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# (8a*RS*)-8,8a-Dihydrofuro[3,2-*f*]-indolizine-6,9(4*H*,7*H*)-dione

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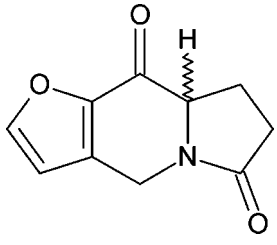
Key indicators: single-crystal X-ray study; $T$ = 298 K; mean $\sigma$(C–C) = 0.002 Å; $R$ factor = 0.040; $wR$ factor = 0.120; data-to-parameter ratio = 17.4.

The title compound, $C_{10}H_9NO_3$, is a chiral molecule with one stereogenic carbon atom, but which crystallizes as a racemate in the centrosymmetric space group $P2_1/n$. The central six-membered ring of the indolizine moiety adopts a definite envelope conformation, while the conformation of the oxopyrrolidine ring is close to that of a flat-envelope with a maximum deviation of 0.352 (1) Å for the flap atom.

## Related literature

For properties of indolizine derivatives, see: Malonne *et al.* (1998); Medda *et al.* (2003); Sonnet *et al.* (2000); Campagna *et al.* (1990); Pearson & Guo (2001); Gupta *et al.* (2003); Teklu *et al.* (2005). For their role as synthetic targets for pharmaceuticals, see: Gubin *et al.* (1992); Ruprecht *et al.* (1989). For the synthesis of the title compound, see: Szemes *et al.* (1998). For metric comparison with related compounds, see: Pedersen (1967).




## Experimental

### Crystal data

$C_{10}H_9NO_3$
$M_r$ = 191.18
Monoclinic, $P2_1/n$
$a$ = 7.63534 (19) Å
$b$ = 11.7583 (2) Å
$c$ = 9.9234 (3) Å
$\beta$ = 105.775 (3)°
$V$ = 857.35 (4) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.11 mm$^{-1}$
$T$ = 298 K
0.49 × 0.23 × 0.13 mm

### Data collection

Oxford Diffraction Gemini R CCD diffractometer
Absorption correction: analytical (Clark & Reid, 1995)
$T_{min}$ = 0.952, $T_{max}$ = 0.992
14552 measured reflections
2213 independent reflections
1646 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.018

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.120
$S$ = 1.03
2213 reflections
127 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.20 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.16 e Å$^{-3}$

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg, 2001); software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BG2407).

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# supporting information

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## (8a*RS*)-8,8a-Dihydrofuro[3,2-*f*]indolizine-6,9(4*H*,7*H*)-dione

**Viktor Vrábel, Július Sivý, Ľubomír Švorc, Peter Šafář and Štefan Marchalín**

### S1. Comment

Indolizine derivatives have been found to possess a variety of biological activities such as antiinflammatory (Malonne *et al.*, 1998), antiviral (Medda *et al.*, 2003), aromatase inhibitory (Sonnet *et al.*, 2000), analgestic (Campagna *et al.*, 1990) and antitumor (Pearson & Guo, 2001) activities. They have also shown to be calcium entry blockers (Gupta *et al.*, 2003) and potent antioxidants inhibiting lipid peroxidation *in vitro* (Teklu *et al.*, 2005). As such, indolizines are important synthetic targets in view of developing new pharmaceuticals for the treatment of cardiovascular diseases (Gubin *et al.*, 1992) and HIV infections (Ruprecht *et al.*, 1989).

Based on these facts and in continuation of our interest in developing simple and efficient route for the synthesis of novel indolizine derivatives, we report here the synthesis, molecular and crystal structure of the title compound, (I). The molecular structure and the atom labeling scheme are shown in Fig. 1.

The molecule crystallizes in the monoclinic space group P21/n. Accordingly, the compound is a racemate and consists of two enantiomeric pairs in the unit cell with relative configuration *R* and S on the C5 carbon atom. The central N-heterocyclic ring is not planar and adopts an envelope conformation for both enantiomers. A calculation of least-squares planes shows that this ring is puckered in such a manner that the five atoms C5, C6, C7, C10 and C11 are coplanar, while atom N1 is displaced from this plane with an out-of-plane displacement of 0.479 (2) Å.

The oxopyrrolidine ring attached to the indolizine ring system has a flat-envelope conformation, with atom C4 on the flap. The maximum deviation from planarity for C4 is 0.352 (1) Å. Obviously, the change of stereochemical centre on C5 from *R* to S causes changes in orientation of N1, C2, O1, C3 and C4.

