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Tetrahedron Letters 44 (2003) 8513–8518

TETRAHEDRON LETTERS

Reaction of tertiary cyclopropyl silyl ethers with diethylaminosulfur trifluoride: the effects of substituents on the cleavage of the cyclopropane ring

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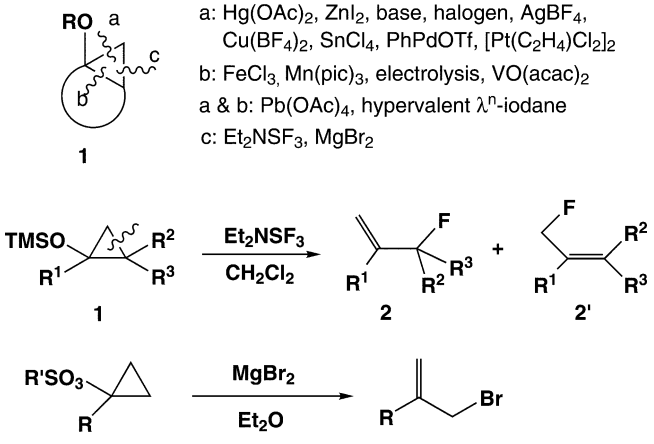
Received 9 July 2003; revised 1 September 2003; accepted 5 September 2003

Abstract—The reaction of tertiary cyclopropanol silyl ethers with diethylaminosulfur trifluoride usually causes ring opening to produce allylic fluorides. However, cyclopropyl silyl ethers bearing a strong electron-donating substituent at C1 or an electron-withdrawing substituent at C2 do not afford allylic fluorides but fluorocyclopropanes. It has also been proved that an electron-donating substituent at C2 of the tertiary cyclopropanol silyl ethers promotes ring opening in the reaction with diethylaminosulfur trifluoride.

Tertiary cyclopropyl systems (**1**) are important synthetic intermediates due to their high reactivity.[1] Several methods have been developed to achieve specific cleavage at bond 'a' or 'b'.[2,3] The methods of bond cleavage at both 'a' and 'b' have been reported by Rubottom[4] and ourselves.[5] We have also reported that the reaction of **1** with diethylaminosulfur trifluoride (DAST)[6] causes ring fragmentation at bond 'c' to provide allylic fluorides.[7] Allylic bromides or chlorides have been synthesized from the reaction of tertiary cyclopropoxy sulfonates with metal halides (magnesium bromide etc.) by Kulinkovich (Scheme 1).[8†]

The plausible mechanism of the reaction of DAST with **1** is shown in Scheme 2. This reaction proceeds through allylic cations (**A** and **A′**) which are produced by the elimination of the oxygen functionality from **1**.

In most cases, **1** reacted with DAST to afford allylic fluorides (**2** and/or **2′**), whereas substrates bearing a strong electron-donating substituent at C1 only gave a fluorocyclopropane (**3**).[9] In this case, the strong electron-donating substituent stabilized the cyclopropyl cation (**B**) derived from **1**, and hence **B** could survive long enough to react with the fluoride ion.



Scheme 1.

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† Some stereochemical and kinetic studies of 'c' bond cleavage of **1** have been reported by several groups.[1b]

