Chemistry of Heterocyclic Compounds, Vol. 34, No. 10, 1998

STRUCTURAL INVESTIGATIONS IN THE SERIES OF SPIRO(THIA)CHROMANS

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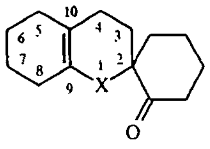
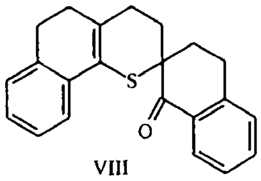
A comparative assessment was made of the reactivity of carbonyl-containing spirohydrochromans in their reaction with hydrogen sulfide under the conditions of acid catalysis. The special features of the structure of one of the obtained condensed spiro(thia)chromans are examined on the basis of the results from x-ray crystallographic analysis, the ^{13}C NMR spectra, and quantum-chemical calculations.

In the reaction of carbonyl-containing spirohydrochromans containing cyclohexane (I) or tetrahydronaphthalene (II) residues at position 2 of the heterocycle with hydrogen sulfide and acids, certain special features due to the specific nature of the structure of these compounds are observed [1, 2].

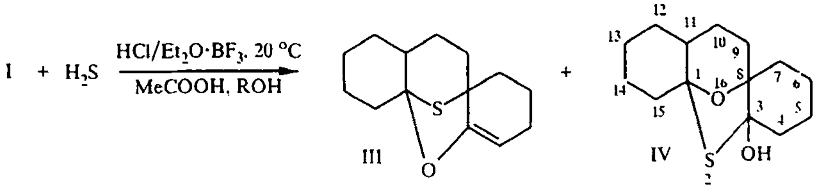


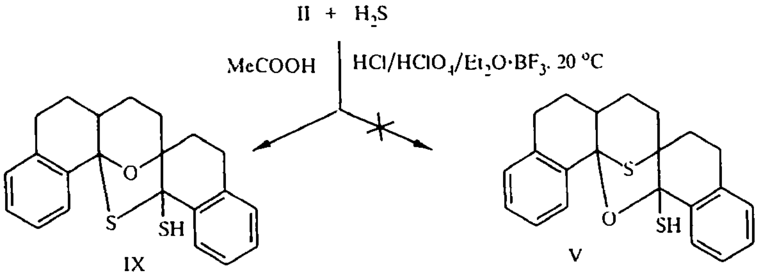
I, II, VII

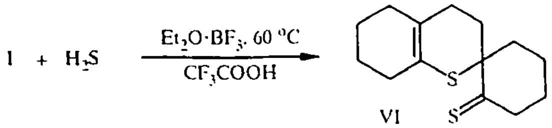
I, II X = O; VII X = S



VIII







The action of hydrogen sulfide and mineral acids or boron trifluoride etherate on the spiro compound (I) at room temperature may be accompanied both by opening of the dihydrochroman ring with the formation of 2-oxa-16-thiatetracyclo-$[7.6.1.0^{3,8}.0^{1,11}]$hexadec-3-ene (III), and by nucleophilic attack by the hydrogen sulfide at the carbonyl group followed by heterocyclization to 16-oxa-2-thiatetracyclo$[7.6.1.0^{3,8}.0^{1,11}]$hexadecan-3-ol (IV) [2]. From compound (II) under analogous conditions the product (V), for which the structure of 2-oxa-16-thia-4,5:14,15-dibenzotetracyclo$[7.6.1.0^{3,8}.0^{1,11}]$hexadecane-3-thiol was proposed [1], is obtained.

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0009-3122/98/3410-1137$20.00

TABLE 1. ^{13}C NMR Spectra of Compounds (II, III-V, VIII) (δ, ppm)

Compound	Chemical shifts, δ, ppm									
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$
II	–	77,08	32,71	23,07	25,55	27,91	–	–	142,94	107,09
III	97,64	–	139,45	112,72	25,00	25,34	25,84	47,97	34,04	25,15
IV	98,95	–	84,98	34,54	23,26	25,27	33,12	82,89	34,25	24,62
V	96,65	–	84,14	–	–	28,30	26,61	67,40	35,12	24,19
VIII	–	50,72	34,72	27,94	25,37	27,97	–	–	130,18	119,57

