

## Synthesis of Vinylsulfanyl-Substitued Polyfluorobenzenes from Perfluorotoluene

S. V. Amosova, G. M. Gavrilova, and A. V. Afonin

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences,  
ul. Favorskogo 1, Irkutsk, 664033 Russia  
e-mail: amosova@irioch.irk.ru

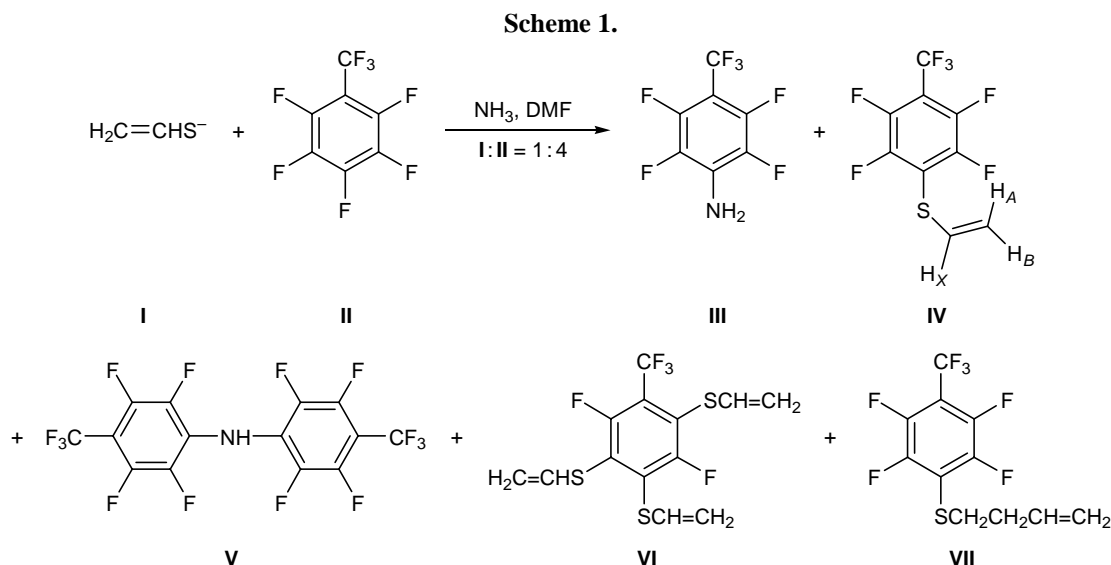
Received July 9, 2004

**Abstract**—The reaction of octafluorotoluene in DMF with vinylthiolate ion generated from divinyl sulfide by the action of sodium in liquid ammonia afforded 2,3,5,6-tetrafluoro-4-trifluoromethylaniline, 3,6-difluoro-4-trifluoromethyl-1,2,5-tris(vinylsulfanyl)benzene, and 3,6-difluoro-*N,N*-dimethyl-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline. Under the same conditions, 2,3,5,6-tetrafluoro-4-trifluoromethylaniline gave rise to 3,6-difluoro-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline.

By reaction of hexafluorobenzene with vinylthiolate ion (**I**) (which is readily generated by the action of metallic sodium on divinyl sulfide in liquid ammonia) we previously synthesized in preparative yields bis- and tetrakis(vinylsulfanyl)fluorobenzenes which are reactive monomers and intermediate products in fine organic synthesis [1, 2]. The yields and ratio of these products depended on the basicity of the medium, reactant ratio, and order of their mixing.

