Available online at www.sciencedirect.com

ScienceDirect

Journal of Fluorine Chemistry 128 (2007) 1087–1090

JOURNAL OF FLUORINE CHEMISTRY

www.elsevier.com/locate/fluor

Fluoride ion-catalyzed desilylative-defluorination for synthetic organic chemistry

Kenji Uneyama [*]

Department of Applied Chemistry, Okayama University, Okayama 700-8530, Japan

Received 12 April 2007; received in revised form 9 May 2007; accepted 10 May 2007
Available online 17 May 2007

Abstract

Two types of fluoride ion-catalyzed desilylative-defluorination (intermolecular and intramolecular versions) have been reported. The intermolecular desilylative-defluorination consists of sequential reactions: generation of a nucleophile by fluoride ion-promoted desilylation, its reaction with a fluorinated electrophile, and simultaneous formation of a final product and regeneration of fluoride ion. Precursors of nucleophiles used in the catalytic reaction system involve disilane, silyl ethers, CF_3-TMS, and $FSO_2CF_2CO_2TMS$. The intramolecular version is quite useful for the preparation of *gem*-difluoroalkenes including α-substituted 2,2-difluorostyrenes, 2-trimethylsilyloxy-3,3-difluoroacrylate, tetrafluoroquinodimethane, which arise from 1,2-, 1,4- and 1,6-desilylative-defluorination, respectively. The potential advantages for both types of the desilylative-defluorinations are (1) effective preparation of base or nucleophile-sensitive products, (2) very mild and essentially neutral conditions, and (3) use of a catalytic amount of fluoride ion.

© 2007 Elsevier B.V. All rights reserved.

Keywords: Desilylative-defluorination; *gem*-Difluoroalkenes; 2,2-Difluorostyrene; 3,3-Difluoroacrylate; Desilylation; Defluorination; Fluoride ion

Fluoride ion-promoted silicon–carbon and silicon–oxygen bonds cleavage and generation of carbanion and oxyanion are one of the most frequently employed reactions in organic synthesis. Generations of enolate from silyl enol ethers, benzyne from *o*-Me_3Si-aryl triflates, and CF_3-anion equivalent from Ruppert-Prakash reagent, Tamao oxidation, and Pd-catalyzed Hiyama coupling, all of these synthetically useful reactions are initiated by fluoride ion endowed with a strong affinity to silicon atom [1].

However, most of these reactions require the use of a stoichiometric or excess amount of fluoride ion, which causes sometimes undesirable side-reactions due to the strong basic conditions. On this basis, it is more feasible to design any practical syntheses, which consist of a sequence of fluoride ion-catalyzed desilylation, generation of reactive intermediates leading to the expected desired reactions, and regeneration of fluoride ion at the final stage of the reaction.

There are two potentially feasible reaction systems in fluoride ion-catalyzed desilylative-defluorination: the one is *intermolecular* desilylative-defluorination and the other is *intramolecular* version. The former consists of an intermolecular reaction of a nucleophile generated by fluoride ion-promoted desilylation reaction with fluorinated electrophile bearing a potentially removable fluorine atom. In this reaction, a final product is formed by a combination of desilylated nucleophile and defluorinated electrophile as shown in Scheme 1. The latter is intramolecular desilylative-defluorination, in which a substrate bearing both of removable silyl moiety and fluorine atom undergoes fluoride ion-promoted desilylation followed by defluorination leading to formation of a final product and along with regeneration of fluoride ion (Scheme 1).

This short review describes two types of the fluoride ion-catalyzed desilylative-defluorination reactions as shown in Scheme 1.

