ELSEVIER

Journal of Fluorine Chemistry 92 (1998) 181–187

JOURNAL OF FLUORINE CHEMISTRY

Effective methods for preparing *S*-(trifluoromethyl)dibenzothiophenium salts

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Received 10 March 1998; received in revised form 12 June 1998; accepted 4 September 1998

Abstract

New effective methods were developed for the preparation of useful electrophilic trifluoromethylating agents, *S*-(trifluoromethyl)dibenzothiophenium tetrafluoroborate (**3**) and triflate (**4**) and *S*-(trifluoromethyl)dibenzothiophenium-3-sulfonate (**6**). Thus, salts **3** and **4** were produced by the intramolecular cyclization of sulfoxide **1** with fuming sulfuric acid, followed by the counteranion replacement reaction of the intermediate (**2**) with sodium tetrafluoroborate and triflate, and salt **6** was directly produced from **1** by treatment with excess fuming sulfuric acid. Useful preparative methods for **1** were also described.

Keywords: Electrophilic trifluoromethylating agents; *S*-(trifluoromethyl)dibenzothiophenium salts; *S*-(trifluoromethyl)dibenzothiophenium sulfonates; Trifluoromethylation

1. Introduction

The introduction of a trifluoromethyl group into an organic molecule often greatly changes the original chemical, biochemical, or physical properties of the molecule, owing to the high electronegativity, stability and lipophilicity of the trifluoromethyl group [1–3]. Accordingly, considerable attention has been directed to the trifluoromethylation of organic compounds in fields of medicine [4–8], agricultural chemicals [9,10] and new material science [11].

In the previous studies, we developed a series of *S*-, *Se*-, and *Te*-(trifluoromethyl)dibenzo-thio-, -seleno-, and -telluro-phenium salts and their 3-sulfonates as power-variable electrophilic trifluoromethylating agents [12,13,15]. We also established a new method for the trifluoromethylation of enolate anions using a *S*-(trifluoromethyl)dibenzothiophenium salt and borane Lewis acid in combination [14].

S-(Trifluoromethyl)dibenzothiophenium tetrafluoroborate (**3**) and triflate (**4**) were synthesized by direct fluorination of 2-[(trifluoromethyl)thio]biphenyl (**9**) in the presence of tetrafluoroboric acid or boron trifluoride and triflic acid, respectively [12,13].[1] Triflate **4** was also prepared by treatment of 2-[(trifluoromethyl)sulfinyl]biphenyl (**1**) with triflic anhydride [12–15] or trifluoroacetyl triflate [16]. However, special technique is required when using potentially dangerous molecular fluorine (F_2), and triflic anhydride or trifluoroacetyl triflate is expensive and difficult to obtain in bulk quantity. In the case of triflic anhydride, an equimolar amount of triflic acid is produced as a byproduct. *S*-(Trifluoromethyl)dibenzothiophenium-3-sulfonate (**6**) was syn-

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[1] *N*-Fluoropyridinium tetrafluoroborate (**3**) and triflate (**4**) were prepared by using $CFCl_3$ or CCl_2FCClF_2 as a solvent [12,13], which has now been forbidden to use because it is one of the ozone layer depletion compounds. They can be prepared by using dry and alcohol-free chloroform instead of $CFCl_3$ or CCl_2FCClF_2. The dry and alcohol-free chloroform was prepared by distilling commercially available chloroform on P_2O_5. In particular, tetrafluoroborate **3** can be prepared in high yield by using chloroform containing a small amount of acetonitrile. This procedure is as follows. Gaseous boron trifluoride [5.4 l (240 mmol)] was introduced at a rate of 50 ml/min to a stirred solution of 50.9 g (299 mmol) of sulfide **9** in a mixture of 200 ml of dry and alcohol-free chloroform and 11.5 ml (220 mmol) of dry acetonitrile at −10°C. Then, 1:9 (v/v) mixture of F_2 and N_2 gas was introduced at a rate of 200 ml/min to the stirred mixture at −10°C. The total amount of F_2 used was 248 mmol. After the atmosphere in the flask was replaced with N_2 gas, the reaction mixture was warmed to room temperatue. Addition of diethyl ether to the reaction mixture resulted in a precipitate of **3**, which was collected by filtration and recrystallized from acetonitrile–diethyl ether to give 63.4 g (93%) of pure **3**.

