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N-[Glycyl-(*Z*)-α,β-dehydrophenylalanyl-glycyl-(*Z*)-α,β-dehydrophenylalanyl]-glycine trifluoroacetate methanol solvate

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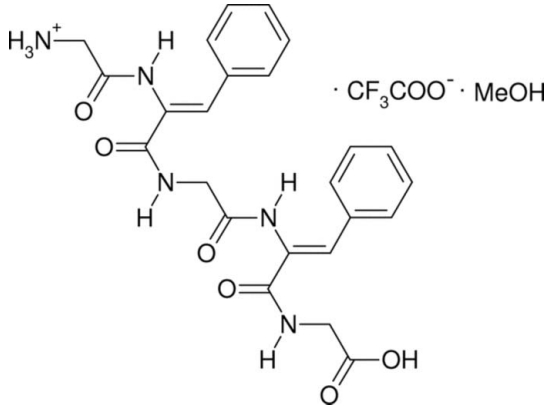
Key indicators: single-crystal X-ray study; T = 100 K; mean σ(C–C) = 0.003 Å; R factor = 0.048; wR factor = 0.144; data-to-parameter ratio = 14.2.

The molecular conformation of the title dehydropeptide, H^+-Gly^1–Δ^ZPhe^2–Gly^3–Δ^ZPhe^4–Gly^5-OH·CF_3COO^-·CH_3OH or $C_{24}H_{26}N_5O_6^+$·CF_3COO^-·CH_3OH, is characterized by the presence of two intramolecular N—H···O hydrogen bonds that stabilize two type III β-turns, at the Δ^ZPhe^2 (Δ^ZPhe is the *Z* isomer of the α,β-dehydrophenylalanine residue) and Gly^3, and Gly^3 and Δ^ZPhe^4 residues. As a result, the pentapeptide adopts a right-handed 3_{10}-helical conformation. All peptide units are linked *trans* to each other.

Related literature

For related literature, see: Ciajolo *et al.* (1990, 1991); Ejsmont *et al.* (2001); Goel *et al.* (2005); Jain *et al.* (1997); Makowski *et al.* (2005, 2006, 2007*a*,*b*); Tuzi *et al.* (1997); Venkatachalam (1968); Vijayaraghavan *et al.* (1998).



Experimental

Crystal data

$C_{24}H_{26}N_5O_6^+$·$C_2F_3O_2^-$·CH_4O
M_r = 625.56
Monoclinic, $P2_1/c$
a = 13.267 (7) Å
b = 16.660 (8) Å
c = 13.459 (7) Å
β = 96.93 (3)°
V = 2953 (3) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 1.02 mm^{-1}
T = 100 (2) K
0.24 × 0.19 × 0.05 mm

Data collection

Oxford Excalibur PX κ-geometry diffractometer plus CCD area detector
Absorption correction: numerical (*CrysAlis RED*; Oxford Diffraction, 2003)
T_{min} = 0.792, T_{max} = 0.951
24725 measured reflections
5723 independent reflections
4191 reflections with $I > 2\sigma(I)$
R_{int} = 0.032

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.144
S = 1.03
5723 reflections
402 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.46 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O9—H9···O8	0.84	1.95	2.781 (2)	169
O5—H5···O9^{i}	0.84	1.77	2.600 (3)	172
N1—H1*D*···O7	0.91	2.05	2.873 (2)	150
N1—H1*E*···O4^{ii}	0.91	1.90	2.755 (2)	155
N1—H1*F*···O8^{iii}	0.91	1.94	2.812 (2)	160
N2—H2*D*···O3^{iv}	0.88	2.04	2.829 (2)	148
N3—H3*D*···O7	0.88	2.30	3.007 (3)	137
N4—H4*D*···O1	0.88	1.97	2.821 (2)	163
N5—H5*D*···O2	0.88	2.14	2.991 (2)	161
N1—H1*D*···F1	0.91	2.34	3.054 (3)	135

Symmetry codes: (i) $-x+1, -y+1, -z$; (ii) $-x+1, -y+1, -z+1$; (iii) $x, -y+\frac{3}{2}, z+\frac{1}{2}$; (iv) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXL97*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LW2007).

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supplementary materials

Acta Cryst. (2007). E**63**, o2709-o2710 [**doi:10.1107/S1600536807016613**]

N-[Glycyl-(*Z*)-α,β-dehydrophenylalanylglycyl-(*Z*)-α,β-dehydrophenylalanyl]glycine trifluoroacetate methanol solvate

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Comment

Continuing our studies (Makowski *et al.*, 2005, 2006, 2007*a*,*b*) of dehydropeptides containing the ΔPhe residue/s, in this paper we present the crystal structure of the title peptide, H^+—Gly^1–$\Delta^Z Phe^2$–Gly^3–$\Delta^Z Phe^4$–Gly^5—OH·CF_3COO^-·CH_3OH, (I). This pentapeptide contains two dehydrophenylalanyl residues of the *Z* configuration, each situated between two flexible glycine residues. There is one molecule in the asymmetric unit, but two types of molecules occur in the crystal, each represented by the opposite torsion angles. One of them is shown in Fig. 1. The most important geometric parameters are presented in Table 1.

