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Synthesis of New Synthons for Organofluorine Compounds from Halothane Containing Sulfur Functional Groups[1)]

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To develop new synthons for the syntheses of organofluorine compounds, the treatment of Halothane, 2-bromo-2-chloro-1,1,1-trifluoroethane, (1) with 4-methylbenzenethiol (2) in the presence of sodium hydride gave 1-chloro-2,2,2-trifluoroethyl 4-methylphenyl sulfide (3), which was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA) to the corresponding sulfoxide (4) and sulfone (5). Reaction of 3 and 5 with allyltributyltin in the presence of 2,2′-azobis(isobutyronitrile) (AIBN) gave 1-(trifluoromethyl)-3-butenyl compounds (9, 11). Sulfoxide 4 was decomposed in this condition. The treatment of 3 with allyltrimethylsilane in the presence of Lewis acids gave 1-(trifluoromethyl)-3-butenyl compounds (9) in good yield. This result suggests that 4-methylphenylthio substituent stabilizes the α-carbocation effectively, though the trifluoromethyl group destabilizes it strongly. Aromatic compounds similarly reacted with 3 in the presence of titanium(IV) chloride to give 2-aryl-1,1,1-trifluoro-2-(4-methylphenylthio)ethanes. Thus, sulfur compounds derived from Halothane were found to be useful new synthons for organofluorine compounds.

Key words Halothane; 2-bromo-2-chloro-1,1,1-trifluoroethane; methylbenzenethiol; radical reaction; allylation; carbocation

Nowadays, organofluorine compounds are attracting much attention in biomedicinal fields, and many new medicines containing fluorine substituents have been developed.[2)] New methodologies for organofluorine compounds have been developed, too. However, new methods for syntheses of new types of organofluorine compounds are still required. We are engaged in finding new synthons for the synthesis of organofluorine compounds, especially for trifluoromethyl compounds. In the course of this study, we found Halothane, 2-bromo-2-chloro-1,1,1-trifluoroethane (**1**), to be a useful synthon for organofluorine compounds.[3)] Now, we would like to report the synthesis of new synthons by modification of the reactivity of **1** introducing sulfur substituents.

Reaction of **1** with 4-methylbenzenethiol (**2**) in the presence of sodium hydride was examined in aprotic solvents. After **2** was treated with sodium hydride in dimethylformamide (DMF), one equivalent of **1** was added at 0 °C and allowed to warm up to room temperature to give 1-chloro-2,2,2-trifluoroethyl 4-methylphenyl sulfide (**3**) in a yield of 32% (Chart 1).

MS of **3** showed a mother ion at *m*/*z*: 240 and 242 in a ratio of 3 : 1, which revealed the presence of one chlorine atom and no bromine atom. ^{19}F-NMR showed a doublet at -8.7 ppm. ^{1}H-NMR showed a quartet at δ 5.20 ($J_{\text{H—F}}=$ 6.6 Hz). The structure of **3** was supported by these spectral data.

Since **1** is highly volatile, two equivalents of **1** were used. The yield of **3** was improved to 55%. To improve the yield of **3** further, reactions in other solvents were examined. Results are summarized in Table 1.

N-Methylpyrrolidone (NMP) gave the best result. These results suggested that a less polar solvent gave a better yield of **3**. Thus, a less polar tetrahydrofuran (THF) was examined, but this did not dissolve the sodium thiolate, and the reaction was not examined further.

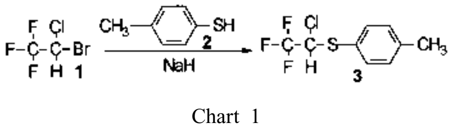

Chart 1

Table 1. Reaction of **1** with **2** in Aprotic Solvents

Entry	**1** (eq)	Solvent	Time (h)	Yield (%)
1	1	DMF	3.5	32
2	2	DMF	4.0	55
3	2	DMSO	4.0	21
4	2	DMI	4.0	60
5	1	NMP	3.5	34
6	2	NMP	4.0	73
7	2	THF	—	—

DMSO: dimethyl sulfoxide; DMI: 1,3-dimethyl-2-imidazolidinone.