The N1—C5 and N1—C11 bonds are approximately equivalent and both are much longer than the N1—C2 bond. Moreover, the N1 atom is $sp^2$ hybridized, as evidenced by the sum of the valence angles around it [358.8 (3)° ]. These data are consistent with conjugation of the lone-pair electrons on N1 with the adjacent carbonyl and agree with literature values for simple amides (Pedersen, 1967).

### S2. Experimental

The title compound rac-(8a)-8,8a-dihydrofuro[3,2-*f*]indolizine-6,9 (4*H*,7*H*)-dione was prepared according to a standard protocol described in literature (Szemes *et al.*, 1998).

### S3. Refinement

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances in the range 0.93 - 0.98Å and O—H distance 0.85Å and $U_{iso}$ set at 1.2$U_{eq}$ of the parent atom.

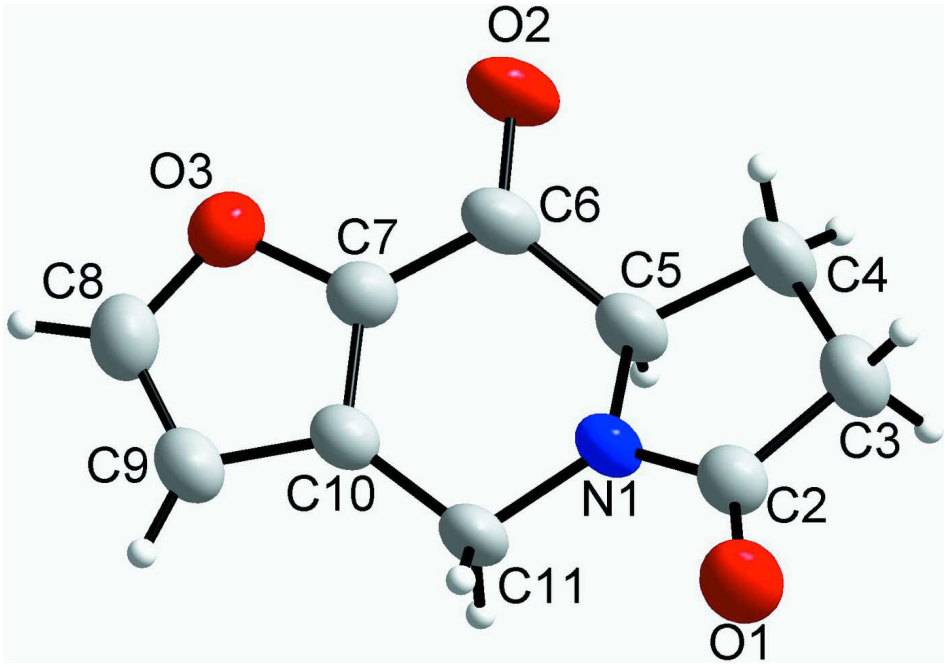


**Figure 1**

Molecular structure of (I) with the atomic numbering scheme; the chiral centre is C5. Displacement ellipsoids are drawn at the 50% probability level (Brandenburg, 2001).

