

Fig. 3. Projection de la structure selon l'axe cristallin c .

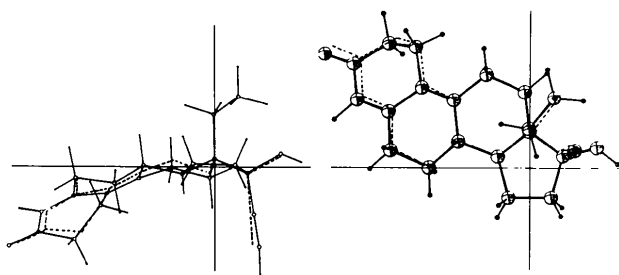


Fig. 4. Conformère isolé théorique (traits pleins) et conformère expérimental cristallin (traits pointillés) représentés dans le repère D .

l'aide de la mécanique moléculaire (Delettré & Mornon, 1980) (Fig. 4). Comme pour RU3097 le champ cristallin ne doit donc induire que de faibles contraintes sur la géométrie moléculaire.

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3-Chloro-3-cyano-1-cyclohexyl-4-(phenylthio)-2-azetidinone. A Substituted Monocyclic β -Lactam

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Abstract. $C_{16}H_{17}ClN_2OS$, orthorhombic, $Pbca$, $a = 10.331(2)$, $b = 15.212(2)$, $c = 21.661(4)$ Å, $V = 3404(1)$ Å³, $Z = 8$, $D_m = 1.269$, $D_c = 1.252$ Mg m⁻³, $\mu(\text{Mo } K\alpha) = 0.346$ mm⁻¹. The four-membered ring of the β -lactam is nearly planar, with a *trans* stereochemistry of the Cl and *S*-phenyl substituents and long C–C bonds of 1.566 (5) and 1.561 (6) Å.

Introduction. A new and versatile synthetic route to 3-cyano-2-azetidinones (3-cyano- β -lactams) involving the cycloaddition of cyanoketenes to formimidates has recently been developed (Moore, Hernandez & Sing, 1976; Moore, Hernandez & Chambers, 1978). The structure of the title compound was investigated in

order to definitively establish its stereochemistry. This was of importance with respect to the synthetic utility of the methodology as well as for providing structural data used for mechanistic arguments. In addition, we were seeking structural information which might suggest a reason for the unusual observation that many monocyclic β -lactams in this series show antibiotic as well as antifungal activity (Inderlied & Sypher, 1977).

Colorless crystals of the title compound were obtained by recrystallization from hexane/diethyl ether. Preliminary precession photographs showed orthorhombic symmetry with systematic absences ($0kl$, $k \neq 2n$; $h0l$, $l \neq 2n$; $hk0$, $h \neq 2n$) uniquely defining space group $Pbca$ (No. 61). Cell parameters ($T = 296$ K)

were determined by least-squares refinement of the setting angles of 15 reflections with $30^\circ \leq 2\theta \leq 35^\circ$ measured on a Syntex $P2_1$ diffractometer with graphite-monochromatized Mo $K\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$). The crystal used for data collection was a rectangular prism measuring approximately $0.8 \times 0.2 \times 0.2 \text{ mm}$. All independent data with $2^\circ \leq 2\theta \leq 43^\circ$ were collected by the θ - 2θ scan technique in bisecting geometry. Peaks were scanned at a rate of $2.0^\circ \text{ min}^{-1}$ over a range of 2θ from 1.0° below the $K\alpha_1$ peak to 1.1° above the $K\alpha_2$ peak. A stationary background count was taken at each end of the scan for half the scan time. Standard deviations were assigned as described by Corfield, Doedens & Ibers (1967) with $p = 0.05$. Of 1886 reflections measured in this manner, 1231 had peak intensities exceeding background by three or more standard deviations; these data formed the basis for subsequent calculations. Intensities were converted to F^2 values by application of Lorentz and polarization corrections and by scaling to compensate for a small (<2%) decay in standard reflections during data collection.

The structure solution was achieved by use of the direct-methods program *MULTAN 77* (Main, Lesinger, Woolfson, Germain & Declercq, 1977). Full-matrix least-squares refinement employed the local program *UCIGLS* (Doedens, 1978) with anisotropic thermal parameters for all nonhydrogen atoms. The H atoms were located on a difference Fourier map and included in the later stages of refinement at fixed idealized positions (C-H = 0.95 \AA ; tetrahedral or trigonal angles as appropriate) with isotropic temperature factors based on those of the corresponding C

Table 1. *Positional parameters of nonhydrogen atoms*

Throughout this paper, numbers in parentheses are standard deviations of the least significant figures.

