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β-Trifluoromethyl-α-functionalized-vinyl sulfides as a potential synthetic intermediate

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ABSTRACT

The β-(trifluoromethyl)vinyl sulfides on treatment with *n*-BuLi/TMEDA at −78 °C were readily lithiated at an α-position of the sulfanyl group, and the generated β-trifluoromethyl-α-sulfanylvinyl anions were reacted with a variety of electrophiles to give the corresponding β-trifluoromethyl-α-functionalized-vinyl sulfides **4aa**–**4aq** in good to excellent yields. The reactivity of some products has been examined. The palladium-catalyzed cross-coupling reaction as well as homo-coupling reaction of **4af** provided the corresponding products in good yields, respectively. The Diels–Alder reaction of cyclic dienes and **14** derived from **4ao** provided the desired six-membered cyclic products with high *endo*-trifluoromethyl group selectivity.

1. Introduction

The significant expansion in the use of fluorinated compounds has drawn much attention to chemists in various fields such as agrochemicals, pharmaceuticals, polymers, and dyes.[1] For example, a great advantage of biologically active fluorinated compounds over non-fluorinated ones is probably considered to appear in its increasing lipophilicity and metabolic stability. Among them, the trifluoromethyl moiety (CF_3) is particularly encountered in many biologically active pharmaceutical and agrochemical compounds presumably due to its intrinsic properties. Therefore, the development of a new methodology for the selective introduction of trifluoromethyl group into readily available promising organic compounds constitutes most important study on organofluorine chemistry.[2] As part of our research to develop versatile fluorinated building blocks,[3] we have interested in the preparation of bifunctionalized olefins containing the trifluoromethyl group. One of the straightforward ways to prepare such olefins seemed to be the introduction of another functional group to trifluoromethylated olefins bearing one functional group in advance. We sought an appropriate scaffolding molecule in view of this strategy.[4] By literature survey we concluded that β-(trifluoromethyl)vinyl sulfide would be the best precursor to our purpose due to its easy availability and promising reactivity.[5] Moreover, the report concerning the preparation of α-sulfanylvinyl anion and its synthetic application also encouraged us to examine this strategy.[6] Although some reactions of vinyl sulfoxide and sulfone have been reported in the literature, no detailed examination has been made in associated research.[7] The preliminary results have been reported in our previous communication.[8] We report here a full account of our studies on the synthesis of various β-trifluoromethyl-α-functionalized-vinyl sulfides from β-(trifluoromethyl)vinyl sulfides and their synthetic applications.

2. Results and discussion

2.1. Synthesis of β-(trifluoromethyl)vinyl sulfides

According to the reported procedure, we found that the simple addition–elimination reaction of 2-bromo-3,3,3-trifluoropropene **1** and thiophenols **2** under basic conditions afforded the corresponding aryl β-(trifluoromethyl)vinyl sulfides **3** in good yields.[5] The reactions smoothly proceeded giving the *E*-isomers preferentially in all cases (Scheme 1). The obtained *E*/*Z*-isomers could be easily separated from each other by column chromatography on silica gel.

2.2. α-Functionalization of β-(trifluoromethyl)vinyl sulfide

Taguchi et al. reported one α-substitution reaction using β-(trifluoromethyl)vinyl sulfone as the related compound, however

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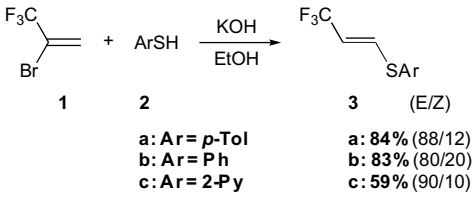
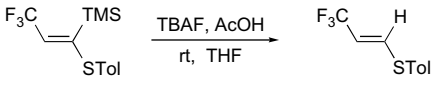


Scheme 1. Preparation of β-(trifluoromethyl)vinyl sulfide **3**.



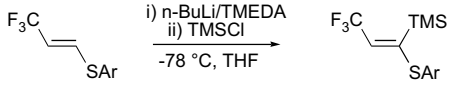
Scheme 2. Desilylation of **4aa** by means of TBAF.

the product yield was reasonable.[4] One the other hand, Takeda et al. reported the successful α-substitution reaction employing (β-methyl or β-phenyl)vinyl sulfides, which lead us to examine **3a** under the similar conditions.[6] Using the reaction of (*E*)-**3a** and TMSCl as a model, we screened reaction conditions (Table 1). The (*E*)-β-trifluoromethyl-α-(*p*-tolylsulfanyl)vinyl anion was generated in situ by addition of *n*-BuLi (1.2 equiv) to a solution of (*E*)-**3a** in the presence of TMEDA (1.2 equiv) in THF at −78 °C, and the resulting anion was treated with TMSCl (1.1 equiv) at this temperature to afford the desired product **4aa** in 82% yield (entry 2).[9] It is noteworthy that the combined use of *n*-BuLi and TMEDA is essential to the successful reaction.[6] The use of *n*-BuLi alone substantially decreased the yield (entry 1). On the contrary to our expectation, the reaction using 2-pyridyl sulfide **3c** gave no desired product and recovered **3c** almost intact (entry 4). This finding suggested that an electron-withdrawing group attached to sulfur atom did not necessarily stabilize the adjacent vinyl anion.

Although it is well accepted that vinyl anions have a tendency toward their configuration with retention to a high degree,[10] we decided to confirm the configuration of the product as follows. We conducted the desilylation–protonation process of the product **4aa** by means of TBAF in the presence of a small amount of acetic acid (Scheme 2). The clean reaction proceeded giving a single product by monitoring the GC–MS analysis of the crude reaction mixture. The structural assignment of this sulfide **3a**′ was performed on the basis of comparison of its ^{1}H NMR spectrum and GC–MS data. The spectrum chart and retention time of **3a**′ were identical with those of the parent sulfide (*E*)-**3a**. We therefore assigned the *E* configuration to the product **4aa**.

Table 2 illustrates the wide generality of this substitution reaction. The reactions with a variety of electrophiles such as chlorosilanes, iodoalkanes, chlorostannane, iodine, thiosulfonates, isocyanate, aldehydes, acyl chloride, cyanoformate, chloroformates proceeded well to provide the corresponding products in good to excellent yields except for acetophenone (entry 13). These results indicate that the β-trifluoromethyl-α-sulfanylvinyl anion should provide useful β-(trifluoromethyl)vinyl compounds in organic synthesis. We therefore present here a facile and efficient protocol for the synthesis of β-trifluoromethyl-α-functionalized-vinyl sulfides. It is noteworthy that the sulfanyl group should play an important role of these substitution reactions in comparison with the corresponding sulfonyl group.[4]

Table 1
Synthesis of (*E*)-aryl β-trifluoromethyl-α-(trimethylsilyl)vinyl sulfide **4**[a]



Entry	Vinyl sulfide	Additive	Product[b] (yield, %)
1	**3a**	None	**4aa** (45)
2	**3a**	TMEDA	**4aa** (82)
3	**3b**	TMEDA	**4ba** (90)
4	**3c**	TMEDA	**4ca** (0)

[a] All reactions were conducted in THF at −78 °C.
[b] Isolated yield.