An α,β-dehydrophenylalanyl residue contains a double bond between the Cα and Cβ atoms. The C^α—C^β distances (C3═C4 and C14═C15) agree with the double-bond distances found in other dehydropeptides containing two ΔPhe residues (Tuzi *et al.*, 1997; Makowski *et al.*, 2006, 2007*a*,*b*). A shortening of the Cα═Cβ distance because of the double bond causes unfavourable steric contacts between the side-chain and main-chain atoms of the dehydrophenylalanyl residues, which are partially relaxed by rearrangement of the N—C^α—C', N—C^α—C^β and C^α—C^β—C^γ bond angles. The same effects have been observed in other similar peptide structures (Jain *et al.*, 1997; Vijayaraghavan *et al.*, 1998; Ejsmont *et al.*, 2001; Goel *et al.*, 2005; Makowski *et al.*, 2005, 2006, 2007*a*,*b*).

All the amino acids in the title peptide are linked *trans* to each other. The deviations from the ideal values are not larger than 10°. The torsion angles χ^2 [−4.7 (3)°], $\chi^{2,1}$ [−28.3 (3)°] and $\chi^{2,2}$ [152.9 (2)°] of the first ΔPhe residue and χ^4 [−1.1 (3)°], $\chi^{4,1}$ [17.5 (3)°] and $\chi^{4,2}$ [−163.7 (2)°] of the second one suggest a synperiplanar conformation of the side chains. The Φ and Ψ torsion angles of the $\Delta^Z Phe^2$, Gly^3, and $\Delta^Z Phe^4$ residues correspond to the standard values for a type III β-turn (Venkatachalam, 1968). The ΔPhe residues are located at the (i+1) position of the first β-turn and the (i+2) position of the second β-turn. As a result, $\Delta^Z Phe^2$–Gly^3–$\Delta^Z Phe^4$ fragment adopts a right-handed 3_{10}-helical conformation. In this case, and in our earlier paper, the same significant deviations were observed for the Ψ torsion angles of the Gly residue surrounded by dehydrophenylalanyl residues (Makowski *et al.*, 2007*b*). In the pentapeptide Boc-Ala–ΔPhe-Gly–ΔPhe–Ala-OMe, where the identical central fragment adopts a right-handed helix, the same deviation is present (Ciajolo *et al.*, 1990). When two ΔPhe moieties are linked by Ala or Val residues, the 3_{10}-helix is less distorted (Ciajolo *et al.*, 1991; Tuzi *et al.*, 1997).

Both β-turns are stabilized by two intramolecular 4→1 hydrogen bonds between the CO and NH groups. All data concerning the hydrogen bonds are shown in Table 2. Each peptide cation forms two hydrogen bonds (N1—H1D···O7 and N1—H1D···F1) with the trifluoroacetate anion, and this ion interacts in turn with the methanol molecule (O9—H9···O8) and the next peptide moiety (N1—H1F···O8). Additionally, there are short C═O···C═O (C2═ O1···C26═O7) interactions between the peptide and methanol molecules. The molecular packing is presented in Fig. 2. Consecutive helical molecules, which form columns running parallel to the *c* axis, are linked by intermolecular N—H···O and C—H···O hydrogen bonds. The hydrogen-bonding pattern of the TFA-O^- ions and MeOH molecules makes a bridging support for connections between

consecutive peptide molecules in individual columns. The O5—H5···O9^{i} [symmetry code: (i) 1 − *x*, 1 − *y*, −*z*] hydrogen bond, with an O5···O9^{i} distance of 2.6 Å and O5—H5···O9^{i} angle of 172°, is exceptionally strong. The only interactions between the helices are hydrophobic contacts between the dehydrophenylalanyl rings and the methyl groups of the methanol molecules.

Experimental

The synthesis of the pentapeptide Boc-Gly–Δ^{Z}Phe–Gly–Δ^{Z}Phe–Gly-OMe has been described by Makowski *et al.* (2007*b*). Boc-Gly–Δ^{Z}Phe–Gly–Δ^{Z}Phe–Gly-OMe (0.059 g, 0.1 mmol) was dissolved in MeOH (1.5 ml), and then H_2O (0.1 ml) and NaOH (0.3 ml, 0.3 mmol) were added. The reaction was carried out for 30 min at room temperature. The reaction mixture was then acidified to pH 3 and brine (~10 ml) was added. The mixture was extracted with EtOAc (5 × 3 ml). The acetate extracts were washed with 0.5 *M* HCl (2 × 2 ml) and brine (2 × 2 ml), and filtered on anhydrous $MgSO_4$. After removal of EtOAc, Boc-Gly–Δ^{Z}Phe–Gly–Δ^{Z}Phe–Gly-OH was crystallized from EtOAc–hexane (Ratio?) [yield 0.056 g, 97%; m.p. 474–477 K (decomposition)]. Elemental analysis, calculated for $C_{29}H_{33}N_5O_8$: C 60.09, H 5.74, N 12.08%; found: C 59.89, H 5.98, N 12.12%. Boc-Gly–Δ^{Z}Phe–Gly–Δ^{Z}Phe–Gly-OH (0.058 g, 0.1 mmol) was dissolved in trifluoroacetic acid (TFA-OH; 1.0 ml) at room temperature and after 5 min, CH_2Cl_2 (~10 ml) was added. Solvents were evaporated and the resulting oil was evaporated twice with ~10 ml of CH_2Cl_2 and twice with ~10 ml of diethyl ether. The residue (a very dense oil) was dissolved in iPr-OH (1 ml) and the product was precipitated with hexane. Yield of Gly–Δ^{Z}Phe–Gly–Δ^{Z}Phe–Gly-OH·TFA was 0.056 g (94%). Elemental analysis for $C_{26}H_{26}N_5O_8F_3$ (593.52), calculated: C 52.62, H 4.41, N 11.80%; found: C 52.83, H 4.59, N 12.09%. Crystals were grown by slow diffusion of hexane into an EtOAc–methanol (1:3 *v*/*v*) solution of the compound at room temperature.

