

## Boron trifluoride-catalyzed reaction of alkyl fluoride with silyl enolate, allylsilane, and hydrosilane

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**Abstract**—Alkylation of silyl enolates with *tert*-alkyl or allylic fluorides proceeds smoothly in the presence of a catalytic amount of boron trifluoride to afford the corresponding carbonyl compounds. Allylation and reduction of alkyl fluorides with allylsilane and hydrosilane, respectively, occur under  $\text{BF}_3$  catalysis.

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Alkyl fluoride is rarely the choice of alkylation agents because of the poor ability of fluoride as a leaving group. Alkylation of enolate mostly utilizes alkyl chloride, bromide, and iodide.<sup>1,2</sup> Alkylation of ketene silyl acetal with alkyl fluoride was accomplished by using trimethylaluminum.<sup>3</sup> However, the considerable reactivity of alkylaluminum reagent may undermine functional group compatibility. Moreover, air-sensitive alkylaluminum is bothersome to handle. Other fluorophilic Lewis acids can be alternatives to trimethylaluminum. Here we report alkylation reaction of silyl enolate with alkyl fluoride in the presence of a catalytic amount of boron trifluoride.

Treatment of 3-fluoro-3-methyl-1-phenylbutane<sup>4</sup> (**1a**, 1.0 mmol) with silyl enolate **2a** (3.0 mmol) in the presence of 2 mol% of  $\text{BF}_3 \cdot \text{OEt}_2$  in dichloromethane (3 mL) at  $-20^\circ\text{C}$  for 15 h afforded ketone **3a** in 89% yield (Table 1, entry 1). Other enolates underwent alkylation reaction with **1a**. The enolate of propiophenone **2b** was alkylated to afford  $\alpha,\beta,\beta$ -trimethyl ketone **3b** in 65% yield (entry 2). The presence of the aromatic rings of **2a** and **2b** was not essential. Alkylation of 2-siloxyprene **2c** and 1-siloxycyclohexene **2d** gave the corresponding ketones in good yields (entries 3 and 4). Reaction of trimethylsilyl enolate of acetaldehyde **2e** resulted in recovery of **1a**

(entry 5). Reaction of **2f** failed, even at elevated temperature, probably due to the steric hindrance (entry 6). On the other hand, ketene silyl acetal **2g** reacted with **1a** smoothly to furnish ester **3g** in spite of two methyl groups (entry 7). Whereas tertiary alkyl fluoride **1b** also participated in the reaction (entry 8), reaction of secondary alkyl fluorides resulted in formation of alkenes. For instance, 3-fluoro-1-phenylbutane was consumed under the same reaction conditions to afford 2- or 3-butenylbenzene with contamination by trace of the desired product. Primary alkyl fluorides resisted the reaction and were completely recovered after workup.

Boron trifluoride was more effective than trimethylaluminum<sup>3</sup> as a catalyst. Treatment of a mixture of **1a** and **2a** with 10 mol% of trimethylaluminum at  $-20^\circ\text{C}$  for 15 h afforded **3a** in 46% yield, along with unchanged **1a** (52%). Fluoride **1c** having a ketone moiety was subjected to the  $\text{BF}_3$ -catalyzed reaction to furnish the desired diketone **3i** in 54% yield (entry 9). On the other hand,  $\text{Me}_3\text{Al}$ -catalyzed reaction (10 mol%,  $-20^\circ\text{C}$ , 15 h) gave no **3i** and **1c** remained unchanged. Ether and ester functionalities were compatible under the reaction conditions (entries 10 and 11).

Besides tertiary alkyl fluoride, allylic fluoride<sup>5</sup> underwent the reaction to afford  $\gamma,\delta$ -unsaturated ketone (Table 2). Unfortunately, the reaction always yielded a mixture of regioisomers **5** and **6**. Moreover, **6b** and **6c** were obtained as 1:1 mixtures of *syn* and *anti* isomers. In contrast to the reaction of **2f** with **1a**,  $\alpha,\alpha$ -dimethyl ketones **5d** and **6d** were obtained (entry 4).

