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Mechanistic Studies on the Catalytic Cycle of Metal Fluoride-Catalyzed Allylation Using Allyltrimethoxysilane in Protic Solvents

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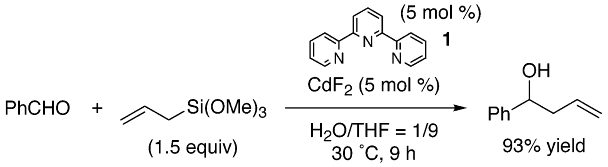
The catalytic cycles of CdF_2·**1**-catalyzed and AgF·BINAP-catalyzed allylation using allyltrimethoxysilane in protic solvents were investigated. The experimental and ^{19}F NMR studies strongly supported that metal fluorides were regenerated from silyl fluoride species, and that these reactions were truly fluoride-catalyzed reactions. It was revealed that these catalytic cycles were much different from that of TBAF-catalyzed allylation using allyltrimethylsilane in THF.

Introduction

Allylation of carbonyl compounds to afford synthetically useful homoallylic alcohols has been a subject of extensive investigations.[1] While numerous allyl organometallic reagents have been used so far,[2] among them, allylsilanes have been widely used and are more desirable reagents than some other allylating agents such as allyltins because of their lower toxicities.[3] Not only Lewis or Brønsted acids but also fluoride anion sources such as tetrabutylammonium fluoride (TBAF) can be employed as catalysts for allylation using allylsilanes, especially allyltrimethylsilane.[4] Recently, allyltri*methoxy*silane[5] has also been used because it is activated more easily by fluoride anion.[6] For example, Yamamoto et al. reported AgF·BINAP-catalyzed enantioselective allylation of aldehydes,[7] and Shibasaki et al. reported CuCl−tetrabutylammonium difluorotriphenylsilicate-catalyzed allylation of aldehydes, ketones, and imines.[8] Quite recently, we have also reported CdF_2[9]·terpyridine (**1**)-catalyzed allylation using allyltrimethoxysilane in aqueous media (Scheme 1).[10] Interestingly, CdF_2·**1**-catalyzed reactions in anhydrous THF or methanol gave only a trace amount of the product. These results show that water is essential for this catalytic system. Our next interest was the mechanism of these fluoride-catalyzed reactions, and it is indeed an important issue to clarify how fluoride anion is involved in the reactions. Herein, we report studies on the mechanism of catalytic cycle of the CdF_2·**1**-catalyzed allylation in aqueous media. Furthermore, based on the insight into the CdF_2·**1** catalysis, we also studied the mechanism of the AgF·BINAP-catalyzed allylation in methanol. These studies revealed that the catalytic cycles of these reactions using allyltrimethoxysilane in protic solvents differ greatly from the cycle of the TBAF-catalyzed reaction using allyltrimethylsilane.

SCHEME 1. CdF_2·1-Catalyzed Allylation Reaction in Aqueous Media



For the TBAF-catalyzed allylation using allyltrimethylsilane in THF, two possible mechanisms of the catalytic cycle have been proposed by Sakurai et al. The first

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(1) For reviews, see: (a) Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 563. (b) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; p 299.

(2) For a review, see: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(3) For reviews, see: (a) Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1. (b) Fleming, I. *Org. React.* **1989**, *37*, 57. (c) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200. (d) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293.

(4) For examples of fluoride-catalyzed allylation reactions using allylsilanes, see: (a) Hosomi, A.; Shirahata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, *19*, 3043. (b) Wang, D.-K.; Zhou, Y.-G.; Tang, Y.; Hou, X.-L.; Dai, L.-X. *J. Org. Chem.* **1999**, *64*, 4233. (c) Asao, N.; Shibato, A.; Itagaki, Y.; Jourdan, F.; Maruoka, K. *Tetrahedron Lett.* **1998**, *39*, 3177. (d) Shibato, A.; Itagaki, Y.; Tayama, E.; Hokke, Y.; Asao, N.; Maruoka, K. *Tetrahedron* **2000**, *56*, 5373. (e) Nakamura, K.; Nakamura, H.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2614.

