

# Reactions of 1,2,4,5-Tetrafluoro-3,6-bis(vinylsulfonyl)benzene with Nucleophilic Reagents Containing a Mercapto Group

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**Abstract**—Addition of 2-aminoethanethiol and 2-mercaptoethanol at both vinylsulfonyl groups of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene occurs through the thiol group of the reagent and yields the corresponding 3,6-bis[2-(2-aminoethylthio)ethylsulfonyl] and 3,6-bis[2-(2-hydroxyethylthio)ethylsulfonyl] derivatives. The reaction of the title compound with 1,2-ethanedithiol leads to formation of only polymeric addition products.

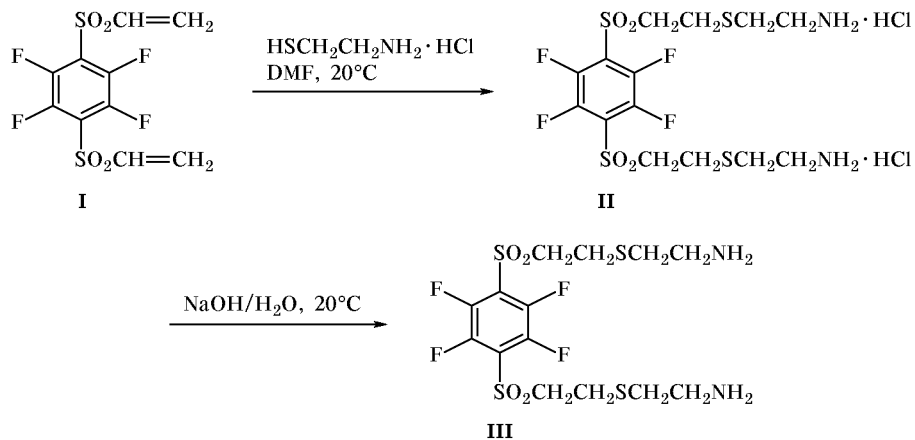
We previously studied reactions of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**I**) and 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene with 2-aminoethanol [1] and allylamine [2] and found that these compounds are promising for building up new heterocyclic systems through simultaneous nucleophilic addition of the amino group at the activated double bonds and replacement of fluorine atoms in the benzene ring.

While continuing studies on reactions of tetrafluorobenzene **I** with difunctional nucleophiles we now report on its reaction with 2 equiv of 2-aminoethanethiol hydrochloride in DMF at 20°C. The reaction follows the nucleophilic addition pattern at activated double bonds of the substrate and yields 59% of 3,6-bis[2-(2-aminoethylthio)ethylsulfonyl]-

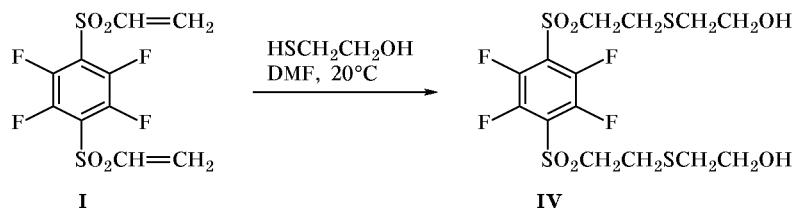
1,2,4,5-tetrafluorobenzene dihydrochloride (**II**) (Scheme 1). The structure of product **II** was proved by elemental analysis and IR and <sup>1</sup>H and <sup>19</sup>F NMR spectra.

Treatment of a solution of **II** in water with 2 equiv of aqueous sodium hydroxide at room temperature gave 75% of the corresponding free base, 3,6-bis[2-(2-aminoethylthio)ethylsulfonyl]-1,2,4,5-tetrafluorobenzene (**III**) whose structure was derived from its elemental composition and IR spectrum. The band due to SO<sub>2</sub> group appears in the IR spectrum of **III** at lower frequencies (by ~15–20 cm<sup>-1</sup>) relative to its position in the spectrum of **II**. This may be due to formation of hydrogen bonds between the amino and sulfonyl groups in **III**. Compound **III** is insoluble in common organic solvents, so that we failed to effect

Scheme 1.



Scheme 2.



intramolecular nucleophilic replacement of fluorine in the benzene ring by amino group with a view to obtain new heterocyclic systems.

