Chemistry of Heterocyclic Compounds, Vol. 32, No. 9, 1996

FLUOROBENZO-1,4-THIAZINE OXIDES FROM BIS-(VINYLSULFINYL)- AND BIS(VINYLSULFONYL)-FLUOROBENZENES AND 2-AMINOETHANOL

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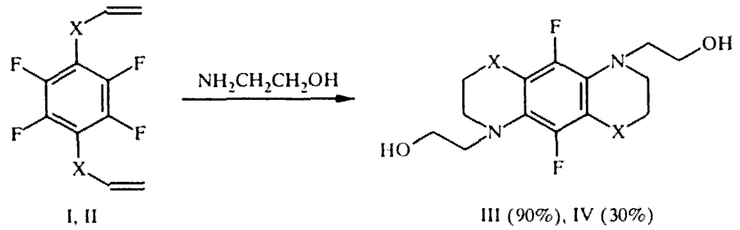
It has been established that 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfinyl)- and 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzenes react with 2-aminoethanol by nucleophilic addition at the activated double bond with replacement of fluorine atoms on the benzene ring by the amino group of 2-aminoethanol to give 4,9-bis(2-hydroxyethyl)-5,10-difluoro-1,2,3,4,6,7,8,9-octahydrobenzo[1,2-b; 5,4-b]di-1,4-thiazine 1,6-dioxide and 1,1,6,6-tetraoxide respectively.

The synthesis of new heterocyclic compounds containing various substituents, including fluorine, and also the search for new routes for making known compounds is an urgent question for solving both practical and theoretical problems in organic chemistry [1, 2]. We showed previously [3], using the reaction of 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (I) with allylamine as an example, that bis(vinylsulfonyl)fluorobenzene, which has several reactive centers in the molecule, is a convenient substance for constructing new heterocyclic systems based on nucleophilic addition and substitution reactions.

As a continuation of these investigations we reacted 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfonyl)benzene (I) and 1,2,4,5-tetrafluoro-3,6-bis(vinylsulfinyl)benzene (II) with 2-aminoethanol in DMF or ethanol at 50-55°C to give high melting (up to 300°C) yellow crystalline substances.

If both hydrogen atoms of the NH_2 group participate in the reaction of bis(vinylsulfonyl)fluorobenzene (I) with allylamine by adding to the activated double bond and substituting fluorine atoms on the benzene ring [3], then the formation of products of reaction at both the amino and hydroxyl group of 2-aminoethanol might have been expected.

It was established unequivocally by x-ray structural investigation that bis(vinylsulfonyl)fluorobenzene (I) forms a product (III) of nucleophilic addition and replacement of fluorine atoms only by the amino group. The hydroxyl group does not react under these conditions. The reaction of bis(vinylsulfinyl)fluorobenzene (II) with 2-aminoethanol proceeded in a similar way leading to the dioxide (IV). The structure of heterocycles (III) and (IV) was confirmed by data of IR, NMR (^1H, ^{13}C, ^{19}F), mass spectrometry, and elemental analysis.



I, II

III (90%), IV (30%)

I, III X = SO_2; II, IV X = SO

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*Deceased.

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TABLE 1. Valence Angles ω (deg) in the Compound (III) Molecule

Angle	ω, deg	Angle	ω, deg
$O_{(1)}-S_{(1)}-O_{(2)}$	117,0(2)	$C_{(2)}-C_{(1)}-C_{(3a)}$	124,9(3)
$O_{(1)}-S_{(1)}-C_{(2)}$	109,4(2)	$S_{(1)}-C_{(2)}-C_{(1)}$	117,3(3)
$O_{(2)}-S_{(1)}-C_{(2)}$	108,2(2)	$S_{(1)}-C_{(2)}-C_{(3)}$	122,1(3)
$O_{(1)}-S_{(1)}-C_{(4)}$	110,8(2)	$C_{(1)}-C_{(2)}-C_{(3)}$	120,6(3)
$O_{(2)}-S_{(1)}-C_{(4)}$	108,8(2)	$N_{(1)}-C_{(3)}-C_{(2)}$	124,3(3)
$C_{(2)}-S_{(1)}-C_{(4)}$	101,5(2)	$N_{(1)}-C_{(3)}-C_{(1a)}$	121,0(3)
$C_{(3)}-N_{(1)}-C_{(5)}$	116,4(3)	$C_{(2)}-C_{(3)}-C_{(1a)}$	114,5(3)
$C_{(3)}-N_{(1)}-C_{(6)}$	119,3(3)	$S_{(1)}-C_{(4)}-C_{(5)}$	108,9(3)
$C_{(5)}-N_{(1)}-C_{(6)}$	116,2(3)	$N_{(1)}-C_{(5)}-C_{(4)}$	112,9(3)
$F_{(1)}-C_{(1)}-C_{(2)}$	117,1(3)	$N_{(1)}-C_{(6)}-C_{(7)}$	112,5(3)
$F_{(1)}-C_{(1)}-C_{(3a)}$	118,0(3)	$O_{(3)}-C_{(7)}-C_{(6)}$	109,2(4)

