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# 4′-Amino-2,2″-dioxo-2,2″,3,3″-tetrahydro-1*H*-indole-3-spiro-1′-cyclopent-3′-ene-2′-spiro-3″-1*H*-indole-3′,5′,5′-tricarbonitrile dihydrate

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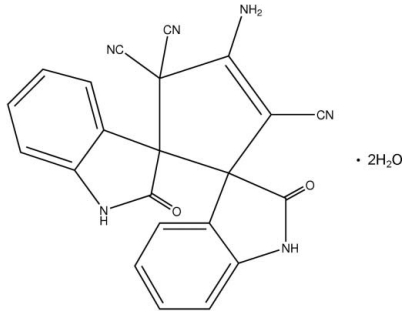
Key indicators: single-crystal X-ray study; $T$ = 293 K; mean $\sigma$(C–C) = 0.003 Å; $R$ factor = 0.042; $wR$ factor = 0.109; data-to-parameter ratio = 8.2.

In the title compound, $C_{22}H_{12}N_6O_2\cdot 2H_2O$, the cyclopentene ring adopts an envelope conformation, with the spiro C atom bonded to the dicyano-substituted C atom deviating by 0.437 (2) Å from the plane of the remaining four atoms in the ring. The puckering and smallest displacement asymmetry parameters for the ring are $q_2$ = 0.275 (2) Å, $\varphi$ = 212.4 (4)° and $\Delta_s(C_2)$ = 2.7 (2). The dihedral angle between the two indole groups is 60.1 (1)°. The structure contains intermolecular N—H···O hydrogen bonds involving the indole groups and O—H···O and O—H···N hydrogen bonds involving the water molecules.

## Related literature

For related literature, see: Akai *et al.* (2004); Cremer & Pople (1975); Gallagher *et al.* (1985); Nagata *et al.* (2001); Nardelli (1983); Williams & Cox (2003); Zaveri *et al.* (2004).




## Experimental

### Crystal data

$C_{22}H_{12}N_6O_2\cdot 2H_2O$
$M_r$ = 428.41
Orthorhombic, $Pna2_1$
$a$ = 17.1850 (16) Å
$b$ = 8.9849 (9) Å
$c$ = 13.3275 (13) Å
$V$ = 2057.8 (3) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.10 mm$^{-1}$
$T$ = 293 (2) K
0.25 × 0.24 × 0.20 mm

### Data collection

Bruker SMART APEX CCD diffractometer
Absorption correction: none
16968 measured reflections
2551 independent reflections
2367 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.022

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.108
$S$ = 1.06
2551 reflections
313 parameters
9 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.27 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.14 e Å$^{-3}$

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1—H1···O2$^{i}$ | 0.86 | 2.09 | 2.905 (2) | 158 |
| N2—H2···O3$^{i}$ | 0.86 | 2.22 | 3.032 (3) | 157 |
| O3—H3$A$···O1$^{ii}$ | 0.85 (1) | 2.00 (2) | 2.795 (3) | 157 (4) |
| O3—H3$B$···N6$^{iii}$ | 0.85 (1) | 2.22 (5) | 2.834 (3) | 129 (5) |
| O3—H3$B$···O4$^{iv}$ | 0.85 (1) | 2.62 (3) | 3.381 (4) | 149 (5) |
| O4—H4$A$···N4$^{v}$ | 0.85 (1) | 2.38 (3) | 3.171 (5) | 155 (7) |
| O4—H4$B$···N3 | 0.85 (1) | 2.68 (4) | 3.392 (4) | 142 (6) |
| N5—H5$A$···O3$^{vi}$ | 0.90 (1) | 1.97 (1) | 2.860 (3) | 175 (3) |
| N5—H5$B$···O4$^{vi}$ | 0.90 (1) | 2.17 (1) | 3.061 (4) | 171 (3) |

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

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BI2273).

## References

Akai, S., Tsujino, T., Akiyama, E., Tanimoto, K., Naka, T. & Kita, Y. (2004). *J. Org. Chem.* **69**, 2478–2486.
Bruker (2001). *SMART* (Version. 5.625/NT/2000) and *SAINT* (Version 6.28a). Bruker AXS Inc., Madison, Wisconsin, USA.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Gallagher, G., Lavanchi, P. G., Wilson, J. W., Hieble, J. & Demmarinis, R. M. (1985). *J. Med. Chem.* **28**, 1533–1536.

Nagata, R., Tokunaga, T., Hume, W., Umezone, T., Okazaki, U., Ueki, Y., Kumagai, K., Hourai, S., Nagamine, J., Seki, H., Taiji, M. & Noguchi, H. (2001). *J. Med. Chem.* **44**, 4641–4649.
Nardelli, M. (1983). *Acta Cryst.* C**39**, 1141–1142.
Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Williams, R. M. & Cox, R. (2003). *Acc. Chem. Res.* **36**, 127–139.
Zaveri, N. T., Jiang, F., Olsen, C. M., Deschamps, J. R., Parrish, D., Polgar, W. & Toll, L. (2004). *J. Med. Chem.* **47**, 2973–2976.

