

Triethylborane-Induced Hydrodehalogenation of Organic Halides by Tin Hydrides

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The reduction of organic halides with tributyltin hydride in the presence of a catalytic amount of triethylborane has been studied. (1) Alkyl iodides and alkyl bromides reacted easily with tin hydride at -78°C to give the corresponding hydrocarbons, while alkyl chlorides were sluggish to react and recovered unchanged. (2) The reduction of alkenyl halides such as 1-deuterio-1-iodo-1-dodecene and 1-iodo-1-triethylsilyl-1-dodecene proceeded nonstereospecifically. (3) The reduction of aryl halides with $n\text{-Bu}_3\text{SnH-Et}_3\text{B}$ system was not so effective as the reduction of alkyl halides and alkenyl halides. Whereas aryl iodides were reduced at room temperature with $n\text{-Bu}_3\text{SnH}$, aryl bromides hardly reacted with $n\text{-Bu}_3\text{SnH}$ even at 80°C .

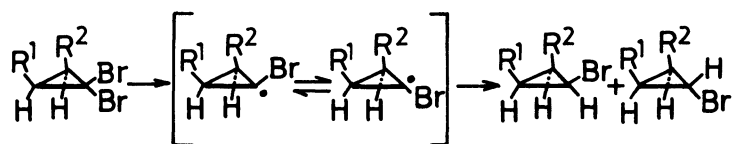
The free radical halogen abstraction from a C-Hal bond opens a broad variety of synthetic possibilities.^{1,2} The simplest version is trapping of the outcoming radical by tin hydride, providing us with a facile route to replacement of halogen by hydrogen at the same carbon atom. The reactions are initiated by generation of tin radicals, which are produced mostly by radical initiators such as azobisisobutyronitrile (AIBN) or benzoyl peroxide. Recently we have found that Et_3B is an efficient radical initiator for generation of tin radicals from tin hydrides and applied this methodology to a couple of organic syntheses.³ We would now like to report on a more detailed study on the reduction of organic halides with R_3SnH in the presence of Et_3B under mild reaction conditions.

Reduction of Alkyl Halides. A number of organic halides were reduced with $n\text{-Bu}_3\text{SnH-Et}_3\text{B}$ system and the results are summarized in Table 1. Treatment of a solution of 1-bromododecane and tributyltin hydride in toluene with a catalytic amount of Et_3B (hexane solution, 10 mol%) gave dodecane quantitatively. It is worth noting that the reaction proceeded at low temperature such as -78°C . Without Et_3B , 1-bromododecane was recovered quantitatively after treatment with $n\text{-Bu}_3\text{SnH}$ in toluene at -78°C for 3 h. Secondary bromoalkane and tertiary bromides were also easily reduced. The reactivity of the halides depends on the nature of the halogen. Iodides and bromides reacted easily with tin hydride in the presence of Et_3B , while chlorides were sluggish to react and were recovered practically unchanged. Heating a benzene solution of 1-chlorododecane with $n\text{-Bu}_3\text{SnH}$ or Ph_3SnH in the presence of a catalytic amount of

Et_3B at 70°C for 5 h resulted in a recovery of the starting 1-chlorododecane quantitatively. Taking advantage of the difference in reactivity between bromide and chloride, it was possible to reduce one halogen in the presence of the other (Run 10).

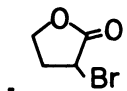
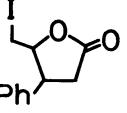
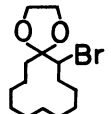
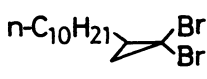
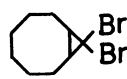
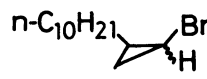
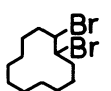
Reduction of halides containing other functional groups such as ether, hydroxyl, or carbonyl proved that these functionalities could be present in the molecule without perturbing the course of reduction, although the nature of the functional group slightly influences the development of the reaction. For example, β -bromopropiophenone (Run 7) and ethylene acetal (Run 13) were reduced slowly at -78°C . The reaction mixture was allowed to come to room temperature and then stirred for several hours to complete the reduction. 11-Bromo-1-undecanol could not be reduced at low temperature because of its low solubility in toluene and the reaction was performed at 0°C .