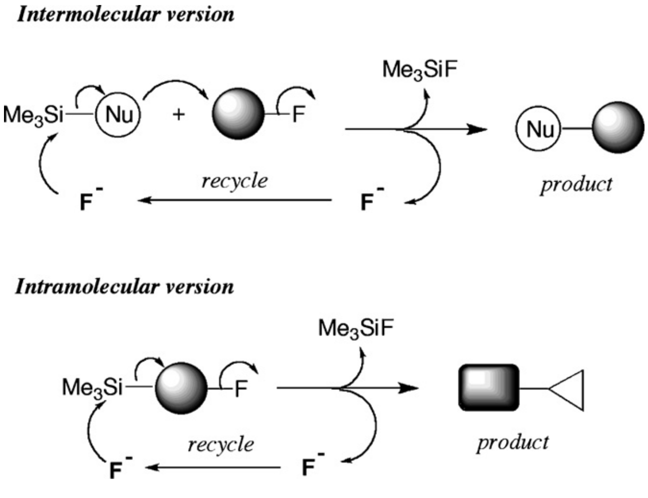
1. Intermolecular desilylative-defluorination reaction

The S_N2' type dimethylphenylsilylation of **1** is shown in Scheme 2 is one of the typical intermolecular desilylative-defluorination, where fluoride ion initiates the heterolytic Si–Si bond cleavage of disilane **2** to generate dimethylphenylsilyl anion, which then attacks trifluoropropene **1** in an S_N2'

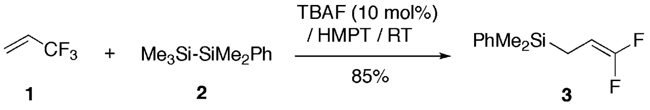
---

[*] Tel.: +81 86 251 8075; fax: +81 86 251 8021.
E-mail address: uneyamak@cc.okayama-u.ac.jp.

0022-1139/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2007.05.008



Scheme 1.

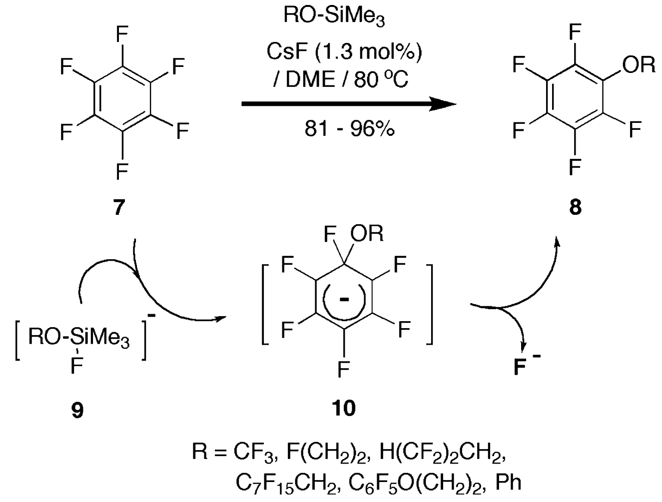


Scheme 2.

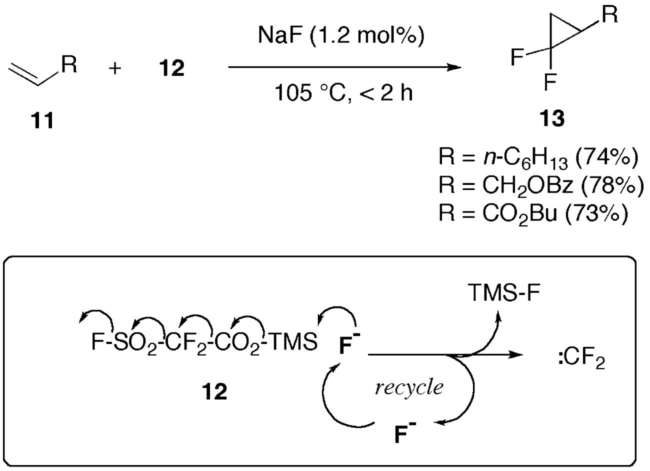
reaction, providing difluoroallyl silane **3** as a final product along with a fluoride ion [2]. A catalytic amount of TBAF (10 mol%) is enough to complete the overall reaction.

