Table 2. *Selected geometric parameters (Å, °)*

S1—C1	1.741 (9)	C2—C3	1.42 (1)
S1—C2	1.780 (7)	C2—C11	1.36 (1)
N1—N2	1.371 (9)	C3—C4	1.37 (1)
N1—C1	1.341 (9)	C4—C5	1.40 (1)
N2—N3	1.303 (9)	C5—C10	1.44 (1)
N3—N4	1.375 (8)	C10—C11	1.41 (1)
N4—C1	1.34 (1)		
C1—S1—C2	105.2 (4)	S1—C1—N1	122.1 (6)
N2—N1—C1	107.6 (6)	S1—C1—N4	127.9 (6)
C1—N1—C12	132.5 (7)	S1—C2—C3	122.3 (6)
N1—N2—N3	106.5 (6)	S1—C2—C11	115.7 (6)
N2—N3—N4	111.3 (6)	C3—C2—C11	121.1 (7)
N3—N4—C1	104.7 (6)		
S1—C1—N1—N2	−176.2 (7)	N1—C1—S1—C2	−171.0 (8)
S1—C1—N1—C12	2 (2)	N3—N2—N1—C12	−178.6 (8)
S1—C1—N4—N3	176.3 (8)	C1—S1—C2—C3	45 (1)
S1—C2—C3—C4	170.9 (9)	C1—S1—C2—C11	−146.0 (8)
S1—C2—C11—C10	−168.9 (8)	C7—C8—C9—C10	0 (2)

The rather low precision found for the molecular geometry parameters reflects limited crystal quality and the low fraction of data which could therefore be considered significant.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN PROCESS* (Molecular Structure Corporation, 1993). Program(s) used to refine structure: *TEXSAN LS*. Software used to prepare material for publication: *TEXSAN FINISH*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: BM1096). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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(3*S*,5*S*,1′*S*)-3-Benzyl-5-[1′-(*tert*-butoxycarbonylamino)-2′-phenylethyl]-4,5-dihydrofuran-2(3*H*)-one

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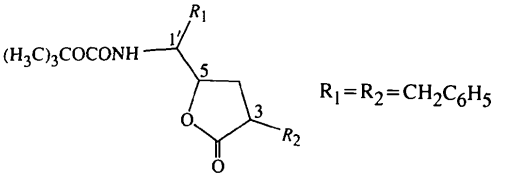
Abstract

The crystal structure of the title lactone, $C_{24}H_{29}NO_4$, contains three chiral centres which are in the *S* configuration. The dihydrofuranone ring takes an envelope conformation.

Comment

Potent synthetic inhibitors of many aspartic proteases such as pepsin, renin, HIV-1 protease or candida protease have been described [for a review see Davies (1990)]. The design of the majority of protease inhibitors is now based on the replacement of a cleaved amide bond in a short substrate peptide by a non-hydrolysable hydroxyethylene isostere [—CH(OH)CH_2—] which resembles the tetrahedral intermediate formed during hydrolysis of a peptide (Greenlee, 1990).



(1)

Butyrolactones are crucial synthones for hydroxyethylene isostere synthesis. They contain three chiral centres at C3, C5 and C1′; the one at C1′ is derived from a natural amino acid of *S* configuration. Recently, we have prepared all four possible diastereoisomers of lactone (1) and transformed them in several series of protease inhibitors in order to study structure–activity relationships (Litera, 1995). The stereochemistry of all of the lactones was determined by ^1H and ^{13}C NMR spectroscopy after the necessary chemical transformations had been made. To confirm the structure of the lactone from which the best inhibitors were derived, we crystallized it from cyclohexane solution by slow evaporation of the solvent. The molecular structure of the resulting lactone together with the atom-

numbering scheme is shown in Fig. 1. The potential chiral centres (atoms C2, C4 and C5) are in the *S* configuration (Prelog, 1976), in agreement with our previous assumptions. The dihydrofuranone ring is in an envelope conformation. The atoms C1, C2, C4 and O1 are situated in a plane (r.m.s. deviation of the fitted least-squares plane through these atoms is about 0.004 Å) and the atom C3 deviates from this plane by −0.427 Å. The carbamate amide bond has a distinctive *trans* configuration and it deviates from a planar arrangement, the r.m.s. deviation of the fitted atoms being about 0.063 Å. More exactly, this non-planarity is caused by a pyramidal deformation of the N atom (τ_N = −14.5°; Ramachandran & Koloskar, 1973). Both benzyl groups are in an analogous position with respect to the dihydrofuranone ring (see Fig. 1), with a very similar conformation. The difference between corresponding torsion angles is at most 10% for the two benzyl groups (see Table 2).