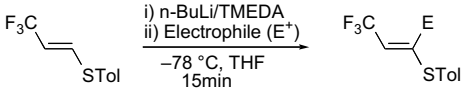
2.3. Synthetic application of β-trifluoromethyl-α-functionalized-vinyl *p*-tolyl sulfides

After having examined the preparation of various β-trifluoromethyl-α-functionalized-vinyl *p*-tolyl sulfides, we embarked on the next study to explore their useful transformation. It is well accepted that fluoride ion initiated allylation of carbonyl compound with allylsilanes.[11] We initially investigated the generation of allyl anion equivalent from vinyl sulfide **4ae** and its subsequent addition reaction to aldehyde (Scheme 3). Thus, to a solution of **4ae** and benzaldehyde in THF was added a catalytic amount of TBAF in THF solution under various conditions. Although complete consumption of **4ae** was observed, no adducts were obtained and benzaldehyde remained intact. Attempts to isolate the main by-product from the reaction mixture gave the difluorobutadiene **5** along with a small amount of contaminants. Although the complete separation of **5** wasn't successful, the structure of **5** was determined by ^{1}H NMR and ^{19}F NMR spectroscopy. The existence of the CF_2=CH– group was confirmed by appearance of two signals of fluorine atoms with typically geminal coupling constants (J=22.9 Hz) and trans and cis coupling of fluorines to single hydrogen atom (J=22.9 and 2.7 Hz, respectively). These results suggested that rapid elimination of the fluoride ion from the generated allyl anion equivalent occurred prior to addition to aldehyde on the contrary to our expectation. On the basis of these findings we preliminary examined the Diels–Alder reaction of **5**.[12] Heating a mixture of **5** and *N*-phenylmaleimide in toluene in a sealed tube at 110 °C for 12 h caused only decomposition of **5**.

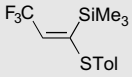
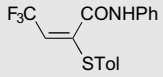
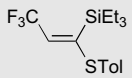
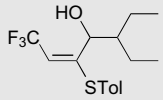
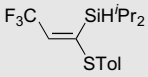
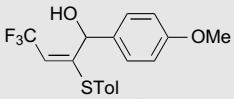
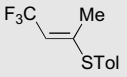
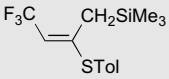
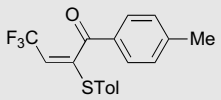
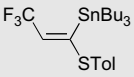
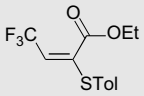
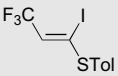
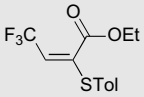
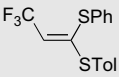
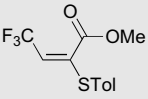
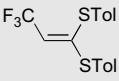
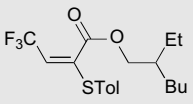
We next briefly investigated the cross-coupling reaction of **4af** having tributylstannyl moiety. After several attempts, according to Corey's procedure of the Stille cross-coupling reaction of vinylstannane and aryl halide,[13] the reaction of **4af** with 4′-iodoacetophenone in the presence of [Pd(PPh_3)$_4$] (5 mol %), LiCl (5 mol %), CuTC (20 mol %) in DMSO at 50 °C for 2 h smoothly proceeded affording the desired cross-coupling product **6** in 87% yield (Scheme 4).

In addition to the cross-coupling reaction of **4af**, the corresponding homo-coupling reaction for the synthesis of bis(trifluoromethyl)butadiene **7** was also attractive for us.[14] Extensive screening of the reaction conditions using $Cu(NO_3)_2\cdot 3H_2O$ revealed that trimethyl orthoformate as a solvent was effective for this homo-coupling reaction.[15] The results are shown in Table 3. Moreover, conducting the homo-coupling reaction at lower temperature improved the product yield (entry 9). On the other hand, the corresponding vinyl chloride **8** and vinyl bromide **9** as a major product, respectively, were obtained in good yield along with a small amount of **7** when we employed $CuCl_2$ or $CuBr_2$ in the presence of $Pd(OAc)_2$ instead of using $Cu(NO_3)_2\cdot 3H_2O$ for this homo-coupling reaction (Scheme 5).[16] These vinyl halides also could be a useful intermediate for the synthesis of trifluoromethyl compounds.

Table 2
Synthesis of β-trifluoromethyl-α-functionalized-vinyl *p*-tolyl sulfide (**4a**)[a]



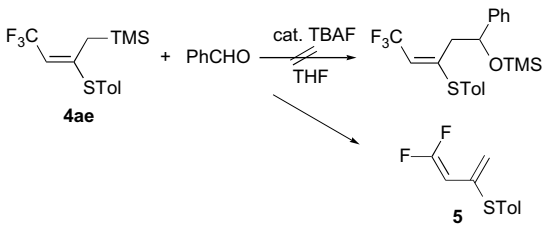
E-**3a** **4a**

Entry	Electrophile	Product	Yield[b] (%)	Entry	Electrophile	Product	Yield[b] (%)
1	Me_3SiCl		**4aa** (82)	10	Phenylisocyanate		**4aj** (54)
2	Et_3SiCl		**4ab** (71)	11	2-Ethylbutanal		**4ak** (98)
3	$^{i}Pr_2HSiCl$		**4ac** (81)	12	Anisaldehyde		**4al** (86)
4	MeI		**4ad** (83)	13	Acetophenone	No reaction	**4am** (0)
5[c]	Me_3SiCH_2I		**4ae** (91)	14	*p*-Toluoyl chloride		**4an** (79)
6	Bu_3SnCl		**4af** (81)	15	Ethyl cyanoformate		**4ao** (60)
7	I_2		**4ag** (91)	16	Ethyl chloroformate		**4ao** (72)
8	$PhSS(O)_2Ph$		**4ah** (95)	17	Methyl chloroformate		**4ap** (75)
9	$TolSS(O)_2Tol$		**4ai** (58)	18	2-Ethylhexyl chloroformate		**4aq** (76)

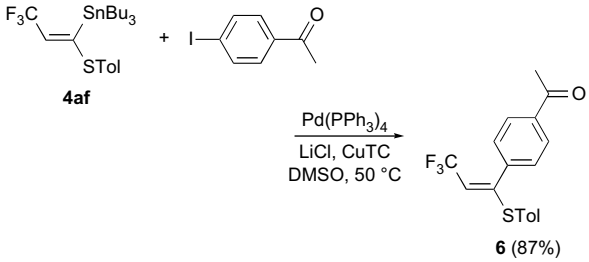
[a] All reactions were conducted using *E*-**3a** (1 equiv) with electrophiles (1.1 equiv) at −78 °C for 15 min.
[b] Isolated yield.
[c] Reaction time was 4 h.

With **7** in hand, we successively examined the thermal Diels–Alder reaction. A toluene solution of **7** and *N*-phenylmaleimide in a sealed tube was refluxed for 12 h then heated up to 180 °C for 6 h. However, no desired cycloadduct was obtained and only a small amount of partially isomerized product derived from **7** was observed by GC–MS analysis in the reaction mixture. This observation suggested that no reactivity of **7** as a diene for the Diels–Alder reaction may attribute to have difficulty with *s*-cis conformation due to steric bulkiness of the CF_3 group at the 1,4-positions of the butadiene.

We next tried to construct the CF_3-containing heterocyclic compound. Thus, the reaction of α,β-unsaturated ketone **4an** with hydrazine monohydrate was conducted in ethanol for 15 h under reflux conditions. On the contrary to our expectation, the corresponding 3-*p*-tolyl-5-trifluoromethyl-1*H*-pyrazole **10** was obtained

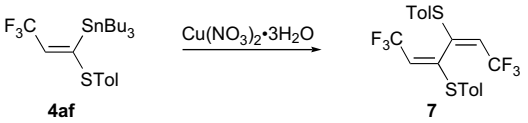


Scheme 3. Reaction of **4ae** with PhCHO in the presence of TBAF.



Scheme 4. Cross-coupling reaction of **4af** with 4′-iodoacetophenone.

