Acta Crystallographica Section B
Structural Science
ISSN 0108-7681

Supramolecular assembling using synthons with NH—CO(S)—CS—NH and NH—CO—CO—NH functionalities: crystal structures of (*S*,*S*)-*N*,*N*′-monothiooxalyldileucine methyl ester and its dithio analogue

Biserka Kojić-Prodić,[a]* Berislav Perić,[a] Zoran Štefanić,[a] Anton Meden,[b] Janja Makarević,[a] Milan Jokić[a] and Mladen Žinić[a]

[a]Rudjer Bošković Institute, PO Box 180, HR-10002, Zagreb, Croatia, and [b]Faculty of Chemistry and Chemical Technology, University of Ljubljana, POB 537, 1001 Ljubljana, Slovenia

Correspondence e-mail: kojic@rudjer.irb.hr

Received 25 July 2003
Accepted 17 December 2003

To compare the structural properties of oxalamide and thiooxalamide groups in the formation of hydrogen bonds suitable for supramolecular assemblies a series of retropeptides was studied. Some of them, having oxalamide bridges, are gelators of organic solvents and water. However, retropeptides with oxygen replaced by the sp^2 sulfur have not exhibited such properties. The crystal structures of the two title compounds are homostructural, *i.e.* they have similar packing arrangements. The monothio compound crystallizes in the orthorhombic space group $P2_12_12_1$ with two molecules in the asymmetric unit arranged in a hydrogen-bond network with an approximate 4_1 axis along the crystallographic *b* axis. However, the dithio and dioxo analogues crystallize in the tetragonal space group $P4_1$ with similar packing patterns and hydrogen-bonding systems arranged in agreement with a crystallographic 4_1 axis. Thus, these two analogues are isostructural having closely related hydrogen-bonding patterns in spite of the different size and polarity of oxygen and sulfur which serve as the proton acceptors.

1. Introduction

In order to understand the gelating properties of the small organic molecules, particularly amino acid derivatives having functionalities with high hydrogen-bonding capabilities, a series of retropeptides with oxalamide bridges was synthesized, structurally characterized and their gelation properties were determined (Makarević *et al.*, 2001, 2003). We focused on ambidextrous gelators that gelatinize both lipophilic organic solvents and water (Jokić *et al.*, 1995). The gelation properties of L-*N*,*N*′-oxalylbis(ValOH) and *rac*-*N*,*N*′-oxalylbis(PhgOH) were studied by X-ray structure analysis, transmission (TEM) and scanning (SEM) electron microscopy, FTIR and NMR (Makarević *et al.*, 2001). Supramolecular assembling in the solid state governed by extensive hydrogen bonding can be studied in detail by X-ray diffraction methods (using single-crystal and fibre diffraction) to obtain closer insight into hydrogen-bond formation and rupture during gelation processes. For this purpose the roles of the oxalamide and thiooxalamide functionalities in hydrogen bonding were studied. So far, we have also studied the hydrogen-bonding motifs in the crystal structures of *meso*-*N*,*N*′-oxalyldivaline (Perić *et al.*, 2001*a*) and 2,2′-*N*,*N*′-oxalyldiiminobis(3-phenylpropaneamide) dimethyl sulfoxide solvate (Perić *et al.*, 2001*b*). In the compounds synthesized the presence of more potential

Table 1
Experimental table.

	I	II
Crystal data		
Chemical formula	$C_{16}H_{28}N_2O_5S$	$C_{16}H_{28}N_2O_4S_2$
M_r	360.46	376.52
Cell setting, space group	Orthorhombic, $P2_12_12_1$	Tetragonal, $P4_1$
a, b, c (Å)	12.562 (9), 16.156 (5), 21.086 (8)	11.3877 (4), 11.3877 (4), 15.9829 (6)
V (Å^3)	4279 (4)	2072.66 (13)
Z	8	4
D_x (Mg m^{-3})	1.119	1.207
Radiation type	Cu $K\alpha$	Mo $K\alpha$
No. of reflections for cell parameters	20	1504
θ range (°)	9–19	2.5–23.0
μ (mm^{-1})	1.55	0.27
Temperature (K)	293 (2)	293 (2)
Crystal form, colour	Prism, yellow	Prism, yellow
Crystal size (mm)	0.4 × 0.2 × 0.15	0.5 × 0.2 × 0.2
Data collection		
Diffractometer	Enraf–Nonius CAD4	KappaCCD
Data collection method	Non-profiled $\omega/2\theta$ scans	CCD rotation images, thick slices
Absorption correction	ψ scan	None
T_{min}	0.752	–
T_{max}	0.791	–
No. of measured, independent and observed reflections	9699, 8972, 4033	2866, 2851, 2608
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.035	0
θ_{max} (°)	76.4	25.0
Range of h, k, l	$0 \Rightarrow h \Rightarrow 15$ $0 \Rightarrow k \Rightarrow 20$ $-26 \Rightarrow l \Rightarrow 26$	$-12 \Rightarrow h \Rightarrow 12$ $-8 \Rightarrow k \Rightarrow 8$ $-17 \Rightarrow l \Rightarrow 17$
No. and frequency of standard reflections	3 every 120 min	–
Intensity decay (%)	5	–
Refinement		
Refinement on	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.060, 0.174, 1.01	0.038, 0.112, 1.10
No. of reflections	8972	2851
No. of parameters	433	217
H-atom treatment	Mixture of independent and constrained refinement	Mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0634P)^2 + 0.8826P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0638P)^2 + 0.7469P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.002	<0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.24, −0.16	0.20, −0.21
Absolute structure	Flack (1983)	Flack (1983)
Flack parameter	−0.01 (3)	0.33 (2)
Rogers parameter	5	–

