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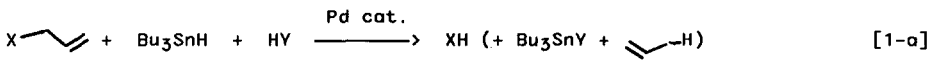
PALLADIUM CATALYZED HYDROSTANNATION OF ALKYNES AND PALLADIUM-CATALYZED HYDROSTANNOLYSIS OF PROPARGYL OR PROPARGYLOXYCARBONYL DERIVATIVES OF VARIOUS FUNCTIONAL GROUPS

Zhang H.X., F. Guibé* and G. Balavoine

Institut de Chimie Moléculaire d'Orsay, Laboratoire de Chimie Organique des Eléments de Transition UA-CNRS n° 255, Bât. 420, 91405 ORSAY cedex, France

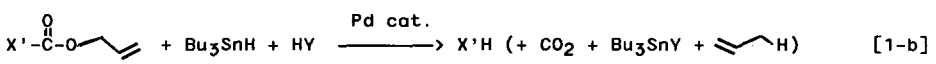
Abstract : $PdCl_2(PPh_3)$ catalyses, under very mild conditions, the cis-hydrostannation of acetylenic compounds by tributyltin hydride and the hydrostannolytic cleavage of propargyl carboxylates, phosphates, carbonates and carbamates. The latter reaction should find use in protective group chemistry.

In the past few years, we have shown that the allyl derivatives of carboxylic acids or phenols and the allyloxy carbonyl derivatives of alcohols and amines may be deprotected in a straightforward and very selective manner by palladium-catalyzed cleavage with tributyltin hydride (equations 1-a and 1-b)[1-4].



[1-a]

X = RCO_2-, ArO-



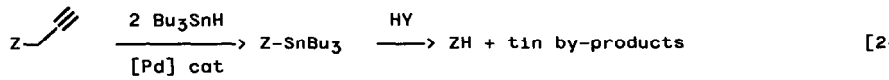
[1-b]

X' = RO-, RNH- ; YH = H_2O, pNO_2-PhOH, AcOH...

We have applied this procedure to the preparation of tributyltin β-ketoesters from allyl β-ketoesters[2], in the selective protection-deprotection of various allyl and allyloxycarbonyl derivatives of amino-acids[3] and in a solid-phase synthesis of the undecapeptide substance P in which the allyloxycarbonyl group was used for the temporary protection of the α-amino functions[4]. In this communication we report : 1) that the catalytic hydrostannolytic deprotection procedure also applies to the propargyl and propargyloxycarbonyl groups ; 2) that palladium complexes catalyze the tributyltin hydride hydrostannation of simple acetylenic compounds ; 3) that the hydrostannation of the triple bond probably represents the first step of the hydrostannolytic cleavage of propargylic esters mentionned above.

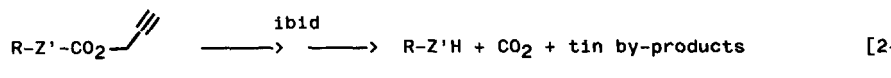
When 2 to 2.2 equivalents of tributyltin hydride were added dropwise over a period of a

few minutes to a benzene, THF or CH_2Cl_2 solution (5 mL) of propargyl acetate (1 mmole) and of dichloro-bis(triphenylphosphine)palladium(II) (2.10^{-2} equivalents) an immediate and exothermic reaction ensued. After 10 min, IR analysis (CCl_4) showed a total conversion of propargyl acetate (υ_{CO} = 1730 cm^{-1}) into tributyltin acetate ((υ_{CO} = 1635 cm^{-1}). Quantitative deprotection (NMR, GC) was also achieved, in CH_2Cl_2, starting from propargyl p-methylbenzoate, diethylpropargyl phosphate, propargyl benzyl carbonate and benzylamine propargyl carbamate.



[2-a]

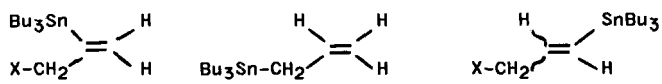
Z = $(EtO)_2$ P(O)-O-, pMe-Ph-CO_2-



[2-b]

R-Z' = $PhCH_2O$, $PhCH_2$-NH

No formation of allenic or propargylic amines or ethers could be detected in the hydrostannolytic deprotection of propargyl carbonate or carbamate[5]. Apart from the tributyltin salts Bu_3SnY -whose nature depends on the final work-up[6]- and a small amount of hexabutyldistannane[1b], the tin by-products of these reactions consist mainly of 2-tributylstannylpropene 1 (X = H) together with 3-tributylstannylpropene 2 and small quantities of Z and E 1-tributylstannyl propene 3 (X = H)[7].