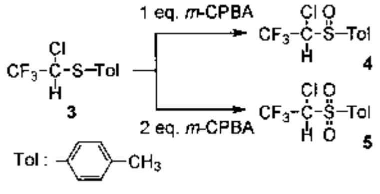

Chart 2

To modify the reactivity of **3**, it was oxidized with one equivalent of *m*-chloroperbenzoic acid (*m*-CPBA) to the corresponding sulfoxide (**4**) and with two equivalents to the sulfone (**5**) (see Chart 2).

Compound **4** has two chiral centers, and its GC and ^{19}F-NMR spectra showed that it was a mixture of two diastereomers (ratio 3 : 2).

A radical generated from the reaction of α-chlorosulfide with tributyltin hydride was reported to add to a carbon–carbon double bond intramolecularly,[4)] as shown at the top of Chart 3.

If this reaction proceeds with **3**, **4** or **5** intermolecularly, it will provide a new methodology for organic fluorine compounds. Thus, we examined their reaction with α-methylstyrene, expecting the reaction shown in the middle of Chart

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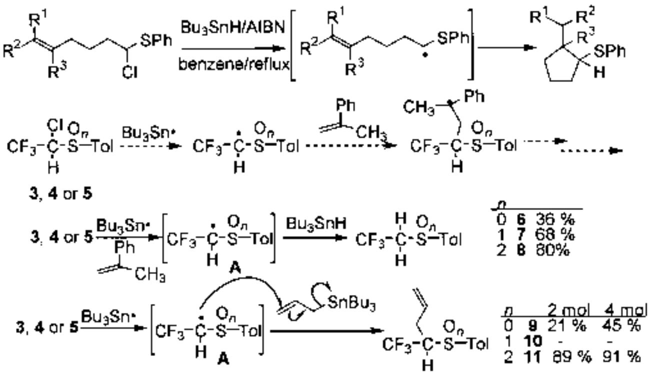


Chart 3

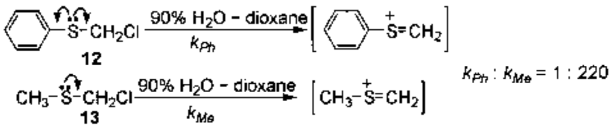


Chart 4

3. When a mixture of **3** and tributyltin hydride was refluxed in benzene with a catalytic amount of 2,2′-azobis(isobutyronitrile) (AIBN), only the reduction product (**6**) was obtained in 36% yield, and the expected product was not obtained at all. Compounds **4** and **5** gave similar results. These facts suggested that radical intermediates were formed. However, they did not react with the olefin, but with tributyltin hydride to give the reduction products (**7** or **8**).

To avoid this undesirable reduction, we examined the reaction of **3** with allyltributyltin, which has no hydrogen and was reported to react through an S_H2' mechanism.[5] A solution of **3** and two equivalents of allyltributyltin in benzene was refluxed with a catalytic amount of AIBN, then an allyl group was introduced in the place of the chlorine atom to give 5,5,5-trifluoro-4-(4-methylphenylthio)-1-pentene (**9**) in the yield of 21%. The use of four equivalents of allyltributyltin improved the yield to 45%. These low yields might be due to the attack by an radical A on the sulfur atom of **3**, since the sulfone **5** gave a much better yield, as shown below.

The same reaction of sulfoxide **4** did not give the objective allyl compound (**10**) at all, even after prolonged reaction time. We could not recover **4**. This suggested that the sulfoxide group is unstable in this reaction condition. On the other hand, the sulfone **5** gave much better yields of the allyl compound (**11**) in a much shorter reaction time than in the case of **3**. These reactions are shown in the bottom of Chart 3.

