likely to contribute electrons to the conduction bands than absorb them.

We are grateful to the National Research Council of Canada for support of this work. We also acknowledge the help of Mr V. Fronz in preparing single crystals of Cr_5Al_8 and V_5Al_8, and for much work in attempting to establish the identity of the various Cr–Al γ-phases.

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The Crystal and Molecular Structure of (±)-Azabiotin Hydrochloride Monohydrate, the Nitrogen Analog of Biotin

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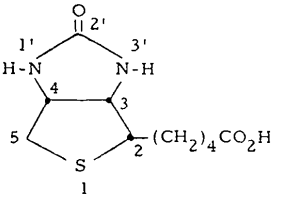
The structure and stereochemistry of (±)-azabiotin hydrochloride has been accurately established by three-dimensional X-ray diffraction techniques. The crystals are triclinic, $P\bar{1}$, with crystal data $a = 7{\cdot}628\,(2)$, $b = 13{\cdot}145\,(3)$, $c = 7{\cdot}185\,(1)$ Å, $\alpha = 99{\cdot}70\,(1)$, $\beta = 106{\cdot}37\,(2)$, $\gamma = 90{\cdot}27\,(2)°$, $Z = 2$ formula units of $C_{10}H_{20}ClN_3O_4$. The structure was solved by direct methods and refined to a conventional discrepancy index $R = 0{\cdot}039$ for 1455 diffractometer data for which $I \geq 3\sigma(I)$. The crystals comprise a racemic mixture of the azabiotin cation protonated at N(1), with one chloride anion and one water of solvation per cation. The three asymmetric centers have the same relative stereochemistry found in biotin. The relevant bond distances and angles are similar to those found in biotin and dethiobiotin. This includes an elongated carbonyl distance [1·243 (4) Å] and shortened C–N distances [1·344 (4) and 1·349 (4) Å] in the ureido moiety. The bicyclic ring system is highly asymmetric in contrast to those found in biotin and dethiobiotin. The valeryl side chain is fully extended and essentially strain-free. A complex three-dimensional hydrogen-bonding network binds the entire crystal together.

Introduction

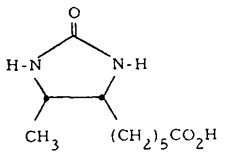
Biotin (I), a member of the B complex of vitamins, serves as a coenzyme for several important carboxylases including propionyl CoA carboxylase, β-methylcrotonyl CoA carboxylase, acetyl CoA carboxylase, and oxalosuccinate-acetyl CoA transcarboxylate (Langer & Gyorgy, 1968). The vitamin is covalently linked to the enzyme *via* an amide bond involving the carboxyl group of biotin and the ϵ-amino group of a lysine residue. There is much evidence to suggest that, prior to transfer to the substrate, carbon dioxide

becomes fixed to N(1′) of biotin while the latter is bound to the enzyme (Knappe, 1970).

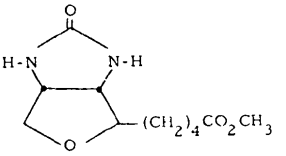


(I)

It is well known that some analogs of biotin have growth-promoting properties in microorganisms comparable to those of the natural vitamin. For example, (+)-dethiobiotin (II) (Melville, Dittmer, Brown & du Vigneaud, 1943), (+)-biotin methyl ester (Kögl & Tönnis, 1936), and (+)-biotin sulfoxide methyl ester (du Vigneaud, 1945) promote the growth of *Saccharomyces cerevisiae* to the same extent as (+)-biotin. (±)-Oxybiotin methyl ester (III) (Winnick, Hofmann, Pilgrim & Axelrod, 1945) has 10–16% of the activity of (+)-biotin in this organism.

