organic compounds

5′-Chlorospiro[1,3-dioxolane-2,3′-indolin]-2′-one: a potential anti-convulsant

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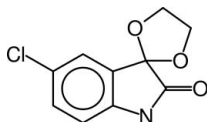Correspondence e-mail: amitde03@yahoo.com

The title compound, $C_{10}H_8ClNO_3$, is a significant anti-convulsant agent. The indolinone system is essentially planar, the dihedral angle between the rings being 2.24 (8)°. The dioxolane ring adopts an envelope conformation; the dihedral angle between the plane through its four coplanar atoms and the indolinone system is 89.8 (1)°. The crystal structure is stabilized by a three-dimensional network of intermolecular N—H···O hydrogen bonds.

Related literature

For related literature, see: Codding *et al.* (1984); De (1990, 1992); De & Kitagawa (1991*a*,*b*); De & Kusunoki (1991); Dickerson & Geis (1969); Itai *et al.* (1978); James & Williams (1972); Popp (1977, 1984); Rajopadhye & Popp (1988); Chakraborty & Talapatra (1985); Chakraborty *et al.* (1985).

Experimental

Crystal data

$C_{10}H_8ClNO_3$	$V = 1990.0$ (4) Å^3
$M_r = 225.62$	$Z = 8$
Monoclinic, $I2/c$	Mo $K\alpha$ radiation
$a = 18.266$ (2) Å	$\mu = 0.37$ mm^{-1}
$b = 7.360$ (1) Å	$T = 298$ (2) K
$c = 14.821$ (1) Å	$0.50 \times 0.30 \times 0.30$ mm
$\beta = 92.855$ (7)°	

Data collection

Rigaku AFC-4 diffractometer	2479 measured reflections
Absorption correction: none	2297 independent reflections
1591 reflections with $I > 2\sigma(I)$	3 standard reflections
$R_{int} = 0.042$	every 100 reflections
	intensity decay: 0.2%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$	H atoms treated by a mixture of
$wR(F^2) = 0.189$	independent and constrained
$S = 0.83$	refinement
2297 reflections	$\Delta\rho_{max} = 0.34$ e Å^{-3}
160 parameters	$\Delta\rho_{min} = -0.52$ e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^i	0.82 (3)	2.11 (3)	2.885 (4)	157.4 (3)

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

Data collection: *AFC-4 Diffractometer Control Software* (Rigaku, 1997); cell refinement: *AFC-4 Diffractometer Control Software*; data reduction: *AFC-4 Diffractometer Control Software*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP* (Johnson, 1965); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1983).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: ER2049).

References

Chakraborty, D. K. & Talapatra, S. K. (1985). *Acta Cryst.* C**41**, 1365–1366.
Chakraborty, D. K., Talapatra, S. K. & Chatterjee, A. (1985). *Acta Cryst.* C**41**, 1363–1364.
Codding, P. W., Lee, T. A. & Richardson, J. F. (1984). *J. Med. Chem.* **27**, 649–654.
De, A. (1990). *Acta Cryst.* C**46**, 1891–1893.
De, A. (1992). *Acta Cryst.* C**48**, 660–662.
De, A. & Kitagawa, Y. (1991*a*). *Acta Cryst.* C**47**, 2179–2181.
De, A. & Kitagawa, Y. (1991*b*). *Acta Cryst.* C**47**, 2384–2386.
De, A. & Kusunoki, M. (1991). *J. Crystallogr. Spectrosc. Res.* **21**, 57–60.
Dickerson, R. E. & Geis, I. (1969). *The Structure and Function of Proteins.* Menlo Park, California: Benjamin.
Itai, A., Iitaka, Y. & Kubo, A. (1978). *Acta Cryst.* B**34**, 3775–3777.
James, M. N. G. & Williams, G. J. B. (1972). *Can. J. Chem.* **50**, 2407–2412.
Johnson, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Nardelli, M. (1983). *Comput. Chem.* **7**, 95–97.
Popp, F. D. (1977). In *Anticonvulsants*, edited by J. A. Vida. New York: Academic Press.
Popp, F. D. (1984). *J. Heterocycl. Chem.* **21**, 1641–1643.
Rajopadhye, M. & Popp, F. D. (1988). *J. Med. Chem.* **31**, 1001–1005.
Rigaku (1997). *AFC-4 Diffractometer Control Software.* Rigaku Corporation, Tokyo, Japan.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