# supporting information

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# 4′-Amino-2,2′′-dioxo-2,2′′,3,3′′-tetrahydro-1*H*-indole-3-spiro-1′-cyclopent-3′-ene-2′-spiro-3′′-1*H*-indole-3′,5′,5′-tricarbonitrile dihydrate

**D. Gayathri, D. Velmurugan, G. Shanthi, P. T. Perumal and K. Ravikumar**

## S1. Comment

The indole template is generally recognized as an important structure in medicinal chemistry, and in particular, oxindoles are important constituents of natural indole alkaloids as well as drugs in development and also in the clinic (Akai *et al.*, 2004). Among them, the spiro-oxindole framework is an important structural motif in biologically relevant compounds such as natural products and pharmaceuticals (Williams & Cox, 2003). The oxindole motif is present in the anti-Parkinson's drug ropinirole (Gallagher *et al.*, 1985), in non-opioid nociceptin receptor ligands (Zaveri *et al.*, 2004), and in the growth hormone secretagogues (Nagata *et al.*, 2001). As the title compound is biologically important, we have determined its crystal structure using X-ray diffraction.

One of the oxindole moieties (C2/C13/N2/C14/C19) is planar with atom O2 deviating by 0.127 (1) Å from the plane of five-membered ring. The dihedral angle between the five- (C2/C13/N2/C14/C19) and six-membered (C14—C19) rings is 1.6 (1)°. The cyclopentene ring adopts an envelope conformation with C2 deviating by 0.437 (2) Å from the plane of the rest of the atoms in the ring. The five-membered ring (N1/C6/C1/C12/C7) in the oxindole moieties adopts a slightly twisted conformation. The puckering parameters (Cremer & Pople, 1975) and the smallest displacement asymmetry parameters (Nardelli, 1983) for the cyclopentene ring and the five-membered ring (N1/C6/C1/C12/C7) are $q_2$ = 0.275 (2)Å and 0.091 (2) Å, $\varphi$ = 212.4 (4)° and 56.3 (12)° and $\Delta_s(C_2)$ = 2.7 (2) and $\Delta_2(C_7)$ = 0.5 (2), respectively.

## S2. Experimental

To a stirred mixture of isatylidene malononitrile (2 mmol) and Hantzsch dihydropyridine ester (1 mmol) in ethanol (10 ml), a catalytic amount of indium(III) chloride (20 mol%) was added and the mixture was stirred at room temperature for about 1–2 h. After complete conversion (as indicated by TLC), the reaction mixture was poured into water and extracted with ethyl acetate (2 × 15 ml). The combined extracts were dried over anhydrous $Na_2SO_4$ and concentrated *in vacuo*. The resulting product was purified by column chromatography on silica gel (Merck, 60–120 mesh, ethyl acetate-hexane, 4:6) to afford the pure product in 88% yield as a white solid. Crystals were grown by slow evaporation from ethanol.

## S3. Refinement

H atoms of the $NH_2$ group and water molecules were located in a difference Fourier map and refined with the N—H and O—H distances restrained to 0.90 (1) and 0.85 (1) Å, respectively. H atoms bound to C atoms and the N atoms of the indole rings were placed geometrically and refined using a riding model with d(C—H) = 0.93 Å, d(N—H) = 0.86 Å, and $U_{iso}$(H) = 1.2 $U_{eq}$(C/N). In the absence of significant anomalous scattering effects, 2271 Friedel pairs were merged as equivalent data.