One of the advantages of the fluoride-ion-catalyzed desilylative-defluorination is a suitable control of the rate of generation of a reactive nucleophile *in situ*. This protocol is particularly useful for the reaction with very reactive fluorinated electrophile like perfluorocyclobutene **4** (Scheme 3) and hexafluorobenzene **7** (Scheme 4). As shown in Scheme 3, the desired substitution proceeds smoothly by a combined use of trimethylsilyl ether as a precursor of nucleophile and a trace amount of CsF. In this reaction system, a reactive nucleophile can be generated in a stepwise manner only after one cycle of the expected reaction sequence (generation of alkoxide equivalent from **5**, nucleophilic attack to perfluorocyclobutene **4**, and formation of product **6** *via* addition-elimination along with regeneration of fluoride ion) completes. Therefore, the reaction system is equivalent to the experimental conditions in which addition rate of a nucleophile is adjusted so as to control the reaction rate [3].

Similar nucleophilic substitution of alkoxide anion equivalent **9** on an aromatic ring was achieved by the reaction of silyl ethers with hexafluorobenzene **7** in the presence of a catalytic amount of CsF as an initiator (Scheme 4) [4]. It was reported that the use of silyl ethers was more favorable for polyalkoxylation of **7** than alkali metal alkoxide.



Scheme 4.

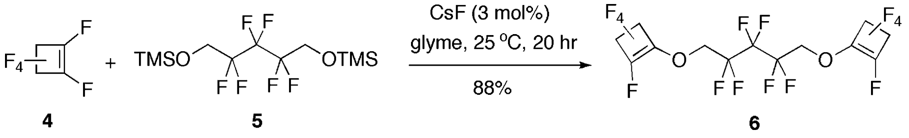


Scheme 5.

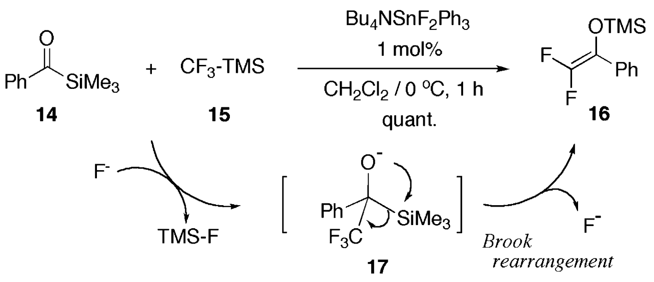
Transformation of benzenesulfonyl fluoride to the corresponding sulfonates ($PhSO_2OR$) with trimethylsilyl ethers ($ROSiMe_3$) was also catalyzed by a catalytic amount of tetraethylammonium fluoride [5].

Fluoride ion-catalyzed generation of difluorocarbene from trimethylsilyl fluorosulfonyldifluoroacetate **12** and the subsequent cyclopropanation of alkenes **11** provide difluorocyclopropanes **13**. The overall reactions can be classified into the intermolecular desilylative-defluorination (Scheme 5) [6]. Here again only 1.2 mol% of NaF can transform all of the silyl acetate **12** to difluorocarbene.

Successive reactions starting from fluoride ion-catalyzed generation of trifluoromethyl carbanion equivalent from Ruppert-Prakash reagent **15** and its subsequent addition to acyl silane **14** followed by Brook rearrangement of



Scheme 3.



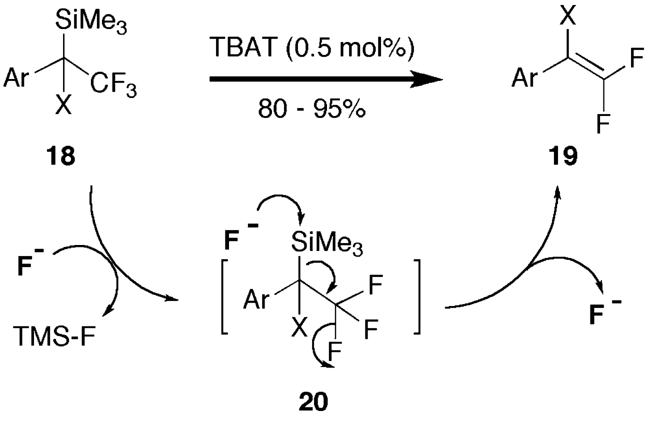
Scheme 6.