1 2 3

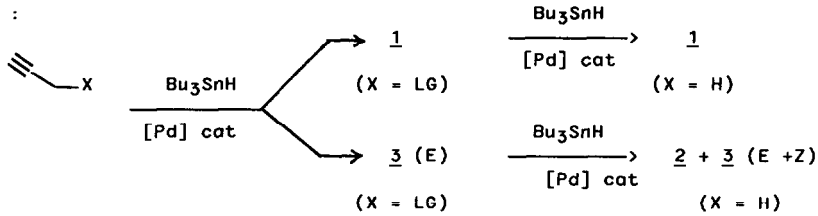
When applied to propargylphenoxide, the catalytic reaction with tributyltin hydride gave different results. Upon addition of one equivalent of tributyltin hydride, propargyl phenoxide was essentially converted to a ca. 95/5 mixture of 2-tributylstannyl- and (presumably) E-1-tributylstannyl-3-phenoxy propene 1 and 3 (X = OPh)[7,8]. Further addition of tributyltin hydride resulted only in partial release (ca 40 %) of tributyltin phenoxide. Extensive decomposition of tributyltin hydride into hexabutyldistannane[1b] and formation of allyl phenoxide (up to 20 %) were also observed.

The formation of tributyltin-substituted allylic phenoxides 1 and 3 (X = OPh) suggested that $PdCl_2(PPh_3)_2$ could act as a catalyst in the hydrostannation of carbon-carbon triple bonds. We were able to confirm this property with a series of simple acetylenic compounds[9]. From the preliminary results listed in the table, the reaction seems to be stereospecific (cis-hydrostannation leading to E-tributylstannyl olefinic compounds, entries 1, 2, 4 and 5)[10-12] but not regiospecific (entries 1, 2) unless electronic factors are involved (entries 3, 6).

From the above results, the following mechanism for the hydrostannolytic deprotection of propargylic esters may be tentatively proposed. In a first step, a palladium-catalyzed cis hydrostannation of the triple bond would lead to the tributyltin-substituted allylic interme-

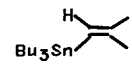
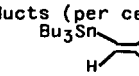
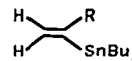
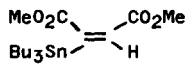
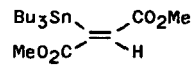
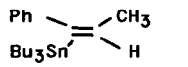
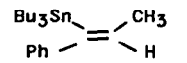
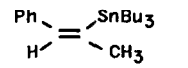
diates 1 and 3 E (X = leaving group : LG) ; in a fast step, these intermediates would then undergo a palladium-catalyzed hydrostannolytic cleavage -probably through the formation of a π-allyl palladium complex[13]- leading to the isomeric tributylstannylpropenes 1, 2 and 3 (X = H) (Scheme I).

Scheme I :



In the case of propargyl phenoxide, due to the poor leaving group ability of the phenoxy group, the intermediate 1 and 3 (X = OPh) are stable enough to be characterized upon addition of one equivalent of tributyltin hydride ; further addition would then lead not only to hydrostannolytic cleavage but also to other side-reactions[14].

Table : Palladium-catalyzed hydrostannation of acetylenic compounds(a)

Entry	Starting compounds H-≡-R	Products (per cent)(b)			Overall isolated yield(%) (d)
					
1	R = CH_2OH	45 %	(c)	55 %	41(e)
2	R = CH_2OTHP	32 %	(c)	68 %	68(e)
3	R = CO_2Me	100 %	(c)	(c)	90
4	MeO_2C-≡-CO_2Me	 83 %	 17 %		
5	Ph-≡-CH_3	 100 % (f)	 (c)	 (c)	79

(a) Bu_3SnH 1 to 1.2 equivalents, $PdCl_2(PPh_3)_2$ 2.10^{-2} equivalents, benzene (entries 1, 2) or THF (entries 3, 4, 5) as the solvent ; room temperature, a few minutes.
(b) Determined by NMR (250 MHz) on the crude reaction mixture.
(c) Undetected.
(d) Analytical overall yields, as determined by NMR on the crude reaction mixture using an internal standard, were found to be in all cases quantitative within experimental errors. Loss of product during purification by column chromatography is mainly due to silica-induced protodestannylation. All purified compounds gave satisfactory elemental analysis.
(e) Mixture of regioisomers.
(f) Stereochemical assignment based on NMR spectroscopy[12].

In conclusion, the allyl and propargyloxycarbonyl groups can be removed under very mild conditions by use of the hydrostannolytic system Bu_3SnH/Pd catalyst. The fact that conditions can often be found for the catalytic selective cleavage of the allyl and allyloxycarbonyl groups in the presence of the propargyl and propargyloxycarbonyl groups, as shown in the accompanying paper, should make these groups useful in protective group chemistry.