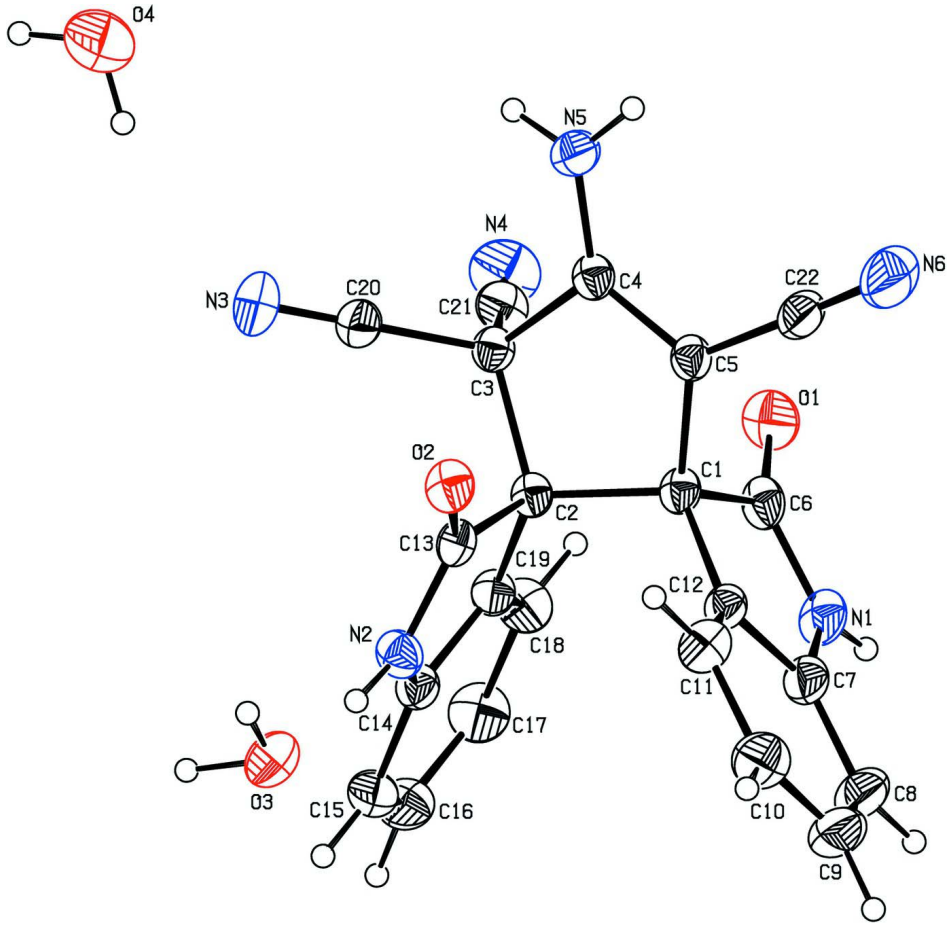


**Figure 1**

The molecular structure of title compound, showing 30% probability displacement ellipsoids for non-H atoms.

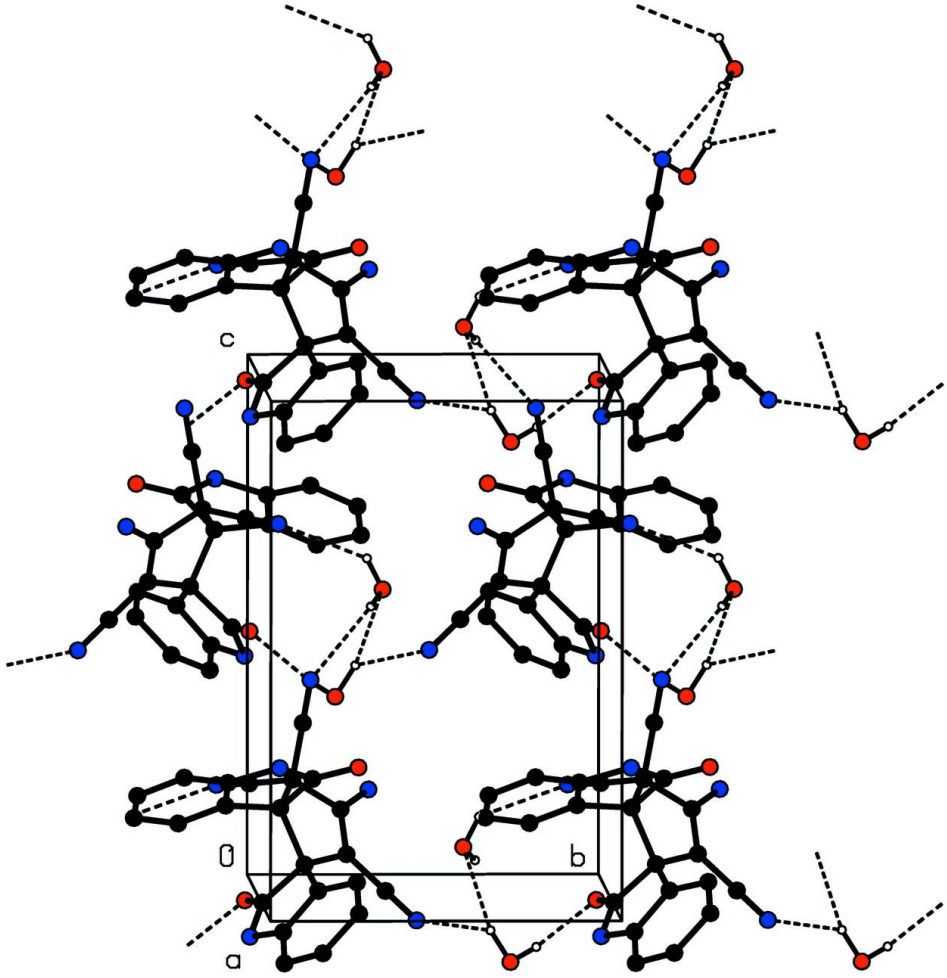


**Figure 2**

The molecular packing viewed down the *a* axis, showing O—H···N and O—H···O intermolecular interactions.