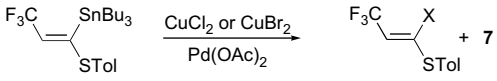
Table 3
Homo-coupling reaction of **4af** under various conditions



4af **7**

Entry	Solvent	$Cu(NO_3)_2 \cdot 3H_2O$ (equiv)	Temp (°C)	Yield[a] (%)
1	Ether	1.0	25	Trace
2	Ether	2.0	25	19
3	Ether	5.0	25	11
4	Hexane	2.0	25	NR[c]
5	THF	2.0	25	20
6	Dioxane	2.0	25	46
7	MTBE[b]	2.0	25	29
8	$CH(OMe)_3$	2.0	25	55
9	$CH(OMe)_3$	2.0	−50 to 0	74

[a] Isolated yield.
[b] Methyl *tert*-butyl ether.
[c] No reaction occurred.

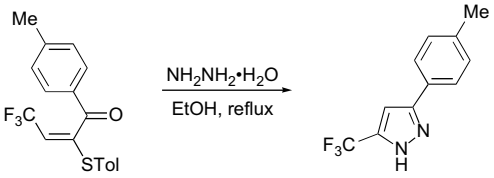


4af

X= Cl (74%) **8**
X= Br (68%) **9**

Scheme 5. Halogenation of **4af** with $CuCl_2$ or $CuBr_2$.

as a desulfurization product in 88% yield (Scheme 6).[17] Although the detailed reaction mechanism is not clear, the plausible mechanism of the formation of **10** was depicted in Scheme 7.

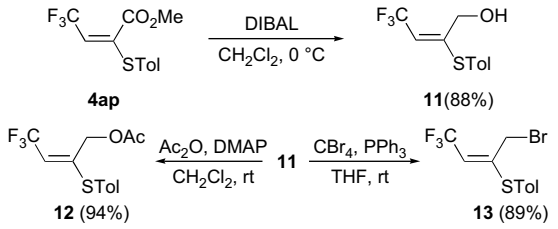


4an **10**, 88%

Scheme 6. Synthesis of pyrazole **10**.

We have also explored the possibility of ordinary functional transformation of an ester group at position α. Reduction of **4ap** with DIBAL in CH_2Cl_2 at 0 °C afforded the allylic alcohol **11** in 88% yield.[18] The use of $LiAlH_4$ in the same reaction resulted in contamination of the saturated alcohol as an over-reduction product. Acetylation and bromination of **11** smoothly proceeded giving the corresponding allylic acetate **12** and allylic bromide **13** as a potential synthetic intermediate in 94% and 89%, respectively (Scheme 8).

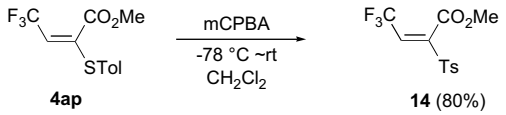
As a further application of **4ap**, the thermal Diels–Alder reaction was investigated.[7c,19] When a mixture of **4ap** and cyclopentadiene was refluxed in toluene for 1 h, only a trace amount of the cycloadduct was detected by GC–MS analysis. To enhance the reactivity of the dienophile **4ap**, we planed to transfer the sulfanyl group into the sulfonyl group as a stronger electron-withdrawing group.



4ap **11**(88%)

12 (94%) **13** (89%)

Scheme 8. Transformation of **4ap**.

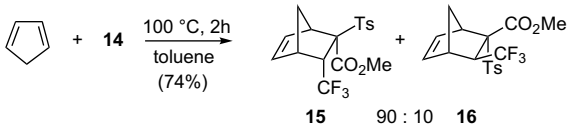


4ap **14** (80%)

Scheme 9. Oxidation of **4ap** with *m*-CPBA.

Oxidation of **4ap** with *m*-CPBA afforded the desired product **14** in 80% yield (Scheme 9).

We subsequently examined the Diels–Alder reaction of **14** with cyclopentadiene. The reaction was conducted using **14** and an excess of cyclopentadiene in toluene at 100 °C for 2 h giving the cycloadducts with a ratio of 90:10 in 74% combined yield (Scheme 10). When the same reaction was carried out in a sealed tube in CH_2Cl_2 at 60 °C for 2 h, the diastereoselectivity of the products slightly improved to 92:8 in 65% yield. The diastereomer was separated from the reaction mixture using silica gel chromatography. The structure of the main product **15** was successfully determined to be *endo*-CF_3-*endo*-CO_2Me-*exo*-Ts after its X-ray crystallography analysis (Fig. 1).



15 90 : 10 **16**

Scheme 10. Diels–Alder reaction of cyclopentadiene and **14**.

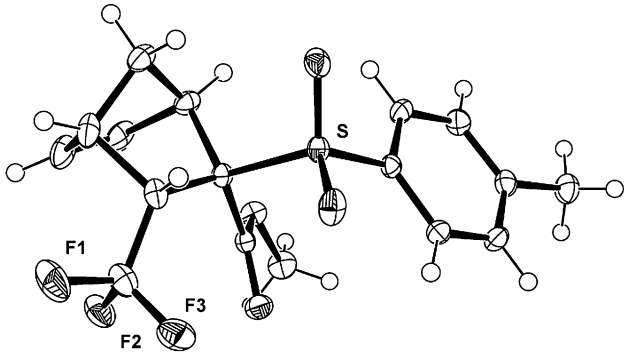
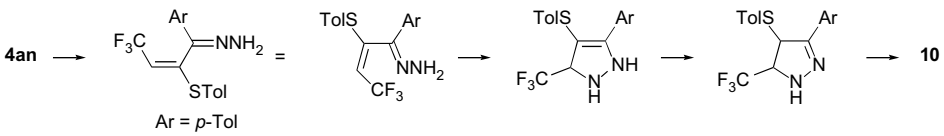
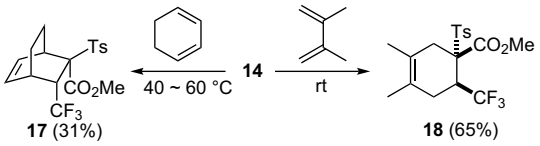


Figure 1. X-ray structure of **15** (50% probability level).



Scheme 7. Plausible mechanism for the formation of **10**.

On the other hand, the reaction of 1,4-cyclohexadiene with **14** in toluene at 40–60 °C for 84 h afforded the single diastereomer **17** albeit in 31% yield. The structure of **17** was also assigned the *endo*-CF_3-*endo*-CO_2Me-*exo*-Ts configuration on the basis of its ^1H NMR and ^{19}F NMR data in comparison with that of **15**. Finally, the Diels–Alder reaction of **14** and 2,3-dimethylbutadiene under mild conditions provided the corresponding cyclohexene derivative **18** in 65% yield (Scheme 11).



Scheme 11. Diels–Alder reaction of **14** with two dienes.

In summary, we have demonstrated the convenient synthesis of **4aa**–**4aq** as a promising trifluoromethylated building block from readily available β-(trifluoromethyl)vinyl sulfide. Actually we have illustrated the cross-coupling reactions, reduction, cyclization, and Diels–Alder reaction of selected products by taking advantage of potential functional groups introduced. These products were also expected to be useful candidates for building up more complex trifluoromethylated compounds.

3. Experimental

3.1. General

Melting points are uncorrected. Infrared (IR) spectra are reported in cm^{-1}. ^1H, ^{19}F, and ^{13}C NMR spectra were measured in $CDCl_3$ solutions. Chemical shifts were given by δ relative to that of an internal Me_4Si (TMS) for ^1H NMR and ^{13}C NMR spectra, and benzylidyne trifluoride ($CF_3C_6H_5$) or hexafluorobenzene (C_6F_6) for ^{19}F NMR spectra.