Computer programs used: *CAD4 Express* (Enraf–Nonius, 1994), *Collect* (Nonius BV, 1997–2000), *HKL Scalepack* (Otwinowski & Minor, 1997), *XCAD4* (Harms & Wocadlo, 1995), *HKL Denzo and Scalepack* (Otwinowski & Minor, 1997, *SHELX*97 (Sheldrick, 1997), *ORTEP-3 for Windows* (Farrugia, 1997), *PLATON* (Spek, 2003), *WinGX publication routines* (Farrugia, 1999).

donor and acceptor functionalities in the molecules would be preferred. However, due to the extremely low solubility of the compounds with a free terminal carboxyl group, an analogous ester was used. The structures of the two novel thioretropeptides (I) and (II) were determined and compared with the structure of the dioxo analogue (III) solved by Karle *et al.* (1994; refcode YIDGAT; data retrieved from Cambridge Structural Database, CSD; Allen, 2002). In addition to the crystal engineering aspect, retropeptides are very interesting for protein engineering as well. They can enhance stability toward enzymatic degradation or they can modify the native conformation required for higher selectivity in biological activity (Puiggali & Subirana, 1998; Subirana, 1997).

2. Experimental

2.1. Synthesis and chemical characterization

^{1}H and ^{13}C NMR spectra were recorded on a Varian 300 spectrometer (300/75 MHz); IR spectra were recorded in KBr pallets on a Perkin–Elmer 297 spectrometer. Optical rotations were measured on an optical activity AA-10 automatic polarimeter using a wavelength of 589.3 nm. Melting points (uncorrected) were determined on a Kofler hot-stage apparatus.

2.1.1. (*S,S*)-*N,N*′-Monothiooxalyl-bis-leucine methyl ester (I). A solution of *N,N*′-oxalyl-*bis*-L-leucine methyl ester (0.692 g, 2.009 mmol) and Lawesson's reagent (0.408 g, 1.009 mmol) in a dry benzene solution (20 ml) was heated to reflux for 30 min. The solvent was evaporated and the residue was partitioned between EtOAc and 5% $NaHCO_3$ (aq); the organic layer was washed with water, dried (Na_2SO_4) and evaporated. Purification by preparative TLC (CH_2Cl_2:light petroleum, 9:1) gave 0.040 g, 5.0% of the dithio derivative and 0.553 g, 76.4% of the title compound: m.p. 367 K (CH_2Cl_2:light petroleum); $[\alpha]_D$: 8 (c 1, CH_2Cl_2:MeOH, 1:4); IR (cm^{-1}): 3275, 1753, 1740, 1663, 1512, 1503; ^{1}H NMR ($CDCl_3$): 9.56 (1H, d, J = 7.3, NH_{thio}), 8.41 (1H, d, J = 8.2, NH_{oxo}), 5.05–4.97 [1H, m, $CH_{\alpha(thio)}$], 4.61–4.53 [1H, m, $CH_{\alpha(oxo)}$], 3.76 [6H, s, $CH_{3(OMe)}$], 1.86–1.62 [6H, m, $CH_{2(\beta)}$ and CH_γ], 0.97 and 0.95 [6H each, 2s, $CH_{3(\delta)}$]; ^{13}C NMR ($CDCl_3$): 186.0 (CSNH), 171.9 and 170.8 (COOMe), 157.7 (CONH), 56.6 [$CH_{\alpha(thio)}$], 52.3 and 52.2 [$CH_{3(OMe)}$], 51.9 [$CH_{\alpha(oxo)}$], 40.9 and 40.1 [$CH_{2(\beta)}$], 24.65 and 24.55(CH_γ), 22.4, 22.2, 21.9 and 21.5 [$CH_{3(\delta)}$]; Anal.: calc.

Table 2
Selected torsion angles for (I), (II) and (III) (°).

