REGIOSELECTIVE RING-OPENING FLUORINATION OF OXETANES WITH SILICON TETRAFLUORIDE†

Makoto Shimizu[a] *, Shigekazu Kanemoto,[b] and Yuko Nakahara[b]

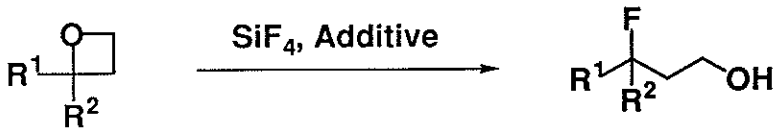
[a]Department of Chemistry for Materials, Mie University, Tsu, Mie 514-8507, Japan

[b]The Institute of Physical and Chemical Research (Riken), Wako, Saitama 351-0198, Japan

†*This paper is dedicated to Professor Teruaki Mukaiyama in recognition of his significant contributions to organic synthesis*

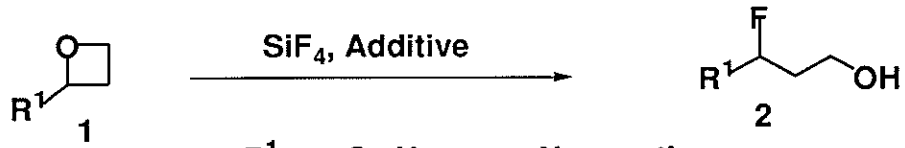
Abstract - Oxetanes were regioselectively cleaved with silicon tetrafluoride to give γ-fluoro alcohols in good yields, in which effects of additives and stereoselectivities were investigated.

Although oxetanes are readily accessible using a variety of synthetic methods and have received considerable attentions as useful C-3 building blocks,[1] their use as substrate for fluorination is limited because of relatively low electrophilicity of the oxetane ring.[2] We have already published that silicon tetrafluoride is a useful reagent for the ring-opening fluorination of oxiranes to give β-fluoro alcohols.[3] In the present study we have found that silicon tetrafluoride is also good fluorination reagent for oxetanes, and wish to describe herein a facile synthesis of γ-fluoro alcohols.



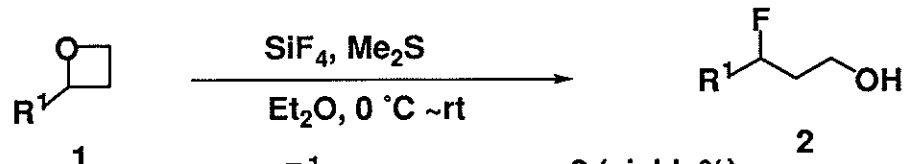
1 2

Initial examination into the ring-opening fluorination of the oxetane (**1a**) met with recovery of the starting materials under a variety of reaction conditions studied for the fluorination of oxiranes (in the presence of *i*-Pr_2NEt, Me_2S, *n*-Bu_4NF, or H_2O).[3] This may be due to the less cation stabilizing ability of the dodecyl group attached to the oxetane, and therefore, the phenyl-substituted analogue (**1b**) was next examined. As expected, this substrate underwent ring-opening fluorination reaction with SiF_4-Me_2S in ether to give γ-fluoro alcohol (**2b**) in 70% yield as the sole product.[4]



a: R^1 = *n*-$C_{11}H_{23}$ No reaction
b: R^1 = Ph 70%

Other mono-substituted oxetanes (**1c** ~ **f**) were examined under the same conditions found for the ring-opening fluorination of 2-phenyloxetane (**1b**) (*vide infra*).

