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L-Methioninamide ester amide of squaric acid diethyl ester

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.006 Å
R factor = 0.047
wR factor = 0.122
Data-to-parameter ratio = 9.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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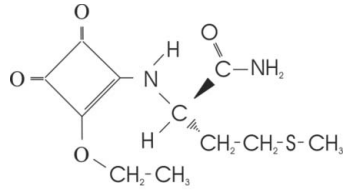
Molecules of the title compound, 2-(2-ethoxy-3,4-dioxocyclobutenylamino)-2-[2-(methylsulfanyl)ethyl]acetamide, $C_{11}H_{16}N_2O_4S$, are connected into chains in the [010] direction by intermolecular N—H···O hydrogen bonds involving the L-methioninamide N atoms and its carbonyl O atom.

Comment

In the course of our systematic spectroscopic and structural investigations of some optically active derivatives of amino acids (Kolev, Petrova & Spiteller, 2004; Kolev, Wortmann *et al.*, 2004; Kolev *et al.*, 2005, 2006) with potential non-linear optical and electro-optical properties (Nalwa *et al.*, 1997; Wolff & Wortmann, 1999; Chemla & Zyss, 1987), the crystal structure of the L-methioninamide ester amide of squaric acid diethyl ester, (I), has been determined. Squaric acid diethyl ester is known as a coupling reagent for the formation of drug biopolymer conjugates, especially to bind pharmacologically active molecules to polymers; the use of such biopolymer drug conjugates represents a promising approach to the treatment and diagnosis of many diseases. Tietze *et al.* (1991) noted that the advantage of employing conjugates lies in the selective delivery to the target site and also in the possible protection of drugs against fast enzymatic degradation and excretion, thereby leading to higher drug concentration in the tumour. Squaric acid and its derivatives, when crystallized non-centrosymmetrically, are of great interest for non-linear optical, electro-optical and photorefractive applications due to their specific properties. The derivatives of squaric acid have large hyperpolarizability values, large differences in the molecular dipole moments between the ground and excited states, large transition dipole moments and a small band gap energy.



(I)

Compound (I) belongs to the C-amidated amino acids, whose salts and ester amides of squaric acid represent a new class of compounds, having great biological importance. A structural study on protonated forms of the C-amidated amino acids Ile, Val, Thr, Ser, Met, Trp, Gln and Arg has previously been performed by In *et al.* (2001).

The IR spectrum of (I) (KBr pellet) exhibits bands at 3393, 3197, 3153 and 3074 cm^{-1}, which could be assigned to the ν^{as}

NH_2 and ν NH modes. The last two peaks are typical for a ν^s NH_2 mode split by Fermi resonance. This phenomenon is observed in cases when the $-NH_2$ group is involved in asymmetric hydrogen bonds similar to those of compound (I), as well as other methionine-containing peptides (Arnaudov *et al.* 2005; Ivanova, 2006*a*,*b*; Ivanova & Arnaudov, 2006; Ivanova *et al.*, 2006). The broad band at 3078 (IR) and 3080 cm^{-1} (Raman) was assigned to N1—H1 stretching in the amide function. Full vibrational analysis of (I) is now in progress and will be published at a later date.

The molecular structure of (I) is shown in Fig. 1, with a packing diagram in Fig. 2. The molecules are connected into chains through two strong N—H···O hydrogen bonds (Table 1). A weaker N—H···O interaction is also observed between the amide N3 group and O41 of the hydrogen squarate part of the molecule. A way of describing the structure is to regard it as being composed of a hydrophilic part, which includes the amino acid amide functional group, and a hydrophobic part composed of the squaric acid units and their ethyl substituents.

Experimental

The starting compound L-methionine amide was received as a white powder from Bachem (Switzerland) and recrystallized from methanol. (I) was prepared in good yield according to the general synthetic scheme described by Tietze *et al.* (1991) *via* condensation of L-methionine amide and diethyl squarate in ethanol at room temperature. A solution of L-methionine amide hydrochloride (3 mmol, 666 mg) in 4 ml ethanol and 1 ml water was added to an ethanol solution (1 ml) of triethylamine (0.41 ml) and diethyl squarate (0.44 ml). The reaction mixture was stirred at room temperature until reaction was complete (2 h). On leaving the solution to stand, the product began to crystallize after 2 h. The precipitate was separated by filtration and recrystallized from ethanol. Colourless crystals that formed after three weeks were filtered off and dried in air at room temperature. Single prismatic, colourless crystals, suitable for X-ray analysis, were grown from ethanol by slow evaporation at room temperature over a period of two weeks.