While continuing studies in this line, we examined vinylsulfanylation of perfluorotoluene (**II**) and found that the presence of an electron-acceptor trifluoromethyl group in the substrate molecule considerably

affects the process and product structure. In the reaction with hexafluorobenzene, 1,2,4,5-tetrafluoro-3,6-di(vinylsulfanyl)benzene was formed in up to 80% yield in DMF at a  $C_6F_6$ -to-**I** ratio of (4–5):1. When the reaction was performed with 5 equiv of vinylthiolate ion, the major product was 1,4-difluoro-2,3,5,6-tetrakis(vinylsulfanyl)benzene (yield up to 90%) [1]. The reaction of perfluorotoluene (**II**) with **I** under the conditions described in [1] for the synthesis of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfanyl)benzene, i.e., with the use of 4 equiv of perfluorotoluene in DMF, incomplete removal of ammonia from the reaction mixture, and subsequent addition of DMF, gave a mixture of



five products **III–VII** (Scheme 1). According to the spectral data (GC–MS, IR, NMR), the fraction boiling in the range from 53 to 62°C (3 mm), 85.2% of the entire reaction mixture, contained 78.8% of 2,3,5,6-tetrafluoro-4-trifluoromethylaniline (**III**) and 19.4% of 2,3,5,6-tetrafluoro-4-trifluoromethyl-1-vinylsulfanylbenzene (**IV**). In the still residue (14.8%) we identified 1,1'-bis(2,3,5,6-tetrafluoro-4-trifluoromethylphenyl)amine (**V**, 70%), 3,6-difluoro-4-trifluoromethyl-1,2,5-tris(vinylsulfanyl)benzene (**VI**, 11%), 4% of compound **III**, 6% of **IV**, and 1.5% of 1-(3-butenylsulfanyl)-2,3,5,6-tetrafluoro-4-trifluoromethylbenzene (**VII**) (Scheme 1). The latter is likely to be formed due to the presence of a small amount of 3-butene-1-thiolate ion in the reaction mixture [3].

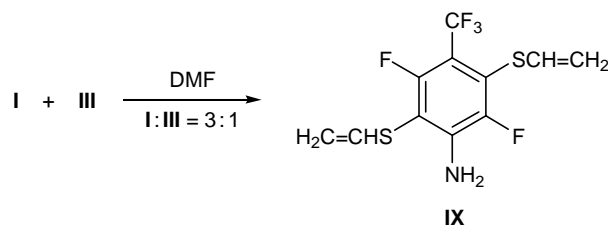
Compounds **V** and **VI** were isolated by column chromatography on aluminum oxide using hexane as eluent. The formation of product **VI** is explained by the *ortho/para*-orienting effect of trifluoromethyl group in nucleophilic substitution reactions [4], as well as by the ability of an RS group to activate fluorine atom in the *para*-position of the benzene ring [5]. The structure of **VI** is confirmed by the IR and  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{19}\text{F}$  NMR spectra. The synthesis of **V** was described in [6]. Our results indicate that, unlike hexafluorobenzene, the main pathway in the reaction with perfluorotoluene is amination, i.e., substitution of the fluorine atom in the *para*-position with respect to the trifluoromethyl group by ammonia which remains in the reaction mixture after partial replacement by DMF.

In order to obtain vinylsulfanyl derivatives of perfluorotoluene we used a different ratio of the reactants (perfluorotoluene–sodium vinylthiolate, 1:3) and changed the order of their mixing (see Experimental). In addition, it was necessary to thoroughly remove ammonia while replacing it by DMF. Under these conditions, the formation of a product with a molecular weight of 341 (according to the GC–MS data) was unexpected. On the basis of the IR and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, this product was assigned the structure of 3,6-difluoro-*N,N*-dimethyl-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline (**VIII**) (up to 70%). The reac-

tion also afforded about 13% of compound **VI** and three unidentified products in an overall yield of no more than 12% (Scheme 2). Compound **VIII** was formed as a result of nucleophilic replacement of two fluorine atoms by vinylsulfanyl groups and of the *para*-fluorine atom by dimethylamine which arises from reaction of DMF with liquid ammonia [7, 8].

