New Electrophilic Trifluoromethylating Agents

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Synthetic routes to *S*-(trifluoromethyl)phenyl-4-fluorophenylsulfonium triflate (**8**), *S*-(trifluoromethyl)phenyl-2,4-difluorophenylsulfonium triflate (**9**), *S*-(trifluoromethyl)phenyl-3-nitrophenylsulfonium triflate (**10**), and *S*-(trifluoromethyl)-4-fluorophenyl-3-nitrophenylsulfonium triflate (**11**) are described. They are stable molecules and conveniently prepared by treating phenyl trifluoromethyl sulfoxide with benzene and its derivatives. These novel electrophilic trifluoromethylating agents react under mild conditions with a variety of aromatic rings (*p*-hydroquinone, pyrrole, and aniline) to give trifluoromethylated compounds (2-trifluoromethyl-*p*-hydroquinone, 2-trifluoromethylpyrrole, 2-trifluoromethylaniline, and 4-trifluoromethylaniline) in moderate to high yields. The electrophilic trifluoromethylating potential can be altered by placing electron-withdrawing substituents on the benzene rings.

Introduction

The trifluoromethyl group (CF_3) is an important structural moiety in diverse classes of bioactive organic molecules. The CF_3 group has a bigger van der Waals radius than that of a CH_3 group and the same electronegativity as oxygen (Table 1).[1]

The C−F bond in trifluoromethylated compounds results in added stability and lipophilicity of the molecule. As a consequence the introduction of a trifluoromethyl group into organic molecules often changes their physical, chemical, and physiological properties.[2] Compounds containing the trifluoromethyl group are found in a variety of commercially important dyes,[3,4] polymers,[5,6] pharmaceuticals,[7] and agrochemicals.[8] The dye industry has found that trifluoromethylated chromophores exhibit increased light fastness[3,4] compared with the nonfluorinated compounds. Trifluoromethylated polymers have high thermal stability and enhanced mechanical and electrical properties. Many of these polyfluorinated polymers find application as liquid crystals.[5,6] In a wide variety of agrochemicals and pharmaceuticals, the properties of the trifluoromethyl group, i.e., to increase lipophilicity and to act as an inhibitor of enzyme action, are key reasons for incorporation.[7,8] Thus, a variety of reagents have been developed in order to introduce the CF_3 group into organic molecules.[9−11] Currently, there are three available methods for directly introducing a CF_3 group into target compounds: (i) organometallic based on CF_3Cu,[9] (ii) nucleophilic based on CF_3SiMe_3,[10] and (iii) electrophilic based on *S*-(trifluoromethyl)dibenzothiophenium triflate.[11]

Table 1. van der Waals Radius and Electronegativity of Different Groups

group/atom	van der Waals radius (Å)	group/atom	electronegativity
CF_3	2.7	CF_3	3.5
CH_3	2.0	CH_3	2.3
CCl_3	3.5	C	2.5
F	1.4	F	4.0
H	1.2	H	2.1
O	1.5	O	3.5
		Cl	3.0

The introduction of a CF_3 group into an electron-rich environment is becoming more and more important in organic and bioorganic synthesis. It is not a trivial task, however. It is extremely difficult to generate the CF_3 cation chemically, due to its high electronegativity (3.45).[12] In 1984, Yagupol'skii[13] reported two trifluoromethyl sulfonium salts, trifluoromethyl-*p*-chlorophenyl(2,4-dimethylphenyl)sulfonium hexafluoroantimonate (**1**) and trifluoromethyl-*p*-chlorophenyl-*p*-anisylsulfonium hexafluoroantimonate (**2**), that were capable of acting as trifluoromethylating reagents. Compounds **1** and **2** react with sodium *p*-nitrothiophenolate in DMF to give *p*-nitrophenyl trifluoromethyl sulfide in high yield. However, **1** and **2** were synthesized from the extremely hygroscopic intermediate fluoro(trifluoromethyl)-*p*-chlo-

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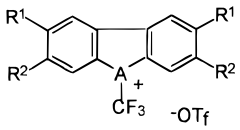
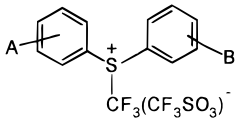


A = S, Se, Te
R^1 = H, R^2 = NO_2

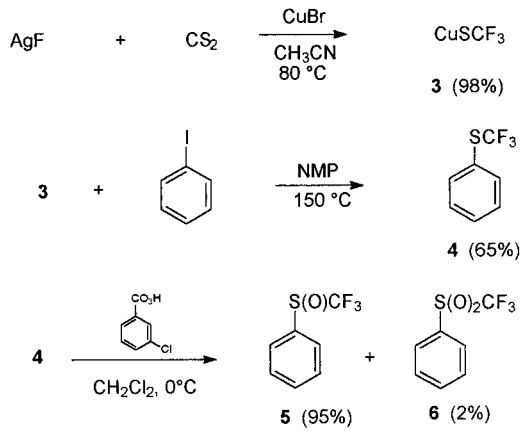
Figure 1.