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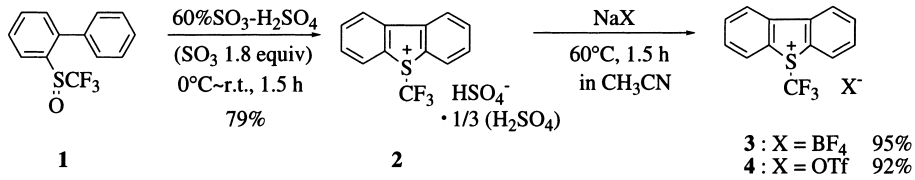


1 2

Scheme 1.

thesized in a stepwise manner by sulfonation of triflate **4** with fuming sulfuric acid [15].

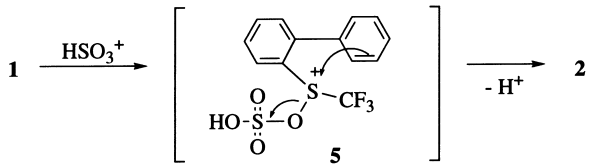
This paper describes new effective methods for preparing useful trifluoromethylating agents **3**, **4** and **6** via the intramolecular cyclization of sulfoxide **1** as a key step, and also useful preparative methods for the starting material **1**.

2. Results and discussion

2.1. Intramolecular cyclization of 2-[(trifluoromethyl)sulfinyl]biphenyl (1) with fuming sulfuric acid

Sulfoxide **1** dissolved in a small amount of dichloromethane was treated with 60% fuming sulfuric acid (SO_3 1.8 equiv.) at 0°C to room temperature for 1.5 h (Scheme 1). The recrystallized product was adduct (**2**) of *S*-(trifluoromethyl)dibenzothiophenium hydrogen sulfate with 1/3 (H_2SO_4) and its yield was 79%. This structural formula was assigned based on the results of spectral and elemental analysis. The ready intramolecular cyclization may be explained as due to the activation of the sulfinyl group (S=O) with reactive species HSO_3^+ in fuming sulfuric acid, as shown in Scheme 2.

Adduct **2** underwent a counteranion replacement reaction with sodium tetrafluoroborate and sodium triflate in acetonitrile to give tetrafluoroborate **3** and triflate **4** with 95% and 92% yields, respectively. To trap sulfuric acid liberated from crystalline **2**, powdered sodium hydrogen carbonate was added in excess to the reaction mixture.



Scheme 2.

Subsequent to treating sulfoxide **1** with 60% fuming sulfuric acid (SO_3 1.8 equiv.) as above, 60% fuming sulfuric acid (SO_3 3.15 equiv.) was added to the reaction mixture which was then stirred at 42°C for 17 h (Scheme 3). This reaction produced *S*-(trifluoromethyl)dibenzothiophenium-3-sulfonate (**6**) in high yield (ca. 80%). It is thus shown possible to obtain sulfonate **6** in 84% yield by treatment of **1** with excess fuming sulfuric acid (SO_3 4.95 equiv.) added to the reaction system in one portion, as seen in Scheme 3.

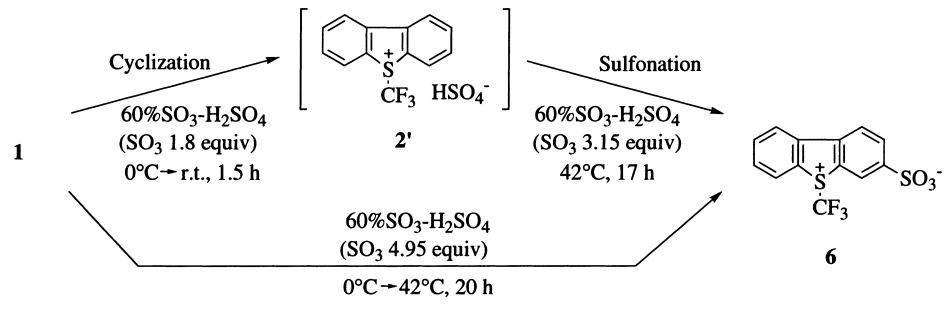
Stirring the resulting oily residue in ethanol made it possible to isolate **6** as a 1:1 crystalline adduct of **6** with the ethanol molecule in high yield.

As shown in Scheme 4, the starting material sulfoxide **1** was prepared in essentially quantitative yield by the selective oxidation of sulfide **9** with hydrogen peroxide–acetic acid. The corresponding sulfone as a byproduct was produced in only 1–2% yield and thus may be used in subsequent reactions without further purification.