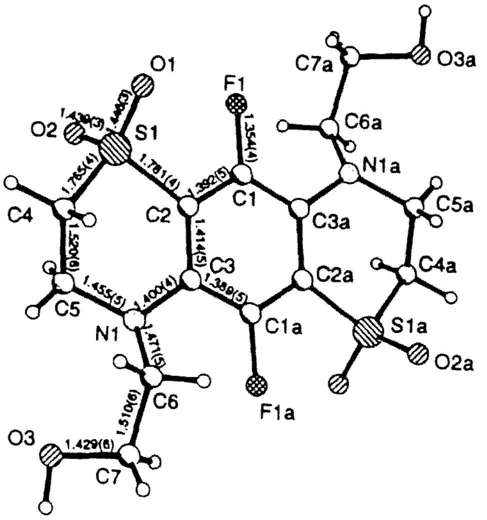

Fig. 1. General form of the centrosymmetric molecule with bond lengths in the symmetrically independent part.

It should be noted that the substitution of a fluorine atom by the amino group in compounds (I) and (II) was affected under milder conditions (50-55°C, DMF) than for 1,2,4,5-tetrafluoro-3,6-bis(vinylthio)benzene (100°C, DMF) [4]. This may be explained by the effect of the two electron-accepting groups in bis(vinylsulfonyl)- (I) and bis(vinylsulfinyl)fluorobenzenes (II) facilitating nucleophilic substitution.

The valence angles for compound (III) are given in Table 1. In this compound the six-membered heterocycles have a half-chair conformation. The $C_{(4)}$ and $C_{(5)}$, $C_{(4a)}$ and $C_{(5a)}$ atoms deviate from the plane of the remaining four atoms (the planes are achieved with a precision of +0.019 Å) by −0.371 and 0.446 Å, and 0.371 and −0.446 Å respectively. On the whole, the approximately flat fragment of the molecule includes the phenyl ring and the atoms adjacent to it, viz. $S_{(1)}$, $N_{(1)}$, $F_{(1)}$ and $S_{(1a)}$, $N_{(1a)}$, $F_{(1a)}$. The hydroxyethyl substituents unfold significantly on different sides of the planar portion of the molecule (torsion angles $C_{(3)}-N_{(1)}-C_{(6)}-C_{(7)}$ −120.7° and $N_{(1)}-C_{(6)}-C_{(7)}-O_{(3)}$ −59.9°). The intermolecular hydrogen bonds in the crystal at $O_{(3)}-H_{(3)}...O_{(2)}$ (0.5 + x, 1.5 − y, 0.5 + z) [$O_{(3)}...O_{(2)}$ 2.927(4), $O_{(3)}-H_{(3)}$ 0.91(7), $H_{(3)}...O_{(2)}$ 2.03(1) Å, angle $O_{(3)}-H_{(3)}...O_{(2)}$ 169(3)°] join the molecules of compound (III) in a strip along the (111) direction. The remaining geometric parameters in compound (III) have the usual values [5].

The examples investigated have shown that bis[vinylsulfonyl(sulfinyl)]fluorobenzenes are convenient substances for obtaining new heterocyclic systems by reacting them with bifunctional nucleophiles.

TABLE 2. Coordinates of Atoms ($\times 10^4$; for H $\times$ 10^3) in the Compound (III) Molecule

Atom	x	y	z
$S_{(1)}$	6262(1)	2099(2)	8425(1)
$F_{(1)}$	3871(2)	2016(5)	8479(2)
$O_{(1)}$	5937(2)	-547(5)	8430(2)
$O_{(2)}$	6021(2)	3405(5)	7450(2)
$O_{(3)}$	9463(3)	8717(6)	10889(3)
$N_{(1)}$	7410(2)	5797(6)	10216(2)
$C_{(1)}$	4415(3)	3552(7)	9236(3)
$C_{(2)}$	5597(3)	3804(7)	9323(3)
$C_{(3)}$	6235(3)	5307(7)	10114(3)
$C_{(4)}$	7728(3)	2491(7)	8959(3)
$C_{(5)}$	7929(3)	5218(8)	9325(3)
$C_{(6)}$	8153(3)	5501(7)	11232(3)
$C_{(7)}$	8766(3)	7931(9)	11609(3)
$H_{(3)}$	991(6)	979(16)	1133(5)
$H_{(41)}$	795(4)	146(9)	961(4)
$H_{(42)}$	810(3)	210(7)	832(3)
$H_{(51)}$	866(4)	545(9)	952(3)
$H_{(52)}$	756(3)	614(8)	872(3)
$H_{(61)}$	869(4)	427(9)	1111(3)
$H_{(62)}$	771(3)	507(7)	1174(3)
$H_{(71)}$	817(4)	920(9)	1161(3)
$H_{(72)}$	916(3)	751(8)	1224(3)

