Acta Cryst. (1990). C46, 299–301

Structure of 3-(4-Nitrobenzoyl)-4-thiazolidinecarboxylic Acid Ethyl Ester

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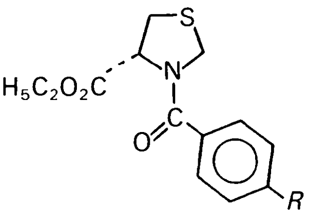
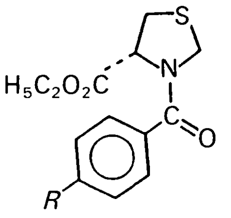
(*Received* 10 *May* 1989; *accepted* 13 *June* 1989)

Abstract. $C_{13}H_{14}N_2O_5S$, $M_r = 310{\cdot}315$, monoclinic, $P2_1$, $a = 5{\cdot}607\ (5)$, $b = 13{\cdot}296\ (5)$, $c = 9{\cdot}833\ (8)$ Å, $\beta = 90{\cdot}67\ (5)°$, $V = 733\ (1)$ Å^3, $Z = 2$, $D_x = 1{\cdot}406$ Mg m^{-3}, λ(Mo $K\bar{\alpha}$) = 0·7107 Å, $\mu = 0{\cdot}245$ mm^{-1}, $F(000) = 324$, $T = 295$ K, final $R = 0{\cdot}045$ for 1280 unique observed reflections. In the solid state the C_6H_4—NO_2 group is *s-trans* with respect to the ethyl ester: this structure corresponds to the major component in solution. The N(2)—C(7) bond length shows that N—CO has a double-bond character. The thiazolidine ring may be considered as of the envelope type.

Introduction. ^{1}H and ^{13}C NMR spectra (Hamri, 1985) of amides of 4-thiazolidinecarboxylic acid ethyl ester, unsubstituted on C2, realized at different temperatures, indicate the existence, in solution, of two different and inseparable conformations.



Major



Minor

The crystallographic analysis of the title compound ($R = NO_2$) (Hamri, Pera, Valenti & Boucherle, 1985) has been performed to compare the conformation of this molecule in solution and in the solid state.

Experimental. Crystals grown from a chloroform solution. Crystal size: 0·20 × 0·20 × 0·20 mm. Density not measured. Enraf–Nonius CAD-4 diffractometer, graphite monochromator. Systematic absences: $0k0$ ($k = 2n$). 20 reflections ($10{\cdot}5 < \theta < 13°$) for refining the unit-cell dimensions. ω scan. 2212 non-zero unique reflections collected ($3 < \theta < 30°$), $\pm h$, k, l; $h_{\max} = 7$, $k_{\max} = 18$, $l_{\max} = 13$. Scan width = 1·20°, scan speed variable between 0·03 and 0·01° s^{-1}. Total background measuring time between 20 and 60 s. Two orientation reflections ($0\bar{7}\bar{2}$ and $0\bar{8}1$) and one intensity reflection ($\bar{2}25$), no variation. Lorentz and polarization corrections. Structure solved by direct methods (*MULTAN*77, Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1977). Anisotropic full-matrix least-squares refinement (on F) for non-H atoms, isotropic for H atoms. Unit weights, final $R = 0{\cdot}045$ ($wR = 0{\cdot}041$) for 1280 reflections ($I > 2\sigma_I$). No extinction correction. $S = 0{\cdot}447$. Max. $\Delta/\sigma = 0{\cdot}19$ [z of H(9)]. Max. peak height in final difference Fourier synthesis: 0·242 e Å^{-3}. H atoms located by difference Fourier map. Scattering factors and f' and f'' from *International Tables for X-ray Crystallography* (1974). Enraf–Nonius (1977) *SDP* employed for all calculations. Computer used: VAX-780.