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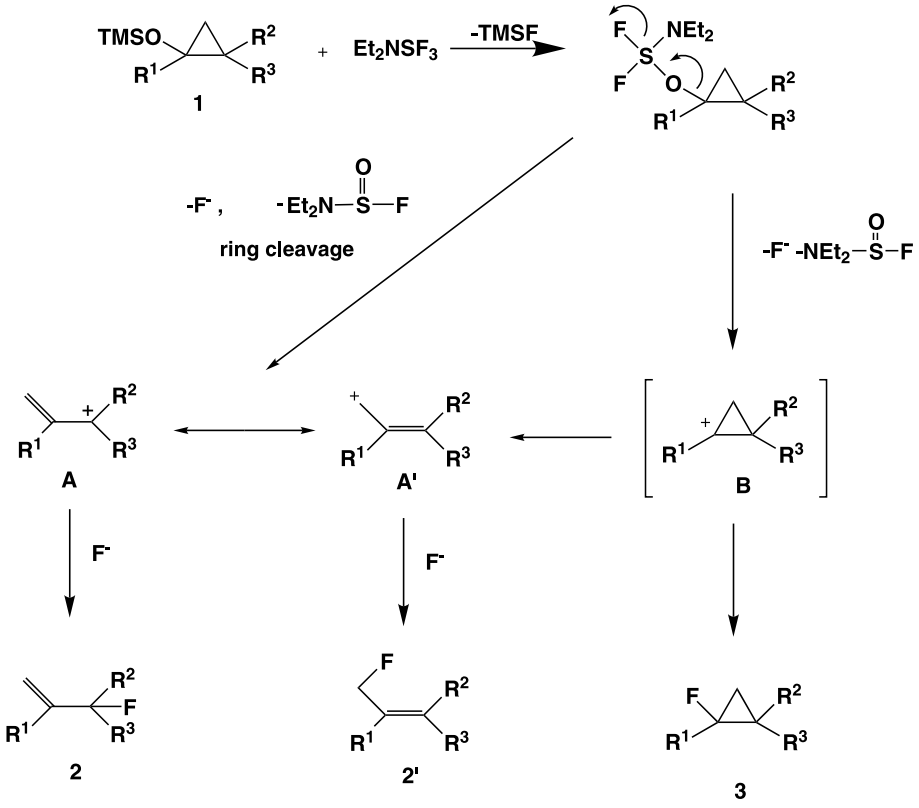
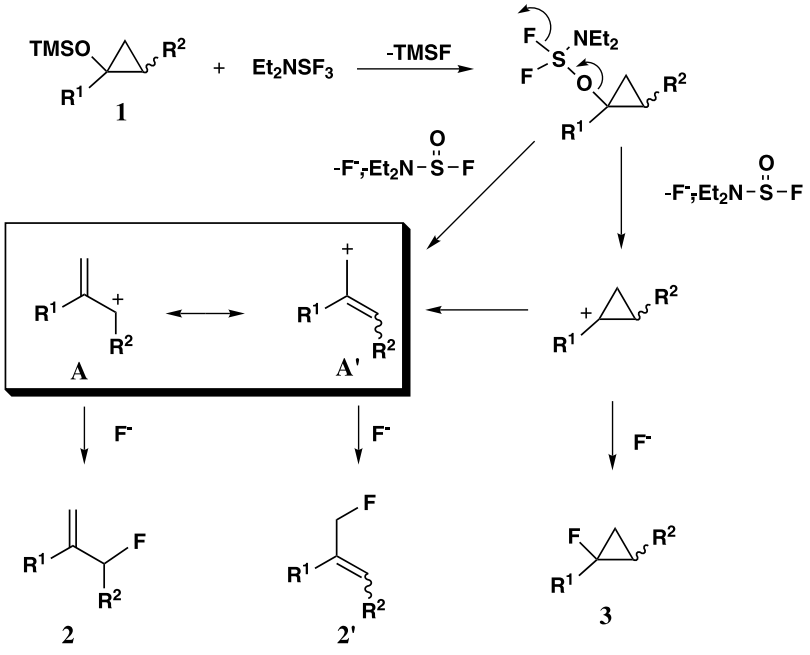
doi:10.1016/j.tetlet.2003.09.089



Scheme 2.