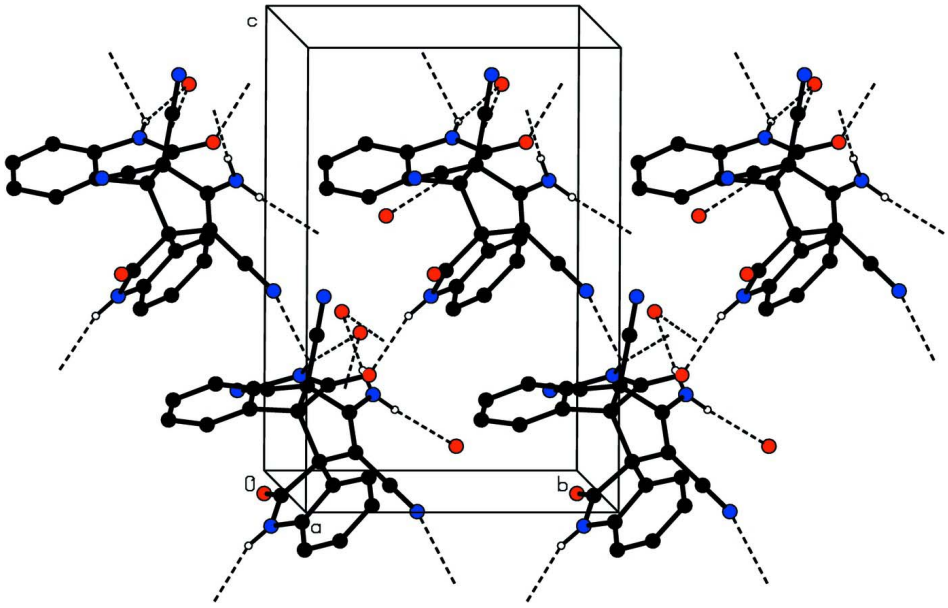


**Figure 3**

The molecular packing viewed down the *a* axis, showing N—H···O intermolecular interactions.

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*Crystal data*

$C_{22}H_{12}N_6O_2·2H_2O$
$M_r = 428.41$
Orthorhombic, $Pna2_1$
Hall symbol: P 2c -2n
$a = 17.1850\ (16)$ Å
$b = 8.9849\ (9)$ Å
$c = 13.3275\ (13)$ Å
$V = 2057.8\ (3)$ Å$^3$
$Z = 4$
$F(000) = 888$
$D_x = 1.383$ Mg m$^{-3}$
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2386 reflections
$\theta = 2.4–28.0°$
$\mu = 0.10$ mm$^{-1}$
$T = 293$ K
Block, colorless
0.25 × 0.24 × 0.20 mm

*Data collection*

Bruker SMART APEX CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
$\omega$ scans
16968 measured reflections
2551 independent reflections
2367 reflections with $I > 2\sigma(I)$
$R_{int} = 0.022$
$\theta_{max} = 28.0°$, $\theta_{min} = 2.4°$
$h = -22\rightarrow22$
$k = -11\rightarrow11$
$l = -17\rightarrow17$

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.108$
$S = 1.06$
2551 reflections
313 parameters
9 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites

H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0751P)^2 + 0.1068P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.27$ e Å$^{-3}$
$\Delta\rho_{min} = -0.14$ 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 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* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| C1 | 0.19406 (12) | 0.1506 (2) | 0.03645 (16) | 0.0341 (4) |
| C2 | 0.19661 (11) | 0.0810 (2) | 0.14549 (15) | 0.0320 (4) |
| C3 | 0.11505 (12) | 0.1206 (2) | 0.19253 (16) | 0.0352 (4) |
| C4 | 0.09089 (12) | 0.2598 (2) | 0.13339 (17) | 0.0349 (4) |
| C5 | 0.13624 (13) | 0.2738 (2) | 0.05081 (16) | 0.0354 (4) |
| C6 | 0.16280 (14) | 0.0331 (2) | −0.03919 (16) | 0.0414 (5) |
| C7 | 0.28704 (15) | 0.0835 (3) | −0.08495 (19) | 0.0452 (5) |
| C8 | 0.35505 (18) | 0.0831 (4) | −0.1392 (2) | 0.0614 (7) |
| H8A | 0.3636 | 0.0143 | −0.1902 | 0.074* |
| C9 | 0.41025 (19) | 0.1889 (4) | −0.1150 (3) | 0.0679 (8) |
| H9A | 0.4570 | 0.1906 | −0.1501 | 0.082* |
| C10 | 0.39785 (17) | 0.2922 (4) | −0.0399 (3) | 0.0612 (7) |
| H10A | 0.4358 | 0.3629 | −0.0256 | 0.073* |
| C11 | 0.32867 (16) | 0.2907 (3) | 0.0144 (2) | 0.0489 (6) |
| H11A | 0.3198 | 0.3607 | 0.0645 | 0.059* |
| C12 | 0.27339 (13) | 0.1839 (2) | −0.00708 (16) | 0.0375 (4) |
| C13 | 0.25886 (12) | 0.1685 (2) | 0.20696 (15) | 0.0340 (4) |
| C14 | 0.29683 (12) | −0.0747 (2) | 0.20308 (17) | 0.0378 (4) |
| C15 | 0.34057 (15) | −0.2019 (3) | 0.2170 (2) | 0.0493 (6) |
| H15A | 0.3882 | −0.1992 | 0.2501 | 0.059* |
| C16 | 0.31063 (17) | −0.3336 (3) | 0.1795 (2) | 0.0564 (7) |
| H16A | 0.3388 | −0.4211 | 0.1878 | 0.068* |
| C17 | 0.24070 (18) | −0.3388 (3) | 0.1305 (2) | 0.0581 (7) |
| H17A | 0.2221 | −0.4293 | 0.1065 | 0.070* |
| C18 | 0.19709 (16) | −0.2097 (2) | 0.1161 (2) | 0.0489 (6) |
| H18A | 0.1497 | −0.2129 | 0.0824 | 0.059* |
| C19 | 0.22569 (13) | −0.0769 (2) | 0.15289 (16) | 0.0364 (4) |
| C20 | 0.12114 (15) | 0.1500 (3) | 0.30204 (19) | 0.0449 (5) |
| C21 | 0.05602 (14) | 0.0018 (3) | 0.1798 (2) | 0.0470 (5) |
| C22 | 0.12327 (16) | 0.3857 (3) | −0.0210 (2) | 0.0506 (6) |
| N1 | 0.22129 (14) | −0.0067 (2) | −0.09965 (16) | 0.0486 (5) |