Finally, cationic reactions of **3** will be discussed. Generally speaking, an α-alkylthio group stabilizes a carbocation. The rate of solvolysis of phenylthiomethyl chloride (**12**) was reported to be 220 times slower than that of methylthiomethyl chloride (**13**), as shown in Chart 4.[6]

This large difference in rates is explained by an electronic effect of the sulfur of the phenylthio group: it stabilizes the carbocation, but is much smaller than that of the methylthio group, since the phenyl group tends to accept the electron pair by resonance, as shown by another arrow in Chart 4. Namely, a change in the structure significantly influences the stability of thioalkyl carbocation.

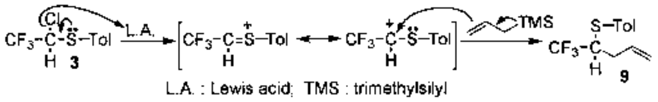


Chart 5

Table 2. Reaction of **3** with Allyltrimethylsilane in the Presence of Lewis Acids

Entry	Allyltrimethylsilane (eq)	Lewis acid (eq)	Time (h)	Yield (%)
1	3	$BF_3 \cdot Et_2O$ (3)	48	Trace
2	3	$SnCl_4$ (3)	48	10
3	3	$ZnBr_2$ (3)	48	30
4	1	$TiCl_4$ (1)	60	80
5	1	$TiCl_4$ (3)	33	70
6	3	$TiCl_4$ (3)	18	94

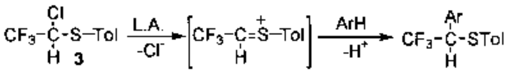


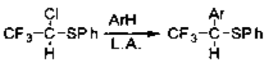
Chart 6

Table 3. Reaction of **3** with Aromatic Compounds in the Presence of $TiCl_4$

Entry	Aromatic compound	Time (h)	Product %	Ref.[7]
1	Benzene	24	**14** 78	66[a]
2	Toluene	12	**15** (*o*-) 16	6 (*o*-)[a]
			16 (*p*-) 82	77 (*p*-)[a]
3	Naphthalene	10	**17** (α-) 90	80 (α-)[b]
4	Phenol	3	**18** (*o*-) 15	
			19 (*p*-) 24	

a) $ZnCl_2/CH_3NO_2$/reflux. *b*) $SnCl_4/ClCH_2CH_2Cl$/reflux.

Cf. Reaction of 1-chloro-2,2,2-trifluoro-1-(phenylthio)ethane with aromatic compounds.



A trifluoromethyl group is a strong electron-withdrawing group and it destabilizes an α-cation to it. Thus, we were interested in which effect, of the phenylthio group or of the trifluoromethyl group, predominates in the reaction of **3**. We treated **3** with allyltrimethylsilane in the presence of several Lewis acids. The results are shown in Chart 5 and Table 2.

These results suggest that the chlorine atom was abstracted with a Lewis acid to give a carbocation, which reacted with allyltrimethylsilane to give an allylated product (**9**). Titanium(IV) chloride was found to work as the best catalyst. It gave a high yield of **9** in the shortest reaction time.

If the carbocation is produced by the reaction of **3** with titanium(IV) chloride, it will react with aromatic compounds to afford 2,2,2-trifluoro-1-(4-methylphenylthio)ethyl derivatives. At first, benzene was treated with **3** in the presence of titanium(IV) chloride at room temperature. When three molar equivalents of aromatic compounds and titanium(IV) chloride were used, moderate to good yields of 2,2,2-trifluoro-1-(4-methylphenylthio)ethyl compounds were obtained, as shown in Chart 6 and Table 3.

Among the aromatics examined, benzene is the least reactive, and it took 24 h for completion of the reaction. However, it gave a fairly good yield of the product. Toluene and naphthalene gave excellent results. Phenol showed the highest reactivity, but the yields of products were not satisfactory due to the difficulty of isolation. The last column of the table shows Uneyama's results of the reaction of a phenylthio homolog of **3** for comparison with ours.[7)] It is clear from the table that the 4-methylphenylthio compound **3** is much more reactive than the phenylthio homolog: the former reacted at a much lower temperature and gave better yields than the latter. This shows that a 4-methylphenylthio group stabilizes an α-cation much better than a phenyl thio group.