Compound	$C_{(11)}$	$C_{(12)}$	$C_{(13)}$	$C_{(14)}$	$C_{(15)}$	$C_{(2')}$	$C_{(3')}$	$C_{(4')}$	$C_{(5')}$	$C_{(6')}$
II	–	–	–	–	–	191,36	–	–	27,39	26,36
III	42,35	37,62	20,81	25,27	30,05	–	–	–	–	–
IV	43,51	38,46	18,27	25,34	30,66	–	–	–	–	–
V	40,90	25,12	30,13	–	–	–	–	–	–	–

TABLE 2. Bond Lengths (d) and Bond Angles (ω) for the Molecule of (V)

Bond	d, Å	Angle	ω, deg
$S_{(1)}-C_{(21)}$	1,805(9)	$C_{(21)}-S_{(1)}-C_{(20)}$	91,9(4)
$S_{(1)}-C_{(20)}$	1,867(9)	$C_{(20)}-O-C_{(8)}$	107,8(6)
$S_{(2)}-C_{(21)}$	1,841(8)	$C_{(2)}-C_{(1)}-C_{(22)}$	120,0(10)
$O-C_{(20)}$	1,427(10)	$C_{(3)}-C_{(2)}-C_{(1)}$	120,7(10)
$O-C_{(8)}$	1,442(9)	$C_{(2)}-C_{(3)}-C_{(4)}$	120,3(11)
$C_{(1)}-C_{(2)}$	1,380(2)	$C_{(5)}-C_{(4)}-C_{(3)}$	121,9(11)
$C_{(1)}-C_{(22)}$	1,408(13)	$C_{(4)}-C_{(5)}-C_{(22)}$	117,5(10)
$C_{(2)}-C_{(3)}$	1,340(2)	$C_{(4)}-C_{(5)}-C_{(6)}$	121,6(12)
$C_{(3)}-C_{(4)}$	1,400(2)	$C_{(22)}-C_{(5)}-C_{(6)}$	120,8(11)
$C_{(4)}-C_{(5)}$	1,380(2)	$C_{(5)}-C_{(6)}-C_{(7)}$	112,9(10)
$C_{(5)}-C_{(22)}$	1,419(14)	$C_{(6)}-C_{(7)}-C_{(8)}$	111,8(8)
$C_{(5)}-C_{(6)}$	1,468(14)	$O-C_{(8)}-C_{(9)}$	109,0(7)
$C_{(6)}-C_{(7)}$	1,520(2)	$O-C_{(8)}-C_{(7)}$	107,7(7)
$C_{(7)}-C_{(8)}$	1,518(13)	$C_{(9)}-C_{(8)}-C_{(7)}$	109,5(8)
$C_{(8)}-C_{(9)}$	1,524(13)	$O-C_{(8)}-C_{(21)}$	103,4(7)
$C_{(8)}-C_{(21)}$	1,561(12)	$C_{(9)}-C_{(8)}-C_{(21)}$	115,1(8)
$C_{(9)}-C_{(10)}$	1,550(2)	$C_{(7)}-C_{(8)}-C_{(21)}$	111,6(8)
$C_{(10)}-C_{(11)}$	1,532(13)	$C_{(8)}-C_{(9)}-C_{(10)}$	113,7(7)