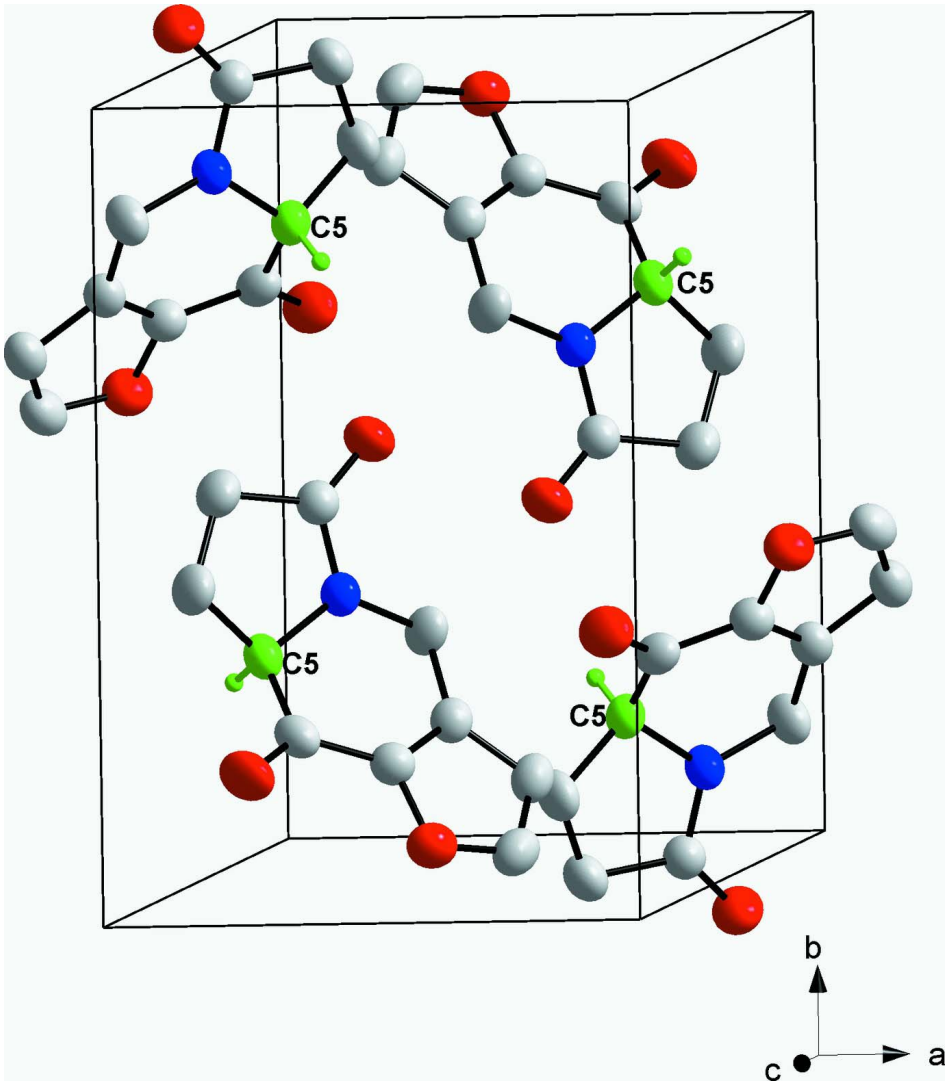


**Figure 2**

Packing diagram.

**(8a*RS*)-8,8a-Dihydrofuro[3,2-*f*]indolizine- 6,9(4*H*,7*H*)-dione**

*Crystal data*

$C_{10}H_9NO_3$
$M_r = 191.18$
Monoclinic, $P2_1/n$
Hall symbol: -P 2yn
$a = 7.63534\ (19)$ Å
$b = 11.7583\ (2)$ Å
$c = 9.9234\ (3)$ Å
$\beta = 105.775\ (3)°$
$V = 857.35\ (4)$ Å$^3$
$Z = 4$
$F(000) = 400$
$D_x = 1.481$ Mg m$^{-3}$
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 7934 reflections
$\theta = 3.5–29.3°$
$\mu = 0.11$ mm$^{-1}$
$T = 298$ K
Block, yellow
0.49 × 0.23 × 0.13 mm

*Data collection*

Oxford Diffraction Gemini R CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 10.4340 pixels $mm^{-1}$
Rotation method data acquisition using $\omega$ and $\varphi$ scans
Absorption correction: analytical (Clark & Reid, 1995)
$T_{min}$ = 0.952, $T_{max}$ = 0.992
14552 measured reflections
2213 independent reflections
1646 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.018
$\theta_{max}$ = 29.4°, $\theta_{min}$ = 3.5°
$h$ = −10→10
$k$ = −15→14
$l$ = −13→13

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.120
$S$ = 1.03
2213 reflections
127 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.063P)^2 + 0.130P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e $Å^{-3}$
$\Delta\rho_{min}$ = −0.16 e $Å^{-3}$

*Special details*

**Experimental**. face-indexed (Oxford Diffraction, 2006)

**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 ($Å^2$)*

| | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| C2 | 1.15109 (18) | 0.99636 (12) | 0.67889 (14) | 0.0438 (3) |
| C3 | 1.3182 (2) | 1.01426 (13) | 0.62848 (17) | 0.0543 (4) |
| H3B | 1.4237 | 1.0285 | 0.7068 | 0.065* |
| H3A | 1.3015 | 1.0783 | 0.5647 | 0.065* |
| C4 | 1.3418 (2) | 0.90534 (14) | 0.55443 (18) | 0.0584 (4) |
| H4B | 1.4692 | 0.8843 | 0.5756 | 0.070* |
| H4A | 1.2938 | 0.9134 | 0.4538 | 0.070* |
| C5 | 1.23351 (17) | 0.81624 (11) | 0.61138 (14) | 0.0439 (3) |
| H5A | 1.3159 | 0.7767 | 0.6906 | 0.053* |
| C6 | 1.13528 (19) | 0.72915 (11) | 0.50495 (14) | 0.0456 (3) |
| C7 | 0.96776 (18) | 0.69128 (11) | 0.53212 (13) | 0.0429 (3) |
| C8 | 0.7398 (2) | 0.58131 (13) | 0.53142 (16) | 0.0539 (4) |
| H8A | 0.6557 | 0.5223 | 0.5095 | 0.065* |
| C9 | 0.74188 (18) | 0.66085 (12) | 0.62999 (14) | 0.0475 (3) |
| H9A | 0.6623 | 0.6671 | 0.6858 | 0.057* |