We also examined vinylsulfanylation of compound **III** containing an electron-donor amino group and electron-acceptor trifluoromethyl group. Its reaction with 3 equiv of vinylthiolate ion in DMF at 15–20°C gave 18% of 3,6-difluoro-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline (**IX**) (according to the GC–MS, IR, and NMR data; Scheme 3). The formation of **VIII** and **IX** may be interpreted in terms of the *meta*-orienting effect of the NMe<sub>2</sub> and NH<sub>2</sub> groups [9] and *ortho*-effect of the CF<sub>3</sub> group which determine the site of fluorine replacement by vinylsulfanyl group. The second vinylsulfanyl group replaces that fluorine atom which appears in the *para*-position with respect to the first vinylsulfanyl group.

Scheme 3.



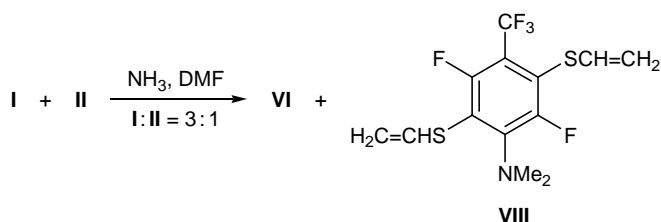
We can conclude that in the reaction of perfluorotoluene with vinylthiolate ion in DMF or liquid ammonia the solvents behave as reactants which strongly compete with vinylthiolate ions in the nucleophilic substitution process. As a result, new polyfunctional vinylsulfanyl-substituted fluorobenzenes containing electron-donor amino or dimethylamino group can be obtained.

## EXPERIMENTAL

The IR spectra were recorded on a Bruker IFS-25 spectrometer from samples prepared as thin films or KBr pellets. The NMR spectra were recorded on a Bruker DPX 400 instrument (400 MHz for  $^1\text{H}$ ) using CDCl<sub>3</sub> as solvent and HMDS ( $^1\text{H}$  and  $^{13}\text{C}$ ) or CFCl<sub>3</sub> ( $^{19}\text{F}$ ) as internal reference. The mass spectra (electron impact, 70 eV) were obtained using an HP 5971A mass-selective detector.

**Reaction of perfluorotoluene with sodium vinylthiolate.** Metallic sodium, 2.3 g (100 mmol), was

Scheme 2.



added in small portions under stirring to a solution of 4.3 g (50 mmol) of divinyl sulfide in 150 ml of liquid ammonia. The ammonia was evaporated, 70 ml of DMF was added, and the resulting solution was added dropwise to a solution of 47 g (200 mmol) of perfluorotoluene in 30 ml of DMF. The mixture was stirred for 5 h, kept for 12 h at 25°C, diluted with 200 ml of water, and extracted with diethyl ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and evaporated under reduced pressure. The residue was subjected to fractional distillation under reduced pressure to isolate 28 g of a fraction with bp 53–62°C (3 mm); repeated fractionation gave 22.4 g (48%) of 2,3,5,6-tetrafluoro-4-trifluoromethylaniline (**III**) with bp 50–52°C (3 mm) [10]. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 1655, 3428, 3525 (NH<sub>2</sub>); 1136, 1181, 1239, 1335 (CF<sub>3</sub>) [11]. Found, %: C 35.85; H 0.91; F 57.61; N 5.82.  $[M]^+$  233. C<sub>7</sub>H<sub>2</sub>F<sub>7</sub>N. Calculated, %: C 36.07; H 0.86; F 57.05; N 6.01. *M* 233. The IR spectrum of 2,3,5,6-tetrafluoro-4-trifluoromethyl-1-vinylsulfanylbenzene (**IV**) contained an absorption band at 1592 cm<sup>-1</sup> (SC=C). <sup>1</sup>H NMR spectrum of **IV**,  $\delta$ , ppm: 5.48 d (1H, H<sub>B</sub>), 5.51 d (1H, H<sub>A</sub>), 6.45 d.d (1H, H<sub>X</sub>), <sup>3</sup>J<sub>BX</sub> = 8.4, <sup>3</sup>J<sub>AX</sub> = 15.4 Hz. Found:  $[M]^+$  276. C<sub>9</sub>H<sub>3</sub>F<sub>7</sub>S. Calculated: *M* 276.

