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Reaction of tertiary cyclopropyl silyl ethers with diethylaminosulfur trifluoride. Part 2: The Friedel–Crafts allylation and cyclopropylation of electron-rich aromatic compounds

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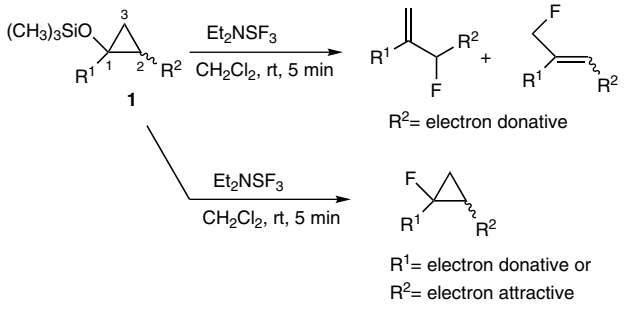
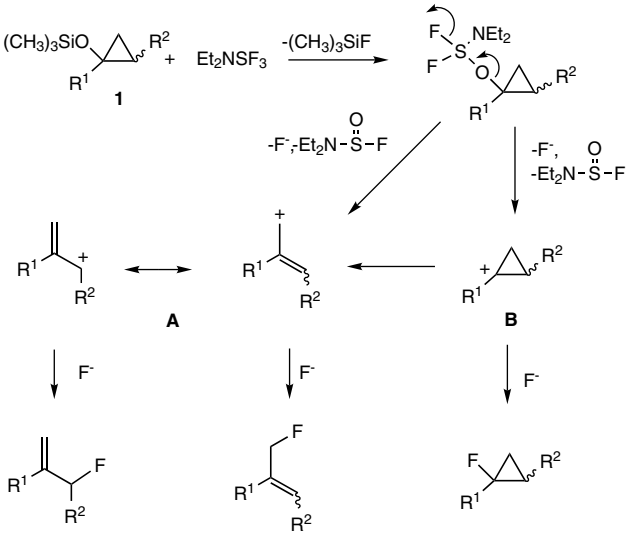
Abstract—The reaction of tertiary cyclopropyl silyl ethers with diethylaminosulfur trifluoride in electron-rich aromatic compounds causes the Friedel–Crafts alkylation to produce allylated or cyclopropylated aromatic compounds.

Tertiary cyclopropyl systems (**1**) are important synthetic intermediates due to their high reactivity and many synthetic methods utilizing **1** have been developed.[1] We previously reported that the reaction of **1** with diethylaminosulfur trifluoride (DAST) causes ring opening to produce an allylic fluoride.[2] We also found that **1** bearing a strong electron-donating substituent at C1 or an electron-withdrawing substituent at C2 does not afford allylic fluorides, but fluorocyclopropanes.[3] It has also been proved that an electron-donating substituent at C2 of **1** promotes ring opening during the reaction with DAST[3] (Scheme 1).



Scheme 1.

This reaction proceeds through carbocation intermediates (allylic cation or cyclopropyl cation) as shown in Scheme 2. In the case of **1** having a strong



Scheme 2.

Keywords: Cyclopropyl silyl ether; Diethylaminosulfur trifluoride; Friedel–Crafts allylation; Friedel–Crafts cyclopropylation.
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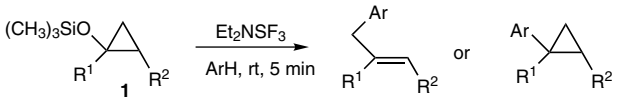
electron-donating substituent at C1, the substituent stabilizes the cyclopropyl cation (**B**) derived from **1**, and therefore, **B** can survive long enough to react with the fluoride ion. Since the electron-donating group at C2 can stabilize the allylic cation (**A**), the ring opening is enhanced. On the other hand, the electron-accepting group at C2 destabilizes the allylic cation (**A**), and the cyclopropyl cation (**B**) survives long enough to react with the fluoride ion[3] (Scheme 2).