| | | | | |
|---|---|---|---|---|
| H1 | 0.2189 | −0.0785 | −0.1422 | 0.058* |
| N2 | 0.31446 (11) | 0.0717 (2) | 0.23268 (15) | 0.0413 (4) |
| H2 | 0.3564 | 0.0962 | 0.2639 | 0.050* |
| N3 | 0.12535 (18) | 0.1713 (4) | 0.38515 (19) | 0.0706 (7) |
| N4 | 0.01054 (15) | −0.0884 (3) | 0.1731 (3) | 0.0727 (8) |
| N5 | 0.03222 (13) | 0.3429 (3) | 0.16605 (18) | 0.0498 (5) |
| H5A | 0.0025 (15) | 0.311 (3) | 0.2169 (17) | 0.048 (7)* |
| H5B | 0.011 (2) | 0.417 (3) | 0.130 (3) | 0.070 (10)* |
| N6 | 0.1106 (2) | 0.4754 (4) | −0.0785 (3) | 0.0916 (11) |
| O1 | 0.09597 (11) | −0.0125 (2) | −0.04096 (16) | 0.0567 (5) |
| O2 | 0.25526 (10) | 0.29951 (16) | 0.22853 (13) | 0.0429 (4) |
| O3 | 0.05768 (12) | 0.7461 (2) | 0.83632 (15) | 0.0540 (4) |
| H3A | 0.073 (3) | 0.830 (3) | 0.858 (3) | 0.107 (15)* |
| H3B | 0.054 (4) | 0.692 (4) | 0.888 (2) | 0.15 (2)* |
| O4 | 0.0238 (2) | 0.3832 (4) | 0.5501 (3) | 0.0938 (9) |
| H4A | 0.020 (4) | 0.322 (6) | 0.599 (4) | 0.16 (3)* |
| H4B | 0.066 (2) | 0.360 (6) | 0.521 (4) | 0.13 (2)* |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C1 | 0.0439 (10) | 0.0289 (9) | 0.0294 (9) | 0.0008 (8) | −0.0003 (8) | −0.0036 (7) |
| C2 | 0.0387 (9) | 0.0268 (9) | 0.0304 (9) | −0.0010 (7) | −0.0022 (8) | −0.0033 (7) |
| C3 | 0.0384 (9) | 0.0334 (9) | 0.0338 (10) | −0.0009 (8) | 0.0006 (8) | 0.0015 (8) |
| C4 | 0.0404 (10) | 0.0319 (9) | 0.0325 (9) | −0.0002 (7) | −0.0024 (8) | −0.0019 (8) |
| C5 | 0.0428 (10) | 0.0329 (10) | 0.0305 (9) | 0.0024 (8) | −0.0017 (8) | −0.0015 (8) |
| C6 | 0.0565 (13) | 0.0354 (10) | 0.0324 (10) | 0.0013 (9) | −0.0081 (10) | −0.0082 (8) |
| C7 | 0.0582 (13) | 0.0408 (11) | 0.0367 (11) | 0.0131 (10) | 0.0031 (10) | −0.0020 (9) |
| C8 | 0.0700 (18) | 0.0639 (17) | 0.0503 (15) | 0.0182 (13) | 0.0193 (14) | −0.0015 (13) |
| C9 | 0.0570 (16) | 0.083 (2) | 0.0642 (18) | 0.0135 (15) | 0.0240 (14) | 0.0145 (17) |
| C10 | 0.0539 (15) | 0.0616 (16) | 0.0682 (19) | −0.0052 (12) | 0.0088 (14) | 0.0140 (14) |
| C11 | 0.0552 (14) | 0.0411 (12) | 0.0504 (14) | −0.0037 (10) | 0.0070 (11) | −0.0017 (10) |
| C12 | 0.0449 (11) | 0.0353 (10) | 0.0321 (10) | 0.0060 (8) | 0.0030 (9) | 0.0003 (8) |
| C13 | 0.0407 (9) | 0.0341 (9) | 0.0271 (9) | −0.0040 (8) | 0.0010 (8) | −0.0036 (7) |
| C14 | 0.0443 (10) | 0.0351 (10) | 0.0340 (10) | 0.0029 (8) | 0.0020 (9) | −0.0012 (8) |
| C15 | 0.0517 (13) | 0.0486 (13) | 0.0476 (13) | 0.0143 (10) | 0.0002 (11) | 0.0010 (11) |
| C16 | 0.0687 (16) | 0.0374 (11) | 0.0632 (16) | 0.0167 (11) | 0.0081 (13) | 0.0036 (11) |
| C17 | 0.0764 (18) | 0.0286 (11) | 0.0692 (18) | 0.0006 (11) | 0.0009 (14) | −0.0073 (11) |
| C18 | 0.0586 (14) | 0.0320 (10) | 0.0563 (14) | −0.0015 (9) | −0.0054 (12) | −0.0061 (10) |
| C19 | 0.0443 (10) | 0.0300 (9) | 0.0351 (10) | 0.0021 (8) | 0.0006 (9) | −0.0004 (8) |
| C20 | 0.0473 (12) | 0.0483 (12) | 0.0392 (13) | 0.0044 (10) | 0.0049 (10) | 0.0056 (10) |
| C21 | 0.0447 (11) | 0.0433 (12) | 0.0530 (14) | −0.0024 (10) | −0.0003 (11) | 0.0055 (10) |
| C22 | 0.0640 (15) | 0.0478 (12) | 0.0400 (12) | 0.0167 (11) | 0.0151 (11) | 0.0054 (10) |
| N1 | 0.0696 (13) | 0.0394 (10) | 0.0368 (10) | 0.0049 (9) | −0.0004 (10) | −0.0135 (8) |
| N2 | 0.0418 (9) | 0.0414 (9) | 0.0406 (10) | 0.0006 (7) | −0.0076 (8) | −0.0047 (8) |
| N3 | 0.0812 (18) | 0.0944 (19) | 0.0363 (13) | 0.0063 (14) | 0.0041 (11) | 0.0020 (12) |
| N4 | 0.0595 (13) | 0.0613 (14) | 0.097 (2) | −0.0217 (12) | −0.0013 (14) | 0.0057 (15) |
| N5 | 0.0509 (11) | 0.0526 (12) | 0.0458 (11) | 0.0136 (9) | 0.0108 (10) | 0.0073 (9) |