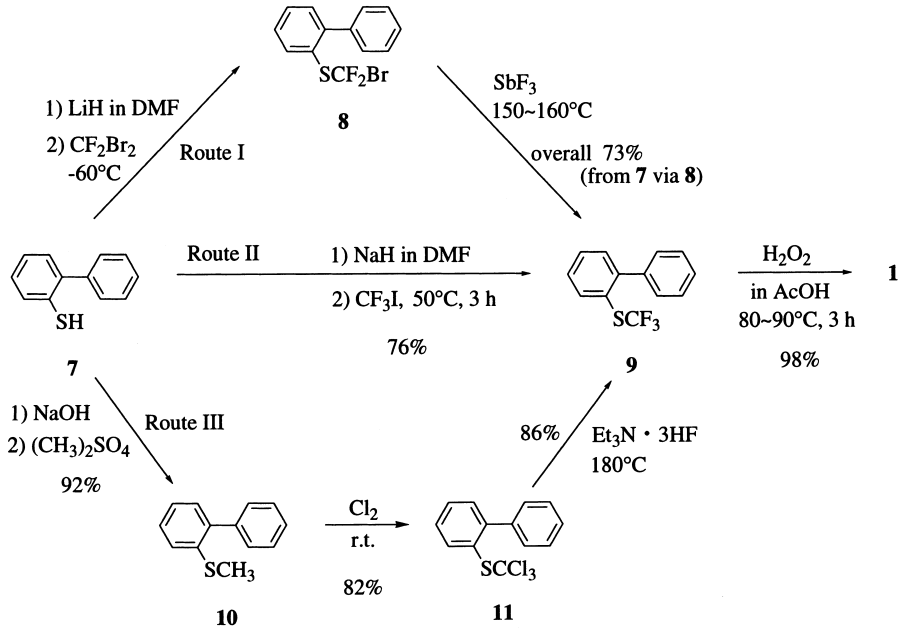
2.2. Preparation of 2-[(trifluoromethyl)thio]biphenyl (9)

Sulfide **9** was previously prepared by photoreaction of the sodium salt of 2-mercaptobiphenyl (**7**) with bromotrifluoromethane in DMF using a high pressure Hg lump. However, this method was not appropriate to a large scale production because of relatively low quantum yield for obtaining **9** by this photoreaction. As shown in Scheme 4, three different routes I, II, and III for preparing **9** from thiol **7** were examined.

As shown in Route I of Scheme 4, in a method using dibromodifluoromethane (CF_2Br_2) in which CF_2Br_2 was



Scheme 3.



Scheme 4.

rapidly added to a solution of lithium salt of **7** in DMF at −60°C under vigorous stirring, 2-[(trifluoromethyl)thio]biphenyl (**8**) was obtained in high yield (ca. 94% crude). However, subsequent to CF_2Br_2 addition, a vigorous exothermic reaction immediately occurred attended with a rapid increase in temperature. When conducting this reaction with the sodium salt of **7** at −20°C to −30°C, bis(2-biphenylyl)disulfide and 2-[(difluoromethyl)thio]biphenyl were formed in considerable amounts as byproducts. On adding CF_2Br_2 dropwise to the solution at −55°C to −50°C to suppress the vigorous reaction, another byproduct was formed. The byproduct was not characterized. The lithium salt of **7** was much better for the reaction than its sodium salt, the latter being insoluble in DMF at low temperature. When heating crude **8** with antimony trifluoride without solvent as the following step, trifluoromethyl sulfide **9** was produced in an overall 73% yield from **7**. It was difficult to suppress the vigorous reaction in the first bromodifluoromethylation step and so Route I using CF_2Br_2 would not be appropriate to a large scale preparation.

Aiken et al. have proposed another method for obtaining **9**, in which sodium 2-bromothiophenolate is allowed to react with CF_2Br_2 in DMF, followed by treatment with silver tetrafluoroborate. 2-Bromo[(trifluoromethyl)thio]benzene thus obtained is coupled with phenylboronic acid in the presence of palladium catalyst to give trifluoromethyl sulfide **9** [17]. But this route is not appropriate for large scale preparation since only limited overall yield is possible and the silver salt is quite expensive.

As shown in Route II of Scheme 4, the direct trifluoromethylation of sodium salt of **7** with iodotrifluoromethane (CF_3I) proceeded smoothly around 50°C in normal room light to give **9** in 76% yield. This method is quite convenient, requiring only one-step from sodium salt of **7** and no special photoirradiation. Thus, the CF_3I method may be considered most suitable for industrial application, provided that CF_3I could be supplied in bulk quantity.