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3) Guibé F, Dangles O., Balavoine G. ; Tetrahedron Lett., 1986, 27, 2368.
4) Dangles O., Guibé F., Balavoine G., Lavielle S., Marquet A. ; J. Org. Chem., 1987, 52, 4984.
5) In palladium-catalyzed deallylation reactions performed on allyl carbamates, competitive allylamine formation may be a serious side reaction[3,4] and ref. therein. In the hydrostannolytic procedure[3,4] the formation of allylamine is completely suppressed in the presence of weak acidic species.
6) Hydrostannolytic deprotection of benzyl propargyl carbonate leads directly to the tributyltin salt of benzyl alcohol which is readily hydrolyzed in water. The deprotection of benzylamine propargyl carbamate yields the corresponding benzylamine tributyltin carbamate (ν_{CO} = 1630 cm^{-1}. Conversion to free amine upon protolysis (aq. HCl, CH_3CO_2H) is immediate. Tin carboxylates are converted into their sodium salt or into carboxylic acids by treatment with aqueous sodium carbonate or with various protonating agents HY.
7) ^1H NMR characteristics (250 MHz, $CDCl_3$) of main products : δ (ppm). 1 (X = H) : 5.7 (dq, $J_1 \simeq J_2 \simeq$1-2 Hz, 1H) and 5.1 (dq, 1H, vinylic H) ; 1.95 (app. t, J ≃ 1.5 Hz, 3H, CH_3). 2 (X = H) : 6.1-5.85 (m, 1H, internal vinylic H) ; 4.80 (dm, J_{trans} = 16 Hz, 1H) and 4.65 (dm, J_{cis} = 10 Hz, 1H, terminal vinylic H) ; allylic H : masked. 1 (X = OPh) : 6.05 (dt, $J_1 \simeq J_2 \simeq$ 1.5-2 Hz, 1H) and 5.45 (dt, 1H, vinylic H) ; 4.60 (app. t, J ≃ 5 Hz, 2H, allylic H).
8) By contrast upon addition of one equivalent of tributyltin hydride, propargyl carboxylates or phosphate gave a 1/1 mixture of unreacted material and of tributyltin carboxylates or phosphate.
9) For a related palladium-catalyzed reaction of silylstannanes with alkynes see : Chenard B.L., Zan Vyl C.M. ; J. Org. Chem., 1986, 51, 3561.
10) Non catalytic polar or radical-initiated hydrostannation of alkynes usually results in trans addition :
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b) Leusink A.J., Budding H.A., Drenth W. ; Ibid, 1967, 9, 295.
c) Leusink A.J., Budding H.A., Marsman J.W. ; Ibid, 1967, 9, 285.
d) Jung M.E., Light L.A. ; Tetrahedron Lett., 1982, 23, 3851.
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Tin hydride addition may also be induced by Et_3B :
f) Nozaki K., Oshima K., Utimoto K. ; J. Am. Chem. Soc., 1987, 109, 2547.
11) The formation of small amounts of trans addition product in the case of diethyl ethyne dicarboxylate (entry 4) may very likely be ascribed to competitive spontaneous (non catalytic) reaction (ref. 9c).
12) Most compounds have already been characterized by NMR spectroscopy (ref. 10c,d).
E-$Bu_3Sn(Ph)C{=}CH(CH_3)$: δ (ppm, $CDCl_3$) : 5.88 (q, J = 7 Hz, 1H) ; 1.67 (d, J = 7 Hz, 3H). The J^3 (^{117}Sn-H) and J^3 (^{119}Sn-H) values (respectively 63 and 67 Hz) for tin and vinylic hydrogen are consistent with a cis relationship (expected values for trans relationship : ca 110-130 Hz, ref 10c).
13) Greenspoon N., Keinan E. ; Tetrahedron Lett., 1982, 21, 241.
Guibé F., Zigna A.M., Balavoine G. ; J. Organomet. Chem., 1986, 306, 257.
Guibé F., Yang T.X., Balavoine G. ; J. Organomet. Chem., 1986, 306, 267.
14) Other mechanistic pathways are conceivable such as the direct hydrostannolysis of σ-allenic or σ-propargylic palladium entities[15,16]. However the need of two equivalents of tributyltin hydride to complete the cleavage of propargyl carboxylates and phosphates is more in favor of a sequential hydrostannation-hydrostannolysis process. We defer a more detailed mechanistic study of this reaction as well as a fuller investigation of the catalytic hydrostannation of alkynes to another report.
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16) For reactions involving such intermediates, see inter alia : Colas Y., Cazes B., Gore J. ; Tetrahedron Lett., 1984, 25, 845 and Bull. Soc. Chim. Fr., 1987, 165.
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