Refinement

All H atoms were positioned geometrically, with C—H distances in the range 0.95–0.99 Å, N—H = 0.88–0.91 Å and O—H = 0.84 Å, and refined with U_{iso}(H) = 1.5U_{eq}(methyl C, N1, O) and U_{iso}(H) = 1.2U_{eq}(non-methyl C, N).

Figures

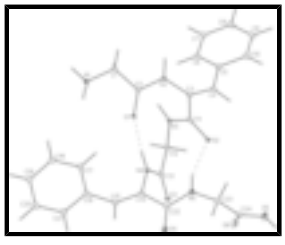


Fig. 1. The molecular structure of the cation of (I). Displacement ellipsoids are drawn at the 10% probability level. Intramolecular hydrogen bonds are shown as dashed lines.

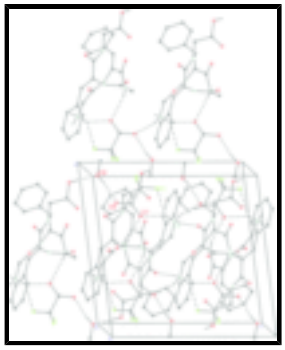


Fig. 2. The crystal packing of (I), viewed along the *b* axis. Dashed lines indicate the most important intermolecular hydrogen bonds, namely O—H···O, N—H···O and N—H···F.

N-[Glycyl-(*Z*)-α,β-dehydrophenylalanylglycyl- (*Z*)-α,β-dehydrophenylalanyl]glycine trifluoroacetate methanol solvate

Crystal data

$C_{24}H_{26}N_5O_6^+ \cdot C_2F_3O_2^- \cdot CH_4O$	F_{000} = 1304
M_r = 625.56	D_x = 1.407 Mg m^{-3}
Monoclinic, $P2_1/c$	Cu $K\alpha$ radiation λ = 1.5418 Å
Hall symbol: -P 2ybc	Cell parameters from 12781 reflections
a = 13.267 (7) Å	θ = 3–76º
b = 16.660 (8) Å	μ = 1.02 mm^{-1}
c = 13.459 (7) Å	T = 100 (2) K
β = 96.93 (3)º	Block, colourless
V = 2953 (3) Å^3	0.24 × 0.19 × 0.05 mm
Z = 4	

Data collection

Oxford Excalibur PX κ-geometry diffractometer plus CCD area detector	5723 independent reflections
Radiation source: fine-focus sealed tube	4191 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.032
T = 100(2) K	θ_{max} = 76.4º
ω and φ scans	θ_{min} = 3.4º
Absorption correction: numerical (CrysAlis RED; Oxford Diffraction, 2003)	h = −14→16
T_{min} = 0.792, T_{max} = 0.951	k = −20→16
24725 measured reflections	l = −14→16

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.048	$w = 1/[\sigma^2(F_o^2) + (0.0995P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$wR(F^2) = 0.144$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.03$	$\Delta\rho_{max} = 0.34$ e Å^{-3}
5723 reflections	$\Delta\rho_{min} = -0.46$ e Å^{-3}
402 parameters	Extinction correction: SHELXL97 (Sheldrick, 1997), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Primary atom site location: structure-invariant direct methods	Extinction coefficient: 0.0014 (2)
Secondary atom site location: difference Fourier map	

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.53257 (10)	0.65963 (7)	0.38921 (9)	0.0226 (3)
O2	0.35789 (10)	0.61904 (7)	0.14489 (10)	0.0289 (3)
O3	0.50702 (10)	0.43833 (7)	0.13987 (9)	0.0250 (3)
O4	0.34387 (11)	0.36464 (8)	0.36263 (10)	0.0349 (3)
O5	0.07560 (11)	0.43507 (11)	0.11459 (13)	0.0502 (5)
H5	0.0581	0.4086	0.0622	0.075*
O6	0.23100 (12)	0.40044 (11)	0.08600 (12)	0.0503 (5)
O7	0.72524 (11)	0.69533 (8)	0.28416 (10)	0.0328 (3)
O8	0.80852 (12)	0.68437 (9)	0.14902 (10)	0.0365 (4)
N1	0.69746 (12)	0.73717 (9)	0.48612 (12)	0.0246 (3)
H1D	0.7292	0.7208	0.4334	0.037*
H1E	0.6789	0.6935	0.5203	0.037*
H1F	0.7405	0.7683	0.5275	0.037*
N2	0.47801 (11)	0.77435 (8)	0.30588 (11)	0.0218 (3)
H2D	0.4893	0.8260	0.2991	0.026*
N3	0.52384 (12)	0.65305 (8)	0.16893 (11)	0.0216 (3)
H3D	0.5703	0.6896	0.1871	0.026*
N4	0.51646 (12)	0.51423 (9)	0.28102 (11)	0.0222 (3)
H4D	0.5325	0.5612	0.3084	0.027*
N5	0.31322 (12)	0.47507 (10)	0.26488 (12)	0.0288 (4)
H5D	0.3397	0.5173	0.2386	0.035*
F1	0.89846 (11)	0.70552 (11)	0.40390 (10)	0.0618 (4)
F2	0.96435 (11)	0.63636 (10)	0.29436 (12)	0.0615 (4)
F3	0.95760 (13)	0.76408 (10)	0.28123 (14)	0.0708 (5)