intermediate **17** lead to the formation of difluoroenol silyl ether **16** successfully (Scheme 6). The reaction with trifluoroacetyl triphenylsilane was firstly discovered by Jin et al. [7], and later on, extensive synthetic application of the corresponding trialkylsilanes was developed by Portella and co-workers [8]. The key step of the net transformation of **14**–**16** is Brook rearrangement, in which intramolecular attack by alkoxide anion to silicon in **17** induces heterolytic carbon–silicon bond cleavage and simultaneous extrusion of β-fluorine atom as a fluoride ion, resulting in the formation of a final product **16** along with regeneration of fluoride ion. This reaction provides aliphatic difluoroenol silyl ethers in more favorable yields than Mg-promoted defluorination of trifluoromethyl alkyl ketones [9].

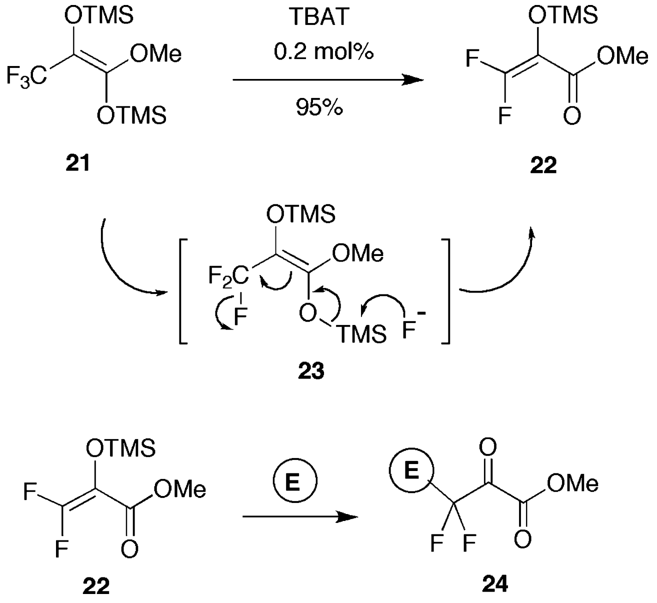
2. Intramolecular desilylative-defluorination reaction

Three kinds of intramolecular desilylative-defluorination have been reported: 1,2- and 1,4- and 1,6-version, respectively. Scheme 7 shows 1,2-desilylative-defluorination, in which the leaving silyl moiety and fluorine atom are located at C1 and C2 carbons. This fluoride ion-catalyzed reaction proceeds within 10 min in the presence of 0.5 mol% of tetrabutylammonium triphenyldifluorosilicate (TBAT) in either CH_2Cl_2 or *n*-hexane, affording 1-substituted (X = F, Cl, and Br) 2,2-difluorostyrenes **19** in excellent yields. The result demonstrates perfect recycling of fluoride ion under the reaction conditions [10].

1,4-Desilylative-defluorination of ketene silylacetal **21** [11] is shown in Scheme 8. Here again only 0.2 mol% of fluoride ion is enough to complete the reaction within 10 min and gives methyl 2,2-difluoro-1-trimethylsilyloxyacrylate **22** in an excellent yield. Particularly interesting and important fact is that the use of 10 mol% of fluoride ion resulted in very poor yield of the desired product **19**. Fig. 1 clearly reveals the yield of **22** decreases sharply as the amount of TBAT increases. The β-carbon of **22** is so highly electrophilic due to both *gem*-fluorines and β-carbomethoxy group that it accepts easily fluoride ion as a nucleophile to generate the corresponding enolate of 2-trimethylsilyloxy-3,3,3-trifluoropropionate, which would undergo condensation with **22**, providing a complex mixture. This reaction system catalyzed with a trace amount of fluoride ion is quite useful when the product is highly reactive with nucleophiles. The product **22** is a good synthetic precursor for 3-substituted 2,2-difluoropyruvates **24** [12].