I(*B*): $\omega, \varphi, \psi, \chi, \omega', \varphi', \psi'$ and χ' angles are defined as C13—C12—N12—C22, C12—N12—C22—C32, N12—C22—C32—O32, N12—C22—C52—C62, C12—C13—N13—C23, C13—N13—C23—C33, N13—C23—C33—O33 and N13—C23—C53—C63, respectively (Fig. 1*a*). III: $\omega, \omega', \varphi', \psi'$ and χ' angles are defined as C9—C1—N1—C2, C1—C9—N2—C10, C9—N2—C10—C11, N2—C10—C11—O6 and N2—C10—C13—C14, respectively (Fig. 1*c*).

	I(*A*)	I(*B*)	II	III
C11—C1—N1—C2 (ω)	174.7 (3)	173.6 (4)	177.8 (3)	173.2
C1—N1—C2—C3 (φ)	−90.8 (5)	−105.5 (5)	−116.0 (4)	−130.4
N1—C2—C3—O3 (ψ)	150.0 (4)	173.6 (5)	173.8 (3)	179.3
N1—C2—C5—C6 (χ)	−69.2 (5)	−68.7 (6)	−67.7 (4)	−67.9
C1—C11—N11—C21 (ω')	175.7 (4)	176.2 (4)	171.9 (3)	172.5
C11—N11—C21—C31 (φ')	−98.7 (5)	−102.7 (6)	−110.3 (4)	−97.1
N11—C21—C31—O31 (ψ')	156.7 (4)	161.0 (5)	133.1 (3)	158.8
N11—C21—C51—C61 (χ')	−59.5 (6)	−60.6 (7)	−69.7 (4)	−63.2

Table 3
Hydrogen-bonding geometry for (I) (Å,°).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
Molecule *A*				
N—H1···O12 (*B*)	0.86	2.38	3.135 (5)	146.1
N11—H11···O22^{i} (*B*)	0.86	2.22	3.021 (5)	155.1
N11—H11···1 (intra)	0.86	2.19	2.596 (5)	109.0
N1—H1···S11 (intra)	0.86	2.58	3.009 (4)	111.9
Molecule *B*				
N12—H12···O1^{ii} (*A*)	0.86	2.36	3.105 (5)	144.7
N13—H13···O2 (*A*)	0.86	2.37	3.155 (6)	151.8
N13—H13···O12 (intra)	0.86	2.19	2.602 (6)	109.0
N12—H12···S13 (intra)	0.86	2.54	2.993 (4)	114.0

Symmetry codes: (i) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$.

for $C_{16}H_{28}N_2O_5S$ (360.466): C 53.31, H 7.83, N 7.77%; found C 53.23, H 8.01, N 7.80%.

The pale-yellow single crystals for X-ray analysis were obtained by vapour diffusion of pentane into a solution of the title compound in diisopropyl ether at room temperature.