(5) For allylation reactions using pentacoordinate silicates prepared from allyltrimethoxysilane, see: (a) Sato, K.; Kira, M.; Sakurai, H. *J. Am. Chem. Soc.* **1989**, *111*, 6429. (b) Hosomi, A.; Kohra, S.; Ogata, K.; Yanagi, T.; Tominaga, Y. *J. Org. Chem.* **1990**, *55*, 2415.

(6) For reviews, see: (a) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. (b) Sakurai, H. *Synlett* **1989**, 1.

(7) (a) Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, H. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3701. (b) During the review of this paper, Yamamoto et al. have reported that BINAP/AgOTf/KF/18-crown-6 was also effective for enantioselective allylation reactions using allyltrimethoxysilane. Wadamoto, M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem.* **2003**, *68*, 5593.

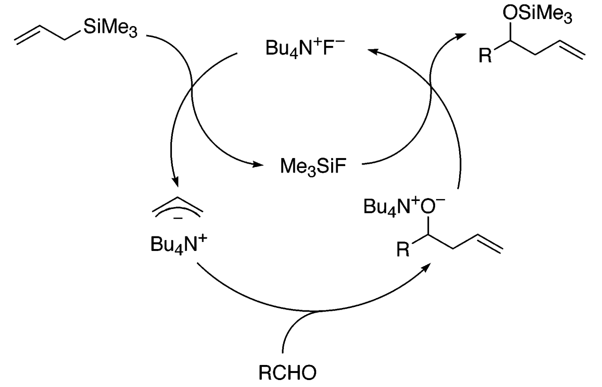
(8) Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M. Shibasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 6536.

(9) According to the literature, the hydrolysis constant (pK_h) of Cd(II) is 10.08. Therefore, Cd(II) is cannot be readily hydrolyzed in water. Baes, C. F., Jr.; Mesmer, R. *The Hydrolysis of Cations*; Wiley: New York, 1976.

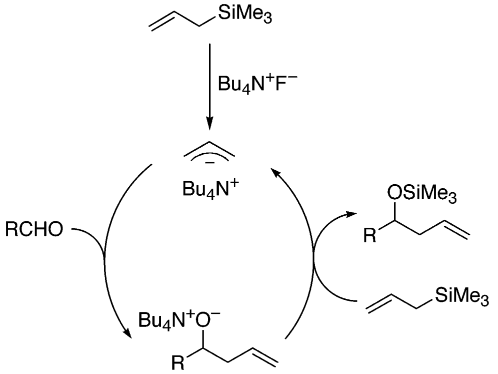
(10) Aoyama, N.; Hamada, T.; Manabe, K.; Kobayashi, S. *Chem. Commun.* **2003**, 676.

10.1021/jo0346196 CCC: $25.00

SCHEME 2. TBAF-Catalyzed Allylation Reaction[4a]



SCHEME 3. TBAF-Initiated Allylation Reaction[4b,11]



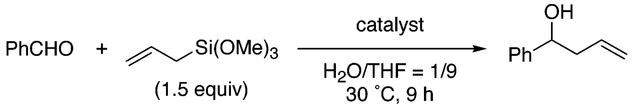
mechanism is a truly fluoride anion-catalyzed reaction (Scheme 2).[4a] The released trimethylsilyl fluoride reacts with the tetrabutylammonium alkoxide to regenerate TBAF in the catalytic cycle. The second mechanism is a fluoride anion-initiated (-triggered) mechanism (Scheme 3). In this mechanism, the fluoride anion just serves as an initiator of the reaction and is not involved in the catalytic cycle. The tetrabutylammonium alkoxide reacts with the allylsilane to regenerate the active species, and the catalytic cycle is completed. Sakurai et al. later stated that the latter mechanism was plausible,[11] and Hou et al. showed experimental evidence which supported the fluoride anion-initiated autocatalytic mechanism.[4b]

Results and Discussion

To elucidate the mechanism of the CdF_2·**1**-catalyzed allylation in aqueous media, at first, we investigated the effect of fluoride anion in the reaction by adding TBAF to $Cd(ClO_4)_2$·**1** complex (Table 1). As a result, only TBAF, only $Cd(ClO_4)_2$·**1**, or $Cd(ClO_4)_2$·**1**:TBAF = 1:1 did not catalyze the allylation (entries 1−3). However, in the case of $Cd(ClO_4)_2$·**1**:TBAF = 1:2, the reaction proceeded smoothly (entry 4). This result suggests that 2 equiv of fluoride anion to $Cd(ClO_4)_2$·**1** is essential for the reaction.

