

Reactions of 1,2,4,5-Tetrafluoro-3,6-bis(vinylsulfonyl)benzene with Cyclic Amines

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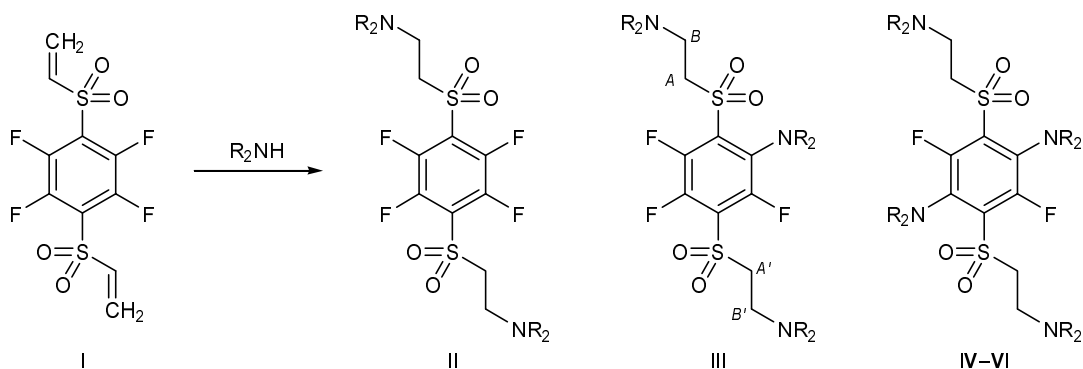
Abstract—Reactions of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene with pyrrolidine, piperidine, and morpholine lead to formation of different products, depending mainly on the reactant ratio. In the presence of 2 equiv of cyclic amine, adducts at both vinylsulfonyl groups are formed, while in reactions with 4 equiv of cyclic amine, the addition at the double bonds is accompanied by nucleophilic replacement of one or two fluorine atoms in the benzene ring.

1,2,4,5-Tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**I**) [1] is readily available via oxidation of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene [2] with hydrogen peroxide. This compound is convenient for the synthesis of various polyfunctional compounds, including heterocycles, by nucleophilic addition and substitution reactions. The double C=C bonds in the vinyl groups of **I** are activated to nucleophilic addition due to electron-acceptor effect of the sulfonyl groups. As we showed previously [3] (in contrast to the data of [4, 5]), this activation is sufficient to ensure addition of 2-aminoethanethiol hydrochloride and 2-sulfanyethanol through their SH groups at both vinylsulfonyl groups in the absence of base catalyst. Likewise, the

corresponding polyaddition product is readily formed from compound **I** and 1,2-ethanedithiol at 20°C.

Unexpectedly, reactions of fluorine-containing bis-sulfone **I** with 2-aminoethanol and allylamine gave rise to heterocyclic systems as a result of nucleophilic addition at the vinyl groups and nucleophilic replacement of fluorine atoms in the benzene ring by the amino group of 2-aminoethanol [6] or allylamine [2]. Compound **I** was found to react with thiosemicarbazide [7, 8] in ethanol or DMF (20°C) in a stepwise mode. At a reactant ratio of 1:2, 1,2,4,5-tetrafluoro-3,6-bis(2-thiosemicarbazidoethylsulfonyl)benzene was obtained in 73% yield. When the reaction was performed in DMF at 75–80°C with 4 equiv of thiosemicarbazide,

Scheme 1.



II-IV, R₂N = piperidino; **V**, R₂N = 1-pyrrolidinyl; **VI**, R₂N = morpholino.

the product was fused N,S-heterocyclic compound which was formed via nucleophilic addition of the 1-NH₂ group of thiosemicarbazide at the vinyl double bonds and subsequent intramolecular replacement of the *ortho*- and *meta*-fluorine atoms by the NH group or sulfur atom, respectively.

The present communication reports the results of our study on the reaction of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**I**) with cyclic amines, such as pyrrolidine, piperidine, and morpholine. The latter were selected, taking into account that their molecules are structural fragments of many biologically active compounds; therefore, introduction of such fragments into the molecule of vinylsulfonylfluorobenzene **I** could give rise to biological activity.