supporting information

5′-Chlorospiro[1,3-dioxolane-2,3′-indolin]-2′-one: a potential anticonvulsant

Amitabha De

S1. Comment

Anti-epileptic drugs have diverse chemical structures and complex physiological and pharmacological actions. The search for potential drugs and their mechanism of action has been difficult because of their complexity. A series of spiro-(1,3-dioxane-2,3′-indolin)-2′-one and structural analogues active against electrically and chemically induced seizures have been studied. These compounds contain both an oxoindole and a dioxolane moiety which have independently been seen in other anticonvulsants (Popp, 1977, 1984). The basic model compound, mentioned above, was used to study the effects of various electron-donating, electron withdrawing and hydrophobic groups on the activity of the molecule. A bulky hydrophobic substituent at the 1′-position (oxoindole) generally tends to decrease the activity. The present compound, a chloro analogue was found to be most potent in the MES test. Since no common target site has yet been established, X-ray analysis was undertaken to search structural information which may help in the understanding of the mechanism of action at the molecular level.

The conformation of the title compound along with the atom-numbering scheme is shown in Fig 1. The carbonyl C atom to tetrahedral C atom distance is typical of a single bond. The C(2) - C(3) bond distance is slightly shorter but closely similar to the values found in other indoline nuclie (Itai *et al.*, 1978; Chakraborty & Talapatra, 1985; Chakraborty *et al.*, 1985; De & Kitagawa, 1991*a*,b; De, 1992). The lone pair of electrons on N(1) is involved in conjugation with the carbonyl group. This is also indicated by the slight lengthening of the C=O double bond [1.220 (4) Å] and the concomitant shortening of the two N - C(sp^2) single bonds [1.341 (4) Å and 1.412 (4) Å] (Codding *et al.*, 1984). The least-squares planes through the five- and six-membered rings are inclined to one another at 2.24 (8)° and each of them are almost planar. The plane containing the atoms C(2), O(2), O(3), C(9) and C(10) is inclined to the overall plane through the indolinone group by 89.8 (1)°. The C—NH—CO—C grouping resembles a *cis* peptide bond. Six atoms of this group [C(8), N(1), H1,*C*(1),*O*(1),*C*(2)] are almost planar. The OC—N bond distance [1.341 (4) Å] is not as short as the normal peptide bond(1.325 Å) (Dickerson & Geis,1969). The packing of the molecule is shown in Fig. 2. The amide nitrogen, N(1), forms a hydrogen bond with the carbonyl oxygen O(1) [N(1) - H1] = 0.82 (3), N(1)···O(1) = 2.885 (4), H1···O(1) = 2.11 (3) Å, N(1) –H1···O(1) = 157.4 (3) °]. The molecules are thus held together by a three-dimensional network of hydrogen bonds.

S2. Experimental

The synthesis of the compound has been described earlier (Rajopadhye & Popp, 1988). Diffraction quality crystals were obtained by slow evaporation of an ethanol solution at room temperature.