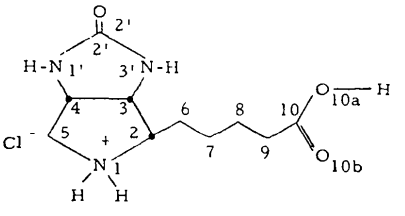


(II)



(III)

As part of a program to synthesize analogs of biotin we have recently reported (Wormser & Abramson, 1976) the development of a facile total synthesis of (±)-azabiotin hydrochloride (IV) in which the S atom of biotin is replaced by a N atom. This analog is envisioned to be a useful biochemical tool in elucidating the active sites of the various carboxylases which utilize biotin. The synthetic procedure developed for (IV) left no doubt concerning the *cis* fusion of the two rings. However, the stereochemical arrangement of the valeric acid side chain relative to the ureido ring remained in question. The present report clarifies the all-*cis* relationship of the three adjacent chiral centers and further defines the important structural features of this molecule.



(IV)

Experimental

A single crystal of (±)-azabiotin hydrochloride with a maximum dimension of 0·25 mm was mounted on a glass fiber with epoxy cement. Initial X-ray examination (Syntex $P2_1$) by rotation and axial photographs yielded approximate lattice constants and showed the crystal to be of triclinic symmetry. Least-squares refinement of 15 reflections with 2θ values between 18 and 30°, which were centered with Mo $K\alpha$ radiation ($\lambda = 0{\cdot}71069$ Å) diffracted from a highly oriented graphite monochromator in the parallel orientation, was used to determine final lattice constants and orientation parameters. The crystal data are $a = 7{\cdot}628\,(2)$, $b = 13{\cdot}145\,(3)$, $c = 7{\cdot}185\,(1)$ Å, $\alpha = 99{\cdot}70\,(1)$, $\beta = 106{\cdot}37\,(2)$, $\gamma = 90{\cdot}27\,(2)°$, $D_c = 1{\cdot}207$ g cm^{-3}, $Z = 2$ formula units of $C_{10}H_{20}ClN_3O_4$, $\mu_a = 2{\cdot}53$ cm^{-1}.

Intensity data for $\sin\theta/\lambda < 0{\cdot}595$ were collected with a scan range from $2\theta(\text{Mo } K\alpha_1) - 1{\cdot}0°$ to $2\theta(\text{Mo } K\alpha_2) + 1{\cdot}0$ and a scan rate of 2·02 deg min^{-1}. Backgrounds were measured at each end of the scan for a total time equal to one-half the scan time. Three standard reflections, measured after every 97 reflections, were statistically constant. Standard deviations (Schmonsees, 1974) were assigned to the intensities according to the formula: $\sigma(I) = [\sigma^2_{\text{counter}} + 0{\cdot}04I^2]^{1/2}$, where $\sigma_{\text{counter}} = (I + 4B)^{1/2}$, I = net intensity, and B = total background counts. Extinction and absorption corrections were not applied. Of the 1966 data examined, 1455 data had net intensities greater than $3\sigma(I)$ and were used in the solution and refinement of the structure.

The structure was solved in $P\bar{1}$ by direct methods with *MULTAN* (Germain, Main & Woolfson, 1971) using 168 reflections with $|E| > 1{\cdot}30$. Of the 16 solutions generated from three origin-fixing reflections and four starting reflections, the non-trivial solution with the largest combined figure of merit was chosen. A computer search of the E map based on this solution revealed the positions of the chloride anion and all non-hydrogen atoms of the cation. Isotropic least-squares refinement (Busing, Martin & Levy, 1962) yielded $R = \Sigma \| F_o| - |F_c\| / \Sigma |F_o| = 0{\cdot}243$. A difference Fourier synthesis (Zalkin, 1966) showed the presence of a water of solvation in the lattice whose inclusion reduced R to 0·149. At this point, idealized positions were calculated (Zalkin, 1974) for all H atoms attached to C atoms and were included after verification from the electron density map. A difference synthesis based upon this model clearly revealed, as the largest peaks, all remaining H atoms at reasonable locations including those on the water molecule. This map unambiguously established the location of the extra proton. Full-matrix least-squares refinement was carried out varying positional and anisotropic thermal parameters of non-hydrogen atoms; H atoms were included as fixed contributions with $B = 4{\cdot}0$ Å^2 at positions described

above. Final discrepancy indices are $R = 0.039$, $wR = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2} = 0.049$. The error of fit is 1.61 and the maximum residual electron density is 0.22 e Å^{-3}. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974).

