JOC Article

Unusual Reaction of 2-(Trifluoromethyl)-1,2-dihydro-3λ^6-thieno-[2,3-*c*]chromen-3,3,4-triones with Hydrazine as a New Route to 3-Hydrazinopyridazine Derivatives

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Oxidation of 2-(trifluoromethyl)-1,2-dihydro-4*H*-thieno[2,3-*c*]chromen-4-ones **2** with H_2O_2 in AcOH gives 2-(trifluoromethyl)-1,2-dihydrothieno[2,3-*c*]chromen-3,3,4-triones **3**, which are transformed into 3-hydrazinopyridazine derivatives **4** in high yields by treatment with hydrazine hydrate in ethanol.

Introduction

Recently[1,2] we have described the reaction of 2-trifluoromethylchromones **1** with ethyl mercaptoacetate in the presence of Et_3N. The reaction turned out to consist of several stages, including the redox stage, and affords dihydrothienocoumarins **2**, which can be considered as useful intermediates for constructing highly functionalized biologically important products. In this work, we report our results of the selective oxidation of sulfides **2** to sulfones **3** and the unusual transformation of sulfones **3** into 3-hydrazinopyridazines **4** under the action of hydrazine hydrate. The latter reaction is undoubtedly of interest since several derivatives of 3-hydrazinopyridazine exhibit different types of biological activity as chemotherapeutics, antiinflammatory agents, CNS depressants and stimulants, and antihypertensives.[3] In particular, prizidilol, a compound combining vasodilator and β-blocker functionalities in the same molecule,[4,5] has been synthesized from 3-hydrazino-6-(2-hydroxyphenyl)-pyridazine, epichlorohydrin, and *tert*-butylamine.[6a,b] In addition, 3-hydrazinopyridazines are widely used in the synthesis of triazolo- and tetrazolopyridazines, which also show interesting pharmaceutical activity and are potential medicinal agents.[7−12]

Results and Discussion

We found that dihydrothienocoumarins **2a**−**f**[1] obtained from ethyl mercaptoacetate and 2-trifluoromethylchromones **1a**−**f** were smoothly oxidized by treatment with H_2O_2 in glacial acetic acid at 100 °C for 2 h and give sulfones **3a**−**f** in 48−83% yields. Nitro derivative **3g** was prepared in 94% yield by the nitration of sulfone **3a** with the nitrating mixture at ∼20 °C for 10 min. The reduction of **3g** with $SnCl_2$ in boiling ethanol gave aminosulfone **3h** in 66% yield (Scheme 1).

Compounds **3** are poorly soluble in alcohol but heating their alcoholic suspension with a 5-fold excess of hydrazine hydrate results in the exothermic reaction during which the solution first becomes homogeneous and a crystalline product immediately precipitates from it. As a rule, 1−2 min of boiling is enough to complete the reaction. On the basis of the data of elemental analysis, IR, NMR, and ^1H and ^{13}C spectroscopy, we established that the reaction products of sulfones **3** with hydrazine are 3-hydrazinopyridazine derivatives **4** (Scheme 2), whose structure was further confirmed by the X-ray diffraction study of crystals of the salt of pyridazine **4b** with $HClO_4$ (cation **5b**, see below).

This unexpected reaction occurs very readily and purely affords in high yields (47−74%) pyridazines **4a**−**c**,**f**−**h** with both electron-donating (Me, MeO, NH_2) and electron-withdrawing (NO_2) groups. However, sulfones **3d**,**e** bearing a substituent in the 9-position did not form the corresponding pyridazines, which can be attributed to repulsive steric interactions between the peri-substituent and the N_2H_4 molecule at the stage of nucleophilic addition of N_2H_4 at the C=C bond of the α-pyrone ring. Note that 4,4,4-trihalo-3-hydroxy-1-(2-hydroxyaryl)bu-