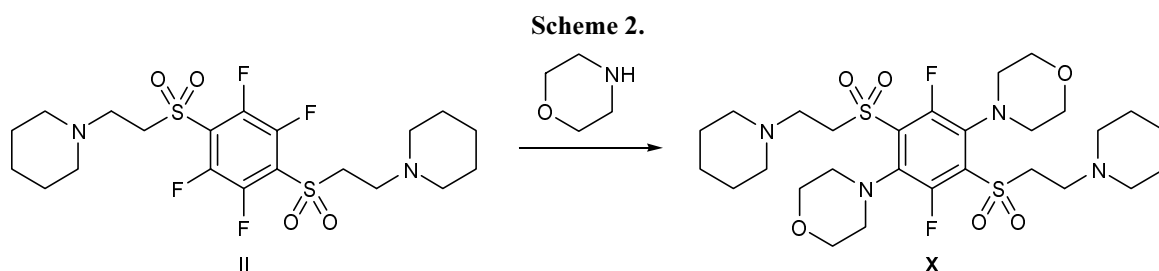
The reactions were carried out in dimethylformamide or ethanol at 55–60°C. Depending on the reactant ratio, either nucleophilic addition or nucleophilic addition and substitution products were formed. The reactions with 2 equiv of amine gave products of addition at both vinylsulfonyl groups. For example, compound **I** reacted with piperidine in DMF to give 40% of 1,2,4,5-tetrafluoro-3,6-bis(2-piperidinoethylsulfonyl)benzene (**II**) (Scheme 1). When the reactant ratio (amine–substrate) was 4:1, the addition process was accompanied by replacement of one or two fluorine atoms in the benzene ring. In the reaction with piperidine we obtained 2,4,5-trifluoro-1-piperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene (**III**) in 47% yield and traces of 1,4-difluoro-2,5-dipiperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene (**IV**). Under the same conditions (DMF, 55–60°C), the reaction of **I** with 4 equiv of pyrrolidine gave 65.5% of 1,4-difluoro-2,5-bis(1-pyrrolidinyl)-3,6-bis[2-(1-pyrrolidinyl)ethylsulfonyl]benzene (**V**), and the reaction with morpholine, 37% of 1,4-difluoro-2,5-dimorpholino-3,6-bis(2-morpholinoethylsulfonyl)benzene (**VI**) (Scheme 1). Obviously, the reaction direction and product yield are determined by excess amine which is necessary to bind hydrogen fluoride liberated as a result of nucleophilic substitution of the fluorine atoms.

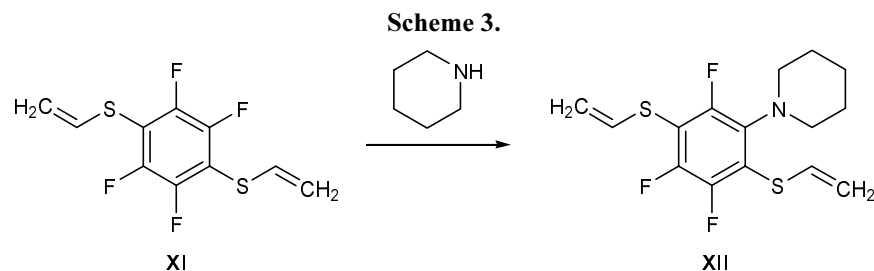
In the reaction of compound **I** with piperidine at a ratio of 1:6, the yield of **IV** increases to 65%. Likewise, 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**I**) reacted with excess morpholine (used as solvent, 55–60°C) to afford 60% of product **VI**. These data suggest that reactions of **I** with cyclic amines can be performed under solvent-free conditions.