In conclusion, **1** reacted with **2** to give a 4-methylphenylthio compound (**3**). This was converted to a sulfoxide (**4**) and sulfone (**5**) selectively using appropriate amounts of *m*-CPBA. Reaction of **3**, **4** or **5** with olefins and tributyltin hydride in the presence of AIBN resulted in the reduction of the chlorine atom to give trifluoroethylsulfur compounds (**6**, **7** or **8**). This suggests that the radical intermediates react more readily with tributyltin hydride than with an olefin. Allyltributyltin reacted with **3** or **5** to give the corresponding allyl compounds (**9** or **11**), while **4** was decomposed in the reaction condition. The reaction of **3** with allyltrimethylsilane in the presence of titanium(IV) chloride gave the allyl compound (**9**) in excellent yield. This result shows that the stabilization of an α-carbocation by a 4-methylphenylthio group exceeded the destabilization by a trifluoromethyl group. The last reaction can be applied to aromatic compounds to give 2,2,2-trifluoro-1-(4-methylphenylthio)ethyl compounds in good yields. Therefore, **3** was found to be useful for the syntheses of organofluorine compounds.

Experimental

General Procedures ^{1}H-NMR were recorded on JEOL-FX90Q and JNM-GX400 spectrometers. Tetramethylsilane was used as an internal standard. ^{19}F-NMR were recorded on Hitachi FT-NMR R-1500 and JEOL-FX90Q spectrometers. Benzotrifluoride was used as an internal standard. Mass spectra were obtained by JEOL JMS-DX-300. Melting point was measured on a Yanagimoto melting point apparatus. Gas-liquid chromatography (GLC) was carried out on a Hitachi 263-50 gas chromatograph (column, 5% SE-30 3 mm×2 m; carrier, N_2 at 30 ml/min). Peak areas were calculated on a Hitachi D-2000 chromato-integrator.

1-Chloro-2,2,2-trifluoroethyl 4-Methylphenyl Sulfide (3) 1) In an atmosphere of Ar, a solution of 4-methylbenzenethiol (**2**, 1.24 g, 10 mmol) in DMF (3 ml) was added dropwise to a suspension of 60% NaH (402 mg, 10 mmol) in DMF (3 ml) at 0 °C. After the mixture was stirred at this temperature for another 10 min, Halothane (**1**, 1.1 ml, 10 mmol) was added, then the mixture was stirred at room temperature for 3.5 h. The whole mixture was poured into ice-water containing 10% HCl, then filtered through a layer of Celite. The Celite layer was washed with Et_2O. All the solutions were combined and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$, then brine, and dried over $MgSO_4$. After the solvent was removed under a vacuum, the residue was separated by column chromatography (SiO_2, hexane) to give **3** (770 mg, 32%). **3**: A colorless oil. bp 101 °C (16 mmHg). MS *m/z*: 240 (M^+). High resolution MS (HR-MS) Calcd for $C_9H_8ClF_3S$ (M^+): 239.999. Found: 239.995. ^{19}F-NMR ($CDCl_3$) δ: -8.74 (3F, d, $J=6.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s), 5.20 (1H, q, $J=6.6$ Hz), 7.47 (2H, d, $J=8.1$ Hz), 7.53 (2H, d, $J=8.1$ Hz).

2) In an atmosphere of Ar, a solution of **2** (1.24 g, 10 mmol) in DMF (3 ml) was added slowly to a suspension of 60% NaH (402 mg, 10 mmol) in DMF (3 ml) at 0 °C. After the mixture was stirred at this temperature for 10 min, **1** (2.1 ml, 20 mmol) was added dropwise to this mixture. After the mixture was allowed to warm to room temperature, it was stirred for another 4 h. The whole mixture was worked up as above to give **3** (1.32 g, 55%).

3) Solvent effects. To investigate solvent effects, the same reaction as above was carried out using the solvents shown in Table 1. The results are summarized in Table 1.