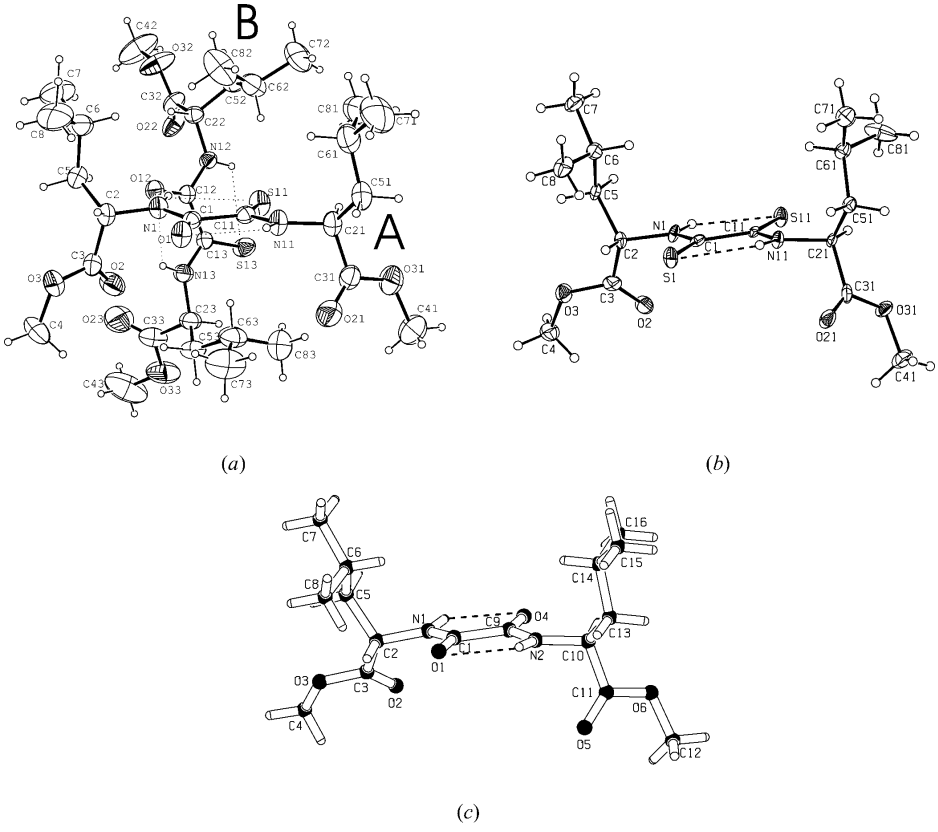

Figure 1
(*a*) *ORTEP*III (Burnett & Johnson, 1996) drawing and atom-labelling of (I) with 30% probability displacement ellipsoids, consisting of an asymmetric unit with two crystallographically independent molecules *A* and *B*. The figure describes their relative orientation and intramolecular hydrogen bonds. (*b*) *ORTEP*III (Burnett & Johnson, 1996) drawing and atom-labelling scheme of (II) with 30% probability displacement ellipsoids. Intramolecular hydrogen bonds are shown. (*c*) Molecular structure and intramolecular hydrogen bonds of (III) with atom-labelling scheme according to Karle *et al.* (1994).

2.1.2. (*S,S*)-*N,N*′-Dithiooxalyl-bis-leucine methyl ester (II). A solution of *N,N*′-oxalyl-*bis*-*l*-leucine methyl ester (0.100 g, 0.290 mmol) and Lawesson's reagent (0.152 g, 0.376 mmol) in a dry benzene solution (9 ml) was heated to reflux overnight. The solvent was evaporated and the residue was partitioned between EtOAc and 5% $NaHCO_3$ (aq); the organic layer was washed with water, dried (Na_2SO_4) and evaporated. Purification on a silica gel column (CH_2Cl_2) gave 0.100 g, 87.3.0% of the title compound: m.p. 305–307 K; $[\alpha]_D$: 48 (c 1, CH_2Cl_2:MeOH, 1:4); IR (cm^{-1}): 3198, 3140, 1748, 1510; ^1H NMR ($CDCl_3$): 10.4 (2H, d, J = 6.4, NH), 5.03–4.95 (2H, m, CH_α), 3.78 [6H, s, $CH_{3(OMe)}$], 1.91–1.64 [6H, m, $CH_{2(\beta)}$ and CH_γ], 1.00 and 0.95 [6H each, 2d, J = 6.4, $CH_{3(\delta)}$]; ^{13}C NMR ($CDCl_3$): 184.4 (CSNH), 170.8 (COOMe), 58.0 (CH_α), 52.4 [$CH_{3(OMe)}$], 39.9 [$CH_{2(\beta)}$], 24.8 (CH_γ), 22.3 and 22.0 [$CH_{3(\delta)}$]; Anal.: calc. for $C_{16}H_{28}N_2O_4S_2$ (394.548): C 48.70, H 7.15, N 7.10%; found C 48.51, H 7.46, N 6.97%.

The yellow single crystals for X-ray analysis were obtained by the vapour diffusion of pentane into a solution of the title compound in diisopropyl ether at 291 K.

2.2. X-ray measurements and structure determination

Details of data collection, structure solution, refinement and the software used are given in Table 1. Diffraction data for (I) were collected on an Enraf–Nonius CAD4 diffractometer using Cu $K\alpha$ radiation and a graphite monochromator. Three standard reflections revealed 5% decay in a crystal of (I) and the data were

Table 4
Hydrogen-bonding geometry for (III) (Å,°).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^{i}	0.96	2.17	3.05	150.0
N2—H15···O2^{ii}	0.96	2.18	3.10	160.3
N2—H15···O1 (intra)	0.96	2.30	2.70	104.3
N1—H1···O4 (intra)	0.96	2.27	2.68	105.7

Symmetry codes: (i) $y, 1-x, -\frac{1}{4}+z$; (ii) $1-y, x, \frac{1}{4}+z$.

Table 5
Hydrogen-bonding geometry for (II) (Å,°).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···S1^{i}	0.86	3.02	3.732 (3)	141.5
N11—H11···O2^{ii}	0.86	2.51	3.280 (4)	149.9
N11—H11···S1 (intra)	0.86	2.44	2.935 (3)	117.3
N1—H1···S11 (intra)	0.86	2.42	2.923 (3)	118.2

Symmetry codes: (i) $-y+2, x, z+\frac{1}{4}$; (ii) $y, -x+2, z-\frac{1}{4}$.

corrected accordingly. The diffraction for (II) was measured on a Nonius Kappa CCD with Mo $K\alpha$ radiation. The structures of (I) and (II) were solved using the program *SHELXS*97 and refined by *SHELXL*97 (Sheldrick, 1997) on F^2 values with a full-matrix least-squares procedure. The H atoms were calculated on stereochemical grounds and refined using the *SHELXL*97 riding model. L-Leucine was used for the preparation of both compounds and enantiomer assignment during the structure determination was in accordance with the configuration of the precursor. The Flack parameter (Flack, 1983) for both structures confirmed the (*S*) configuration [−0.01 (3) for (I) and 0.33 (2) for (II)]. The geometrical parameters were calculated by *PLATON* (Spek, 2003), which was also used to create the illustrations.

