Fig. 1. Perspective view of (4) with thermal ellipsoids scaled to 50% probability. H atoms are denoted by spheres of arbitrary radius.

z) 3.265 (9) Å, and C(2″)···O(1)(x, y, −1 + z) 3.346 (7) Å.

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Structure of a Substituted 2-Thiohydantoin

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Abstract. S-[1-(3-Acetyl-5-oxo-2-thioxo-2,3,4,5-tetrahydro-1H-imidazol-4-yl)ethyl] ethanethioate, $C_9H_{12}N_2O_3S_2$, $M_r = 260.3$, monoclinic, $P2_1/n$, $a = 8.643 (1)$, $b = 15.554 (1)$, $c = 8.898 (1)$ Å, $\beta = 92.05 (1)°$, $V = 1195.4 (3)$ Å^3, $Z = 4$, D_m(flotation) = 1.448 (5), $D_x = 1.446$ Mg m^{-3}, λ(Cu Kα) = 1.5418 Å, μ(Cu Kα) = 3.96 mm^{-1}, $F(000) = 544$, $T = 293 (1)$ K, final $R = 0.046$ for 1708 observed data. Atoms of the thiohydantoin nucleus are approximately coplanar, and the N(3) acetyl group is twisted by about 12° from the mean plane. N(1) of the hydantoin ring is the donor atom in an intermolecular hydrogen bond with the carbonyl oxygen of the N(3) acetyl substituent, the N(1)···O(6) distance being 2.873 (3) Å. These interactions link the molecules into chains along the [101] direction in the crystal.
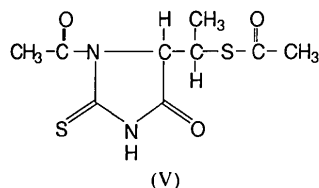
Introduction. Application of the thiocyanate degradation procedure (Schlack & Kumpf, 1926) to a peptide (I) converts the C-terminal amino acid into a substituted thiohydantoin derivative (II), which can

be subsequently cleaved to give a shortened (by one amino-acid residue) peptide (III), together with the C-terminal amino acid thiohydantoin (IV), which can be identified (usually by HPLC analysis).

(i) (CH₃CO)₂O, CH₃COOH, SCN⁻   (ii) Base or acid
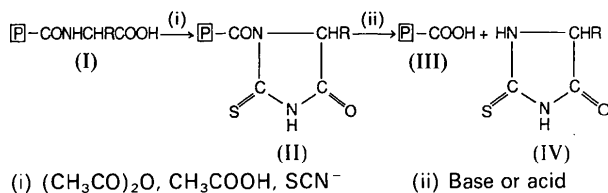
The shortened peptide can then be subjected to further degradation cycles. In this way, the sequencing of the peptide from its C-terminal end is possible. Indeed, recent improvements to the Schlack–Kumpf procedure have enabled the sequences of sizeable peptides to be determined from their C-terminal ends (Inglis, Wilshire, Casagranda & Laslett, 1989, and references cited therein). However, certain amino-acid residues, e.g. those of serine and threonine, have not been successfully sequenced by the thiocyanate degradation procedure.

We have examined the reactions of serine and threonine with a mixture of sodium thiocyanate, acetic anhydride and acetic acid under the Schlack–Kumpf reaction conditions and, from each reaction, have isolated compounds which contain two acetyl groups (^{1}H NMR spectra) and, surprisingly, an extra sulfur atom. The compound isolated from the reaction with threonine was obtained as crystals suitable for an X-ray crystallographic analysis. Its structure proved to be the thiohydantoin (V).

At present, the origin of the sulfur atom in the side chain at C(4) must remain a matter for speculation. However, it is possible that the reactive species responsible for the introduction of the acetylthio group is acetyl thiocyanate (CH₃COSCN), a known reagent (usually prepared *in situ*) (Elmore, Ogle, Fletcher & Toseland, 1956).

Experimental. Colourless tabular crystals from an *n*-heptane/dichloromethane mixture. A fragment *ca* 0.395 × 0.395 × 0.290 mm aligned on a Rigaku-AFC diffractometer; cell parameters determined by least squares from 2θ values for 25 strong reflections ($42 < 2\theta < 82°$); Cu *Kα* radiation (graphite crystal monochromator, $\lambda = 1.5418$ Å); ω–2θ scan, scan

Table 1. *Final atomic coordinates* (S × 10⁵; C, N, O × 10⁴; H × 10³) *and equivalent isotropic temperature factors for the non-*H *atoms (isotropic for* H) *with e.s.d.'s in parentheses*

