Acta Chemica Scandinavica B 39 (1985) 123–129

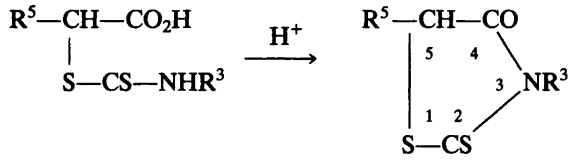
The Crystal and Molecular Structure of 3-Isopropyl-5-phenylrhodanine

KNUT RANG,[a] JAN SANDSTRÖM,[a*] LARS THELL,[b] and QIBIN YANG[b**]

[a] Division of Organic Chemistry 3 and [b] Division of Inorganic Chemistry 2, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden

3-Isopropyl-5-phenylthiazolidin-4-one-2-thione crystallizes in the monoclinic space group $P2_1$. The structure has been determined by single crystal X-ray diffraction and refined to $R=0.022$ and $R_w=0.025$. The bond lengths of the CO–N–CS–S part are discussed in relation to MO calculations. The 3-isopropyl group is bisected by the thiazolidine ring plane, with the methyl groups turned towards the carbonyl oxygen, as expected from steric considerations. The thiazolidine and phenyl rings are practically planar with an 86.2° angle between the planes.

Rhodanines, *i.e.* thiazolidin-4-one-2-thiones (*2*), are formed by cyclization, often spontaneous, of α-carboxymethyl dithiocarbamates (*1*)



1 *2*

a, R^3=iPr, R^5=Ph; *b*, R^3=H, R^5=Me; *c*=R^3=R^5=H

It has been observed[1,2] that cyclization of several optically active precursors (*1*) leads to racemic rhodanines, and therefore H-5 was considered as too mobile to sustain optical activity. In the course of an NMR study of the orientation of alkyl groups in position 3, we also prepared a number of 5-phenylrhodanines (*2*, R^5=Ph). By a high temperature ^{1}H NMR study of *2a* and by the resolution through chromatography on swollen microcrystalline triacetylcellulose of *2a* and two analogues, we found that these compounds retain their chirality in neutral solution at room temperature. Therefore, it now seems likely that the racemization previously observed is due to the acid medium used in the last step of the synthesis.

* Author to whom correspondence should be addressed.
** On leave from Institute of Metal Research, Academia Sinica, Shenyang, China.

0302-4369/85 $2.50

Table 1. Experimental details.

Cell data	a=12.273(3) b=5.245(1) c=9.888(2) β=111.40(2) Z=2
Space group	$P2_1$
D_c	1.36 G cm^{-3}
D_m [a]	1.34 G cm^{-3}
Radiation	MoK_α
θ interval (°)	3–25
$\omega-2\theta$ scand width w (°)	2.4+$\alpha_1\alpha_2$ splitting
Scan rate (°/min)	1.0–29.3
μ (mm^{-1})	0.4
Number of reflections measured [b]	1219
Number of reflections with zero weight	83
Number of reflections used in the final refinement, m	1136
Number of parameters refined, n	196
$R=\sum(\|F_o\|-\|F_c\|)/\sum\|F_o\|$	0.022
$R_w=[\sum w(\|F_o\|-\|F_c\|)^2/\sum w\|F_o\|^2]^{\frac{1}{2}}$	0.025
$S=[\sum w(\|F_o\|-\|F_c\|)^2/(m-n)]^{\frac{1}{2}}$	0.96

[a] Measured by flotation. [b] One set of independent reflections was measured.

As part of a study of the circular dichroism spectra of simple chromophores in rigid molecules, *2a* became of interest as an *N*-acyldithiocarbamate model. A single crystal X-ray diffraction study of this compound was undertaken, in order to provide the geometry necessary for calculation of the rotational strengths of the near UV transitions in the rhodanine system.

EXPERIMENTAL

Preparative part. 3-Isopropyl-5-phenylthiazolidin-4-one-2-thione (2a). Carbon disulfide (7.6 g, 0.1 mol) in dry diethyl ether (25 ml) was added dropwise with cooling (0 °C) and stirring during 1.5 h to a solution of isopropylamine (11.8 g, 0.2 mol) in dry diethyl ether (50 ml). A colourless crystalline precipitate of isopropylammonium *N*-isopropyldithiocarbamate was formed (98 % yield, identified by its ^{1}H NMR spectrum).