Table 1 contains the atomic parameters and Table 2 important distances and angles. Tables 3 and 4 contain chemically important torsion angles and least-squares planes respectively.*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32240 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

The crystallographic study shows the crystals of (±)-azabiotin hydrochloride to comprise a racemic mixture of the azabiotin cation, protonated at N(1), with one chloride anion and one water of solvation per cation. The entire structure is bound together by a complex three-dimensional network of hydrogen bonds. The three asymmetric centers have the same relative stereochemistry found in biotin.

The stereochemistry and thermal ellipsoids (Johnson, 1965; Glick, Anderson, Butler & Corey, 1976) of one formula unit are shown stereoscopically in Fig. 1. Fig. 2 is a stereoscopic view of the packing including hydrogen bonding.

Results and discussion

The following discussion will describe the molecular

Table 1. *Atomic parameters for azabiotin hydrochloride monohydrate (with the standard deviations of the last digit in parentheses)*

Anisotropic thermal parameters are of the form: $T = \exp[-\frac{1}{4}(h^2a^{*2}B_{11} + \cdots + 2hka^*b^*B_{12} + \cdots)]$; the isotropic thermal equivalent has the form: $T = \exp[-B_{iso}(\sin^2\theta/\lambda^2)]$, where $B_{iso} = [V^2 \det(B_{ij})]^{1/3}$.

	x	y	z		x	y	z
Cl	0.6009 (1)	0.1575 (1)	0.3091 (1)	H(3)	0.0966	0.2887	0.7750
N(1′)	0.1460 (4)	0.0879 (2)	0.8998 (4)	H(4)	0.3186	0.2176	0.9980
N(3′)	−0.0239 (3)	0.1453 (2)	0.6432 (4)	H(5)*a*	0.5301	0.1685	0.8421
N(1)	0.3396 (3)	0.1347 (2)	0.5646 (4)	H(5)*b*	0.4326	0.0524	0.7938
O(2′)	−0.1475 (3)	0.0154 (2)	0.7526 (3)	H(2)	0.3185	0.2916	0.6130
O(10)*a*	−0.3356 (4)	0.5654 (2)	−0.0665 (4)	H(6)*a*	0.0164	0.1815	0.3126
O(10)*b*	−0.3166 (5)	0.4065 (2)	−0.2049 (4)	H(6)*b*	0.1932	0.2314	0.2672
C(2′)	−0.0192 (5)	0.0773 (2)	0.7653 (5)	H(7)*a*	0.1222	0.3988	0.3993
C(3)	0.1310 (4)	0.2204 (2)	0.7157 (4)	H(7)*b*	−0.0551	0.3487	0.4433
C(4)	0.2651 (4)	0.1673 (2)	0.8721 (5)	H(8)*a*	−0.1964	0.2970	0.1045
C(5)	0.4121 (5)	0.1266 (3)	0.7790 (5)	H(8)*b*	−0.0151	0.3370	0.0535
C(2)	0.2305 (4)	0.2297 (2)	0.5621 (5)	H(9)*a*	−0.0631	0.5100	0.1872
C(6)	0.1132 (4)	0.2387 (2)	0.3574 (5)	H(9)*b*	−0.2483	0.4687	0.2288
C(7)	0.0232 (5)	0.3412 (3)	0.3530 (5)	H(1′)	0.1750	0.0590	1.0000
C(8)	−0.0938 (5)	0.3504 (3)	0.1461 (5)	H(3′)	−0.1310	0.1610	0.5490
C(9)	−0.1698 (5)	0.4568 (3)	0.1388 (5)	H(1)*a*	0.4390	0.1390	0.4940
C(10)	−0.2789 (5)	0.4716 (3)	−0.0614 (6)	H(1)*b*	0.2660	0.0760	0.4940
O(*w*)	0.5310 (4)	0.3886 (2)	0.3959 (4)	H(*w*)*a*	0.5610	0.3300	0.3660
				H(*w*)*b*	0.5780	0.4050	0.5380
				H(10)*a*	−0.4070	0.5740	−0.2200