Scheme 1



A and B = F, NO_2, CF_3.

Scheme 2



rophenylsulfonium hexafluoroantimonate. Both products, **1** and **2**, are also extremely hygroscopic. Furthermore, they are unreactive with the highly activated aromatic compound *N*,*N*-dimethylaniline. In 1990, Umemoto reported power-variable electrophilic trifluoromethylating agents (Figure 1) that can transfer the CF_3 group to different kinds of organic molecules.[11,14] They react readily with strongly activated aromatic systems, e.g. *N*,*N*-dimethylaniline. Although these reagents are very useful, they are prepared by using multistep, inconvenient synthetic routes that require gaseous CF_3I or CF_3Br for the trifluoromethylation reaction. These reagents, although available commercially, are expensive.

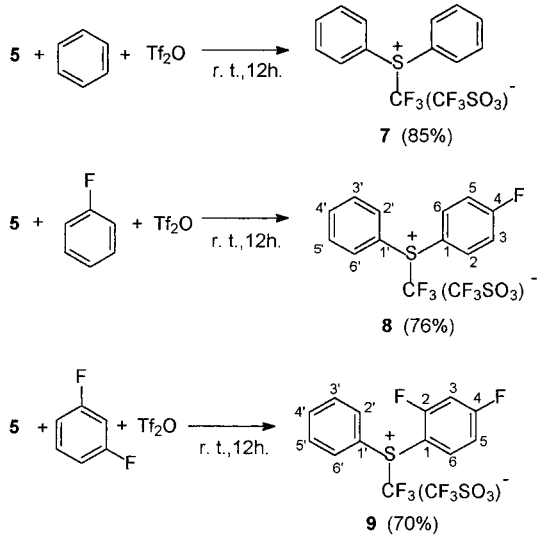
We have developed a new series of *S*-(trifluoromethyl)-diphenylsulfonium triflate derivatives that are easily prepared from inexpensive reagents. We have explored their potential to act as practical, useful electrophilic trifluoromethylating agents, and the results of that exploration are the focus of this paper.

Results and Discussion

Based on the literature,[11−14] and our unpublished work, our synthetic targets were derivatized *S*-(trifluoromethyl)diphenylsulfonium triflates (Scheme 1). We have developed simple, inexpensive routes for their preparation. Reactivity can be tuned via functionalization of the aromatic rings.

The precursors to these compounds were synthesized as described in Scheme 2. Trifluoromethylthiocopper(I) **(3)** was prepared by reacting silver(I) fluoride and carbon disulfide in acetonitrile, followed by a metathetical reaction with copper(I) bromide.[15] The white solid **3** was obtained in high yield (98%) and was reacted with iodobenzene in *N*-methylpyrrolidone (NMP) to give trifluoromethylthiobenzene (**4**) in 65% yield.[15] When this reaction was carried out in a different solvent, e.g. in DMF, the yield was not improved. The product was purified by column chromatography. The ^{19}F NMR spectrum of **4** consisted of a single resonance at −43.0 ppm in $CDCl_3$. Phenyl trifluoromethyl sulfoxide (**5**) was obtained from the oxidation of trifluoromethylthiobenzene with *m*-chloroperbenzoic acid via reaction overnight at 0 °C in CH_2Cl_2. This oxidation reaction is very sensitive to temperature. If the temperature exceeded 0 °C, the yield of sulfone **6** was enhanced. For example, when the reaction was carried out at room temperature for 12 h, the ratio of **5**:**6** was 5:2. On the other hand at 0 °C for 10 h, the ratio of **5**:**6** was 95:2. Compounds **5** and **6** were separated by column chromatography.