S3. Refinement

All the hydrogen atoms in the structure were located in a difference map except the two H-atoms on C10. They were placed at geometrically idealized positions. Geometric calculations were performed using *SHELXL-97*, *PARST* (Nardelli,
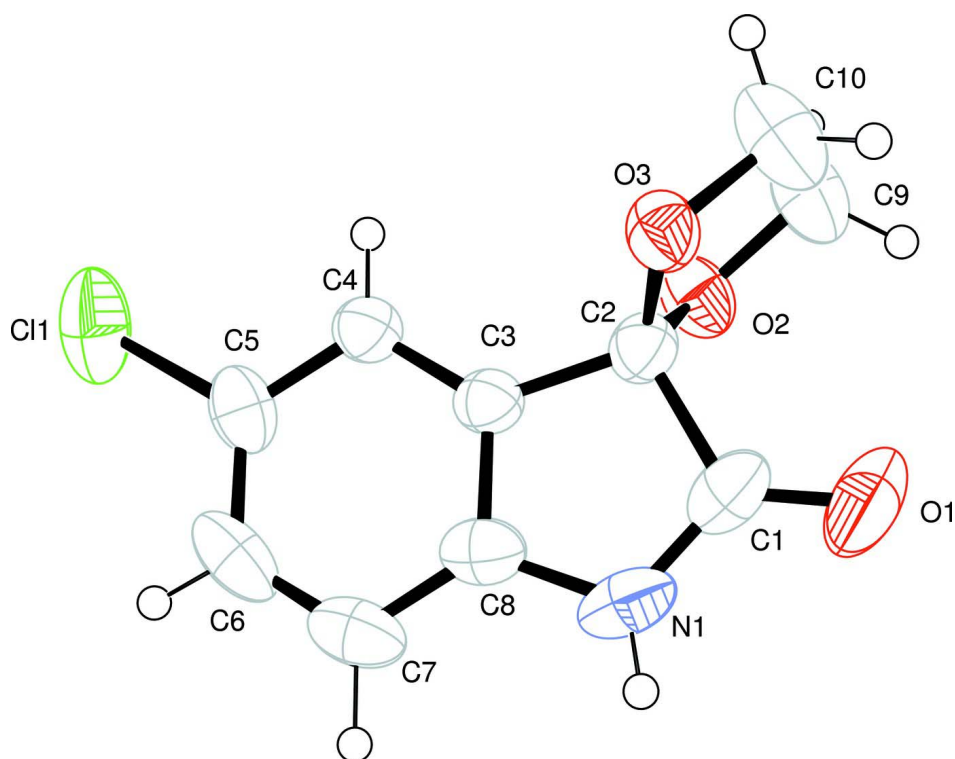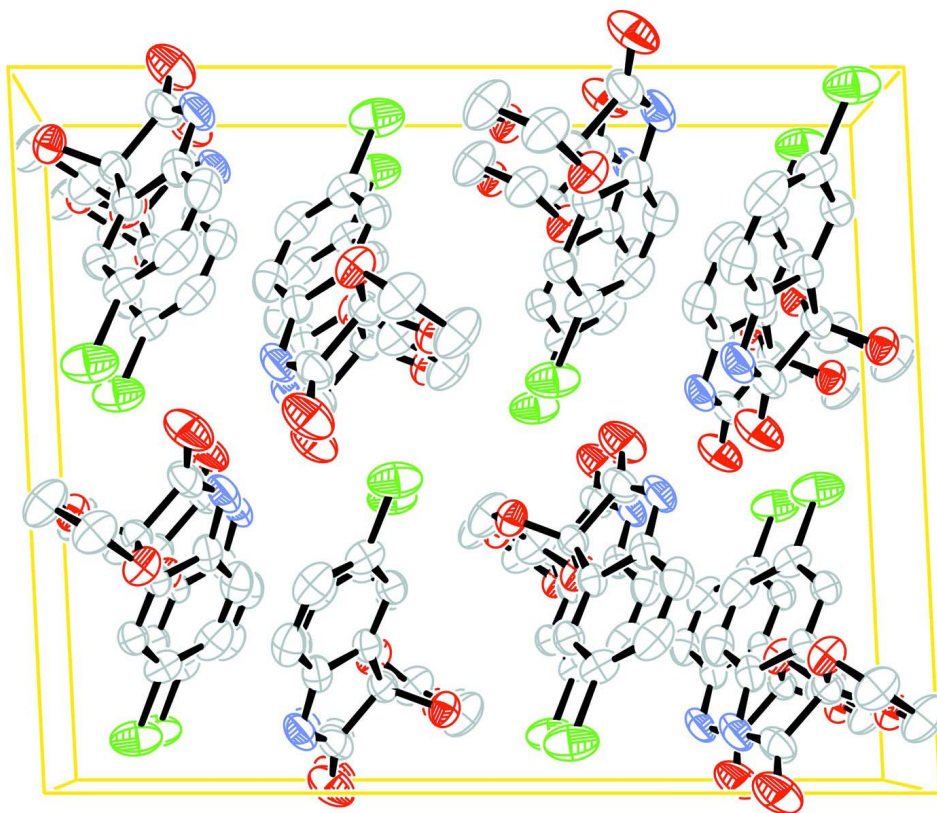
1983) programs.