C1	0.60598 (14)	0.78420 (11)	0.44898 (14)	0.0244 (4)
H1A	0.6260	0.8329	0.4141	0.029*
H1B	0.5703	0.8012	0.5060	0.029*
C2	0.53631 (14)	0.73333 (10)	0.37793 (13)	0.0204 (4)
C3	0.39924 (14)	0.73758 (10)	0.24064 (13)	0.0230 (4)
C4	0.30397 (15)	0.76579 (11)	0.22699 (14)	0.0263 (4)
H4A	0.2595	0.7385	0.1776	0.032*
C5	0.25772 (14)	0.83269 (11)	0.27685 (14)	0.0269 (4)
C6	0.29061 (15)	0.85820 (11)	0.37512 (14)	0.0284 (4)
H6A	0.3453	0.8312	0.4133	0.034*
C7	0.24381 (16)	0.92255 (12)	0.41694 (16)	0.0325 (5)
H7A	0.2672	0.9395	0.4831	0.039*
C8	0.16315 (17)	0.96205 (13)	0.36268 (17)	0.0375 (5)
H8A	0.1317	1.0063	0.3912	0.045*
C9	0.12858 (17)	0.93647 (14)	0.26603 (17)	0.0390 (5)
H9A	0.0730	0.9631	0.2287	0.047*
C10	0.17474 (16)	0.87249 (12)	0.22412 (16)	0.0328 (5)
H10A	0.1498	0.8552	0.1585	0.039*
C11	0.42529 (15)	0.66568 (10)	0.18113 (13)	0.0236 (4)
C12	0.55121 (15)	0.57698 (10)	0.12477 (13)	0.0239 (4)
H12A	0.6254	0.5762	0.1218	0.029*
H12B	0.5171	0.5737	0.0553	0.029*
C13	0.52226 (14)	0.50366 (10)	0.18250 (13)	0.0216 (4)
C14	0.48482 (15)	0.45075 (10)	0.34211 (13)	0.0230 (4)
C15	0.54577 (16)	0.41652 (11)	0.41713 (14)	0.0273 (4)
H15A	0.5138	0.3759	0.4518	0.033*
C16	0.65261 (15)	0.43019 (11)	0.45553 (14)	0.0276 (4)
C21	0.70155 (17)	0.37048 (13)	0.51760 (15)	0.0357 (5)
H21A	0.6644	0.3242	0.5328	0.043*
C20	0.80258 (18)	0.37737 (14)	0.55707 (16)	0.0401 (5)
H20A	0.8342	0.3357	0.5978	0.048*
C19	0.85755 (17)	0.44510 (14)	0.53701 (16)	0.0390 (5)
H19A	0.9270	0.4499	0.5635	0.047*
C18	0.81013 (17)	0.50585 (13)	0.47785 (16)	0.0367 (5)
H18A	0.8471	0.5529	0.4653	0.044*
C17	0.70912 (16)	0.49856 (12)	0.43672 (15)	0.0314 (5)
H17A	0.6782	0.5402	0.3956	0.038*
C22	0.37529 (15)	0.42583 (11)	0.32361 (13)	0.0258 (4)
C23	0.20558 (15)	0.46164 (13)	0.24324 (15)	0.0334 (5)
H23A	0.1697	0.5131	0.2501	0.040*
H23B	0.1840	0.4239	0.2934	0.040*
C24	0.17370 (15)	0.42802 (12)	0.13944 (15)	0.0311 (5)
C25	0.90493 (18)	0.69935 (14)	0.30531 (16)	0.0383 (5)
C26	0.80132 (15)	0.69248 (11)	0.24016 (14)	0.0273 (4)
C27	1.0656 (2)	0.6760 (2)	0.0823 (3)	0.0687 (9)
H27A	1.0552	0.7332	0.0677	0.103*
H27B	1.1174	0.6548	0.0432	0.103*
H27C	1.0882	0.6689	0.1538	0.103*
O9	0.97470 (12)	0.63477 (11)	0.05703 (13)	0.0513 (5)

