Control of the free radical reaction by dynamic coordination: unique reactivity of pyridylethyl-substituted tin hydrides

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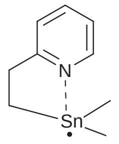
Tin hydrides having one or two pyridyl groups show unique reactivity in the reduction of alkyl halides under radical conditions, indicating the potential of intramolecular coordination for the control of radical reactions.

The importance of polar effects in radical reactions has attracted significant interest for many years,[1] and solvent effects[2] and anchimeric assistance[3] have been reported for various reactions involving free radicals. We report here unique reactivity of tin hydrides having pyridyl groups, suggesting the potential of intramolecular coordination for the control of radical reactions. This opens a new aspect of free radical chemistry. We also report the remarkable intermolecular effect of pyridyl groups in tin hydride reduction.

In recent work we have found the stabilization of cation radical intermediates by dynamic coordination to tin, which in turn favors the electron transfer from tetraalkylstannanes.[4] In connection with our interest in controlling chemical reactions by dynamic intramolecular coordination,[5,6] we envisioned that similar coordination might also be effective for the tin radical **1**. Thus, we synthesized tin hydrides having one or two pyridyl groups for coordination such as **2** and **3** and examined their reaction with organic halides under radical conditions (Scheme 1).[7]



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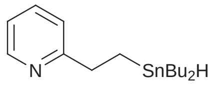

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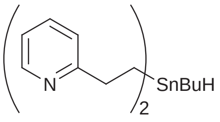

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Tin hydrides **2** and **3** were synthesized by the $LiAlH_4$ reduction of the corresponding tin halides.[4,8] The fact that the chemical shift from the ^{119}Sn NMR spectrum (in C_6D_6) of **2** (δ −88.270) is similar to that of Bu_3SnH (δ −87.210) indicated the absence of coordination of the pyridyl group to tin. This sharply contrasts to the ^{119}Sn NMR spectrum of the corresponding tin halide, which indicates the presence of a definite coordination of the pyridyl group to tin.[4]

The reduction of organic halides with **2**, however, exhibited unique features in contrast to that with Bu_3SnH (Table 1). Although primary alkyl bromides were reduced smoothly with **2**, the corresponding chlorides were unchanged under the same conditions.[9] *sec*-Alkyl chlorides and aromatic chlorides were also completely inactive towards **2** under these conditions. In the case of Bu_3SnH, however, such organic chlorides were reduced, albeit slowly. The unique reactivity of **2** seems to be ascribed to the lower reactivity of tin radical **1** towards organic halides (Scheme 2).

The reduction of alkyl bromides with **2** was completely retarded by the addition of a catalytic amount of hydroquinone (0.1 equiv.), indicating that the reaction proceeded by a radical chain mechanism. The facile 5-*exo* cyclization[10] shown in Scheme 3 also supported a radical mechanism. The ratio of 5-*exo*/6-*endo* was similar to that observed for Bu_3SnH. The high yields of the cyclized products also demonstrates the utility of **2** for radical carbon–carbon bond formation.[11]

In order to get deeper insight into the unique reactivity of **2**, we examined the effect of the pyridyl group on the stability of the tin radical with molecular orbital calculations.[12] The geometry optimization of a model compound, $2\text{-}PyCH_2CH_2SnMe_2$ radical, gave three structures (Fig. 1). The coordinated structures **A** and **B** are more stable than non-coordinated structure **C**, indicating that the coordination does

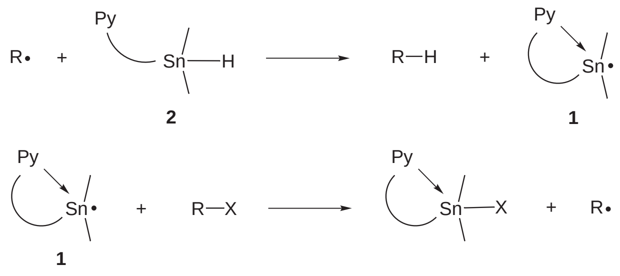
$$R{-}X \xrightarrow[\text{AIBN}]{R'_3SnH} R{-}H$$

Scheme 1

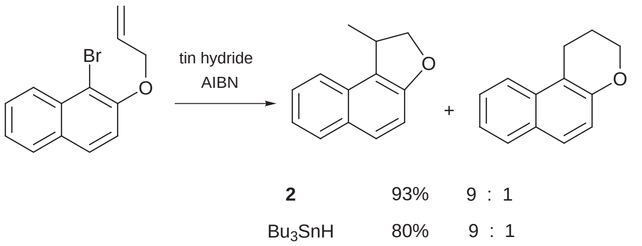
Table 1 Reduction of organic halides with tin hydrides under radical conditions[a]

