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BF_3-promoted hydrostannation of *N*-heteroatom-substituted imines for the reduction of C=N bond

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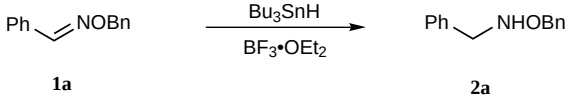
Abstract—Hydrostannation of *N*-heteroatom-substituted imines such as oxime ethers, hydrazones, oximes, nitrones, and *N*-sulfonyl imines using a combination of Bu_3SnH and $BF_3{\cdot}OEt_2$ has been systematically studied. Not only aromatic aldimines but also kitimines and aliphatic imines were reduced to give the corresponding amines.

Organotin hydrides are known as a mild reagent for the reduction of aldehydes and ketones by hydrostannation, and a variety of useful methods have been available.[1,2] In contrast, the corresponding hydrostannation of imine derivatives has not been widely studied. Baba's group have shown, in their series of papers, that the reduction of *N*-alkyl or *N*-aryl imines with organotin hydrides or dibutyltin halide hydrides was promoted by the addition of Lewis bases such as HMPA, Bu_4NX and so on. They have successfully extended the reaction to reductive amination of aldehydes and ketones, chemoselective reduction of imino group in the presence of carbonyl group, and tandem reductive amination-Michael reaction.[3] However, the hydrostannation of imines activated by Lewis acids has not been studied.[4] Herein we wish to report the BF_3-promoted hydrostannation of imines providing a new efficient method for the reduction of C=N bond.

The imines of choice were *N*-heteroatom-substituted imines such as oxime ethers, hydrazones, oximes, nitrones, and *N*-sulfonyl imines, since they have been shown to be stable and useful even for aqueous-medium reaction in our recent studies on radical reactions.[5] Additionally, the advantage of *N*-heteroatom-substituted imines is that the resulting *N*-heteroatom-substituted amines can be readily converted to primary amines by cleavage of the nitrogen-heteroatom bond.[6]



1a **2a**

Scheme 1.

We initially investigated the hydrostannation of benzaldoxime ether **1a** (Scheme 1). Among several Lewis acids evaluated, $BF_3{\cdot}OEt_2$ was found to be most effective for the hydrostannation of **1a** using Bu_3SnH.[7] To a solution of oxime ether **1a** in CH_2Cl_2 were added $BF_3{\cdot}OEt_2$ (1 equiv.) and a commercially available Bu_3SnH (2 equiv.), and then the reaction mixture was stirred at room temperature for 2 h. As expected, the reaction proceeded smoothly to give the desired alkoxyamine **2a** in 95% yield (Table 1, entry 1). When the reaction was carried out in the presence of 0.5 equiv. of $BF_3{\cdot}OEt_2$, alkoxyamine **2a** was obtained in 27% yield and 69% yield of starting material **1a** was recovered (entry 2). In the absence of $BF_3{\cdot}OEt_2$, the reaction did not proceed (entries 3 and 4); thus, 1 equiv. of $BF_3{\cdot}OEt_2$ is necessary for completing hydrostannation of **1a**, because $BF_3{\cdot}OEt_2$ is trapped by the nitrogen atom of both the starting material and the product. When the freshly-distilled Bu_3SnH was employed, the reaction proceeded smoothly even with 1 equiv. of Bu_3SnH to give **2a** in 95% yield (entry 5).[8]

We next examined the hydrostannation of hydrazone, oxime, nitrone, and sulfonyl imine **1b–e** in the presence of $BF_3{\cdot}OEt_2$ (Scheme 2, Table 2).

In the presence of 1 equiv. of $BF_3{\cdot}OEt_2$, the hydrostannation of hydrazone **1b** having two nitrogen atoms was less effective to give the corresponding hydrazine **2b** in 65% yield (entry 1). In the case of hydrazone **1b**, 2 equiv. of $BF_3{\cdot}OEt_2$ were required for completing the

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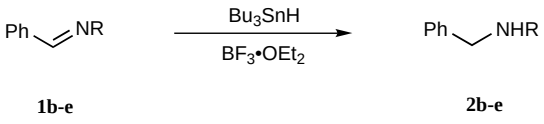
Table 1. Hydrostannation of oxime ether **1a**

Entry	Solvent	Bu_3SnH (equiv.)	$BF_3{\cdot}OEt_2$ (equiv.)	Temp. (°C)	Yield (%)[a]
1	CH_2Cl_2	2	1	20	95
2	CH_2Cl_2	2	0.5	20	27 (69)
3	CH_2Cl_2	2	0	20	No reaction
4	MeOH	1	0	Reflux	No reaction
5	CH_2Cl_2	1[b]	1	20	95

[a] Yields in parentheses were for the starting material.
[b] The reaction was carried out with freshly-distilled Bu_3SnH.

hydrostannation (entries 2 and 3). Only a modest chemical yield was observed in the reaction of oxime **1c**, presumably due to the formation of unidentified complex formed from oxime **1c** and Bu_3SnH in the presence of $BF_3{\cdot}OEt_2$ (entry 4). The reaction of nitrone **1d** proceeded smoothly to give the corresponding amine **2d** in 84% yield (entry 5). In contrast, *N*-sulfonyl imine **1e** exhibited an excellent reactivity toward Bu_3SnH even in the absence of $BF_3{\cdot}OEt_2$, because of the higher reactivity of C=N bond by electron-withdrawing substituent on nitrogen atom (entry 6).