H9	0.9305	0.6526	0.0909	0.077*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0336 (7)	0.0150 (6)	0.0193 (6)	−0.0009 (5)	0.0037 (5)	0.0007 (5)
O2	0.0353 (8)	0.0192 (6)	0.0302 (7)	−0.0025 (6)	−0.0044 (6)	−0.0025 (5)
O3	0.0382 (7)	0.0136 (6)	0.0234 (6)	−0.0007 (5)	0.0046 (6)	−0.0017 (5)
O4	0.0457 (9)	0.0303 (7)	0.0285 (7)	−0.0119 (7)	0.0039 (6)	0.0069 (6)
O5	0.0296 (8)	0.0729 (12)	0.0479 (10)	0.0011 (8)	0.0034 (7)	−0.0217 (9)
O6	0.0356 (9)	0.0695 (12)	0.0449 (9)	0.0118 (8)	0.0018 (7)	−0.0231 (8)
O7	0.0340 (8)	0.0375 (8)	0.0269 (7)	−0.0015 (6)	0.0040 (6)	−0.0032 (6)
O8	0.0433 (8)	0.0416 (8)	0.0245 (7)	0.0123 (7)	0.0030 (6)	0.0008 (6)
N1	0.0290 (8)	0.0224 (8)	0.0223 (8)	−0.0028 (7)	0.0022 (6)	0.0001 (6)
N2	0.0282 (8)	0.0131 (7)	0.0238 (8)	−0.0016 (6)	0.0028 (6)	0.0001 (6)
N3	0.0317 (8)	0.0130 (7)	0.0201 (7)	−0.0009 (6)	0.0032 (6)	−0.0008 (6)
N4	0.0352 (8)	0.0137 (7)	0.0175 (7)	−0.0030 (6)	0.0025 (6)	−0.0007 (5)
N5	0.0318 (9)	0.0258 (8)	0.0288 (8)	−0.0029 (7)	0.0036 (7)	0.0024 (7)
F1	0.0468 (8)	0.1033 (13)	0.0340 (7)	−0.0026 (8)	−0.0001 (6)	−0.0101 (8)
F2	0.0486 (8)	0.0753 (11)	0.0568 (9)	0.0221 (8)	−0.0091 (7)	−0.0060 (8)
F3	0.0626 (10)	0.0738 (11)	0.0754 (11)	−0.0337 (9)	0.0060 (8)	0.0003 (9)
C1	0.0295 (10)	0.0195 (9)	0.0244 (9)	−0.0002 (8)	0.0035 (8)	−0.0010 (7)
C2	0.0274 (9)	0.0169 (8)	0.0181 (8)	0.0007 (7)	0.0076 (7)	−0.0008 (7)
C3	0.0305 (10)	0.0160 (8)	0.0222 (9)	−0.0011 (7)	0.0017 (7)	0.0015 (7)
C4	0.0313 (10)	0.0203 (9)	0.0265 (9)	−0.0021 (8)	0.0007 (8)	0.0024 (7)
C5	0.0278 (10)	0.0237 (9)	0.0298 (10)	0.0003 (8)	0.0062 (8)	0.0050 (8)
C6	0.0303 (10)	0.0261 (10)	0.0292 (10)	0.0019 (8)	0.0056 (8)	0.0023 (8)
C7	0.0361 (11)	0.0323 (11)	0.0304 (10)	0.0027 (9)	0.0095 (9)	0.0007 (8)
C8	0.0419 (12)	0.0313 (11)	0.0422 (12)	0.0089 (10)	0.0163 (10)	0.0033 (9)
C9	0.0373 (12)	0.0402 (12)	0.0402 (12)	0.0141 (10)	0.0072 (10)	0.0074 (9)
C10	0.0330 (11)	0.0336 (11)	0.0315 (10)	0.0049 (9)	0.0033 (8)	0.0038 (8)
C11	0.0345 (10)	0.0159 (8)	0.0196 (9)	0.0011 (8)	0.0000 (8)	0.0041 (7)
C12	0.0366 (10)	0.0150 (8)	0.0204 (9)	0.0007 (8)	0.0044 (7)	−0.0005 (7)
C13	0.0268 (9)	0.0165 (8)	0.0215 (9)	0.0021 (7)	0.0030 (7)	−0.0001 (7)
C14	0.0349 (10)	0.0161 (8)	0.0186 (8)	−0.0013 (8)	0.0056 (7)	−0.0001 (7)
C15	0.0394 (11)	0.0198 (9)	0.0236 (9)	0.0005 (8)	0.0077 (8)	0.0021 (7)
C16	0.0357 (11)	0.0268 (10)	0.0208 (9)	0.0036 (8)	0.0060 (8)	0.0005 (7)
C21	0.0418 (12)	0.0348 (11)	0.0308 (10)	0.0046 (10)	0.0060 (9)	0.0083 (9)
C20	0.0425 (13)	0.0449 (13)	0.0326 (11)	0.0108 (11)	0.0031 (9)	0.0094 (9)
C19	0.0353 (11)	0.0486 (13)	0.0321 (11)	0.0066 (10)	0.0002 (9)	−0.0030 (10)
C18	0.0398 (12)	0.0338 (11)	0.0359 (12)	−0.0014 (9)	0.0024 (9)	−0.0047 (9)
C17	0.0375 (11)	0.0265 (10)	0.0295 (10)	0.0035 (9)	0.0008 (9)	0.0008 (8)
C22	0.0376 (11)	0.0221 (9)	0.0184 (8)	−0.0034 (8)	0.0066 (8)	−0.0008 (7)
C23	0.0315 (11)	0.0382 (11)	0.0310 (11)	−0.0020 (9)	0.0061 (8)	−0.0019 (9)
C24	0.0298 (11)	0.0276 (10)	0.0362 (11)	0.0013 (8)	0.0048 (9)	−0.0016 (8)
C25	0.0396 (12)	0.0463 (13)	0.0299 (11)	0.0025 (10)	0.0081 (9)	−0.0008 (9)
C26	0.0322 (11)	0.0255 (10)	0.0244 (9)	0.0030 (8)	0.0038 (8)	0.0004 (8)
C27	0.0431 (15)	0.088 (2)	0.077 (2)	−0.0201 (15)	0.0135 (14)	−0.0356 (17)