2-Chloro-1,1,1-trifluoro-2-(4-methylbenzenesulfinyl)ethane (4) In an atmosphere of Ar, **3** (240 mg, 1 mmol) was added drop by drop to a solution of 60% *m*-CPBA (287 mg, 1 mmol) in CH_2Cl_2 (5 ml) at room temperature. After the mixture was stirred for 1 h, it was treated with 20% $NaHSO_3$ and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent under a vacuum, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 3 : 2) to give **4** (221 mg, 86%). **4** was found to be a mixture of two diastereo isomers by ^{19}F-NMR (ratio 3 : 2). The isomers were separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 3 : 2). **4**: One isomer: Colorless crystals. mp 87—88 °C. MS *m/z*: 256 (M^+). HR-MS Calcd for $C_9H_8ClF_3OS$ (M^+): 255.994. Found: 255.987 ^{19}F-NMR ($CDCl_3$) δ: -5.73 (3F, d, $J=7.0$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.44 (3H, s), 4.65 (1H, q, $J=7.0$ Hz), 7.37 (2H, d, $J=8.3$ Hz), 7.58 (2H, d, $J=8.3$ Hz). The other isomer: A colorless oil. MS *m/z*: 256 (M^+). HR-MS Calcd for $C_9H_8ClF_3OS$ (M^+): 255.994. Found: 255.988. ^{19}F-NMR ($CDCl_3$) δ: -3.95 (3F, d, $J=7.0$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.45 (3H, s), 4.81 (1H, q, $J=7.0$ Hz), 7.37 (2H, d, $J=8.3$ Hz), 7.69 (2H, d, $J=8.3$ Hz).

2-Chloro-1,1,1-trifluoro-2-(4-methylbenzenesulfonyl)ethane (5) In an atmosphere of Ar, **3** (240 mg, 1 mmol) was added drop by drop to a solution of 60% *m*-CPBA (862 mg, 3 mmol) in CH_2Cl_2 (15 ml). After the mixture was stirred at room temperature for 1 h, it was treated with 20% $NaHSO_3$ and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 1 : 1) to give **5** (245 mg, 90%). **5**: Colorless crystals. mp 66—68 °C. MS *m/z*: 272 (M^+). HR-MS Calcd for $C_9H_8ClF_3O_2S$ (M^+): 271.989. Found: 271.981. ^{19}F-NMR ($CDCl_3$) δ: -4.07 (3F, d, $J=6.2$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.49 (3H, s), 5.06 (1H, q, $J=6.2$ Hz), 7.42 (2H, d, $J=8.3$ Hz), 7.88 (2H, d, $J=8.3$ Hz).

Reaction of 3 with α-Methylstyrene in the Presence of Tributyltin Hydride In an atmosphere of Ar, tributyltin hydride (0.35 ml, 1.3 mmol) was added to a boiling solution of AIBN (10 mg, 0.06 mmol), α-methylstyrene (0.65 ml, 5 mmol) and **3** (240 mg, 1 mmol) in benzene (10 ml). After the mixture was refluxed for 1 h, it was treated with cold 10% KF, then extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give 2,2,2-trifluoroethyl 4-methylphenyl sulfide (**6**, 75 mg, 36%). **6**: A colorless oil. MS *m/z*: 206 (M^+). HR-MS Calcd for $C_9H_9F_3S$ (M^+): 206.038. Found: 206.038. ^{19}F-NMR ($CDCl_3$) δ: -3.35 (3F, t, $J=9.8$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.34 (3H, s), 3.38 (2H, q, $J=9.8$ Hz), 7.14 (2H, d, $J=9.5$ Hz), 7.40 (2H, d, $J=9.5$ Hz).