The reactivity of cyclic amines toward compound **I** changes in accordance with their basicity (pyrrolidine ≥ piperidine > morpholine; pK_a = 11.27, 11.22, and 8.33, respectively). These amines are strong bases, and they readily react with most acids to give the corresponding salts. By reaction of compound **IV** in chloroform with gaseous hydrogen chloride (20–25°C) we obtained hydrochloride **VII**. Perchlorates **VIII** and **IX** were formed on treatment of solutions of **IV** and **V**, respectively, in chloroform with 30% perchloric acid. According to the data of elemental analysis, only one nitrogen atom is protonated in molecules **IV** and **V**, presumably the one not linked to the aromatic ring. The salts thus formed separate from the solution; they are almost insoluble in water, ethanol, and dimethyl sulfoxide; therefore, interaction of the other basic centers in compounds **VII–IX** with an acid is excluded. Salts **VII–IX** are weakly soluble in water on heating to 80–90°C.

The conditions leading to formation of compounds **II–VI** suggest that the reaction of **I** with cyclic amines can be performed in a stepwise mode to introduce different amine residues into the substrate molecule. By treatment of compound **IV** with morpholine (DMF, 55–60°C) we obtained 1,4-difluoro-2,5-dimorpholino-3,6-bis(2-piperidinoethylsulfonyl)benzene (**X**) in up to 70% yield (Scheme 2).

The reaction of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**XI**) with 4 equiv of piperidine in DMF at 100°C gave product of replacement of only one fluorine atom, 2,4,5-trifluoro-1-piperidino-3,6-bis(vinylsulfonyl)benzene (**XII**, yield 34%; Scheme 3). Disubstituted products **IV–VI** were obtained from bisulfone **I** under analogous conditions, but at a lower





temperature (55–60°C). These data indicate enhanced reactivity of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**I**) as compared to bis-sulfide **XI** and hexafluorobenzene [9] in nucleophilic substitution processes. Obviously, the reason is activating effect of the electron-acceptor sulfonyl groups, which is consistent with the data of Rodionov *et al.* [10] who studied the effect of sulfur-containing substituents in polyfluorinated benzene ring on the rate of fluorine replacement by various nucleophiles, including piperidine.

Compounds **II–X** are light yellow high-melting crystalline substances. Their structure was proved by the IR and ^1H , ^{13}C , and ^{19}F NMR spectra and elemental analyses.

EXPERIMENTAL

The IR spectra were obtained on a Bruker IFS-25 spectrometer from samples dispersed in mineral oil or pelleted with KBr. The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 instrument (400 MHz for ^1H) in CDCl_3 . The chemical shifts were measured relative to HMDS (^1H and ^{13}C), CFCl_3 (^{19}F), or CH_3NO_2 (^{15}N). The GC–MS data were obtained using an HP 5971A mass-selective detector (electron impact, 70 eV) coupled with a gas chromatograph.

1,2,4,5-Tetrafluoro-3,6-bis(2-piperidinoethylsulfonyl)benzene (II). A solution of 1 g of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene in 17 ml of DMF was heated to 55°C, a solution of 0.5 g of piperidine in 3 ml of DMF was added, and the mixture was stirred for 6 h at 55–60°C. The mixture was treated with water and extracted with chloroform. The extract was washed with water and dried over MgSO_4 . The solvent was removed to obtain 1.1 g of a crystalline substance which was washed with ethanol and ether and recrystallized from chloroform. Yield 0.61 g (40%), light yellow crystals, mp 176–177°C (from chloroform). IR spectrum, ν , cm^{-1} : 1141, 1339 (SO_2). ^1H NMR spectrum (CDCl_3), δ , ppm: 1.20 br.m and 1.30 br.m (4H each, CH_2 , piperidine), 2.25 br.m (4H, NCH_2 , piperidine), 2.86 t (4H, $\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$, $^3J = 5.92$ Hz), 3.48 t

(4H, CH_2SO_2 , $^3J = 5.92$ Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 23.72 (C^4 , piperidine), 25.68 (C^3 , piperidine), 52.40 ($\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 54.30 (C^2 , piperidine), 54.91 (CH_2SO_2), 125.22 (C^6 , C^3 , arom.), 144.59 d.d (C^1 , C^2 , C^4 , C^5 , arom., $^1J_{\text{CF}} = 267.6$, $^2J_{\text{CF}} = 12.27$ Hz). ^{19}F NMR spectrum: $\delta_{\text{F}} -135.31$ ppm, s. Found, %: C 47.91; H 6.23; F 14.91; N 6.12; S 12.98. $\text{C}_{20}\text{H}_{28}\text{F}_4\text{N}_2\text{O}_4\text{S}_2$. Calculated, %: C 47.98; H 5.64; F 15.18; N 5.60; S 12.81.