O9	0.0359 (9)	0.0674 (12)	0.0510 (10)	−0.0082 (8)	0.0067 (7)	−0.0200 (9)

Geometric parameters (Å, °)

O1—C2	1.239 (2)	C6—C7	1.391 (3)
O2—C11	1.239 (2)	C6—H6A	0.9500
O3—C13	1.236 (2)	C7—C8	1.387 (3)
O4—C22	1.242 (2)	C7—H7A	0.9500
O5—C24	1.309 (3)	C8—C9	1.393 (3)
O5—H5	0.8400	C8—H8A	0.9500
O6—C24	1.199 (3)	C9—C10	1.383 (3)
O7—C26	1.231 (3)	C9—H9A	0.9500
O8—C26	1.249 (2)	C10—H10A	0.9500
N1—C1	1.480 (2)	C12—C13	1.522 (2)
N1—H1D	0.9100	C12—H12A	0.9900
N1—H1E	0.9100	C12—H12B	0.9900
N1—H1F	0.9100	C14—C15	1.342 (3)
N2—C2	1.351 (2)	C14—C22	1.503 (3)
N2—C3	1.420 (2)	C15—C16	1.467 (3)
N2—H2D	0.8800	C15—H15A	0.9500
N3—C11	1.354 (3)	C16—C17	1.403 (3)
N3—C12	1.464 (2)	C16—C21	1.406 (3)
N3—H3D	0.8800	C21—C20	1.386 (3)
N4—C13	1.349 (2)	C21—H21A	0.9500
N4—C14	1.433 (2)	C20—C19	1.388 (3)
N4—H4D	0.8800	C20—H20A	0.9500
N5—C22	1.349 (3)	C19—C18	1.391 (3)
N5—C23	1.440 (3)	C19—H19A	0.9500
N5—H5D	0.8800	C18—C17	1.392 (3)
F1—C25	1.344 (3)	C18—H18A	0.9500
F2—C25	1.331 (3)	C17—H17A	0.9500
F3—C25	1.346 (3)	C23—C24	1.517 (3)
C1—C2	1.508 (3)	C23—H23A	0.9900
C1—H1A	0.9900	C23—H23B	0.9900
C1—H1B	0.9900	C25—C26	1.543 (3)
C3—C4	1.340 (3)	C27—O9	1.394 (3)
C3—C11	1.504 (3)	C27—H27A	0.9800
C4—C5	1.473 (3)	C27—H27B	0.9800
C4—H4A	0.9500	C27—H27C	0.9800
C5—C10	1.402 (3)	O9—H9	0.8400
C5—C6	1.407 (3)		
C24—O5—H5	109.5	N3—C12—H12B	108.9
C1—N1—H1D	109.5	C13—C12—H12B	108.9
C1—N1—H1E	109.5	H12A—C12—H12B	107.7
H1D—N1—H1E	109.5	O3—C13—N4	123.10 (16)
C1—N1—H1F	109.5	O3—C13—C12	120.47 (16)
H1D—N1—H1F	109.5	N4—C13—C12	116.42 (15)
H1E—N1—H1F	109.5	C15—C14—N4	123.6 (2)
C2—N2—C3	122.72 (15)	C15—C14—C22	119.3 (2)