*3.1.1. Preparation of (E)-(3,3,3-trifluoro-1-(p-tolylthio)prop-1-enyl)trimethylsilane (**4aa**)*

To a solution of *E*-**3a** (84.0 mg, 0.385 mmol)[8] in THF (2 mL) under argon was added TMEDA (74 μL, 0.46 mmol) at room temperature, and the whole mixture was cooled to −78 °C. After being stirred for 10 min at this temperature, to this mixture was added *n*-BuLi (2.71 M in hexane solution, 170 μL, 0.46 mmol) dropwise via syringe. After being stirred for 10 min, TMSCl (54 μL, 0.42 mmol) was added to the solution, and the whole mixture was stirred for 15 min. The reaction was quenched with water at this temperature and extracted with hexane/ether=3:1. Additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by Florisil chromatography (hexane as eluant) to give 91.7 mg of **4aa** as pale yellow oil in 82% yield: IR (neat) 3025, 2957, 1585, 1276, 1135, 1109, 847, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.34 (9H, s), 2.39 (3H, s), 5.22 (1H, q, J=9.2 Hz), 7.24 (2H, d, J=8.4 Hz), 7.32 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.49 (q, J=2.5 Hz), 21.3, 117.8 (q, J=35.5 Hz), 123.6 (q, J=270.3 Hz), 126.2, 130.8, 135.7, 140.1, 155.9 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −56.9 (d, J=10.0 Hz); GC–MS *m*/*z* 290 (0.5, M^+), 141 (48), 107 (47), 91 (21), 77 (55), 73 (100), 65 (17). Anal. Calcd for $C_{13}H_{17}F_3SSi$: C, 53.76; H, 5.90. Found: C, 53.87; H, 5.78%.

*3.1.2. (E)-Triethyl(3,3,3-trifluoro-1-(p-tolylthio)prop-1-enyl)silane (**4ab**)*

Colorless oil; yield 71%; IR (neat) 3024, 2959, 2878, 1620, 1581, 1274, 1134, 1004, 811, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.82–0.91 (6H, m), 0.99–1.06 (9H, m), 2.39 (3H, s), 5.26 (1H, q, J=9.4 Hz), 7.22 (2H, d, J=7.7 Hz), 7.35 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 3.4 (q, J=2.5 Hz), 7.3, 21.3, 118.2 (q, J=35.5 Hz), 123.5 (q, J=270.3 Hz), 126.3, 130.8, 135.8, 140.1, 153.8 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.2 (d, J=10.0 Hz); GC–MS *m*/*z* 332 (4, M^+), 179 (43), 141 (34), 105 (30), 91 (52), 77 (100), 59 (31). Anal. Calcd for $C_{16}H_{23}F_3SSi$: C, 57.80; H, 6.97. Found: C, 57.70; H, 6.83%.

*3.1.3. (E)-(3,3,3-Trifluoro-1-(p-tolylthio)prop-1-enyl)-diisopropylsilane (**4ac**)*

Colorless oil; yield 81%; IR (neat) 2945, 2890, 2867, 1583, 1492, 1463, 1316, 1270, 1135, 1114, 1009, 909, 847, 809, 785, 664 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.12 (6H, d, J=7.0 Hz), 1.14 (6H, d, J=7.0 Hz), 1.22–1.35 (2H, m), 2.40 (3H, s), 3.82 (1H, sxt, J=4.8 Hz), 5.30 (1H, q, J=8.4 Hz), 7.25 (2H, d, J=8.1 Hz), 7.33 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.06 (d, J=3.1 Hz), 11.08 (d, J=3.1 Hz), 18.85, 18.87, 21.3, 118.9 (q, J=34.9 Hz), 123.4 (q, J=270.3 Hz), 126.1, 130.8, 135.6, 140.3, 152.0 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.5 (dd, J=7.3, 5.5 Hz); GC–MS *m*/*z* 332 (3, M^+), 269 (27), 179 (40), 161 (42), 141 (92), 123 (70), 91 (100), 77 (58), 63 (55). Anal. Calcd for $C_{16}H_{23}F_3SSi$: C, 57.80; H, 6.97. Found: C, 57.80; H, 6.93%.

*3.1.4. (E)-(4,4,4-Trifluorobut-2-en-2-yl)(p-tolyl)sulfane (**4ad**)*

Colorless oil; yield 83%; IR (neat) 3026, 2927, 1638, 1581, 1274, 1134, 1004, 811, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.13 (3H, dq, J=1.1, 2.2 Hz), 2.39 (3H, s), 4.93 (1H, qq, J=8.3, 1.1 Hz), 7.23 (2H, d, J=7.9 Hz), 7.37 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.5 (q, J=1.2 Hz), 21.3, 109.4 (q, J=34.3 Hz), 123.5 (q, J=270.3 Hz), 125.9, 130.6, 135.5, 140.3, 151.5 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.2 (d, J=6.4 Hz); GC–MS *m*/*z* 232 (8, M^+), 148 (14), 91 (50), 77 (22), 65 (15), 59 (100). Anal. Calcd for $C_{11}H_{11}F_3S$: C, 56.88; H, 4.77. Found: C, 57.06; H, 4.85%.

*3.1.5. (E)-(4,4,4-Trifluoro-2-(p-tolylthio)but-2-enyl)trimethylsilane (**4ae**)*

White solid; yield 91%; mp 29.8–32.5 °C; IR (KBr) 3025, 2957, 2927, 1611, 1494, 1351, 1258, 1188, 1135, 1079, 915, 840, 811 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.16 (9H, s), 2.09 (2H, q, J=1.8 Hz), 2.38 (3H, s), 4.70 (1H, q, J=8.4 Hz), 7.22 (2H, d, J=7.7 Hz), 7.35 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.68, 21.3, 24.4, 105.6 (q, J=34.3 Hz), 123.8 (q, J=270.3 Hz), 125.9, 130.6, 135.5, 140.3, 154.9 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −56.4 (d, J=8.8 Hz); GC–MS *m*/*z* 304 (0.6, M^+), 196 (5), 123 (9), 107 (17), 91 (22), 77 (48), 73 (100). Anal. Calcd for $C_{14}H_{19}F_3SSi$: C, 55.23; H, 6.29. Found: C, 55.53; H, 6.31%.

*3.1.6. (Z)-Tributyl(3,3,3-trifluoro-1-(p-tolylthio)prop-1-enyl)-stannane (**4af**)*

Colorless oil; yield 81%; IR (neat) 2958, 2923, 1578, 1302, 1271, 1128, 1106, 880, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (9H, t, J=7.2 Hz), 1.09–1.21 (6H, m), 1.30–1.42 (6H, m), 1.51–1.62 (6H, m), 2.38 (3H, s), 5.37 (1H, q, J=7.9 Hz), 7.23 (2H, d, J=8.3 Hz), 7.31 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 13.6, 21.3, 27.2, 28.4, 116.3 (q, J=33.6 Hz), 124.1 (q, J=269.1 Hz), 127.2, 130.6, 135.2, 139.8, 156.5 (q, J=7.5 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.3 (d, J=6.1 Hz); GC–MS *m*/*z* 450 (4.3, M^+−Bu), 179 (75), 178 (100), 135 (2), 123 (10), 119 (16), 107 (41), 91 (72), 65 (8). Anal. Calcd for $C_{22}H_{35}F_3SSn$: C, 52.09; H, 6.95. Found: C, 51.82; H, 6.99%.

*3.1.7. (Z)-(3,3,3-Trifluoro-1-iodoprop-1-enyl)(p-tolyl)sulfane (**4ag**)*

Colorless oil; yield 91%; IR (neat) 3038, 2924, 1597, 1492, 1400, 1286, 1260, 1132, 832, 810, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (3H, s), 5.82 (1H, q, J=7.2 Hz), 7.27 (2H, d, J=8.3 Hz), 7.42 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 103.8 (q, J=6.2 Hz), 119.3 (q, J=36.7 Hz), 121.8 (q, J=270.9 Hz), 129.2, 130.9, 134.8, 141.3; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.2 (d, J=8.4 Hz); GC–MS *m*/*z* 344 (0.4, M^+), 343 (0.6), 217 (26), 173 (9), 148 (31), 147 (31), 123 (33), 91

(68), 77 (20), 65 (100). Anal. Calcd for $C_{10}H_8F_3IS$: C, 34.90; H, 2.34. Found: C, 35.07; H, 2.36%.