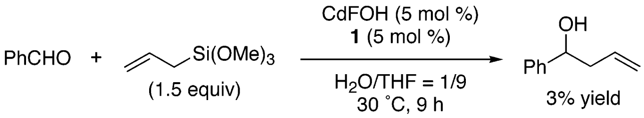
Next, we used CdFOH[12]·**1** as a catalyst. If the CdF_2·**1**-catalyzed allylation is a fluoride-initiated autocatalytic reaction, CdFOH, which is formed by hydrolysis of $CdFOCH(Ph)CH_2CH{=}CH_2$, should catalyze the reaction. However, CdFOH·**1** was found to be totally ineffective for the allylation (Scheme 4). This result suggests that the mechanism of the catalytic cycle is not a fluoride-initiated one.

TABLE 1. Effect of Fluoride Anion

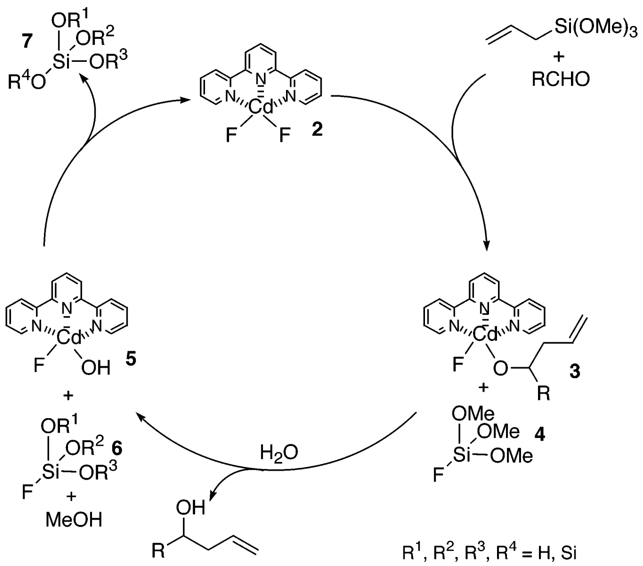


entry	catalyst (mol %)	yield (%)
1	TBAF (10)	1
2	$Cd(ClO_4)_2$ (5) **1** (5)	0
3	$Cd(ClO_4)_2$ (5) **1** (5) TBAF (5)	0
4	$Cd(ClO_4)_2$ (5) **1** (5) TBAF (10)	95

SCHEME 4. CdFOH·1-Catalyzed Allylation Reaction in Aqueous Media



SCHEME 5. Catalytic Cycle of CdF_2·1-Catalyzed Allylation Reaction in Aqueous Media



From the results mentioned above, we propose the catalytic cycle of the CdF_2·**1**-catalyzed allylation as shown in Scheme 5. In the first step, complex **2**, an aldehyde, and allyltrimethoxysilane react to give adduct **3**[13] and fluorotrimethoxysilane **4**. At this moment, it is unclear whether an allylcadmium or allylsilicate species is involved in this step.[14] In the second step, adduct **3** is hydrolyzed to give complex **5** and the product as the alcohol form. Fluorotrimethoxysilane is also hydrolyzed

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[11] Sakurai, H.; Hosomi, A.; Saito, M.; Sasaki, K.; Iguchi, H.; Sasaki, J.; Araki, Y. *Tetrahedron* **1983**, *39*, 883.

[12] For preparation of CdFOH, see: Srivastava, O. K.; Secco, E. A. *Can. J. Chem.* **1967**, *45*, 1375.

[13] A possibility that allylcadmium (or allylsilver) species affords the product without forming adduct **3** (or **9**) may not be excluded.