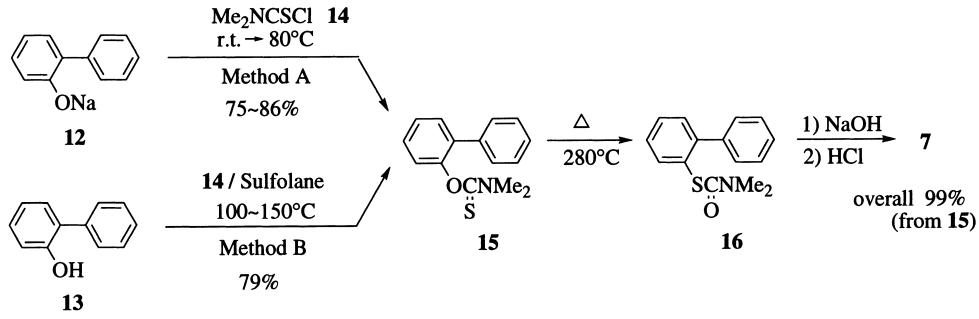
Methylation/chlorination/Cl–F exchange method is shown as Route III in Scheme 4. 2-(Methylthio)biphenyl (**10**) [18] derived by methylation of thiol **7** was chlorinated by photochlorination with chlorine in a small amount of carbon tetrachloride or chlorobenzene at room temperature or under cooling in an ice bath to produce 2-[(trichloromethyl)thio]biphenyl (**11**) in 82% yield. As described in Section 3.11, **10** could be prepared from **15** via **16** and **7** by a one-batch method with an overall 74% yield.

The chlorination of **10** occurred very rapidly. Chlorination at 80°C caused cleavage of the C–S bond, thus producing 2-chlorobiphenyl. The Cl–F exchange of **11** was carried out using triethylamine trihydrofluoride, an easy-to-handle compound in contrast to hydrogen fluoride. A mixture of **11** and 3.1 equimolar amount of triethylamine trihydrofluoride was heated in an autoclave at 180°C for 9 h to give **9** in 86% yield.[2] Chlorination and Cl–F exchange (without purification of intermediate **11**) in combination produced **9** as the final product from **10** in 66% yield. This method is appropriate for large scale production of **9** owing to its high production efficiency per reactor.

2.3. Preparation of 2-mercaptobiphenyl (7)

Thiol **7** was prepared as shown in Scheme 5. Thiocarbamate **15** could be obtained by two methods: reaction of dry sodium salt **12** of 2-hydroxybiphenyl (**13**) with

[2] A stainless-steel autoclave used for this reaction was slightly corroded.



Scheme 5.

N,*N*-dimethylthiocarbamoyl chloride (**14**) in DMF solvent at room temperature to 80°C (Method A) [19,20,21] or reaction of **13** with **14** in a small amount of dry sulfolane at 100–150°C (Method B). Method B is highly production efficient per reactor. The recrystallized and dried solid of **15** was heated at 280°C [21] and the rearrangement product **16** thus obtained was hydrolyzed by sodium hydroxide in methanol under a nitrogen atmosphere [19,20]. Following neutralization, thiol **7** was obtained in essentially quantitative yield from **15**.

3. Experimental

3.1. General

Melting and boiling points were uncorrected. ^{1}H and ^{19}F NMR spectra were recorded with 200 and 188 MHz NMR spectrometers, respectively. ^{19}F NMR chemical shifts are given in ppm downfield from CCl_3F as an internal standard. Mass spectra were recorded at 70 eV. The structural assignment of the products was carried out by comparison with authentic samples or spectral and elemental analyses. The data of new compounds are shown below.

3.2. Materials

Sulfolane was dried by distillation under reduced pressure. Sodium 2-phenylphenolate (**12**) was dried at 200°C for 12 h under vacuum. 2-Phenylphenol (**13**) was dried at 50°C for 12 h under vacuum. *N*,*N*-Dimethylformamide (DMF) was dried by distillation on calcium hydride. Other commercially available chemicals were used without further purification, unless otherwise noted.

3.3. Preparation of S-(trifluoromethyl)dibenzothiophenium hydrogen sulfate 1/3(H_2SO_4) (2)

60% fuming sulfuric acid [180 ml (SO_3: 2.66 mol)] was dropwise added over a period of 35 min to a stirred solution of 400 g (1.48 mol) of [(trifluoromethyl)sulfinyl]biphenyl (**1**) in 1 l of dichloromethane cooled on an ice bath and the mixture was stirred at room temperature for 1.5 h. Methanol [107 ml (2.63 mol)] and diisopropyl ether [ca. 3 l] were carefully added to the stirred reaction mixture cooled on an ice bath. A vigorous exothermic reaction occurred on mixing. The resulting solid was collected by filtration and purified by recrystallization from methanol–ethyl acetate to give 448 g (79%) of **2** as crystals. The elemental analysis indicated that *S*-[(trichloromethyl)dibenzothiophenium hydrogen sulfate exists as adduct with 1/3(H_2SO_4) in the crystals.