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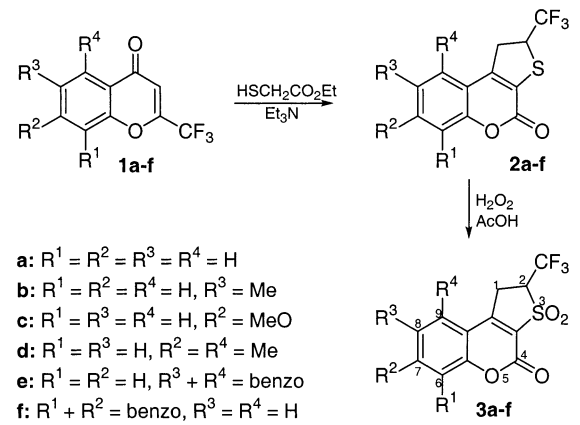
SCHEME 1



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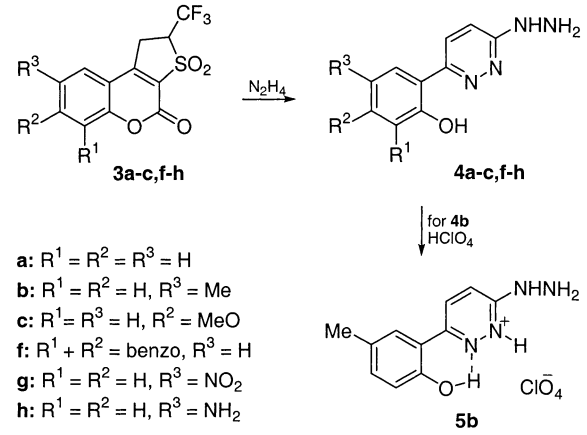

tan-1-ones obtained by reaction of the appropriate 2-hydroxyacetophenones with chloral or bromal react with hydrazine at elevated temperatures to give 6-(2-hydroxyaryl)-3-pyridazinones in good yields.[6c]

The reaction of N_2H_4 with sulfone **3g** is very helpful in revealing the mechanism of the transformation **3** → **4**. Under standard conditions, this reaction gave a mixture of pyridazine **4g** with an unknown product in a ratio of 3:1, respectively. Since the minor product could be one of the intermediates of the transformation we are interested in, the reaction was studied in more detail. It turned out that if the heating time was increased from 2 to 15 min, pure hydrazinopyridazine **4g** was formed in 73% yield, while if the reaction is conducted at 0 °C for 20 min, the treatment of the homogeneous solution with dilute AcOH resulted in the starting sulfone **3g** containing 9% of the same unknown admixture. However, when the reaction temperature was increased to 20 °C, after 30 min the individual substance of molecular formula $C_{12}H_{15}N_7O_6S$ was isolated from the reaction mixture, which decomposes on heating above 200 °C to evolve SO_2 and has an ^{1}H NMR spectrum identical with that of the

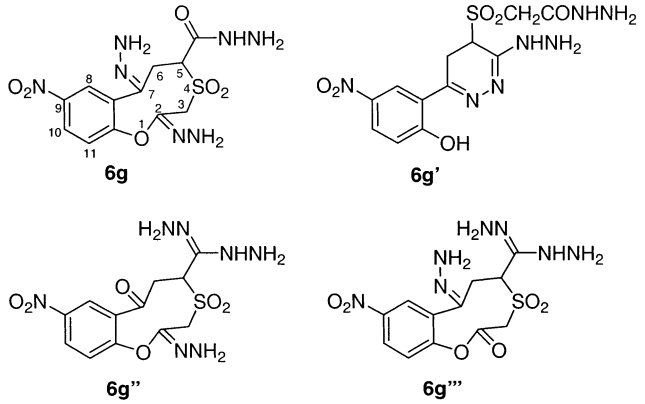

FIGURE 1.

minor component of the mixture obtained in the first experiment. When this compound, the molecular formula of which corresponds to the addition of 3 molecules of N_2H_4 to sulfone **3g** with elimination of 3 molecules of HF, was boiled in alcohol in the presence of hydrazine hydrate or ammonia, pyridazine **4g** was formed, which finally proves its intermediacy. As expected, the reaction did not occur without a base additive.