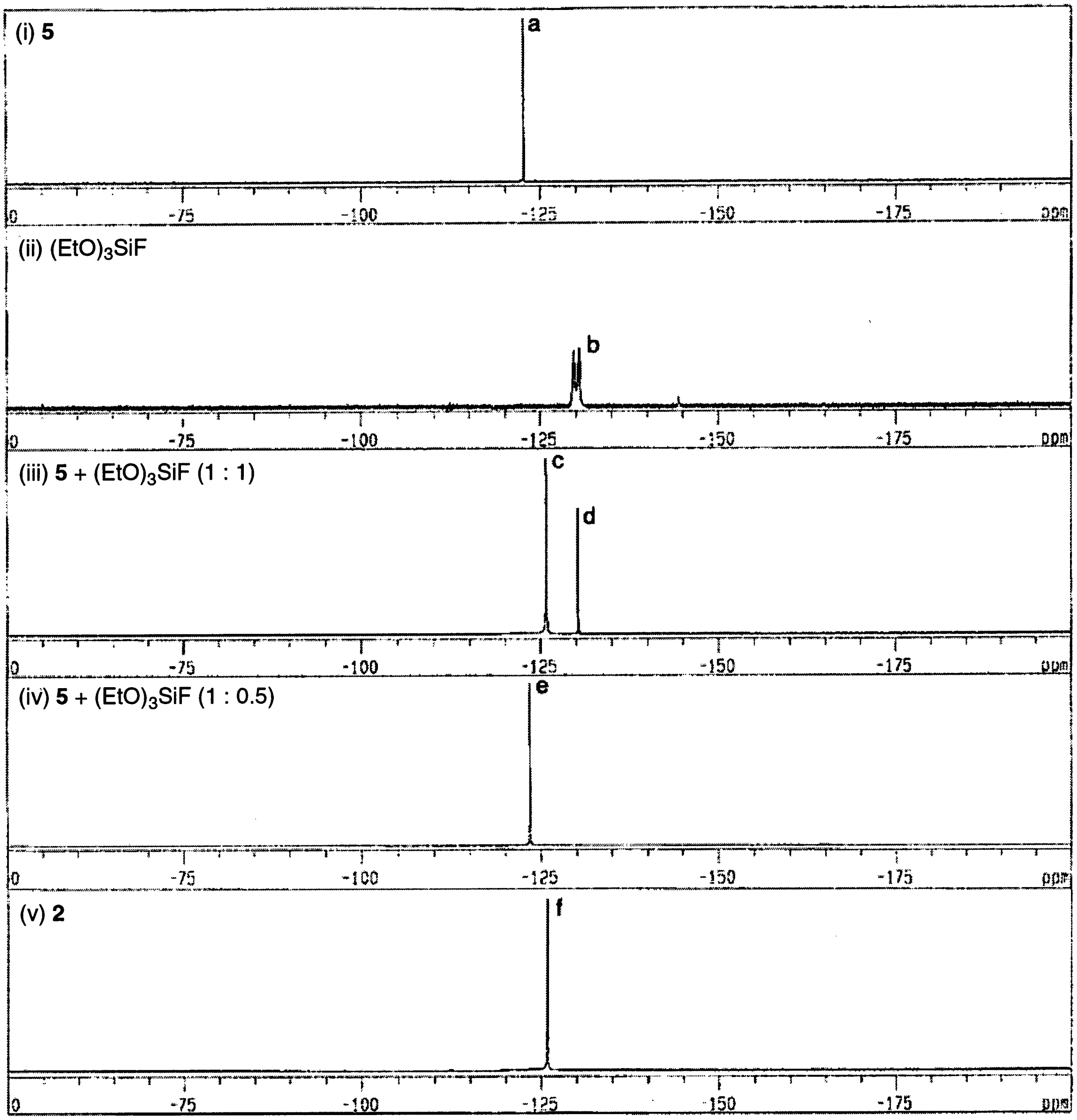
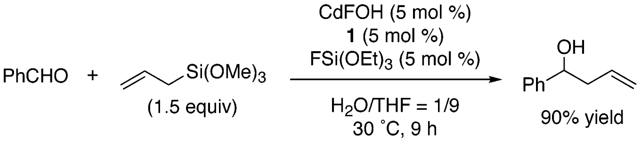


FIGURE 1. ^{19}F NMR spectra (at 282.65 MHz in D_2O at 30 °C) of (i) complex **5**, (ii) $(EtO)_3SiF$, (iii) a mixture of complex **5** and $(EtO)_3SiF$ (1:1), (iv) a mixture of complex **5** and $(EtO)_3SiF$ (1:0.5), and (v) complex **2**.

to give **6** along with generation of methanol. These hydrolyses should occur rapidly in the presence of water. In the third step, complex **5** reacts with **6** to regenerate CdF_2·**1** complex (**2**) for the next catalytic cycle.

