Conformational peculiarities of a new heterocyclic dihydrothienothiopyranoisoxazole system

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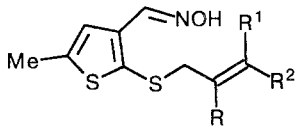
The crystalline and molecular structures of 3*H*-3a,4-dihydro-7-methylthieno[3′,2′:5,6]thiopyrano[4,3-*c*]isoxazole and 3*H*-3a,4-dihydro-3-isopropoxycarbonyl-3a,7-dimethylthieno[3′,2′:5,6]thiopyrano[4,3-*c*]isoxazole are determined by X-ray analysis. The effect of steric factors on intramolecular 1,3-dipolar cycloaddition is shown.

Key words: 3*H*-3a,4-dihydro-7-methylthieno[3′,2′:5,6]thiopyrano[4,3-*c*]isoxazole, 3*H*-3a,4-dihydro-3-isopropoxycarbonyl-3a,7-dimethylthieno[3′,2′:5,6]thiopyrano-[4,3-*c*]isoxazole, X-ray analysis, conformation.

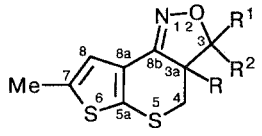
It has previously been shown[1–2] that oxime **1a** is oxidized by NaOCl to form the tricyclic system **2a**. The reaction occurs as intramolecular 1,3-dipolar cycloaddition (IMCA) of allylthionitrile oxides to the allyl double bond.



1

NaOCl

a: R = R¹ = R² = H
b: R = H, R¹ = R² = Me
c: R = Me, R¹ = R² = H
d: R = Me, R¹ = H
R² = COOPr^i



2

The oxidation of oxime **1b**, which has two α,α-Me groups at the multiple bond of the substituent, occurs similarly. However, attempts to involve oxime **1c** with the methyl group at the β-position in cyclization have failed. Only unidentified resins were formed as the reaction products.[2] However, the introduction of an ester group to the terminal carbon atom of the molecule changes the situation sharply: **1d** reacts with NaOCl to form the tricyclic structure **2d** in a satisfactory yield (see Ref. 2).

In this work, the attempt is made to explain the results obtained on the basis of the geometric and conformational parameters of the crystalline products of the cyclization, 3*H*-3a,4-dihydrothienothiopyranoisooxazoles.

Structures **2a** and **2d** were determined by X-ray structural analysis. The conformations of the molecules are presented in Fig. 1, *a*, *b*. The thiopyran cycle (*B*) in **2a** takes the half-chair conformation HC with an up-

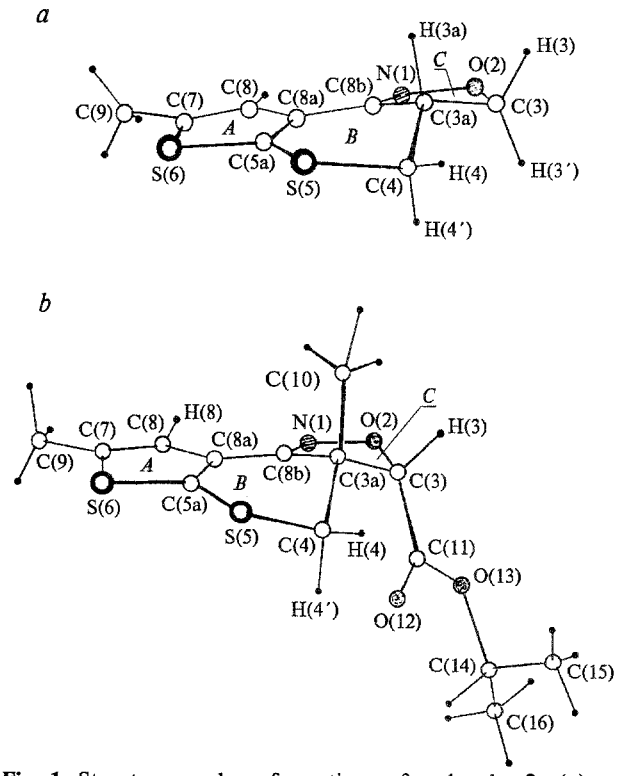


Fig. 1. Structures and conformations of molecules **2a** (*a*) and **2d** (*b*).