**Keywords:** Alkyl fluoride; Alkylation; Silyl enolate; Boron trifluoride; Silane.

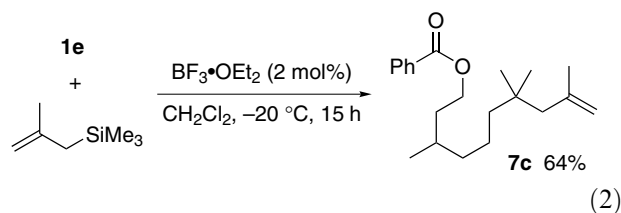
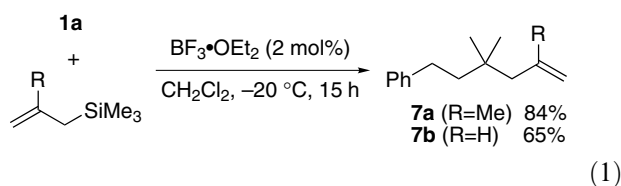
\* Corresponding author. Tel.: +81-75-383-2437; fax: +81-75-383-2438; e-mail: [oshima@fm1.kuic.kyoto-u.ac.jp](mailto:oshima@fm1.kuic.kyoto-u.ac.jp)

**Table 1.** Reaction of alkyl fluoride with silyl enolate in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$ 

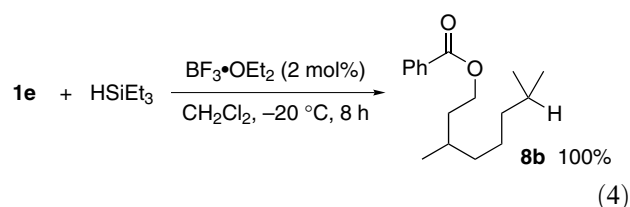
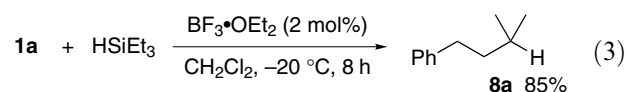
Entry	$\text{R}^1\text{-F}$ <b>1</b>	<b>2</b>	$\text{R}^2$	$\text{R}^3$	$\text{R}^4$	<b>3</b>	Yield, %
1		<b>2a</b>	H	H	Ph	<b>3a</b>	89
2	<b>1a</b>	<b>2b</b>	H	Me	Ph	<b>3b</b>	65
3	<b>1a</b>	<b>2c</b>	H	H	Me	<b>3c</b>	62
4	<b>1a</b>	<b>2d</b>	H	$-(\text{CH}_2)_4-$		<b>3d</b>	53
5	<b>1a</b>	<b>2e</b>	H	H	H	<b>3e</b>	0
6 <sup>a</sup>	<b>1a</b>	<b>2f</b>	Me	Me	Ph	<b>3f</b>	0
7	<b>1a</b>	<b>2g</b>	Me	Me	OMe	<b>3g</b>	81
8		<b>2a</b>	H	H	Ph	<b>3h</b>	79
9		<b>2a</b>	H	H	Ph	<b>3i</b>	54
10		<b>2a</b>	H	H	Ph	<b>3j</b>	56
11		<b>2a</b>	H	H	Ph	<b>3k</b>	75

<sup>a</sup> At reflux.

Alkyl fluoride **1a** was allylated with methallyl- and allyltrimethylsilane to form **7a** and **7b**, respectively, in good yields (Eq. 1). Reaction of **1e** with methallyltrimethylsilane afforded **7c** in 64% yield (Eq. 2).



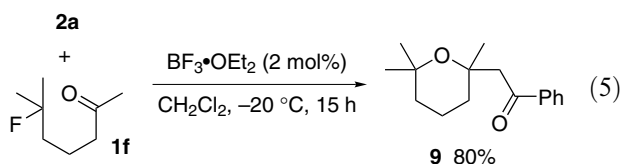
Reduction of **1a** and **1e** with triethylsilane also occurred under similar conditions (Eqs. 3 and 4).