A comparison of the bond lengths of the two molecules in the asymmetric unit is, on the basis of the r.m.s. bond fit, an option used in *PLATON* (Spek, 2003), giving a value of 0.0181 Å.[1]

3. Results and discussion

3.1. Molecular structures

The crystal structure of (I) includes two molecules in the asymmetric unit, whereas the crystal structures of (II) and (III) contain only one molecule in the asymmetric unit. In both conformers of (I) and in the molecules of (II) and (III), leucyl residues are *cis*-positioned with respect to the (thio)oxalamide bridge (Fig. 1). The characteristic torsional angles of leucyl residues are listed in Table 2. The angles are labelled according to the convention used in the literature (Karle *et al.*, 1994; Makarević *et al.*, 2001; Perić *et al.*, 2001*a*,*b*). The signs of the torsional angles are in accordance with the selected (*S*) configuration of the leucyl residue. The values of the C═S bonds are in the range 1.627 (4)–1.664 (3) Å.

[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: SN0036). Services for accessing these data are described at the back of the journal.

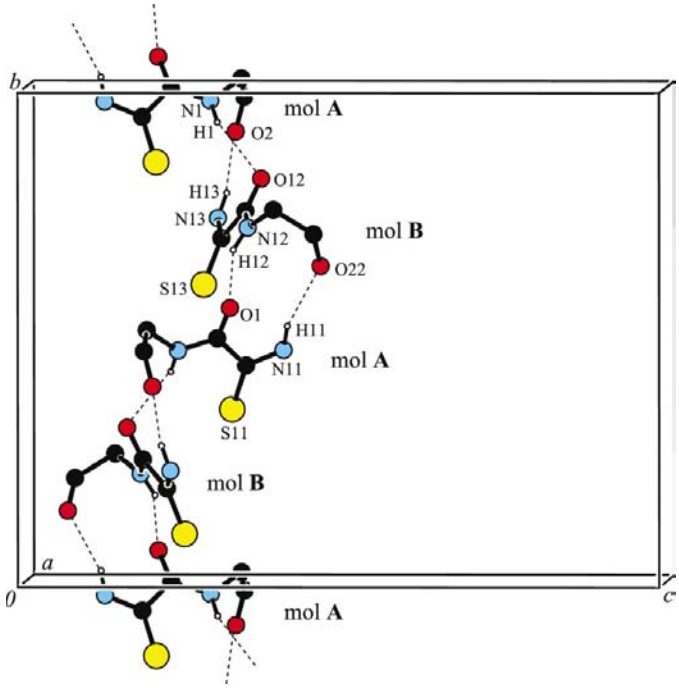

Figure 2
Intermolecular hydrogen bonds in the crystal packing of (I). Atoms involved in intermolecular hydrogen bonds are labelled, as well as the S11 and S13 atoms. For the sake of clarity, only hydrogen-bonding functionalities are shown.

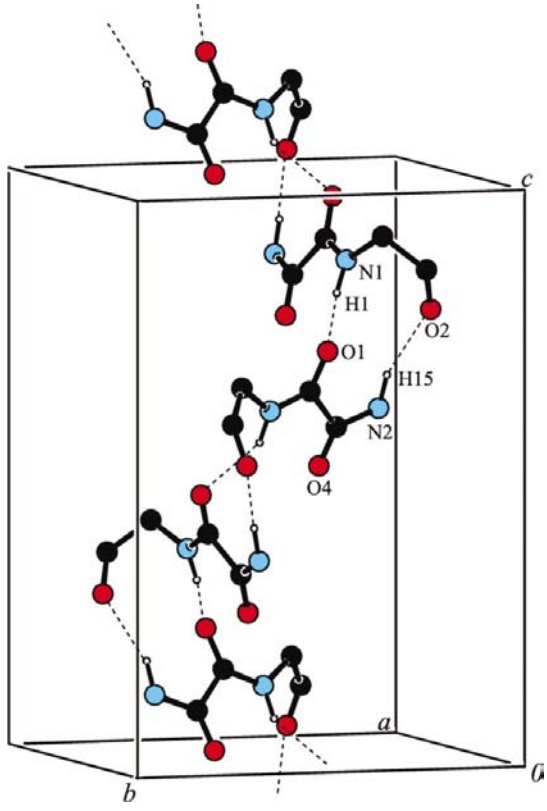

Figure 3
Intermolecular hydrogen bonds in the crystal packing of (III). Atoms involved in intermolecular hydrogen are labelled. For the sake of clarity, only hydrogen-bonding functionalities are shown.

Compounds with dithiooxalamide bridges extracted from the Cambridge Structural Database, version 5.24, Release December 2002 (Allen, 2002), revealed a symmetrical substitution (on both sides of the thiooxalamide bridge) of the alkyl or aryl substituents with the molecules exhibiting C_i symmetry. Also, the compounds with monothiooxalamide bridges extracted from the database revealed chemically different substituents. Thus, the structures (I) and (II) presented in this paper are novel representatives of this class of compound which have been deposited in the Cambridge Structural Database so far.