*3.1.8. (E)-4-(3,3,3-Trifluoro-1-(phenylthio)prop-1-enylthio)-1-methylbenzene (**4ah**)*

Colorless oil; yield 95%; IR (neat) 3058, 3025, 2924, 1586, 1296, 1259, 1138, 841, 809, 746, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.37 (3H, s), 5.38 (1H, q, J=7.9 Hz), 7.15–7.25 (3H, m), 7.34–7.40 (4H, m), 7.45–7.53 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0, 113.1 (q, J=35.5 Hz), 122.8 (q, J=270.9 Hz), 126.6, 128.8, 129.8, 130.6, 134.2, 135.0, 139.4, 140.4, 151.4 (q, J=5.0 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −56.8 (d, J=8.7 Hz); GC–MS m/z 326 (2.2, M^+), 217 (5), 183 (7), 153 (18), 134 (50), 124 (54), 91 (67), 77 (100), 65 (69). Anal. Calcd for $C_{16}H_{13}F_3S_2$: C, 58.88; H, 4.01. Found: C, 58.99; H, 4.06%.

*3.1.9. 4-(3,3,3-Trifluoro-1-(p-tolylthio)prop-1-enylthio)-1-methylbenzene (**4ai**)*

White solid; yield 58%; mp 57.5–59.0 °C; IR (KBr) 3059, 3024, 2922, 2861, 1574, 1295, 1258, 1137, 1104, 845, 809, 663 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.37 (3H, s), 2.38 (3H, s), 5.27 (1H, q, J=7.9 Hz), 7.18 (4H, d, J=8.1 Hz), 7.24 (2H, d, J=8.1 Hz), 7.40 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 113.1 (q, J=35.5 Hz), 122.8 (q, J=270.9 Hz), 126.6, 126.8, 129.8, 130.6, 134.2, 135.0, 139.4, 140.4, 151.4 (q, J=5.0 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.0 (d, J=8.8 Hz); GC–MS m/z 340 (6, M^+), 217 (19), 167 (29), 148 (25), 124 (44), 107 (13), 91 (100), 77 (32), 65 (80). Anal. Calcd for $C_{17}H_{15}F_3S_2$: C, 59.98; H, 4.44. Found: C, 60.20; H, 4.43%.

*3.1.10. (E)-4,4,4-Trifluoro-N-phenyl-2-(p-tolylthio)but-2-enamide (**4aj**)*

White solid; yield 54%; mp 126.9–128.3 °C; IR (KBr) 3301, 1663, 1536, 1446, 1336, 1273, 1143, 1107, 858, 809, 757, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (3H, s), 5.24 (1H, q, J=7.9 Hz), 7.10–7.50 (9H, m), NH proton is missing; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 112.2 (q, J=36.1 Hz), 120.5, 122.0 (q, J=270.9 Hz), 123.6, 125.4, 129.1, 130.9, 135.2, 136.6, 141.1, 148.7 (q, J=5.6 Hz), 161.0; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −58.8 (d, J=8.0 Hz); GC–MS m/z 337 (6, M^+), 268 (2), 217 (5), 148 (19), 123 (49), 107 (24), 91 (74), 77 (84), 65 (100). Anal. Calcd for $C_{17}H_{14}F_3NOS$: C, 60.52; H, 4.18; N, 4.15. Found: C, 60.43; H, 4.16; N, 4.16%.

*3.1.11. (E)-5-Ethyl-1,1,1-trifluoro-3-(p-tolylthio)hept-2-en-4-ol (**4ak**)*

Pale yellow oil; yield 98%; IR (neat) 3439, 2966, 2937, 1626, 1493, 1326, 1267, 1112, 1021, 913, 857, 812, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (3H, t, J=7.3 Hz), 0.95 (3H, t, J=7.3 Hz), 1.20–1.46 (2H, m), 1.52–1.70 (1H, m), 1.70–1.95 (3H, m), 2.40 (3H, s), 4.75 (1H, d, J=8.6 Hz), 4.84 (1H, q, J=8.8 Hz), 7.25 (2H, d, J=7.9 Hz), 7.38 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.4, 11.1, 20.1, 21.1, 21.3, 44.5, 71.5, 110.7 (q, J=35.5 Hz), 123.2 (q, J=270.9 Hz), 125.2, 130.9, 135.9, 140.4, 160.1 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −55.1 (d, J=9.2 Hz); GC–MS m/z 318 (0.8, M^+), 248 (9), 124 (100), 91 (59), 77 (21), 65 (15). Anal. Calcd for $C_{16}H_{21}F_3OS$: C, 60.36; H, 6.65. Found: C, 60.30; H, 6.72%.

*3.1.12. (E)-4,4,4-Trifluoro-1-(p-methoxyphenyl)-2-(p-tolylthio)but-2-en-1-ol (**4al**)*

Pale yellow oil; yield 86%; IR (neat) 3443, 2936, 1612, 1512, 1264, 1149, 1109, 1033, 856, 813, 670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.37 (3H, s), 2.51 (1H, d, J=5.1 Hz), 3.82 (3H, s), 4.92 (1H, q, J=8.8 Hz), 6.05 (1H, d, J=5.0 Hz), 6.93 (2H, d, J=8.8 Hz), 7.21 (2H, d, J=7.9 Hz), 7.33 (2H, d, J=8.1 Hz), 7.48 (2H, d, J=8.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 55.2, 70.8 (q, J=1.9 Hz), 110.3 (q, J=34.9 Hz), 113.8, 123.1 (q, J=271.5 Hz), 125.4, 127.4, 130.8, 132.0, 135.7, 140.3, 159.4, 159.8 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −55.4 (d, J=8.4 Hz); GC–MS m/z 354 (0.01, M^+), 217 (9), 137 (100), 123 (12), 94 (35), 77 (44), 65 (20). Anal. Calcd for $C_{18}H_{17}F_3O_2S$: C, 61.00; H, 4.84. Found: C, 60.94; H, 4.92%.

*3.1.13. (E)-4,4,4-Trifluoro-1-p-tolyl-2-(p-tolylthio)but-2-en-1-one (**4an**)*

White solid; yield 79%; mp 61.8–62.5 °C; IR (KBr) 3030, 2958, 2925, 1676, 1606, 1334, 1276, 1147, 1015, 858, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (3H, s), 2.44 (3H, s), 5.28 (1H, q, J=7.9 Hz), 7.22 (2H, d, J=8.1 Hz), 7.29 (2H, d, J=8.1 Hz), 7.40 (2H, d, J=8.1 Hz), 7.84 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 21.8, 110.8 (q, J=35.5 Hz), 122.1 (q, J=270.9 Hz), 129.1, 129.5, 129.6, 129.8, 130.8, 135.8, 141.0, 145.5, 151.1 (q, J=5.6 Hz), 190.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −58.7 (d, J=8.8 Hz); GC–MS m/z 336 (0.8, M^+), 119 (100), 91 (39), 65 (15). Anal. Calcd for $C_{18}H_{15}F_3OS$: C, 64.27; H, 4.49. Found: C, 64.26; H, 4.52%.