	<i>x</i>	<i>y</i>	<i>z</i>
Cl	0.93834 (12)	0.20691 (8)	0.59685 (6)
S	0.81488 (11)	0.46759 (7)	0.53829 (6)
O	1.1668 (3)	0.3011 (2)	0.5046 (6)
N(1)	0.9550 (3)	0.3442 (2)	0.4779 (2)
N(2)	1.0533 (6)	0.4092 (3)	0.6619 (3)
C(1)	1.0560 (5)	0.3175 (3)	0.5126 (2)
C(2)	0.9679 (4)	0.3157 (3)	0.5712 (2)
C(3)	0.8607 (4)	0.3530 (3)	0.5272 (2)
C(4)	1.0119 (5)	0.3687 (4)	0.6222 (3)
C(5)	0.9410 (4)	0.3643 (3)	0.4111 (2)
C(6)	0.8067 (4)	0.3379 (4)	0.3906 (2)
C(7)	0.7914 (5)	0.3563 (4)	0.3217 (2)
C(8)	0.8931 (9)	0.3090 (4)	0.2853 (3)
C(9)	1.0269 (7)	0.3347 (5)	0.3061 (3)
C(10)	1.0449 (5)	0.3181 (4)	0.3754 (2)
C(11)	0.6707 (5)	0.4546 (3)	0.5812 (2)
C(12)	0.6660 (7)	0.4743 (4)	0.6429 (3)
C(13)	0.5505 (12)	0.4665 (5)	0.6746 (4)
C(14)	0.4399 (10)	0.4420 (5)	0.6449 (6)
C(15)	0.4440 (6)	0.4229 (4)	0.5844 (4)
C(16)	0.5589 (6)	0.4287 (3)	0.5518 (2)

atoms. At convergence the final conventional *R* factor was 0.041. In all least-squares refinements, the function minimized was $\sum w(|F_o| - |F_c|)^2$ where $w = 4F_o^2/\sigma^2(F_o^2)$. Scattering factors (including anomalous terms for S and Cl) were taken from *International Tables for X-ray Crystallography* (1974). A final difference Fourier map showed no peaks $>0.3 \text{ e \AA}^{-3}$ and a structure factor calculation for the data not included in the refinement yielded no unreasonably large F_o^2 values.

Positional parameters of nonhydrogen atoms are listed in Table 1 and selected bond distances and angles are given in Table 2.* Fig. 1 provides an overall view of

* Lists of structure factors, thermal parameters, H atom positional parameters and bond distances and angles in the cyclohexyl and phenyl rings have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34582 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond distances (Å) and angles (°) in the central portion of the molecule*

Internal distances and angles within the phenyl and cyclohexyl rings are not included in this table.

N(1)—C(1)	1.348 (5)	C(2)—Cl	1.773 (4)
N(1)—C(3)	1.452 (5)	C(2)—C(4)	1.441 (7)
N(1)—C(5)	1.487 (5)	C(3)—S	1.823 (4)
C(1)—C(2)	1.561 (6)	S—C(11)	1.767 (5)
C(1)—O	1.184 (5)	C(4)—N(2)	1.142 (6)
C(2)—C(3)	1.566 (5)		
C(1)—N(1)—C(3)	97.9 (3)	C(3)—C(2)—C(4)	119.1 (4)
C(1)—N(1)—C(5)	132.8 (4)	N(1)—C(3)—C(2)	86.5 (3)
C(3)—N(1)—C(5)	129.2 (3)	N(1)—C(3)—S	111.0 (3)
N(1)—C(1)—C(2)	90.4 (3)	C(2)—C(3)—S	116.7 (3)
N(1)—C(1)—O	136.8 (4)	C(3)—S—C(11)	100.4 (2)
C(2)—C(1)—O	132.8 (4)	S—C(11)—C(12)	121.2 (5)
C(1)—C(2)—C(3)	85.0 (3)	S—C(11)—C(16)	119.7 (4)
C(1)—C(2)—Cl	111.8 (3)	C(2)—C(4)—N(2)	176.4 (6)
C(1)—C(2)—C(4)	115.4 (4)	N(1)—C(5)—C(6)	108.7 (3)
C(3)—C(2)—Cl	114.0 (3)	N(1)—C(5)—C(10)	109.7 (4)