Compound **2**. mp 122–127°C (with dec.). ^{1}H NMR (CD_3CN) δ: 7.86 (2H, td, J=8, 1 Hz, 3-H, 7-H); 8.07 (2H, td, J=8, 1 Hz, 2-H, 8-H); 8.35 (2H, dd, J=8, 1 Hz, 1-H, 9-H); 8.44 (2H, d, J=8 Hz, 4-H, 6-H). ^{19}F NMR (CD_3CN) δ: −52.8 (s). IR (KBr) (cm^{-1}): 3418; 3072; 2300; 1284; 1208; 1177; 1087; 1078; 1040; 1009; 887; 851; 766; 576. Mass spectrum (FAB) *m/z*: 253 (M^{+}–HSO_4). Analysis: Calc. for $C_{13}H_9F_3O_4S_2 \cdot 1/3(H_2SO_4)$: C, 40.77; H, 2.54; S, 19.53%. Found: C, 40.03; H, 2.87; S, 19.83%.

3.4. Preparation of 2-[(trichloromethyl)dibenzothiophenium tetrafluoroborate and triflate, (3) and (4)

Under an argon atmosphere, 600 g (1.57 mol) of **2** was added by portions to a stirred solution of 176 g (1.57 mol) of sodium tetrafluoroborate in 2.5 l of acetonitrile over a period of 5–10 min at 60°C and the mixture was stirred at the temperature for 1.5 h. After cooling to room temperature, ca. 600 g of powdered sodium hydrogen carbonate was added to the mixture. The mixture was stirred at room temperature for 3 h and insoluble materials were removed by filtration. After evaporation of the solvent from the filtrate, the residue was recrystallized from acetonitrile–diethyl ether to give 508 g (95%) of tetrafluoroborate **3**. Similarly, triflate **4** was prepared from **2** in 92% yield with sodium triflate instead of sodium tetrafluoroborate.

3.5. Preparation of 2-[(trichloromethyl)dibenzothiophenium-3-sulfonate (6)

A solution of 350 g (1.3 mol) of 2-[(trichloromethyl)sulfinyl]biphenyl (**1**) in 1 l of dichloromethane was placed in a flask to which a Dimroth condenser with a calcium chloride-drying tube was attached. To the stirred solution cooled on an ice bath, 434 ml (SO_3: 6.4 mol) of 60% fuming sulfuric acid was dropwise added over a period of 40 min and the

mixture was stirred at 42°C for 20 h. Diisopropyl ether (ca. 3.3 l) was carefully added to the stirred reaction mixture cooled on an ice bath. A vigorous exothermic reaction occurred on mixing with the ether. The resulting gummy oil was separated from the solution by decanting and then washed repeatedly with diisopropyl ether. Ethanol (ca. 1 l) was then added to the gummy oil and the mixture was stirred till all of the oil became white powdered crystals; it took ca. 2 h. The crystals were collected by filtration, washed with ethanol (2 times), and dried under vacuum for 6.5 h at 60°C to give 413 g (84%) of **6**. ^{1}H NMR indicated that **6** exists as adduct with one molecule of ethanol in the crystal (**6**: C_2H_5OH=1:1).

Compound **6**. mp 142–147°C (with dec.). ^{1}H NMR (CD_3CN) δ: 1.17 (3H, t, J=7 Hz, CH_3); 3.60 (2H, q, J=7 Hz, CH_2); 7.92 (1H, td, J=8, 1 Hz, 7-H); 8.10 (1H, td, J=8, 1 Hz, 8-H); 8.42 (1H, dd, J=8, 1 Hz, 2-H); 8.46–8.57 (3 H, m, 1-H, 6-H, 9-H); 8.90 (1H, d, J=1 Hz, 4-H). ^{19}F NMR (CD_3CN) δ: −53.9 (s). IR (KBr) (cm^{-1}): 3454; 1229; 1198; 1120; 1082; 1031; 773; 665; 614; 515. Mass spectrum (FAB) *m/z*: 333 (M^++1). Analysis: Calc. for $C_{13}H_7F_3O_3S_2 \cdot C_2H_6O$: C, 47.61; H, 3.46%. Found: C, 46.77; H, 3.46%.

