

Crystal and molecular structure of 4-amino-4-carboxyl thiapyran†

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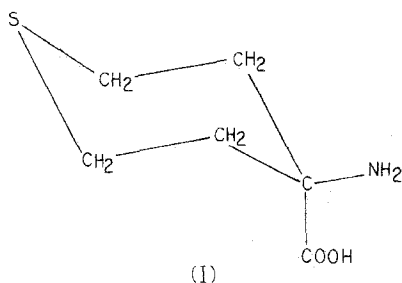
Abstract

4-Amino-4-carboxylthiapyran crystallizes in space group $P2_1/c$ with $a = 10.61$, $b = 6.55$, $c = 10.97$ Å, $\beta = 96.3^\circ$, and $Z = 4$. The structure was solved by the heavy-atom method, with 897 observed reflections, and refined to an R of 0.093. The packing of the structure is found to be very similar to that in the structure of 1-aminocyclohexane carboxylic acid. The conformation of the thiapyran ring exists in the “puckered chair” form.

Introduction

The structural formula of 4-amino-4-carboxylthiapyran(I) (hereinafter 4-THIA), $C_6H_{11}NO_2S$, is very similar to that of 1-aminocyclohexane-1-carboxylic acid (hereinafter 1-HEX) reported by Varughese et al. (1975); the C(4) methylene group of 1-HEX is replaced by a sulfur atom in 4-THIA. The

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study of 4-THIA was carried out to investigate the structural and packing changes that are introduced into the cyclohexane system when a hetero atom like sulfur replaces a methylene group in the ring. A similar investigation has been carried out on the structure of 4-amino-4-carboxylthiapyran hydrobromide (hereinafter 4-THIA HBR), which showed interesting conformational and packing features of the structure due to the presence of a weak $N-H \cdots S$ interaction in the structure (Chacko et al., 1975).

Experimental

Rotation, Weissenberg, and precession photographs were taken with $Cu K\alpha$ ($\lambda = 1.5418 \text{ \AA}$). The unit-cell dimensions were determined from precession photographs. The relevant crystal data are listed below.

Crystal system	Monoclinic
Unit-cell dimensions	$a = 10.61(1) \text{ \AA}$ $b = 6.55(1)$ $c = 10.97(1)$ $\beta = 96.3 (5)^\circ$
Space group	$P2_1/c$
Molecular formula	$C_6H_{11}NO_2S$
Z	4
D_m	1.39 g cm^{-3}
D_c	1.41
$\mu(Cu K\alpha)$	32 cm^{-1}
$F(000)$	344

The intensities were collected about b for hkl ($k = 0-5$) and about c for hkl ($l = 0, 1, \text{ and } 2$) by the multiple film equi-inclination method. The crystal used for the b axis data had cross-sectional dimensions 0.15, 0.25 mm, those for the c axis data were 0.25, 0.35 mm. The intensities were estimated visually and corrected for Lorentz, polarization and spot shape effects. The common reflections from the two sets of data were used to get a scale factor

by the method of Rollett and Sparks (1960). There was a total of 897 observed independent reflections.

Structural determination and refinement

The cell dimensions of 4-THIA were close to those of 1-HEX, which also belongs to space group $P2_1/c$. A three-dimensional Patterson was computed for 4-THIA to locate the sulfur atom. A sulfur-phased Fourier synthesis was computed, which revealed all the nonhydrogen atoms in the structure; they were close to the corresponding atomic positions in 1-HEX, except for sulfur and its immediate neighbors. The initial R index for all nonhydrogen atoms was 0.30. Four cycles of least-squares refinement (Gantzel et al., 1961) with isotropic temperature factors gave an R of 0.14. Hydrogens, located at this stage from a difference electron density synthesis, were included subsequently in the structure factors during further refinement cycles. Three cycles of anisotropic refinement for the nonhydrogen atoms gave a final R of 0.093. The weighting scheme employed was that of Cruickshank et al. (1961), given by $W = 1/(A + |F_o| + C|F_o|^2)$, where the constants A and C were 8.0 and 0.04, respectively.