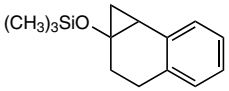
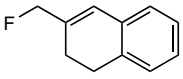
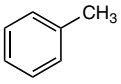
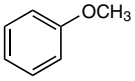
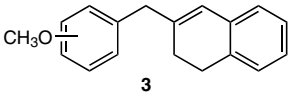
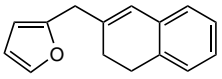
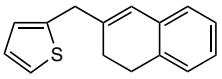
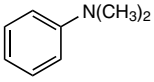
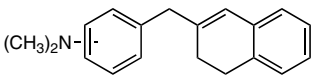
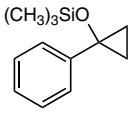
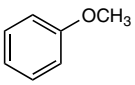
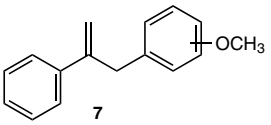
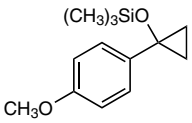
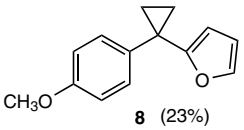
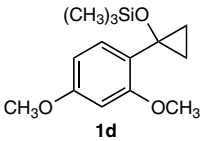
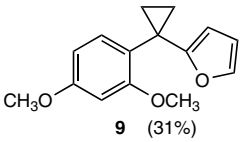
In this letter, we report that the reaction of DAST with **1** in an electron-rich aromatic compound as the solvent causes Friedel–Crafts allylation or cyclopropylation of the aromatic compound (Scheme 3).



Scheme 3.

The results of this reaction are shown in Table 1. Initially, we examined the reaction of DAST with **1a** in benzene or toluene; however, the allylic fluoride (**2a**) was obtained as the sole product. These aromatic compounds are not electron rich enough to react with a carbocation intermediate. Therefore, we then evaluated the reaction of DAST with **1a** in electron-rich aromatic

Table 1.

1	ArH	Products
 **1a**		 **2a** (36%)
1a		**2a** (21%)
1a		 **3** *o*-isomer (7%) *p*-isomer (88%)
1a		 **4** (95%)
1a		 **5** (67%)
1a		 **6** (64%) mixture of *o*- and *p*-isomers
 **1b**		 **7** *o*-isomer (11%) *p*-isomer (44%)
 **1c**		 **8** (23%)
 **1d**		 **9** (31%)

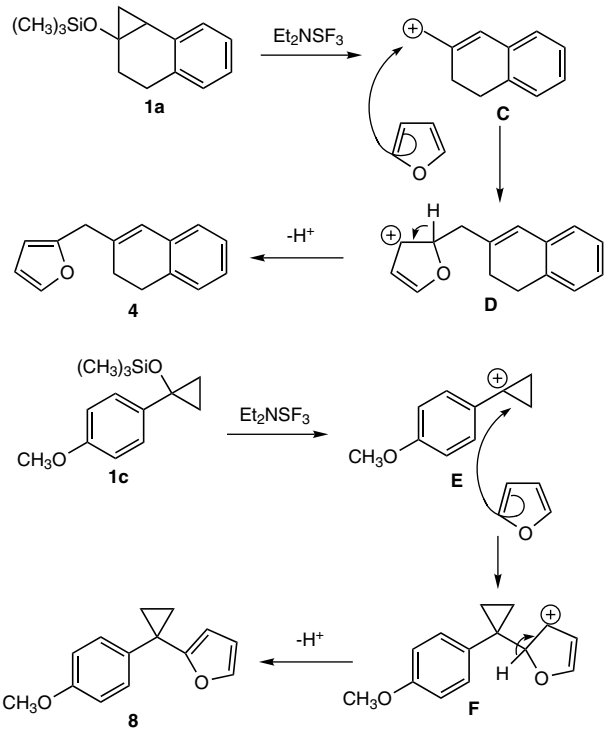
compounds such as anisole, furan, thiophene, or *N*,*N*-dimethylaniline. In all cases, the major products were allylated aromatic compounds (**3**–**6**). Anisole was also allylated during the reaction of **1b** with DAST to give the product (**8**) as a mixture of *o*- and *p*-isomers. The reaction of **1c** and **1d** bearing a strongly electron-donating group at C1 with DAST in furan provided cyclopropyl compounds (**8**, **9**), respectively. The isolated yields of **8** and **9** were not high because the fluorocyclopropane and an unidentified complex mixture were also obtained.

The reaction of **1a** with DAST was attempted for the synthesis of **4** by use of a mixed solvent of dichloromethane and furan.[4] The results of this reaction are shown in Table 2. This reaction gave monosubstituted compound (**4**) and bisubstituted compound (**10**) in all cases, and the yields of **4** decreased with a decrease in the amount of furan in the solvent.