	Yield of RH (%)[b]		
Organic halide	Bu_3SnH	**2**	**3**
$C_{12}H_{25}Cl$	75	0	0
$C_{12}H_{25}Br$	97	97	39
$C_{12}H_{25}I$	96	98	97
$Ph(CH_2)_3Cl$	52	0	0
$Ph(CH_2)_3Br$	100	99	56
$Ph(CH_2)_3I$	100	99	94
1-Naphthyl-Cl	12	0	0
1-Naphthyl-Br	93	90	20
1-Naphthyl-I	97	97	96
$C_8H_{17}CClHCH_3$	75	0	0

[a] Reactions were normally carried out with 0.10 mmol of organic halide, 0.12 mmol of tin hydride, and 0.01 mmol of AIBN in 0.4 ml of benzene at 60 °C for 2 h under an atmosphere of argon. [b] Determined with GC using an internal standard.



Scheme 2



Scheme 3

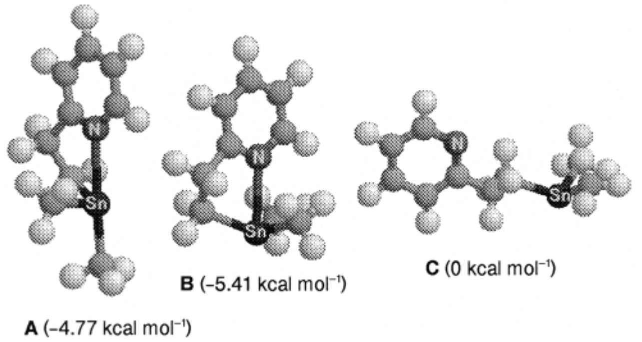


Fig. 1 Optimized structures of the 2-$PyCH_2CH_2SnMe_2$ radicals and their relative energies obtained by molecular orbital calculations (MP2/LANL2DZ).

take place at the radical. Such stabilization might decrease the reactivity of tin radicals towards organic halides,[13] although a detailed discussion should be reserved until kinetic data are available.

The reactivity of the tin hydride having two pyridyl groups, compound **3**, was also studied (Table 1). Although organic iodides were reduced smoothly with **3**, the reactions of organic bromides were much slower. Organic chlorides were almost inactive towards **3**. These data naturally imply that the second pyridyl group further decreases the reactivity of the tin radical.

It is notable that the introduction of the second pyridyl group gives us a bonus, *i.e.* easy separation and recovery of the tin halide after the reaction.[14] The tin halide derived from **3** can be completely separated by acid extraction and recovered by a follow-up base extraction, although the tin halide derived from **2** cannot be separated in a similar fashion. The easy protonation of the second pyridyl group seems to be responsible for this phenomena because the first pyridyl group should be used for coordination to the tin halide (*vide supra*).

In order to examine the effect of intermolecular coordination on the reactivity of the tin radical, we carried out the radical reduction of organic halides with Bu_3SnH in the presence of an additive such as pyridine and 2,2’-bipyridyl (Fig. 2). For the reduction of the alkyl bromide, the reaction took place smoothly even in the presence of such additives. The reduction of the alkyl chloride, however, was retarded significantly with an increase in the amount of additive. It is especially remarkable that the reaction was almost completely suppressed in the presence of 0.25 equiv. of bipyridyl. These results clearly indicate that the reactivity of tin radicals can be controlled even by intermolecular coordination.

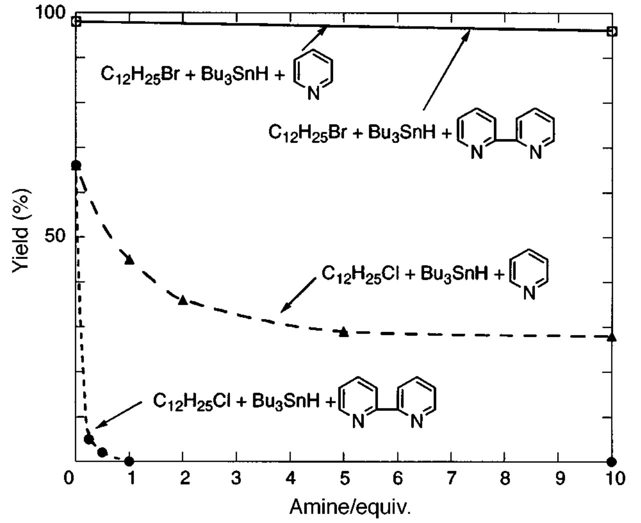


Fig. 2 Effect of pyridine and 2,2′-bipyridyl as additives on the reduction of alkyl halides by Bu_3SnH.

In summary, the results described above demonstrate the potential of dynamic coordination for the control of radical reactions. Future studies will hopefully delineate the detailed mechanistic role of the coordination.

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