Scattering factors were taken from the *International Tables of X-ray Crystallography* (1962). Anomalous dispersion correction factors applied to sulfur are those given by Cromer and Liberman (1970). The final positional and thermal parameters are given in Table 1. Table 2 gives the hydrogen atom coordinates.

Discussion of the structure

Intramolecular features

The bond lengths and angles are listed in Table 3. The average standard deviation of the C–S, C–C, and C–O bonds are 0.010, 0.011, and 0.010 Å, respectively. The mean C–C bond length of the thiapyran ring is 1.515 Å and is slightly smaller than the mean value of 1.527 Å in the structure of 4-THIA HBR. The C–S bond lengths of 1.808 and 1.780 Å are close to the expected value of 1.81 Å (Pauling, 1960) and are equivalent within the limits of accuracy of the structure. The C–S–C angle of 97.5° agrees very well with the value of 98.7° in the structure of 4-THIA HBR. The mean C–C–C bond angle of 112.8° of the thiapyran ring shows that it is slightly larger than the value of 111.5° of the cyclohexane *chair* conformation (Bixon and Lifson, 1967). The slight increase in this mean value seems to compensate for the small value of the C–S–C valency angle, as was also observed in the structure of 4-THIA HBR.

The carboxyl group exists in this structure in the ionized form CO₂⁻ with the amino group in the NH₃⁺ state. The C^α–N distance of 1.50 Å agrees

Table 1. Fractional atomic coordinates and thermal parameters (all $\times 10^4$), with esd's in parentheses^a

X	Y	Z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
S	9571(2)	1502(5)	1509(3)	62(2)	565(12)	139(3)	-9(7)	-30(3)
C(4)	6595(6)	2207(11)	936(5)	57(6)	183(21)	41(4)	-13(16)	5(8)
C(3)	7492(7)	4019(14)	1130(8)	84(7)	235(23)	77(7)	-63(20)	12(12)
C(2)	8745(8)	3572(17)	675(9)	82(8)	462(36)	115(9)	-127(27)	34(14)
C(2')	8380(7)	-399(15)	1189(9)	65(6)	338(30)	114(10)	80(22)	-19(12)
C(3)	7110(7)	278(12)	1574(7)	64(6)	194(22)	74(6)	42(18)	-13(9)
C(5)	6142(6)	1917(14)	-438(6)	52(6)	318(27)	45(5)	-56(21)	3(9)
N	5427(5)	2806(9)	1505(5)	75(5)	172(17)	44(4)	29(14)	10(7)
O(1)	5581(6)	3357(9)	-966(4)	132(7)	285(18)	47(4)	32(17)	-20(8)
O(2)	6330(5)	279(9)	926(4)	82(5)	304(18)	63(4)	-6(15)	-6(7)

^a The thermal parameters is of the form $T = \exp - [b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl]$.

Table 2. *Coordinates of the hydrogen atoms from the difference synthesis*

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)	Bonded to
H(1)	0.461	0.169	0.125	1.64	N
H(2)	0.564	0.307	0.225	1.64	N
H(3)	0.505	0.409	0.100	1.64	N
H(4)	0.766	0.431	0.203	2.45	C(3)
H(5)	0.707	0.524	0.071	2.45	C(3)
H(6)	0.928	0.488	0.070	3.91	C(2)
H(7)	0.858	0.323	-0.027	3.91	C(2)
H(8)	0.827	-0.069	0.028	3.44	C(2')
H(9)	0.867	-0.171	0.162	3.44	C(2')
H(10)	0.647	-0.085	0.142	2.22	C(3')
H(11)	0.722	0.053	0.250	2.22	C(3')