Scheme 3



S-(Trifluoromethyl)diphenylsulfonium triflate and its derivatives were obtained by an intermolecular condensation reaction of phenyl trifluoromethyl sulfoxide with benzene, 1-fluorobenzene, or 1,3-difluorobenzene by the action of trifluoromethanesulfonic anhydride at room temperature (Scheme 3). The products were easily purified by column chromatography and recrystallization. Compound **7** was obtained in a yield of 85%. A parent ion for **7** appears in the mass spectrum at *m*/*z* 255 (FAB-MS). When 1-fluorobenzene or 1,3-difluorobenzene was reacted with phenyl trifluoromethyl sulfoxide, we expected two major products, the *ortho*- and *para*-substituted isomers. In this reaction, however, we obtained the *para*-isomer of **8** in a yield of 76% and the *para*-isomer of **9** in a yield of 70%. The structure of these products was confirmed based on their ^1H and ^{19}F NMR and mass spectra. The FAB-MS for **8** showed a parent ion at *m*/*z* 273. In the ^1H NMR spectrum, H2 and H6 gave peaks that are a doublet of doublets, with coupling constants of J_{23} = 6.0 Hz and J_{2F} = 4.0 Hz. Protons H3 and H5 resonate as another set of doublet of doublets, J_{32} = 6.0 Hz and J_{3F} = 9.0 Hz. These two types of protons

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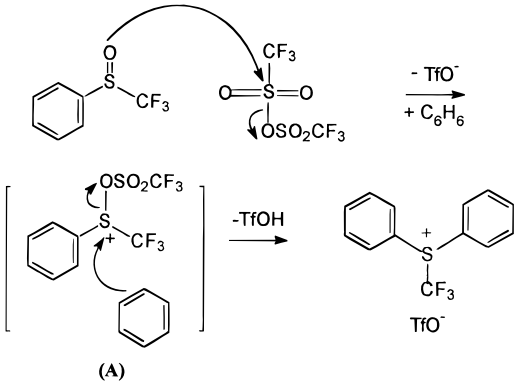
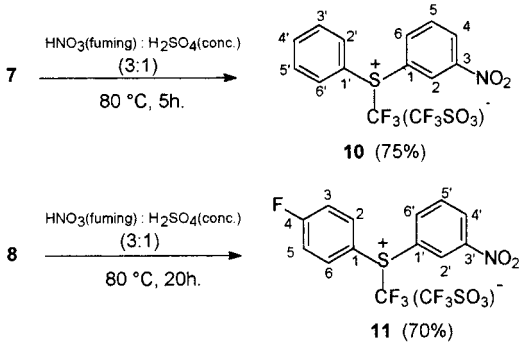
Scheme 4



(A)

Scheme 5



confirm that the F group is at the *para*-position. If the F atom were located at the *ortho*-position or the *meta*-position, the ^{1}H NMR would show four types of protons and much more complex fine coupling. For compound **9**, the ^{19}F NMR spectrum showed two types of fluorine atoms on the benzene ring. One gave rise to a resonance at −91.74 ppm and the second at −98.22 ppm. The ^{1}H NMR spectrum showed a resonance at 7.90 ppm for H6, as a broad doublet $J_{65} = 7.5$ Hz. H5 is at 7.45 ppm as a doublet of doublets with coupling constants of $J_{56} = 8.10$ Hz, $J_{54F} = 7.8$ Hz. Proton H3 is at 7.25 ppm and is also a doublet of doublets with coupling constants of $J_{32F} = 9.0$ Hz, $J_{34F} = 9.0$ Hz. There are three different types of protons on the fluorinated benzene ring, confirming the structure of **9** as shown. The FAB-MS shows a parent ion for **9** at *m*/*z* 291. From these results, it is seen that steric factors are important with respect to the isomer formed. When either the group on the ring or the attacking group is large, steric hindrance inhibits the formation of the *ortho*-product, and the amount of *para*-isomer obtained is increased.

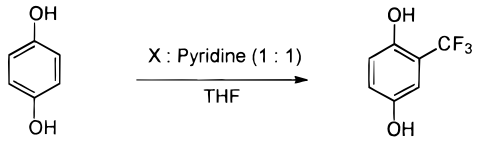
When 1,2,4-trifluorobenzene or pentafluorobenzene was the substrate in this intermolecular condensation reaction, mixtures of products were obtained because of interfering nucleophilic reactions. The $CF_3SO_3^-$ nucleophile attacked the fluorobenzene ring and replaced fluorine atoms. No reaction occurred when the substrate used was nitrobenzene or trifluoromethylbenzene. Not surprisingly the reactivity toward electrophiles of the benzene ring substituted with electron-withdrawing groups (NO_2, CF_3) was greatly reduced.

The intermolecular condensation reaction of phenyl trifluoromethyl sulfoxide (**5**) with benzene induced by Tf_2O apparently proceeds via intermediate A (Scheme 4). This is also consistent with the fact that electron-withdrawing groups on the benzene-ring reduced its reactivity with the sulfoxide.