2,4,5-Trifluoro-1-piperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene (III) was synthesized in a similar way, but using 4 equiv of piperidine. Yield 47%, mp 141–142°C (from ethanol). IR spectrum, ν , cm^{-1} : 1140, 1327 (SO_2). ^1H NMR spectrum (CDCl_3), δ , ppm: 1.17 m (4H, C^4H_2 , piperidine- CH_2), 1.33 m [8H, C^3H_2 , C^5H_2 , piperidine- CH_2], 2.25 m and 2.30 m (4H, NCH_2 , piperidine- CH_2), 1.69 m (6H, CH_2 , piperidine- C_{arom}), 3.14 m and 3.07 m (4H, NCH_2 , piperidine- C_{arom}), 2.86 t (2H, H_{B} , $^3J = 6$ Hz), 3.47 t (2H, H_{A}), 2.80 t (2H, H_{B}), 3.70 t (2H, H_{A}). ^{13}C NMR spectrum, δ_{C} , ppm: 23.73 (C^2 , C^6 , piperidine- CH_2), 23.82 (C^2 , C^6 , piperidine- C_{arom}), 25.74 and 25.67 (C^3 , C^5 , piperidine- CH_2), 26.12 (C^3 , C^5 , piperidine- C_{arom}), 52.40 (C^{B}), 52.32 ($\text{C}^{\text{B}'}$), 52.86 (C^2 , C^6 , piperidine- C_{arom}), 54.42 and 54.25 (C^2 , C^6 , piperidine- CH_2), 54.54 (C^4), 54.20 (C^4), 155 d (C^1 , arom., $^1J_{\text{CF}} = 263.39$ Hz), 145.90 d.d (C^4 , arom., $^1J_{\text{CF}} = 266.36$, $^2J_{\text{CF}} = 16.2$ Hz), 146.80 d.d (C^5 , arom., $^1J_{\text{CF}} = 263.38$, $^2J_{\text{CF}} = 18.0$ Hz), 136.67 d.d (C^3 , arom., $^2J_{\text{CF}} = 16.3$, $^3J_{\text{CF}} = 4.8$ Hz), 133.38 (C^2 , arom.), 124.55 d.d (C^6 , arom., $^2J_{\text{CF}} = 18.4$, $^3J_{\text{CF}} = 13.0$ Hz). ^{19}F NMR spectrum, δ_{F} , ppm: -118.36 d (2-F, $^5J_{\text{FF}} = 14.3$ Hz), -131.48 d (4-F, $^3J_{\text{FF}} = 23.5$ Hz), -135.43 d.d (5-F). ^{15}N NMR spectrum, δ_{N} , ppm: -330.6, -331.4 [$\text{CH}_2\text{N}(\text{CH}_2)_2$]. Found, %: C 52.84; H 6.72; F 9.24; N 7.55; S 11.52. $\text{C}_{25}\text{H}_{38}\text{F}_3\text{N}_3\text{O}_4\text{S}_2$. Calculated, %: C 53.07; H 6.77; F 10.07; N 7.42; S 11.33.