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}/B_{iso}(Å²)
N(1)	4618 (3)	−2234 (1)	9913 (3)	2.84 (5)
C(2)	4787 (3)	−3037 (2)	9307 (3)	2.46 (5)
S(2)	62940 (8)	−36516 (5)	96666 (9)	3.70 (2)
N(3)	3466 (2)	−3180 (1)	8402 (2)	2.25 (4)
C(4)	2367 (3)	−2460 (2)	8494 (3)	2.34 (5)
C(5)	3239 (3)	−1831 (2)	9526 (3)	2.85 (6)
O(5)	2834 (2)	−1138 (1)	9938 (3)	4.27 (6)
C(6)	3153 (3)	−3818 (2)	7322 (3)	2.49 (5)
O(6)	2031 (2)	−3712 (1)	6481 (2)	3.10 (4)
C(7)	4165 (4)	−4587 (2)	7219 (4)	3.66 (8)
C(8)	791 (3)	−2725 (2)	9104 (3)	2.67 (5)
S(8)	9313 (8)	−30351 (4)	110783 (7)	3.29 (2)
C(9)	−392 (3)	−2000 (2)	8887 (4)	3.59 (7)
C(10)	1284 (3)	−4168 (2)	10971 (3)	3.28 (7)
O(10)	1500 (2)	−4529 (1)	9798 (2)	4.19 (5)
C(11)	1254 (5)	−4607 (3)	12469 (4)	4.81 (9)
H(1)	537 (4)	−200 (2)	1041 (4)	4.5 (8)
H(4)	219 (3)	−220 (2)	753 (4)	3.0 (6)
H(7a)	518 (4)	−441 (2)	695 (4)	4.1 (7)
H(7b)	363 (4)	−495 (2)	648 (4)	5.0 (8)
H(7c)	418 (4)	−482 (3)	812 (5)	5.3 (9)
H(8)	45 (3)	−325 (2)	848 (3)	2.9 (5)
H(9a)	−133 (4)	−217 (2)	922 (4)	5.0 (8)
H(9b)	−54 (4)	−187 (2)	782 (4)	4.9 (8)
H(9c)	−5 (4)	−155 (3)	942 (4)	5.6 (10)
H(11a)	167 (6)	−517 (4)	1245 (6)	9.3 (14)
H(11b)	160 (6)	−425 (3)	1326 (6)	8.3 (14)
H(11c)	21 (6)	−469 (3)	1281 (6)	8.5 (13)

Table 2. *Bond lengths* (Å), *valence and selected torsion angles* (°) *with e.s.d.'s in parentheses*

N(1)—C(1)	1.370 (4)	C(5)—O(5)	1.195 (3)
N(1)—C(5)	1.379 (4)	C(6)—O(6)	1.215 (3)
C(2)—S(2)	1.638 (3)	C(6)—C(7)	1.487 (4)
C(2)—N(3)	1.391 (3)	C(8)—S(8)	1.822 (3)
N(3)—C(4)	1.473 (3)	C(8)—C(9)	1.530 (4)
N(3)—C(6)	1.401 (3)	S(8)—C(10)	1.791 (3)
C(4)—C(5)	1.523 (4)	C(10)—O(10)	1.206 (3)
C(4)—C(8)	1.540 (4)	C(10)—C(11)	1.499 (5)

C(2)—N(1)—C(5)	114.8 (2)	C(4)—C(5)—O(5)	128.3 (2)
N(1)—C(2)—S(2)	123.4 (2)	N(3)—C(6)—O(6)	117.2 (2)
N(1)—C(2)—N(3)	106.1 (2)	N(3)—C(6)—C(7)	120.8 (2)
S(2)—C(2)—N(3)	130.6 (2)	O(6)—C(6)—C(7)	122.0 (2)
C(2)—N(3)—C(4)	111.3 (2)	C(4)—C(8)—S(8)	112.4 (2)
C(2)—N(3)—C(6)	130.1 (2)	C(4)—C(8)—C(9)	110.7 (2)
C(4)—N(3)—C(6)	117.9 (2)	S(8)—C(8)—C(9)	109.8 (2)
N(3)—C(4)—C(5)	102.5 (2)	C(8)—S(8)—C(10)	102.4 (1)
N(3)—C(4)—C(8)	113.4 (2)	S(8)—C(10)—O(10)	122.4 (2)
C(5)—C(4)—C(8)	112.6 (2)	S(8)—C(10)—C(11)	113.1 (2)
N(1)—C(5)—C(4)	105.3 (2)	O(10)—C(10)—C(11)	124.5 (2)
N(1)—C(5)—O(5)	126.4 (2)		

N(1)—C(2)—N(3)—C(4)	−3.2 (3)	C(4)—N(3)—C(6)—O(6)	3.5 (3)
C(2)—N(3)—C(4)—C(5)	2.8 (3)	C(8)—C(4)—C(5)—O(5)	−58.6 (4)
N(3)—C(4)—C(5)—N(1)	−1.3 (3)	C(5)—C(4)—C(8)—C(9)	75.3 (3)
C(4)—C(5)—N(1)—C(2)	−0.6 (3)	C(4)—C(8)—S(8)—C(10)	−90.5 (2)
C(5)—N(1)—C(2)—N(3)	2.3 (3)	C(8)—S(8)—C(10)--O(10)	6.2 (3)
S(2)—C(2)—N(3)—C(6)	−13.1 (4)	C(9)—S(8)—C(10)—C(11)	−172.9 (2)

rate 2° min⁻¹, scan range $\Delta\omega = 1.2° + 0.5°\tan\theta$, $2\theta_{max} = 130°$, 10 s stationary background counts; three standard reflections ($\overline{2}0\overline{2}$, $\overline{1}5\overline{1}$, 320) monitored every 50 reflections, no significant intensity variation; 1977 unique data, h − 10 to 10, k 0 to 18, l 0 to 10, 1708 for which $I \geq 1.5\sigma(I)$ used for refinement; intensities corrected for Lorentz and polarization effects and for absorption, transmission factors