Since crystals of the isolated intermediate were inappropriate for X-ray diffraction study, its structure was established from the data of IR and ^{1}H and ^{13}C NMR spectra. The IR spectrum of the intermediate contains no absorption bands of the ketone or ester carbonyl group (1670−1740 cm^{-1}) but exhibits several bands in the regions of 1520−1660 ($\nu_{C=N}$, δ_{NH}, amide-I) and 3090−3400 cm^{-1} (ν_{NH}).[13] The ^{1}H NMR spectrum in DMSO-d_6 exhibits signals from 3 aromatic protons (δ 7.7−8.3 ppm) and from 5 aliphatic protons of two CH_2 and one CH groups forming AMX and AB spin systems in a region of 2.8−4.8 ppm. One of the CH_2 groups is in a weak field (4.18 ppm), which indicates that it is adjacent to two electron-withdrawing groups as, for example, in the diketo form of β-diketones.[14] In addition, the spectrum contains signals from 7 mobile protons, which appear as 3 two-proton (4.5, 6.7, and 7.3 ppm) and 1 one-proton (9.6 ppm) singlets and disappear when CD_3CO_2D is added. On the basis of these data, we can propose two alternative structures for the intermediate in the reaction of **3g** with N_2H_4: benzocyclononene **6g** (closer in structure to initial sulfone **3g**) and dihydropyridazine **6g′** (closer in structure to product **4g**), among which we prefer the first one (Figure 1).

The following facts favor structure **6g**. First, the chemical shifts of singlets from NH and NH_2 protons, which are in the composition of the hydrazino (−$NHNH_2$) and hydrazono (=NNH_2) groups, agree well only with structure **6g**: the downfield one-proton and upfield two-proton signals correspond to the $CONHNH_2$ group, and 2 two-proton peaks at 6.7 and 7.3 ppm correspond to two hydrazono groups. Structure **6g′** contains only two hydrazino groups, whose NH_2 protons are usually more shielded, and the NH protons, as well as phenolic hydroxyl, in a solution of DMSO-d_6 should appear in a

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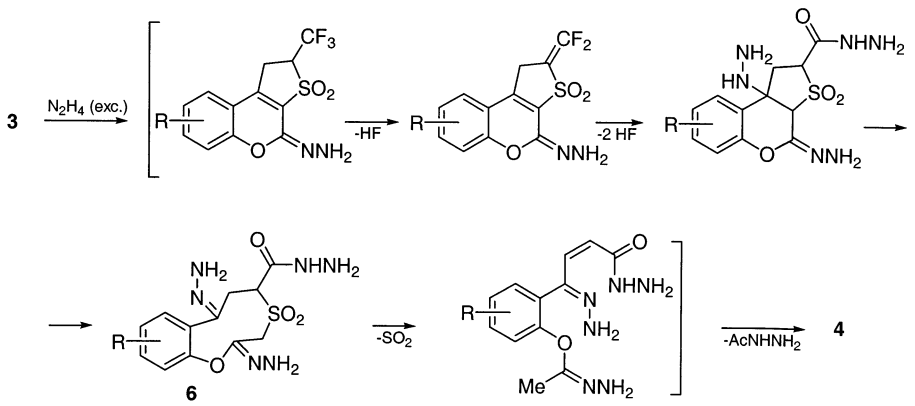
SCHEME 3



lower field (~8−10 ppm). Second, the aromatic proton in the ortho position to oxygen is manifested in initial sulfone **3g** at 7.81 ppm, in the intermediate it appears at 7.69 ppm, and in product **4g**, in which the oxygen atom is not involved in cycle formation, the aromatic proton appears at 7.10 ppm. Since the considered proton in the intermediate is deshielded by 0.6 ppm compared to the similar proton in pyridazine **4g**, we may conclude that the oxygen atom is in the composition of the cycle and, hence, the intermediate has structure **6g** rather than **6g′**. Structures **6g″** and **6g‴**, which differ from **6g** only by the localization of the carbonyl oxygen atom, were rejected on the basis of the data of IR and ^{13}C NMR spectra (Figure 1).