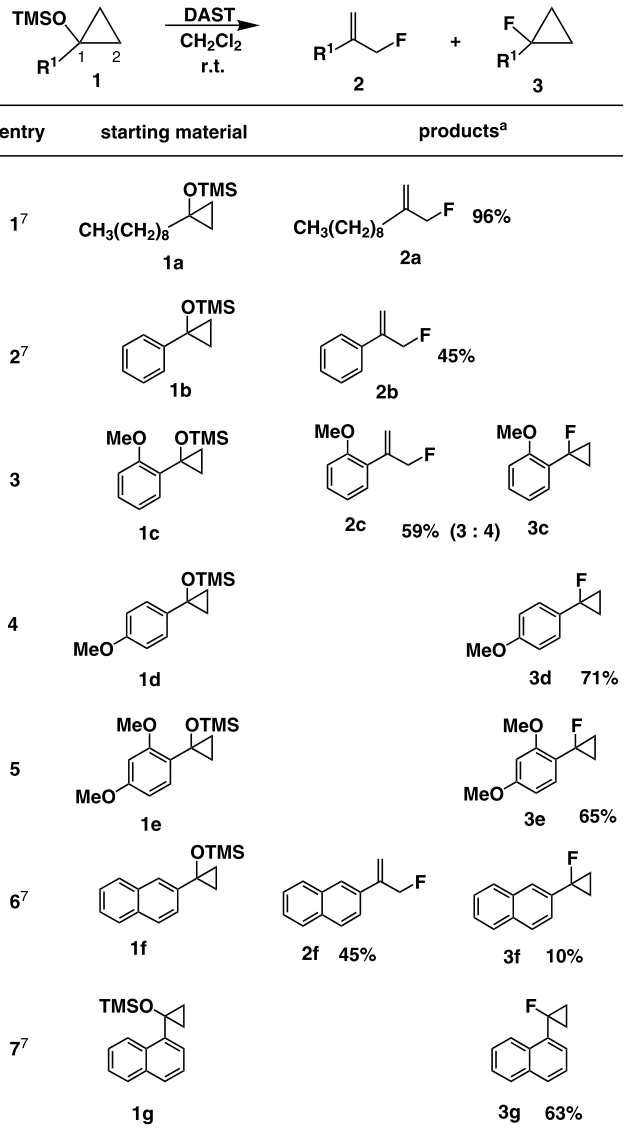


Scheme 3.

We further examined the reaction of several kinds of **1** with DAST and found that the electronic property of the substituents on the cyclopropane ring of **1** influenced the reactivity for the cleavage of cyclopropane ring. We would now like to report the results of this study.

First, we investigated the effect of the C1 substituent of **1** on the reaction. Tertiary cyclopropylsilylethers (**1a**–**g**) were treated with DAST in dichloromethane and the results are shown in Table 1. In all cases, allylic fluorides and/or fluorocyclopropanes were effectively obtained. The difference in yield mainly depends on the stability of the products during the silica-gel column chromatography. As we expected, the tendency for the cleavage of a cyclopropane ring decreased further with an increase in the electron donating ability of the substituent on C1. For example, (**1b**) having the phenyl group, which is a relatively weak electron releasing group, afforded only an allylic fluoride (**2b**) (entry 2). On the other hand, **1e** having the 2,4-dimethoxyphenyl group, which is a strong electron releasing group, furnished only fluorocyclopropane (**3e**) (entry 5). The compound (**1c**) bearing the 2-methoxyphenyl group, whose electron donativity is between phenyl and 2,4-dimethoxyphenyl, produced a mixture of allylic fluoride (**2c**) and fluorocyclopropane (**3c**) (entry 3).

Table 1.



[a]All compounds were characterized on the basis of their mass, IR, ^{1}H and ^{19}F-NMR spectral data. The ratio of the products was determined on the basis of their ^{1}H and ^{19}F-NMR spectral data.

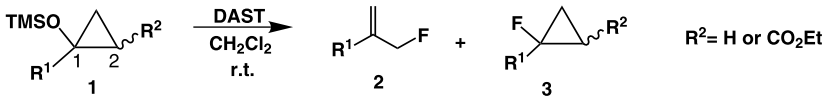
We then examined the reaction of DAST with **1** having an electron-withdrawing substituent (CO_2Et) at C2. We summarized these results in Table 2 and also showed the results of the reaction with **1** having no substituent at C2 for comparison. Interestingly, fluorocyclopropanes are the only products for **1** having the CO_2Et group at C2 (entries 2, 4, 6, 8, 10 and 12).[‡] These results are in sharp contrast to the reaction of DAST with tertiary cyclopropylsilylethers which have no substituents at C2 (entries 1, 3, 5 and 9). The reaction of **1** containing an electron-attracting group at C2 with DAST must be a good method to synthesize the fluorocyclopropanes. As noted in entry 12, the *cis*-isomer (**1m**) gave a mixture of the *cis*- and *trans*-fluorocyclopropanes (**3m**). This result confirms that the reaction proceeds through a cyclopropyl cation intermediate.