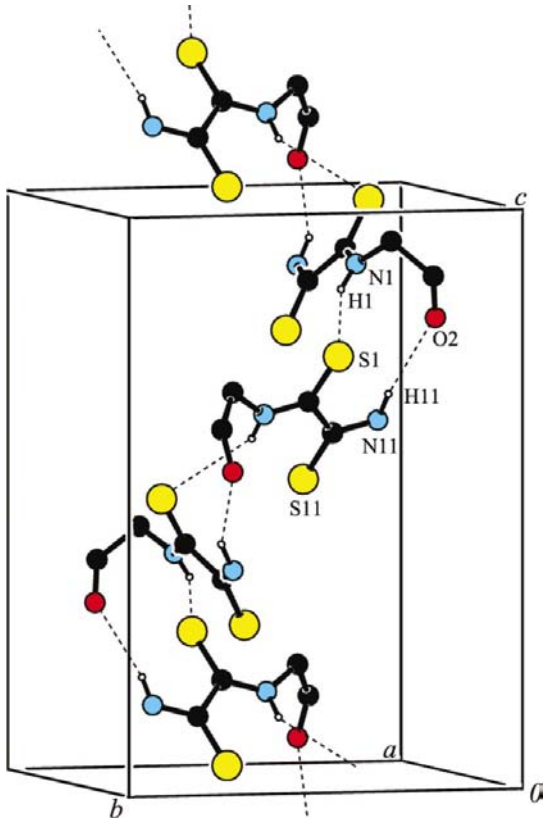

Figure 4
Intermolecular hydrogen bonds in the crystal packing of (II). Atoms involved in intermolecular hydrogen bonds are labelled. For the sake of clarity, only hydrogen-bonding functionalities are shown.

In the structure of (I) the two molecules (*A* and *B*) revealed slightly different conformations (Table 2). The conformational difference between chemically identical moieties within one molecule are comparable to the differences observed between crystallographically independent molecules. The characteristic angle pairs (φ, ψ) and their analogues (φ', ψ') in (II) are similar to the values typical of β-sheets (±anticlinal range of the torsional angles; Creighton, 1993). However, in (I), with a monothiooxalamide bridge, the φ and φ' values are in the antiperiplanar range. The monothiooxalamide group in (I) deviates from planarity as illustrated by the torsion angles O═C—C═S 172.6 (3)° in *A* and 177.2 (3)° in *B*, and by displacements from the best least-squares planes through the oxalyl bridges [S11 by 0.233 (1) Å (A), least-squares plane defined by five atoms (N1, C1, O1, C11, N11) with the mean deviation of 0.032 (4) Å and S13 by 0.090 (2) Å (*B*), least-squares plane defined by five atoms (N12, C12, O12, C13, N13) with the mean deviation of 0.012 (4) Å]. The analogous torsion angle in (II) is 178.5 (2)° and the six atoms of the dithiooxalamide bridge are coplanar [with a mean deviation of 0.006 (3) Å]. The retropeptide units in (I), (II) and (III) are involved in the intramolecular hydrogen bonds N—H···O and N—H···S, forming the five-membered *pseudo*-C_5 ring pattern ('*pseudo*' is related to the retropeptide unit, see Figs. 1*a*–*c*). According to the graph-set notation proposed by Etter *et al.* (1990), these hydrogen bonds form motifs with an *S*(5) graph-set descriptor (Tables 3–5). From the spectroscopic evidence of thioamide peptides the enhanced acidity of the thioamide N—H proton, as the strong hydrogen-bonding donor, promotes the formation of the C_5 ring structure that is not so common in unsubstituted peptides (Shaw *et al.*, 1995). This intramolecular hydrogen bond can stabilize the conformation and diminish some effects introduced by the replacement of C═O by C═S, *i.e.* steric hindrance due to the larger van der Waals radius of the S atom. The different polarity which affects the strength of the hydrogen bonding and steric hindrance usually disturbs the secondary structures (α-helices and β-sheets of thiopeptides; Shaw *et al.*, 1995; Tran *et al.*, 2001). Different properties of C═O and C═ functionalities in hydrogen bonding found a practical application in the kinetic