1,4-Difluoro-2,5-dipiperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene (IV). A solution of 0.8 g of compound **I** in 25 ml of ethanol was heated to 55–60°C, a solution of 1.2 g of piperidine in 5 ml of ethanol was added, and the mixture was stirred for 6 h at that temperature. The precipitate was filtered off and

washed with ethanol and diethyl ether. Yield 1 g (65%), light yellow crystals, mp 167–168°C. IR spectrum, ν , cm^{-1} : 1133, 1320 (SO_2). ^1H NMR spectrum (CDCl_3), δ , ppm: 1.20 br.m (4H, C^4H_2 , piperidine- CH_2), 1.73 br.m [8H, C^3H_2 , C^5H_2 , piperidine- CH_2], 2.25 and 2.32 br.m (8H, C^2H_2 , C^6H_2 , piperidine- CH_2), 2.82 t (4H, $\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 3.07 m and 3.15 m (8H, C^2H_2 , C^6H_2 , piperidine- C_{arom}), 3.69 t (4H, CH_2SO_2). ^{13}C NMR spectrum, δ_{C} , ppm: 23.81 (C^4 , piperidine- CH_2), 23.91 (C^4 , piperidine- C_{arom}), 25.73 (C^3 , C^5 , piperidine- CH_2), 25.99 (C^3 , C^5 , piperidine- C_{arom}), 52.17 ($\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 52.62 (C^2 , C^6 , piperidine), 54.40 (SO_2CH_2), 132.37 d.d (C^3 , C^6 , arom.), 139.11 d.d (C^1 , C^4 , arom.), 155.19 (C^2 , arom.), 157.84 (C^5 , arom.). Found, %: C 57.09; H 7.71; F 6.94; N 9.17; S 10.71. $\text{C}_{30}\text{H}_{48}\text{F}_2\text{N}_4\text{O}_4\text{S}_2$. Calculated, %: C 57.11; H 7.67; F 6.02; N 8.81; S 10.16.

1,4-Difluoro-2,5-bis(1-pyrrolidinyl)-3,6-bis[2-(1-pyrrolidinyl)ethylsulfonyl]benzene (V). A solution of 1.4 g of compound **I** in 20 ml of DMF was heated to 55°C, and a solution of 1.2 g of pyrrolidine in 5 ml of DMF was added dropwise from a dropping funnel (the reaction was accompanied by a slight evolution of heat). The mixture was stirred for 6 h at 55–60°C and was left overnight. The precipitate was filtered off and washed with ethanol and diethyl ether. Yield 1.6 g (65.5%), light brown crystals, mp 191–192°C (decomp.). IR spectrum, ν , cm^{-1} : 1136, 1319 (SO_2). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 1.54 m (8H, C^3H_2 , C^4H_2 , pyrrolidine- CH_2), 1.85 m [8H, C^3H_2 , C^4H_2 , pyrrolidine- C_{arom}], 2.36 m [8H, C^2H_2 , C^5H_2 , pyrrolidine- CH_2], 2.83 t (4H, $\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 3.15 m (8H, C^2H_2 , C^5H_2 , pyrrolidine- C_{arom}), 3.66 t (4H, CH_2SO_2). ^{13}C NMR spectrum, δ_{C} , ppm: 23.06 (C^3 , C^4 , pyrrolidine- CH_2), 25.48 (C^3 , C^4 , pyrrolidine- C_{arom}), 48.31 ($\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 52.62 (C^2 , C^5 , pyrrolidine- C_{arom}), 52.99 (C^2 , C^5 , pyrrolidine- CH_2), 55.15 (CH_2SO_2). Found, %: C 53.60; H 7.06; F 6.85; N 9.78; S 11.03. $\text{C}_{26}\text{H}_{40}\text{F}_2\text{N}_4\text{O}_4\text{S}_2$. Calculated, %: C 54.33; H 7.01; F 6.61; N 9.75; S 11.16.