Reaction of 4 with α-Methylstyrene in the Presence of Tributyltin Hydride In an atmosphere of Ar, tributyltin hydride (0.35 ml, 1.3 mmol) was added to a boiling solution of AIBN (10 mg, 0.06 mmol), **4** (256 mg, 1 mmol) and α-methylstyrene (0.65 ml, 5 mmol) in benzene (10 ml). After the mixture was refluxed for 1 h, it was treated with cold 10% KF and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 3 : 2) to give 1,1,1-trifluoro-2-(4-methylbenzenesulfinyl)ethane (**7**, 151 mg, 68%). **7**: Colorless crystals. mp 58—59 °C. MS *m/z*: 222 (M^+). HR-MS Calcd $C_9H_9F_3OS$ (M^+): 222.033. Found: 222.033. ^{19}F-NMR ($CDCl_3$) δ: 1.59 (3F, dd, $J=10.1$, 10.1 Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.44 (3H, s), 3.38 (1H, dq, $J=14.3$, 10.1 Hz), 3.55 (1H, dq, $J=14.3$, 10.1 Hz), 7.38 (2H, d, $J=8.2$ Hz), 7.59 (2H, d, $J=8.2$ Hz).

Reaction of 5 with α-Methylstyrene in the Presence of Tributyltin Hydride In an atmosphere of Ar, tributyltin hydride (0.35 ml, 1.3 mmol) was added dropwise to a boiling solution of AIBN (10 mg, 0.06 mmol), **5** (272 mg, 1 mmol) and α-methylstyrene (0.65 mg, 5 mmol) in benzene (10 ml). After the mixture was refluxed for 1 h, it was treated with cold 10% KF and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent under a vacuum, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 1 : 1) to give 1,1,1-trifluoro-2-(4-methylbenzenesulfonyl)ethane (**8**, 190 mg, 80%). **8**: Colorless crystals. mp 80—81 °C. MS *m/z*: 238 (M^+). HR-MS Calcd for $C_9H_9F_3O_2S$ (M^+): 238.028. Found: 238.027. ^{19}F-NMR ($CDCl_3$) δ: 1.31 (3F, t, $J=9.0$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.46 (3H, s), 3.91 (2H, q, $J=9.0$ Hz), 7.39 (2H, d, $J=8.4$ Hz), 7.84 (2H, d, $J=8.4$ Hz).

Reaction of 3 with Allyltributyltin Using 2 eq of Reagent: In an atmosphere of Ar, a solution of AIBN (8 mg, 0.05 mmol), **3** (60 mg, 0.25 mmol) and allyltributyltin (0.16 ml, 0.5 mmol) in benzene (1.5 ml) was refluxed under stirring for 9 h. The cooled mixture was treated with 10% KF and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give 5,5,5-trifluoro-4-(4-methylphenylthio)-1-pentene (**9**, 13 mg, 21%). **9**: A colorless oil. MS *m/z*: 246 (M^+). HR-MS Calcd for $C_{12}H_{13}F_3S$ (M^+): 246.069. Found: 246.068. ^{19}F-NMR ($CDCl_3$) δ: -7.23 (3F, d, $J=8.5$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.34 (3H, s), 2.38 (1H, dddt, $J=15.0$, 9.8, 4.8, 1.2 Hz), 2.64 (1H, dddt, $J=15.0$, 7.0, 4.3, 1.2 Hz), 3.30 (1H, ddq, $J=12.5$, 9.8, 8.5 Hz), 5.18—5.23 (2H, m), 5.89—6.00 (1H, ddm, $J=17.1$, 10.1 Hz), 7.12 (2H, d, $J=7.9$ Hz), 7.41 (2H, d, $J=7.9$ Hz).

Using 4 eq of the Reagent: In an atmosphere of Ar, a solution of AIBN (8 mg, 0.05 mmol), **3** (60 mg, 0.25 mmol) and allyltributyltin (0.31 ml, 1 mmol) in benzene (1.5 ml) was refluxed under stirring for 9 h. The cooled mixture was treated with 10% KF and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give **9** (28 mg, 45%).

The same reactions of **4** with allyltributyltin as those of **3**, with much prolonged reaction times (72 h), did not afford any objective product (**10**). The starting material (**4**) was not recovered. This suggested that **4** was not stable in this reaction condition.