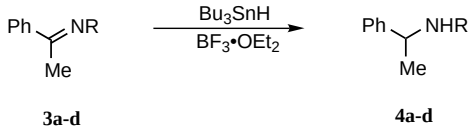
1b-e **2b-e**

Scheme 2.

Table 2. Hydrostannation of *N*-heteroatom-substituted imines **1b–e**[a]

Entry	Substrate	$BF_3{\cdot}OEt_2$ (equiv.)	Product	Yield (%)
1	**1b**: NR = $NNPh_2$	1	**2b**	65
2	**1b**: NR = $NNPh_2$	2	**2b**	76
3[b]	**1b**: NR = $NNPh_2$	2	**2b**	92
4	**1c**: NR = NOH	1	**2c**	48
5	**1d**: NR = $N^+(O^-)Bn$	1	**2d**[c]	84
6	**1e**: NR = NTs	0	**2e**	98

[a] The reactions were carried out with Bu_3SnH (2 equiv.) in CH_2Cl_2 at 20°C for 2 h.
[b] The reaction was carried out with freshly-distilled Bu_3SnH (1 equiv.) in CH_2Cl_2 at 20°C for 2 h.
[c] Product **2d** is $PhCH_2NH(OH)CH_2Ph$.



3a-d **4a-d**

Scheme 3.

Ketimine derivatives **3a–d** worked well under similar reaction conditions using $BF_3{\cdot}OEt_2$ (Scheme 3, Table 3). In the case of ketoxime ether **3a** and hydrazone **3b**, more than 2 equiv. of $BF_3{\cdot}OEt_2$ were required for completing the reactions (entries 1 and 2).[9] The reaction of *N*-sulfonyl ketimine **3d** proceeded smoothly even in the absence of $BF_3{\cdot}OEt_2$ to give the corresponding amine **4d** in 99% yield (entry 4).

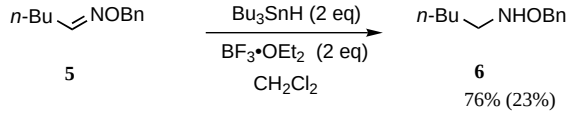
We finally investigated hydrostannation of aliphatic imine derivatives **5** and **7** (Scheme 4). The reactions of pentanal oxime ether **5** proceeded slowly to give alkoxyamine **6** in 76% yield,[10] accompanied with 23% yield of the starting compound **5**. Modest chemical yield was obtained in the reaction of aliphatic ketoxime ether **7**.

In conclusion, we have developed a new method for reduction of *N*-heteroatom-substituted imine derivatives via hydrostannation using Bu_3SnH and $BF_3{\cdot}OEt_2$. The reaction could apply to not only aromatic aldimine derivatives but also aromatic ketimines, providing a

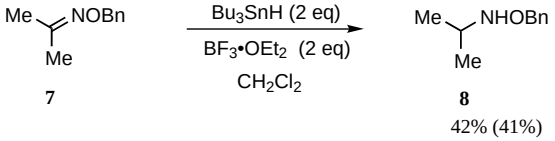
Table 3. Hydrostannation of *N*-heteroatom-substituted imines **3a–d**[a]

Entry	Substrate	$BF_3{\cdot}OEt_2$ (equiv.)	Product	Yield (%)
1	**3a**: R = NOBn	3	**4a**	97
2	**3b**: R = $NNPh_2$	2	**4b**	99
3	**3c**: R = NOH	1	**4c**	70
4	**3d**: R = NTs	0	**4d**	99

[a] The reactions were carried out with Bu_3SnH (2 equiv.) in CH_2Cl_2 at 20°C for 2 h.



5 **6**
76% (23%)



7 **8**
42% (41%)

Scheme 4.

useful route for synthesis of a variety of primary amines from the corresponding carbonyl compounds.

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7. In the presence of other Lewis acids ($InCl_3$, $MgBr_2$ or $Yb(OTf)_3$), the hydrostannation of **1a** did not proceed under the similar reaction conditions.
8. Procedure for hydrostannation of **1a** (Table 1, entry 5): To a solution of oxime ether **1a** (50 mg, 0.24 mmol) in CH_2Cl_2 (5 mL) were added $BF_3{\cdot}OEt_2$ (0.03 mL, 0.24 mmol) and Bu_3SnH (0.06 mL, 0.24 mmol). After being stirred under a nitrogen atmosphere at 20°C for 2 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt = 15:1) afforded **2a** (48.5 mg, 95%) as a colorless oil.
9. Spectral data of **4b**: ^{1}H NMR ($CDCl_3$): δ 1.39 (3H, d, J = 6.0 Hz), 4.04 (1H, q, J = 6.0 Hz), 4.16 (1H, br s), 6.92–7.42 (10H, m). ^{13}C NMR ($CDCl_3$): δ 21.0, 56.8, 120.3, 122.1, 127.2, 127.3, 128.3, 128.9, 143.3, 147.7. HRMS: calcd for $C_{20}H_{20}N_2$ (M^+) 288.1626, found 288.1637.
10. Spectral data of **6**: ^{1}H NMR ($CDCl_3$): δ 0.89 (3H, br t, J = 6.0 Hz), 1.20–1.60 (6H, m), 2.93 (2H, t, J = 7.0 Hz), 4.71 (2H, s), 7.28–7.40 (5H, m). ^{13}C NMR ($CDCl_3$): δ 13.9, 22.4, 26.9, 29.2, 52.1, 76.1, 127.6, 128.2, 137.9. HRMS: calcd for $C_{12}H_{19}NO$ (M^+) 193.1466, found 193.1481.