Probably, the fragment of molecule **6g**, which is fused with the benzene ring, is close to the planar conformation, and the C(3), S(4), C(5), and C(6) atoms take the chairlike conformation in which the hydrazide group occupied the equatorial position. The axial methine proton H(5) (X part of the AMX spin system) is split on the axial and equatorial protons of the C(6)H_2 group (AM part of the AMX spin system) with $J_{XA} = 12.5$ Hz and $J_{XM} = 5.0$ Hz, respectively, the equatorial C(6)H*H* proton (δ = 3.61 ppm) forms a doublet of doublets with $J_{MA} = 14.2$ Hz and J_{MX} = 5.0 Hz, and the axial C(6)H*H* proton (δ = 2.79 ppm) appears as a triplet with J = 13.4 Hz due to the close values of the vicinal ($J_{AX} = 12.5$ Hz) and geminal ($J_{AM} = 14.2$ Hz) constants. Since the molecule contains the chiral center, the protons of the C(3)H_2 group are diastereotopic and form the AB system with $J_{AB} = 14.3$ Hz. Note that the indicated values of spin−spin coupling constants in **6g** agree well with the values of vicinal and geminal constants in cyclohexane.[15]

The ^{13}C NMR spectrum recorded for a solution of the intermediate in DMSO-d_6 without ^{1}H decoupling contains a triplet of doublets, a triplet, and a doublet of doublets of doublets in the region of aliphatic carbon atoms, which makes it possible to assign unambiguously these signals to the C(6), C(3), and C(5) atoms, respectively. Three most downfield signals belong to the C=O, C(11a), and C(9) atoms, which is confirmed by the character of its splitting. The protonated C(11), C(10), and C(8) atoms are at 121.9−123.4 ppm, and the quaternary C(7a), C(7), and C(2) atoms lie in a region of 129.2−134.5 ppm. Note that the signal at 133.9 ppm looks like a noncompletely resolved triplet of doublets of doublets, which allows it to be presumably assigned to the C(7) atom. Thus, analysis of the ^{1}H and ^{13}C NMR spectra of the intermediate favors structure **6g**, which, in turn, suggests the possible mechanism of formation of pyridazines **4** from sulfones **3** (Scheme 3).

We believe that the reaction is started from the attack of the keto group of sulfone **3** by the hydrazine molecule. This interaction through the addition−elimination stages leads to the replacement of the carbonyl oxygen atom of the ester group, by the hydrazono group. At first sight, this transformation seems quite unexpected; however, this is directly confirmed in the literature. Bakre and Merchant[16] showed for several examples that the reaction of hydrazine hydrate with coumarin derivatives bearing the heterocyclic ring in 3- and 4-positions of the coumarin system proceeds at the keto group and leads to the corresponding hydrazones. The subsequent hydrazinolysis and hydrolysis of the CF_3 group to the $CONHNH_2$ moiety as the E−A process, addition to the activated double bond of the hydrazine molecule, and opening of the bond common for the bicycle lead to the formation of the benzocyclononene intermediate **6**, which was isolated in the case of sulfone **3g**. The further transformation of this intermediate is accompanied by the elimination of SO_2 to form the hydrazine derivative of β-aroylacrylic acid, which undergoes intramolecular cyclization and gives 3-hydrazinopyridazines **4** (Scheme 3). The capability of the fluorine atoms of the CF_3 group of substituting under the action of ammonia and primary and secondary amines has previously been observed for α-trifluoromethyl-α-fluoro-2-hydroxyacetophenone[17] and for the reaction of 2- and 4(5)-trifluoromethylimidazoles[18,19] with a 5% solution of NH_4OH. The latter lead through difluorodiazafulvenes to 2- and 4(5)-cyanoimidazoles.

X-ray Diffraction Study of Perchlorate 5b. Structure **5b** consists of the flattened cation and anions associated by hydrogen bonds (Figure 2). In the $[C_{11}H_{13}N_4O]^+$ cation, the angle between the planes of the aromatic cycles is 8.4°, and the hydrazine group is coplanar to the plane of the pyridazine cycle. Flattening of the cation is favored by the formation of the intramolecular O(1)−H(1O)···N(1) hydrogen bond with