The reactivity of the *S*-(trifluoromethyl)diphenylsulfonium triflate salt can be modified by the introduction of different substituents into the ring. Mononitrated thiophenium salts were prepared from the reaction of **7** or **8** with a mixture of fuming HNO_3 and concentrated H_2SO_4 at 80 °C (Scheme 5). Products **10** and **11** were purified by recrystallization. When **7** and **8** were nitrated, the *meta*-substituted products were expected since CF_3S^+ is a *meta*-directing group. Compounds **10** and **11** were obtained in yields of 75% and 70%, respectively. The structures of **10** and **11** were elucidated by NMR and MS spectral analysis. For compound **10**, FAB-MS shows a parent ion at *m*/*z* 300. The ^{1}H NMR spectrum shows H2 at 8.83 ppm as a doublet of doublets with coupling constants of $J_{24} = J_{26} = 2.0$ Hz. Proton H4 resonates at 8.75 ppm as a doublet of doublets of doublets, with coupling constants of $J_{45} = 6.0$ Hz and $J_{42} = J_{46} = 2.0$ Hz. Proton H6 is found at 8.42 ppm, as a multiplet, with one measurable coupling constant of $J_{65} = 6.0$ Hz. The other six hydrogenatoms appear as two multiplets at 8.15 and 7.90 ppm. The presence of four different types of protons and their fine structure in the NMR spectra confirmed the structure of **10**. For compound **11**, the FAB-MS spectrum shows a parent ion at *m*/*z* 318. The ^{1}H NMR shows H2′ at 8.81 ppm as a doublet of doublets with coupling constants of $J_{2'4'} = J_{2'6'} = 2.0$ Hz. Proton H4′ is at 8.73 ppm as a doublet of doublets of doublets with coupling constants of $J_{4'5'} = 6.0$ Hz, $J_{4'2'} = J_{4'6'} = 2.0$ Hz. Proton H5′ is found at 8.10 ppm as a doublet of doublets with coupling constants of $J_{5'4'} = J_{5'6'} = 8.0$ Hz, while a complex multiplet at 8.42 ppm was assigned to H6′. One measurable coupling constant is $J_{6'5'} = 8.0$ Hz. For H2 and H6 at 8.24 ppm, a doublet of doublets resonance is seen and the coupling constants are $J_{23} = 8.0$ Hz and $J_{2F} = 8.0$ Hz. H3 and H5 are at 7.67 ppm also as a doublet of doublets with coupling constants of $J_{32} = 8.0$ Hz, $J_{3F} = 8.1$ Hz. These data are consistent with the presence of a single NO_2 group on the nonfluorinated benzene ring. Only two types of protons are present on the benzene ring that contains a fluorine atom. The other four types of protons and their coupling constants confirm the fact that the NO_2 group is at the *meta*-position of the nonfluorinated benzene ring. When **8** was nitrated, the nitro group was not incorporated into the fluorobenzene ring under the reaction conditions used. Only the nonfluorinated benzene ring could be nitrated. The electrophilic nitration reaction becomes more difficult when more fluoro groups are on the benzene ring. For example, the compound *S*-(trifluoromethyl)phenyl-2,4-difluorophenylsulfonium triflate was examined, and no nitration reaction occurred under any of the reaction conditions employed.

Tables 2−4 compare the reactivities of a series of *S*-(trifluoromethyl)diphenylsulfonium triflates and derivatives with respect to their ability to transfer CF_3 to different substrates. Relative amounts of products formed were determined based on ^{19}F NMR spectral analysis. Because of the electron-withdrawing properties of the nitro group on the benzene ring, compounds **10** and **11** are more effective transfer reagents than **7** and **8**. When there are two fluorine atoms on the benzene ring, the electrophilic trifluoromethylating ability of the sulfonium

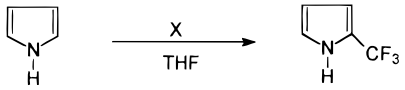
Table 2. Trifluoromethylation of *p*-Hydroquinone by Various Trifluoromethylating Agents



X	molar ratio[a]	condition	yield, %[b]
7	2:1	rt, 5 h	5
10	2:1	rt, 5 h	40
8	2:1	rt, 5 h	6
11	2:1	rt, 5 h	40
9	2:1	rt, 5 h	10
9	2:1	reflux, 10 h	85

[a] Molar ratio = substrate:CF_3^+. [b] Yields determined from ^{19}F NMR spectra. Reference 16.