Monodehalogenation of alkyl-substituted *gem*-dibromocyclopropanes with $n\text{-Bu}_3\text{SnH-Et}_3\text{B}$ proceeded easily at -78°C to provide stereoisomeric mixtures of monobromocyclopropanes. The isomeric ratios were almost the same as those obtained by reported ordinary procedure (without Et_3B).⁴ The formation of *endo*- or *cis*-bromocyclopropanes as major products is explained as follows: (1) Tin radical attacks bromine to give a radical, (2) the intermediate radical equilibrates faster than hydrogen is transferred, (3) finally the less hindered approach of tin hydride provide *endo* or *cis* isomer selectively (Scheme 1). Reduction of monobromocyclopropanes to cyclopropanes did not proceed at -78°C and it took prolonged reaction time (10 h) at



Scheme 1.

Table 1. Reduction of Alkyl Halides with *n*-Bu₃SnH-Et₃B

Run	Substrate	Reaction conditions		Procedure	Yield of alkane %
		Temp °C	Time h		
1	1-Iodododecane	-78	0.5	A	95
2	2-Iodododecane	-78	0.5	A	90
3	1-Bromododecane	-78	0.5	A	100
4	2-Bromododecane	-78	0.5	A	98
5	1-Bromoadamantane	-78	0.5	A	75
6	BrCH ₂ CH ₂ CH ₂ OTHP	-78	0.5	B	77
7	PhCOCH ₂ CH ₂ Br	25	10	B	87
8	HOCH ₂ (CH ₂) ₉ CH ₂ Br	0	0.5	B	94
9	MeOOC(CH ₂) ₉ CH ₂ Br	-78	0.5	B	95
10	Cl(CH ₂) ₃ COO(CH ₂) ₃ Br	-78	0.5	B	87
11		-78	0.5	B	90
12		-78	0.5	B	87
13		-78, 1; 20, 3		A	80
14		-78	1.0	A	 92(67/33) ^{a)}
		20	15 ^{b)}	A	 84
15		-78	1.0	A	Monobromide 80(82/18) ^{c)}
16		20	11	A	83
17	CH ₃ (CH ₂) ₉ CHBrCH ₂ Br	-78	0.5	A	1-Dodecene 99
18		-78	0.5	A	Cyclododecene 96

a) Isomeric ratio (cis/trans). b) 2.2 mol of *n*-Bu₃SnH was employed. c) Isomeric ratio (endo/exo).

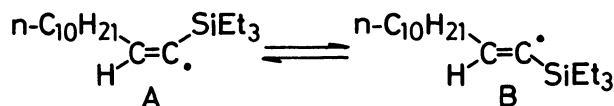
room temperature to complete the reaction. Treatment of dibromocyclopropanes with 2.2 mol of tin hydride at room temperature for 15 h afforded cyclopropanes directly in high yields.

β -Elimination has been achieved by treatment of *vic*-dibromoalkanes with *n*-Bu₃SnH-Et₃B system. *meso*-1,2-Dibromocyclododecane gave a mixture of *trans*- and *cis*-cyclododecene in an 1:1 ratio (Run 18).