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}	B_{iso}
Cl	3.08 (4)	4.64 (5)	3.68 (4)	0.66 (3)	0.60 (3)	1.42 (4)	3.68 (2)
N(1′)	3.70 (13)	3.93 (14)	2.83 (13)	−0.19 (11)	0.05 (11)	1.79 (11)	3.20 (6)
N(3′)	2.78 (12)	4.28 (14)	3.00 (13)	−0.05 (10)	0.21 (10)	1.90 (11)	3.06 (6)
N(1)	2.90 (12)	3.11 (13)	2.93 (13)	0.43 (10)	0.74 (10)	0.72 (10)	2.96 (6)
O(2′)	4.26 (12)	3.83 (11)	3.24 (11)	−0.98 (10)	0.83 (10)	0.98 (9)	3.60 (5)
O(10)*a*	6.82 (15)	3.64 (12)	4.61 (14)	0.89 (11)	−0.25 (12)	1.39 (11)	4.78 (7)
C(10)*b*	13.42 (26)	5.28 (16)	3.27 (14)	3.30 (16)	−1.17 (15)	0.45 (13)	5.90 (8)
C(2′)	3.65 (16)	2.89 (15)	2.41 (15)	0.08 (13)	0.79 (13)	0.74 (12)	2.90 (7)
C(3)	3.24 (15)	2.56 (14)	2.28 (14)	0.25 (12)	0.54 (12)	0.57 (12)	2.68 (7)
C(4)	3.38 (15)	3.06 (15)	2.37 (15)	0.09 (12)	0.18 (12)	0.72 (12)	2.94 (7)
C(5)	3.45 (16)	4.09 (17)	3.06 (16)	0.51 (13)	0.20 (13)	1.13 (13)	3.50 (8)
C(2)	3.05 (15)	2.56 (14)	2.74 (15)	0.00 (11)	0.65 (12)	0.83 (12)	2.74 (7)
C(6)	3.46 (15)	3.36 (16)	2.45 (15)	0.25 (12)	0.77 (12)	0.78 (12)	3.02 (7)
C(7)	3.92 (16)	3.36 (15)	2.73 (16)	0.41 (13)	0.65 (13)	0.94 (13)	3.27 (7)
C(8)	4.27 (17)	3.62 (17)	2.79 (16)	0.47 (14)	0.56 (14)	1.12 (14)	3.45 (8)
C(9)	4.48 (17)	3.80 (17)	2.91 (16)	0.66 (14)	0.60 (14)	1.04 (14)	3.64 (8)
C(10)	4.81 (19)	3.58 (19)	3.17 (18)	0.44 (15)	0.47 (15)	0.94 (16)	3.82 (9)
O(*w*)	7.61 (16)	4.68 (13)	4.01 (13)	1.89 (12)	0.27 (12)	1.53 (11)	5.01 (6)

stereochemistry of the cation and compare it with that found in biotin (DeTitta, Edmonds, Stallings & Donohue, 1976; Traub, 1956, 1959) and dethiobiotin (Chen, Parthasarathy & DeTitta, 1976). For convenience, the numbering scheme used [see (IV)] corresponds to that adopted in the other two structures and the discussion parallels that presented for these two structures.

Table 2. *Distances* (Å) *and angles* (°) *for azabiotin hydrochloride monohydrate*

Those hydrogens which were assigned calculated positions are 1·00 Å from the atoms to which they are bonded.

C(2′)–O(2′)	1·243 (4)	C(6)–C(7)	1·516 (4)
C(2′)–N(1′)	1·344 (4)	C(7)–C(8)	1·528 (4)
C(2′)–N(3′)	1·349 (4)	C(8)–C(9)	1·520 (5)
C(1′)–C(4)	1·456 (4)	C(9)–C(10)	1·490 (5)
N(3′)–C(3)	1·452 (4)	C(10)–O(10)*a*	1·312 (4)
C(3)–C(4)	1·555 (4)	C(10)–O(10)*b*	1·188 (4)
C(4)–C(5)	1·516 (5)	N(1′)–H(1′)	0·85
C(3)–C(2)	1·525 (4)	N(3′)–H(3′)	0·95
C(5)–N(1)	1·505 (4)	N(1)–H(1)*a*	1·03
C(2)–N(1)	1·503 (4)	N(1)–H(1)*b*	0·93
C(2)–C(6)	1·515 (4)	O(10)*a*–H(10)*a*	1·11