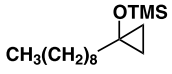
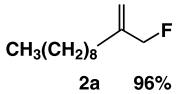
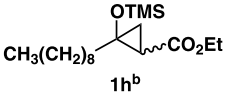
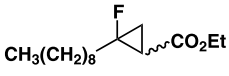
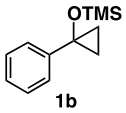
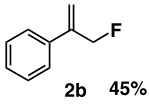
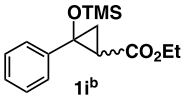
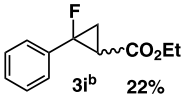
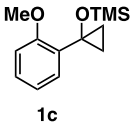
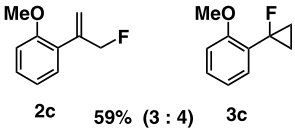
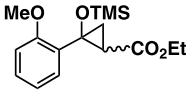
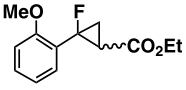
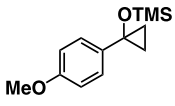
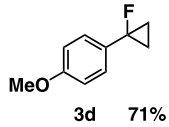
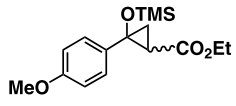
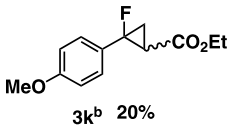
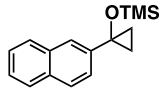
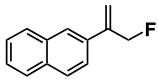
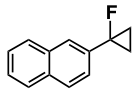
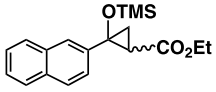
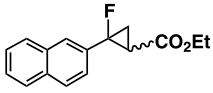
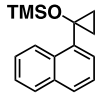
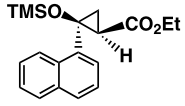
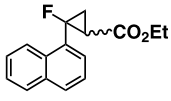
We next investigated the reaction of DAST toward **1** bearing an electron-releasing substituent (Me or Ph) at C2 and found that allylic fluorides were obtained in all cases (Table 3).[‡] Even if **1** had a strong electron-releasing group at C1, no fluorocyclopropane was produced (entries 2, 3 and 6). These results are contrary to the results of **1** having an electron-withdrawing substituent.

Our results suggest that the electronic property of the substituents at C2 strongly affects the reactivity of the cyclopropane ring in **1**. We depicted the plausible reaction mechanism of **1** containing a substituent at C2 in Scheme 3. Since the electron-donating group at C2 can stabilize the allylic cation (**A**), the cleavage of the cyclopropane ring is stimulated. On the other hand, the electron-accepting group at C2 destabilizes the allylic cation (**A**), and the cyclopropyl cation can survive long enough to react with the fluoride ion. Further details of this reaction are currently under investigation.

[‡] Since some products (**2**, **3**) were unstable to silica gel column chromatography, the isolated yields of the products were very low in some cases. The unstable compounds easily decomposed to afford complex mixtures. We measured the ^{1}H NMR of the crude products and confirmed that the desired products (**2**, **3**) were effectively obtained.

Table 2.



entry	starting material	products[a]
1[7]	 1a	 2a 96%
2	 1h[b]	 3h[b] 22%
3[7]	 1b	 2b 45%
4	 1i[b]	 3i[b] 22%
5	 1c	 2c 59% (3 : 4) 3c
6	 1j[b]	 3j[b] 25%
7	 1d	 3d 71%
8	 1k[b]	 3k[b] 20%
9[7]	 1f	 2f 45%  3f 10%
10	 1l[b]	 3l[b] 84%
11[7]	 1g	 3g 63%
12	 1m	 3m 45% 3:2 mixture of stereoisomers

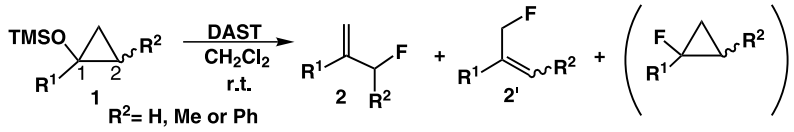
[a] All compounds were characterized on the basis of their mass, IR, ^{1}H and ^{19}F-NMR spectral data. The ratio of the products was determined on the basis of their ^{1}H and ^{19}F-NMR spectral data.