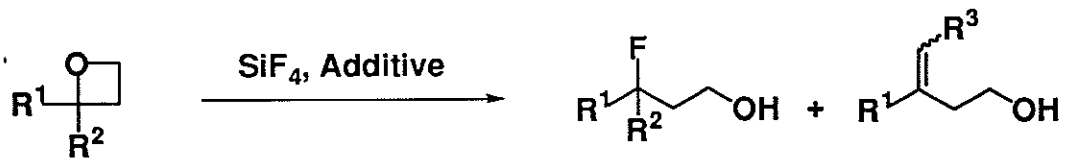


R^1	2 (yield, %)
c: *trans*-PhCH=CH	Complex
d: *trans*-C_5H_{11}CH=CH	Complex
e: PhC≡C	52
f: *n*-C_6H_{13}C≡C	65

While alkene-substituted derivatives (**1c**, **d**) did not give the desired fluorinated products but rather complicated reaction mixtures were obtained, alkyne-substituted oxetanes (**1e**, **f**) underwent ring-opening fluorination reaction to give γ-fluoro alcohols in good yields. This may be due to the susceptibility of alkenes to acid catalyzed polymerization.

In the cases with 2,2-disubstituted oxetanes, the reaction conditions for the desired regioselective ring-opening fluorination were relatively tricky, and olefinic compounds were obtained as by-products which were, however, always readily separable by chromatography on silica gel. Results are summarized in Table 1.

The ring-opening fluorination reaction was highly influenced by the additive. In the presence of TBAF in ether the reaction gave the desired fluorinated product in good yield, whereas the reaction did not afford the ring-opened product in the presence of *i*-Pr_2NEt / H_2O, which effected the ring-opening fluorination of epoxides previously reported. In the case of the aliphatic oxetane (**1h**), the reaction was also highly



g: R^1 = Ph, R^2 = CH_3, R^3 = H
h: R^1 = R^2 = *n*-C_5H_{11}, R^3 = *n*-C_4H_9

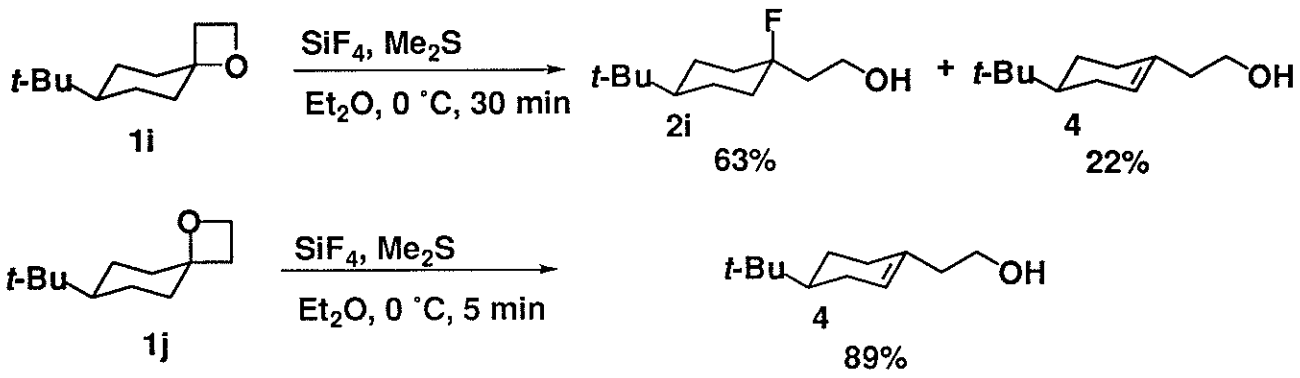
Table 1 Ring-opening Fluorination of 2,2-Disubstituted Oxetanes.[a]

Entry	Oxetane	Additive	Solvent	Yield/%[b]	2:3[c]
1	**1g**	*n*-Bu_4NF	Et_2O	78	83 : 17
2	**1g**	*i*-Pr_2NEt	$ClCH_2CH_2Cl$	67	67 : 33
3	**1g**	*i*-Pr_2NEt / H_2O	Et_2O	0	- : -
4	**1h**	None	Et_2O	88	66 : 34
5	**1h**	Ph_3P	Et_2O	87	70 : 30
6	**1h**	Ph_3P / CCl_4	Et_2O	92	71 : 29
7	**1h**	$Ph_2PCH_2CH_2PPh_2$	Et_2O	85	51 : 49
8	**1h**	Me_2S	Et_2O	89	78 : 22
9	**1h**	DMF	Et_2O	69	29 : 71
10	**1h**	*i*-Pr_2NEt	$ClCH_2CH_2Cl$	70	10 : 90

a) The reaction was carried out according to the typical experimental procedure. b) Isolated yields. c) Based on isolated materials.

dependent on the additive and solvent. In 1,2-dichloroethane, formation of the olefin (**3h**) predominated, whereas fluorinated compound was obtained as a major product in ether even in the absence of the additive.