*3.1.14. (E)-Ethyl 4,4,4-trifluoro-2-(p-tolylthio)but-2-enoate (**4ao**)*

Pale yellow oil; yield 72%; IR (neat) 2985, 1741, 1629, 1493, 1448, 1370, 1334, 1275, 1223, 1140, 1018, 984, 852, 811, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (3H, t, J=7.5 Hz), 2.39 (3H, s), 4.20 (2H, q, J=7.2 Hz), 5.23 (1H, q, J=7.9 Hz), 7.25 (2H, d, J=8.1 Hz), 7.42 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.7, 21.3, 62.6, 113.3 (q, J=36.7 Hz), 120.0, 121.8 (q, J=270.0 Hz), 130.8, 135.5, 141.1, 145.4 (q, J=5.6 Hz), 163.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.6 (d, J=8.1 Hz); GC–MS m/z 290 (7, M^+), 217 (3), 149 (94), 123 (53), 108 (18), 91 (87), 77 (29), 65 (100). Anal. Calcd for $C_{13}H_{13}F_3O_2S$: C, 53.78; H, 4.51. Found: C, 53.83; H, 4.40%.

*3.1.15. (E)-Methyl 4,4,4-trifluoro-2-(p-tolylthio)but-2-enoate (**4ap**)*

Pale yellow oil; yield 75%; IR (neat) 2956, 1744, 1626, 1493, 1436, 1339, 1276, 1230, 1139, 1017, 927, 856, 812 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (3H, s), 3.75 (3H, s), 5.24 (1H, q, J=7.8 Hz), 7.25 (2H, d, J=8.1 Hz), 7.42 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 53.0, 113.5 (q, J=36.5 Hz), 121.7 (q, J=270.5 Hz), 123.8, 130.8, 135.4, 141.1, 145.1 (q, J=5.8 Hz), 163.8; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.9 (d, J=6.9 Hz); GC–MS m/z 275 (34, M^+), 244 (3), 217 (15), 173 (23), 148 (95), 123 (54), 91 (80), 65 (100). Anal. Calcd for $C_{12}H_{11}F_3O_2S$: C, 52.17; H, 4.01. Found: C, 52.43; H, 3.99%.

*3.1.16. (E)-2-Ethylhexyl 4,4,4-trifluoro-2-(p-tolylthio)but-2-enoate (**4aq**)*

Pale yellow oil; yield 76%; IR (neat) 2961, 2931, 1741, 1629, 1493, 1463, 1382, 1335, 1276, 1223, 1141, 1018, 855, 811, 670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (3H, t, J=7.5 Hz), 0.90 (3H, t, J=7.2 Hz), 1.20–1.42 (8H, m), 1.50–1.65 (1H, m), 2.39 (3H, s), 4.00 (1H, dd, J=11.0, 5.7 Hz), 4.05 (1H, dd, J=10.6, 5.5 Hz), 5.26 (1H, q, J=7.9 Hz), 7.24 (2H, d, J=8.1 Hz), 7.42 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.8, 14.0, 21.3, 22.9, 23.5, 28.8, 30.1, 38.5, 68.8, 113.4 (q, J=36.7 Hz), 121.7 (q, J=270.3 Hz), 124.0, 130.8, 135.4, 140.9, 145.4 (q, J=5.6 Hz), 163.7; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.7 (d, J=8.0 Hz); GC–MS m/z 374 (0.7, M^+), 373 (4, M^+−1), 261 (3), 216 (4), 173 (2), 149 (22), 123 (20), 91 (24), 77 (7), 69 (54), 65 (21), 57 (100). Anal. Calcd for $C_{19}H_{25}F_3O_2S$: C, 60.94; H, 6.73. Found: C, 61.18; H, 6.67%.

3.2. Preparation of (*E*)-1-(4-(3,3,3-trifluoro-1-(*p*-tolylthio)prop-1-enyl)phenyl)ethanone (6)

To a solution of **4af** (101.5 mg, 0.200 mmol) in DMSO (1 mL) under argon were successively added 4′-iodoacetophenone (43.0 mg, 0.175 mmol), CuTC (1.9 mg, 0.01 mmol), LiCl (3.1 mg, 0.07 mmol), and $Pd(PPh_3)_4$ (12.5 mg, 0.01 mmol) at room temperature. The whole mixture was heated to 80 °C for 2 h. After the mixture was cooled to room temperature, the reaction was quenched with water and extracted with hexane/ethyl acetate=3:1. Additional extraction was repeated twice. The

combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/ethyl acetate=20:1 as eluant) to give 51.0 mg of **6** as a white solid in 87% yield. Mp 135.5–136.8 °C; IR (KBr) 3042, 1682, 1634, 1600, 1494, 1403, 1346, 1269, 1187, 1135, 1098, 1016, 962, 822, 811, 776, 666 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.40 (3H, s), 2.62 (3H, s), 5.16 (1H, q, J=7.9 Hz), 7.25 (2H, d, J=7.9 Hz), 7.43 (2H, d, J=8.1 Hz), 7.49 (2H, d, J=8.3 Hz), 7.95 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 26.6, 110.6 (q, J=34.9 Hz), 122.6 (q, J=270.9 Hz), 125.6, 128.0, 128.76, 128.77, 130.8, 135.4, 137.4, 140.0, 140.7, 153.6 (q, J=5.6 Hz), 197.3; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −55.9 (d, J=7.6 Hz); GC–MS m/z 336 (5, M^+), 267 (19), 163 (90), 124 (37), 101 (34), 91 (100), 77 (45), 65 (33). Anal. Calcd for $C_{18}H_{15}F_3OS$: C, 64.27; H, 4.49. Found: C, 64.18; H, 4.43%.

3.3. (2*E*,4*E*)-1,1,1,6,6,6-Hexafluoro-3,4-bis(*p*-tolylthio)hexa-2,4-diene (7)

To a solution of **4af** (88.5 mg, 0.174 mmol) in $CH(OMe)_3$ (1 mL) under argon was added $Cu(NO_3)_2\cdot 3H_2O$ (85.6 mg, 0.348 mmol) at −50 °C, and the whole mixture was gently warmed to 0 °C over 2 h. The reaction was quenched with water and extracted with hexane/ether=3:1 solution. Additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/triethylamine=200:1 as eluant) to give 28.0 mg of **7** as a white solid in 74% yield. Mp 100.8–102.1 °C; IR (KBr) 3068, 2924, 1651, 1614, 1596, 1491, 1361, 1295, 1280, 1162, 1138, 1107, 1017, 908, 852, 814, 807, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.41 (6H, s), 4.69 (2H, br q, J=7.0 Hz), 7.26 (4H, d, J=8.1 Hz), 7.42 (4H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 111.7 (q, J=35.5 Hz), 122.1 (q, J=270.9 Hz), 124.7, 130.8, 136.0, 141.1, 146.9; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.7 (d, J=8.5 Hz); GC–MS m/z 434 (7, M^+), 291 (3), 241 (10), 214 (6), 155 (11), 125 (100), 91 (97), 79 (59), 77 (43), 65 (17). Anal. Calcd for $C_{20}H_{16}F_6S_2$: C, 55.29; H, 3.71. Found: C, 55.45; H, 3.84%.