$C_{(11)}-C_{(20)}$	1,516(11)	$C_{(11)}-C_{(10)}-C_{(9)}$	110,1(8)
$C_{(11)}-C_{(12)}$	1,535(14)	$C_{(20)}-C_{(11)}-C_{(10)}$	109,6(7)
$C_{(12)}-C_{(13)}$	1,487(13)	$C_{(20)}-C_{(11)}-C_{(12)}$	109,0(8)
$C_{(13)}-C_{(14)}$	1,530(2)	$C_{(10)}-C_{(11)}-C_{(12)}$	113,8(8)
$C_{(14)}-C_{(19)}$	1,387(12)	$C_{(13)}-C_{(12)}-C_{(11)}$	112,2(8)
$C_{(14)}-C_{(15)}$	1,402(13)	$C_{(12)}-C_{(13)}-C_{(14)}$	112,9(8)
$C_{(15)}-C_{(16)}$	1,410(2)	$C_{(19)}-C_{(14)}-C_{(15)}$	118,3(9)
$C_{(16)}-C_{(17)}$	1,341(13)	$C_{(19)}-C_{(14)}-C_{(13)}$	123,1(9)
$C_{(17)}-C_{(18)}$	1,367(11)	$C_{(15)}-C_{(14)}-C_{(13)}$	118,6(9)
$C_{(18)}-C_{(19)}$	1,398(13)	$C_{(14)}-C_{(15)}-C_{(16)}$	120,4(8)
$C_{(19)}-C_{(20)}$	1,507(11)	$C_{(17)}-C_{(16)}-C_{(15)}$	118,5(10)
$C_{(21)}-C_{(22)}$	1,540(13)	$C_{(16)}-C_{(17)}-C_{(18)}$	122,8(9)
		$C_{(17)}-C_{(18)}-C_{(19)}$	119,3(8)
		$C_{(14)}-C_{(19)}-C_{(18)}$	120,4(8)
		$C_{(14)}-C_{(19)}-C_{(20)}$	120,2(9)
		$C_{(18)}-C_{(19)}-C_{(20)}$	119,4(8)
		$O-C_{(20)}-C_{(19)}$	108,2(7)
		$O-C_{(20)}-C_{(11)}$	111,3(7)
		$C_{(19)}-C_{(20)}-C_{(11)}$	112,4(7)
		$O-C_{(20)}-S_{(1)}$	103,1(5)
		$C_{(19)}-C_{(20)}-S_{(1)}$	110,3(6)
		$C_{(11)}-C_{(20)}-S_{(1)}$	111,1(6)
		$C_{(22)}-C_{(21)}-C_{(8)}$	112,7(8)
		$C_{(22)}-C_{(21)}-S_{(1)}$	109,3(6)
		$C_{(8)}-C_{(21)}-S_{(1)}$	105,0(5)
		$C_{(22)}-C_{(21)}-S_{(2)}$	106,5(6)
		$C_{(8)}-C_{(21)}-S_{(2)}$	111,5(6)
		$S_{(1)}-C_{(21)}-S_{(2)}$	112,0(5)
		$C_{(1)}-C_{(22)}-C_{(5)}$	119,5(10)
		$C_{(1)}-C_{(22)}-C_{(21)}$	117,3(10)
		$C_{(5)}-C_{(22)}-C_{(21)}$	123,2(9)