C2—N2—H2D	118.6	N4—C14—C22	116.9 (2)
C3—N2—H2D	118.6	C14—C15—C16	131.9 (2)
C11—N3—C12	118.31 (15)	C14—C15—H15A	114.0
C11—N3—H3D	120.8	C16—C15—H15A	114.0
C12—N3—H3D	120.8	C17—C16—C21	117.57 (19)
C13—N4—C14	121.53 (14)	C17—C16—C15	125.24 (17)
C13—N4—H4D	119.2	C21—C16—C15	117.18 (18)
C14—N4—H4D	119.2	C20—C21—C16	121.7 (2)
C22—N5—C23	122.99 (17)	C20—C21—H21A	119.2
C22—N5—H5D	118.5	C16—C21—H21A	119.2
C23—N5—H5D	118.5	C21—C20—C19	120.0 (2)
N1—C1—C2	109.37 (15)	C21—C20—H20A	120.0
N1—C1—H1A	109.8	C19—C20—H20A	120.0
C2—C1—H1A	109.8	C20—C19—C18	119.4 (2)
N1—C1—H1B	109.8	C20—C19—H19A	120.3
C2—C1—H1B	109.8	C18—C19—H19A	120.3
H1A—C1—H1B	108.2	C19—C18—C17	120.8 (2)
O1—C2—N2	124.15 (16)	C19—C18—H18A	119.6
O1—C2—C1	120.66 (16)	C17—C18—H18A	119.6
N2—C2—C1	115.15 (15)	C18—C17—C16	120.57 (19)
C4—C3—N2	123.0 (2)	C18—C17—H17A	119.7
C4—C3—C11	118.7 (2)	C16—C17—H17A	119.7
N2—C3—C11	118.3 (2)	O4—C22—N5	122.34 (18)
C3—C4—C5	129.9 (2)	O4—C22—C14	121.60 (17)
C3—C4—H4A	115.1	N5—C22—C14	116.03 (16)
C5—C4—H4A	115.1	N5—C23—C24	113.77 (17)
C10—C5—C6	117.92 (18)	N5—C23—H23A	108.8
C10—C5—C4	118.17 (18)	C24—C23—H23A	108.8
C6—C5—C4	123.90 (17)	N5—C23—H23B	108.8
C7—C6—C5	120.65 (19)	C24—C23—H23B	108.8
C7—C6—H6A	119.7	H23A—C23—H23B	107.7
C5—C6—H6A	119.7	O6—C24—O5	124.3 (2)
C8—C7—C6	120.4 (2)	O6—C24—C23	124.56 (19)
C8—C7—H7A	119.8	O5—C24—C23	111.11 (17)
C6—C7—H7A	119.8	F2—C25—F1	106.18 (18)
C7—C8—C9	119.5 (2)	F2—C25—F3	105.86 (19)
C7—C8—H8A	120.2	F1—C25—F3	105.86 (19)
C9—C8—H8A	120.2	F2—C25—C26	112.18 (18)
C10—C9—C8	120.3 (2)	F1—C25—C26	114.09 (19)
C10—C9—H9A	119.8	F3—C25—C26	112.06 (18)
C8—C9—H9A	119.8	O7—C26—O8	129.84 (19)
C9—C10—C5	121.1 (2)	O7—C26—C25	116.73 (17)
C9—C10—H10A	119.4	O8—C26—C25	113.43 (18)
C5—C10—H10A	119.4	O9—C27—H27A	109.5
O2—C11—N3	121.10 (17)	O9—C27—H27B	109.5
O2—C11—C3	120.50 (17)	H27A—C27—H27B	109.5
N3—C11—C3	118.40 (16)	O9—C27—H27C	109.5
N3—C12—C13	113.41 (15)	H27A—C27—H27C	109.5
N3—C12—H12A	108.9	H27B—C27—H27C	109.5

C13—C12—H12A	108.9	C27—O9—H9	109.5
N1—C1—C2—N2	−150.7 (2)	C6—C5—C10—C9	2.0 (3)
C3—N2—C2—C1	−171.8 (2)	C4—C5—C10—C9	−179.15 (19)
C2—N2—C3—C11	−55.0 (2)	C12—N3—C11—O2	−8.9 (2)
N2—C3—C11—N3	−19.0 (2)	C4—C3—C11—O2	−21.9 (3)
C12—N3—C11—C3	170.6 (2)	N2—C3—C11—O2	160.54 (16)
N2—C3—C4—C5	−4.7 (3)	C4—C3—C11—N3	158.56 (17)
C3—C4—C5—C6	−28.3 (3)	C14—N4—C13—O3	−4.5 (3)
C3—C4—C5—C10	152.9 (2)	N3—C12—C13—O3	154.67 (17)
C11—N3—C12—C13	−57.6 (2)	C13—N4—C14—C15	114.5 (2)
N3—C12—C13—N4	−26.5 (2)	C22—C14—C15—C16	−177.20 (18)
C14—N4—C13—C12	176.7 (2)	C17—C16—C21—C20	−1.6 (3)
C13—N4—C14—C22	−69.4 (2)	C15—C16—C21—C20	179.50 (19)
N4—C14—C22—N5	−12.0 (2)	C16—C21—C20—C19	1.1 (3)
C23—N5—C22—C14	−177.3 (2)	C21—C20—C19—C18	0.5 (3)
N4—C14—C15—C16	−1.1 (3)	C20—C19—C18—C17	−1.6 (3)
C14—C15—C16—C17	17.5 (3)	C19—C18—C17—C16	1.0 (3)
C14—C15—C16—C21	−163.7 (2)	C21—C16—C17—C18	0.5 (3)
C22—N5—C23—C24	−103.4 (2)	C15—C16—C17—C18	179.33 (18)
N5—C23—C24—O5	−164.7 (2)	C23—N5—C22—O4	0.7 (3)
C3—N2—C2—O1	5.9 (3)	C15—C14—C22—O4	−13.7 (3)
N1—C1—C2—O1	31.5 (2)	N4—C14—C22—O4	169.95 (16)
C2—N2—C3—C4	127.6 (2)	C15—C14—C22—N5	164.33 (17)
C11—C3—C4—C5	177.90 (17)	N5—C23—C24—O6	13.6 (3)
C10—C5—C6—C7	−1.9 (3)	F2—C25—C26—O7	122.5 (2)
C4—C5—C6—C7	179.30 (18)	F1—C25—C26—O7	1.7 (3)
C5—C6—C7—C8	0.7 (3)	F3—C25—C26—O7	−118.6 (2)
C6—C7—C8—C9	0.5 (3)	F2—C25—C26—O8	−57.2 (2)
C7—C8—C9—C10	−0.5 (3)	F1—C25—C26—O8	−177.97 (18)
C8—C9—C10—C5	−0.8 (3)	F3—C25—C26—O8	61.7 (2)

