

Reduction of α -Chlorocarbonyl Compounds by the Tributyltin Hydride–Phosphine Oxide Combined System. Chemoselective Reduction of the Carbonyl Group

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α -Chlorocarbonyl compounds undergo selective reduction at the carbonyl group with tributyltin hydride–phosphine oxide combined systems to yield chlorohydrins.

Triorganotin hydrides are known as efficient reagents for the reduction of the carbon–halogen bond.¹ Generally, these reactions have been reported to proceed by a free radical mechanism, and radical initiators such as azoisobutyronitrile (AIBN) and u.v. irradiation accelerate the dehalogenation. Even the carbon–halogen bond in a α -chlorocarbonyl compound, which includes a reducible carbonyl group, is selectively and cleanly reduced to give the corresponding unhalogenated ketone.²

In contrast, here we report the unusual reaction of tributyltin hydride (Bu_3SnH) with α -chlorocarbonyl com-

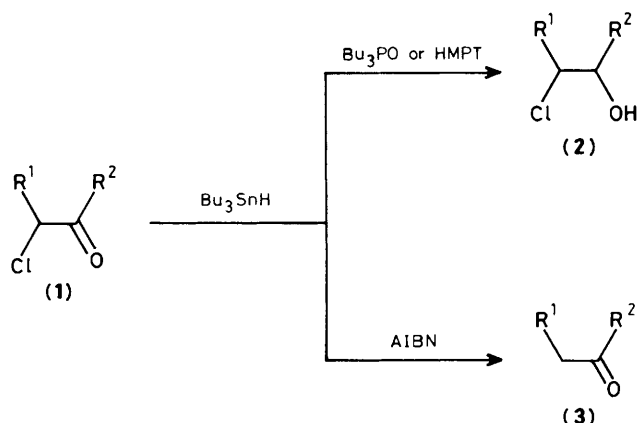
pounds. The opposite chemoselectivity, that is, reduction of the carbonyl group, is observed when tributyltin hydride is combined with phosphine oxides such as hexamethylphosphoric triamide (HMPT) and tributylphosphine oxide (Bu_3PO) (Scheme 1). To the best of our knowledge, few examples have been reported of the reduction of the carbonyl group in α -halogenoketones by organotin hydrides,³ and these results were in any case not satisfactory.

Some examples are shown in Table 1. In the reduction of α -chloroacetone (**1a**), free radical conditions using the Bu_3SnH –AIBN system induced selective reduction at the

Table 1. Reaction of compounds (1).^a

	(1)		Additive	Conditions	Ratio (2):(3) ^b	% Yield ^b
a	H	Me	Bu ₃ PO	0°C, 24 h	100: 0	67
			HMPT	"	100: 0	72
			AIBN	0°C, 72 h	0: 100	50
b	Me	Me	Bu ₃ PO	0°C, 24 h	100: 0	75 ^c
			HMPT	"	100: 0	78 ^d
			AIBN	0°C, 72 h	0: 100	79
c	-(CH ₂) ₃ -		HMPT	60°C, 1 h	73: 27	90 ^e
			AIBN	60°C, 6 h	0: 100	86
d	n-C ₅ H ₁₁	H	Bu ₃ PO	60°C, 1 h	100: 0	75
			HMPT	"	100: 0	67
			AIBN	60°C, 2 h	27: 73	74
e	=CHPh	H	HMPT	60°C, 2 h	100: 0	98
			AIBN	60°C, 4 h	60: 40	20

^a (1) 2.5 mmol, Bu₃SnH 5 mmol, phosphine oxide 5 mmol, AIBN 0.01 mmol. ^b Determined by g.l.c. ^c (2) *erythro:threo* 54:46. ^d (2) *erythro:threo* 63:37. ^e (2) *cis:trans* 41:59.

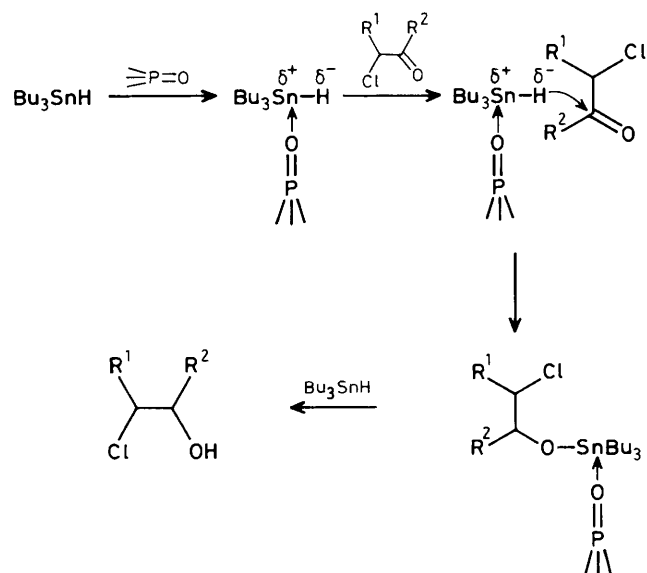


Scheme 1. a, R¹ = H, R² = Me; b, R¹ = R² = Me; c, R¹, R² = -(CH₂)₃-; d, R¹ = C₅H₁₁, R² = H; e, R¹ = =CHPh, R² = H.

chloro group to yield acetone (3a). On the other hand, the addition of HMPT and Bu₃PO to Bu₃SnH markedly affected the reaction, and chemoselective reduction occurred at the carbonyl group to give the chlorohydrin (2a). No (3a) could be detected. Moreover, the reaction rate was accelerated compared with the Bu₃SnH-AIBN system. The use of phosphine oxides is important, because other ligands such as amines and phosphines did not offer such a feature. As demonstrated in Table 1, further types of α -chloro ketones and aldehydes were reduced at the carbonyl group selectively or predominantly to yield chlorohydrins. The chemoselectivity observed is in opposition to that for the Bu₃SnH-AIBN system which induces dehalogenation.

As to the reduction of carbonyl compounds, a trialkyltin hydride, being a typical agent of free radical reduction, has exhibited a hydride donor ability in several cases; either in reactions in a highly polar solvent such as MeOH,⁴ in the presence of a Lewis acid catalyst,⁵ or with strongly electrophilic carbonyl compounds.⁶ The Bu₃SnH-phosphine oxide combined reducing system seems to act as a hydride donor. As shown in Scheme 2, the Sn-H bond is activated in the presence of a phosphine oxide, and the nucleophilicity of a hydride ion is increased to attack the carbonyl group. The organotin alkoxide generated *in situ* subsequently reacts with free Bu₃SnH, to give chlorohydrins.

Thus, the organotin hydride-phosphine oxide combined system is an excellent reagent for the reduction of carbonyl

**Scheme 2**

groups, and we are now investigating the further use of this reducing system.

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