To elucidate this third step, a mixture of complex **5** and fluorotriethoxysilane was used as a catalyst. Fluorotriethoxysilane was used as an analogue of **4**[15] and should have been hydrolyzed to **6** in situ. It is noteworthy that the reaction proceeded smoothly in the presence of complex **5** and fluorotriethoxysilane (Scheme 6), contrary to the reaction without fluorotriethoxysilane (Scheme 4).

SCHEME 6. CdFOH·1 and $FSi(OEt)_3$ as a Catalyst



Regeneration of complex **2** was also confirmed by ^{19}F NMR studies. ^{19}F NMR of complex **5** in D_2O[16] at 30 °C showed a peak at −122.67 ppm (Figure 1 (i)). Fluorotriethoxysilane was readily hydrolyzed by D_2O and showed broad peaks at −129.62 and −130.41 ppm (Figure 1 (ii)). On the other hand, a mixture of complex **5** and fluorotriethoxysilane in D_2O showed new peaks at −125.81 ppm (peak **c**) and −130.26 ppm (peak **d**) (Figure 1 (iii)). The peak **d** was assigned to be **6** on the basis of the satellite peak derived from coupling with ^{29}Si (J = 108 Hz). Although peak **d** remained, the integration of peak **d** was much smaller than that of peak **c** (the ratio of integration was peak **c**/peak **d** = 9/1), and peak **d** was consumed completely when using 0.5 equiv of fluorotriethoxysilane (Figure 1 (iv)). As a result of fast equilibrium between

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(14) Crotylation reactions are known to give information on the transition state structure. However, CdF_2·**1**-catalyzed crotylation reaction using (*E*)-crotyltrimethoxysilane (*E*/*Z* = 96/4, 2 equiv) resulted in low yield and low selectivity (12% yield, *syn*/*anti* = 46/54). Therefore, we could not get a clue for the first step from crotylation.

(15) Fluorotriethoxysilane is commercially available in high purity.

(16) D_2O was used as a solvent because complex **5** is hardly soluble in organic and other aqueous solvents.

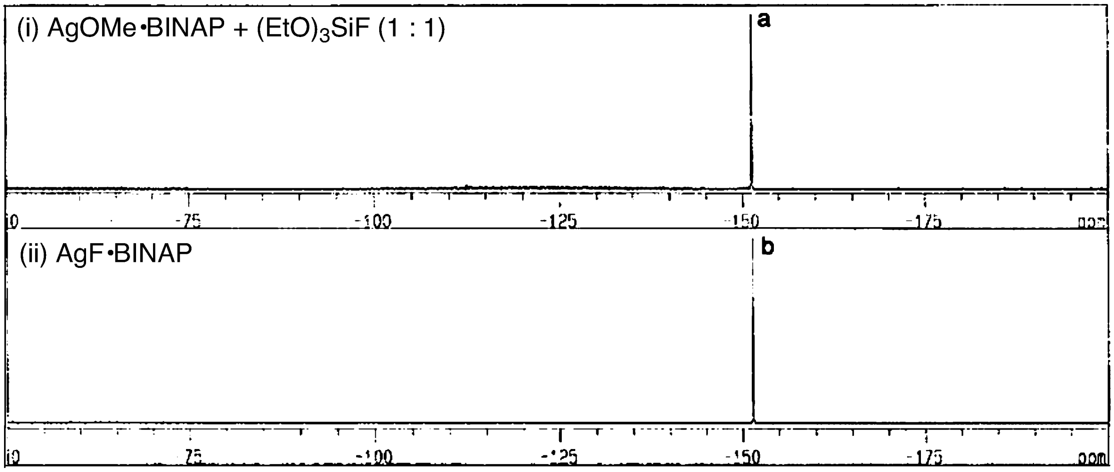
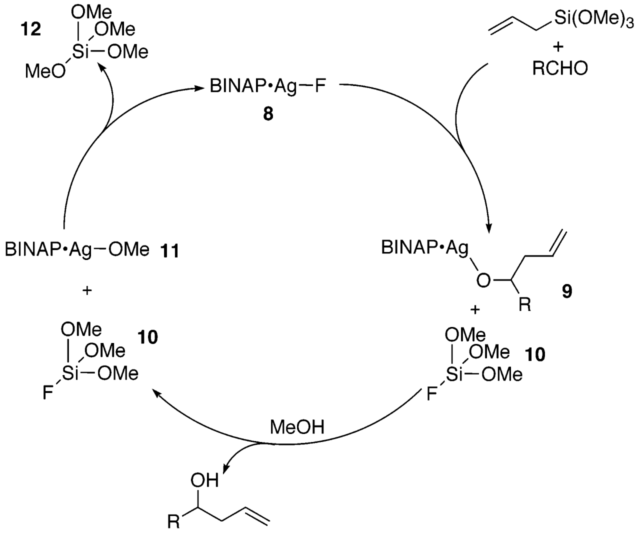