Figure 1

ORTEP (Johnson, 1965) diagram of the Molecular structure with atom labels showing displacement ellipsoids at 50% probablity.

Figure 2

Packing of the molecule viewed down the *b* axis.

5′-Chlorospiro[1,3-dioxolane-2,3′-indolin]-2′-one

Crystal data

$C_{10}H_8ClNO_3$	$D_x = 1.506$ Mg m^{-3}
$M_r = 225.62$	$D_m = 1.498$ Mg m^{-3}
Monoclinic, $I2/c$	D_m measured by flotation
Hall symbol: -I 2yc	Melting point: 460 K
$a = 18.266$ (2) Å	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$b = 7.360$ (1) Å	Cell parameters from 25 reflections
$c = 14.821$ (1) Å	$\theta = 2.2–27.5°$
$\beta = 92.855$ (7)°	$\mu = 0.37$ mm^{-1}
$V = 1990.0$ (4) Å^3	$T = 298$ K
$Z = 8$	Needle, colourless
$F(000) = 928$	$0.50 \times 0.30 \times 0.30$ mm

Data collection

Rigaku AFC-4 diffractometer	$R_{int} = 0.042$
Radiation source: fine-focus sealed tube	$\theta_{max} = 27.5°$, $\theta_{min} = 2.2°$
Graphite monochromator	$h = -23 \rightarrow 23$
ω scans	$k = 0 \rightarrow 9$
2479 measured reflections	$l = 0 \rightarrow 19$
2297 independent reflections	3 standard reflections every 100 reflections
1591 reflections with $I > 2\sigma(I)$	intensity decay: 0.2%

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	
$R[F^2 > 2\sigma(F^2)] = 0.049$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.189$	
$S = 0.83$	H atoms treated by a mixture of independent and constrained refinement
2297 reflections	
160 parameters	$w = 1/[\sigma^2(F_o^2) + (0.1365P)^2 + 2.6179P]$
0 restraints	where $P = (F_o^2 + 2F_c^2)/3$
Primary atom site location: structure-invariant direct methods	$(\Delta/\sigma)_{max} = 0.006$
	$\Delta\rho_{max} = 0.34$ e Å^{-3}
	$\Delta\rho_{min} = -0.52$ e Å^{-3}

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 on F^2 for ALL reflections except for 0 with very negative F^2 or flagged by the user for potential systematic errors. Weighted R-factors wR and all goodnesses 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 observed criterion of $F^2 > \sigma(F^2)$ is used only for calculating _R_factor_obs *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 (Å²)