Table 3. *Bond lengths (Å) and angles (deg) with esd's in parentheses*

S-C(2)	1.808(11)	C(2)-S-C(2')	97.5(6)
S-C(2')	1.780(9)	S-C(2)-C(3)	112.1(7)
C(3)-C(4)	1.522(11)	S-C(2')-C(3')	111.9(7)
C(3')-C(4)	1.517(11)	C(2)-C(3)-C(4)	111.4(7)
C(2)-C(3)	1.499(13)	C(3)-C(4)-C(3')	113.4(6)
C(2')-C(3')	1.522(12)	C(4)-C(3')-C(2')	113.5(6)
C(4)-C(5)	1.543(9)	C(3)-C(4)-C(5)	110.8(6)
C(4)-N	1.500(10)	C(3')-C(4)-C(5)	113.9(6)
C(5)-O(1)	1.226(10)	C(4)-C(5)-O(1)	116.7(6)
C(5)-O(2)	1.225(10)	C(4)-C(5)-O(2)	119.1(6)
		C(3)-C(4)-N	105.7(6)
		C(3')-C(4)-N	107.3(5)
		C(5)-C(4)-N	104.8(5)
		O(1)-C(5)-O(2)	124.1(6)

Table 4. *Torsion angles (deg) of the thiapyran ring, with esd's in parentheses*

C(4)-C(3)-C(2)-S	-63.1(8)
C(3)-C(2)-S-C(2')	58.3(7)
C(2)-S-C(2')-C(3')	-55.5(7)
S-C(2')-C(3')-C(4)	59.8(8)
C(2')-C(3')-C(4)-C(3)	-57.5(8)
C(3')-C(4)-C(3)-C(2)	58.9(8)
Mean torsion angle (ϕ_{av})	58.9

Table 5. Equation of and deviation from the best plane through the atoms C(4), C(5), O(1), and O(2)

$0.9050x + 0.3493y - 0.2424z = 6.4913$	
Deviations (Å)	
C(4)	-0.003
C(5)	0.009
O(1)	-0.003
O(2)	-0.003
N	-1.200

Table 6. Hydrogen bond lengths (Å) and angles (deg)

Donor	Acceptor	$D \cdots A$	$H \cdots A$	$D-H \cdots A$	$C-D \cdots A$	$H-D \cdots A$
C(4)-N	$\cdots O(1)^i$	2.77	1.80	150	117.7	19
C(4)-N	$\cdots O(2)^{ii}$	2.77	1.64	168	106.2	7
C(4)-N	$\cdots O(1)^{iii}$	2.86	2.18	139	111.8	30
C(4)-N	$\cdots O(2)^{iii}$	3.14	2.32	163	107.1	12
<i>Symmetry code</i>						
(i)		$1 - x,$	$1 - y,$	$- z$		
(ii)		$1 - x,$	$- y,$	$- z$		
(iii)		$x,$	$\frac{1}{2} - y,$	$\frac{1}{2} + z$		

closely to the mean $C^\alpha-N$ distance of 1.487Å observed in amino acids (Marsh and Donohue, 1967) and is within the limits of the accuracy of the structure determination. It is interesting to note that all three C-C-N angles in this structure are significantly smaller than the tetrahedral value, whereas only one of these angles is found to be significantly smaller in the structure of 1-HEX.

Molecular conformation

The thiapyran ring in this structure exists in a "puckered chair" form, as indicated by the torsion angles about bonds given in Table 4. The mean torsion angle (ϕ_{av}) of 58.9° shows the significant puckering of the thiapyran ring, as it is larger than the value of 54.7° expected for the *chair* form of cyclohexane (Bixon and Lifson, 1967). The puckering of the thiapyran ring observed in 4-THIA HBR ($\phi_{av} = 56.2^\circ$) is smaller than that found in this structure, and this feature has been attributed to a weak $N \cdots S$ interaction of 3.34Å observed in the structure of 4-THIA HBR. The carboxyl group

