PALLADIUM-CATALYZED CONJUGATE REDUCTION OF α,β-UNSATURATED CARBONYL COM-

POUND WITH TRIBUTYLTIN HYDRIDE. THE PROMOTING INFLUENCE OF THE PRESENCE OF

PROTONIC OR LEWIS ACIDS.

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Abstract : Acetic acid or $ZnCl_2$ promote the palladium-catalyzed selective conjugate reduction of α,β-unsaturated carbonyl compounds with tributyltin hydride. Protonic agents also promote the palladium-catalyzed hydrogenolysis of aryl allyl ethers and allyl carbamates.
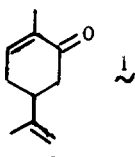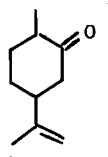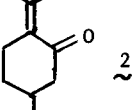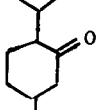
During the past few years, we have been investigating the hydride donor properties of tributyltin hydride in the presence of soluble palladium catalysts such as tetrakis(triphenyl-phosphine)palladium. Acyl chlorides were thus reduced selectively to aldehydes [1] . We also observed [1b] that $Pd(PPh_3)_4$ catalyzes the hydrostannation of α,β-unsaturated carbonyl compounds. Finally in connection with problems related to protective group chemistry we used tri-butyltin hydride and $Pd(PPh_3)_4$ as a catalyst to unblock allyloxycarbonyl derivatives of alco-hols through hydrogenolysis of the allyl carbonate function [2] . In order to avoid possible side reactions, some of these unblocking reactions were tentatively performed in the presence of a protonic agent, namely p-nitrophenol [2] . Successfull results encouraged us to further explore the potentialities of the Bu_3SnH/Palladium catalyst reducing system in the presence of proton donors. Recent publications by Keinan and coworkers concerning the palladium-cata-lyzed hydrogenolysis of allyl carboxylates [3] and the palladium-catalyzed conjugate reduc-tion of α,β-unsaturated carbonyl compounds [4] with tributyltin hydride prompt us to report our own observations in these fields.

We have studied the palladium-catalyzed tributyltin hydride reduction of α,β-unsatura-ted compounds in the presence of acetic acid as the proton donor (method A). Since $ZnCl_2$ was known to catalyze the hydrostannation of saturated carbonyl compounds [5] and to promote the palladium-catalyzed cross-coupling of allylic bromides and acetates with tetraallyltin [6] we have also investigated the use of anhydrous $ZnCl_2$, instead of acetic acid, as the coactiva-ting agent (method B).

Bu_3SnH(1.2 mmole) was added dropwise over a period of a few minutes and at room tempe-rature to a stirred oxygen-free solution (1 to 1.5 ml) of the unsaturated carbonyl compound (1 mmole) and $Pd(PPh_3)_4$ [7] (1 or 2 10^{-2} mmole) either in benzene/acetic (1.05 mmole) or in THF/$ZnCl_2$(argon atmosphere). Reactions were slightly exothermic and complete within 10 minu-tes. Analytical yields [8] were then determined by g.l.c. and/or NMR spectroscopy (after con-ventionnal work-up in method B). The results are given in the table.

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TABLE   Palladium-catalyzed reduction of α,β-unsaturated carbonyl compounds with tributyltin hydride.

Substrate	Condition [a]	Product	Yield %	% recovered starting material
Crotonaldehyde	A	Butyraldehyde	76	0
Cinnamaldehyde	A	3-Phenylpropanal	82	0
Citral	A	Citronellal	83	0
Cyclohexenone	A	Cyclohexanone	98	0
	B(0.2)		93	0
Benzalacetone	A	4-phenyl-2-propanone	94	0
3-methyl-2-cyclohexenone	A	3-methylcyclohexanone	23	76
	B(0.2)		40	58
	B(1.0)		95	0

	A	[b]	18	80
	B(0.45)		95	5
	A	[b]	12	88
	B(2.2)		64	23

(a) Bu₃SnH was added over a period of 2 to 10 min.. Figures in parentheses refer to the amount (equiv. based on starting α-enone) of $ZnCl_2$ used in method B.

(b) Mixture of epimers.

The reactions were found to be highly selective towards the formation of the conjugate reduction product (the saturated carbonyl compound). In no cases could any appreciable amounts of allylic or saturated alcohols be detected.

The presence of acetic acid significantly improves the scope of the reaction , thus α,β-unsaturated aldehydes, cyclohexenone and benzalacetone are now reduced in good to excellent yields Perhaps owing to the occurence of side reactions such as aldol condensation, lower yields of saturated aldehydes were obtained from crotonaldehyde or cinnamaldehyde in the absence of proton donors by us in earlier experiments [1b, 9] . Similarly, only partial reduction of cyclohexenone to cyclohexanone was observed due to a competitive decomposition of tributyltin hydride. The question wether the role of acetic acid in the present experiments is to slow down decomposition of the tin hydride or if it has a truly accelerating effect on the catalytic process has not yet been elucidated.
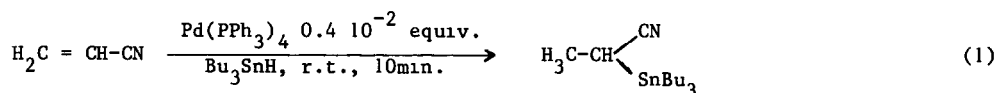
Further inspection of the table shows that α-enones which bear two or more substituents on the ethylenic bond are not reduced in reasonable yields ; thus rather severe limitations are encountered with method A resulting from its sensitivity to steric factors. The thermal non catalytic conjugate reduction of α-enone with tributyltin hydride in the presence of methanol as a proton source has been described [10]. It is much less sensitive to steric congestion but requires rather drastic conditions