	x	y	z	U_{iso}*/U_{eq}
Cl1	0.40898 (6)	−0.00775 (11)	0.43060 (5)	0.0825 (4)
O1	0.3184 (2)	0.5049 (4)	0.0001 (2)	0.0931 (9)
O2	0.37608 (10)	0.5934 (2)	0.18885 (12)	0.0534 (5)
O3	0.45532 (9)	0.4244 (2)	0.11210 (12)	0.0494 (4)
N1	0.28723 (12)	0.2542 (4)	0.0815 (2)	0.0612 (6)
C1	0.3263 (2)	0.4038 (4)	0.0651 (2)	0.0596 (7)
C2	0.38452 (12)	0.4261 (3)	0.1450 (2)	0.0442 (5)
C3	0.36853 (11)	0.2671 (3)	0.20354 (15)	0.0418 (5)
C4	0.40017 (12)	0.2147 (3)	0.2858 (2)	0.0446 (5)
C5	0.3712 (2)	0.0628 (3)	0.3264 (2)	0.0516 (6)
C6	0.3125 (2)	−0.0317 (4)	0.2873 (2)	0.0634 (8)
C7	0.2809 (2)	0.0217 (4)	0.2041 (2)	0.0606 (7)
C8	0.31030 (12)	0.1704 (3)	0.1639 (2)	0.0484 (5)
C9	0.4219 (2)	0.7216 (4)	0.1450 (2)	0.0678 (8)
C10	0.4787 (2)	0.6085 (4)	0.1035 (3)	0.0759 (9)
H4	0.4389 (16)	0.275 (4)	0.3142 (18)	0.051 (7)*
H6	0.2955 (19)	−0.126 (5)	0.316 (2)	0.069 (9)*
H7	0.234 (2)	−0.037 (5)	0.181 (2)	0.077 (10)*
H1	0.2565 (18)	0.206 (5)	0.047 (2)	0.062 (9)*
H91	0.393 (2)	0.792 (6)	0.102 (3)	0.110 (14)*
H92	0.441 (2)	0.808 (7)	0.189 (3)	0.086 (11)*
H101	0.5260	0.6263	0.1351	0.08*
H102	0.4822	0.6401	0.0403	0.08*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.1293 (9)	0.0619 (5)	0.0567 (5)	0.0119 (4)	0.0092 (5)	0.0165 (3)
O1	0.099 (2)	0.100 (2)	0.077 (2)	0.0173 (14)	−0.0313 (13)	0.0273 (14)
O2	0.0595 (10)	0.0389 (9)	0.0630 (10)	0.0018 (7)	0.0167 (8)	−0.0016 (7)
O3	0.0459 (8)	0.0434 (9)	0.0594 (10)	0.0071 (7)	0.0089 (7)	0.0065 (7)
N1	0.0475 (11)	0.0723 (15)	0.0617 (13)	0.0053 (11)	−0.0181 (10)	−0.0182 (12)
C1	0.0552 (13)	0.065 (2)	0.0573 (14)	0.0149 (12)	−0.0140 (11)	0.0000 (12)
C2	0.0427 (10)	0.0426 (11)	0.0467 (11)	0.0043 (8)	−0.0024 (8)	0.0014 (9)
C3	0.0367 (9)	0.0384 (10)	0.0500 (11)	0.0013 (8)	−0.0004 (8)	−0.0026 (9)
C4	0.0426 (11)	0.0400 (11)	0.0509 (12)	−0.0019 (9)	−0.0016 (9)	−0.0015 (9)
C5	0.0677 (14)	0.0371 (11)	0.0514 (12)	0.0043 (10)	0.0157 (11)	0.0016 (9)
C6	0.077 (2)	0.0349 (11)	0.081 (2)	−0.0119 (12)	0.031 (2)	−0.0082 (12)
C7	0.0508 (13)	0.0505 (14)	0.081 (2)	−0.0119 (11)	0.0094 (12)	−0.0206 (13)
C8	0.0393 (10)	0.0447 (11)	0.0608 (13)	0.0020 (9)	0.0001 (9)	−0.0156 (10)
C9	0.083 (2)	0.0459 (14)	0.076 (2)	−0.0025 (13)	0.022 (2)	0.0066 (14)
C10	0.086 (2)	0.051 (2)	0.095 (2)	−0.0020 (15)	0.041 (2)	0.005 (2)

Geometric parameters (Å, º)

