Oxidative Generation of 2-(Trifluoromethyl)- and 2-(Chlorodifluoromethyl)allylic Cations and Its Synthetic Application[1]

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Oxidative generation of allylic cations having strong electron-withdrawing CF_3 and CF_2Cl groups from 2-(trifluoromethyl)- and 2-(chlorodifluoromethyl)allylsilanes was successfully carried out for the first time. The generated cation was trapped with nucleophiles such as arenes and acetonitrile.

Studies on electronegatively substituted carbocations are important from both mechanistic and synthetic aspects.[2] Since a CF_3 group is one of the most potent electron-withdrawing groups, α-CF_3 substituted carbocations should be highly destabilized. Furthermore, compounds having a CF_3 group are highly useful for the preparation of pharmaceuticals, agrochemicals, and functional materials.[3] Therefore, great efforts have been made for the generation of α-CF_3 carbocations and their synthetic utilization so far.[2] Recently, we found that anodic oxidation was quite effective for the generation of α-CF_3 cations stabilized by adjacent sulfur,[4] nitrogen,[5] or selenium atoms.[6] On the other hand, Yoshida[7] and we[8] first demonstrated generation of allylic cations using anodically oxidizable umpolung of the corresponding allylsilanes.

These facts prompted us to investigate electrochemical and chemical oxidative generation of 2-(trifluoromethyl)- and 2-(chlorodifluoromethyl)allylic cations **3** and **4** from 2-(trifluoromethyl)- and 2-(chlorodifluoromethyl)allylsilanes **1** and **2** in the presence of nucleophiles. There has been no example of successful generation of such 2-(fluoromethyl)allylic cations so far although the generation of perfluoroanalogue of **3**[9] and various α-CF_3 substituted carbocations have been attempted.[2]

Anodic oxidation (constant current, 2 × 96480 C mol^{-1}) of **1** was first carried out at platinum electrodes in Et_4NOTs/MeCN using an undivided cell. However, only trace amount of acetamidation product **5** was detected from the electrolytic solution by mass spectrometry [m/z 167 (M^+), 125 ($CH_2{=}C(CF_3)CH_2NH_2^+$), 109 (M^+-CH_3CONH), 69 (CF_3^+)]. In this case, no tosylation product was formed at all.

Since electrochemical oxidation was not effective for the generation of such allylic cation, we employed chemical oxidation using a strong oxidizing reagent, $Tl(OCOCF_3)_3$, which has been used for the generation of nonfluorinated allylic cation from simple allylsilane.[10] Oxidation of **1** was attempted using two equiv. of $Tl(OCOCF_3)_3$ in acetonitrile at room temperature.[11] After overnight reaction, **5** was found to be formed in a reasonable yield as 10 % (Scheme 1).[12] Next, oxidation of **1** and **2** was carried out similarly in the presence of arenes such as benzene and *p*-xylene to provide 2-(trifluoromethyl)- and 2-(chlorodifluoromethyl)allylated benzene derivatives **6** and **7** in relatively good yields (Scheme 2, Table 1).[11,13,14]

Thus, we have demonstrated the first successful oxidative generation of allylic cations having strong electron-withdrawing CF_3 and CF_2Cl groups together with their synthetic application: We have achieved efficient introduction of such 2-(fluoromethyl)allyl groups into arenes in one step, which is difficult to achieve by other method.

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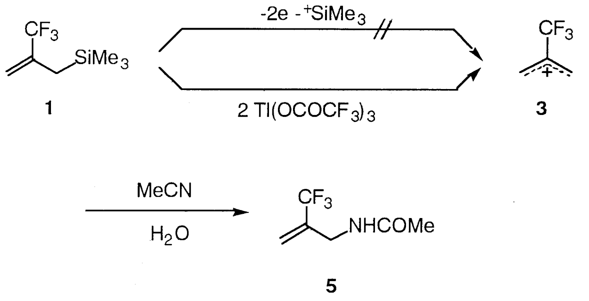
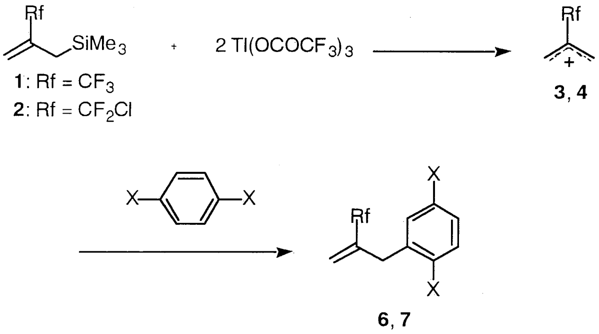


Scheme 1.