α-Bromophenylacetic acid (4.3 g, 0.02 mol) was dissolved with sodium bicarbonate (1.9 g, 0.023 mol) in water (20 ml). Solid isopropylammonium *N*-isopropyldithiocarbamate (3.9 g, 0.02 mol) was added, and after 5 h the solution was acidified with 5 M HCl to pH≈1. A colourless oil separated, which was decanted and brought to crystallization by trituration with a small quantity of ethanol. Recrystallization from absolute ethanol gave colourless prisms in 30 % yield, m.p. 124–126 °C. ^{1}H NMR (100 MHz, CD_2Cl_2): δ 1.43 and 1.48 (6H, d of d, J 6.8 Hz), 5.07 (1H, s), 5.25 (1H, sept, J 6.8 Hz), 7.31 (5H, m). In *o*-dichlorobenzene the corresponding chemical shifts are δ 1.17 and 1.23 (6H, d of d, J 6.8 Hz), 4.72 (1H, s), 5.10 (1H, sept, J 6.8 Hz). The doublet of doublets due to the diastereotopic methyl groups showed no significant broadening below 172 °C in this solvent, corresponding to a free energy barrier to racemization ≥110 kJ mol^{-1}.

Structure determination and refinement. The cell dimensions shown in Table 1 were refined by least-squares from 25 single indexed lines of a powder pattern obtained in a Guinier-Hägg focusing camera with CuK_α radiation. Silicon was used as an internal

Table 2. Final positional parameters and isopropic *B*-values [Å^2]. *B*-values [Å^2] are converted from anisotropic to isotropic. Standard deviations in parentheses. For numbering, see Fig. 1.

	X	*Y*	*Z*	*B*
C1	.2782(2)	.6412(6)	.7611(3)	3.48(7)
C2	.2762(2)	.6312(7)	.9010(3)	4.06(7)
C3	.3296(2)	.8123(7)	.0002(3)	4.15(7)
C4	.3856(3)	.0041(6)	.9631(3)	4.23(8)
C5	.3883(2)	.0157(6)	.8237(3)	3.49(7)
C6	.3344(2)	.8361(5)	.7229(2)	2.67(5)
C7	.3355(2)	.8561(5)	.5711(2)	2.79(6)
C8	.2118(2)	.8605(5)	.4567(2)	2.89(6)
C9	.2871(2)	.5264(5)	.3665(2)	2.68(5)
C10	.0751(2)	.6296(6)	.2400(3)	3.37(6)
C11	.0415(3)	.8417(7)	.1341(3)	4.61(9)
C12	−.0144(3)	.5708(10)	.3078(4)	5.36(10)
S1	.2948(1)	.3072(0)	.2556(1)	3.75(2)
S2	.4086(0)	.5997(2)	.5193(1)	3.23(2)
N1	.1929(2)	.6710(4)	.3551(2)	2.73(5)
O1	.1399(2)	.0102(4)	.4563(2)	4.15(5)
H1	.241(3)	.522(7)	.691(3)	4.1(6)
H2	.238(3)	.504(6)	.917(3)	4.0(6)
H3	.324(3)	.799(7)	1.094(3)	4.6(6)
H4	.418(3)	.138(12)	1.027(4)	7.1(10)
H5	.421(2)	.136(7)	.800(3)	3.6(6)
H7	.374(2)	.993(6)	.564(3)	2.9(5)
H10	.088(2)	.499(6)	.189(3)	3.2(6)
H111	.031(3)	.982(8)	.182(4)	6.3(9)
H112	.107(3)	.873(8)	.093(4)	5.9(8)
H113	.029(39)	.287(8)	.938(3)	5.0(7)
H121	−.087(4)	.531(8)	.230(4)	6.2(8)
H122	.012(4)	.448(11)	.380(5)	7.4(11)
H123	.019(3)	.222(8)	.641(4)	5.8(9)

Table 3. Interatomic distances (Å). Standard deviations in parentheses.

C1–C2	1.393(4)	C9–S2	1.738(2)
C1–C6	1.387(4)	C9–N1	1.368(3)
C2–C3	1.374(5)	C10–C11	1.509(5)
C3–C4	1.369(5)	C10–C12	1.515(4)
C4–C5	1.392(4)	C10–N1	1.494(3)
C5–C6	1.379(4)		
C6–C7	1.510(3)		
C7–C8	1.527(3)		
C7–S2	1.827(3)		
C8–O1	1.198(3)		
C8–N1	1.397(3)		
C9–S1	1.643(2)		

Table 4. Selected bond and torsion angles and R.M.S. deviations (Å) from the least-squares planes through the two rings.