| | | | | |
|---|---|---|---|---|
| C10 | 0.89106 (17) | 0.73291 (11) | 0.63038 (13) | 0.0408 (3) |
| C11 | 0.96560 (19) | 0.83359 (13) | 0.71747 (14) | 0.0483 (3) |
| H11B | 0.8692 | 0.8880 | 0.7146 | 0.058* |
| H11A | 1.0172 | 0.8106 | 0.8140 | 0.058* |
| N1 | 1.10563 (14) | 0.88532 (10) | 0.66294 (11) | 0.0425 (3) |
| O1 | 1.07083 (16) | 1.06761 (9) | 0.72905 (13) | 0.0636 (3) |
| O2 | 1.19841 (17) | 0.69185 (9) | 0.41368 (12) | 0.0654 (3) |
| O3 | 0.87461 (14) | 0.59746 (9) | 0.46802 (10) | 0.0535 (3) |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C2 | 0.0435 (6) | 0.0436 (7) | 0.0472 (7) | 0.0004 (5) | 0.0176 (5) | 0.0013 (5) |
| C3 | 0.0515 (8) | 0.0506 (8) | 0.0679 (9) | −0.0066 (6) | 0.0282 (7) | 0.0042 (7) |
| C4 | 0.0544 (8) | 0.0586 (9) | 0.0760 (10) | −0.0066 (7) | 0.0412 (8) | −0.0008 (7) |
| C5 | 0.0412 (6) | 0.0457 (7) | 0.0519 (7) | 0.0039 (5) | 0.0249 (6) | 0.0033 (6) |
| C6 | 0.0541 (7) | 0.0405 (7) | 0.0511 (7) | 0.0077 (6) | 0.0294 (6) | 0.0049 (5) |
| C7 | 0.0476 (7) | 0.0408 (7) | 0.0437 (7) | 0.0003 (5) | 0.0180 (6) | −0.0004 (5) |
| C8 | 0.0480 (8) | 0.0501 (8) | 0.0624 (9) | −0.0075 (6) | 0.0131 (7) | 0.0025 (7) |
| C9 | 0.0428 (7) | 0.0526 (8) | 0.0495 (7) | −0.0036 (6) | 0.0169 (6) | 0.0068 (6) |
| C10 | 0.0419 (6) | 0.0441 (7) | 0.0392 (6) | −0.0003 (5) | 0.0161 (5) | 0.0044 (5) |
| C11 | 0.0504 (7) | 0.0550 (8) | 0.0492 (7) | −0.0092 (6) | 0.0301 (6) | −0.0073 (6) |
| N1 | 0.0428 (6) | 0.0440 (6) | 0.0487 (6) | −0.0026 (5) | 0.0263 (5) | −0.0035 (5) |
| O1 | 0.0681 (7) | 0.0486 (6) | 0.0852 (8) | 0.0021 (5) | 0.0396 (6) | −0.0122 (5) |
| O2 | 0.0849 (8) | 0.0569 (6) | 0.0742 (7) | 0.0039 (6) | 0.0552 (7) | −0.0080 (5) |
| O3 | 0.0584 (6) | 0.0480 (6) | 0.0559 (6) | −0.0029 (4) | 0.0188 (5) | −0.0085 (4) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| C2—O1 | 1.2211 (16) | C6—C7 | 1.4472 (18) |
| C2—N1 | 1.3492 (18) | C7—C10 | 1.3578 (17) |
| C2—C3 | 1.5062 (18) | C7—O3 | 1.3717 (16) |
| C3—C4 | 1.512 (2) | C8—C9 | 1.350 (2) |
| C3—H3B | 0.9700 | C8—O3 | 1.3579 (18) |
| C3—H3A | 0.9700 | C8—H8A | 0.9300 |
| C4—C5 | 1.5345 (19) | C9—C10 | 1.4188 (18) |
| C4—H4B | 0.9700 | C9—H9A | 0.9300 |
| C4—H4A | 0.9700 | C10—C11 | 1.4848 (19) |
| C5—N1 | 1.4651 (15) | C11—N1 | 1.4562 (15) |
| C5—C6 | 1.515 (2) | C11—H11B | 0.9700 |
| C5—H5A | 0.9800 | C11—H11A | 0.9700 |
| C6—O2 | 1.2176 (16) | | |
| | | | |
| O1—C2—N1 | 124.75 (12) | C7—C6—C5 | 111.91 (10) |
| O1—C2—C3 | 127.14 (13) | C10—C7—O3 | 110.64 (11) |
| N1—C2—C3 | 108.08 (11) | C10—C7—C6 | 126.76 (13) |
| C2—C3—C4 | 105.48 (12) | O3—C7—C6 | 122.29 (11) |
| C2—C3—H3B | 110.6 | C9—C8—O3 | 112.18 (12) |