Reaction of 5 with Allyltributyltin Using 2 eq of the Reagent: In an atmosphere of Ar, a solution of AIBN (8 mg, 0.05 mmol), **5** (68 mg, 0.25 mmol) and allyltributyltin (0.16 ml, 0.5 mmol) in benzene (1.5 ml) was refluxed under stirring for 3 h. The cooled mixture was treated with 10% KF and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent under a vacuum, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 1 : 1) to give 5,5,5-trifluoro-4-(4-methylbenzensulfonyl)-1-pentene (**11**, 62 mg, 89%). **11**: Colorless crystals. mp 42 °C. MS *m/z*: 278 (M^+). HR-MS Calcd for $C_{12}H_{13}F_3O_2S$ (M^+): 278.059. Found: 278.059. ^{19}F-NMR ($CDCl_3$) δ: -0.84 (3F, d, $J=7.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s), 2.68 (1H, dddt, $J=15.3$, 7.6, 7.6, 1.2 Hz), 2.97 (1H, ddm, $J=15.6$, 5.2 Hz), 3.69 (1H, dqd, $J=7.7$, 7.6, 5.1 Hz), 5.14—5.22 (2H, m), 5.86 (1H, ddm, $J=16.8$, 10.1 Hz), 7.38 (2H, d, $J=8.2$ Hz), 7.81 (2H, d, $J=8.2$ Hz).

Using 4 eq of the Reagent: In an atmosphere of Ar, a solution of AIBN (8 mg, 0.05 mmol), **5** (68 mg, 0.25 mmol) and allyltributyltin (0.31 ml, 1 mmol) in benzene (1.5 ml) was refluxed under stirring for 3 h. The cooled mixture was worked up as above to give **11** (63 mg, 91%).

5,5,5-Trifluoro-4-(4-methylphenylthio)-1-pentene (9) through a Cationic Reaction of 3 Using $BF_3 \cdot Et_2O$ as a Lewis Acid: In an atmosphere of Ar, BF_3 Et_2O (0.38 ml, 3 mmol) was added slowly to a solution of **3** (240 mg, 1 mmol) and allyltrimethylsilane (0.27 ml, 3 mmol) in CH_2Cl_2 (5 ml) at room temperature. After the mixture was stirred for 48 h at room temperature, it was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent under a vacuum, the residue was purified by column chromatography (SiO_2, hexane) to give **9** (10 mg, 4%).

The results of reactions using other Lewis acids are summarized in Table 3.

1,1,1-Trifluoro-2-(4-methylphenylthio)-2-phenylethane (14) In an atmosphere of Ar, $TiCl_4$ (0.33 ml, 3 mmol) was added slowly to a solution of **3** (240 mg, 1 mmol) and benzene (0.27 ml, 3 mmol) in CH_2Cl_2 (5 ml) at room temperature. After the mixture was stirred for 24 h at this temperature, it was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent under a vacuum, the residue was purified by column chromatography (SiO_2, hexane) to give **14** (219 mg, 78%). **14**: A colorless oil. MS *m/z*: 282 (M^+). HR-MS Calcd for $C_{15}H_{13}F_3S$: 282.070 (M^+). Found: 282.070. ^{19}F-NMR ($CDCl_3$) δ: -4.54 (3F, d, $J=8.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.31 (3H, s), 4.45 (1H, q, $J=8.6$ Hz), 7.06—7.33 (9H, m).