Reduction of Alkenyl Halides. The reduction of alkenyl iodides and bromides was also examined in the presence of a catalytic amount of Et₃B. Whereas iodides reacted easily with tin hydrides at -78 °C, bromides reacted slowly compared with iodides and it took 10 h to complete the reduction at room

temperature. The effectiveness of Et₃B catalyst was confirmed by the fact that treatment of a solution of (*E*)-1-bromo-1-dodecene with *n*-Bu₃SnH in the absence of Et₃B at room temperature for 15 h resulted in quantitative recovery of (*E*)-1-bromo-1-dodecene. The typical results are summarized in Table 2. Treatment of (*E*)-1-deuterio-1-iodo-1-dodecene or (*Z*)-isomer with *n*-Bu₃SnH-Et₃B at -78 °C resulted in a formation of similar isomeric mixtures of (*E*)- and (*Z*)-1-deuterio-1-dodecene (*E*:*Z*=61:39—63:37). Thus, the reduction proceeded nonstereospecifically. Same stereochemical results were obtained with *n*-Bu₃SnH-AIBN system. The reaction of (*E*)- or (*Z*)-1-deuterio-1-iodo-1-dodecene with *n*-Bu₃SnH in the presence of AIBN at 50 °C

provided similar isomeric mixtures of (*E*)- and (*Z*)-1-deuterio-1-dodecene (*E*:*Z*=60:40). The reduction of alkenyl halides having silyl group on the same carbon bearing iodine also followed non-stereospecific course (Runs 6 and 7). (*E*)-1-Iodo-1-triethylsilyl-1-dodecene (**1**) gave a mixture of (*Z*)-1-triethylsilyl-1-dodecene and (*E*)-isomer (*Z*:*E*=56:44) and (*Z*)-isomer **2** afforded a *Z*:*E*=57:43 mixture upon treatment with *n*-Bu₃SnH-Et₃B at -78 °C.⁵⁾ The results have been explained by fast equilibration of two configurations of the alkenyl radical before hydrogen transfer (Scheme 2).



Scheme 2.

gem-Dibromoalkene provided monobromoalkene. For instance, reduction of 1,1-dibromo-1-dodecene gave an 1:1 mixture of 1-bromo-1-dodecene.

Reduction of Aryl Halides. The reduction of aryl iodides and bromides proceeded slowly with *n*-Bu₃SnH-Et₃B system.⁶⁾ 1-Iodonaphthalene reacted at room temperature, while 1-bromonaphthalene were inert. Aryl bromides were reduced at 80 °C, however, when more reactive Ph₃SnH was employed. The reaction was successively applied to the cyclization reaction. For instance, a mixture of five-membered ring and six-membered ring products was obtained upon treatment of aryl iodide **3** with *n*-Bu₃SnH-Et₃B (Scheme 3).

The Et₃B-induced reaction has following characteristics compared to ordinary reaction. (1) Tributyltin radical or triphenyltin radical can be generated at low

Table 2. Reduction of Alkenyl Halides with *n*-Bu₃SnH-Et₃B

$ \begin{array}{ccc} R^1 & & R^2 \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ R^3 & & X \end{array} \longrightarrow \begin{array}{ccc} R^1 & & R^2 \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ R^3 & & H \end{array} $				
Run	Substrate	Reaction conditions Temp/°C	Time/h	Yield of alkene/%
1	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad I \end{array} $	20	0.5	1-Dodecene 77
2	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad Br \end{array} $	20	12	1-Dodecene 98
3	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad D \end{array} $	-78, 2;	20, 0.5	$ \begin{array}{cc} \begin{array}{c} R \\ \\ C=H \\ \quad \\ H \quad D \end{array} & \begin{array}{c} R \\ \\ C=D \\ \quad \\ H \quad H \end{array} \\ 83 & (63:37) \end{array} $
4	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad I \end{array} $	-78, 2;	20, 0.5	$ \begin{array}{cc} \begin{array}{c} R \\ \\ C=H \\ \quad \\ H \quad D \end{array} & \begin{array}{c} R \\ \\ C=D \\ \quad \\ H \quad H \end{array} \\ 87 & (61:39) \end{array} $
5	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad Me \end{array} $	-78	0.5	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad Me \end{array} $ 84
6	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad SiEt_3 \end{array} $ 1	-78	0.5	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad SiEt_3 \end{array} $ 95 (<i>Z</i> / <i>E</i> =56/44)
7	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad SiEt_3 \end{array} $ 2	-78	0.5	$ \begin{array}{c} n-C_{10}H_{21} \\ \\ C=C \\ \quad \\ H \quad SiEt_3 \end{array} $ 98 (<i>Z</i> / <i>E</i> =57/43)
8	$ \begin{array}{c} n-C_8H_{17} \\ \\ C=C \\ \quad \\ H \quad Br \end{array} $	-78	0.5	$ \begin{array}{c} n-C_8H_{17} \\ \\ C=C \\ \quad \\ H \quad Br \end{array} $ 80 (<i>Z</i> / <i>E</i> =1:1)