| | | | | | | |
|---|---|---|---|---|---|---|
| N6 | 0.121 (3) | 0.084 (2) | 0.0696 (18) | 0.0470 (19) | 0.0373 (18) | 0.0380 (16) |
| O1 | 0.0578 (11) | 0.0560 (10) | 0.0563 (11) | −0.0089 (8) | −0.0123 (9) | −0.0163 (9) |
| O2 | 0.0552 (9) | 0.0330 (7) | 0.0404 (8) | −0.0026 (6) | −0.0050 (7) | −0.0110 (6) |
| O3 | 0.0606 (11) | 0.0517 (9) | 0.0498 (10) | 0.0029 (9) | −0.0094 (9) | −0.0077 (8) |
| O4 | 0.093 (2) | 0.091 (2) | 0.097 (2) | 0.0319 (15) | −0.0022 (16) | 0.0075 (18) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| C1—C5 | 1.500 (3) | C11—H11A | 0.930 |
| C1—C12 | 1.511 (3) | C13—O2 | 1.213 (3) |
| C1—C6 | 1.556 (3) | C13—N2 | 1.337 (3) |
| C1—C2 | 1.583 (3) | C14—C15 | 1.380 (3) |
| C2—C19 | 1.508 (3) | C14—C19 | 1.394 (3) |
| C2—C13 | 1.560 (3) | C14—N2 | 1.406 (3) |
| C2—C3 | 1.576 (3) | C15—C16 | 1.384 (4) |
| C3—C21 | 1.482 (3) | C15—H15A | 0.930 |
| C3—C20 | 1.487 (3) | C16—C17 | 1.369 (4) |
| C3—C4 | 1.535 (3) | C16—H16A | 0.930 |
| C4—N5 | 1.328 (3) | C17—C18 | 1.394 (4) |
| C4—C5 | 1.354 (3) | C17—H17A | 0.930 |
| C5—C22 | 1.406 (3) | C18—C19 | 1.380 (3) |
| C6—O1 | 1.220 (3) | C18—H18A | 0.930 |
| C6—N1 | 1.337 (3) | C20—N3 | 1.126 (4) |
| C7—C8 | 1.374 (4) | C21—N4 | 1.130 (3) |
| C7—C12 | 1.395 (3) | C22—N6 | 1.133 (4) |
| C7—N1 | 1.404 (3) | N1—H1 | 0.860 |
| C8—C9 | 1.381 (5) | N2—H2 | 0.860 |
| C8—H8A | 0.930 | N5—H5A | 0.90 (1) |
| C9—C10 | 1.382 (5) | N5—H5B | 0.90 (1) |
| C9—H9A | 0.930 | O3—H3A | 0.85 (1) |
| C10—C11 | 1.392 (4) | O3—H3B | 0.85 (1) |
| C10—H10A | 0.930 | O4—H4A | 0.85 (1) |
| C11—C12 | 1.380 (3) | O4—H4B | 0.85 (1) |
| | | | |
| C5—C1—C12 | 120.04 (17) | C12—C11—H11A | 120.4 |
| C5—C1—C6 | 110.78 (17) | C10—C11—H11A | 120.4 |
| C12—C1—C6 | 101.37 (17) | C11—C12—C7 | 119.2 (2) |
| C5—C1—C2 | 101.12 (16) | C11—C12—C1 | 132.7 (2) |
| C12—C1—C2 | 113.93 (17) | C7—C12—C1 | 108.0 (2) |
| C6—C1—C2 | 109.64 (16) | O2—C13—N2 | 127.39 (19) |
| C19—C2—C13 | 102.28 (17) | O2—C13—C2 | 125.34 (19) |
| C19—C2—C3 | 118.76 (17) | N2—C13—C2 | 107.25 (16) |
| C13—C2—C3 | 106.69 (16) | C15—C14—C19 | 122.0 (2) |
| C19—C2—C1 | 116.18 (17) | C15—C14—N2 | 128.3 (2) |
| C13—C2—C1 | 107.57 (15) | C19—C14—N2 | 109.72 (18) |
| C3—C2—C1 | 104.56 (15) | C14—C15—C16 | 117.2 (2) |
| C21—C3—C20 | 106.75 (19) | C14—C15—H15A | 121.4 |
| C21—C3—C4 | 110.04 (18) | C16—C15—H15A | 121.4 |