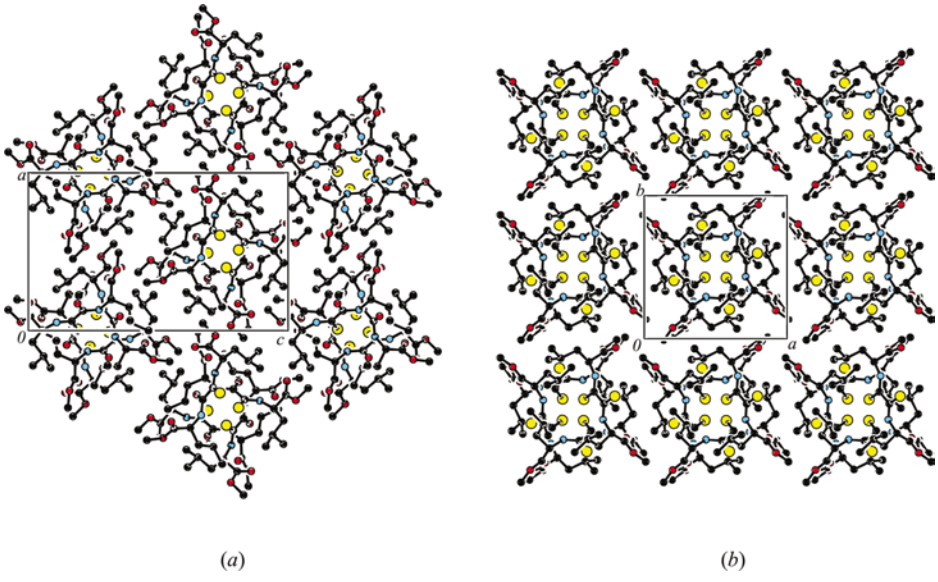

Figure 5
(*a*) Assemblies of the one-dimensional helices in the crystal structure of (I). The different appearance of yellow-coloured S atoms indicate the opposite orientations of the helices. (*b*) Assemblies of the one-dimensional helices in the crystal structure of (II). The crystal structure of (II) is isostructural to (III).

studies of the enzymatic activity of cysteine proteinases *versus* serine proteases (Menard & Storer, 1992). Thus, the peptidyl thioamides were used as substrates and inhibitors of papain and as probes of the kinetic significance of the oxyanion hole (Foje & Hanzlik, 1994).

3.2. Hydrogen bonds and crystal packings

The presence of carbonyl and thiocarbonyl groups makes an asymmetrical thiooxalamide bridge in the retropeptide (I). Intermolecular hydrogen bonds of the N—H···O type act between:

(i) amide and oxalyl groups, and

(ii) amide end ester groups (Table 3, Fig. 2)

connecting molecules *A* and *B* into a helix arranged in accordance with a non-crystallographic, fourfold screw axis in the direction of the crystallographic axis *b*, also detected by a NONSYM search in *PLATON* (Spek, 2003). The analogous hydrogen bonds (*A*) N1—H1···O12 (*B*) and (*B*) N12—H12···O1^{ii} (*A*) [Table 3, symmetry code: (ii) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$] connect molecules by the 2_1 symmetry operating along *b*. The antiparallel hydrogen-bonding pattern in the non-polar space group $P2_12_12_1$ emulates the 4_1 operation. The function of these two hydrogen bonds, described by the graph-set descriptor $C(4)$ is comparable to N1—H1···O1^{i} in (III) [Fig. 3, Table 4, symmetry code (i) $y, 1-x, -\frac{1}{4}+z$). The pattern generated by intermolecular hydrogen bonds between the oxalamide bridge and a carbonyl of the ester moiety (*B*), N13—H13···O1 (*A*) and (*A*) N11—H11···O22^{i} (*B*) [Table 3, symmetry code (i) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$], can be described by the descriptor $C(8)$. The analogous pattern in (III) is formed by the intermolecular hydrogen bond N2—H15···O2^{ii} [Fig. 3, Table 4, symmetry code (ii) $1-y, x, \frac{1}{4}+z$], which completes a helix pattern along the 4_1 axis running along the tetragonal *c* axis. In the structure of (III) the analogous motif involves N—H···O interactions (Table 4). In this structure the O4 atom, a part of the oxalamide bridge, does not participate in intermolecular hydrogen bonding, whereas in the structure of the monothio analogue (I) this very atom is substituted by sulfur. In the crystal structures of (I) and (III) the system of hydrogen bonds can be uniquely described by the first-level graph-set descriptor $N_1 = S(5)S(5)C(8)C(4)$.

The analogous chemical formula, similar values of the unit-cell parameters of (II) and (III), and the same space group $P4_1$ suggest their close structural relationship. Along the crystallographic axis *c* (being coaxial with the screw axis 4_1) there is a lengthening of *ca* 1.5% for (II) owing to the larger van der Waals radius of sulfur (1.80 Å) than oxygen (1.40 Å) in (III). Thus, in these two structures the patterns running along the direction of *c*, Tables 4 and 5) should be very similar. The analysis of the hydrogen-bonding patterns leads to the same graph-set descriptor as already mentioned above. It also reveals that the O4 atom, part of the oxalamide bridge in (III), and its analogue S11 in (II), do not act as acceptors in intermolecular hydrogen bonds (Figs. 3 and 4). Hydrogen-bonding patterns found in (I), (II) and (III) lead to similar supramolecular assemblies as illustrated (Figs. 2, 3, and 4). Molecules are assembled into helices, their inner parts reveal $R_2^2(10)$ hydrogen-bonded rings, whereas hydrophobic leucyl residues and ester groups are on the outer parts of the helices (Fig. 5).