Crystal data

$C_{11}H_{16}N_2O_4S$
M_r = 272.32
Monoclinic, $P2_1$
a = 9.5810 (11) Å
b = 7.3961 (12) Å
c = 9.9354 (13) Å
β = 103.355 (7)°
V = 685.00 (16) Å^3
Z = 2
D_x = 1.320 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 7.3–15.1°
μ = 0.25 mm^{-1}
T = 294 (2) K
Prism, colourless
0.55 × 0.48 × 0.22 mm

Data collection

Siemens P4 four-circle diffractometer
ω scans
Absorption correction: ψ scan (*XPREP* in *SHELXTL-Plus*; Sheldrick, 1995)
T_{min} = 0.873, T_{max} = 0.948
1754 measured reflections
1487 independent reflections
1294 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 25.0°
$h = -1 \rightarrow 11$
$k = -1 \rightarrow 8$
$l = -11 \rightarrow 11$
3 standard reflections
every 100 reflections
intensity decay: 1%

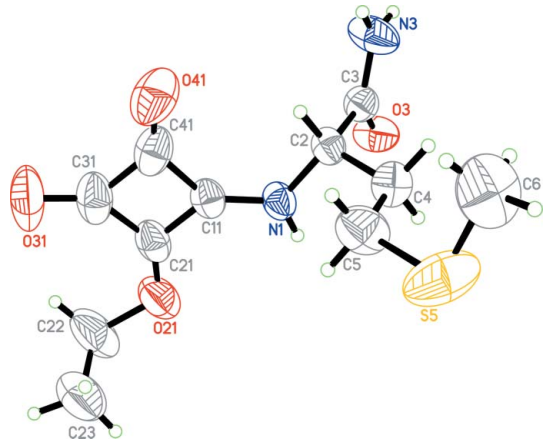


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

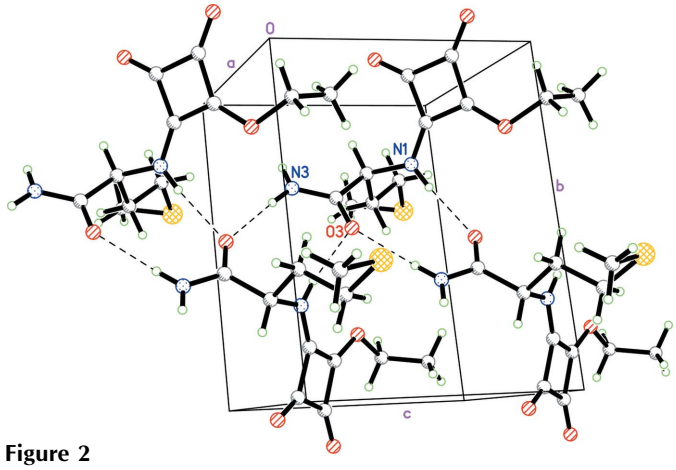


Figure 2
Projection of (I), showing the construction of a three-dimensional network through intermolecular hydrogen bonds (dashed lines).

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.122
S = 1.05
1487 reflections
166 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0523P)^2 + 0.2827P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.009
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.09 (2)
Absolute structure: Flack (1983), 204 Friedel pairs
Flack parameter: 0.05 (19)

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O3^{i}	0.86	1.98	2.829 (4)	169
N3—H31···O3^{ii}	0.86	2.14	2.999 (4)	177
N3—H32···O41^{iii}	0.86	2.51	3.241 (5)	143

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

The *S* configuration of the L-methioninamide α-carbon atom C2 is known and was confirmed by the Flack (1983) parameter x = 0.05 (19). The H atoms were constrained to idealized positions and

refined using a riding model, with C—H distances ranging from 0.96 to 0.98 Å and an N—H distance of 0.86 Å. Isotropic displacement parameters $U_{iso}(H) = 1.5U_{iso}(C_{methyl})$, $1.2U_{iso}(C)$ and $1.2U_{iso}(N)$ were employed for the respective H atoms. The methyl groups were allowed to rotate but not to tip.

Data collection: *R3m/V User's Guide* (Siemens, 1989); cell refinement: *R3m/V User's Guide*; data reduction: *XDISK* (Siemens, 1989); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97*.

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