EXPERIMENTAL

The IR spectra were recorded on a Specord 75 IR spectrometer in thin films with KBr. The NMR spectra were described on a JEOL FX 90Q instrument. Mass spectra were taken on a LKB 2091 spectrometer, electron ionizing energy 14 eV, 70 eV.

X-ray Structural Investigation. Crystals of compound (III) were monoclinic, at −80°C a = 11.863(2) Å, b = 5.265(3) Å, c = 13.187(4) Å, β = 100.48(2)°, V = 809.9(9) Å^3, d_{calc} = 1.691 g/cm^3, space group $P2_1/n$, Z = 2, the molecules of (III) were located at the crystallographic centers of symmetry. Unit cell parameters and the intensity of 2263 independent reflections were measured on a Syntex $P2_1$ four-circle automatic diffractometer (λMoKα, β filter, $\theta/2\theta$ scanning to θ_{max} = 27°). The structure was solved by the direct method showing all the nonhydrogen atoms, and was refined by the full matrix least squares method in the anisotropic approach for the nonhydrogen atoms using 1345 reflections with $I > 3\sigma(I)$. All the hydrogen atoms were substantially revealed by difference syntheses and refined isotropically. The final value for the divergence factor R = 0.049 (R_w = 0.049). All calculations were carried out with the SHELXTL PLUS program (PC version) [6]. The coordinates of atoms are given in Table 2.

5,10-Difluoro-4,9-bis(2-hydroxyethyl)-1,2,3,4,6,7,8,9-octahydrobenzo[1,2-b; 5,4-b]di-1,4-thiazine 1,1,6,6-Tetraoxide (III). 2-Aminoethanol (10 mmole) in DMF (5 ml) was added to a solution of compound (I) (3.6 mmole) in DMF (15 ml) at 50°C, and the mixture was stirred for 5 h at 50-55°C. The solvent was removed under reduced pressure, the residual mass poured into ether, and washed with ether. The yellow powder was recrystallized from ethanol. Compound (III) (1.35 g: 90%) of mp 300°C (ethanol) was obtained. IR spectrum: 1120, 1325 cm^{-1} (νSO_2). PMR spectrum (DMF-D_6): 3.49-3.88 ppm coalesced m ($NCH_2CH_2SO_2$, NCH_2CH_2O). ^{13}C NMR spectrum, ppm: 126.47 (C^3), 141.94 (C^2), 143.31 (C^1), 57.47 (C^7), 60.72 (C^4), 50.38 (C^5), 48.76 (C^6) (numbering of the C atoms differs from the IUPAC recommendations and corresponds with those given in Fig. 1). ^{19}F NMR spectrum (CCl_3F) ppm: −126.17 s. Mass spectrum, m/z: 412 $[M]^+$. Found, %: C 40.47; H 4.39; F 9.21; N 6.79; S 15.00. $C_{14}H_{18}F_2N_2O_6S_2$. Calculated, %: C 40.57; H 4.?9; F 9.46; N 6.52; S 14.61.

5,10-Difluoro-4,9-bis(2-hydroxyethyl)-1,2,3,4,6,7,8,9-octahydrobenzo[1,2-b; 5,4-b]di-1,4-thiazine 1,6-Dioxide (IV). This compound was obtained according to the procedure described above. Yield was 0.4 g (30%) of mp 260°C (ethanol). IR spectrum: 1050 cm^{-1} (ν SO). PMR spectrum (DMF-D_6): 3.24-3.70 ppm coalesced m (NCH_2CH_2SO, NCH_2CH_2O). Mass spectrum, m/z: 380 $[M]^+$. Found, %: C 43.61; H 4.69; F 9.94; N 7.05; S 16.21. $C_{14}H_{18}F_2N_2O_4S_2$. Calculated, %: C 44.20; H 4.77; F 9.99; N 7.36; S 16.82.

The work was carried out with the support of the Russian Funds for Fundamental Investigations (Project No. 96-03-33264).

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