1,4-Difluoro-2,5-dimorpholino-3,6-bis(2-morpholinoethylsulfonyl)benzene (VI). A solution of 1 g of compound **I** in 20 ml of DMF was heated to 55°C, a solution of 1 g of morpholine in 5 ml of DMF was added, and the mixture was stirred for 6 h at 55–60°C. The precipitate was filtered off and washed with ethanol and diethyl ether. Yield 0.7 g (37%), light yellow crystals, mp 273°C (decomp.). IR spectrum, ν , cm^{-1} : 1139, 1320 (SO_2). ^1H NMR spectrum (CDCl_3), δ , ppm: 2.43 br.t (8H, NCH_2 , morpholine- CH_2), 2.93 br.m and 3.43 br.m (4H each, NCH_2 , morpholine-

C_{arom}), 2.92 t (4H, $\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$, $^3J = 6.8$ Hz), 3.55 br.t (8H, CH_2OCH_2 , morpholine- CH_2 , $^3J = 4$ Hz), 3.72 t (4H, CH_2SO_2), 3.84 br.m (8H, CH_2OCH_2 , morpholine- C_{arom}). ^{13}C NMR spectrum, δ_{C} , ppm: 51.58 ($\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 51.80 (CH_2NCH_2 , morpholine- C_{arom}), 53.48 (CH_2NCH_2 , morpholine- CH_2), 54.66 (SO_2CH_2), 66.70 (CH_2OCH_2 , morpholine- CH_2), 67.13 (CH_2OCH_2 , morpholine- C_{arom}), 156.10 d.d (C_{arom} , $^1J_{\text{CF}} = 266.1$, $^4J_{\text{CF}} = 3.45$ Hz), 133.12 d.d (C_{arom} , $^2J_{\text{CF}} \approx ^3J_{\text{CF}} \approx 7.7$ Hz), 137.87 d.d (C_{arom} , $^2J_{\text{CF}} = 11.5$, $^3J_{\text{CF}} = 6.9$ Hz). ^{19}F NMR spectrum: $\delta_{\text{F}} -117.11$ ppm, s. Found, %: C 48.57; H 6.38; F 5.43; N 9.00; S 9.36. $\text{C}_{26}\text{H}_{40}\text{F}_2\text{N}_4\text{O}_8\text{S}_2$. Calculated, %: C 48.89; H 6.31; F 5.95; N 8.77; S 10.04.

1,4-Difluoro-2,5-dimorpholino-3,6-bis(2-piperidinoethylsulfonyl)benzene (X). A solution of 0.4 g of compound **II** in 8 ml of DMF was heated to 55°C, a solution of 0.21 g of morpholine in 4 ml of DMF was added, and the mixture was stirred for 6 h at 55–60°C and left overnight. It was then diluted with 25 ml of water and extracted with chloroform, the extract was washed with water and dried over MgSO_4 , and the solvent was removed to obtain 0.8 g of a solid substance which was recrystallized from hot ethanol. Yield 0.35 g (69%), light yellow crystals, mp 208–210°C (decomp.). IR spectrum, ν , cm^{-1} : 1137, 1324 (SO_2). ^1H NMR spectrum (CDCl_3), δ , ppm: 1.68 br.m and 1.8 br.m (6H each, CH_2 , piperidine), 2.42 br.m (8H, CH_2NCH_2), 2.87 t (4H, $\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 3.06 br.m and 3.15 br.m (4H each, NCH_2 , morpholine), 3.55 t (4H, SO_2CH_2), 3.75 m (8H, CH_2OCH_2). ^{13}C NMR spectrum, δ , ppm: 23.61 (C^4 , piperidine), 26.00 (C^3 , C^5 , piperidine), 52.60 ($\text{SO}_2\text{CH}_2\text{CH}_2\text{N}$), 53.31 (C^2 , C^6 , piperidine), 54.36 (SO_2CH_2), 66.62 (CH_2OCH_2), 51.61 (CH_2NCH_2 , morpholine), 132.25 d.d (C^3 , C^6 , arom.), 137.40 d.d (C^2 , C^5 , arom.), 157.59 d.d and 154.95 d.d ($\text{C}-\text{F}$). ^{19}F NMR spectrum: $\delta_{\text{F}} -117.86$ ppm. Found, %: C 52.98; H 7.41; F 5.93; N 9.58; S 10.68. $\text{C}_{28}\text{H}_{44}\text{F}_2\text{N}_4\text{O}_6\text{S}_2$. Calculated, %: C 52.97; H 6.98; F 5.98; N 8.82; S 10.10.