Scheme 2.

Table1. Oxidative 2-(fluoromethyl)allylation of arenes

Rf	X	Yield/%
CF_3	H	**6a** 89
CF_2Cl	H	**6b** 64
CF_3	Me	**7a** 82
CF_2Cl	Me	**7b** 75

References and Notes

1 A part of this work is "Electrolytic Reactions of Fluoro Organic Compounds. Part 15." Part 14: Ref. 5.

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11 In the case of nonfluorinated simple allylsilane, one equiv. of $Tl(OCOCF_3)_3$ is enough for the oxidative generation of allylic cation.[10] However, two equiv. of $Tl(OCOCF_3)_3$ were necessary in the cases of **1** and **2**. When one equiv. of $Tl(OCOCF_3)_3$ was used, about 50% of starting **1** and **2** remained and the product yields decreased to about half (for example, **6a**: 89% → 43% yield). This is probably due to extremely high oxidation potentials of **1** and **2** (E_p^{ox}, 2.80 and 2.85 V vs. SCE, respectively) compared with that of simple nonfluorinated allylsilane (E_p^{ox}, 2.29 V).

12 Compound **5**: colorless solid; mp 39.5-41.2 °C; IR 1660 (νC=O) cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.00 (s, 3H), 3.92 (S, 1H), 4.03 (s, 1H), 5.45 (m, 1H), 5.74 (m, 1H), 5.80-6.60 (broad, 1H); HRMS Found: m/z 167.0559 (M^+). Calcd for $C_6H_8F_3NO$: m/z 167.0557.

13 A typical procedure is as follows: To a stirred solution of 6 mmol of $Tl(OCOCF_3)_3$ in benzene or *p*-xylene (100 equiv. to **1** or **2**) was added **1** or **2** (3 mmol) under a nitrogen atmosphere at room temperature. After overnight, the reaction mixture was mixted with brine (30 ml). The resulting precipitates were removed by filtration and the filtrate was extracted with ether (20 ml × 3). The extracts were washed with brine and water, and then dried over anhydrous Na_2SO_4. The products **6** and **7** were isolated by TLC or column chromatography using hexane-AcOEt (20:1) as an elution solvent.

14 Spectral data. **6a**: colorless oil; ^{1}H NMR ($CDCl_3$): δ 3.47 (s, 2H), 5.00 (m, 1H), 5.70 (m, 1H), 6.90–7.50 (m, 5H); MS m/z 186 (M^+), 117 (M^+-CF_3); HRMS Found: m/z 186.0661 (M^+). Calcd for $C_{10}H_9F_3$: m/z 186.0656. **6b**: colorless oil; ^{1}H NMR ($CDCl_3$): δ 3.54 (s, 2H), 4.90 (m, 1H), 5.66 (m, 1H), 6.90-7.60 (m, 5H); MS m/z 204 (M^++2), 202 (M^+), M^+-CF_2Cl); HRMS Found: m/z 204.0322 (M^++2), 202.0355 (M^+). Calcd for $C_{10}H_9ClF_2$: 204.0331 (M^++2), 202.0360 (M^+). **7a**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H), 2.27 (s, 3H), 3.39 (s, 2H), 4.77 (m, 1H), 5.60 (m, 1H), 6.80-7.30 (m, 3H); MS m/z 214 (M^+), 199 (M^+-CH_3), 145 (M^+-CF_3), 105 (M^+-CH_2=C(CF_3)CH_2); HRMS Found: m/z 214.0944. Calcd for $C_{12}H_{13}F_3$: m/z 214.0969.**7b**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H), 2.28 (s, 3H), 3.46 (s, 2H), 4.62 (m, 1H), 5.52 (m, 1H), 6.70-7.20 (m, 3H); MS m/z 232 (M^++2), 230 (M^+), 215 (M^+-CH_3), 145 (M^+-CF_2Cl), 105 (M^+-CH_2=C(CF_2Cl)CH_2); HRMS Found: m/z 232.0644 (M^++2), 230.0691 (M^+). Calcd for $C_{12}H_{13}ClF_2$: m/z 232.0644 (M^++2), 230.0673 (M^+).