Discussion. Atomic coordinates are reported in Table 1, main interatomic distances and bond angles in the atomic arrangement in Table 2.* Crystal packing is shown in Fig. 1. In the solid state, the title compound has only one conformation. In this conformation:

- The configuration of C(4) fixed by the starting molecule, the cysteine ethyl ester hydrochloride, has not been modified during the amidification process and is still *R*.
- The groups C_6H_4—NO_2 and COO—C_2H_5 are in an *s-trans* situation.

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* Lists of structure factors, anisotropic thermal parameters for non-H atoms, H-atom coordinates, and bond lengths and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52324 (16 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/90/020299-03$03.00

Table 1. *Final atomic coordinates and B_{eq} values*

The e.s.d.'s are given in parentheses.

$$B_{\text{eq}} = (4/3)\textstyle\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
C(1)	0·903 (1)	−0·2706 (6)	0·2514 (7)	8·4 (2)
C(2)	0·150 (1)	−0·2503 (5)	0·2340 (7)	8·1 (2)
C(3)	0·6539 (9)	0·1187 (4)	0·6270 (5)	5·0 (1)
C(4)	0·5379 (7)	0·0916 (3)	0·4926 (5)	3·83 (9)
C(5)	0·6019 (9)	−0·0137 (3)	0·4468 (6)	5·3 (1)
C(6)	0·8173 (8)	0·1255 (3)	0·3060 (5)	4·6 (1)
C(7)	0·4765 (7)	0·2379 (3)	0·3494 (4)	3·32 (7)
C(8)	0·5661 (6)	0·3079 (3)	0·2410 (4)	3·04 (7)
C(9)	0·7799 (7)	0·3600 (3)	0·2604 (4)	3·55 (8)
C(10)	0·8473 (8)	0·4325 (3)	0·1693 (4)	3·90 (9)
C(11)	0·7005 (8)	0·4515 (3)	0·0585 (4)	3.88 (9)
C(12)	0·5085 (9)	−0·1011 (4)	0·9648 (5)	4·4 (1)
C(13)	0·4243 (7)	0·3275 (3)	0·1273 (4)	3·87 (9)
N(1)	0·7681 (7)	0·5306 (3)	−0·0381 (4)	5·3 (1)
N(2)	0·6095 (6)	0·1579 (3)	0·3824 (3)	3·41 (7)
O(1)	0·2613 (8)	−0·2888 (3)	0·3706 (4)	7·32 (9)
O(2)	0·3373 (7)	−0·4371 (3)	0·2776 (4)	7·5 (1)
O(3)	0·2882 (5)	0·2589 (2)	0·4049 (3)	4·50 (7)
O(4)	0·3533 (8)	0·0452 (4)	0·1382 (4)	8·8 (1)
O(5)	0·0493 (8)	0·0768 (4)	0·0153 (4)	8·4 (1)
S	0·8870 (3)	0·000	0·3662 (2)	7·08 (4)

– The N(2)—C(7) bond distance (1·337 Å), if compared with the N(2)—C(4) distance (1·457 Å) or with N(2)—C(6) (1·459 Å), indicates a double-bond character for N—CO. The N atom is thus in an sp^2 hybridization state. This double-bond character is confirmed by the planarity observed for the C(6)—N(2)—C(7)—C(8) group of atoms for which the torsion angle is about 10° and by the sum of the valency angles (359·7°) around this N atom.

– The values of the dihedral angles corresponding to the three following planes: *P*(1): C(4), N(2), C(6), S (thiazolidine ring); *P*(2): N(2), C(7), C(8), O(3) (amide group); *P*(3): C(8), C(9), C(11), C(12), C(13), N(1), O(4), O(5), C(10) (nitrophenyl group), show that the amide group and the thiazolidine ring are almost coplanar [*P*(1),*P*(2) ~ 10°]. In addition the dihedral angles of the mean plane of the nitrophenyl group [*P*(3)] with the plane *P*(2) of the amide group and with the plane *P*(1) of the thiazolidine ring are 55 and 65° respectively.