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Table 1. Torsion angles (φ) in the *B* and *C* cycles in structures **2a,d**

Angle	φ/deg	
	2a	**2d**
C(8a)—C(5a)—S(5)—C(4)	−12.1	−17.1
C(5a)—S(5)—C(4)—C(3a)	39.6	48.0
S(5)—C(4)—C(3a)—C(8b)	−55.9	−63.7
C(4)—C(3a)—C(8b)—C(8a)	40.7	44.5
C(3a)—C(8b)—C(8a)—C(5a)	−10.4	−10.3
C(8b)—C(8a)—C(5a)—S(5)	1.0	1.1
N(1)—C(8b)—C(3a)—C(3)	−12.1	−15.7
C(8b)—C(3a)—C(3)—O(2)	16.1	23.4
C(3a)—C(3)—O(2)—N(1)	−16.1	−25.1
C(3)—O(2)—N(1)—C(8b)	8.8	16.1
O(2)—N(1)—C(8b)—C(3a)	2.7	1.0

declined C(3a) atom and a down-declined C(4) atom relative to the main plane of the cycle. The isoxaline cycle (*C*) has the shape of a flattened envelope ($_3$E), whose C(3) angle is bent aside by 13° from the central plane of the cycle. All of the bond lengths and bond angles in the tricyclic system are close to the standard values.[4] However, the deformations of the H—C—C and H—C—S exocyclic bond angles at the C(3a) and C(4) atoms are unusually large (H(3a)—C(3a)—C(4) 89.7°, H(3a)—C(3a)—C(3) 121.4°, H(4)—C(4)—C(3a) 120.9°, H(4)—C(4)—S(5) 95.3°), which indicates considerable steric hindrances between the vicinal protons in the tricyclic framework of molecule **2a**. We believe that the bulkier CH_3 group at the C(3a) position of this tricyclic system would result in greater steric hindrances. The

Table 2. Bond lengths (*d*) in molecules **2a,d**

Bond	*d*/Å	
	2a	**2d**
N(1)—O(2)	1.429(8)	1.434(5)
O(2)—C(3)	1.440(7)	1.445(6)
C(3)—C(3a)	1.530(8)	1.559(6)
C(3a)—C(4)	1.436(9)	1.519(5)
C(4)—S(5)	1.817(8)	1.822(4)
S(5)—C(5a)	1.730(6)	1.747(4)
C(5a)—S(6)	1.733(6)	1.706(4)
S(6)—C(7)	1.719(6)	1.740(4)
C(7)—C(8)	1.349(6)	1.344(7)
C(8)—C(8a)	1.423(7)	1.435(6)
C(8a)—C(8b)	1.462(6)	1.424(6)
C(8b)—N(1)	1.278(8)	1.287(6)
C(5a)—C(8a)	1.367(8)	1.384(6)
C(8b)—C(3a)	1.500(7)	1.516(6)
C(7)—C(9)	1.534(7)	1.500(6)
C(3)—C(11)		1.501(7)
C(3a)—C(10)		1.502(7)
C(11)—O(12)		1.200(7)
C(11)—O(13)		1.347(5)
O(13)—C(14)		1.472(6)
C(14)—C(15)		1.493(6)
C(14)—C(16)		1.500(5)