O(2′)···H(1)*b* ($\bar{x}, \bar{y}, 1-z$)	1·94
O(10)*b*···H(*w*)*b* ($x-1, y, z-1$)	1·79
H(10)*a*···O(*w*) ($\bar{x}, 1-y, \bar{z}$)	1·51
O(2′)···H(1′) ($\bar{x}, \bar{y}, 2-z$)	2·23
Cl···H(1)*a*	2·09
Cl···H(3′) ($x+1, y, z$)	2·27
Cl···H(*w*)*a*	2·27
O(2′)···N(1) ($\bar{x}, \bar{y}, 1-z$)	2·795 (3)
O(10)*b*···O(*w*) ($x-1, y, z-1$)	2·743 (4)
O(10)*a*···O(*w*) ($\bar{x}, 1-y, \bar{z}$)	2·587 (4)
O(2′)···N(1′) ($\bar{x}, \bar{y}, 2-z$)	3·034 (3)
Cl···N(1)	3·111 (3)
Cl···N(3′) ($x+1, y, z$)	3·200 (3)
Cl···O(*w*)	3·076 (3)
O(2′)–C(2′)–C(1′)	126·6 (3)
O(2′)–C(2′)–N(3′)	124·9 (3)
N(1′)–C(2′)–N(3′)	108·6 (3)
C(2′)–N(1′)–C(4)	112·5 (3)
C(2′)–N(3′)–C(3)	112·3 (3)
N(1′)–C(4)–C(3)	102·1 (2)
N(3′)–C(3)–C(4)	101·6 (2)
C(3)–C(4)–C(5)	105·6 (3)
C(4)–C(3)–C(2)	101·2 (2)
C(4)–C(5)–N(1)	105·4 (2)
C(3)–C(2)–N(1)	102·2 (2)
C(5)–N(1)–C(2)	105·0 (2)
C(3)–C(2)–C(6)	116·9 (2)
C(1)–C(2)–C(6)	112·9 (3)
C(2)–C(6)–C(7)	112·2 (3)
C(6)–C(7)–C(8)	112·1 (3)
C(7)–C(8)–C(9)	111·9 (3)
C(8)–C(9)–C(10)	114·2 (3)
C(9)–C(10)–O(10)*a*	113·3 (3)
C(9)–C(10)–O(10)*b*	125·2 (3)
O(10)*a*–C(10)–O(10)*b*	121·5 (3)

Ureido ring

Much of the discussion regarding biological activity in biotin-type structures has centered on the unusual C=O and C–N bond distances found in these compounds. In azabiotin hydrochloride, the C=O distance of 1·243 (4) Å is consistent with the values of 1·25 and 1·244 Å reported in biotin and dethiobiotin respectively. These distances are significantly longer than those found in barbiturate structures (Craven, Cusatis, Gartland & Vizzini, 1973) and compare with that of 1·270 Å found in urea (Caron & Donohue, 1969). The C–N distances of 1·344 (4) and 1·349 (4) Å compare favorably with those of 1·34 (av.) and 1·347 Å (av.) for biotin and dethiobiotin respectively. These are shorter than the 1·370 Å found in barbiturate structures and are comparable with the 1·326 Å value reported for urea. It may thus be seen that the presence of resonance forms with a partial negative charge on the carbonyl O noted for biotin and dethiobiotin is also important in azabiotin. This five-membered ring in biotin was found to be virtually planar. In azabiotin hydrochloride and in dethiobiotin, this ring departs significantly from planarity in a comparable fashion. In azabiotin hydrochloride, C(3) is displaced 0·26 Å from the plane formed by the other four atoms.