While continuing systematic research into the reactivity of condensed spirohydrochromans, we found that the use of trifluoroacetic acid and increase in temperature promoted recyclization of the spiran (I) and nucleophilic substitution of its C=O group under the influence of hydrogen sulfide. Thus, at 60°C the reaction of compound (I) with hydrogen sulfide and an aprotic reagent (boron trifluoride etherate), fulfilling the functions of Lewis acid, results in the formation of 3,4,5,6,7,8-hexahydrospiro[thiochromene-2,1′-cyclohexane]-2′-thione (VI) with a yield of 74%. The IR spectrum of the latter does not contain a band for the stretching vibrations of the C=O group (1720 cm^{-1}), which is present in the spectrum of the substrate (I), and absorption bands for the C=S (~1375 cm^{-1}) and C—S—C (~730 cm^{-1}) groups appear.

TABLE 3. Coordinates of the Nonhydrogen Atoms ($\times 10^4$) and Their Equivalent Isotropic Factors ($\times 10^3$) for the Molecule of (V)

Atom	x	y	z	$U_{(eq)}$
$S_{(1)}$	4677(3)	4189(3)	6181(1)	55(1)
$S_{(2)}$	4695(3)	5507(3)	7238(1)	81(1)
O	2925(7)	6568(7)	5887(2)	53(2)
$C_{(1)}$	2232(14)	2790(14)	6962(4)	73(3)
$C_{(2)}$	909(19)	1879(14)	7073(4)	85(4)
$C_{(3)}$	-544(18)	2479(19)	7005(4)	93(4)
$C_{(4)}$	-742(13)	4053(21)	6831(4)	88(4)
$C_{(5)}$	525(13)	5033(14)	6725(3)	69(3)
$C_{(6)}$	308(14)	6682(14)	6540(4)	79(3)
$C_{(7)}$	1762(15)	7734(12)	6618(4)	77(3)
$C_{(8)}$	3241(11)	6965(11)	6403(3)	56(3)
$C_{(9)}$	4603(15)	8161(12)	6425(3)	79(3)
$C_{(10)}$	6110(13)	7584(13)	6147(4)	80(3)
$C_{(11)}$	5668(11)	6877(11)	5635(4)	62(3)
$C_{(12)}$	7024(12)	5975(14)	5377(4)	79(3)
$C_{(13)}$	6601(12)	5450(15)	4861(4)	90(4)
$C_{(14)}$	4909(12)	4817(10)	4822(3)	60(3)
$C_{(15)}$	4447(15)	4031(12)	4381(3)	72(3)
$C_{(16)}$	2865(17)	3522(13)	4316(4)	81(3)
$C_{(17)}$	1862(12)	3667(11)	4703(4)	64(3)
$C_{(18)}$	2271(12)	4397(11)	5143(3)	57(3)
$C_{(19)}$	3815(12)	4959(10)	5207(3)	50(2)
$C_{(20)}$	4274(11)	5747(11)	5694(3)	53(2)
$C_{(21)}$	3581(11)	5295(11)	6649(3)	51(3)
$C_{(22)}$	2060(12)	4369(12)	6779(3)	54(3)

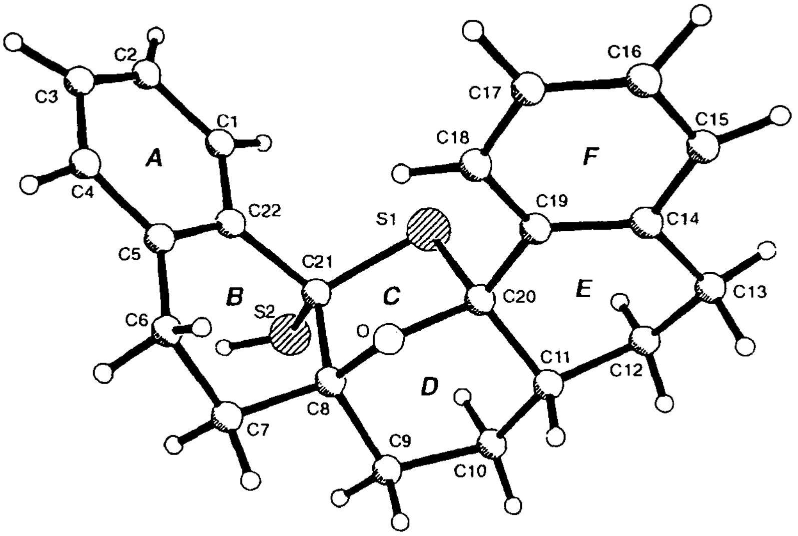

Fig. 1. General appearance and numbering of atoms in the molecule of compound (V).

Use of the data from quantum-chemical calculations (by the LCAO-MO SCF method in the CNDO/2 approximation), which make it possible to compare the values of the effective charges at the $C_{(10)}$ ($\delta-$ 0.057 and 0.041) and $C_{(2')}$ ($\delta+$ 0.225 and 0.215) atoms in the spirohydrochromans (I) and (II), shows that protonation of the π bond of the spiran (I) must take place more readily than that of its benzannelated analog (II), leading to opening of the heterocycle with subsequent cyclization to the spirohydrochromans (VII) and (VI). On the basis of the closeness of the values of the effective charges at the spiran carbon atoms in the substrates (I) and (II) ($\delta+$ 0.149 and 0.144 respectively) it can be supposed that recyclization is also possible for the latter but under more rigorous conditions. In this connection further refinement of the structure of the product obtained earlier by the action of hydrogen sulfide and boron trifluoride etherate on the spirohydrochroman (II) at 20°C, to which the structure of the thiol (V) was assigned, is required.