Scheme 7.



Scheme 8.

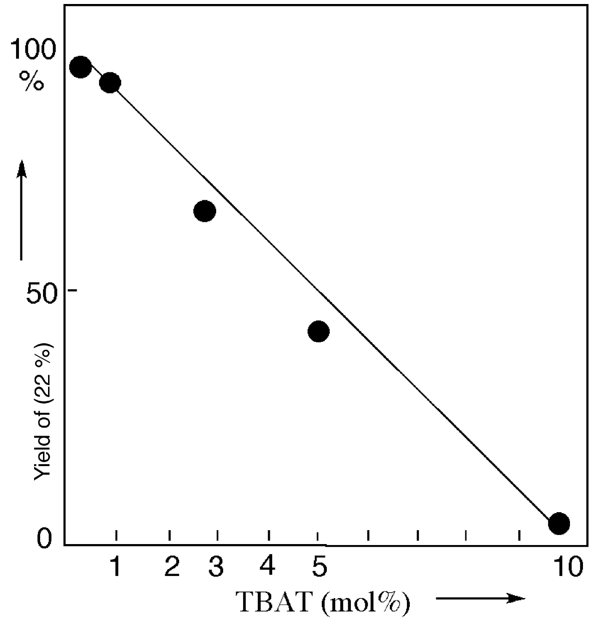
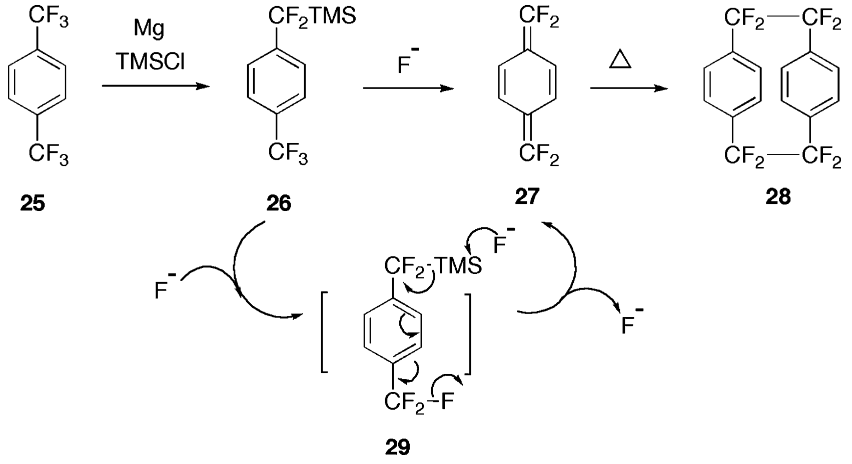


Fig. 1. Relation between yield of **22** and amount of TBAT.



Scheme 9.

1,6-Desilylative-defluorination is also feasible for the preparation of tetrafluoroquinodimethane **27** from **26** as shown in Scheme 9 [13]. The fluorinated quinodimethane is so reactive and unstable that use of the minimum amount of fluoride ion is essential to avoid unfavorable fluoride ion-induced oligomerization of **27**. The octafluoroparacyclophane **28** is an excellent precursor for the insulating fluoroparylene polymer [14].

3. Conclusion

Two types of fluoride ion-catalyzed desilylative-defluorination (intermolecular and intramolecular version) have been reported. The intermolecular desilylative-defluorination consists of sequential reactions: generation of a nucleophile by fluoride ion-promoted desilylation, its reaction with a fluorinated electrophile, and simultaneous formation of a final product and regeneration of fluoride ion. The intramolecular version is quite useful for the preparation of *gem*-difluoroalkenes which arise from 1,2-, 1,4- and 1,6-desilylative-defluorination. The potential advantages for both types of the desilylative-defluorinations are (1) effective preparation of base or nucleophile sensitive products, (2) very mild and essentially neutral conditions, and (3) use of catalytic amount of fluoride ion.

