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Generation of a Cation Radical from 2-Pivaloyl-1-tributylstannyl-1,2,3,4-tetrahydroisoquinoline and the Reaction with Carbon Nucleophiles

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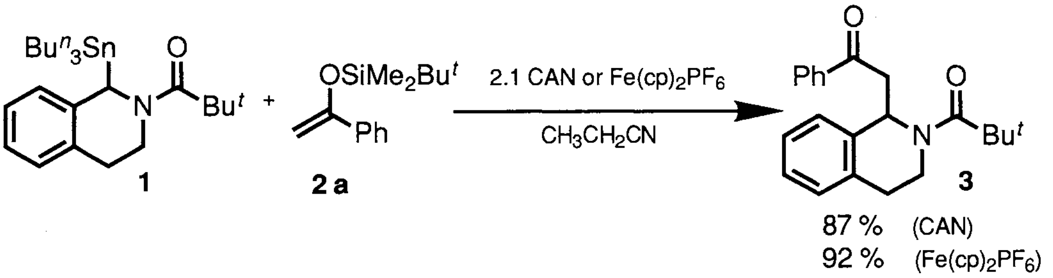
Oxidation of 2-pivaloyl-1-tributylstannyl-1,2,3,4-tetrahydroisoquinoline with metallic oxidants generates a reactive species such as the hydroisoquinolin-1-yl cation by eliminating the stannyl group. This intermediate reacts with various carbon nucleophiles to give the corresponding addition products.

For the purpose to utilize various cation radicals for carbon-carbon bond forming reactions, we recently reported a method for the transformation of cation radicals of sulfides into the carbon (C)-radicals and/or C-cations.[1)] That is, the cation radicals of α-stannyl sulfides are converted into the C-radicals and/or cations of the sulfides by the elimination of the stannyl group.

Application of this method was further examined to generate reactive carbon intermediates from cation radicals of nitrogen compounds, and our attention has been focussed on the generation of C-cation of 1,2,3,4-tetrahydroisoquinoline derivative, because isoquinoline derivatives occupy an important class of intermediates for the synthesis of various natural products and medicines.[2)]

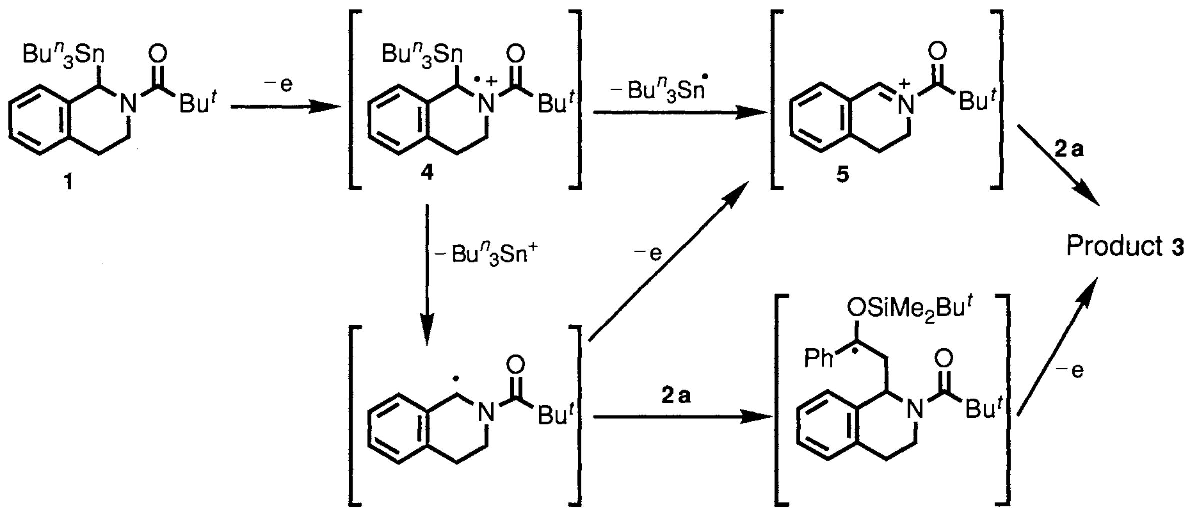
2-Pivaloyl-1-tributylstannyl-1,2,3,4-tetrahydroisoquinoline (**1**) was chosen as a cation radical source and was prepared by the stannylation of the anion generated according to the Seebach's method.[3)] Reaction of **1** with α-(t-butyldimethylsiloxy)styrene (**2a**) was examined in the presence of 2.1 mole equivalents of various metallic oxidants such as Mn^{III}, Ag^{II}, Fe^{III}, Ce^{IV} compounds. Among these oxidants examined, the use of ammonium cerium(IV) nitrate (CAN), ferricenium hexafluorophosphate ($Fe(cp)_2PF_6$)[4)] gave the addition product **3** in high yield (Eq. 1). Thus the treatment of a mixture of **1** and 2 mole equivalents of **2a** in propionitrile with CAN at -23 °C or with $Fe(cp)_2PF_6$ at 0 °C gave the corresponding addition product **3** in 87% yield or 92% yield, respectively.