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|---|---|---|---|
| C20—C3—C4 | 112.24 (19) | C17—C16—C15 | 121.9 (2) |
| C21—C3—C2 | 113.62 (17) | C17—C16—H16A | 119.1 |
| C20—C3—C2 | 111.58 (18) | C15—C16—H16A | 119.1 |
| C4—C3—C2 | 102.72 (16) | C16—C17—C18 | 120.6 (2) |
| N5—C4—C5 | 130.6 (2) | C16—C17—H17A | 119.7 |
| N5—C4—C3 | 119.7 (2) | C18—C17—H17A | 119.7 |
| C5—C4—C3 | 109.72 (18) | C19—C18—C17 | 118.6 (3) |
| C4—C5—C22 | 121.9 (2) | C19—C18—H18A | 120.7 |
| C4—C5—C1 | 114.59 (18) | C17—C18—H18A | 120.7 |
| C22—C5—C1 | 123.10 (19) | C18—C19—C14 | 119.7 (2) |
| O1—C6—N1 | 127.3 (2) | C18—C19—C2 | 132.2 (2) |
| O1—C6—C1 | 124.5 (2) | C14—C19—C2 | 107.96 (18) |
| N1—C6—C1 | 108.2 (2) | N3—C20—C3 | 179.4 (3) |
| C8—C7—C12 | 122.4 (3) | N4—C21—C3 | 178.0 (3) |
| C8—C7—N1 | 127.5 (2) | N6—C22—C5 | 178.1 (3) |
| C12—C7—N1 | 110.0 (2) | C6—N1—C7 | 111.51 (19) |
| C7—C8—C9 | 117.3 (3) | C6—N1—H1 | 124.2 |
| C7—C8—H8A | 121.3 | C7—N1—H1 | 124.2 |
| C9—C8—H8A | 121.3 | C13—N2—C14 | 112.51 (18) |
| C8—C9—C10 | 121.7 (3) | C13—N2—H2 | 123.7 |
| C8—C9—H9A | 119.1 | C14—N2—H2 | 123.7 |
| C10—C9—H9A | 119.1 | C4—N5—H5A | 119.9 (19) |
| C9—C10—C11 | 120.1 (3) | C4—N5—H5B | 123 (3) |
| C9—C10—H10A | 119.9 | H5A—N5—H5B | 115 (3) |
| C11—C10—H10A | 119.9 | H3A—O3—H3B | 105.1 (17) |
| C12—C11—C10 | 119.1 (2) | H4A—O4—H4B | 104.8 (17) |

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|---|---|---|---|
| C5—C1—C2—C19 | 158.77 (17) | C9—C10—C11—C12 | 0.7 (4) |
| C12—C1—C2—C19 | −71.0 (2) | C10—C11—C12—C7 | −2.2 (4) |
| C6—C1—C2—C19 | 41.8 (2) | C10—C11—C12—C1 | 179.7 (2) |
| C5—C1—C2—C13 | −87.37 (18) | C8—C7—C12—C11 | 2.5 (4) |
| C12—C1—C2—C13 | 42.8 (2) | N1—C7—C12—C11 | −175.0 (2) |
| C6—C1—C2—C13 | 155.61 (17) | C8—C7—C12—C1 | −179.0 (2) |
| C5—C1—C2—C3 | 25.79 (18) | N1—C7—C12—C1 | 3.5 (3) |
| C12—C1—C2—C3 | 155.99 (17) | C5—C1—C12—C11 | 48.3 (4) |
| C6—C1—C2—C3 | −91.22 (18) | C6—C1—C12—C11 | 170.6 (2) |
| C19—C2—C3—C21 | −37.6 (3) | C2—C1—C12—C11 | −71.8 (3) |
| C13—C2—C3—C21 | −152.32 (18) | C5—C1—C12—C7 | −130.0 (2) |
| C1—C2—C3—C21 | 93.88 (19) | C6—C1—C12—C7 | −7.7 (2) |
| C19—C2—C3—C20 | 83.1 (2) | C2—C1—C12—C7 | 110.0 (2) |
| C13—C2—C3—C20 | −31.6 (2) | C19—C2—C13—O2 | −173.2 (2) |
| C1—C2—C3—C20 | −145.38 (18) | C3—C2—C13—O2 | −47.8 (3) |
| C19—C2—C3—C4 | −156.44 (18) | C1—C2—C13—O2 | 63.9 (3) |
| C13—C2—C3—C4 | 88.85 (18) | C19—C2—C13—N2 | 5.2 (2) |
| C1—C2—C3—C4 | −24.95 (19) | C3—C2—C13—N2 | 130.60 (18) |
| C21—C3—C4—N5 | 72.4 (3) | C1—C2—C13—N2 | −117.67 (18) |
| C20—C3—C4—N5 | −46.3 (3) | C19—C14—C15—C16 | −0.5 (4) |
| C2—C3—C4—N5 | −166.3 (2) | N2—C14—C15—C16 | −179.2 (2) |