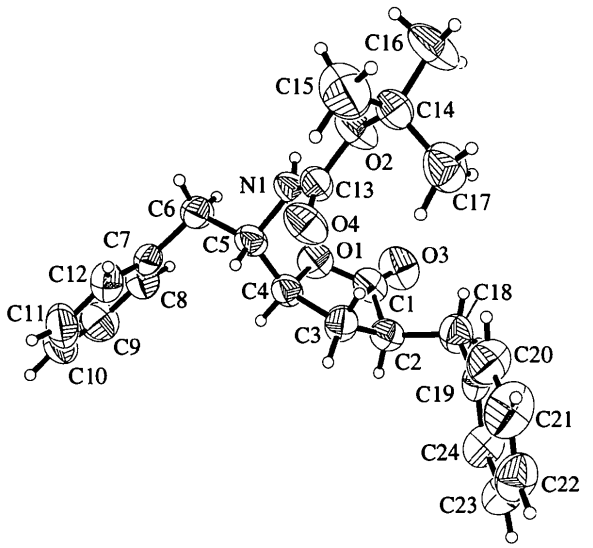


Fig. 1. Perspective view of the title lactone with the atomic labelling scheme for non-H atoms. Displacement ellipsoids are shown at the 50% probability level.

The packing of the molecules in the title lactone is controlled predominantly by intermolecular hydrogen bonds which connect the molecules [H1···O3^{i} 2.32 (3) Å, N1—H1···O3^{i}; (i) = (−*x*, *y*−1/2, 1/2−*z*) 155 (3)°] in two antiparallel helices along the *b* axis. A second type of packing is also observed in the crystal structure. It results from the stacking between neighbouring phenyl groups (see Fig. 2). The distance between their centres of mass is about 4.99 Å and they form an acute angle of 71°. This type of packing results from interactions between the slightly positively charged H atoms of one aromatic group and the electron-rich π-electron system of another aromatic group (Glusker, Lewis & Rossi, 1994).

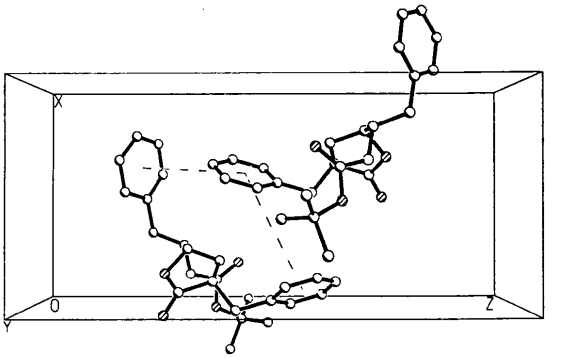


Fig. 2. Packing of the molecules in the crystal (projected on the *ac* plane). Dashed lines connect the centres of mass of interacting aromatic rings.

Experimental

The title lactone was crystallized by slow evaporation from a cyclohexane solution.

Crystal data

$C_{24}H_{29}NO_4$
M_r = 395.50
Orthorhombic
$P2_12_12_1$
a = 9.4429 (6) Å
b = 11.3908 (8) Å
c = 21.123 (2) Å
V = 2272.0 (3) Å^3
Z = 4
D_x = 1.156 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 14–15°
μ = 0.078 mm^{-1}
T = 293 (2) K
Irregular bar
0.4 × 0.4 × 0.3 mm
Colourless

Data collection

Enraf–Nonius CAD-4 MACHIII four-circle diffractometer
θ/2θ scans
Absorption correction: none
4312 measured reflections
4000 independent reflections
2885 observed reflections [$I > 2\sigma(I)$]

R_{int} = 0.0289
θ_{max} = 24.97°
h = −11 → 11
k = 0 → 13
l = 0 → 25
3 standard reflections
frequency: 60 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0325
$wR(F^2)$ = 0.0876
S = 1.045
3512 reflections
379 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0416P)^2 + 0.0484P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = −0.004
$\Delta\rho_{max}$ = 0.088 e Å^{-3}
$\Delta\rho_{min}$ = −0.092 e Å^{-3}