In the reaction of tetrafluorobenzene **I** with 2-aminoethanethiol hydrochloride in the presence of KOH in the system 50% aqueous 2-propanol–DMF (1:1) we could expect formation of different products, depending on the amount of potassium hydroxide. At an equimolar ratio of KOH and 2-aminoethanethiol hydrochloride (to release two  $\text{NH}_2$  groups), addition of the amino groups at both vinyl sulfonyl group is possible with subsequent replacement of fluorine in the benzene ring by the same amino group in a way similar to that reported in [1, 2]. Another possible pathway includes addition of thiol groups at the vinyl double bonds and subsequent replacement of fluorine with participation of the amino group. When 2 equiv of KOH is taken (with respect to 2-aminoethanethiol hydrochloride), fluorine atoms in the benzene ring may be replaced by the sulfide moiety with formation of only substitution products; an alternative route includes subsequent addition of the  $\text{NH}_2$  group to the double bond. However, our experiments resulted in isolation of products which were insoluble in common organic solvents, and we were unable to examine them by  $^1\text{H}$  NMR spectroscopy. Their IR spectra contained absorption bands typical of stretching vibrations of  $\text{SO}_2$  group and  $\text{C}-\text{F}_{\text{arom}}$  bond, whereas bands assignable to vinylsulfonyl group were absent. Obviously, these data are insufficient to unambiguously determine the structure of the isolated compounds.

The reaction of tetrafluorobenzene **I** with 2 equiv of 2-mercaptoethanol in DMF at  $20^\circ\text{C}$  resulted in nucleophilic addition through the thiol group and

formation of 1,2,4,5-tetrafluoro-3,6-bis[2-(2-hydroxyethylthio)ethylsulfonyl]benzene (**IV**) in 48% yield (Scheme 2). Its structure was confirmed by the IR and NMR spectra.

The result of the reaction of 1,2-ethanedithiol with compound **I** indicates easy addition of the thiol group at the double  $\text{C}=\text{C}$  bond of the vinylsulfonyl moiety. The reaction was carried out in DMF at  $20^\circ\text{C}$ , and it led to formation of polymeric product **V** in up to 40% yield (Scheme 3). The structure of its monomeric unit was derived from the elemental analysis and IR spectrum which contained bands typical of stretching vibrations of the  $\text{SO}_2$  group and  $\text{C}-\text{F}_{\text{arom}}$  bond. We failed to record NMR spectra of **V** because of its poor solubility in organic solvents.

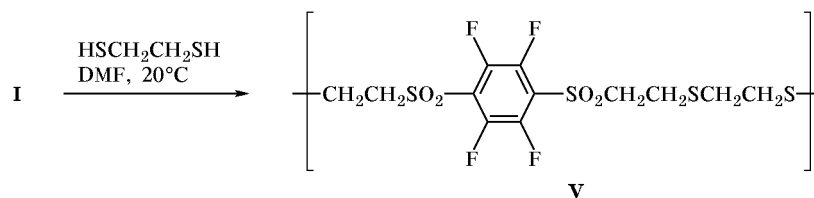
Our results suggest that, contrary to the data of [3, 4], the acceptor power of a sulfonyl group directly attached to polyfluorinated benzene ring is sufficient to activate the adjacent double bond for selective nucleophilic addition of thiol groups in the absence of base catalyst.

## EXPERIMENTAL

The IR spectra were recorded on a Bruker IPS-25 spectrometer from samples pelleted with KBr. The  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra were obtained on a JEOL FX-90Q instrument at 89.55 MHz for  $^1\text{H}$  and 84.25 MHz for  $^{19}\text{F}$ ; HMDS ( $^1\text{H}$ ) and  $\text{CF}_3\text{C}_6\text{H}_5$  ( $^{19}\text{F}$ , the chemical shifts were recalculated to  $\text{CFCl}_3$ ) were used as internal standards.