| | | | |
|---|---|---|---|
| C21—C3—C4—C5 | −106.6 (2) | C14—C15—C16—C17 | 0.1 (4) |
| C20—C3—C4—C5 | 134.7 (2) | C15—C16—C17—C18 | 0.4 (5) |
| C2—C3—C4—C5 | 14.7 (2) | C16—C17—C18—C19 | −0.4 (5) |
| N5—C4—C5—C22 | −3.5 (4) | C17—C18—C19—C14 | 0.0 (4) |
| C3—C4—C5—C22 | 175.3 (2) | C17—C18—C19—C2 | 175.9 (3) |
| N5—C4—C5—C1 | −176.4 (2) | C15—C14—C19—C18 | 0.4 (4) |
| C3—C4—C5—C1 | 2.4 (3) | N2—C14—C19—C18 | 179.4 (2) |
| C12—C1—C5—C4 | −144.5 (2) | C15—C14—C19—C2 | −176.4 (2) |
| C6—C1—C5—C4 | 97.9 (2) | N2—C14—C19—C2 | 2.6 (3) |
| C2—C1—C5—C4 | −18.3 (2) | C13—C2—C19—C18 | 179.1 (3) |
| C12—C1—C5—C22 | 42.7 (3) | C3—C2—C19—C18 | 62.1 (4) |
| C6—C1—C5—C22 | −74.9 (3) | C1—C2—C19—C18 | −64.0 (3) |
| C2—C1—C5—C22 | 168.9 (2) | C13—C2—C19—C14 | −4.6 (2) |
| C5—C1—C6—O1 | −41.8 (3) | C3—C2—C19—C14 | −121.6 (2) |
| C12—C1—C6—O1 | −170.3 (2) | C1—C2—C19—C14 | 112.2 (2) |
| C2—C1—C6—O1 | 68.9 (3) | O1—C6—N1—C7 | 171.7 (2) |
| C5—C1—C6—N1 | 138.14 (19) | C1—C6—N1—C7 | −8.3 (3) |
| C12—C1—C6—N1 | 9.6 (2) | C8—C7—N1—C6 | −174.1 (3) |
| C2—C1—C6—N1 | −111.1 (2) | C12—C7—N1—C6 | 3.2 (3) |
| C12—C7—C8—C9 | −1.1 (4) | O2—C13—N2—C14 | 174.4 (2) |
| N1—C7—C8—C9 | 176.0 (3) | C2—C13—N2—C14 | −4.0 (2) |
| C7—C8—C9—C10 | −0.5 (5) | C15—C14—N2—C13 | 179.9 (2) |
| C8—C9—C10—C11 | 0.7 (5) | C19—C14—N2—C13 | 1.0 (3) |

*Hydrogen-bond geometry (Å, º)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1···O2$^{i}$ | 0.86 | 2.09 | 2.905 (2) | 158 |
| N2—H2···O3$^{i}$ | 0.86 | 2.22 | 3.032 (3) | 157 |
| O3—H3*A*···O1$^{ii}$ | 0.85 (1) | 2.00 (2) | 2.795 (3) | 157 (4) |
| O3—H3*B*···N6$^{iii}$ | 0.85 (1) | 2.22 (5) | 2.834 (3) | 129 (5) |
| O3—H3*B*···O4$^{iv}$ | 0.85 (1) | 2.62 (3) | 3.381 (4) | 149 (5) |
| O4—H4*A*···N4$^{v}$ | 0.85 (1) | 2.38 (3) | 3.171 (5) | 155 (7) |
| O4—H4*B*···N3 | 0.85 (1) | 2.68 (4) | 3.392 (4) | 142 (6) |
| N5—H5*A*···O3$^{vi}$ | 0.90 (1) | 1.97 (1) | 2.860 (3) | 175 (3) |
| N5—H5*B*···O4$^{vi}$ | 0.90 (1) | 2.17 (1) | 3.061 (4) | 171 (3) |

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