FIGURE 2. ^{19}F NMR spectra (at 282.65 MHz in methanol-d_4 at −20 °C) of (i) a mixture of AgOMe•BINAP and $(EtO)_3SiF$ (1:1) and (ii) AgF•BINAP.

SCHEME 7. Catalytic Cycle of AgF·BINAP-Catalyzed Allylation Reaction



CdF_2·**1** and CdFOH·**1** on the NMR time scale, only one peak was observed. The peak **c** coincided with the signal of complex **2** (**f**) whose chemical shift was −125.89 ppm (Figure 1 (v)). Therefore, the peak **c** is assigned to be complex **2**. These experimental and ^{19}F NMR results strongly support the regeneration of complex **2** from complex **5** and fluorotriethoxysilane in the presence of water and, as a consequence, the truly fluoride-catalyzed mechanism. It should be also mentioned that, while a strong silicon−fluoride bond is generally considered hard to cleave, the bond was cleaved under the present conditions.

Next, we turned our attention to the mechanism of AgF·BINAP-catalyzed allylation in methanol. A proposed catalytic cycle is shown in Scheme 7.[17] Although the reaction of adduct **9**[13] with **10** to give the corresponding trimethoxysilyl ether as the product was conceivable, monitoring the reaction by TLC did not show the formation of the trimethoxysilyl ether. Therefore, adduct **9** is considered to react with methanol to give the alcohol product and AgOMe•BINAP. The next step was evaluated experimentally. AgOMe•BINAP was prepared by mixing $AgClO_4$•BINAP and NaOMe in methanol at −20 °C. This catalyst was found to be ineffective for the reaction of benzaldehyde with allyltrimethoxysilane at −20 °C for 5 h (2% yield and 59% ee). However, when fluorotriethoxysilane was added to this catalyst solution and then benzaldehyde and allyltrimethoxysilane were added successively, the desired homoallylic alcohol was obtained in 63% yield with 93% ee. Although the yield was slightly lower, the result is close to that of AgF•BINAP-catalyzed reaction (82% yield and 93% ee, lit.[7a] 92% yield and 94% ee). Furthermore, ^{19}F NMR of AgOMe•BINAP and fluorotriethoxysilane in methanol-d_4 at −20 °C showed a peak at −151.26 ppm (Figure 2 (i)), which coincided with the signal of AgF•BINAP in methanol-d_4 (−151.36 ppm (Figure 2 (ii)). These results suggest the regeneration of AgF•BINAP from AgOMe•BINAP and fluorotriethoxysilane.