References

[1] K. Uneyama, Organofluorine Chemistry, Blackwell Publishing, Oxford, UK, 2006.
[2] (a) T. Hiyama, M. Obayashi, M. Sawahara, Tetrahedron Lett. 24 (1983) 4113–4116;
(b) M. Fujita, M. Obayashi, T. Hiyama, Tetrahedron 44 (1988) 4135–4145.
[3] W.B. Farnham, D.C. Roe, D.A. Dixon, J.C. Calabrese, R.L. Harlow, J. Am. Chem. Soc. 112 (1990) 7707–7718.
[4] (a) Y.F. Zhang, R.L. Kirchmeier, J.M. Shreeve, J. Fluorine Chem. 68 (1994) 287–292;
(b) N.R. Patel, J. Chen, Y.F. Zhang, R.L. Kirchmeier, J.M. Shreeve, Inorg. Chem. 33 (1994) 5463–5470.
[5] P. Ykman, K.H. Hall, J. Organomet. Chem. 116 (1976) 153–159.
[6] (a) F. Tian, V. Kruger, O. Bautista, J.-X. Duan, A.-R. Li, W.R. Dolbier Jr., Q.-Y. Chen, Org. Lett. 2 (2000) 563–564;
(b) W. Xu, Q.-Y. Chen, J. Org. Chem. 67 (2002) 9421–9427;
(c) W. Xu, Q.-Y. Chen, Org. Biomol. Chem. 1 (2003) 1151–1156;
(d) Z.L. Cheng, Q.-Y. Chen, J. Fluorine Chem. 126 (2005) 39–43;
(e) Z.-L. Cheng, Q.-Y. Chen, Synletters (2006) 478–480;
(f) Z.-L. Cheng, Q.-Y. Chen, J. Fluorine Chem. 127 (2006) 894–900;
(g) W.R. Dolbier Jr., M.A. Battiste, Chem. Rev. 103 (2003) 1071–1098 (review of fluorocyclopropanes).
[7] (a) F. Jin, B. Jiang, Y. Xu, Tetrahedron Lett. 33 (1992) 1221–1224;
(b) F. Jin, Y. Xu, W. Huang, J. Chem. Soc., Perkin Trans. I (1993) 795–799.
[8] (a) T. Brigaud, P. Doussot, C. Portella, J. Chem. Soc. Chem. Commun. (1994) 2117–2118;
(b) O. Lefebvre, T. Brigaud, C. Portella, Tetrahedron 54 (1998) 5939–5948.
[9] H. Amii, T. Kobayashi, Y. Hatamoto, K. Uneyama, Chem. Commun. (1999) 1323–1324.
[10] Y. Nakamura, K. Uneyama, J. Org. Chem., in press.
[11] G. Takikawa, T. Katagiri, k. Uneyama, J. Org. Chem. 70 (2005) 8811–8816.
[12] G. Takikawa, K. Toma, K. Uneyama, Tetrahedron Lett. 47 (2006) 6509–6511.
[13] H. Amii, Y. Hatamoto, M. Seo, K. Uneyama, J. Org. Chem. 66 (2001) 7216–7218.
[14] (a) W.R. Dolbier Jr., M.A. Asghar, H.-Q. Pan, L. Celewicz, J. Org. Chem. 58 (1993) 1827–1830;
(b) W.R. Dolbier Jr., X.X. Rong, Y. Xu, W.F. Beach, J. Org. Chem. 62 (1997) 7500–7503;
(c) W.R. Dolbier Jr., J.-X. Duan, A.J. Roche, Org. Lett. 2 (2000) 1867–1869;
(d) H.H. Wenk, W. Sander, A. Leonov, A. de Meijere, Eur. J. Org. Chem. (1999) 3287–3290.