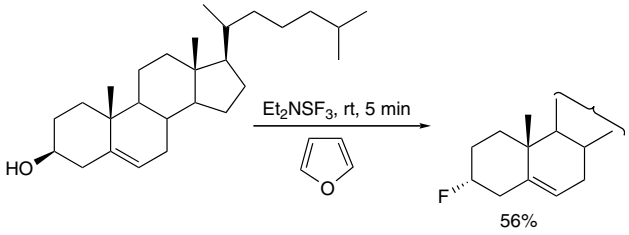
The plausible reaction mechanisms are shown in Scheme 4 with **1a** and **1c** as examples. In the case of **1a**, DAST reacts with **1a** to afford the allylic cation (**C**), and an aromatic compound attacks **C**. The proton was eliminated from the resulting adduct (**D**) to give the aromatized product (**5**). In the case of **1c**, DAST reacts with **1c** to provide the cyclopropyl cation (**E**) and **E** proceeds through a similar mechanism of **C** to afford the product (**8**). The cyclopropyl silyl ethers (**1c**,**d**) have an electron-rich aromatic moiety in their own structure; therefore, they could react with the cyclopropyl cation to afford the complex mixture.

It has been known that DAST generally reacts with alcohols via an S_N2 or S_Ni mechanism.[5] In these cases, the reaction of DAST with alcohols was expected not to react with aromatic compounds but with the fluoride ion. Actually, the treatment of cholesterol with DAST in furan provided only the fluorinated compound (Scheme 5). This result is in sharp contrast to the reaction of DAST with the cyclopropyl silyl ethers (**1**) in an electron-rich aromatic compound.

In conclusion, the reaction of **1** with DAST in an electron-rich aromatic compound causes Friedel–Crafts allylation or cyclopropylation of the aromatic compound.

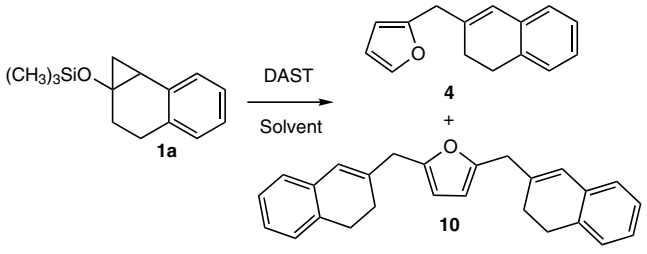


Scheme 4.



Scheme 5.

Table 2.



Run	Solvent	Products (%)	
	CH_2Cl_2 (2 ml) in Furan (equiv)	**4**	**10**
1	1.0	28	20
2	2.0	50	17
3	5.0	67	12

The general experimental procedure is as follows: To a solution of cyclopropyl silyl ether (0.5 mmol) in an aromatic compound (2 ml) was added DAST (1.5 mmol) at room temperature under an inert atmosphere, and the reaction mixture was stirred for 30 min. Saturated aqueous sodium bicarbonate was added to the reaction mixture and the resulting mixture was extracted with ethyl acetate. The extract was washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated to afford the crude product. Chromatography on silica gel gave a pure sample.

References and notes

1. Reviews: (a) Murai, S.; Ryu, I.; Sonoda, N. *J. Organomet. Chem.* **1983**, *250*, 121–133; (b) Kuwajima, I.; Nakamura, E. *Top. Curr. Chem.* **1990**, *155*, 1–39; (c) Ryu, I.; Murai, S. In *Methoden der Organisches Chemie (Houben-Weyl)*;

deMeijere, A., Ed.; Georg Thieme: New York, 1997; Vol. E17, pp 1985–2040; (d) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597–2632.
2. Kirihara, M.; Kambayashi, T.; Momose, T. *Chem. Commun.* **1996**, 1103–1104.
3. Kirihara, M.; Kakuda, H.; Tsunooka, M.; Shimajiri, A.; Takuwa, T.; Hatano, A. *Tetrahedron Lett.* **2003**, *44*, 8513–8518.
4. To a solution of cyclopropyl silyl ether (0.5 mmol) in a mixed solvent of dichloromethane (2 ml) and furan (0.5, 1.0, or 2.5 mmol) was added DAST (1.5 mmol) at room temperature under an inert atmosphere, and the reaction mixture was stirred for 30 min. The reaction mixture was worked up and purified as described in the general experimental procedure of the text.
5. Hudlicky, M. *Org. React. (N.Y.)* **1988**, *35*, 513–637.