The experimental results stated above strongly support the truly fluoride-catalyzed mechanism for both the CdF_2•**1**-catalyzed allylation in H_2O−THF and the AgF•BINAP-catalyzed allylation in methanol. This conclusion is contrary to the catalytic cycle of TBAF-catalyzed allylation using allyltrimethylsilane in THF.[4b,11] In the CuCl−tetrabutylammonium difluorotriphenylsilicate-catalyzed allylation using allyltrimethoxysilane in THF, Shibasaki et al. also proposed another mechanism where the initially formed CuF was not regenerated, and instead, allylfluorodimethoxysilane was involved in the catalytic cycle.[8] We assume that in the former two reactions (the CdF_2•**1**-catalyzed and the AgF•BINAP-catalyzed ones) the protic solvents play important roles and facilitate the regeneration of the metal fluoride species probably due to effective solvation of fluoride anion.[18]

In conclusion, we have investigated the catalytic cycles of CdF_2•**1**-catalyzed and AgF•BINAP-catalyzed allylation using allyltrimethoxysilane in protic solvents. The ex-

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[17] In the crotylation reaction, Yamamoto et al. noted that the occurrence of transmetalation gives crotylsilver species. Therefore, it is likely that allylsilver species is involved in the first step. See ref 7a.

[18] Hefter reported in his review that fluoride anion solvation by nonprotic solvents (DMSO, DMF, THF) requires much more Gibbs energies compared to protic solvents (H_2O, MeOH). Hefter, G. H. *Pure Appl. Chem.* **1991**, *63*, 1749.

perimental evidence described here shows that each metal fluoride is regenerated from silyl fluoride species and that these reactions are interesting examples in which truly fluoride-catalyzed mechanisms are operative. These catalytic cycles are much different from that of TBAF-catalyzed allylation using allyltrimethylsilane in THF. Thus, the studies in this paper will provide a new aspect in fluoride-catalyzed allylation using allylsilanes.

Experimental Section

General Methods. All reactions were performed under an argon atmosphere. Chemical shifts are reported in δ ppm referenced to an internal standard (tetramethylsilane, 0 ppm) for ^{1}H NMR, an internal standard ($CDCl_3$, 77.0 ppm) for ^{13}C NMR, and an external standard ($CFCl_3$, 0 ppm) for ^{19}F NMR.

Typical Procedures for Allylation Reactions. For $Cd(ClO_4)_2$·1 and TBAF-Catalyzed Allylation Reaction in Aqueous Media (Table 1, Entry 4). To a solution of $Cd(ClO_4)_2$ (6.5 mg) and **1** (3.6 mg) in H_2O (145 μL) were added TBAF in H_2O (75 wt %, 10.5 μL) and THF (1.40 mL). The mixture was stirred at 30 °C for 30 min, and then benzaldehyde (33.1 mg) and allyltrimethoxysilane (75.5 mg) were added successively. The mixture was stirred at 30 °C for 9 h and diluted with water (ca. 5 mL). The aqueous layer was extracted with CH_2Cl_2 three times, and the organic layer was washed with saturated NaCl and dried over Na_2SO_4. The solvents were evaporated after filtration. The residual crude product was purified by preparative TLC on silica gel to give 1-phenyl-3-buten-1-ol[19] as a colorless oil (44.0 mg, 95% yield).

1-Phenyl-3-buten-1-ol: ^{1}H NMR (300.4 MHz, $CDCl_3$) δ 2.05 (br, 1H), 2.43−2.56 (m, 2H), 4.72 (dd, 1H, J = 5.7, 7.3 Hz), 5.11−5.19 (m, 2H), 5.79 (ddt, 1H, J = 7.1, 10.2, 17.1 Hz), 7.24−7.36 (m, 5H); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 43.8, 73.3, 118.3, 125.8, 127.5, 128.4, 134.4, 143.8.

For CdFOH·1- and $FSi(OEt)_3$-Catalyzed Allylation Reaction in Aqueous Media (Scheme 6). To a suspension of CdFOH[12] (2.3 mg) and **1** (3.6 mg) in H_2O (155 μL) was added THF (1.40 mL). The mixture was stirred at 30 °C for 30 min, and then benzaldehyde (32.8 mg), allyltrimethoxysilane (75.5 mg), and fluorotriethoxysilane (2.8 mg) were added successively. The mixture was stirred at 30 °C for 9 h and diluted with water (ca. 5 mL). The aqueous layer was extracted with CH_2Cl_2 three times, and the organic layer was washed with saturated NaCl and dried over Na_2SO_4. The solvent was evaporated after filtration. The residual crude product was purified by preparative TLC on silica gel to give 1-phenyl-3-buten-1-ol[19] as a colorless oil (41.2 mg, 90% yield).