3.6. Preparation of 2-[(trichloromethyl)sulfinyl]biphenyl (1)

31% hydrogen peroxide [132 g (1.20 mol)] was added dropwise to a stirred solution of 245 g (0.96 mol) of 2-[(trichloromethyl)thio]biphenyl (**9**) in 1250 ml of acetic acid over a period of 40 min at 70–84°C. After the addition, the mixture was stirred at 80–88°C for 3 h, cooled and poured into ca. 3 l of ice-water. The resulting precipitate was collected by filtration, washed with water, and dissolved in diethyl ether. The ether layer was washed with water (2 times), aqueous sodium carbonate (2 times), water and saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 256 g (98%) of **1**. ^{19}F NMR indicated that the product was contaminated with ca. 2% of the corresponding sulfone.

3.7. Preparation of 2-[(bromodifluoromethyl)thio] biphenyl (8)

Under an argon atmosphere, a solution of 246 g (1.32 mol) of 2-mercaptobiphenyl (**7**) in 350 ml of dry DMF was added dropwise to a stirred suspension of 10.6 g (1.33 mol) of lithium hydride in 1.15 l of dry DMF cooled on an ice bath. After an exothermic reaction ceased, the mixture was stirred at room temperature for 20 min and cooled to −60°C (the reaction solution's temperature) on a dry ice–acetone bath. Dibromodifluoromethane [145 ml (1.58 mol)] was rapidly added to the stirred solution; it took ca. 1–2 min. At this time, a vigorous exothermic reaction immediately occurred and the reaction mixture's temperature rose up to nearly −5°C. After the exothermic reaction ceased, the reaction mixture was stirred for 10 min on the dry ice–acetone bath cooling and then for 30 min at room temperature, poured into ice-water, and extracted with ethyl acetate. The extract was washed with saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 393 g (ca. 94%) of crude **8**, which was a solid containing a small amount of oil and could be used for the next halogen exchange reaction without further purification. Purification of the crude **8** was carried out by distillation under reduced pressure to give pure **8** (bp 136–139°C/6 mmHg).

Compound **8**. mp 45–46°C. ^{1}H NMR ($CDCl_3$) δ: 7.27–7.59 (8H, m); 7.81 (1H, dm, J=8 Hz, 3-H) ppm. ^{19}F NMR ($CDCl_3$) δ: −217 (s) ppm. IR (KBr) (cm^{-1}): 1463; 1444; 1082; 1057; 842; 755; 699; 505. Mass spectrum *m/z*: 314, 316 (M^+). Analysis: Calc. for $C_{13}H_9BrF_2S$: C, 49.54; H, 2.88. Found: C, 49.75; H, 2.67%.

3.8. Preparation of 2-[(trifluoromethyl)thio]biphenyl (9) from 8

Under an argon atmosphere, a mixture of 392 g (ca. 1.24 mol) of crude **8** and 81.4 g (0.45 mol) of antimony trifluoride was heated gradually to 150°C and maintained at 150–160°C for ca. 2 h under stirring. After cooling, hexane was added to the reaction mixture and insoluble materials were removed by filtering through celite. The filtrate was washed twice with 2–3 N aqueous HCl solution and then twice with saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 280 g of an oil, which was purified by distillation under reduced pressure to give 245 g (overall 73% from **7**) of **9** (bp 109–111°C/6 mmHg).

3.9. Preparation of 2-[(trifluoromethyl)thio]biphenyl (9) from 7 and iodotrifluoromethane

Under nitrogen atmosphere, 5.59 g (30 mmol) of 2-mercaptobiphenyl (**7**) in 30 ml of dry DMF was placed in a 100 ml reaction flask. Into it, 1.21 g (32 mmol) of NaH (60% in oil) was added under stirring and cooling on an ice bath. The reaction mixture was stirred at the temperature for 10 min and then at room temperature for 20 min. The pressure in the reaction flask was reduced by vacuum pump and then the atmosphere in the flask was filled with ca. 37 mmol (7.3 g) of gaseous iodotrifluoromethane by connecting a balloon containing the amount of iodotrifluoromethane and additionally with N_2 till the pressure became atmospheric pressure. An exothermic reaction occurred soon. After the exothermic reaction ceased, the reaction mixture was stirred at 50°C for 3 h, poured into water and extracted with hexane. The extract was washed with water and saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. After evaporation of the solvent, the residue was column chromatographed on silica gel using hexane as an eluent to give 5.8 g (76%) of **9**.