3.3. Concluding remarks

In spite of the chemical replacement of the sp^2 oxygen by sulfur, similar hydrogen-bond patterns were described by the first-level graph-set descriptor $N_1 = S(5)S(5)C(8)C(4)$. Helices formed in these structures revealed 4_1 symmetry: in (I) there is a local 4_1 axis of pseudo character (Fig. 5*a*), whereas in (II) and (III) there is the crystallographic 4_1 symmetry (Fig. 5*b*). In (II) and (III) oxalamide and dithiooxalamide bridges are symmetrical and the hydrogen bonds formed obey the polar 4_1 symmetry. However, the asymmetrical monothiooxalamide bridges generate hydrogen bonds between the two molecules *A* and *B* in the asymmetric unit connected into helices that fit into the non-polar space group $P2_12_12_1$ (Fig. 5*a*). However, in (II) and (III) helices are repeated by translation only, always keeping the same orientation as required by the tetragonal polar space group $P4_1$ (Fig. 5*b*). Thus, the structures (II) and (III) are isostructural, whereas structure (I) is homostructural to them (Kálmán *et al.*, 1993, 2001; Kálmán & Párkányi, 1997). Their crystal packings include one-dimensional α-networks generated by hydrogen bonds (N—H···O) between neighbouring oxalamide groups previously described for oxalamides used as synthons for molecular assembling (Coe *et al.*, 1997).

Financial support from the Croatian Ministry of Science and Technology for the projects 0098036 and 0098053 is gratefully acknowledged. The crystallographic data set was collected on the Nonius KappaCCD diffractometer at the Laboratory of Inorganic Chemistry, Faculty of Chemistry and Chemical Technology, University of Ljubljana, Slovenia. We acknowledge with thanks the financial contribution of the Ministry of Science and Technology, Republic of Slovenia, through grants No. X-2000 and No. PS-511-102, which made the purchase of the apparatus possible.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Burnett, M. N. & Johnson, C. K. (1996). Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
Coe, S., Kane, J. J., Nguyen, T. L., Toledo, L. M., Winiger, E., Fowler, F. W. & Lauher, J. W. (1997). *J. Am. Chem. Soc.* **119**, 86–93.
Creighton, T. E. (1993). *Proteins: Structures and Molecular Properties*, 2nd ed. New York: Freeman and Co.
Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* B**46**, 256–262.
Enraf–Nonius (1994). *CAD*4 *Express Software.* Delft, The Netherlands.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Foje, L. K. & Hanzlik, R. P. (1994). *Biochim. Biophys. Acta*, **1201**, 447–453.
Harms, K. & Wocadlo, S. (1995). *XCAD*-4. University of Marburg, Germany.

Jokić, M., Makarević, J. & Žinić, M. (1995). *J. Chem. Soc. Chem. Commun.* pp. 1723–1724.
Kálmán, A., Argay, Gy., Fabiau, L., Bernáth, G. & Fülöp, F. (2001). *Acta Cryst.* B**57**, 539–550.
Kálmán, A. & Párkányi, L. (1997). *Adv. Mol. Struct. Res.* **3**, 160–165.
Kálmán, A., Párkányi, L. & Argay, Gy. (1993). *Acta Cryst.* B**49**, 1039–1049.
Karle, I. L., Ranganathan, D., Shah, K. & Vaish, N. K. (1994). *Int. J. Pept. Protein Res.* **46**, 160–165.
Makarević, J., Jokić, M., Perić, B., Tomišić, V., Kojić-Prodić, B. & Žinić, M. (2001). *Chem. Eur. J.* **7**, 3328–3341.
Makarević, J., Jokić, M., Raza, Z., Štefanić, Z., Kojić-Prodić, B. & Žinić, M. (2003). *Chem. Eur. J.* **9**, 5567–5580.
Menard, R. & Storer, A. C. (1992). *Biol. Chem. Hoppe-Seyler*, **373**, 384–400.
Nonius (1997–2000). *Collect.* Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. **276**, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Perić, B., Kojić-Prodić, B., Makarević, J., Jokić, M. & Žinić, M. (2001*a*). *Acta Cryst.* C**57**, 747–748.
Perić, B., Makarević, J., Jokić, M., Kojić-Prodić, B. & Žinić, M. (2001*b*). *Acta Cryst.* C**57**, 865–867.
Puiggali, J. & Subirana, J. A. (1998). *Biopolymers*, **45**, 149–155.
Shaw, R. A., Kollát, E., Hollósi, M. & Mantsch, H. H. (1995). *Spectrochim. Acta Part A*, **51**, 1399–1412.
Sheldrick, G. M. (1997). *SHELX*97, Release 97–2. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Subirana, J. A. (1997). *FEBS Lett.* **417**, 352–354.
Tran, T. T., Treutlein, H. & Burgess, A. W. (2001). *J. Comput. Chem.* **22**, 1026–1037.