Tetrasubstituted tetrahydropyran **9** was obtained in 80% yield when a mixture of fluoro ketone **1f** and **2a** was treated with 2 mol% of  $\text{BF}_3 \cdot \text{OEt}_2$  (Eq. 5). The formation of **9** strongly suggests that the reaction proceeds via a carbocation intermediate.<sup>6</sup>

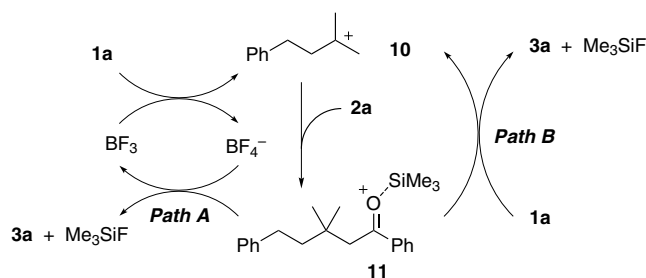
**Table 2.** Reaction of silyl enolate with allylic fluoride

Entry	4	2	Yield, %
1		2a	75 (5a/6a = 56/44)
2	4a	2b	82 (5b/6b <sup>a</sup> = 49/51)
3	4a	2d	85 (5c/6c <sup>a</sup> = 51/49)
4	4a	2f	91 (5d/6d = 70/30)
5		2a	73 (5e/6e = 71/29)
6	4b	2d	65 (5f/6f = 72/28)

<sup>a</sup> *syn/anti* = 1/1.

We are tempted to assume the mechanism for the alkylation of enolate as follows (Scheme 1). Boron trifluoride would abstract the fluoride of alkyl fluoride to form the corresponding alkyl cation **10** and tetrafluoroborate. Nucleophilic attack of silyl enolate, **2a** for instance, affords oxonium cation **11**, followed by desilylation by the action of tetrafluoroborate to give the product and to regenerate  $\text{BF}_3$  (path A). Alternatively, the oxonium cation **11** may also work as a fluorine abstracting agent<sup>7</sup> (path B), that is,  $\text{BF}_3$  may be the initiator of this reaction.

In summary, *tert*-alkyl and allyl fluorides serve as promising electrophiles in the reaction with silanes such

**Scheme 1.**

as silyl enolate, allylsilane, and hydrosilane in the presence of  $\text{BF}_3$ .  $\text{BF}_3$  catalyzes the reaction more efficiently than  $\text{Me}_3\text{Al}$ .

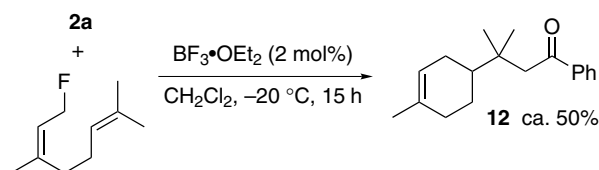
**Experimental procedure.** Boron trifluoride diethyl etherate (0.03 mL, 0.02 mmol) was added to a solution of 2-fluoro-2-methyl-4-phenylbutane (**1a**, 166 mg, 1.00 mmol) and silyl enolate **2a** (576 mg, 3.00 mmol) in dichloromethane (3 mL) at  $-20^\circ\text{C}$ . After being stirred for 15 h, the mixture was poured into hydrochloric acid (1 M, 20 mL). Extraction with hexane/ethyl acetate (10/1, 25 mL  $\times$  3) followed by silica gel column purification afforded 3,3-dimethyl-1,5-diphenyl-1-pentanone (**3a**, 237 mg, 0.89 mmol) in 89% yield.

### Acknowledgements

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- Alkyl fluorides were prepared by treatment of the corresponding alkenes with HF-pyridine. See: Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872–3881.
- Allylic fluorides were prepared by treatment of the corresponding allylic bromide with tetrabutylammonium fluoride and were purified by distillation. Purification by chromatography on silica gel resulted in decomposition. See: Ichihara, J.; Takai, Y.; Hanafusa, T.; Tomioka, K. *J. Fluorine Chem.* **1995**, *71*, 131–133. Allylic fluorides we employed are stable at  $-10^\circ\text{C}$  at least for 1 month.
- Treatment of neryl fluoride with **2a** gave cyclohexene derivative **12**, which was tentatively assigned, in ca. 50% yield with contamination by several unidentified byproducts.



- Trimethylsilyl trifluoromethanesulfonate did not effect the reaction of **2a** with **1a** at all.