Table 3. Bond angles (ω) in molecules **2a,d**

Angle	ω/deg	
	2a	**2d**
N(1)—O(2)—C(3)	108.6(7)	108.6(6)
O(2)—C(3)—C(3a)	105.6(8)	103.4(6)
C(3)—C(3a)—C(8b)	99.3(7)	98.7(6)
C(8b)—C(3a)—C(4)	114.8(8)	110.3(5)
C(3)—C(3a)—C(4)	119.8(8)	114.5(5)
C(3a)—C(8b)—N(1)	115.1(9)	114.7(4)
C(8b)—N(1)—O(2)	108.4(7)	108.2(7)
C(8a)—C(8b)—C(3a)	121.1(6)	121.1(7)
C(3a)—C(4)—S(5)	115.1(5)	111.2(4)
C(4)—S(5)—C(5a)	99.2(3)	98.4(3)
S(5)—C(5a)—C(8a)	129.1(7)	126.9(3)
S(5)—C(5a)—S(6)	120.4(5)	120.8(4)
S(6)—C(5a)—C(8a)	110.5(5)	112.3(6)
C(5a)—S(6)—C(7)	91.4(7)	92.1(4)
S(6)—C(7)—C(8)	112.2(7)	110.7(4)
S(6)—C(7)—C(9)	119.7(6)	119.5(5)
C(9)—C(7)—C(8)	128.0(7)	129.8(9)
C(7)—C(8)—C(8a)	112.4(7)	113.8(8)
C(8)—C(8a)—C(5a)	113.3(8)	111.1(4)
C(8)—C(8a)—C(8b)	127.4(6)	126.2(7)
C(5a)—C(8a)—C(8b)	119.3(6)	121.7(7)
C(8a)—C(8b)—N(1)	123.8(7)	124.2(8)
H(3a)—C(3a)—C(3)	121.4(8)	
H(3a)—C(3a)—C(8b)	112.9(10)	
H(3a)—C(3a)—C(4)	89.7(9)	
H(4')—C(4)—C(3a)	108.2(8)	
H(4')—C(4)—S(5)	108.3(7)	
H(4)—C(4)—C(3a)	120.9(11)	
H(4)—C(4)—S(5)	95.3(12)	
O(2)—C(3)—C(11)		108.5(7)
C(3a)—C(3)—C(11)		114.9(8)
C(11)—O(3)—C(14)		117.9(6)
H(3)—C(3)—C(3a)		105.9(11)
C(10)—C(3a)—C(3)		109.3(4)
C(10)—C(3a)—C(8b)		108.9(6)
C(10)—C(3a)—C(4)		113.6(7)
H(3)—C(3)—O(2)		110.9(11)

calculation performed by the MOLDRAW program[5] shows that in this case the energy of the nonvalence interaction is increased by 17.1 kcal mol^{-1}. In our opinion, this may be one of the reasons for the absence of thienothiopyran **2c** in the IMCA reaction products.

The formation of thiopyran **2d** may also be made possible by the specific features of its spatial structure. The molecule of *trans*-isomer **2d** is shown in Fig. 1, *b*. In this case, the conformations of cycles *B* and *C* are the same as that in **2a** (HC and $_3$E, respectively), but the ester group bends the C(3) angle of the envelope 26.3° from the plane of the *C* cycle. As a result, the distances between the vicinal substituents, C(10)···H(3) (2.50 Å) and C(10)···H(4) (2.74 Å), increase to the usually observed C···H contacts (2.5—2.8 Å)[6] without any significant deformation of the exocyclic bond angles: C(10)—C(3a)—C(4) 113.6(7)°, C(10)—C(3a)—C(3) 109.3(4)°, and C(10)—C(3a)—C(8b) 108.9(6)°.

Table 4. Atomic coordinates (for non-hydrogen atoms $\times 10^4$, for H atoms $\times 10^3$) and isotropic heat parameters (Å^2) in molecule **2a**

Atom	x	y	z	U_{iso}
N(1)	−605(4)	−583(5)	−2279(8)	5.3
O(2)	−938(4)	575(4)	−1759(8)	6.2
C(3)	−49(5)	1760(6)	−2007(10)	5.6
C(3a)	−50(6)	1245(7)	−2194(10)	6.4
C(4)	1781(6)	1878(7)	−3440(15)	6.8
S(5)	2852(1)	1058(1)	−3692(2)	5.5
C(5a)	2086(5)	−613(6)	−3619(8)	4.8
S(6)	2656(1)	−1900(1)	−4164(2)	5.4
C(7)	1470(5)	−3109(6)	−3733(9)	5.7
C(8)	680(5)	−2565(6)	−3208(9)	5.0
C(8a)	1032(4)	−1131(6)	−3136(8)	4.4
C(8b)	411(5)	−215(6)	−2559(10)	5.2
C(9)	1430(7)	−4608(8)	−3864(12)	6.4
H(3)	9(8)	232(9)	−78(13)	6.7
H(3′)	−22(7)	239(8)	−331(11)	5.6
H(4)	237(7)	298(9)	−315(12)	7.6
H(4′)	140(7)	189(9)	−475(11)	7.8
H(3a)	162(8)	140(9)	−95(10)	8.5
H(8)	−12(8)	−318(8)	−290(11)	6.5
H(9)	65(7)	−527(8)	−400(11)	8.5
H(9′)	161(7)	−478(10)	−503(10)	7.5
H(9′′)	204(7)	−486(8)	−298(10)	8.5