**3,6-Bis[2-(2-aminoethylthio)ethylsulfonyl]-1,2,4,5-tetrafluorobenzene dihydrochloride (II).** To a solution of 0.55 g of 2-aminoethanethiol hydrochloride in 15 ml of DMF we added at  $20^\circ\text{C}$  with stirring

Scheme 3.



a solution of 0.8 g of compound **I** in 15 ml of DMF. After 20 h, the solvent was removed under reduced pressure, and the residue was washed with ethanol and diethyl ether. Yield 0.8 g (59%), light yellow powder, mp 180–185°C (decomp.). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1149, 1341 ( $\text{SO}_2$ ); 1487 (C–F); 2956 br.s ( $\text{NH}_3^+$ ).  $^1\text{H}$  NMR spectrum ( $\text{D}_2\text{O}$ ),  $\delta$ , ppm: 3.02 t (4H,  $2\text{SCH}_2\text{CH}_2\text{NH}_2$ ), 3.10 t (4H,  $2\text{SCH}_2\text{CH}_2\text{SO}_2$ ), 3.27 t (4H,  $2\text{CH}_2\text{SO}_2$ ), 4.09 t (4H,  $2\text{CH}_2\text{NH}_2$ ).  $^{19}\text{F}$  NMR spectrum ( $\text{D}_2\text{O}$ ):  $\delta_{\text{F}}$  –131.96 ppm, s. Found, %: C 30.44; H 3.99; Cl 12.77; F 13.64; N 5.39; S 23.06.  $\text{C}_{14}\text{H}_{22}\text{Cl}_2\text{F}_4\text{N}_2\text{O}_4\text{S}_2$ . Calculated, %: C 30.16; H 3.98; Cl 12.72; F 13.63; N 5.02; S 23.00.

**3,6-Bis[2-(2-aminoethylthio)ethylsulfonyl]-1,2,4,5-tetrafluorobenzene (III)**. To a solution of 1 g of compound **II** in 20 ml of water we added at 20°C with stirring an aqueous solution of 0.15 g of NaOH. A yellow solid precipitated; after 5 h, it was filtered off, washed in succession with water, ethanol, and diethyl ether, and dried under reduced pressure. Yield 0.65 g (75%), yellow powder, decomposition point 230–232°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1123, 1336 ( $\text{SO}_2$ ); 1456 (C–F); 3372, 3434 ( $\text{NH}_2$ ). Found, %: C 34.64; H 4.22; F 15.25; N 6.21; S 26.61.  $\text{C}_{14}\text{H}_{20}\text{F}_4\text{N}_2\text{O}_4\text{S}_2$ . Calculated, %: C 34.70; H 4.16; F 15.68; N 5.78; S 26.45.

**1,2,4,5-Tetrafluoro-3,6-bis[2-(2-hydroxyethylthio)ethylsulfonyl]benzene (IV)**. To a solution of 0.47 g of 2-mercaptoethanol in 10 ml of DMF we added at 20°C with stirring a solution of 1 g of compound **I** in 15 ml of DMF, and the mixture was kept for 17 h at 20°C. The solvent was removed under reduced pressure, and the light yellow finely crystalline residue was washed with chloroform and diethyl ether. Yield 0.7 g (48%), colorless fine crystals,

mp 135–137°C (decomp.). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1145, 1341 ( $\text{SO}_2$ ); 1490.5 (C–F); 3581 (OH).  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 2.68 t (4H,  $2\text{SCH}_2\text{CH}_2\text{OH}$ ), 3.00 t (4H,  $2\text{SCH}_2\text{CH}_2\text{SO}_2$ ), 3.10 s (OH), 3.68 t (4H,  $2\text{CH}_2\text{SO}_2$ ), 3.86 t (4H,  $2\text{CH}_2\text{OH}$ ).  $^{19}\text{F}$  NMR spectrum (acetone- $d_6$ ):  $\delta_{\text{F}}$  –131.21 ppm, s. Found, %: C 34.60; H 4.01; F 15.33; S 26.15.  $\text{C}_{14}\text{H}_{18}\text{F}_4\text{O}_6\text{S}_4$ . Calculated, %: C 34.37; H 3.73; F 15.62; S 26.35.

**Reaction of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (I) with 1,2-ethanedithiol**. To a solution of 0.29 g of 1,2-ethanedithiol in 10 ml of DMF we added at 20°C with stirring a solution of 1 g of compound **I** in 10 ml of DMF, and the mixture was kept for 16 h at 20°C. The colorless precipitate was separated, washed with acetone and diethyl ether, and dried under reduced pressure to obtain 0.5 g (40%) of product **V** as a colorless powder. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1145, 1325 ( $\text{SO}_2$ ); 1490 (C–F). Found, %: C 33.77; H 3.04; F 16.59; S 31.18.  $\text{C}_{12}\text{H}_{12}\text{F}_4\text{O}_4\text{S}_4$ . Calculated, %: C 33.96; H 2.85; F 17.90; S 30.21.

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