– The thiazolidine ring can be considered as of the envelope type given the small value of the torsion angle in *P*(1) (about 7·5°) and the small value of the maximum distance from this mean plane [*P*(1)—N(1) = 0·048 Å] showing almost coplanarity. The atom C(5) is located at a distance of 0·64 Å from this plane in the opposite direction to the ethyl ester group as indicated by the value of the torsion angle C(5)—C(4)—N(2)—C(6)(−31·5°). Such a conformation has already been reported for the thiazolidine ring in *cyclo*(-glycyl-4-thiaprolyl-) (Haar, Fermandjian, Robert, Lefebvre-Soubeyran & Savrda, 1976) and in 2-benzoylimino-3-methyl-1,3-thiazolidine (Kálmán & Párkányi, 1980).

Table 2. *Main interatomic distances* (Å) *and bond angles* (°)

E.s.d.'s are given in parentheses.

C(1)—C(2)	1·42 (2)	C(1)—C(2)—O(1)	102 (1)
C(2)—O(1)	1·56 (1)	C(2)—O(1)—C(3)	117·5 (7)
C(3)—O(1)	1·32 (1)	O(1)—C(3)—O(2)	123·5 (8)
C(3)—O(2)	1·20 (1)	C(4)—C(3)—O(1)	112·9 (7)
C(3)—C(4)	1·51 (1)	C(5)—C(4)—N(2)	105·7 (7)
C(4)—C(5)	1·52 (1)	C(3)—C(4)—C(5)	112·3 (7)
C(5)—S	1·80 (1)	C(4)—C(5)—S	104·6 (5)
S—C(6)	1·811 (7)	C(5)—S—C(6)	92·7 (3)
C(6)—N(2)	1·459 (9)	S—C(6)—N(2)	105·9 (5)
N(2)—C(7)	1·337 (8)	C(4)—N(2)—C(6)	115·6 (6)
N(2)—C(4)	1·457 (9)	C(4)—N(2)—C(7)	120·3 (6)
C(7)—O(3)	1·226 (8)	C(6)—N(2)—C(7)	123·8 (6)
C(7)—C(8)	1·505 (9)	N(2)—C(7)—O(3)	123·6 (6)
C(8)—C(9)	1·396 (9)	O(3)—C(7)—C(8)	118·1 (6)
C(9)—C)10)	1·372 (10)	N(2)—C(7)—C(8)	118·3 (5)
C(10)—C11)	1·381 (10)	C(7)—C(8)—C(9)	120·2 (6)
C(11)—C(12)	1·382 (10)	C(7)—C(8)—C(13)	119·5 (6)
C(12)—C(13)	1·368 (11)	C(9)—C(8)—C(13)	119·9 (6)
C(13)—C(8)	1·389 (9)	C(8)—C(9)—C(10)	120·2 (6)
C(11)—N(1)	1·470 (9)	C(9)—C(10)—C(11)	118·5 (7)
N(1)—O(4)	1·206 (8)	C(11)—N(1)—O(4)	119·7 (8)
N(1)—O(5)	1·213 (9)	O(4)—N(1)—O(5)	122·5 (8)
		C(11)—N(1)—O(5)	117·8 (7)
		C(10)—C(11)—C(12)	122·3 (6)
		C(10)—C(11)—N(1)	119·0 (7)
		C(12)—C(11)—N(1)	118·7 (7)
		C(13)—C(12)—C(11)	118·8 (7)
		C(12)—C(13)—C(8)	120·2 (7)

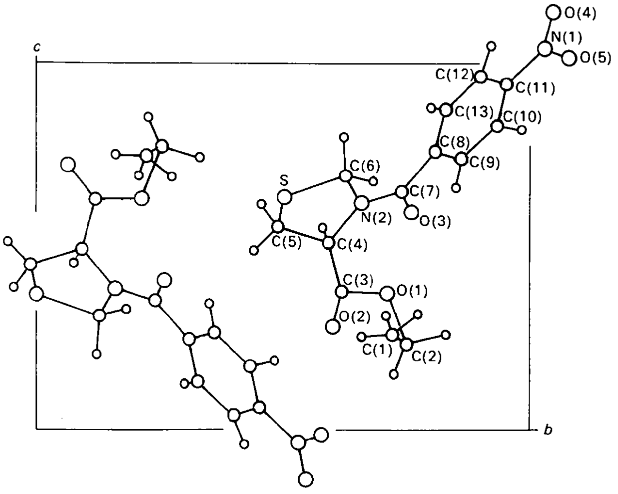

Fig. 1. Crystal packing.