C6–C1–C2	119.4(3)		
		C7–C8–N1	112.4(2)
C1–C2–C3	120.2(3)	C7–C8–O1	123.0(2)
		O1–C8–N1	124.6(2)
		N1–C9–S1	127.8(2)
C2–C3–C4	120.6(2)	N1–C9–S2	111.9(2)
		S1–C9–S2	120.3(1)
		C8–N1–C9	116.7(2)
C3–C4–C5	119.7(3)	C10–N1–C8	121.3(2)
		C10–N1–C9	122.0(2)
		C9–S2–C7	93.7(1)
C4–C5–C6	120.3(3)	C11–C10–C12	114.1(3)
		N1–C10–C11	110.9(2)
		N1–C10–C12	110.5(2)
C1–C6–C7	120.7(2)		
C5–C6–C1	119.8(2)		
C5–C6–C7	119.5(2)		
C8–C7–C6	111.7(2)		
C8–C7–S2	105.2(2)		
S2–C7–C6	114.1(2)		
Plane	R.M.S. Deviations	Group	
I	0.0055	C(1)–C(2)–C(3)–C(4)–C(5)–C(6)	
II	0.0441	C(7)–S(2)–C(9)–N(1)–C(8)	
Angle between plane I and II (°)		86.2(1)	

standard. A stout prismatic crystal ($0.5\times0.12\times0.12$ mm^3), selected with polarization and Weissenberg techniques, was mounted on a Nicolet P3M four-circle diffractometer. Table 1 gives information on the data collection, reduction of the intensities, and subsequent refinement. Systematic absences were $0k0$: $k\neq2n$ which is consistent with the space group $P2_1$. A refinement of 28 accurately measured θ-values confirmed the unit cell parameters.

No systematic variation was observed in the intensity of a standard reflection (2.1.2), which was checked every 50 reflections. I and σ_c (I) (based on counting statistics) were corrected for Lorentz and polarization effects.

The positions for the sulfur atoms were determined by direct methods, while for the rest of the atoms they were determined by difference synthesis. Scattering factors for neutral atoms[3] were used in the least-squares refinement.

Without correction for absorption and extinction, the least-squares refinement, including anisotropic temperature factors for non-hydrogen atoms, gave the final R=0.022 and

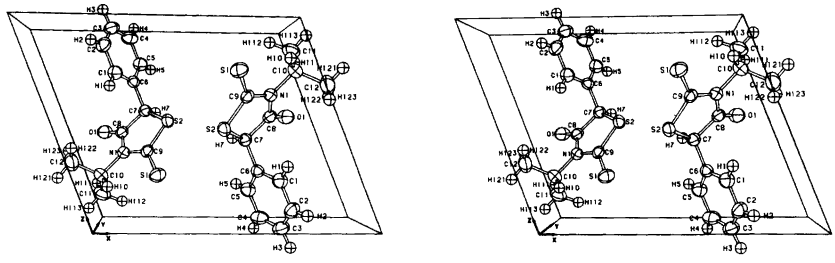


Fig. 1. Stereoview of the unit cell of *2a*.

Table 5. Bond lengths (in Å) in simple amides and thioamides, and in *2a–c*.

Compound	R(CO–N)	R(C=O)	R(CS–N)	R(C=S)	Ref.
Formamide	1.352	1.224	–	–	6
Acetamide	1.38	1.28	–	–	7
N-Methyl-*N*-benzyl-thioformamide	–	–	1.35	1.66	8
Thioacetamide	–	–	1.32	1.71	9
IIa	1.397	1.198	1.368	1.643	This work
IIb	1.370	1.210	1.370	1.639	4
IIc	1.38	1.23	1.37	1.64	5

R_w=0.025 with weights $w^{-1}=\sigma_c^2(|F_o|)+(0.03|F_o|)^2$. The highest peaks in the final difference synthesis corresponded to 0.13 $e^- Å^{-3}$.

Final positional parameters are given in Table 2 and bond lengths (in Å) and angles in Tables 3 and 4. A stereoview of the unit cell is shown in Fig. 1.

RESULTS AND DISCUSSION

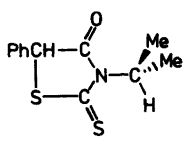
The bond lengths and angles in the thiazolinethione ring of IIa agree well with those reported recently by Gattow *et al.*[4] for 5-methylrhodanine (IIb), as well as with earlier data for the unsubstituted rhodanine (IIc).[5] It is obvious from both structures that the C=O and C=S bonds in most cases are shorter and the C–N bonds longer than in simple amides and thioamides (Table 5), as should be expected from simple resonance arguments. MO calculations with an HMO method, self-consistent in charges and bond orders,[10,11] and CNDO calculations[12] give larger C=O and smaller C–N π bond orders for the

–CO–N–CS–S= system than for the simple –CO–N and N–CS–S systems (Table 6).