Compared to method A, the scope of method B is wider. Carvone 1 and 3-methyl-2-cyclohe-

xenone are now essentially quantitatively reduced to saturated ketones, and pulegone $\underline{2}$ is reduced selectively (63% yield) to menthone-isomenthone. Anhydrous $ZnCl_2$ may be used in catalytic amount but with poorly reactive α-enones much better yields are obtained by using large amounts. The absence of any alcohol formation is worthy of note since $ZnCl_2$ is known to strongly activate carbonyl functions towards nucleophilic agents, including tributyltin hydride [5] and to strongly favor 1-2 versus 1-4 reduction of α-enones [11,12]. Note that pulegone has been hydrosilylated with triethyl- or phenyldimethylsilane in the presence of $RhCl(PPh_3)_3$ apparently in quantitative yield but with a poor or no selectivity at all towards formation of the 1,4-adduct [13].
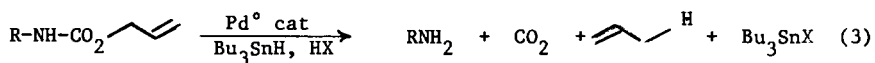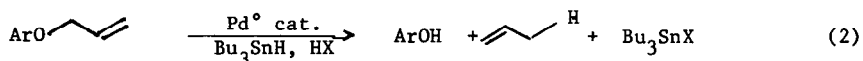
Method B could also constitute an useful way of generating enolstannanes [14], allylated derivatives of cyclohexanone – almost exclusively the mono-C-allylated one – were obtained upon treatment of the reduction mixture of cyclohexenone with allyl bromide. Note that tetrakis (triphenylphosphine)palladium is known to catalyze the allylation of enol stannanes [15].

We have also studied the hydrostannation of acrylonitrile in the presence of tetrakis (triphenylphosphine)palladium, without any added $ZnCl_2$ or acetic acid. α-Tributyltin proprionitrile, $\nu_{C=N}=2\ 210cm^{-1}$, was exclusively obtained. (eq. 1) Since radical conditions

$$H_2C = CH\text{-}CN \xrightarrow[\text{Bu}_3\text{SnH, r.t., 10min.}]{Pd(PPh_3)_4\ 0.4\ 10^{-2}\ equiv.} H_3C\text{-}CH \Big\langle \begin{array}{l} CN \\ SnBu_3 \end{array} \qquad (1)$$

are known to favor the formation of isomeric β-trialkyltin derivatives [16] our result strongly suggests that the palladium- catalyzed hydrostannation of activated double bonds occurs by an ionic mechanism [17].

To conclude we want also to report that proton donors (acetic acid, p-nitrophenol) also promote the hydrogenolysis of allyl aryl ethers and allyl carbamates with Bu_3SnH (eq.2 and 3)

$$ArO\diagup\diagup \xrightarrow[\text{Bu}_3\text{SnH, HX}]{Pd^\circ\ cat.} ArOH + \diagup\diagdown^H + Bu_3SnX \qquad (2)$$

$$R\text{-}NH\text{-}CO_2\diagup\diagup \xrightarrow[\text{Bu}_3\text{SnH, HX}]{Pd^\circ\ cat} RNH_2 + CO_2 + \diagup\diagdown^H + Bu_3SnX \qquad (3)$$

Incomplete unblocking of the phenol or amine functions are observed in the absence of a proton source These results which are part of our continuing studies [2] on the use of allyl and allyloxycarbonyl groups in protective group chemistry will be reported later in more details.

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(7) Pd(PPh$_3$)$_4$ was freshly recrystallized from benzene containing triphenylphosphine. A catalyst of good quality is desirable to prevent decomposition of tributyltin hydride by metallic or organometallic impurities.

(8) For preparative scale experiments various methods are available for the isolation of the reaction product from organotin compounds (see for exemple ref. 1b and ref. therein).

(9) Note however that Keinan obtained good results in the reduction of cinnamaldehyde by slowly adding (1hr) Bu$_3$SnH in THF solution. The same author used water as an in situ proton source to promote the catalytic reduction of β-ionone (see ref. 4).

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(12) For the sake of comparaison, cyclohexenone was reacted at room temperature in THF/ZnCl$_2$ (0.2 equivalent) without palladium catalyst. After 18hr, 44% of cyclohexanone, 5% cyclohexanol and, traces of cyclohexene-3-ol were found together with 48% of unreacted cyclohexenone.

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(14) The exact nature of the enolate species in the presence of ZnCl$_2$ remains however to be clarified. Enolstannanes have been obtained from α-enones and Bu$_3$SnH under UV irradiation : M. Pereyre and J. Valade, Bull. Soc. Chim. Fr., 1928 (1967).

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(17) See also ref. 4. Similarly, an ionic mechanism is also very probable in the case of the palladium-catalyzed tributyltin hydride reduction of acyl chlorides to aldehyde (ref.1b).