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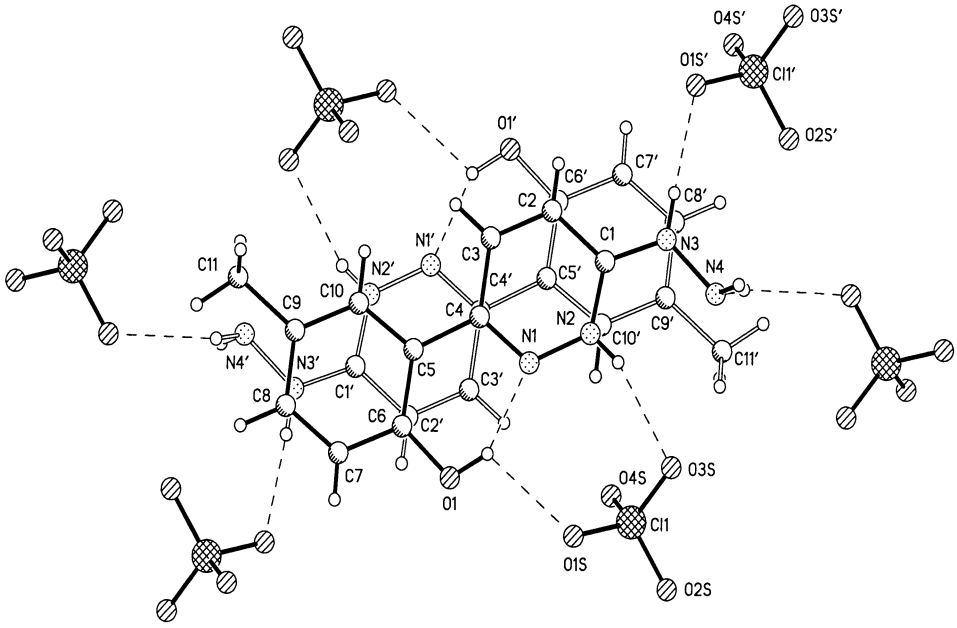

FIGURE 2. General view of the dimer of **5b** in the projection along the *b* axis. The labeling scheme of non-hydrogen atoms, dimer cations, and some anions is shown. Hydrogen bonds in the crystal are presented by dotted lines.

the following parameters: H···N 1.88(4) Å, O−H 0.88(3) Å, O···N 2.653(2) Å, and O(1)−H(1O)···N(1) 146(3)°. According to the published data,[20] the interatomic distances for the O−H···N hydrogen bonds in analogous fragments vary in the following characteristic ranges: O···N 2.471−2.668 Å (average 2.586 Å) and H···N 1.354−2.090 Å (average 1.732 Å). Therefore, the O−H···N hydrogen bond can be considered as relatively weak (for further discussion see the Supporting Information).

In conclusion, the reaction described above has wide applicability and represents a new route to synthesize 3-hydrazinopyridazines with 2-hydroxyaryl substituents. Our approach makes it possible to obtain these compounds from 2-hydroxyacetophenones and ethyl trifluoroacetate (starting substances for the synthesis of 2-trifluoromethylchromones[21]) in four stages, whereas the method for synthesis of similar pyridazines described in the patent literature[6a] consists of seven stages and starts from phenols and succinic anhydride via 6-(2-hydroxyaryl)-3-pyridazinones.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively; chemical shifts are given in δ ppm downfield from tetramethylsilane as internal standard. IR spectra were measured in Nujol. Elemental analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Urals Branch of the Russian Academy of Sciences. Melting points are uncorrected. The starting dihydrothienocoumarins **2a**−**f** were prepared by reaction of the appropriate 2-trifluoromethylchromone **1a**−**f**[21] and ethyl mercaptoacetate according to the procedure described.[1]

Crystallographic Data for 5b ($C_{11}H_{13}N_4O\cdot ClO_4$). The crystal system is monoclinic at 140 K; a = 25.369(3) Å, b = 12.5402(15) Å, c = 8.5014(11) Å, β = 104.312(3)°, V = 2620.6(5) Å^3, d_{calc} = 1.605 g cm^{-3}, μ = 0.322 mm^{-1}, space group *C*2/*c*, *Z* = 8. The intensities of 3817 independent reflections (R_{int} = 0.04) were measured on a Bruker SMART 1K CCD diffractometer, λ(Mo Kα) = 0.71073 Å, graphite monochromator, ω scans (scan step in ω 0.3°, exposition time of the frame 30 s), $2\theta_{max}$ = 60°, data completeness 99%. The intensities of all reflections were obtained by the use of the SAINT Plus and SADABS program packages (maximum and minimum transmission coefficients 0.977 and 0.715).[22,23] The structure was solved by the direct method using the SHELXTL-97[24] program package. Non-hydrogen atoms were refined by the full-matrix least-squares procedure on F^2 in an anisotropic approximation. The positions of hydrogen atoms were found by a difference Fourier synthesis and refined isotropically. The hydrogen atoms of the Me group were refined by using the riding model with isotropic displacement parameters U_{iso}(H) = 1.5U_{eq}(C), where U_{eq}(C) were equivalent isotropic displacement parameters of corresponding C atoms. The final discrepancy factors were as follows: R_1 = 0.059 (based on F for 2213 reflections with $I > 2\sigma(I)$), wR_2 = 0.150 (calculated based on F^2 for all 3817 reflections, used at the final stage of the refinement); the total number of the parameters in the refinement was 230, GOOF = 0.882.