(1)

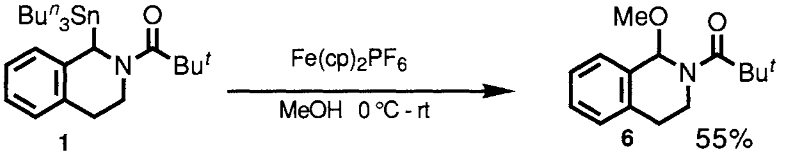
It was not obvious in the above reaction whether the stannyl group eliminates as the stannyl radical or as the stannyl cation, because both of the intermediates are able to react with the silyl enol ether **2a** as shown in the

Scheme 1. However, by considering the stability of both of the stannyl radical and the acyliminium ion, it was supposed that the cation radical **4** would cleave to give the acyliminium cation **5**, which reacts with the silyl enol ether **2a**.



Scheme 1.

In fact, when **1** was treated with only $Fe(cp)_2PF_6$ in methanol, the 1-methoxy-tetrahydroisoquinoline derivative **6** was obtained in moderate yield (Eq. 2). This result apparently confirms that the acyliminium cation **5** is the actual intermediate to react with the silyl enol ether **2a**.

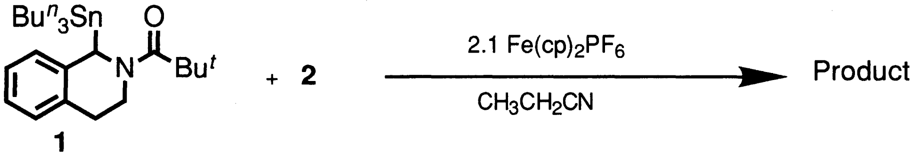
 (2)

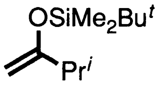
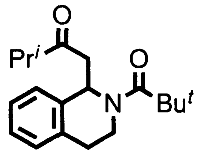
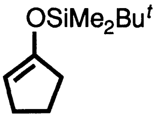
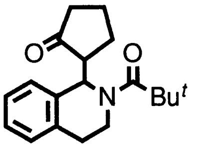
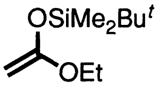
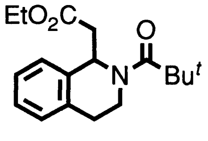
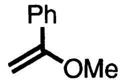
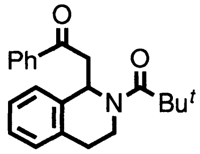
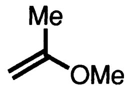
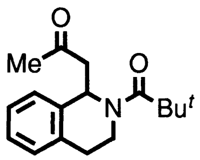
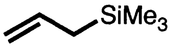
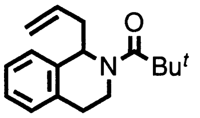
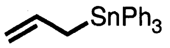
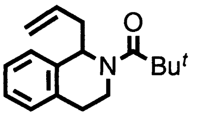
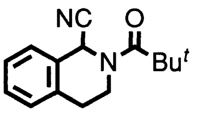
Since the reaction was found to proceed via the acyliminium cation **5**, the reaction of the stannylisoquinoline **1** and various carbon nucleophiles **2** was tried in the presence of $Fe(cp)_2PF_6$. As shown in Table, **1** reacted with various electron rich olefinic compounds such as aromatic and alkyl silyl enol ethers **2a-c**, a ketene silyl acetal **2d** and vinyl ethers **2e** and **2f** to give the addition products in good yields. Moreover, the adducts were obtained by the reaction with nucleophiles such as allyltrimethylsilane **2g** and allyltriphenylstannane **2h** and cyanotrimethylsilane **2i**, in moderate yields.

