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## Aminium Salt Promoted Catalytic Substitution Reactions of Acetals with Silylated Nucleophiles

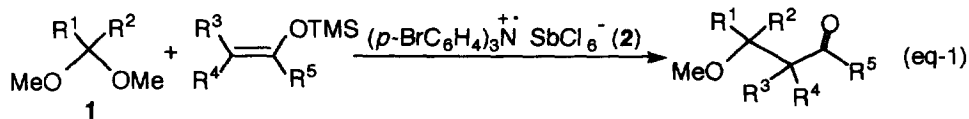
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**Abstract:** A catalytic amount of tris(*p*-bromophenyl)aminium hexachloroantimonate promoted the substitution reactions of dimethylacetals with various silylated nucleophiles through an electron transfer mechanism. Silyl compounds include silyl enol ether, ketene silyl acetal, and allylsilane. One methoxy group of the substrates was effectively substituted by nucleophiles to form carbon-carbon bonds.

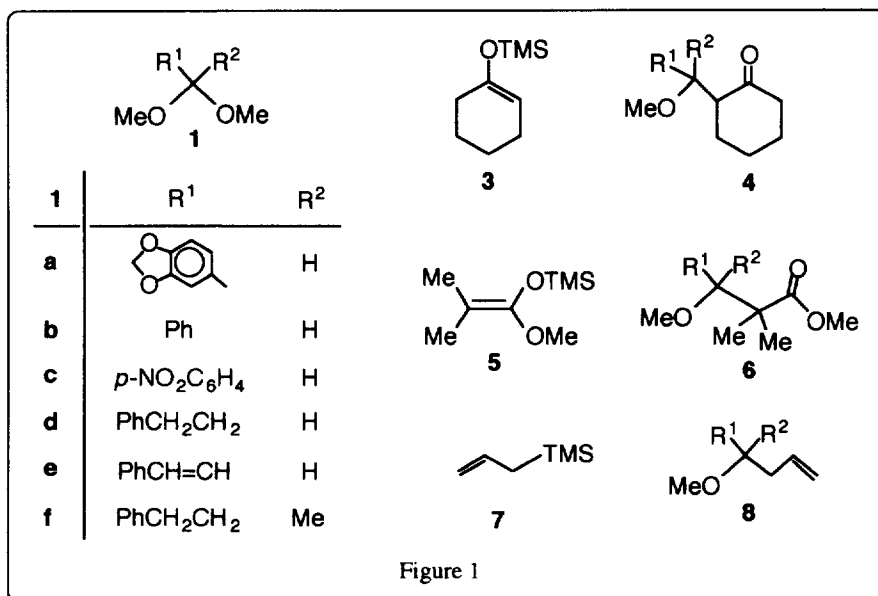
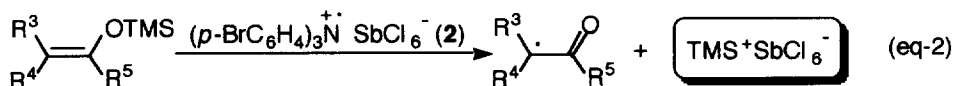
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Cationic transformations of acetals include synthetically important deprotection and nucleophilic substitution reactions.<sup>1</sup> We have recently demonstrated how electron transfer processes are useful for the transformations of the related sulfur compounds.<sup>2</sup> Although aminium salts are considered to be feasible reagents for electron transfer reactions, the scope of their synthetic applications is still limited.<sup>3</sup> This may be due to the anticipation that typical aminium salt, tris(*p*-bromophenyl)aminium salt, would not be effective for the oxidation of weak electron donors because of the low oxidation potential of tris(*p*-bromophenyl)amine ( $E_0^{ox} = 1.05$  V vs SCE).<sup>4</sup> Therefore, it must be an interesting challenge to determine the applicability of this aminium salt to the oxidative transformations of acetals since their oxidation potentials are relatively high (2.00–3.00 V).<sup>5</sup> For this task, we chose the reaction systems of acetals **1** and silyl enol ethers to achieve carbon-carbon bond formations (eq-1). Our basic idea shown in eq-2 and eq-3 is unique, however, plausible.



Namely, oxidation of silyl enol ethers with aminium salt first occurs to generate trimethylsilyl hexachloroantimonate (TMSSbCl<sub>6</sub>) since the oxidation potentials of such silyl compounds are relatively low (eq-2).<sup>3g, 6</sup> Then, the TMSSbCl<sub>6</sub> attacks acetals to produce oxonium species which subsequently react with silyl enol ethers (eq-3).<sup>7</sup> Overall reaction pathways finally give  $\beta$ -methoxy carbonyl compounds (eq-1). We also planned to conduct the reactions of **1** with other silyl compounds. Acetals and silyl compounds used for the reactions are shown together with the products in Figure 1. All the results are summarized in Table 1.<sup>8</sup>

We first conducted the reaction of piperonal dimethyl acetal **1a** with 1-(trimethylsilyloxy)cyclohexene **3**. When tris(*p*-bromophenyl)aminium hexachloroantimonate **2** (0.01 mmol) was added to a dry acetonitrile solution containing **1a** (1.00 mmol) and **3** (1.05 mmol) at 0 °C, characteristic deep blue color of **2** immediately disappeared. After TLC separation of the crude reaction mixture,  $\beta$ -methoxy ketone **4a** was isolated in 95%



yield as the diastereomeric mixture (70/30) (entry 1). Methylene chloride was also found to be a suitable solvent for the reaction. Similarly, the reactions of **1b-1f** with **3** gave products **4b-4f** in good yields (entry 2-6). For the reaction of **1a** with 1,1-dimethylketene methyltrimethylsilylacetal **5** under the **2** promoted conditions, nearly quantitative formation of  $\beta$ -methoxy ester **6a** was observed (entry 7). Compounds **6b-6f** were also obtained in good yields for the reactions of **1b-1f** with **5** (entry 8-12). These results encouraged us to perform the reactions of **1** with relatively weak electron donor, such as allyltrimethylsilane **7**. Unlike the reactions with **3** or **5**, the color of **2** lasted for a while during the reaction. However, the reaction of **1a** and **7** with a catalytic amount of **2** gave 95% of **8a** (entry 13). Other acetals **1b-1f** also reacted with **7** to give the corresponding products **8b-8f** in good to excellent yields (entry 14-18).