General Procedure for the Synthesis of Sulfones 3a−f. A mixture of dihydrothienocoumarin **2** (0.022 mol), 33% H_2O_2 (18 mL), and AcOH (60 mL) was heated on a water bath for 2 h and then cooled to room temperature. The crystalline product that precipitated was filtered off, washed with aqueous acetic acid (1:1), and dried.

2-(Trifluoromethyl)-1,2-dihydro-3λ^6-thieno[2,3-*c*]-chromen-3,3,4-trione (3a): yield 64%; mp 244−246 °C; ^{1}H NMR (DMSO-d_6) δ 3.87 (dd, 1H, J = 19.0, 5.9 Hz), 4.11 (dd, 1H, J = 19.0, 9.1 Hz), 5.23−5.33 (m, 1H), 7.55 (ddd, 1H, J = 7.9, 7.4, 0.9 Hz), 7.59 (dd, 1H, J = 8.5, 0.9 Hz), 7.88 (ddd, 1H, J = 8.5, 7.4, 1.5 Hz), 8.05 (dd, 1H, J = 7.9, 1.5 Hz); IR (Nujol) 1745 (C=O), 1630, 1615, 1570 cm^{-1}. Anal. Calcd for $C_{12}H_7F_3O_4S$: C, 47.37; H, 2.32. Found: C, 47.53; H, 2.10.

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8-Methyl-2-(trifluoromethyl)-1,2-dihydro-3λ⁶-thieno-[2,3-*c*]chromen-3,3,4-trione (3b): yield 83%; mp 282−283 °C; ^{1}H NMR (DMSO-d_6/CCl_4) δ 2.46 (s, 3H), 3.70 (dd, 1H, J = 18.9, 5.7 Hz), 4.04 (dd, 1H, J = 18.9, 9.2 Hz), 5.07−5.17 (m, 1H), 7.41 (d, 1H, J = 8.5 Hz), 7.64 (ddq, 1H, J = 8.5, 2.1, 0.5 Hz), 7.82 (br d, 1H, J = 1.7 Hz); IR (Nujol) 1735 (C=O), 1630, 1580 cm^{-1}. Anal. Calcd for $C_{13}H_9F_3O_4S$: C, 49.06; H, 2.85. Found: C, 49.02; H, 2.80.

7-Methoxy-2-(trifluoromethyl)-1,2-dihydro-3λ⁶-thieno-[2,3-*c*]chromen-3,3,4-trione (3c): yield 77%; mp 246−247 °C; ^{1}H NMR (DMSO-d_6/CCl_4) δ 3.66 (dd, 1H, J = 18.8, 5.9 Hz), 3.94 (s, 3H), 4.01 (dd, 1H, J = 18.8, 9.2 Hz), 5.00−5.10 (m, 1H), 7.05 (dd, 1H, J = 8.9, 2.4 Hz), 7.11 (d, 1H, J = 2.4 Hz), 7.90 (d, 1H, J = 8.9 Hz); IR (Nujol) 1730 (C=O), 1615, 1560 cm^{-1}. Anal. Calcd for $C_{13}H_9F_3O_5S$: C, 46.71; H, 2.71. Found: C, 46.97; H, 2.68.