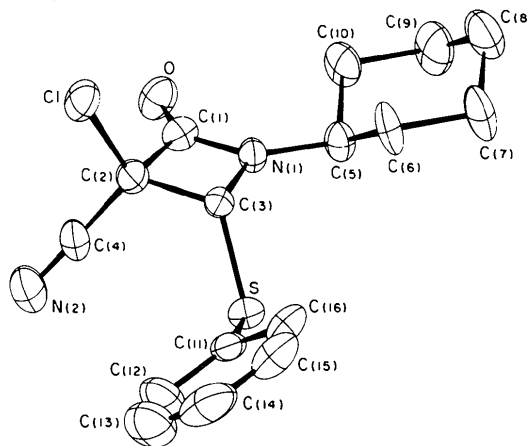


Fig. 1. Perspective view of the molecular structure with the atom-numbering scheme. Hydrogen atoms have been omitted for clarity.

Table 3. Distances and angles within the four-membered ring of five substituted monocyclic 2-azetidiones

Substituents on the four-membered ring					
N	CO- <i>m</i> -BrC ₆ H ₄	<i>p</i> -ClC ₆ H ₄	<i>p</i> -BrC ₆ H ₄	C ₆ H ₅	C ₆ H ₁₁
C(2)	H, H	H, C ₆ H ₅	H, H	C ₆ H ₅ , Cl	CN, Cl
C(3)	H, CH ₃	H, <i>i</i> -C ₃ H ₇	H, H	H, C ₆ H ₅	H, SC ₆ H ₅
Distances (Å)					
C(1)–C(2)	1.52 (1.5)	1.518 (5)	1.518 (7)	1.530 (12)	1.561 (6)
C(2)–C(3)	1.58 (1.5)	1.575 (4)	1.539 (7)	1.602 (10)	1.566 (5)
C(3)–N	1.48 (1.5)	1.481 (4)	1.459 (7)	1.498 (10)	1.452 (5)
N–C(1)	1.40 (1.5)	1.367 (4)	1.363 (7)	1.342 (10)	1.348 (5)
Angles (°)					
C(2)–C(1)–N	–*	93.0 (3)	92.0 (3)	92.9 (6)	90.4 (3)
C(3)–C(2)–C(1)	–	85.5 (3)	85.4 (3)	85.6 (5)	85.0 (3)
N–C(3)–C(2)	–	86.5 (3)	87.9 (3)	84.5 (5)	86.5 (3)
C(1)–N–C(3)	–	95.0 (3)	94.5 (3)	96.9 (6)	97.9 (3)
Reference	Paulus <i>et al.</i> (1969)	Parthasarathy (1970)	Kartha & Ambady (1973)	Colens <i>et al.</i> (1974)	This work

* Angles were not given and could not be calculated from published data.

the molecular structure and a definition of the atom-numbering scheme.

Discussion. The molecular structure of 3-chloro-3-cyano-1-cyclohexyl-4-(phenylthio)-2-azetidione, shown in Fig. 1, confirms in all major respects the structure assigned to this material on the basis of mechanistic considerations (Kunert, Chambers, Mercer, Hernandez & Moore, 1978) and further documented by magnetic resonance experiments (Chambers, Kunert, Hernandez, Mercer & Moore, 1978). The crucial stereochemical feature is the *trans* relationship of the Cl and SC₆H₅ groups. The stereospecificity of the formation of the C(2)–C(3) bond is an important factor in the synthetic utility of the cyanoketene/imidate cycloaddition reaction.

The principal stereochemical features of the central portion of the molecule are similar to those observed in other monocyclic β -lactams (Paulus, Kobelt & Jensen, 1969; Parthasarathy, 1970; Kartha & Ambady, 1973; Colens, Declercq, Germain, Putzeys & Van Meersehe, 1974). In particular, the four-membered ring is nearly planar (maximum deviation from least-squares plane = 0.022 Å) and the ring N atom is within 0.026 Å of the plane defined by C(1), C(3), and C(5). The N(1)–C(1) distance of 1.348 (5) Å is substantially shorter than the value expected for a single bond. In contrast to these results, the fused-ring β -lactam systems found in the penicillins and cephalosporins usually, but not always, exhibit substantial deviations of the ring N atom from its coordination plane and a concomitant nonplanarity of the four-membered ring (Sweet, 1972, and refer-

ences therein; Applegate, Dolfini, Puar, Slusarchyk, Toeplitz & Gougoutas, 1974; Albers-Schönberg *et al.*, 1978).