Although an electron transfer from the silyl compounds **3**, **5**, or **7** to **2** are considered to be thermodynamically unfavorable,<sup>9</sup> following reactions of the formed cation radicals of the silyl compounds must be efficient.<sup>3</sup> If an electron transfer from the silyl compounds to **2** first occurs, the efficient fragmentation of

Table 1. Aminium Salt Promoted Reactions of Acetals with Silyl Compounds.

entry	<b>1</b> <sup>a</sup>	TMSNu	<b>2</b> /mol%	reaction time/min.	product	yield/% <sup>b</sup>
1	<b>1a</b>	<b>3</b>	1	10	<b>4a</b>	95 <sup>c</sup>
2	<b>1b</b>	<b>3</b>	2	10	<b>4b</b>	75 <sup>c</sup>
3	<b>1c</b>	<b>3</b>	3	60	<b>4c</b>	98 <sup>c</sup>
4	<b>1d</b>	<b>3</b>	3	120	<b>4d</b>	93 <sup>c</sup>
5	<b>1e</b>	<b>3</b>	1	10	<b>4e</b>	86 <sup>c</sup>
6	<b>1f</b>	<b>3</b>	3	30	<b>4f</b>	72 <sup>c</sup>
7	<b>1a</b>	<b>5</b>	3	10	<b>6a</b>	100
8	<b>1b</b>	<b>5</b>	3	20	<b>6b</b>	90
9	<b>1c</b>	<b>5</b>	10	300	<b>6c</b>	86
10	<b>1d</b>	<b>5</b>	10	240	<b>6d</b>	92
11	<b>1e</b>	<b>5</b>	3	20	<b>6e</b>	77
12	<b>1f</b>	<b>5</b>	5	120	<b>6f</b>	78
13	<b>1a</b>	<b>7</b>	1	10	<b>8a</b>	95
14	<b>1b</b>	<b>7</b>	1	30	<b>8b</b>	87
15	<b>1c</b>	<b>7</b>	2	180	<b>8c</b>	92
16	<b>1d</b>	<b>7</b>	5	60	<b>8d</b>	94
17	<b>1e</b>	<b>7</b>	2	180	<b>8e</b>	85
18	<b>1f</b>	<b>7</b>	5	60	<b>8f</b>	83

<sup>a</sup> **1** (1.00 mmol); MeCN (10 mL); silyl compounds (1.05-1.10 mmol). <sup>b</sup> Isolated yields.

<sup>c</sup> Compounds **4** were obtained as diastereomeric mixtures: **4a** (70/30), **4b** (81/19), **4c** (50/50), **4d** (55/45), **4e** (80/20), **4f** (54/46). The assignment of relative configuration was not determined.

the cation radicals would produce  $\text{TMSSbCl}_6$ .<sup>3g, 10</sup> We suspected that  $\text{TMSSbCl}_6$  probably promoted the reactions and still remained in the solutions at the completion of the reactions. To substantiate this, we conducted the following experiments. To the decolorized solution obtained by the treatment of **2** (0.03 mmol) with **5** (1.10 mmol) in a dry acetonitrile solution for 10 sec (the time required for decolorization was about 1 sec), **1a** (1.00 mmol) was added and stirred for 10 min. Then, 63% of **6a** was isolated at 71% conversion of **1a**. Interestingly, only 7% conversion of **1a** and no isolation of **6a** was observed when **1a** was added to the decolorized solution after 1 min. These results suggest that  $\text{TMSSbCl}_6$  must be formed, however, no longer active enough to promote the reaction smoothly after the complete consumption of **2**. Further, to compare the catalytic ability of **2** with that of trimethylsilyl triflate (TMSOTf), we conducted the reaction of **1a** and **3** with TMSOTf (1 mol%) under the similar reaction conditions to that with **2**. The substituted product **4a** was obtained in 95% yield as the diastereomeric mixture (71/29). This result implies that **2** has almost comparable activity to that of TMSOTf.

In conclusion, we have first found that a catalytic amount of aminium salt **2** promoted the reactions of acetals with various silyl compounds. In these reactions, **2** is considered to act as single-electron oxidant to generate silyl cationic species.<sup>11</sup> Thus, aminium salts should be recognized as more widely applicable reagents

to the synthetically useful oxidative transformations since they can be easily prepared, handled, used under mild conditions, and recyclable. We will conduct the further studies to elucidate the more detailed mechanism for the reactions and to apply this methodology to the other synthetically useful reactions.

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- All products were isolated by silica gel TLC and characterized by their spectroscopic data.
- The oxidation peak potentials ( $E_p^{ox}$  vs. SCE) of the acetals **1** and the silyl compounds were measured by cyclic voltammetry at  $v = 100$  mV/sec in MeCN containing 0.1M  $Et_4NClO_4$ : **1a** (1.84 V), **1b** (> 3.00 V), **1c** (> 3.00 V), **1d** (2.45 V), **1e** (2.25 V), **1f** (2.75 V), **3** (1.15 V), **5** (1.05 V), **7** (2.24V).
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