The still residue (4.85 g) was treated with hot hexane, and the hexane solution was subjected to column chromatography on aluminum oxide using hexane as eluent. We isolated 0.5 g (3%) of 3,6-difluoro-4-trifluoromethyl-1,2,5-tris(vinylsulfanyl)benzene (**VI**) as a light brown liquid and 2 g (2%) of compound **V** as a colorless crystalline substance [6]. IR spectrum of **VI**,  $\nu$ , cm<sup>-1</sup>: 864, 876 sh, 982, 1590 (SC=C), 1142, 1179, 1299 (CF<sub>3</sub>). <sup>1</sup>H NMR spectrum of **VI**,  $\delta$ , ppm: 5.23 d, 5.25 d, and 5.32 d (1H, H<sub>B</sub>); 5.35 d, 5.37 d, and 5.40 d (1H, H<sub>A</sub>); 6.35 d.d, 6.38 d.d, and 6.46 d.d (1H, H<sub>X</sub>); <sup>3</sup>J<sub>BX</sub> = 8.4, <sup>3</sup>J<sub>AX</sub> = 15.4 Hz. <sup>13</sup>C NMR spectrum of **VI**,  $\delta_C$ , ppm: 116.48, 116.57, 117.40 (C<sup>β</sup>); 129.60, 129.90, 130.42 (C<sup>α</sup>). <sup>19</sup>F NMR spectrum of **VI**,  $\delta_F$ , ppm: -54.77 d (CF<sub>3</sub>), -94.65 d (6-F), -104.22 q.d (3-F). Found:  $[M]^+$  356. C<sub>13</sub>H<sub>9</sub>F<sub>5</sub>S<sub>3</sub>. Calculated: *M* 356. Compound **V**: Found:  $[M]^+$  449. C<sub>14</sub>H<sub>9</sub>F<sub>14</sub>N. Calculated: *M* 449.

**3,6-Difluoro-*N,N*-dimethyl-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline (VIII)**. Metallic sodium, 2.3 g (100 mmol), was added in small portions under stirring to a solution of 4.3 g (50 mmol) of divinyl sulfide in 100 ml of liquid ammonia. The ammonia was evaporated, 40 ml of DMF was added to the residue, and argon was bubbled through the mixture. A solution of 4 g (17 mmol) of perfluorotoluene in

10 ml of DMF was added. During the addition, the mixture slightly warmed up, and it was cooled using a cold water bath. The mixture was stirred for 5 h, kept for 12 h at 25°C, diluted with water, and treated with diethyl ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and evaporated under reduced pressure to leave 3.3 g of a dark brown viscous material which contained (according to the GC-MS data) 73.5% of compound **VIII** and 13.4% of **VI**. By treatment with hot hexane and ethanol we isolated 0.17 g (3%) of **VI** and 2.4 g (42%) of **VIII**. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 1585 (SC=C); 3001, 3036, 3089 (=C-H); 1135, 1157, 1229, 1337 (CF<sub>3</sub>). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.93 d [6H, N(CH<sub>3</sub>)<sub>2</sub>], 5.04 d and 5.07 d (1H each, H<sub>B</sub>), 5.28 d and 5.31 d (1H each, H<sub>A</sub>), 6.23 d.d and 6.30 d.d (1H each, H<sub>X</sub>); <sup>3</sup>J<sub>BX</sub> = 8.4, <sup>3</sup>J<sub>AX</sub> = 15.4 Hz. <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 113.68 and 113.84 (C<sup>β</sup>), 131.24 and 132.01 (C<sup>α</sup>). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: -52.74 d (CF<sub>3</sub>), -94.45 d (6-F), -103.92 q.d (3-F). Found:  $[M]^+$  341. C<sub>13</sub>H<sub>12</sub>F<sub>5</sub>NS<sub>2</sub>. Calculated: *M* 341.