General Procedure for the Synthesis of 3-Hydrazinopyridazines 4a−c,f−h. Hydrazine hydrate (30%, 10 mL) was added to a suspension of sulfone **3** (4.7 mmol) in boiling ethanol (20 mL). The mixture was boiled for 1−2 min in the case of **3a**−**c**,**h** and for 15 min in the case of **3f**,**g**. In most cases, pyridazine **4** is crystallized almost immediately after the initial sulfone **3** was dissolved in the reaction mixture. Then the mixture was cooled to room temperature, and the product was filtered off, washed with ethanol, and dried. In the case of **3h**, the reaction mixture, before the isolation of pyridazine **4h**, was diluted with 40% ethanol (25 mL).

2-(6-Hydrazinopyridazin-3-yl)phenol monohydrate (4a): yield 72% as colorless needles from ethanol; mp 184−186 °C; ^{1}H NMR (DMSO-d_6/CCl_4) δ 4.35 (br s, 2H), 6.83−6.88 (m, 2H), 7.19 (ddd, 1H, J = 8.4, 7.4, 1.5 Hz), 7.24 (d, 1H, J = 9.6 Hz), 7.73 (br d, 1H, J = 7.9 Hz), 8.04 (d, 1H, J = 9.6 Hz), 8.21 (br s, 1H), 13.71 (br s, 1H); IR (Nujol) 3350, 3180−3300, 1645, 1610, 1590 cm^{-1}. Anal. Calcd for $C_{10}H_{10}N_4O\cdot H_2O$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.37; H, 5.25; N, 25.61.

2-(6-Hydrazinopyridazin-3-yl)-5-methoxyphenol monohydrate (4c): yield 67% as colorless crystals; mp 206−207 °C; ^{1}H NMR (DMSO-d_6/CCl_4) δ 3.78 (s, 3H), 4.24 (br s, 2H), 6.40 (d, 1H, J = 2.6 Hz), 6.43 (dd, 1H, J = 8.6, 2.6 Hz), 7.20 (d, 1H, J = 9.7 Hz), 7.63 (d, 1H, J = 8.6 Hz), 7.95 (d, 1H, J = 9.7 Hz), 8.06 (br s, 1H), 14.06 (br s, 1H); IR (Nujol) 3420, 3210−3360, 1620, 1590, 1575 cm^{-1}. Anal. Calcd for $C_{11}H_{12}N_4O_2\cdot H_2O$: C, 52.79; H, 5.64; N, 22.39. Found: C, 52.41; H, 5.47; N, 22.31.

2-(6-Hydrazinopyridazin-3-yl)-1-naphthol (4f): yield 61% as a colorless crystals; mp 222−223 °C dec; ^{1}H NMR (DMSO-d_6) δ 4.46 (s, 2H), 7.32 (d, 1H, J = 9.7 Hz), 7.44 (d, 1H, J = 8.8 Hz), 7.50−7.56 (m, 2H), 7.86 (d, 1H, J = 7.3 Hz), 7.95 (d, 1H, J = 8.8 Hz), 8.31 (d, 1H, J = 9.7 Hz), 8.32 (d, 1H, J = 7.3 Hz), 8.38 (s, 1H), 15.6 (br s, 1H); IR (Nujol) 3300, 3125, 1640, 1585, 1520 cm^{-1}. Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.66; H, 4.79; N, 22.21. Found: C, 66.81; H, 4.84; N, 22.20.

2-(6-Hydrazinopyridazin-3-yl)-4-nitrophenol (4g): yield 73% as a colorless crystals; mp 280−282 °C dec; ^{1}H NMR (DMSO-d_6) δ 4.60 (br s, 2H), 7.10 (d, 1H, J = 9.1 Hz), 7.30 (d, 1H, J = 9.6 Hz), 8.14 (dd, 1H, J = 9.1, 2.8 Hz), 8.35 (d, 1H, J = 9.6 Hz), 8.57 (br s, 1H), 8.71 (d, 1H, J = 2.8 Hz), 15.1 (br s, 1H); IR (Nujol) 3370, 3240, 1640, 1620, 1590 cm^{-1}. Anal. Calcd for $C_{10}H_9N_5O_3$: C, 48.59; H, 3.67; N, 28.33. Found: C, 48.54; H, 3.58; N, 28.25.