Table 3. Trifluoromethylation of Pyrrole by Various Trifluoromethylating Agents



X	molar ratio[a]	condition	yield, %[b]
7	1:2.5	reflux, 2 h	6
10	1:2.5	reflux, 2 h	80
8	1:2.5	reflux, 2 h	10
11	1:2.5	reflux, 2 h	85
9	1:2.5	reflux, 2 h	50
9	1:2.5	reflux, 10 h	87

[a] Molar ratio = substrate:CF_3^+. Yields determined from ^{19}F NMR spectra. Reference 17.

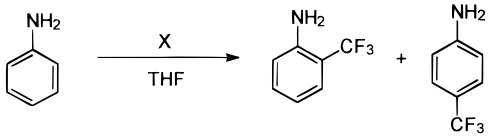
triflate is enhanced. Thus **9** is also more reactive than either **7** or **8**.

p-Hydroquinone was trifluoromethylated with reagents **7**−**11** in the presence of pyridine as a base (Table 2), and the yields of 2-trifluoromethyl-*p*-hydroquinone obtained were determined by ^{19}F NMR and ^1H NMR spectral analysis. At rt, the abilities of **10** and **11** to transfer CF_3 appeared about equal. At higher temperatures, **9** functioned very effectively as an electrophilic trifluoromethylating reagent, but increase in temperature did not impact the ability of the other four reagents to transfer CF_3.

2-Trifluoromethylpyrrole was the product of trifluoromethylation of pyrrole under reflux conditions (Table 3). No products containing more than one CF_3 group were isolated. When the reactions were carried out at room temperature, the yields were poor, e.g., for compounds **7** and **8**, only starting material was recovered, and for compounds **9**, **10**, and **11**, the yields were less than 10%. However, at reflux, **9**, **10**, and **11** gave yields of 2-trifluoromethylpyrrole of 80% or better. With **9** a longer reflux time was required.

p-Hydroquinone is more electron-rich than pyrrole, and consequently its reactivity is higher as demonstrated by the fact that transfer of CF_3 takes place readily at room temperature.

Table 4. Trifluoromethylation of Aniline by Various Trifluoromethylating Agents



12 **13**

X	molar ratio[a]	condition	yield (**12**:**13**), %
7	1:2	reflux, 10 h	trace, trace
10	1:2	reflux, 10 h	70, 18
8	1:2	reflux, 10 h	trace, trace
11	1:2	reflux, 10 h	66, 17
9	1:2	reflux, 10 h	33, 31

[a] Molar ratio = substrate:CF_3^+. [b] Yields determined from ^{19}F NMR spectra. Reference 18.

Table 4 shows the results of the trifluoromethylation of aniline and the two products identified when treating aniline with reagents **7**−**11** in THF at reflux. When the reactions were carried out at room temperature, only starting materials were obtained.

Conclusion

We have demonstrated that aromatic ring substituted *S*-(trifluoromethyl)diphenylsulfonium triflates react with aromatic ring substrates to give aromatic compounds containing the trifluoromethyl group. The electrophilic trifluoromethylating reagents that we have described are stable molecules and are inexpensive and convenient to prepare. Their electrophilic trifluoromethylating potential can be altered by changing the substitutents on the benzene rings. When electron-withdrawing groups (NO_2, F) were present on the benzene ring, transfer of the CF_3 group to electron-rich substrates was enhanced.

Experimental Section

^{19}F, ^1H, and ^{13}C NMR spectra were obtained with a 200 MHz NMR spectrometer using $CDCl_3$ as solvent unless otherwise indicated. Chemical shifts are reported with respect to $(CH_3)_4Si$ or $CFCl_3$. Products were separated by column chromatography with 70−230 mesh silica gel.