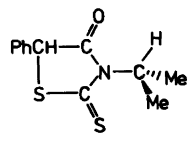
It is worth noting (Fig. 1) that although the sample is racemic *2a*, each crystal contains only one enantiomer.

The conformational behaviour of isopropyl groups bonded to the 3-nitrogen atoms in azoline-2-thiones with methyl or other alkyl groups in position 4 have been studied by low-temperature NMR spectroscopy[13,14] and by force-field calculations.[13] In general, the isopropyl group has been found to adopt one of the two possible "bisected" conformations, with the methyl groups on either side of the plane through the heterocyclic ring. For *2a* the corresponding rotamers should be *A* and *B*, the former being found in the crystal.

Since the rotamer with the methyl groups turned away from the larger one of the flanking groups generally is the favoured one, rotamer *A* should dominate also in solution. In fact,



A



B

Table 6. π-Bond orders (p) calculated by a HMO[10,11] and a CNDO[12] (bold) method.

Bond system	Amide		Thioamide	
	p_{C-N}	$p_{C=O}$	p_{C-N}	$p_{C=S}$
N–C=O	**0.434**	**0.836**	–	–
	0.501	0.850	–	–
N–CS–S	–	–	**0.642**	**0.627**
	–	–	0.600	0.731
–CO–N–CS–S[a]	**0.325**	**0.886**	**0.472**	**0.758**
	0.345	0.923	0.528	0.754

[a] The CNDO calculations are performed on a 3-methylrhodanine molecule with the geometry from *2a*.

low temperature ^{1}H NMR studies of 3-isopropylrhodanine and its 5-phenyl analogue failed to detect any line-broadening due to slow exchange between the *A* and *B* forms above −100 °C, which probably indicates a very strong dominance of rotamer *A*. The barriers for isopropyl group rotation in near analogues, such as 3-isopropyl-4-methylthiazoline-2-thione, -imidazoline-2-thione, and -oxazoline-2-thione fall in the range of 43.0–61.0 kJ mol^{-1}.[14] Aksaç *et al.*[15] have found high barriers to rotation of 3-aryl substituents in rhodanines. Therefore, the steric hindrance to rotation of a 3-isopropyl group in a rhodanine ring certainly would have been sufficient to give an exchange effect on the ^{1}H NMR spectrum above −100 °C, had not the $A \rightleftharpoons B$ equilibrium been strongly biased. The conclusion is that the conformation found in the crystal also is the dominating one in solution.

We will report on the resolution of *2a* and its CD spectrum in a subsequent communication.

Acknowledgement. We thank Drs Lars Fälth and Christer Svensson for valuable discussions, Mr Ulf Håkansson for help with the Weissenberg and Guinier photographs and for collecting the X-ray intensity data, and the Swedish Natural Science Research Council for financial support. Qibin Yang thanks the Royal Swedish Academy of Engineering Sciences for a fellowship.

REFERENCES

1. Kallenberg, S. *Diss.*, Lund 1919.
2. Sandström, J. *Arkiv Kemi 8* (1955) 487.
3. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1974, Vol. 4.
4. Gattow, G., Kiel, G. and Rach, W. *Z. Anorg. Allg. Chem. 506* (1983) 145.
5. van der Helm, D., Lessor, A.E., Jr. and Merrit, L.L., Jr. *Acta Cryst. 15* (1962) 1227.
6. Hirota, E., Sugisaki, R., Nielsen, C.J. and Sörensen, G.O. *J. Mol. Spectrosc. 49* (1974) 251.
7. Senti, F. and Harker, D. *J. Am. Chem. Soc. 62* (1940) 2008.
8. Piazzesi, A.M., Bardi, R., Mammi, M. and Walter, W. *Ric. Sci. Rend. 34* (1964) 173.
9. Truter, M.R. *J. Chem. Soc.* (1960) 997.
10. Sandström, J. *Acta Chem. Scand. 16* (1962) 1616.

11. Sandström, J. *Acta Chem. Scand. 17* (1963) 678.
12. Guimon, C., Gonbeau, D. and Pfister-Guillouzo, G. *Tetrahedron 29* (1973) 3399.
13. Roussel, C., Lidén, A., Chanon, M., Metzger, J. and Sandström, J. *J. Am. Chem. Soc. 98* (1976) 3847.
14. Djafri, A., Roussel, C. and Sandström, J. *J. Chem. Soc. Perkin Trans. 2. In press.*
15. Aksaç, Z., Pinar, E. and Içli, S. *Org. Magn. Reson. 21* (1983) 548.

Received April 13, 1984.