Table 3. *Torsion angles and asymmetry parameters in azabiotin hydrochloride monohydrate* (°)

These torsion angles are based on a right-handed Klyne–Prelog convention (Glick *et al.*, 1976)

φ_2	C(2′)–N(3′)–C(3)–C(4)	16·9
$\varphi_{2'}$	C(2′)–N(1′)–C(4)–C(3)	10·2
	N(3′)–C(3)–C(4)–N(1′)	−15·2
φ_1, φ_5	C(3)–N(3′)–C(2′)–N(1′)	−11·3
$\varphi_{1'}, \varphi_{5'}$	C(4)–N(1′)–C(2′)–N(3′)	0·0
	C(5)–C(4)–C(3)–C(2)	−12·9
φ_3	N(1)–C(2)–C(3)–C(4)	32·9
$\varphi_{3'}$	N(1)–C(5)–C(4)–C(3)	−12·3
φ_3, φ_8	C(5)–N(1)–C(2)–C(3)	−41·3
$\varphi_{4'}, \varphi_{8'}$	C(2)–N(1)–C(5)–C(4)	33·7
φ_6	C(2′)–N(3′)–C(3)–C(2)	129·1
$\varphi_{6'}$	C(2′)–N(1′)–C(4)–C(5)	−103·6
φ_7	N(3′)–C(3)–C(2)–N(1)	−77·1
$\varphi_{7'}$	N(1′)–C(4)–C(5)–N(1)	99·3
	C(3)–C(2)–C(6)–C(7)	69·2
	N(1)–C(2)–C(6)–C(7)	−172·6
	C(2)–C(6)–C(7)–C(8)	−180·0
	C(6)–C(7)–C(8)–C(9)	−174·9
	C(7)–C(8)–C(9)–C(10)	−177·6
	C(8)–C(9)–C(10)–O(10)*a*	176·8
	C(8)–C(9)–C(10)–O(10)*b*	4·5

$$\varphi_U = \sqrt{[(\varphi_1 + \varphi_{1'})^2 + (\varphi_2 + \varphi_{2'})^2/2]} = 20{\cdot}76\,°.$$

$$\varphi_T = \sqrt{[(\varphi_3 + \varphi_{3'})^2 + (\varphi_4 + \varphi_{4'})^2/2]} = 15{\cdot}53\,°.$$

$$\varphi_B = \sqrt{[(\varphi_5 + \varphi_{5'})^2 + (\varphi_6 + \varphi_{6'})^2 + (\varphi_7 + \varphi_{7'})^2 + (\varphi_8 + \varphi_{8'})^2/4]} = 18{\cdot}22°.$$

Table 4. *Least-squares planes in azabiotin hydrochloride monohydrate*

The equations of the planes are $aX + bY + cZ = d$ where X, Y, and Z are orthonormal vectors (Å) in the directions corresponding to **a***, **b**, and **a*** × **b** respectively.

Equations

Plane	Atoms	*a*	*b*	*c*	*d*
1	N(1′), C(2′), N(3′)	0·539	−0·589	−0·602	−4·10
2	N(1′), C(4), C(3), N(3′)	0·586	−0·497	−0·640	−4·29
3	C(2), C(3), C(4), C(5)	−0·400	−0·759	−0·514	−3·92
4	C(2), N(1), C(5)	−0·833	−0·549	−0·072	−2·07

Displacements (Å)

Plane 1		Plane 2		Plane 3		Plane 4	
N(1′)	0·0	N(1′)	−0·063	C(2)	−0·049	C(2)	0·0
C(2′)	0·0	C(4)	0·089	C(3)	0·075	N(1)	0·0
N(3′)	0·0	C(3)	−0·089	C(4)	−0·076	C(5)	0·0
C(3)	−0·265	N(3′)	0·063	C(5)	0·049	C(3)	0·984
C(4)	0·002	C(2′)	−0·073	N(1)	0·564	C(4)	0·811
O(2′)	0·000	O(2′)	−0·182				