Preparation of Phenyl Trifluoromethyl Sulfoxide (5) and Phenyl Trifluoromethyl Sulfone (6). To a stirred solution of phenyl trifluoromethyl sulfide (1.0 g, 5.6 mmol) in dry CH_2Cl_2 (40 mL) at 0 °C under N_2 was added *m*-chloroperbenzoic acid (1.46 g, 7.3 mmol) in small portions. After the reaction mixture was stirred for 10 h at 0 °C, and then rt for 1 h, the solution was filtered and evaporated. The residue was subjected to silica gel column chromatography using a mixture of ethyl acetate and hexanes (30:1) as eluent to give product **5**[19] (0.981 g, 90%). IR (film): 3067 (w), 2359 (w), 1448 (m), 1370 (m), 1191 (s), 1141 (s), 1089 (s), 688 (m), 606 (m) cm^{-1}; ^1H NMR ($CDCl_3$): 7.54−8.06 (m, 5H); ^{19}F NMR ($CDCl_3$): −74.9 (s); ^{13}C NMR ($CDCl_3$): 134, 131, 130, 126, 121 (q, J = 260 Hz) ppm; EI-MS [*m/e* (species, intensity)]: 194 (M^+, 4.8), 141 ($M^+ - C_4H_5$, 13), 125 ($M^+ - CF_3$, 100), 109 ($M^+ - CF_3 - O$, 8), 77 (C_6H_5, 65), 69 (CF_3, 7.2). Phenyl trifluoromethyl sulfone (**6**)[20] (30.1 mg, 3%). IR (film): 3070 (w), 1585 (w), 1451 (m), 1370 (s), 1221 (s), 1143 (s), 1075 (m), 605 (m), 576 (m) cm^{-1}; ^1H NMR ($CDCl_3$): 8.04 (bd, J_{23} = 11.2 Hz, 2H), 7.84 (dt, J_{43} = 8.0 Hz, J_{42} = 2.0 Hz, 1H), 7.63 (dt, J_{32} = 8.0 Hz, J_{34} = 8.0 Hz, 2H); ^{19}F NMR ($CDCl_3$): −78.8 (s, 3F); ^{13}C NMR ($CDCl_3$): 137, 131, 130,

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129, 124 (q, $J = 261$ Hz) ppm; EI-MS [*m/e* (species, intensity)]: 210 (M^+, 2.7), 141 ($M^+ - CF_3$, 44.8), 125 ($M^+ - CF_3 - O$, 2.9), 77 ($C_6H_5^+$, 100), 69 (CF_3^+, 2.9). These compounds were previously synthesized but characterized based on ^{19}F NMR spectral data and boiling points only.

Preparation of *S*-(Trifluoromethyl)diphenylsulfonium Triflate (7). To a solution of phenyl trifluoromethyl sulfoxide (194.17 mg, 1.0 mmol) in dry benzene (2.6 mL, 30 mmol) was added $(CF_3SO_2)_2O$ (0.84 mL, 5.0 mmol) at 0 °C. The resulting solution was stirred for 1 h at 0 °C and then rt for another 24 h. The solvent was evaporated, and the residue was purified by column chromatography on silica gel with $CH_3CN-CH_2Cl_2$ (1:4) as eluent. The product was obtained as a white crystal (343.4 mg, 85%), mp 84−5 °C (recrystallized from ethyl acetate/hexanes). IR (Nujol): 3115 (w), 1263 (s), 1224 (s), 1146 (s), 1083 (s), 513 (s) cm^{-1}; ^1H NMR ($CDCl_3$): 8.15 (d, $J_{23} = 7.6$ Hz, 4H), 7.82 (m, 6H); ^{19}F NMR ($CDCl_3$): −49.6 (s, 3F), −78.6 (s, 3F); ^{13}C NMR ($CDCl_3$): 137, 133, 132, 127 (q, $J = 252$ Hz), 122 (q, $J = 253$ Hz), 117 ppm; FAB$^+$-MS [*m/e* (species, intensity)]: 255 ($(C_{13}H_{10}F_3S)^+$, 100), 186 ($(C_{13}H_{10}F_3S)^+ - CF_3$, 81.2), 178 ($(C_{13}H_{10}F_3S)^+ - C_6H_5$, 2.1), 109 ($(C_{13}H_{10}F_3S)^+ - C_6F_5 - CF_3$, 14.6). Anal. Calcd for $C_{14}H_{10}F_6O_3S_2$: C, 41.58; H, 2.49; F, 28.22. Found: C, 41.62; H, 2.57; F, 28.60.

