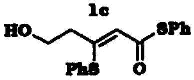
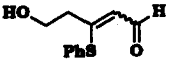
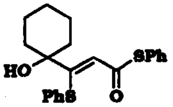
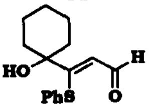
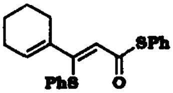
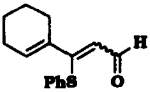
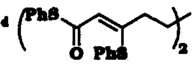
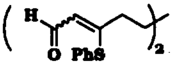


entry	catalyst	(mol%)	period of addition (min)	yield of 3a (%)[b]	(E/Z)[c]
1	$Pd(PPh_3)_4$	0.4	7	93[d]	(1/99)
2	$Pd(PPh_3)_4$	0.025	10	33	only Z
3[e]	$Pd(PPh_3)_4$	0.4	1	89	only Z
4	$Pd(PPh_3)_2Cl_2$	1.0	4	90	(7/93)
5	$Pd(OAc)_2$	1.0	11	26	(17/83)
6[f]	10% Pd on carbon	3.0	—	0[g]	
7[h]	$Pd(PPh_3)_4$	1.0	—	0[i]	
8[j]	AIBN	10	—	trace[k]	
9[l]	Et_3B	120		0[m]	

[a] A solution of n-Bu_3SnH (1.2 mmol in PhH 10 mL) was added to a solution of **1a** (1.0 mmol in PhH 20 mL) and catalyst at 25 °C. [b] NMR yield. [c] The *E/Z* ratio in crude reaction mixture. [d] Isolated yield (*E/Z* = 6/94). [e] 3.1 equiv of n-Bu_3SnH was used. [f] The solution of Et_3SiH (2.3 mmol) and **1a** (1.0 mmol) with Pd/C in CH_2Cl_2 (1 mL) was stirred at 25 °C for 50 min, see ref 5b. [g] The *E/Z* ratio of recovered **1a** was 23/77. [h] Et_3SiH was used in lieu of n-Bu_3SnH. [i] No reaction. [j] n-Bu_3SnH (0.75 mmol) was added to a 5 mL of PhH solution of **1a** (0.5 mmol) and AIBN (0.05 mmol) at 70 °C over a period of 40 min. Then the mixture was refluxed for 4 h. [k] The *E/Z* ratio of recovered **1a** was 68/32. [l] n-Bu_3SnH (0.6 mmol) was added to a 10 mL of PhH solution of **1a** (0.5 mmol) and Et_3B over a period of 40 min. Then, the mixture was stirred at 25 °C for 16 h. [m] The *E/Z* ratio of recovered **1a** was 86/14.

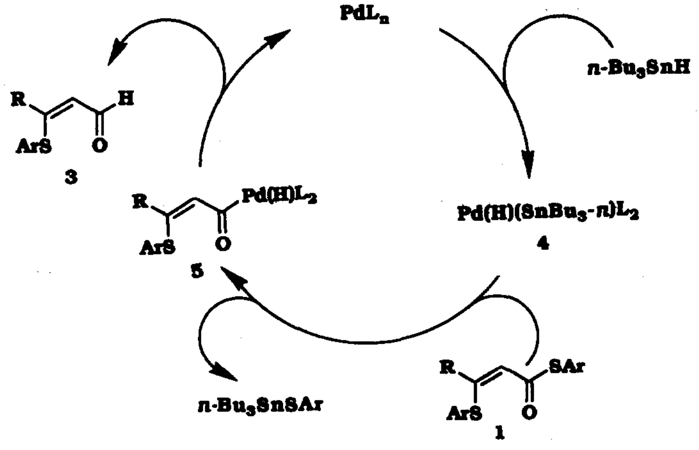
The results of the $Pd(PPh_3)_4$-catalyzed reduction of some (*Z*)-1,3-bis(arylthio)-2-alken-1-ones (**1**) with n-Bu_3SnH were listed in Table 2. The reactions proceeded successfully to give the corresponding aldehydes (**3**) in good yields, although some double bond isomerization took place during the isolation of **3**. Hydroxy group and tethered olefinic unit did not affect the reduction (entries 3, 4, and 5).

Table 2. **Palladium-Catalyzed Reduction of 1 with n-Bu_3SnH^a**

entry	substrate	product	yield (%)[b]	(E/Z)
1	 ArS = CH_3-C₆H₄-S **1b**	 **3b**	96	(4/96)
2	 **1c**	 **3c**	89	(9/91)
3	 **1d**	 **3d**	91	(2/98)
4	 **1e**	 **3e**	94	(0/100)
5	 **1f**	 **3f**	98	(15/85) (0/100)[c]
6[d]	 **1g**	 **3g**	86	(Z,E/Z,Z = 2/98)

[a] Procedure: n-Bu_3SnH (1.1-1.3 mmol in PhH 10 mL) was added to a solution of 1 (1.0 mmol in PhH 20 mL) in the presence of 0.4 mol% of $Pd(PPh_3)_4$ over a period of 7-20 min at 25 °C. [b] Isolated yield. [c] The *E/Z* ratio in crude reaction mixture. [d] 0.5 mmol of 1 g was used.

Scheme 1 illustrates one of the possible reaction paths for the present palladium-catalyzed reduction of 1 with n-Bu_3SnH. The reaction proceeds *via* the oxidative addition of n-Bu_3SnH to low-valent palladium complex to form Pd-H species **4**. The following ligand exchange of **4** with **1** generates the acylpalladium complex **5**, accompanied by the formation of n-Bu_3SnSAr. The subsequent reductive elimination from **5** affords **3** and regenerates the low-valent palladium catalyst.



Scheme 1. A Possible Reaction Path

Scheme 2

In conclusion, this study reveals the chemoselective and site-selective palladium-catalyzed reduction of (Z)-1,3-bis(arylthio)-2-alken-1-ones (1) to give (Z)-3-(arylthio)-2-alkenals (3). The carbonylative addition (eq 1) and subsequent reduction with tin hydride (eq 2) realizes the regio- and stereoselective thioformylation of terminal acetylenes (Scheme 2). Work is ongoing in efforts to further clarify the generality of this transformation and will be reported in due course.

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