**3,6-Difluoro-4-trifluoromethyl-2,5-bis(vinylsulfanyl)aniline (IX)**. Metallic sodium, 2.3 g (100 mmol), was added in small portions under stirring to a solution of 4.3 g (50 mmol) of divinyl sulfide in 100 ml of liquid ammonia. The ammonia was evaporated, 40 ml of DMF was added to the residue, and argon was bubbled through the mixture. A solution of 4.2 g (18 mmol) of 2,3,5,6-tetrafluoro-4-trifluoromethylaniline (**III**) in 25 ml of DMF was added dropwise, and the mixture was stirred for 5 h at 20–25°C, kept for 12 h at 25°C, diluted with water, and treated with diethyl ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and evaporated under reduced pressure. The residue was 1.2 g of a dark brown liquid. It was treated with hot hexane, and from the hexane solution we isolated 1 g (18%) of compound **IX**. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 1587 (SC=C); 3010, 3085 (=C-H); 3384, 3494 (NH<sub>2</sub>); 1124, 1162, 1229, 1368 (CF<sub>3</sub>). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 5.04 d and 5.18 d (1H each, H<sub>B</sub>), 5.27 d and 5.28 d (1H each, H<sub>A</sub>), 6.16 d.d and 6.34 d.d (1H each, H<sub>X</sub>); <sup>3</sup>J<sub>BX</sub> = 8.4, <sup>3</sup>J<sub>AX</sub> = 15.4 Hz. <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 113.81 and 114.30 (C<sup>β</sup>), 127.52 and 129.88 (C<sup>α</sup>). <sup>19</sup>F NMR spectrum,  $\delta_F$ , ppm: -52.64 d [CF<sub>3</sub>, <sup>4</sup>J(CF<sub>3</sub>, 3-F) = 33.56 Hz], -106.67 q.d [3-F, <sup>4</sup>J(CF<sub>3</sub>, 3-F) = 33.56, <sup>5</sup>J(3-F, 6-F) = 13.48 Hz], -124.95 d (6-F). Found, %: C 42.50; H 2.36; F 30.67; N 4.19; S 20.07.  $[M]^+$  313. C<sub>11</sub>H<sub>8</sub>F<sub>5</sub>NS<sub>2</sub>. Calculated, %: C 42.17; H 2.57; F 30.32; N 4.47; S 20.47. *M* 313.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 02-03-32844).

## REFERENCES

1. Amosova, S.V., Gostevskaya, V.I., Gavrilova, G.M., Afonin, A.V., Romanenko, L.S., and Stefanik, L., *Zh. Org. Khim.*, 1992, vol. 28, p. 1463.
2. Amosova, S.V., Gostevskaya, V.I., Gavrilova, G.M., Afonin, A.V., and Toryashinova, D.-S.D., *Zh. Org. Khim.*, 1993, vol. 29, p. 2416.
3. Amosova, S.V., Gostevskaya, V.I., Gavrilova, G.M., and Afonin, A.V., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 713.
4. Ishikawa, N. and Kobayashi, E., *Ftor, khimiya i primeneniye* (Fluorine. Chemistry and Applications), Moscow: Mir, 1982, p. 156.
5. Burdon, J.A., Damadaran, V.A., and Tatlow, J.C., *J. Chem. Soc.*, 1964, p. 763.
6. Kobrina, L.S., *Fluorine Chemistry Reviews*, New York: Marcel Dekker, 1974, p. 112.
7. Abezgauz, F.I. and Sokolov, S.V., *Zh. Obshch. Khim.*, 1967, vol. 37, p. 809.
8. Gerasimova, T.N. and Kargapolova, I.Yu., *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim.*, 1986, vol. 15, p. 112.
9. Yakobson, G.G., Shteingarts, V.D., Furin, G.G., and Vorozhtsov, N.N., *Zh. Obshch. Khim.*, 1964, vol. 34, p. 3514.
10. Alsop, D.J., Burdon, J.A., and Tatlow, J.C., *J. Chem. Soc.*, 1962, p. 1801.
11. Poleshchuk, O.Kh., Korobeinicheva, I.K., Fugaeva, O.M., and Furin, G.G., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1603.