3.10. Preparation of 2-(methylthio)biphenyl (**10**) from **7**

Into a solution of 36.0 g (0.86 mol) of sodium hydroxide in 150 ml of water 140.0 g (0.75 mol) of 2-mercaptobiphenyl (**7**) was added. Into the solution stirred and cooled on an ice bath, 78.3 ml (0.83 mol) of dimethyl sulfate was dropwise added over a period of 25 min, and the reaction mixture was heated at 110°C for 140 min. After cooling, the reaction mixture was extracted with diethyl ether. The organic layer was washed with water and then saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 150.5 g of oil, which was then distilled under reduced pressure to give 138 g (92%) of **10** (bp 135–137°C/4 mmHg).

3.11. Preparation of 2-(methylthio)biphenyl (**10**) from **15**

Under an argon atmosphere, 329 g (1.28 mol) of *O*-(2-biphenylyl)-*N*,*N*-dimethylthiocarbamate (**15**) was heated to 280°C and maintained at the temperature for 1 h under stirring. After cooling, the reaction mixture was dissolved in 880 ml of methanol which was degassed (O_2) with argon. Sodium hydroxide [107 g (2.56 mol)] was added to the solution, and the solution was again degassed (O_2) with argon and heated under reflux for 18 h. Then, dimethyl sulfate [134 ml (1.41 mol)] was dropwise added over a period of 45 min to the reaction mixture stirred and cooled on an ice bath. The mixture was stirred for 2 h at room temperature, heated under reflux for 1 h, cooled, poured into water and extracted with hexane (3 times). The extract was washed with water (2 times) and saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave an oil, which was then distilled under reduced pressure to obtain 190 g (74%) of **10** (bp 154–160°C)/8 mmHg).

3.12. Preparation of 2-[(trichloromethyl)thio]biphenyl (**11**) from **10**

A solution of 80.0 g (0.40 mol) of **10** in 140 ml of carbon tetrachloride was placed in a flask and the atmosphere in the flask was replaced with chlorine (Cl_2). The reaction mixture was irradiated with a high-pressure Hg lamp (450 W) during introduction of Cl_2 for 105 min while cooling on an ice bath. The flow rate of Cl_2 was controlled so that Cl_2 was almost completely absorbed into the reaction solution. After absorption of Cl_2 ceased, excess Cl_2 in the reaction vessel was removed by flowing N_2. The reaction mixture was then washed with aqueous sodium thiosulfate solution. The organic layer was separated, washed with water and saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 100 g (82%) of **11**. For further purification, distillation under reduced pressure was carried out (bp 173–175°C/5–6 mmHg).

Compound **11**. mp 59–60°C. ^{1}H NMR ($CDCl_3$) δ: 7.32–7.42 (5H, m); 7.45–7.51 (2H, m, 4-H, 6-H); 7.59 (1H, td, J=8, 1 Hz, 5-H); 8.05 (1H, dd, J=8, 1 Hz, 3-H). IR (KBr) (cm^{-1}): 1463; 1447; 788; 759; 747; 733; 722; 500. Mass spectrum *m*/*z*: 302, 304, 306 (M^+). Analysis: Calc. for $C_{13}H_9Cl_3S$: C, 51.42; H, 2.99%. Found: C, 51.37; H, 2.88%.

3.13. Preparation of 2-[(trichloromethyl)thio]biphenyl (**9**) from **11**

A mixture of 3.0 g (9.9 mmol) of **11** and 5.0 ml (30.7 mmol) of triethylamine trihydrofluoride was placed in an autoclave (inside this was a container made of polytetrafluoroethylene) and heated at 180°C for 9 h. After cooling, the reaction mixture was poured into water and extracted with hexane. The extract was washed with water (2 times) and saturated aqueous NaCl solution, dried with $MgSO_4$, and filtered. After evaporation of the solvent, the residue was column chromatographed on silica gel using hexane as an eluent to give 2.2 g (86%) of **9**.