| | | | |
|---|---|---|---|
| C4—C3—H3B | 110.6 | C9—C8—H8A | 123.9 |
| C2—C3—H3A | 110.6 | O3—C8—H8A | 123.9 |
| C4—C3—H3A | 110.6 | C8—C9—C10 | 105.49 (12) |
| H3B—C3—H3A | 108.8 | C8—C9—H9A | 127.3 |
| C3—C4—C5 | 104.60 (11) | C10—C9—H9A | 127.3 |
| C3—C4—H4B | 110.8 | C7—C10—C9 | 106.58 (12) |
| C5—C4—H4B | 110.8 | C7—C10—C11 | 122.24 (11) |
| C3—C4—H4A | 110.8 | C9—C10—C11 | 131.16 (11) |
| C5—C4—H4A | 110.8 | N1—C11—C10 | 108.71 (10) |
| H4B—C4—H4A | 108.9 | N1—C11—H11B | 109.9 |
| N1—C5—C6 | 111.56 (10) | C10—C11—H11B | 109.9 |
| N1—C5—C4 | 103.12 (11) | N1—C11—H11A | 109.9 |
| C6—C5—C4 | 114.77 (12) | C10—C11—H11A | 109.9 |
| N1—C5—H5A | 109.1 | H11B—C11—H11A | 108.3 |
| C6—C5—H5A | 109.1 | C2—N1—C11 | 123.51 (10) |
| C4—C5—H5A | 109.1 | C2—N1—C5 | 113.76 (10) |
| O2—C6—C7 | 125.20 (14) | C11—N1—C5 | 121.64 (11) |
| O2—C6—C5 | 122.74 (13) | C8—O3—C7 | 105.10 (10) |

| | | | |
|---|---|---|---|
| O1—C2—C3—C4 | −170.54 (15) | C8—C9—C10—C7 | −0.07 (15) |
| N1—C2—C3—C4 | 11.15 (17) | C8—C9—C10—C11 | −178.40 (15) |
| C2—C3—C4—C5 | −20.30 (17) | C7—C10—C11—N1 | 9.17 (19) |
| C3—C4—C5—N1 | 21.70 (16) | C9—C10—C11—N1 | −172.72 (13) |
| C3—C4—C5—C6 | 143.24 (13) | O1—C2—N1—C11 | −6.8 (2) |
| N1—C5—C6—O2 | 152.99 (13) | C3—C2—N1—C11 | 171.60 (12) |
| C4—C5—C6—O2 | 36.17 (19) | O1—C2—N1—C5 | −174.95 (14) |
| N1—C5—C6—C7 | −31.17 (16) | C3—C2—N1—C5 | 3.41 (16) |
| C4—C5—C6—C7 | −147.98 (12) | C10—C11—N1—C2 | 153.77 (12) |
| O2—C6—C7—C10 | −178.15 (14) | C10—C11—N1—C5 | −38.95 (17) |
| C5—C6—C7—C10 | 6.1 (2) | C6—C5—N1—C2 | −139.84 (12) |
| O2—C6—C7—O3 | 9.0 (2) | C4—C5—N1—C2 | −16.15 (16) |
| C5—C6—C7—O3 | −166.75 (11) | C6—C5—N1—C11 | 51.73 (16) |
| O3—C8—C9—C10 | −0.56 (16) | C4—C5—N1—C11 | 175.42 (12) |
| O3—C7—C10—C9 | 0.67 (15) | C9—C8—O3—C7 | 0.96 (16) |
| C6—C7—C10—C9 | −172.91 (13) | C10—C7—O3—C8 | −0.99 (15) |
| O3—C7—C10—C11 | 179.19 (12) | C6—C7—O3—C8 | 172.92 (13) |
| C6—C7—C10—C11 | 5.6 (2) | | |