Preparation of *S*-(Trifluoromethyl)phenyl-4-fluorophenylsulfonium Triflate (8). To a solution of phenyl trifluoromethyl sulfoxide (582 mg, 3.0 mmol) in dry 1-fluorobenzene (8.4 mL, 30 mmol) was added $(CF_3SO_2)_2O$ (2.5 mL, 15 mmol) at 0 °C. The reaction mixture was stirred for 10 h at 0 °C and then at rt for another 2 h. Removal of the solvent left a crude residue that was subjected to column chromatography on silica gel using $CH_3CN-CH_2Cl_2$ (1:4) as eluent to give the product as a white crystal (886 mg, 70%), mp 80−1 °C (recrystallized from ethyl acetate/hexanes). IR (Nujol): 3108 (m), 1719 (w), 1589 (m), 1494 (m), 1255 (s), 1171 (s), 640 (s) cm^{-1}; ^1H NMR ($CDCl_3$): 8.35 (dd, $J_{23} = 6.0$ Hz, $J_{2F} = 4.0$ Hz, 2H), 8.19 (bd, $J_{2'3'} = 6.0$ Hz, 2H), 7.83 (m, 3H), 7.51 (dd, $J_{32} = 6.0$ Hz, $J_{3F} = 9.0$ Hz, 2H); ^{19}F NMR ($CDCl_3$): −50.7 (s, 3F), −78.7 (s, 3F), −95.5 (s, 1F); ^{13}C NMR ($CDCl_3$): 170 (d, $J = 261$ Hz), 139, 137, 135, 135, 127 (q, $J = 265$ Hz), 126 (q, $J = 263$ Hz), 121, 116 ppm; FAB$^+$-MS [*m/e* (species, intensity)]: 273 ($(C_{13}H_9F_4S)^+$, 100), 272 ($(C_{13}H_8F_4S)^+$, 14.2), 254 ($(C_{13}H_9F_3S)^+$, 5.9), 204 ($(C_{13}H_9F_4S)^+ - CF_3$, 98.0), 196 ($(C_{13}H_9F_4S)^+ - C_6H_5$, 5.3), 178 ($(C_{13}H_9F_4S)^+ - C_6H_4F$, 3.4), 127 ($(C_6H_4FS)^+$, 13.0), 109 ($(C_6H_5S)^+$, 20.1)). Anal. Calcd for $C_{14}H_9F_7O_3S_2$: C, 39.81; H, 2.15. Found: C, 39.45; H, 2.17.

Preparation of *S*-(Trifluoromethyl)phenyl-2,4-difluorophenylsulfonium Triflate (9). To a solution of phenyl trifluoromethyl sulfoxide (485 mg, 2.5 mmol) in dry 1,3-difluorobenzene (7.4 mL, 75 mmol) was added $(CF_3SO_2)_2O$ (2.10 mL, 12.5 mmol) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then at rt for another 20 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using $CH_3CN-CH_2Cl_2$ (1:4) as eluent. The product was obtained as a white crystal (770 mg, 70%), mp 78−9 °C (recrystallized from ethyl acetate/hexanes). IR (Nujol): 3099 (s), 1600 (s), 1479 (s), 1450 (s), 1200 (s) (cm^{-1}); ^1H NMR ($CDCl_3$): 8.26 (d, $J_{2'3'} = 8.1$ Hz, $J_{4'3'} = 8.1$ Hz, 3H), 7.90 (bd, $J_{65} = 7.5$ Hz, 1H), 7.75 (dd, $J_{3'2'} = 7.8$ Hz, $J_{3'4'} = 7.8$ Hz, 2H), 7.45 (dd, $J_{56} = 8.1$ Hz, $J_{54F} = 7.8$ Hz, 1H), 7.25 (dd, $J_{32F} = 9.0$ Hz, $J_{34F} = 9.0$ Hz, 1H); ^{19}F NMR ($CDCl_3$): −47.6 (s, 3F), −78.3 (s, 3F), −91.7 (s, 1F), −98.2 (s, 1F); ^{13}C NMR ($CDCl_3$): 168 (d, $J = 261$ Hz), 163 (d, $J = 262$), 138, 137, 133, 132, 126 (q, $J = 262$), 123 (q, $J = 262$ Hz), 120, 117, 115, 108 ppm; FAB$^+$-MS [*m/e* (species, intensity)]: 291 ($(C_{13}H_8F_5S)^+$, 100), 222 ($(C_{13}H_8F_5S)^+ - CF_3$, 80.6), 145 ($(C_{13}H_8F_5S)^+ - C_6H_5 - CF_3$, 15.0)). Anal. Calcd for $C_{14}H_8F_8O_3S_2$: C, 38.18; H, 1.83; F, 34.52. Found: C, 37.97; H, 1.88; F, 34.90.