Cl1—C5	1.740 (3)	C4—C5	1.386 (3)
O1—C1	1.220 (4)	C4—H4	0.92 (3)
O2—C2	1.404 (3)	C5—C6	1.381 (4)
O2—C9	1.438 (3)	C6—C7	1.392 (5)
O3—C2	1.405 (3)	C6—H6	0.88 (4)
O3—C10	1.429 (4)	C7—C8	1.369 (4)
N1—C1	1.341 (4)	C7—H7	1.01 (4)
N1—C8	1.412 (4)	C9—C10	1.487 (4)
N1—H1	0.82 (3)	C9—H91	0.96 (4)
C1—C2	1.560 (3)	C9—H92	0.96 (4)
C2—C3	1.494 (3)	C10—H101	0.97
C3—C4	1.378 (3)	C10—H102	0.97
C3—C8	1.386 (3)		
C2—O2—C9	106.6 (2)	C4—C5—Cl1	118.8 (2)
C2—O3—C10	107.9 (2)	C5—C6—C7	120.6 (2)
C1—N1—C8	112.1 (2)	C5—C6—H6	119 (2)
C1—N1—H1	127 (2)	C7—C6—H6	121 (2)
C8—N1—H1	121 (2)	C8—C7—C6	117.2 (2)
O1—C1—N1	127.0 (3)	C8—C7—H7	123 (2)
O1—C1—C2	125.8 (3)	C6—C7—H7	119 (2)
N1—C1—C2	107.3 (2)	C7—C8—C3	122.4 (2)
O3—C2—O2	107.0 (2)	C7—C8—N1	128.2 (2)
O3—C2—C3	113.9 (2)	C3—C8—N1	109.4 (2)
O2—C2—C3	112.9 (2)	O2—C9—C10	104.7 (2)
O3—C2—C1	109.8 (2)	O2—C9—H91	110 (3)
O2—C2—C1	110.9 (2)	C10—C9—H91	114 (3)

C3—C2—C1	102.3 (2)	O2—C9—H92	109 (2)
C4—C3—C8	120.7 (2)	C10—C9—H92	115 (2)
C4—C3—C2	130.3 (2)	H91—C9—H92	105 (4)
C8—C3—C2	108.9 (2)	O3—C10—C9	106.0 (2)
C3—C4—C5	117.2 (2)	O3—C10—H101	110.3
C3—C4—H4	123.2 (17)	C9—C10—H101	111.0
C5—C4—H4	119.6 (17)	O3—C10—H102	110.3
C6—C5—C4	122.0 (3)	C9—C10—H102	110.3
C6—C5—Cl1	119.2 (2)	H101—C10—H102	110.0
C9—O2—C2—O3	28.9 (2)	O2—C2—C3—C8	118.8 (2)
C9—O2—C2—C1	−90.9 (2)	O3—C2—C3—C4	63.6 (3)
C9—O2—C2—C3	155.0 (2)	O3—C2—C3—C8	−118.9 (2)
C2—O2—C9—C10	−23.5 (3)	C1—C2—C3—C4	−177.9 (2)
C10—O3—C2—O2	−22.6 (3)	C1—C2—C3—C8	−0.4 (2)
C10—O3—C2—C1	97.9 (2)	C2—C3—C4—C5	177.2 (2)
C10—O3—C2—C3	−148.1 (2)	C2—C3—C8—N1	0.9 (3)
C2—O3—C10—C9	7.5 (3)	C2—C3—C8—C7	−176.9 (2)
C8—N1—C1—O1	−179.1 (3)	C4—C3—C8—N1	178.7 (2)
C8—N1—C1—C2	0.8 (3)	C4—C3—C8—C7	0.9 (4)
C1—N1—C8—C3	−1.1 (3)	C3—C4—C5—Cl1	−179.6 (2)
C1—N1—C8—C7	176.6 (3)	C3—C4—C5—C6	−0.9 (4)
O1—C1—C2—O2	59.0 (4)	Cl1—C5—C6—C7	179.8 (2)
O1—C1—C2—O3	−59.1 (4)	C4—C5—C6—C7	1.0 (4)
O1—C1—C2—C3	179.7 (3)	C5—C6—C7—C8	−0.2 (4)
N1—C1—C2—O2	−120.9 (2)	C6—C7—C8—N1	−178.1 (3)
N1—C1—C2—O3	121.0 (2)	C6—C7—C8—C3	−0.7 (4)
N1—C1—C2—C3	−0.2 (3)	O2—C9—C10—O3	9.7 (3)
O2—C2—C3—C4	−58.7 (3)		

Hydrogen-bond geometry (Å, º)

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1[i]	0.82 (3)	2.11 (3)	2.885 (4)	157.4 (3)

Symmetry code: (i) −x+1/2, y−1/2, −z.