4-Amino-2-(6-hydrazinopyridazin-3-yl)phenol (4h): yield 47% as yellow crystals; mp 221−222 °C; ^{1}H NMR (DMSO-d_6) δ 4.40 (br s, 2H), 4.54 (br s, 2H), 6.58 (dd, 1H, J = 8.5, 2.5 Hz), 6.67 (d, 1H, J = 8.5 Hz), 7.01 (d, 1H, J = 2.5 Hz), 7.24 (d, 1H, J = 9.6 Hz), 7.91 (d, 1H, J = 9.6 Hz), 8.24 (s, 1H), 12.56 (s, 1H); IR (Nujol) 3450, 3370, 3350, 3210−3270, 1650, 1620, 1600, 1570, 1515 cm^{-1}. Anal. Calcd for $C_{10}H_{11}N_5O$: C, 55.29; H, 5.10; N, 32.24. Found: C, 55.30; H, 5.14; N, 32.36.

2,7-Dihydrazono-9-nitro-4,4-dioxo-4,5,6,7-tetrahydro-1,4-benzoxathionin-5(3*H*)-carbohydrazide (6g). Aqueous 30% $N_2H_4\cdot H_2O$ (2 mL) was added to a suspension of nitrosulfone **4g** (0.50 g, 1.4 mmol) in 6 mL of ethanol cooled to 0 °C. The obtained mixture was stirred at ∼20 °C for 30 min, and the product that formed was filtered off then washed with aqueous ethanol (1:1), ethanol, and chloroform to give compound **6g** (0.40 g, 73%) as colorless powder: mp 200−202 °C dec. ^{1}H NMR (DMSO-d_6) δ 2.79 (t, 1H, J = 13.4 Hz), 3.61 (dd, 1H, J = 14.2, 5.0 Hz), 4.18 (AB-system, 2H, $\Delta\delta$ = 0.10, J = 14.3 Hz), 4.51 (br s, 2H), 4.78 (dd, 1H, J = 12.5, 5.0 Hz), 6.72 (s, 2H), 7.28 (s, 2H), 7.69 (d, 1H, J = 9.0 Hz), 8.14 (dd, 1H, J = 9.0, 2.9 Hz), 8.31 (d, 1H, J = 2.9 Hz), 9.57 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 22.46 (td, C,[6] ^1J = 134.3, ^2J = 3.9 Hz), 54.88 (t, C,[3] ^1J = 139.5 Hz), 61.36 (ddd, C,[5] ^1J = 145.5, ^2J = 6.4, ^2J = 3.7 Hz), 121.91 (d, C,[11] ^1J = 168.4 Hz), 122.92 (dd, C[8] or C,[10] ^1J = 169.6, ^3J = 4.6 Hz), 123.39 (dd, C[10] or C,[8] ^1J = 171.1, ^3J = 5.4 Hz), 129.23 (br s, C[7a]), 133.89 (tdd, C,[7] $^3J \sim 7.2$, $^2J \sim 4.0$, $^2J \sim 2.0$ Hz), 134.45 (br s, C[2]), 143.36 (dt, C,[9] ^3J = 10.3, ^2J = 3.6 Hz), 157.13 (ddd, C,[11a] ^3J = 10.3, ^3J = 8.7, ^2J = 3.6 Hz), 160.25 (q, C=O, $^2J \sim {}^3J \sim 4.0$ Hz); IR (Nujol) 3400, 3360, 3225, 3090 (NH, NH_2), 1660 (C=O), 1615, 1600, 1585, 1560, 1520 cm^{-1}. Anal. Calcd for $C_{12}H_{15}N_7O_6S$: C, 37.40; H, 3.92; N, 25.44. Found: C, 37.32; H, 3.91; N, 25.41.

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Supporting Information Available: ^{1}H NMR spectra for compounds **3a**, **3g**, **3h**, **4a**, **4b**, **4g**, **4h**, **6g**, and a mixture of **4g** + **6g**; ^{13}C NMR spectra for compound **6g** (decoupling, coupling); complete listing of IR and ^{1}H NMR peaks and elemental analyses of compounds **3d**−**h**, **4b**, and **5b** and ^{13}C NMR peaks for **4b**; and a discussion and X-ray data for compound **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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