Angles between planes

1–2	6·4°	2–3	61·9°
1–3	57·3	2–4	99·7
1–4	94·7	3–4	38·1

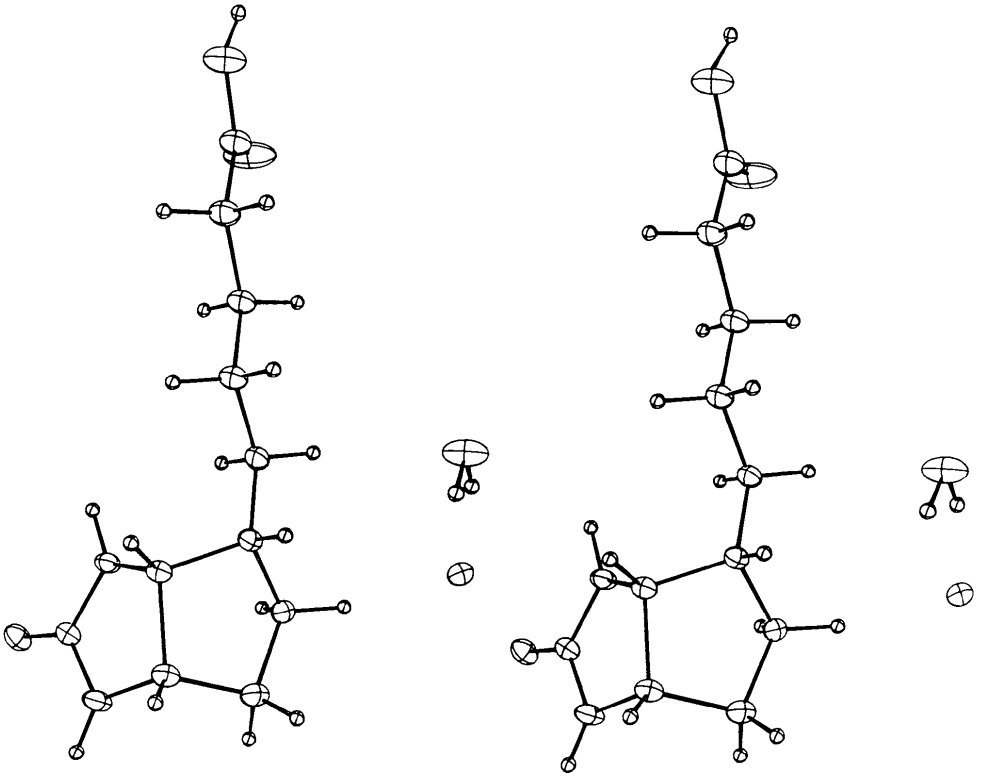


Fig. 1. Stereoscopic view of azabiotin hydrochloride monohydrate with 20% probability ellipsoids.