3.3.1. (*Z*)-(1-Chloro-3,3,3-trifluoroprop-1-enyl)(p-tolyl)sulfane (*8*)

To a solution of **4af** (370.6 mg, 0.731 mmol) in THF (3 mL) under argon were added $CuCl_2$ (201.7 mg, 1.50 mmol) and $Pd(OAc)_2$ (16.6 mg, 0.074 mmol) at 25 °C, and the whole mixture was stirred for 2 h. The reaction was quenched with water and extracted with hexane/ethyl acetate=3:1 solution. Additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/triethylamine=200:1 as eluant) to give 136.9 mg of **8** as colorless oil in 74% and 31.7 mg of **7** as a white solid in 20% yield, respectively. IR (neat) 3070, 2927, 1619, 1493, 1293, 1257, 1141, 1125, 915, 848, 810, 691, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.40 (3H, s), 5.48 (1H, q, J=7.1 Hz), 7.26 (2H, d, J=8.1 Hz), 7.43 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 112.6 (q, J=36.7 Hz), 121.8 (q, J=270.3 Hz), 125.3, 130.9, 135.1, 141.3, 144.8 (q, J=6.2 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.1 (d, J=7.5 Hz); GC–MS m/z 254 (10, M^+ [^{37}Cl]), 252 (24, M^+ [^{35}Cl]), 217 (10), 183 (41), 148 (90), 123 (64), 91 (48), 77 (37), 65 (100). Anal. Calcd for $C_{10}H_8ClF_3S$: C, 47.53; H, 3.19. Found: C, 47.57; H, 3.19%.

3.3.2. (*Z*)-(1-Bromo-3,3,3-trifluoroprop-1-enyl)(p-tolyl)sulfane (*9*)

Colorless oil; yield 68%; IR (neat) 3055, 2926, 1611, 1492, 1289, 1256, 1134, 843, 810, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.40 (3H, s), 5.72 (1H, q, J=7.0 Hz), 7.27 (2H, d, J=8.1 Hz), 7.43 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 114.8 (q, J=36.7 Hz), 121.9 (q, J=270.3 Hz), 126.6, 130.9, 132.6 (q, J=6.3 Hz), 135.0, 141.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −59.4 (d, J=7.1 Hz); GC–MS m/z 298 (7, M^+ [^{81}Br]), 296 (6, M^+ [^{79}Br]), 227 (4), 217 (30), 173 (26), 148 (83), 123 (40), 91 (43), 77 (22), 65 (100). Anal. Calcd for $C_{10}H_8BrF_3S$: C, 40.42; H, 2.71. Found: C, 40.56; H, 2.73%.

3.4. 5-Trifluoromethyl-3-*p*-tolyl-1*H*-pyrazole (10)[17a]

To a solution of **4an** (23.1 mg, 0.069 mmol) in ethanol (2 mL) under argon was added $NH_2NH_2\cdot H_2O$ (9.0 μL, 0.186 mmol) at room temperature, and the whole mixture was gently warmed up to 80 °C. After the reaction mixture was stirred for 15 h at this temperature, the solution was directly concentrated. To the residue were added ethyl acetate and water. After separation of the organic layer, additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/ethyl acetate=4:1 as eluant) to give 13.6 mg of **10** as a white solid in 88% yield. Mp 155.3–156.8 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (3H, s), 6.70 (1H, s), 7.25 (2H, d, J=8.1 Hz), 7.45 (2H, d, J=8.1 Hz), 11.74 (1H, br s); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −63.6 (s); GC–MS m/z 226 (100, M^+), 205 (19), 177 (17), 157 (27), 130 (49), 90 (37), 63 (42), 51 (75).

3.5. Preparation of (*E*)-4,4,4-trifluoro-2-(*p*-tolylthio)but-2-en-1-ol (11)

To a solution of **4ap** (776.8 mg, 2.81 mmol) in CH_2Cl_2 (10 mL) under argon was added DIBAL (0.98 M in hexane, 6.89 mL, 6.75 mmol) dropwise via syringe at 0 °C, and the whole mixture was stirred for 20 min at this temperature. The reaction was slowly quenched with $Na_2SO_4\cdot 10H_2O$. A small amount of additional Na_2SO_4 and NaF was added to the reaction mixture. The solution was separated and the residual precipitate was washed with hexane/ether=3:1. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/ether=3:1 as eluant) to give 697.3 mg of **11** as pale yellow oil in 88% yield. IR (neat) 3351, 1628, 1450, 1326, 1266, 1107, 1053, 852, 811, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (1H, t, J=6.8 Hz), 2.40 (3H, s), 4.52 (2H, d, J=6.6 Hz), 4.93 (1H, q, J=8.6 Hz), 7.25 (2H, d, J=7.9 Hz), 7.40 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 60.7 (q, J=2.1 Hz), 110.0 (q, J=35.7 Hz), 123.1 (q, J=270.9 Hz), 125.1, 130.9, 131.1, 140.5, 155.9 (q, J=5.4 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −56.6 (dt, J=8.6, 2.1 Hz); GC–MS m/z 248 (19, M^+), 217 (18), 149 (16), 123 (17), 92 (49), 91 (100), 75 (33), 65 (26). Anal. Calcd for $C_{11}H_{11}F_3OS$: C, 53.22; H, 4.47. Found: C, 53.32; H, 4.54%.

3.6. Preparation of (*E*)-4,4,4-trifluoro-2-(*p*-tolylthio)but-2-en-1-yl acetate (12)

To a solution of **11** (443.7 mg, 1.79 mmol) in CH_2Cl_2 (10 mL) were added Ac_2O (0.26 mL, 2.68 mmol) and DMAP (667.0 mg, 5.37 mmol) at room temperature. After being stirred for 15 min, the solution was concentrated to about one tenth of its original volume. The resulting solution was directly purified by silica gel chromatography (hexane/ether=3:1 as eluant) to give 489.4 mg of **12** as pale yellow oil in 94% yield. IR (neat) 3026, 2954, 2927, 1752, 1634, 1326, 1268, 1222, 1163, 1114, 1062, 851, 812, 666 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.15 (3H, s), 2.40 (3H, s), 4.94 (2H, s), 4.99 (1H, q, J=8.4 Hz), 7.26 (2H, d, J=8.4 Hz), 7.39 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 21.3, 61.1 (q, J=2.1 Hz), 111.7 (q, J=35.7 Hz), 122.8 (q, J=270.6 Hz), 124.6, 130.9, 135.6, 140.7, 150.8 (q, J=5.4 Hz), 170.1; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.2 (dt, J=8.2, 1.8 Hz); GC–MS m/z 290 (23, M^+), 230 (16), 161 (47), 124 (70), 105 (25), 91 (100), 77 (59), 65 (48). Anal. Calcd for $C_{13}H_{13}F_3O_2S$: C, 53.79; H, 4.51. Found: C, 53.97; H, 4.62%.

3.7. Preparation of (*E*)-(1-bromo-4,4,4-trifluorobut-2-en-2-yl)(*p*-tolyl)sulfane (13)

To a solution of **11** (610.3 mg, 2.46 mmol) in THF (15 mL) under argon were added PPh_3 (1.00 g, 3.45 mmol) and tetrabromomethane (CBr_4, 1.50 g, 4.43 mmol) at once at room temperature. After being stirred for 5 min, the reaction was quenched with saturated $NaHCO_3$ solution, and extracted with hexane/ether=3:1. Additional extraction was repeated twice. The combined organic solution was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/triethylamine=200:1 as eluant) to give 682.7 mg of **13** as pale yellow oil in 89% yield. IR (neat) 1629, 1493, 1330, 1265, 1116, 811 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.40 (3H, s), 4.17 (2H, d, J=0.9 Hz), 5.13 (1H, q, J=8.3 Hz), 7.26 (2H, d, J=7.7 Hz), 7.42 (2H, d, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 25.4 (q, J=1.9 Hz), 113.0 (q, J=35.5 Hz), 122.6 (q, J=270.9 Hz), 124.9, 130.9, 135.6, 140.8, 151.5 (q, J=5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −57.6 (d, J=8.4 Hz); GC–MS m/z 312 (17, M^+ [^{81}Br]), 310 (16, M^+ [^{79}Br]), 231 (68), 211 (66), 161 (51), 123 (100), 91 (40), 79 (80), 77 (99), 69 (37), 65 (31). Anal. Calcd for $C_{11}H_{10}BrF_3S$: C, 42.46; H, 3.24. Found: C, 42.71; H, 3.28%.