Thus, the formation of the cyclization product, thiopyran **2d**, can be explained by the fact that the CH_3 group at the C(3a) position of this compound has no steric hindrances.

Experimental

The X-ray diffraction experiment for compounds **2a** and **2d** was carried out on a RED-4 automatic four-circle diffractometer (λ(Cu-Kα), graphite monochromator, θ/2θ-scanning, θ ≤ 60°). The structures were solved by the direct method. The coordinates of the non-hydrogen atoms were refined by the least-squares method in the anisotropic approximation. Hydrogen atoms were experimentally located in the difference Fourier syntheses and refined in the isotropic approximation. The calculations were performed on an IBM PC/AT with AREN programs.[7]

Crystals of **2a** ($C_9H_9NOS_2$) prepared by slow evaporation of the solvent (hexane) are monoclinic: a = 12.906(1), b = 10.309(1), c = 7.500(1) Å, γ = 105.93(1)°, V = 959.6(2) Å^3, space group $P2_1/n$, Z = 4. The final value of R is equal to 0.066; 1293 reflections with $I \geq 2\sigma(I)$.

Crystals of **2d** ($C_{14}H_{17}NO_3S_2$) prepared from its ethyl acetate solution are monoclinic: a = 13.921(2), b = 12.969 (2), c = 8.778(1) Å, β = 109.12(1)°, V = 1497.6(3) Å^3, space group $P2_1/a$, Z = 4. The final value of R is equal to 0.065; 1700 reflections with $I \geq 2\sigma(I)$.

Table 5. Atomic coordinates (for non-hydrogen atoms $\times 10^4$, for H atoms $\times 10^3$) and isotropic heat parameters (Å^2) in molecule **2d**

Atom	x	y	z	U_{iso}
N(1)	2567(3)	1721(3)	14585(5)	4.6
O(2)	2921(3)	1413(3)	16245(4)	5.0
C(3)	3057(5)	307(3)	16321(6)	3.9
C(3a)	2321(3)	−76(3)	14667(5)	3.3
C(4)	2733(3)	−945(3)	13900(5)	3.3
S(5)	1871(1)	−1243(1)	11889(1)	3.8
C(5a)	1657(3)	12(3)	11126(5)	3.4
S(6)	1161(1)	230(1)	9103(1)	4.0
C(7)	1190(3)	1560(4)	9383(6)	4.0
C(8)	1575(3)	1800(3)	10955(5)	4.1
C(8a)	1853(3)	920(3)	12000(5)	3.4
C(8b)	2253(3)	912(3)	13716(5)	3.3
C(9)	805(4)	2253(4)	7944(6)	5.6
C(10)	1288(4)	−308(3)	14828(5)	4.8
C(11)	4163(3)	71(4)	16630(5)	3.5
O(12)	4776(2)	636(2)	16386(4)	5.3
O(13)	4364(2)	−886(2)	17247(4)	3.9
C(14)	5421(4)	−1253(5)	17695(5)	4.8
C(15)	5892(2)	−1080(6)	19465(4)	6.3
C(16)	5366(5)	−2360(5)	17180(4)	6.7
H(3)	274(5)	−4(4)	1726(6)	2.0
H(4)	350(3)	−77(4)	1380(6)	1.3
H(4')	279(6)	−162(6)	1455(5)	1.0
H(8)	162(5)	259(5)	1150(7)	4.5
H(14)	577(5)	−82(6)	1684(5)	3.1

The geometric parameters of molecules **2a** and **2d** and the atomic coordinates are presented in Tables 1—5.

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