The typical experimental procedure is as follows: To a propionitrile (15 ml) solution of $Fe(cp)_2PF_6$ (0.70 g, 2.1 mmol) was added a propionitrile (5.0 ml) solution of **1** (0.51 g, 1.0 mmol) and **2a** (0.47 g, 2.0 mmol) at 0 °C under an argon atmosphere. After stirring for 1 h, aq. Na_2CO_3 was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and purified by column chromatography (ethyl acetate:hexane=1:3, v/v) to give the addition product **3** (0.31 g, 92%).

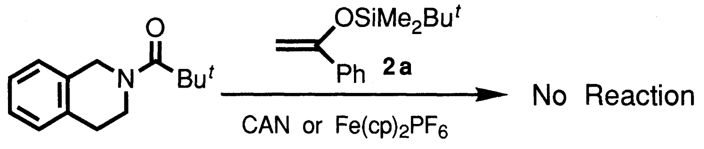
Although the stannyl isoquinoline **1** was readily oxidized with CAN and $Fe(cp)_2PF_6$, N-pivaloyltetrahydroisoquinoline (**7**) having no stannyl group was not oxidized under the same reaction conditions, indicating that the introduction of the stannyl group lowers the oxidation potential of N-pivaloylisoquinoline **7**

Table 1. The Reactions of **1** with Carbon Nucleophiles **2**



Nucleophile	Temp/°C	Product	Yield/%
 **2b**	-23		72
 **2c**	-23		74
 **2d**	0		73
 **2e**	-23		90
 **2f**	-23		76
 **2g**	rt		61
 **2h**	rt		62
Me_3SiCN **2i**	rt		53

(Eq. 3).5) The same effect of a stannyl or a silyl group on lowering the oxidation potential of ethers and sulfides was also reported.6) When 1- tributylstannyl-1,2,3,4-tetrahydroisoquinoline (**8**) having no amido group was treated with the silyl enol ether **2a** and CAN under the same reaction conditions, no addition product was formed but 3,4-dihydroisoquinoline (**9**) was obtained in 98% yield (Eq. 4).



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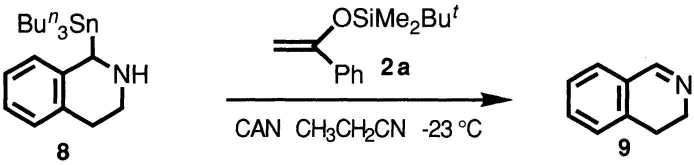
(3)



8 **9** 98% (4)

As mentioned above, this method enables the transformation of the cation radical of the amide into the acyliminium cation, which is utilized for direct carbon-carbon bond formation.7,8) It makes a contrast to the electrooxidation of amines where an alkoxyl or a hydroxyl group is introduced on the α-carbon of nitrogen atom.9)

References

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2) T. Kametani and M. Ihara, *Heterocycles*, **13**, 497 (1979); G. Grethe, "Isoquinolines, part one; The Chemistry of Heterocyclic Compounds," Wiley, New York (1981), Vol. 38; K. Nakanishi, T. Goto, S. Ito, S. Natori, and S. Nozoe, "Natural Products Chemistry," Kodansha, Tokyo (1975), Vol. 2.

3) D. Seebach, J.-J. Lohmann, M. A. Syfrig, and M. Yoshifuji, *Tetrahedron,* **39**, 1963 (1983).

4) Ferricenium hexafluorophosphate was according to the literature procedure: D. N. Hendrickson, Y. S. Sohn, and H. B. Gray, *Inorg. Chem.*, **10**, 1559 (1971).

5) By the cyclic voltammogram measurements, **1** exhibits an oxidation peak at about 1.2 V (Ag/Ag^+ *vs* . SCE, CH_3CN, irreversible), while **6** shows an oxidation peak at about 2.7 V.

6) R. S. Glass, A. M. Radspinner, and W. P. Singh, *J. Am. Chem. Soc.*, **114**, 4921 (1992); J. Yoshida, Y. Ishichi, K. Nishiwaki, S. Shiozawa, and S. Isoe, *Tetrahedron Lett.*, **33**, 2599 (1992).

7) The intramolecular carbon-carbon bond formation is achieved very recently by using α-stannyl ethers in electrooxidation reaction: J. Yoshida, Y. Ishichi, and S. Isoe, *J. Am. Chem. Soc.*, **114**, 7594 (1992). An α-stannyl carbamate is also employed for carbon-carbon bond formation in electrooxidation: Private communication; J. Yoshida, Y. Ishichi, and S. Isoe.

8) Further application of the present method is now in progress. A non-benzylic substrate, 4-tributylstannyl-2-azetidinone derivative, was found to react with the silyl enol ether **2a** to give the addition product.

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