In fact, by examining the signals of the key carbon atoms in the ^{13}C NMR spectra, which determine the structure of this product [1], and comparing them with the signals of compounds (III, IV, VIII) [2], we found that the signal of the spiran carbon atom $C_{(2)}$ can be assigned with equal probability to the carbon attached to the oxygen or the sulfur atom of the heterocyclic fragment [see Table 1, compound (V)]. To obtain final evidence for the structure of the compound its x-ray crystallographic analysis was undertaken, and this showed that the central heterocycle in the molecule is hydropyran (Fig. 1).

It was established that the rings* A and F are planar within 0.02 Å, and the angle between the planes of the rings is 92.8°. In ring B the $C_{(5)}$, $C_{(6)}$, $C_{(8)}$, $C_{(21)}$, and $C_{(22)}$ atoms are coplanar within 0.04 Å; the $C_{(7)}$ atom lies outside of this plane by 0.65 Å; the $S_{(2)}$ atom is in the axial position. Ring E has a similar conformation; the $C_{(12)}$, $C_{(13)}$, $C_{(17)}$, $C_{(19)}$, and $C_{(20)}$ atoms are practically coplanar (maximum deviation 0.07 Å), and the $C_{(11)}$ atom projects from the plane by 0.68 Å. The five-membered ring C has a conformation close to an envelope, and the heteroatom (oxygen) projects from the average plane of the other atoms by 0.65 Å. The tetrahydropyran ring D has the ideal chair conformation, where the $C_{(8)}$ and $C_{(11)}$ atoms project from the plane of the other four atoms by 0.68 and 0.65 Å respectively on different sides.

Thus, according to the data from x-ray crystallographic analysis, ^{13}C NMR, and quantum-chemical calculations, we have shown that the product from the reaction of the spirohydrochroman (II) with hydrogen sulfide and boron trifluoride etherate at 20°C has the structure of 16-oxa-2-thia-4,5,14,15-dibenzotetracyclo[7.6.1.0^{3,8}.0^{1,11}]hexadecane-3-thiol (IX).

The refined spectral characteristics can be used for the identification of new compounds of the investigated series.

EXPERIMENTAL

The IR spectrum was obtained on a UR-20 spectrometer in tablets with potassium bromide and in Vaseline oil. The ^{13}C NMR spectra were recorded on a Varian FT-80A Fourier spectrometer at 30°C in deuterochloroform.

X-ray Crystallographic Analysis. The crystals of compound (V) ($C_{22}H_{22}OS_2$) are rhombic; a = 8.463(2), b = 8.313(2), c = 26.676(5) Å, ρ_{calc} = 1.297 g/cm^3, V = 1876.7 Å^3, Z = 4, space group $P2_12_12_1$. The unit cell parameters and the intensities of 846 unique reflections with $I > 2\sigma(I)$ were measured on a Syntex P-1 diffractometer (MoKα radiation, $\theta/2\theta$ scan). The structure of (VII) was interpreted by means of the SHELXTL-81 and SHELTXTL-93 software [3, 4] and was refined by least-squares treatment in anisotropic approximation. The coordinates of the hydrogen atoms were obtained from a difference synthesis, and their position and temperature parameters were included in the refinement. The final values of the convergence factors were R = 0.442 and R_W = 0.1104.

3,4,5,6,7,8-Hexahydrospiro[thiochromene-2,1′-cyclohexane]-2′-thione (VI). We saturated 30 ml of acetic acid with hydrogen sulfide for 2 h and added 2.2 g (0.01 mole) of compound (I) and 4.14 g (0.03 mole) of boron trifluoride etherate. The delivery of hydrogen sulfide was continued for 3 h at ~60°C. The reaction mixture was treated with 50 ml of water and extracted with ether (2 × 30 ml). The extract was washed with water and sodium carbonate solution and dried with magnesium sulfate. The solvent was evaporated, and 1.85 g (74%) of compound (IV) was obtained; mp 128-129°C (from hexane), R_f 0.88 (Silufol UV-254 plates, eluant 4:1:1 hexane—ether—acetone). Found %: C 66.70; H 7.25; S 24.82. $C_{14}H_{20}S_2$. Calculated %: C 66.66; H 7.94; S 25.39.

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*The numbering of the atoms used during description of the structure differs from the nomenclature.