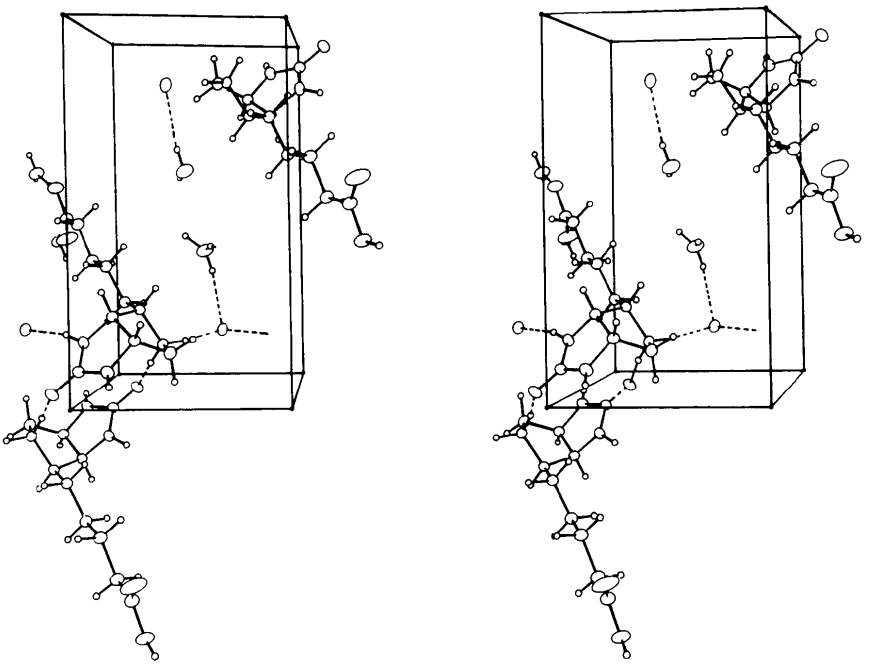


Fig. 2. Packing of azabiotin hydrochloride monohydrate as viewed down the *c* axis. The dashed lines represent hydrogen bonds.

C_4N *ring*

This ring is not present in dethiobiotin. If we compare the ring in azabiotin hydrochloride and biotin we find comparable C—C bond distances. The C—N(1) distances in azabiotin hydrochloride correspond to a normal sp^3–sp^3 C—N bond distance. The substitution of the N atom for a S atom leads to a much larger angle subtended at the hetero-atom (C—N—C, 105·0° *vs* C—S—C, 89·4°). The angles subtended at C(3) and C(4) average 103·4° in azabiotin *vs* 109·2° in biotin; this may also result from the smaller N atom. These latter angles are significantly larger in dethiobiotin (116·3° av.) where there are no ring constraints.

Symmetry of ring system

A calculation for determining the presence of mirror symmetry bisecting a ring system has been reported by Duax & Rohrer (1973). The asymmetry parameters φ_U for the ureido ring, φ_T for the C_4N ring and φ_B for the bicyclic ring are given in Table 3. A value of $\varphi = 0°$ would correspond to exact mirror symmetry and values of 15–35° to high asymmetry with respect to a given plane. These values were reported to range from 2·5 to 4·3° for biotin and dethiobiotin. In azabiotin hydrochloride these values are $\varphi_U = 20·8$, $\varphi_T = 15·5$ and $\varphi_B = 18·2°$. Thus the rings are clearly far more asymmetric in azabiotin hydrochloride than in the previously reported structures. It is significant to emphasize the similarity in bond distances in the three compounds in spite of the differences in conformation.

Valeryl chain

The valeryl chain is in its fully extended form. Torsion angles along the chain are all within 5° of the strain-preferred *anti* conformation. Of particular interest is the value of 180·0° for the torsion angle about C(6)—C(7). This angle was −179·6° in dethiobiotin, but biotin had a highly strained value of 73·9°. The large twisting in biotin has been ascribed (DeTitta *et al.*, 1976) to an attempt to reduce nonbonded interactions between C(7) and S(1). It is interesting to note that the nitrogenous system does not require such a twist even though the hetero ring system is comparable.

The torsion angles about C(9)—C(10) are 176·8 and 4·5° approximating the minimum energy conformation. These values were −163·5 and 21·9° in dethiobiotin and −70·4 and 111·3° in biotin. Thus again, the azabiotin hydrochloride appears to be a system which is stereochemically quite strain-free.

Hydrogen bonding

The entire structure is strongly hydrogen-bonded. Each chloride ion forms three hydrogen bonds with Cl···H distances in the range 2·09–2·27 Å. Each water molecule forms three hydrogen bonds, one from O(*w*) to the carboxylic acid proton (1·51 Å) and two from water protons to a chloride ion and the carboxylic C=O oxygen (1·79 Å).

Perhaps of most interest is the hydrogen bond formed between O(2′) and the proton on a N(1) of an adjacent molecule (1·94 Å). In addition O(2′) may form

a weak hydrogen bond to a hydrogen on N(1′) on a related molecule (2·23 Å). In each of the previous biotin-like structures, O(2′) is hydrogen-bonded to the H on the carboxylate group. The consistent presence of some intermolecular hydrogen bonding to O(2′) is a significant factor in terms of the redistribution of electrons in the ureido ring and in terms of the nucleophilicity of the ureido ring.

We wish to thank Dr George DeTitta for stimulating discussions regarding the significant structural features of the biotin-like structures and for preprints of the structural studies of biotin and dethiobiotin.

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