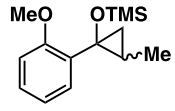
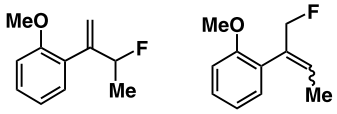
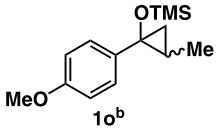
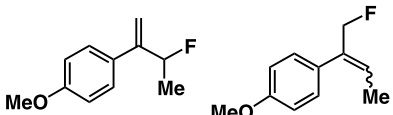
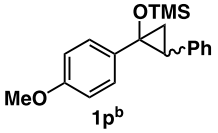
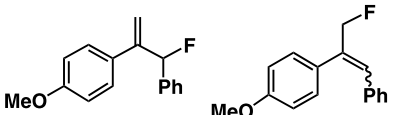
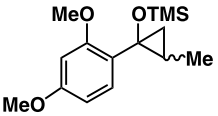
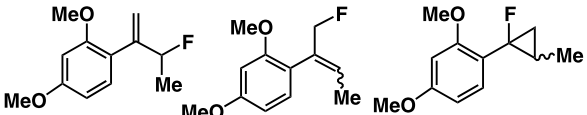
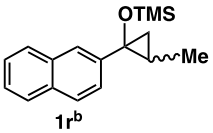
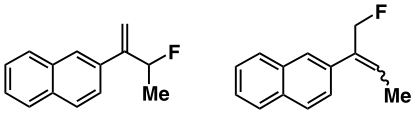
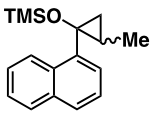
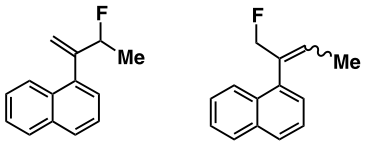
[b] 1:1 mixture of stereoisomers.

References

1. Reviews: (a) Kuwajima, I.; Nakamura, E. *Top. Curr. Chem.* **1990**, *155*, 1–39; (b) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597–2632.
2. Specific 'a'-bond cleavage: (a) Murai, S.; Aya, T.; Renge, T.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1974**, *39*, 858–859; (b) Rubottom G. M.; Lopez, M. I. *J. Org. Chem.* **1973**, *38*, 2097–2099; (c) Conia J. M.; Girard, C. *Tetrahedron Lett.* **1973**, *14*, 2767–2770; (d) Murai, S.; Seki, Y.; Sonoda, N. *J. Chem. Soc. Chem. Commun.* **1974**, 1032–1033; (e) Ryu, I.; Matsumoto, K.; Ando, M.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1980**, *21*, 4283–4286; (f) Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 7192–7194; (g) Ryu, I.; Matsumoto, K.; Kameyama, Y.; Ando, M.; Kusumoto, N.; Ogawa, A.; Kambe, N.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1993**, *115*, 12330–12339; (h) Ryu, I.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1986**, *51*, 2389–2391; (i) Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1988**, *110*, 3296–3298; (j) Ikura, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 1520–1521.
3. Specific 'b'-bond cleavage: (a) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073–2074; (b) Lewicka-Piekut S.; Okamura, W. H. *Synth. Commun.* **1980**, *10*, 415–420; (c) Blanco, L.; Mansouri, A. *Tetrahedron Lett.* **1988**, *29*, 3239–3242; (d) Booker-Milburn, K. I. *Synlett*, **1992**, 809–810; (e) Booker-Milburn K. I.; Thompson, D. F. *Synlett* **1993**, 592–594; (f) Torii, S.; Okamoto T.; Ueno, N. *J. Chem. Soc. Chem. Commun.* **1978**, 293–294; (g) Iwasawa,

Table 3.



entry	starting material	products[a]
1	 1n[b]	 2n quant. (2:1) 2'n[b]
2	 1o[b]	 2o 80% (2:1) 2'o[b]
3	 1p[b]	 2p 52% (2:1) 2'p[b]
4	 1q[b]	 2q 65% (5:4:1) 2'q[b] 3q[b]
5	 1r[b]	 2r 29% (2:1) 2'r[b]
6	 1s[b]	 2s 72% (2:1) 2's[b]

[a]All compounds were characterized on the basis of their mass, IR, ^{1}H and ^{19}F-NMR spectral data. The ratio of the products was determined on the basis of their ^{1}H and ^{19}F-NMR spectral data.

[b] 1:1 mixture of stereoisomers.

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