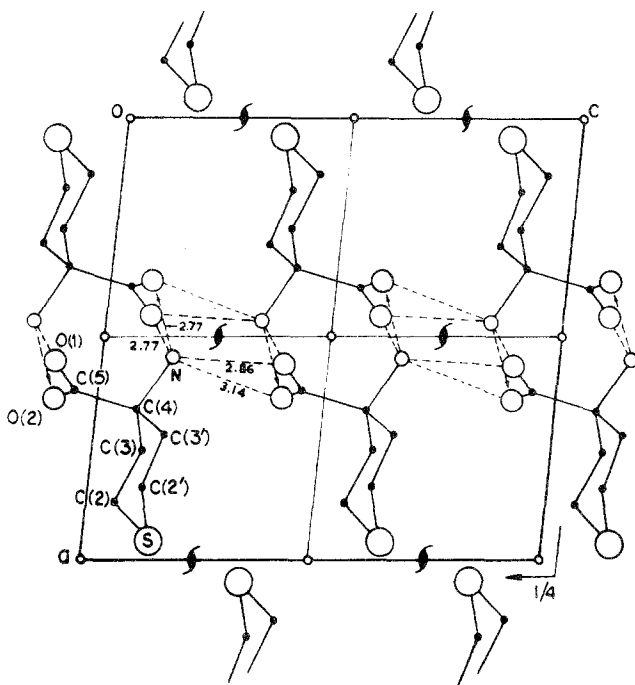


Fig. 1. Packing of the molecule viewed down b .

atoms C(5), O(1), O(2), and C(4) form a mean plane with N deviating from this plane by 1.20 Å. The equation of the plane and deviations of atoms from it are given in Table 5.

Molecular packing and hydrogen bonding

The packing of the molecule viewed down b is shown in Fig. 1. The nitrogen (NH_3^+) has four nearest neighbor oxygens, O(1)(i), O(2)(ii), O(1)(iii), and O(2)(iii), for favorable hydrogen bonds at distances of 2.77, 2.77, 2.86, and 3.14 Å, respectively. H(2) enters into a bifurcated hydrogen bond with O(1)(iii) and O(2)(iii), where the hydrogen to acceptor oxygen distances are 2.18 and 2.32 Å, respectively. In the case of the structure of 1-HEX, the nitrogen to O(2)(iii) distance of 3.25 Å (not mentioned in the paper) was not considered to be a hydrogen bonded contact because it lies outside the limit of $N-H \cdots O$ type of hydrogen bonds (Stout and Jensen, 1968). The projection down the C(4)–N bond of 4-THIA is shown in Fig. 2, indicating all the hydrogen bonded contacts of N. The relevant hydrogen bond distances

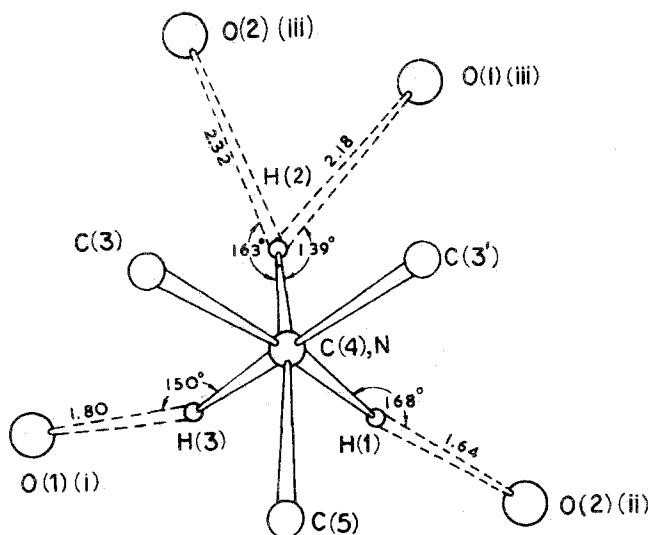


Fig. 2. Projection down the C(4)-N bond of 4-THIA.

and angles are given in Table 6. The packing of the structure of 4-THIA is very similar to that of 1-HEX. The significant differences in packing between the two structures are for the sulfur atom and its immediate neighbors.

Acknowledgments

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