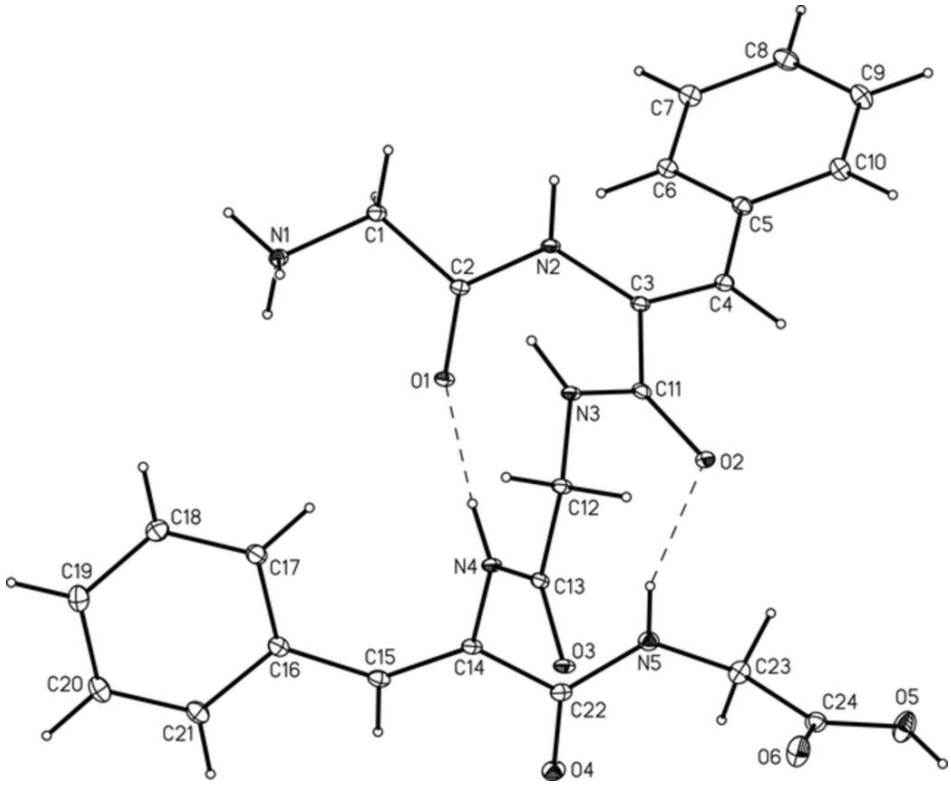
Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O9—H9···O8	0.84	1.95	2.781 (2)	169
O5—H5···O9^{i}	0.84	1.77	2.600 (3)	172
N1—H1D···O7	0.91	2.05	2.873 (2)	150
N1—H1E···O4^{ii}	0.91	1.90	2.755 (2)	155
N1—H1F···O8^{iii}	0.91	1.94	2.812 (2)	160
N2—H2D···O3^{iv}	0.88	2.04	2.829 (2)	148
N3—H3D···O7	0.88	2.30	3.007 (3)	137
N4—H4D···O1	0.88	1.97	2.821 (2)	163
N5—H5D···O2	0.88	2.14	2.991 (2)	161
N1—H1D···F1	0.91	2.34	3.054 (3)	135
N3—H3D···N2	0.88	2.55	2.850 (2)	101
N4—H4D···N3	0.88	2.41	2.769 (2)	105
N5—H5D···N4	0.88	2.35	2.757 (3)	109
C1—H1A···O3^{iv}	0.99	2.53	3.137 (2)	119

C1—H1A···O6^{iv}	0.99	2.21	2.982 (3)	134
C4—H4A···O2	0.95	2.45	2.811 (3)	102
C7—H7A···O2^{iii}	0.95	2.55	3.326 (3)	139
C15—H15A···O4	0.95	2.43	2.826 (3)	105
C15—H15A···O1^{ii}	0.95	2.37	3.184 (3)	143
C23—H23B···O4	0.99	2.42	2.802 (3)	102
C1—H1B···N3^{iii}	0.99	2.47	3.438 (3)	166
C6—H6A···N2	0.95	2.59	3.092 (3)	114
C17—H17A···N4	0.95	2.52	3.114 (3)	120

Symmetry codes: (i) −*x*+1, −*y*+1, −*z*; (ii) −*x*+1, −*y*+1, −*z*+1; (iii) *x*, −*y*+3/2, *z*+1/2; (iv) −*x*+1, *y*+1/2, −*z*+1/2.

Fig. 1


C8
C9
C7
C10
C6
C5
N1
C1
C2
N2
C3
C4
O1
C11
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O2
C12
C18
C19
C17
N4
C13
C15
C16
C14
O3
N5
C23
C20
C22
C24
O5
C21
O6
O4

Fig. 2