Preparation of *S*-(Trifluoromethyl)phenyl-3-nitrophenylsulfonium Triflate (10). To fuming nitric acid (0.12 mL, 2.5 mmol, 90%, $d = 1.5$) was added concentrated H_2SO_4 (0.35 mL, $d = 1.98$). After the mixture was stirred for 0.5 h, *S*-(trifluoromethyl)diphenylsulfonium triflate (1.0 g, 2.5 mmol) was added. The reaction mixture was stirred for 5 h at 100 °C, and then diethyl ether was slowly added to the mixture. The resulting pale yellow crystal was collected by filtration and recrystallized with $CH_3CN-CH_2Cl_2$ to give 833 mg (75%) of **10**, mp 87−9 °C. IR (Nujol): 1450 (s), 1225 (s), 1589 (m), 1031 (s), 639 (s), 585 (s) cm^{-1}; ^1H NMR ($CDCl_3$): 8.83 (dd, $J_{24} = J_{26} = 2.0$ Hz, 1H), 8.75 (ddd, $J_{45} = 6.0$ Hz, $J_{42} = J_{46} = 2.0$ Hz, 1H), 8.42 (dm, $J_{65} = 6.0$ Hz, 1H), 8.15 (m, 4H), 7.90 (m, 2H); ^{19}F NMR ($CDCl_3$): −48.1 (s, 3F), −78.3 (s, 3F); ^{13}C NMR ($CDCl_3$): 139, 138, 137, 136, 135, 134, 133, 132, 129, 123 (q, $J = 264$ Hz), 122 (q, $J = 263$ Hz), 117 ppm; FAB$^+$-MS [*m/e* (species, intensity)]: 300 ($(C_{13}H_9F_3NO_2S)^+$, 100)). Anal. Calcd for $C_{14}H_9F_6NO_5S_2$: C, 37.42; H, 2.02; N, 3.12. Found: C, 37.32; H, 1.98; N, 2.90.

Preparation of *S*-(Trifluoromethyl)-4-fluorophenyl-3-nitrophenylsulfonium Triflate (11). To fuming nitric acid (0.60 mL, 14.2 mmol, 90%, $d = 1.5$) was added concentrated H_2SO_4 (2.0 mL, $d = 1.98$). After the mixture was stirred for 0.5 h, *S*-(trifluoromethyl)phenyl-4-fluorophenylsulfonium triflate (2.0 g, 4.7 mmol) was added to the solution. The reaction mixture was stirred for 20 h at 100 °C. Diethyl ether was slowly added to the mixture. The resulting pale yellow crystal was collected by filtration and then was recrystallized with $CH_3CN-CH_2Cl_2$ to give 1.5 g of **11** (70%), mp 87−8 °C. IR (Nujol): 3105 (m), 1588 (s), 1494 (m), 1450 (s), 1087 (s) cm^{-1}; ^1H NMR ($CDCl_3$): 8.81 (dd, $J_{2'4'} = J_{2'6'} = 2.0$ Hz, 1H), 8.73 (ddd, $J_{4'5'} = 6.0$ Hz, $J_{4'2'} = J_{4'6'} = 2.0$ Hz, 1H), 8.42 (dm, $J_{6'5'} = 8.0$ Hz, 1H), 8.24 (dd, $J_{23} = 8.0$ Hz, $J_{2F} = 8.0$ Hz, 2H), 8.10 (dd, $J_{5'4'} = J_{5'6'} = 8.0$ Hz, 1H), 7.67 (dd, $J_{32} = 8.0$ Hz, $J_{3F} = 8.1$ Hz, 2H); ^{19}F NMR ($CDCl_3$): −48.3 (s, 3F), −78.3 (s, 3F), −95.3 (s, 1F); ^{13}C NMR ($CDCl_3$): 170 (d, $J = 260$ Hz), 152, 138, 137, 135, 132, 129, 127 (q, $J = 262$ Hz), 121, 121, 120 (q, $J = 262$ Hz), 116 ppm; FAB$^+$-MS [*m/e* (species, intensity)]: 318 ($(C_{13}H_8F_4NO_2S)^+$, 100), 300 ($(C_{13}H_8F_4NO_2S)^+ - F + H$, 61.2), 272 ($(C_{13}H_8F_4NO_2S)^+ - NO_2$, 3.6), 250 ($(C_{13}H_8F_4NO_2S)^+ - CF_3 + H$, 2.9)). Anal. Calcd for $C_{14}H_8F_7NO_5S_2$: C, 35.98; H, 1.73; N, 3.00. Found: C, 35.74; H, 1.67; N, 2.92.

General Method for the Trifluoromethylation Reactions. To a stirred solution of 0.9−2.5 mmol of substrate in 10 mL of dry THF under N_2 was added 1 mmol of a trifluoromethyl onium salt. Detailed conditions are shown in Tables 2−4. After the reaction was complete, the reaction mixture was studied by ^1H and ^{19}F NMR. In ^{19}F NMR, the triflate anion of the trifluoromethyl onium triflate was used as an internal standard to determine the yield of product.

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