The structural effect of oxetane ring on the formation of olefinic product was next examined using the oxaspiro type derivative (**1i**, **j**) under rigorously anhydrous conditions. The oxetane (**1i**) possessing the equatorial oxygen gave the fluoride (**2i**) as a major product, whereas the axial counterpart (**1j**) afforded the elimination product (**4**) as the sole product.



These examples indicated that the present fluorination proceeded mostly *via* an S_N2 type attack of the fluoride ion from the back side of the oxetane oxygen, and therefore, in the case of the oxetane (**1j**), the *trans*-diaxial orientation of the alkoxy and a hydrogen made the elimination more favorable, leading to the formation of the olefin (**4**).

Ring-opening fluorination of oxetanes studied here provides a rapid access to γ-fluoro alcohols in good yield. The fluorination was often affected by the formation of elimination product formed under the

influence of the characteristic features of fluoride ion as a base. This type of by-product formation was suppressed in part by the addition of a certain additive in the fluorination media.

REFERENCES AND NOTES

1. a) G. Büchi, J. T. Kofron, E. Koller, and D. Rosenthal, *J. Am. Chem. Soc.*, 1956, **78**, 876. J. D. Coyle and H. A. Carless, *J. Chem. Soc. Rev.*, 1972, **1**, 465. J. A. Porco, Jr. and S. L. Schreiber, in Comprehensive Organic Synthesis, ed. by B. M. Trost and I. Fleming, Vol. 5, pp. 151-192, Pergamon Press, Oxford, 1991, and the references therein. b) H. B. Henbest and B. B. Millard, *J. Chem. Soc.*, 1960, 3575. c) S. C. Welch and A. S. C. Prakasa Rao, *J. Am. Chem. Soc.*, 1979, **101**, 6135. K. Okuma, Y. Tanaka, S. Kaji, and H. Ohta, *J. Org. Chem.*, 1983, **48**, 5133. K. Okuma, K. Nishimura,and H. Ohta, *Chem. Lett*, 1984, 93. W. L. Brown and A. G. Fallis, *Can. J. Chem.*, 1987, **65**, 1828. d) M. Shimizu, R. Ando, and I. Kuwajima, *J. Org. Chem.*, 1981, **46**, 5246. M. Shimizu, R. Ando, and I. Kuwajima, *Ibid.*, 1984, **49**, 753.
2. J. Colonge and P. Rochas, *Bull. Soc, Chim. Fr.*, 1948, 818, 822, 825, 827. S. Searles, *J. Am. Chem. Soc.*, 1954, **76**, 2313.
3. M. Shimizu and H. Yoshioka, *Tetrahedron Lett.*, 1988, **29**, 4101. M. Shimizu and H. Yoshioka, *Heterocycles*, 1988, **27**, 2527. M. Shimizu and H. Yoshioka, *Tetrahedron Lett.*, 1989, **30**, 967. See also, M. Shimizu, Y. Nakahara,and H. Yoshioka, *J. Chem. Soc., Chem. Commun.*, 1989, 1881. M. Shimizu, *Encyclopedia of Reagents for Organic Synthesis*, 1995, Vol. 6, pp. 4442-4444. M. Shimizu, Y. Nakahara, and H. Yoshioka, *J. Fluorine Chem.*, in press.
4. A typical procedure for the ring-opening fluorination of oxetane is as follows: Into a 30 mL round-bottomed flask equipped with a balloon filled with SiF_4 were added ether (3 mL) and Me_2S (37 μL, 0.5 mmol) successively. To it was added a solution of oxetane (**1**) (0.5 mmol) in ether (2 mL) at 0 °C, and the mixture was stirred at that temperature for 1 h. Aqueous KF solution (5 mL) was added and the normal work-up followed by separation on silica gel TLC gave γ-fluoro alcohol (**2**).

Received, 13th April, 1999