Since no other structurally characterized β -lactam has cyano or *S*-phenyl substituents and since compounds with similar substitution patterns exhibit somewhat different patterns of chemical reactivity from those of other monocyclic β -lactams, it is reasonable to inquire whether this molecule shows any structural details which depart significantly from those observed for related systems. The pertinent comparative data are tabulated in Table 3. From these data, two principal differences are apparent. The C(1)–C(2) distance of 1.561 (6) Å is very long for a C(*sp*²)–C(*sp*³) bond and longer than previously observed values, which are in the range 1.518–1.530 Å. The ring angle at C(1) is 90.4 (3)°, a value somewhat smaller than the range of 92.0–93.0° found in analogous molecules. A long C(2)–C(3) distance is frequently observed in these systems; the value of 1.566 (5) Å found in the present case fits this pattern. Whether these structural observations may be related to the differences in chemical reactivity or to the biological activity of certain of these substituted β -lactams remains a subject for further investigation.

Other features of the molecular structure are unremarkable. The bond distances within the phenyl and cyclohexyl groups are somewhat shorter than their expected values; this presumably is a consequence of the rather high thermal motion of these groups. The shortest intermolecular contact is 2.25 Å between O and H(3) of an adjacent molecule. All other contacts are comparable to, or greater than, the sum of the appropriate van der Waals radii.

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Zwitterionic Character of Guanosine 5'-Monophosphate (5'-GMP): Redetermination of the Structure of 5'-GMP Trihydrate

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Abstract. $C_{10}H_{14}N_5O_8P \cdot 3H_2O$, $M_r = 417$, $P2_12_12_1$, $a = 10.649$ (2), $b = 6.185$ (1), $c = 25.514$ (4) Å, $Z = 4$, $V = 1680.3$ Å³, $D_o = 1.644$ (floatation in 2-propanol/CHBr₃), $D_c = 1.648$ Mg m⁻³, $\mu = 2.14$ mm⁻¹ (Cu K α). A redetermination of the structure of 5'-GMP·3H₂O [originally reported by Murayama, Nagashima & Shimizu (1969). *Acta Cryst.* **B25**, 2236–2245] has established that the nucleotide exists as a zwitterion with the N(7) site of the base protonated. The three water molecules of hydration bridge the base N(7) and a phosphate oxygen of the same molecule through hydrogen bonding. One of the H atoms on the base N(2) atom appears to be involved in a bifurcated hydrogen bond, while an anionic phosphate O atom simultaneously accepts hydrogen bonds from the base N(1) and N(2) atoms. There is also a hydrogen bond to the ribose ring O(4') atom.

Introduction. Recently, Sundaralingam & Prusiner (1978) predicted zwitterionic character for the free acid

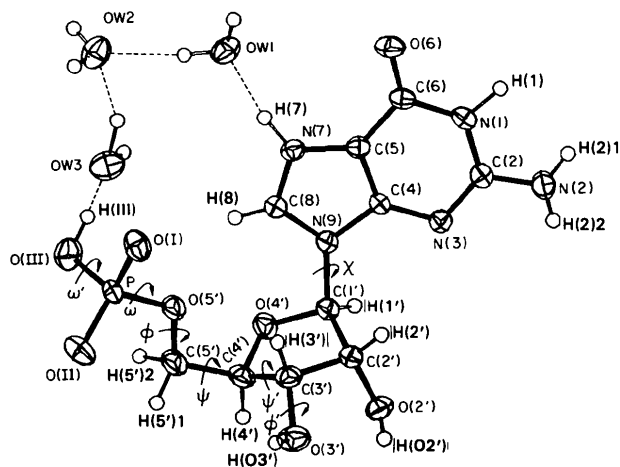


Fig. 1. An ORTEP drawing of 5'-GMP·3H₂O showing the molecular conformation, atom numbering and conformational notations.