From the ^{1}H and ^{13}C NMR studies this atomic arrangement corresponds to the major component in solution. The two conformations observed in solution differ essentially in the geometry of the amide group.

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Acta Cryst. (1990). C**46**, 301–303

Structure of Tetrahydro-*N*-methyl-2-(2-pyridinyl)-2-thiophenecarbothioamide* (Picartamide)

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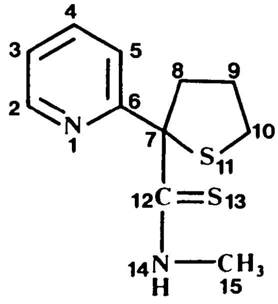
(*Received* 5 *April* 1989; *accepted* 7 *June* 1989)

Abstract. $C_{11}H_{14}N_2S_2$, $M_r = 238{\cdot}37$, monoclinic, $P2_1/c$, $a = 8{\cdot}760\,(3)$, $b = 8{\cdot}732\,(2)$, $c = 16{\cdot}353\,(4)$ Å, $\beta = 112{\cdot}02\,(5)^\circ$, $V = 1185{\cdot}3\,(5)$ Å^3, $Z = 4$, $D_m = 1{\cdot}334\,(2)$, $D_x = 1{\cdot}336$ g cm^{-3}, $\lambda(\text{Cu }K\alpha) = 1{\cdot}5418$ Å, $\mu = 37{\cdot}53$ cm^{-1}, $F(000) = 504$, $T = 293$ K, $R = 0{\cdot}045$ for 1983 observed reflections. The tetrahydro-2-thiophene ring takes a β-envelope configuration and is linked with the thiocarboxamide group by an intramolecular N—H···S hydrogen bond. The NH group is intermolecularly hydrogen-bonded to the pyridine N atom, thus forming a 'cyclic' dimer structure between two centrosymmetrically related molecules.

Introduction. The regulation of gastric acid secretion is very useful for peptic ulcer therapy. H^+,K^+-ATPase inhibitors (ARIs) have been receiving increasing interest (Clissold & Campoli-Richards, 1986; Sachs, Carlsson, Lindberg & Wallmark, 1988), since the enzyme has been recognized as the acid pump involved in the terminal steps of the gastric acid secretory process.

Picartamide [*N*-methyl-2-(2-pyridyl)tetrahydro-2-thiophenethiocarboxamide] (1) could be considered to be a H^+,K^+-ATPase inhibitor inasmuch as it is a potent inhibitor of gastric acid secretion induced by histamide, pentagastric, carbachol and dibutyryl cyclic AMP in rats (Deregnaucourt & Hardy-Houis, 1982) and has no anticholinergic or antihistaminic property (Aloup, Bouchaudon, Farge, James, Deregnaucourt & Hardy-Houis, 1987).



(1)

In order to consider the relationship between the structures and activities of ARIs, it is of special importance to know their stable conformations. This paper deals with the crystal structure of picartamide.

Experimental. Cubic crystals of picartamide were grown from a chloroform/methylene dichloride mixture. Crystal density was measured by the flotation method using a CCl_4–C_6H_6 mixture. A well shaped crystal with approximate dimensions $0{\cdot}2 \times 0{\cdot}2 \times 0{\cdot}3$ mm was mounted on a Rigaku AFC-5 computer-controlled diffractometer with graphite-monochromated Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å). Unit-cell dimensions were determined by a least-squares fit of 2θ values of 25 reflections ($50 < 2\theta < 61^\circ$). Intensities were measured by the ω–2θ scan technique

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