3.8. Preparation of (*E*)-methyl 4,4,4-trifluoro-2-tosylbut-2-enoate (14)

To a solution of **4ap** (209.3 mg, 0.758 mmol) in CH_2Cl_2 (4 mL) under argon was added *m*-CPBA (77%, 464.0 mg, 2.07 mmol) at −78 °C, and the whole mixture was stirred at this temperature for 1 h. The reaction was gently warmed to room temperature over 18 h. The reaction was quenched with saturated $Na_2S_2O_3$ solution and saturated $NaHCO_3$ solution, successively, and extracted with CH_2Cl_2. Additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/ethyl acetate=3:1 as eluant) to give 186.8 mg of **14** as a white solid in 80% yield. Mp 87.3–88.9 °C; IR (KBr) 3064, 2965, 1752, 1747, 1441, 1343, 1328, 1295, 1274, 1236, 1187, 1151, 1082, 818, 683 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.48 (3H, s), 3.82 (3H, s), 6.95 (1H, q, J=7.0 Hz), 7.39 (2H, d, J=8.6 Hz), 7.77 (2H, d, J=8.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 53.7, 120.6 (q, J=273.2 Hz), 127.8 (q, J=38.0 Hz), 129.2, 130.1, 134.5, 146.0 (q, J=4.8 Hz), 146.5, 160.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −63.2 (d, J=7.3 Hz); GC–MS m/z 308 (0.2, M^+), 244 (2), 229 (2), 185 (3), 155 (11), 139 (6), 91 (100), 65 (27). Anal. Calcd for $C_{12}H_{11}F_3O_4S$: C, 46.75; H, 3.60. Found: C, 46.83; H, 3.69%.

3.8.1. Methyl 6-(trifluoromethyl)-5-tosylbicyclo[2,2,1]hept-2-en-5-carboxylate (*15*)

A sealed glass tube was successively charged with **14** (58.2 mg, 0.189 mmol), cyclopentadiene (77.0 μL, 0.934 mmol, freshly prepared from dicyclopentadiene), and toluene (1 mL). The resulting mixture was heated at 100 °C for 2 h. After the mixture was cooled to room temperature, toluene was evaporated at reduced pressure. The residue was purified by silica gel chromatography (hexane/ethyl acetate=10:1 as eluant) to give 52.5 mg of **15** as a mixture of two diastereomers in 74% combined yield. Major isomer **15** (*endo*-CF_3-adduct) was partially obtained by the second silica gel chromatography (hexane/ethyl acetate=20:1 as eluant) in a pure form. White solid; mp 129.5–130.2 °C; IR (KBr) 2954, 1743, 1321, 1312, 1289, 1276, 1265, 1149, 1131, 1119, 824, 707, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.54 (1H, d, J=9.0 Hz), 2.37 (1H, d, J=9.0 Hz), 2.46 (3H, s), 3.27 (1H, br s), 3.51 (3H, s), 3.73 (1H, dq, J=3.0, 9.3 Hz), 3.73 (1H, br s), 6.27 (1H, dd, J=5.3, 2.9 Hz), 6.31–6.37 (1H, m), 7.36 (2H, d, J=8.4 Hz), 7.72 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 44.6 (q, J=2.5 Hz), 45.6, 51.0 (q, J=28.6 Hz), 51.6, 52.5, 82.8 (q, J=1.2 Hz), 125.3 (q, J=278.4 Hz), 129.5, 130.0, 133.7, 137.4, 138.4, 145.7, 165.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −62.4 (br s); GC–MS m/z 374 (0.2, M^+), 235 (7), 219 (50), 199 (15), 159 (19), 139 (14), 109 (20), 91 (100), 66 (57), 65 (27), 59 (55). Anal. Calcd for $C_{17}H_{17}F_3O_4S$: C, 54.54; H, 4.58. Found: C, 54.14; H, 4.66%.

3.8.2. Methyl 6-(trifluoromethyl)-5-tosylbicyclo[2,2,2]oct-2-en-5-carboxylate (*17*)

Colorless syrup; yield 40%; IR (neat) 3056, 2953, 2879, 1761, 1597, 1436, 1319, 1289, 1256, 1161, 1143, 1107, 818, 697, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20–1.45 (2H, m), 1.85–1.96 (1H, m), 2.40–2.50 (1H, m), 2.44 (3H, s), 3.00–3.15 (1H, m), 3.53 (3H, s), 3.62–3.67 (1H, m), 3.68 (1H, q, J=10.3 Hz), 6.20–6.45 (2H, m), 7.32 (2H, d, J=8.1 Hz), 7.70 (2H, d, J=8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.8, 21.7, 25.5, 31.5 (q, J=2.9 Hz), 37.4, 48.6 (q, J=28.4 Hz), 52.6, 80.9, 125.7 (q, J=279.6 Hz), 129.3, 129.7, 130.1, 132.4, 134.4, 145.6, 165.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −62.9 (d, J=9.9 Hz); GC–MS m/z 249 (1), 233 (44), 213 (16), 185 (19), 173 (31), 155 (43), 133 (23), 127 (24), 105 (39), 91 (84), 79 (47), 77 (46), 59 (100). Anal. Calcd for $C_{18}H_{19}F_3O_4S$: C, 55.66; H, 4.93. Found: C, 55.75; H, 4.93%.

3.8.3. Methyl 6-(trifluoromethyl)-3,4-dimethyl-1-tosylcyclohex-3-en-1-carboxylate (*18*)

White solid; yield 65%; mp 117.9–119.7 °C; IR (KBr) 2954, 2928, 2862, 1741, 1322, 1276, 1156, 1109, 814, 708, 661 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.44 (3H, s), 1.49 (3H, s), 2.26 (1H, d, J=17.8 Hz), 2.44 (3H, s), 2.51 (1H, d, J=19.3 Hz), 2.79 (2H, d, J=17.8 Hz), 3.65–3.78 (1H, m), 3.68 (3H, s), 7.32 (2H, d, J=8.1 Hz), 7.72 (2H, d, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.2, 18.5, 21.6, 29.0 (q, J=2.5 Hz), 31.6, 40.6 (q, J=26.8 Hz), 53.0, 73.2, 121.9, 122.3, 126.2 (q, J=283.2 Hz), 129.3, 129.7, 134.0, 145.6, 167.3; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −67.8 (d, J=9.5 Hz); GC–MS m/z 234 (47), 213 (19), 199 (38), 175 (33), 165 (62), 155 (38), 139 (25), 121 (24), 105 (36), 91 (100), 77 (26), 65 (39), 59 (55). Anal. Calcd for $C_{18}H_{21}F_3O_4S$: C, 55.37; H, 5.42. Found: C, 55.31; H, 5.49%.

3.9. Crystal data for 15

$C_{17}H_{17}F_3O_4S$: M=374.37, T=93(2) K, triclinic, space group P-1, a=7.810(7) Å, b=8.731(11) Å, c=12.978(13) Å, V=815.1(15) $Å^3$, Z=2, D_c=1.525 Mg m^{-3}, m=0.251 mm^{-1}, l=0.71073 Å, q_{max}=27.45°, 7946 measured reflection, 3661 independent reflections, 226 refined parameters, GOF=1.038, $R[F^2>2s(F^2)]$=0.0482, $wR(F^2)$=0.1337. The intensity data were collected on a Rigaku RAXIS-RAPID diffractometer. The structure was solved by direct methods (SIR2002[20]) and the non-hydrogen atoms were refined anisotropically by full-matrix least-squares procedures on F^2 for all reductions (SHELXL97[21]). All hydrogen atoms were positioned geometrically and refined as riding. CCDC-715697 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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