For ^{19}F NMR Measurement of a Mixture of Complex 5 and $FSi(OEt)_3$ (1 equiv) in D_2O at 30 °C. To a mixture of CdFOH[12] (11.9 mg) and **1** (18.8 mg) in D_2O (0.8 mL) was added fluorotriethoxysilane (14.6 μL, 1 equiv). The mixture was transferred into a NMR sample tube. After 30 min, ^{19}F NMR was measured, and the spectrum is shown in Figure 1 (iii): ^{19}F NMR (282.65 MHz, D_2O) δ −125.81 (s), −130.26 (s, satellite peak J_{Si-F} = 108 Hz).

^{19}F NMR of complex **5** in D_2O at 30 °C (Figure 1 (i)): ^{19}F NMR (282.65 MHz, D_2O) δ −122.67 (s). ^{19}F NMR of $FSi(OEt)_3$ in D_2O at 30 °C (Figure 1 (ii)): ^{19}F NMR (282.65 MHz, D_2O) δ −129.62 (br), −130.41 (br). ^{19}F NMR of a mixture of complex **5** and $FSi(OEt)_3$ (0.5 equiv) in D_2O at 30 °C (Figure 1 (iv)): ^{19}F NMR (282.65 MHz, D_2O) δ −123.45 (s). ^{19}F NMR of complex **2** in D_2O at 30 °C (Figure 1 (v)): ^{19}F NMR (282.65 MHz, D_2O) δ −125.89 (s).

The Procedure for AgOMe·(*R*)-BINAP- and $FSi(OEt)_3$-Catalyzed Allylation Reaction in Methanol. To a solution of $AgClO_4$ (7.2 mg) and (*R*)-BINAP (13.3 mg) in methanol (2.17 mL) was added NaOMe (1.9 mg) in methanol (1.0 mL), and the mixture was stirred at −20 °C for 10 min with exclusion of direct light. To the mixture were added $FSi(OEt)_3$ (6.4 mg) in methanol (1.0 mL), benzaldehyde (36.7 mg), and allyltrimethoxysilane (84.5 mg) successively at this temperature. The mixture was stirred at −20 °C for 5 h and quenched with 0.2 N HCl (ca. 5 mL). The aqueous layer was extracted with CH_2Cl_2 three times, and the organic layer was washed with saturated NaCl and dried over Na_2SO_4. The solvents were evaporated after filtration. The residual crude product was purified by preparative TLC on silica gel to give 1-phenyl-3-buten-1-ol[19] as a colorless oil (32.5 mg, 63% yield). The enantiomeric excess of the product was determined to be 93% ee by a chiral HPLC analysis (CHIRALCEL OD, hexane/^{i}PrOH = 20/1, flow rate 0.5 mL/min, t_R 18.1 min (major, (*R*)-isomer) and t_R 19.6 min (minor, (*S*)-isomer).[19]

For ^{19}F NMR Measurement of a Mixture of AgOMe·BINAP and $FSi(OEt)_3$ (1 equiv) in Methanol-d_4 at −20 °C. To a mixture of $AgClO_4$ (8.8 mg) and (*R*)-BINAP (26.8 mg) in methanol-d_4 (1.1 mL) was added NaOMe (2.4 mg) in methanol-d_4 (0.53 mL) at −20 °C. After 10 min, to the mixture was added $FSi(OEt)_3$ (7.7 mg) in methanol-d_4 (0.53 mL) at this temperature. After 10 min, the resulting solution was transferred into an NMR sample tube at −20 °C. After 30 min, ^{19}F NMR was measured at −20 °C, and the spectrum is shown in Figure 2 (i): ^{19}F NMR (282.65 MHz, D_2O) δ −151.26 (s).

^{19}F NMR of AgF·(*R*)-BINAP in methanol-d_4 at −20 °C (Figure 2 (ii)): ^{19}F NMR (282.65 MHz, D_2O) δ −151.36 (s).

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(19) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama. T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490.