Extinction correction: *SHELXL*93 (Sheldrick, 1994)
Extinction coefficient: 0.0234 (14)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: Flack (1983)
Flack parameter = −0.8 (10) (inconclusive)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
O1	0.1622 (1)	0.6654 (1)	0.28298 (6)	0.0602 (4)
O2	−0.0172 (1)	0.3265 (2)	0.37692 (6)	0.0679 (4)
O3	−0.0063 (2)	0.8017 (2)	0.28586 (7)	0.0776 (5)
O4	0.1941 (1)	0.3611 (1)	0.42438 (7)	0.0663 (4)
N1	0.1446 (2)	0.4269 (2)	0.32599 (8)	0.0582 (5)
C1	0.0870 (2)	0.7498 (2)	0.3126 (1)	0.0567 (5)
C2	0.1358 (2)	0.7639 (2)	0.38002 (9)	0.0528 (5)
C3	0.2199 (3)	0.6526 (2)	0.39157 (9)	0.0570 (5)
C4	0.2685 (2)	0.6164 (2)	0.32587 (9)	0.0520 (5)
C5	0.2792 (2)	0.4851 (2)	0.31510 (9)	0.0506 (5)
C6	0.3345 (2)	0.4537 (2)	0.2489 (1)	0.0566 (5)
C7	0.4851 (2)	0.4926 (2)	0.23799 (8)	0.0480 (5)
C8	0.5175 (3)	0.5838 (2)	0.1980 (1)	0.0652 (6)
C9	0.6569 (3)	0.6181 (2)	0.1890 (1)	0.0821 (7)
C10	0.7630 (3)	0.5622 (3)	0.2211 (2)	0.0883 (9)
C11	0.7327 (3)	0.4711 (3)	0.2604 (1)	0.0811 (8)
C12	0.5946 (2)	0.4367 (2)	0.2686 (1)	0.0630 (6)
C13	0.1147 (2)	0.3696 (2)	0.37974 (9)	0.0492 (5)
C14	−0.0800 (2)	0.2615 (2)	0.4294 (1)	0.0566 (5)
C15	0.0040 (4)	0.1517 (3)	0.4437 (2)	0.109 (1)
C16	−0.2263 (3)	0.2356 (4)	0.4046 (2)	0.095 (1)
C17	−0.0886 (4)	0.3398 (3)	0.4869 (1)	0.0837 (8)
C18	0.0131 (3)	0.7856 (3)	0.4246 (1)	0.0646 (6)
C19	0.0555 (2)	0.7855 (2)	0.4936 (1)	0.0561 (5)
C20	0.0329 (3)	0.6909 (3)	0.5318 (1)	0.0798 (7)
C21	0.0732 (4)	0.6935 (3)	0.5948 (1)	0.094 (1)
C22	0.1354 (3)	0.7891 (3)	0.6200 (1)	0.0811 (7)
C23	0.1581 (3)	0.8835 (3)	0.5832 (1)	0.0802 (7)
C24	0.1196 (3)	0.8814 (2)	0.5205 (1)	0.0707 (7)

Table 2. *Selected torsion angles (°)*

C4—C5—C6—C7	65.1 (3)
C5—C6—C7—C8	−108.9 (2)
C5—N1—C13—O4	0.7 (3)
C5—N1—C13—O2	179.0 (2)
C3—C2—C18—C19	55.4 (3)
C2—C18—C19—C20	−101.0 (3)
H1—N1—C13—O4	165 (2)
H1—N1—C13—O2	−17 (2)

Data collection: *CAD-4/PC Software* (Enraf–Nonius, 1989*a*). Cell refinement: *CAD-4/PC Software*. Data reduction: *CADRED* (Enraf–Nonius, 1989*b*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1994). Molecular graphics: *O* (Jones & Kjeldgaard, 1993). Software used to prepare material for publication: *SHELXL*93 (Sheldrick, 1994).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: KA1190). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Ethylmethylglyoxal Bis(amidinohydrazonium) Dichloride–Water (1/2)

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Abstract

The title compound, $C_7H_{18}N_8^{2+}.2Cl^-.2H_2O$, has been found to exist as the *anti–anti* isomer, with an all-*trans* configuration of the bis(amidinohydrazone) chain, just like glyoxal bis(amidinohydrazone) and all its mono- and dialkylglyoxal analogues studied so far. The bis(amidinohydrazone) backbone of the dication is planar in contrast to the corresponding sulfate salt.

Comment

Ethylmethylglyoxal bis(amidinohydrazone) (EMGBG) is a potent and highly specific inhibitor of *S*-adenosylmethionine decarboxylase (AdoMetDC), one of the two rate-limiting enzymes of polyamine biosynthesis (Elo *et al.*, 1986). The compound is therefore an important tool in the investigation of polyamine metabolism and of the largely unknown physiological functions of the natural polyamines. Potent polyamine antimetabolites, including EMGBG, may also be potential anticancer agents.

The crystal and molecular structures of several mono- and dialkylglyoxal bis(amidinohydrazones) have been determined previously, including methylglyoxal bis(amidinohydrazone) dichloride monohy-