1,1,1-Trifluoro-2-(2- and 4-methylphenyl)-2-(4-methylphenylthio)-ethanes (15 and 16) In an atmosphere of Ar, $TiCl_4$ (0.33 ml, 3 mmol) was added slowly to a solution of **3** (240 mg, 1 mmol) and toluene (0.32 ml, 3 mmol) in CH_2Cl_2 (5 ml) at room temperature. After the mixture was stirred for 12 h at this temperature, it was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ and brine, then dried over $MgSO_4$. After evaporation of the solvent, the residue was separated by column chromatography (SiO_2, hexane) to give 1,1,1-trifluoro-2-(2-methylphenyl)-2-(4-methylphenylthio)ethane (**15**, 46 mg, 16%) and 1,1,1-trifluoro-2-(4-methylphenyl)-2-(4-methylphenylthio)ethane (**16**, 242 mg, 82%). **15**: A colorless oil. MS *m/z*: 296 (M^+). HR-MS Calcd for $C_{16}H_{15}F_3S$: 296.084 (M^+). Found: 296.084. ^{19}F-NMR ($CDCl_3$) δ: -4.71 (3F, d, $J=8.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, s), 2.34 (3H, s), 4.42 (1H, q, $J=8.6$ Hz), 7.08 (2H, d, $J=8.2$ Hz), 7.15 (2H, d, $J=8.2$ Hz), 7.22 (2H, d, $J=8.2$ Hz), 7.33 (2H, d, $J=8.2$ Hz). **16**: A colorless oil. MS *m/z*: 296 (M^+). HR-MS Calcd for $C_{16}H_{15}F_3S$: 296.085 (M^+). Found: 296.085. ^{19}F-NMR ($CDCl_3$) δ: -3.93 (3F, d, $J=8.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.33 (6H, s), 4.75 (1H, q, $J=8.6$ Hz), 7.09 (2H, d, $J=8.2$ Hz), 7.16—7.42 (4H, m), 7.33 (2H, d, $J=8.2$ Hz).

1,1,1-Trifluoro-2-(4-methylphenylthio)-2-(1-naphthyl)ethane (17) In an atmosphere of Ar, $TiCl_4$ (0.33 ml, 3 mmol) was added slowly to a solution of **3** (240 mg, 1 mmol) and naphthalene (0.38 g, 3 mmol) in CH_2Cl_2 (5 ml) at room temperature. After the mixture was stirred for 10 h, it was worked up as above to give 1,1,1-trifluoro-2-(4-methylphenylthio)-2-(1-naphthyl)ethane (**17**, 298 mg, 90%). **17**: A colorless oil. MS *m/z*: 332 (M^+). HR-MS Calcd for $C_{19}H_{15}F_3S$: 332.085 (M^+). Found: 332.085. ^{19}F-NMR ($CDCl_3$) δ: -3.38 (3F, d, $J=7.3$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.33 (3H, s), 5.39 (1H, br), 7.06—8.01 (11H, m).

1,1,1-Trifluoro-2-(2- and 4-hydroxyphenyl)-2-(4-methylphenylthio)-ethanes (18 and 19) In an atmosphere of Ar, $TiCl_4$ (0.33 ml, 3 mmol) was added slowly to a solution of **3** (240 mg, 1 mmol) and phenol (0.26 ml, 3 mmol) in CH_2Cl_2 (5 ml). After the mixture was stirred for 3 h, it was worked up as above, then separated by column chromatography (SiO_2, hexane to hexane–CH_2Cl_2, 7 : 3) to give 1,1,1-trifluoro-2-(2-hydroxyphenyl)-2-(4-methylphenylthio)ethane (**18**, 44 mg, 15%) and 1,1,1-trifluoro-2-(4-hydroxyphenyl)-2-(4-methylphenylthio)ethane (**19**, 72 mg, 24%). **18**: A colorless oil. MS *m/z*: 298 (M^+). HR-MS Calcd for $C_{15}H_{13}F_3OS$: 298.064 (M^+). Found: 298.064. ^{19}F-NMR ($CDCl_3$) δ: -4.22 (3F, d, $J=8.6$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.45 (3H, s), 5.10 (1H, q, $J=8.6$ Hz), 5.19 (1H, s), 6.78—7.35 (4H, m), 7.08 (2H, d, $J=8.2$ Hz), 7.36 (2H, d, $J=8.2$ Hz). **19**: Colorless crystals. mp 98—100 °C. MS *m/z*: 298 (M^+). HR-MS Calcd for $C_{15}H_{13}F_3OS$: 298.063 (M^+). Found: 298.063. ^{19}F-NMR ($CDCl_3$) δ: -5.23 (3F, d, $J=8.5$ Hz). ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, s), 4.40 (1H, q, $J=8.5$ Hz), 4.81 (1H, s), 6.79 (2H, d, $J=8.5$ Hz), 7.08 (2H, d, $J=7.9$ Hz), 7.21 (2H, d, $J=8.5$ Hz), 7.30 (2H, d, $J=7.9$ Hz).

References and Notes

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