0.2497 to 0.4116. Structure solved by direct methods and refined with *SHELX*76 (Sheldrick, 1976). Refinement with anisotropic temperature factors given to the S, O, N and C atoms and isotropic for H atoms converged at $R = 0.046$, $wR = 0.058$, $S = 1.64$ (194 parameters varied); function minimized $\sum w(|\Delta F|)^2$ with $w = [\sigma^2(|F|) + 0.00095|F|^2]^{-1}$; at convergence $(\Delta/\sigma)_{max} = 0.003$, $(\Delta\rho)_{max}$, $(\Delta\rho)_{min} = +0.46$, -0.38 e Å^{-3}; an isotropic extinction correction of the form $F = F_c\{1 - [3.4\,(2) \times 10^{-6}F^2/\sin\theta]\}$ applied to the calculated structure amplitudes. Atomic scattering factors and anomalous-dispersion factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 99, 149). Figures were prepared from the output of *ORTEP*II (Johnson, 1976). Major calculations performed on a VAX8800 computer.

Discussion. Final atomic coordinates are given in Table 1.* The molecular conformation and numbering scheme are illustrated in Fig. 1, while bond lengths, valence angles and selected torsion angles, the latter referring to the $(4S,8R)$ enantiomer, are given in Table 2.

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* Lists of structure amplitudes, anisotropic thermal parameters, and short intermolecular approaches have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54483 (21 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.
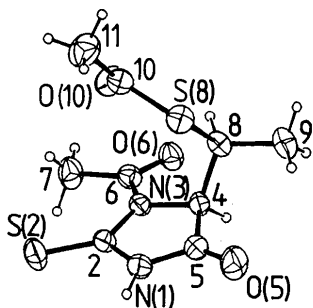

Fig. 1. Perspective view of (V) [$(4S,8R)$ enantiomer] with thermal ellipsoids scaled to 50% probability. The C symbol is omitted and H atoms are denoted by spheres of arbitrary radius.
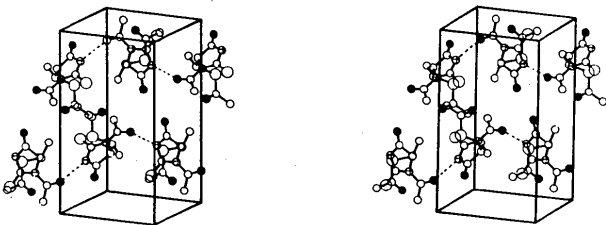

Fig. 2. Stereoview of the crystal packing. Direction of projection a and the b axis is vertical.

The atoms of the thiohydantoin nucleus are co-planar to within $+0.027\,(5)$ Å. There is, however, a slight degree of ring pucker as reflected in the ring torsion angles (see Table 2), while the acetyl group at N(3) is twisted by about 12° from the mean plane of the hydantoin nucleus. Atoms C(8), S(8), C(10), O(10), C(11) of the acetylthio side chain at C(4) are approximately coplanar [r.m.s.d. = 0.051 (5) Å], and the orientation of the group relative to the hydantoin ring is given by the torsion angles N(3)—C(4)—C(8)—S(8) and C(8)—S(8)—C(10)—O(10) of 67.8 (3) and 6.2 (3)° respectively. The bond lengths and angles are in good agreement with those reported for comparable structures. The C(2)—S(2) bond of 1.638 (3) Å has strong double-bond character; *cf.* pure C=S double-bond length 1.608 Å (Abrahams, 1956). As generally observed in acylthiols (Agafonov, Legendre & Rodier, 1989; Deguire & Brisse, 1988; Kakehi, Ito, Ito, Yotsuya & Nagata, 1985), the C(sp^3)—S(8) bond is significantly longer than the C(sp^2)—S(8) bond, in this case by 0.031 (3) Å. To minimize interaction between S(2) and the acetyl group at N(3) both the exocyclic angles, S(2)—C(2)—N(3) and C(2)—N(3)—C(6), have expanded by about 10° from the standard trigonal value of 120°.

The crystal packing is illustrated in Fig. 2. The molecules are linked into chains along the [101] direction by hydrogen bonds in which N(1) of the hydantoin ring is the donor atom to the carbonyl oxygen O(6) of the acetyl substituent at N(3) of a glide-related molecule. For these interactions the N(1)···O(6)(1/2 + x, $-1/2 - y$, 1/2 + z), N(1)—H(1), H(1)···O(6) distances are 2.873 (3), 0.85 (4) and 2.03 (4) Å respectively with the N(1)—H(1)···O(6) angle 172 (3)°. Apart from two short intermolecular contacts, O(10)···O(10)($-x$, $-1 - y$, $2 - z$) 3.012 (3) Å and C(10)···O(10) 3.202 (3) Å, all other contacts are greater than 3.34 Å.

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