for 30 min at -78°C . The disappearance of the starting material was confirmed by thin layer chromatographic assay. The resulting mixture was transferred into 100 ml round-bottomed flask using 25 ml of methanol. The solvent was evaporated as an azeotropic mixture to afford a crude oil which was submitted to silica-gel column chromatography (hexane as an eluant) to give dodecane (0.17 g) quantitatively. (b) **Procedure B:** The procedure was used for the reduction of the compounds which have polar functional groups such as hydroxyl or carbonyl in the molecule. The reduction of 11-bromo-1-undecanol to 1-undecanol is representative. A solution of tributyltin hydride (0.33 g, 1.0 mmol) in toluene (4.0 ml) was added to a solution of 11-bromo-1-undecanol (0.25 g, 1.0 mmol) in toluene (4.0 ml) at 0°C . Et_3B (1.0 M hexane solution, 0.1 ml, 0.1 mmol) was added and the resulting mixture was stirred at 0°C for 30 min. The reaction mixture was diluted with $EtOAc$ (20 ml) and saturated aqueous potassium fluoride (2 ml) and anhydrous potassium fluoride (1.0 g) were added to remove tributyltin bromide.¹⁶ The mixture was stirred for another 30 min and the precipitated tributyltin fluoride was removed by filtration and washed with ethyl acetate. Combined filtrates were washed with brine and dried over anhydrous sodium sulfate and concentrated in vacuo. The residual oil was purified by silica-gel column chromatography (hexane/ethyl acetate=5/1 as an eluant) to give 1-undecanol (0.16 g) in 94% yield.

General Procedure for the Reduction of Alkenyl Halides.

The reactions were performed following the procedure A described for the reduction of alkyl halides. A solution of tributyltin hydride (0.33 g, 1.1 mmol) in toluene (4.0 ml) and Et_3B (1.0 M hexane solution, 0.1 ml, 0.1 mmol) were added successively to a solution of 1,1-dibromo-1-decene (0.30 g, 1.0 mmol) in toluene (4.0 ml) at -78°C and the resulting mixture was stirred at -78°C for 30 min. Concentration followed by purification by silica-gel column chromatography gave 1-bromo-1-decene (0.18 g) in 80% yield as an isomeric mixture ($E/Z=1/1$).

Reduction of Aryl Halide 3 with $n-Bu_3SnH-Et_3B$. A solution of $n-Bu_3SnH$ (0.35 g, 1.2 mmol) in benzene (2.0 ml) was added dropwise over 2 h by syringe pump to a solution of aryl iodide 3 (0.24 g, 1.0 mmol) and Et_3B (1.0 M hexane solution, 0.1 ml, 0.1 mmol) in benzene (10 ml) at 20°C . The resulting mixture was stirred more than 1 h after the completion of the addition. Work-up followed by purification by preparative TLC on silica gel gave a mixture of 1,1-dimethylindan (18%), 2-methyl-1,2,3,4-tetrahydronaphthalene (33%), and (3-methyl-3-butenyl)benzene (6%), whose spectra were identical with those of authentic samples.^{17,18}

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