3.14. Preparation of 2-[(trichloromethyl)thio]biphenyl (**9**) from **10**

Cl_2 [104 l (4.6 mol)] was introduced over a period of 3.5 h to a stirred solution of 301 g (1.5 mol) of 2-(methylthio)biphenyl (**10**) in 250 ml of chlorobenzene in a photoreaction vessel which was irradiated with a high-pressure Hg lamp (450 W) under cooling on an ice bath. The flow rate of Cl_2 was controlled so that Cl_2 was absorbed completely. After removing chlorobenzene by distillation under reduced pressure, 808 ml (4.96 mol) of triethylamine trihydrofluoride was added to the residue. This mixture was placed in a stainless steel autoclave (cf. [2]), heated at 180°C for 12 h, cooled, and poured into ice-water. Then, ca. 1 l of hexane and 744 g (7.43 mol) of calcium carbonate were added to the mixture. After filtration, the filtrate was extracted with hexane. The hexane layer was washed with water (3 times), dried with $MgSO_4$, and filtered. After evaporation of the solvent, the residue was distilled under reduced pressure to give 253 g (66%) of **9** (bp 109–114°C/5–6 mmHg).

3.15. Preparation of O-(2-(biphenylyl)-N,N-dimethylthiocarbamate (**15**)

Method A. Under an argon atmosphere, 714.5 g (5.61 mol) of *N*,*N*-dimethylthiocarbamoyl chloride (**14**) was added to a solution of 1025 g (5.34 mol) of dry sodium 2-phenylphenolate (**12**)[3] in 3.5 l of dry DMF at 5–12°C. The mixture was stirred at room temperature and an exothermic reaction occurred. If needed, the reaction mixture was

[3] As an alternative method, sodium 2-phenylphenolate (**12**) was in situ prepared by reacting dry 2-hydroxybiphenyl (**13**) with sodium hydride (60% in oil) as follows: a solution of **13** in DMF was dropwise added into an equimolar amount of sodium hydride in DMF under stirring and cooling on an ice bath.

cooled on a water bath. After the exothermic reaction ceased, the reaction mixture was heated at 80°C for 45 min. The reaction mixture was concentrated by distillating DMF under reduced pressure at 70–85°C and the concentrated reaction mixture was poured into water. The resulting precipitate was collected by filtration and recrystallized from ethanol (500 g/1 l ethanol). Materials insoluble in hot ethanol were removed by ready filtration. The crystals obtained by the recrystallization were washed with a 3:1 mixture of hexane and ethanol to give 1029 g (75%) of **15**. In s similar experiment using 34.6 g (0.178 mol) of **12**, 25.1 g (0.197 mol) of **14**, and 120 ml of DMF, 39.1 g (86%) of **15** was obtained.

Method B. Under an argon atmosphere, a solution of 70.0 g (0.55 mol) of **14** in 60 ml of dry sulfolane was dropwise added over a period of 25 min to 85.1 g (0.5 mol) of dry 2-phenylphenol (**13**) which was heated and stirred at 85–90°C. Hydrogen chloride was evolved. After the addition of **14**, the mixture was heated gradually to 150°C in a period of 2.5 h, cooled, and poured into ca. 600 ml of water. The resulting precipitate was collected by filtration and purified by recrystallization from ethanol to obtain 100.9 g (79%) of **15**.

3.16. Preparation of 2-mercaptobiphenyl (7) from 15

Under a nitrogen atmosphere, 1166 g (4.54 mol) of **15** was heated to 280°C and maintained at 264–282°C for 35 min under stirring. After cooling, the reaction mixture was dissolved in 4 l of methanol which was degassed (O_2) with argon. Sodium hydroxide [363 g (9.08 mol)] was added to the reaction mixture and the mixture was again degassed with argon and heated under reflux for 12 h. After cooling, the mixture was poured into cold and dilute HCl solution (HCl; ca. 14 mol). The resulting precipitate was collected by filtration and dissolved in dichloromethane. The organic layer was dried with $MgSO_4$, and filtered. Evaporation of the solvent gave 834 g (99%) of **7** (bp 121.5–122°C/4 mmHg).

4. Conclusion

Effective methods using the intramolecular cyclization of sulfoxide **1** with cheap fuming sulfuric acid as a key step have been developed for the production of useful electrophilic trifluoromethylating agents, *S*-(trifluoromethyl)dibenzothiophenium tetrafluoroborate (**3**) and triflate (**4**), and *S*-(trifluoromethyl)dibenzothiophenium-3-sulfonate (**6**). These methods have an advantage that the potentially dangerous molecular fluorine is not used. Methods for effectively obtaining sulfoxide **1**, sulfide **9**, and thiol **7** have also been established. Thus, complete methods starting from 2-hydroxybiphenyl have been developed for the production of **3**, **4**, and **6**.

Acknowledgements

The authors thank M.Sc. Kenji Adachi and M.Eng. Masayuki Harada for their partial technical contribution.

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