2,4,5-Trifluoro-1-piperidino-3,6-bis(vinylsulfonyl)benzene (XII). A solution of 1.53 g of piperidine in 5 ml of DMF was added to a solution of 1.2 g of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (**XI**) in 15 ml of DMF. The mixture was heated for 10 h at 100°C, diluted with 25 ml of water, and extracted with diethyl ether. The extract was washed with water, dried over MgSO_4 , and evaporated. The residue, 0.8 g, was a dark brown liquid containing (according to the GC-MS data) 51.4% of compound **XII**, 12.8% of 6-(3-butenylsulfonyl)-1-dimethylamino-2,4,5-tri-

fluoro-3-vinylsulfanylbenzene [11], 6% of 6-dimethylamino-1,2,4,5-tetrafluoro-3-vinylsulfanylbenzene [12], and 26% of initial compound **XI**. IR spectrum of **XII**: $\nu(\text{SCH}=\text{CH}_2)$ 1590 cm^{-1} . ^1H NMR spectrum (CDCl_3), δ , ppm: 1.55 br.m (2H, C^4H_2 , piperidine), 1.64 m (4H, C^3H_2 , C^5H_2 , piperidine), 3.01 m (4H, CH_2NCH_2), 5.29 d and 5.32 d (2H, $\text{CH}_2=$), 6.33 d.d (1H, 3-SCH=, $^3J_{\text{cis}} = 9.54$, $^3J_{\text{trans}} = 15.21$ Hz), 5.30 d and 5.31 d (2H, $\text{CH}_2=$), 6.37 d.d (1H, SCH=, 6-SCH=, $^3J_{\text{cis}} = 9.67$, $^3J_{\text{trans}} = 16.25$ Hz).

1,4-Difluoro-2,5-dipiperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene hydrochloride (VII). Gaseous hydrogen chloride was passed over a period of 30 min through a solution of 0.5 g of compound **IV** in 5 ml of chloroform at room temperature. The precipitate was filtered off and washed with chloroform and diethyl ether. Yield 0.5 g (82%), light yellow finely crystalline substance, mp 263–265°C (decomp.). Found, %: C 47.58; H 6.97; Cl 17.16; F 4.33; N 7.09; S 8.57. $\text{C}_{30}\text{H}_{49}\text{ClF}_2\text{N}_4\text{O}_4\text{S}_2$. Calculated, %: C 48.30; H 6.41; Cl 16.46; F 4.92; N 7.27; S 8.32.

1,4-Difluoro-2,5-bis(1-pyrrolidinyl)-3,6-bis[2-(1-pyrrolidinyl)ethylsulfonyl]benzene hydroperchlorate (VIII). To a solution of 0.1 g of compound **V** in 3 ml of chloroform we added under stirring 3 ml of 30% HClO_4 . After 3 h, the precipitate was filtered off and washed with ethanol and diethyl ether. Yield 0.1 g (74%), mp 239–240°C (decomp.). Found, %: C 40.95; H 5.46; Cl 15.88; F 5.28; N 7.39; S 8.75. $\text{C}_{26}\text{H}_{41}\text{ClF}_2\text{N}_4\text{O}_8\text{S}_2$. Calculated, %: C 41.64; H 5.31; Cl 16.30; F 4.88; N 7.19; S 8.23.

1,4-Difluoro-2,5-dipiperidino-3,6-bis(2-piperidinoethylsulfonyl)benzene hydroperchlorate (IX) was obtained in a similar way. Yield 77%, mp 250°C

(decomp.). Found, %: C 43.96; H 5.38; Cl 14.88; F 4.03; N 6.25; S 7.32. $\text{C}_{30}\text{H}_{49}\text{ClF}_2\text{N}_4\text{O}_8\text{S}_2$. Calculated, %: C 44.60; H 5.91; Cl 15.20; F 4.55; N 6.71; S 7.68.

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