Crystal structure and Hirshfeld surface analysis of 
\(N\)-(2,6-dimethylphenyl)-2-[3-hydroxy-2-oxo-3-(2-oxopropyl)indolin-1-yl]acetamide

Intissar Nchioua, Abdulsalam Alsubari, Joel T. Mague and Youssef Ramli

1Laboratory of Medicinal Chemistry, Drug Sciences Research Center, Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco, 2Laboratory of Medicinal Chemistry, Faculty of Clinical Pharmacy, 21 September University, Yemen, and 3Department of Chemistry, Tulane University, New Orleans, LA 70118, USA. *Correspondence e-mail: alsubaripharmaco@21umas.edu.ye

The cup-shaped conformation of the title molecule, \(C_{21}H_{22}N_{2}O_{4}\), is largely determined by an intramolecular \(N\cdots H\cdots O\) hydrogen bond. In the crystal, double layers of molecules are formed by \(O\cdots H\cdots O\) and \(C\cdots H\cdots O\) hydrogen bonds. A Hirshfeld surface analysis was performed, which confirms the regions that are active for intermolecular interactions.

1. Chemical context

1H-Indole-2,3-dione, also known as isatin, represents a synthetically useful substrate that can be used to prepare a broad range of heterocyclic compounds, including examples of pharmacological significance (Bekircan & Bektas, 2008). Its derivatives are biologically active and have significant importance in medicinal chemistry (Feng et al., 2010). They show potent anticonvulsant activity at low concentrations (Mathur & Nain, 2014), as well as antibacterial (Hu et al., 2017), anticancer (Ding et al., 2020) and antitubercular (Nath et al., 2020) activities. Arylacetamide-based compounds have attracted increasing attention because of their important pharmacological activities (Beccalli et al., 2007; Valeur & Bradley, 2009; Allen & Williams, 2011; Missioui et al., 2021, 2022a,b,c). As part of our interest in the identification of bioactive compounds, we report herein on the synthesis, crystal structure and Hirshfeld surface analysis of the title arylacetamide-based derivative containing an isatin moiety, namely \(N\)-(2,6-dimethylphenyl)-2-[3-hydroxy-2-oxo-3-(2-oxopropyl)indolin-1-yl]acetamide (Fig. 1)
2. Structural commentary

The molecule adopts a cup-shaped conformation (Fig. 1), which is largely determined by the intramolecular N2—H2...O3 hydrogen bond (Table 1). As this places O3 directly over the five-membered ring [O3...centroid = 2.7062 (8) Å, C10...centroid = 2.9956 (9) Å, C10—O3...centroid = 99.56 (9)°], there is the possibility of an added C—O...N interaction reinforcing the observed conformation. The indole moiety is slightly non-planar as seen from the 1.89 (3)° dihedral angle between the mean planes of its constituent rings. The dihedral angle between the mean plane of the C1/C6/C7/C8/N1 ring and that of the C12/C13/N2/O4 unit is 82.83 (5)° while that between the latter plane and the mean plane of the C14—C19 ring is 72.24 (4)°. All bond distances and bond angles appear as expected for the given formulation.

3. Supramolecular features

In the crystal, centrosymmetric dimers are formed by self-complementary O1—H1...O2 hydrogen bonds (Table 1) and these units are assembled into corrugated layers parallel to the bc plane by C3—H3...O4 hydrogen bonds (Table 1 and Fig. 2). Although these layers clearly contain large pores, they are combined in pairs across centers of symmetry by C9—H9...O4, C11—H11...O4 and C12—H12A...O1 hydrogen bonds (Table 1) so that the pores in one layer are capped by molecules in the second and the resulting double layer has no significant pores (Fig. 3).

4. Database survey

A search of the Cambridge Structural Database (CSD version 5.43 updated to March 2022; Groom et al., 2016) with the fragment A provided 28 hits, most of which contained a benzyl group attached to the ring nitrogen atom. Of these, seven [DEVVUY (Liu et al., 2018), DIDVAO (Makaev et al., 2006), ...]
ODUWIV (Duan et al., 2013), PUZBAQ (Becerra et al., 2020), PUZBEU (Becerra et al., 2020), PUZBIY (Becerra et al., 2020) and PUZBOE (Becerra et al., 2020) are most similar to the title molecule having a \( \beta \)-carbonyl group in the substituent attached to the saturated carbon of the five-membered ring. As in the title compound, all of these form dimers through complementary O—H\( \cdots \)C1/C1/C1/C1 hydrogen bonds between the hydroxy and keto groups and these units are also further assembled into chains and/or layers by hydrogen-bonding interactions.

5. Hirshfeld surface analysis
The analysis was performed with crystalExplorer 21.5 (Spackman et al., 2021) with the details of the pictorial output described in a recent publication (Tan et al., 2019). Fig. 4 shows the \( d_{\text{norm}} \) surface for the asymmetric unit plotted over the limits −0.6060 to 1.5193 a.u. together with three adjacent molecules that are hydrogen-bonded to it. The one on the lower left, adjacent to the pair of intense red spots, is the second half of one inversion dimer with these red spots indicating the strong O1—H1\( \cdots \)O2 hydrogen bonds (cf. Fig. 2). The molecules above and below the surface are members of two adjacent layers of molecules (cf. Fig. 3), which are linked by the C9—H9A\( \cdots \)O4 hydrogen bonds (lighter red spots). Fig. 5a presents a fingerprint plot of all intermolecular interactions while Fig. 5b shows the 55.2% of these attributable to H\( \cdots \)H interactions. Fig. 5c and 5d delineate the O\( \cdots \)H/H\( \cdots \)O (24.1%) and C\( \cdots \)H/H\( \cdots \)C (17.8%) interactions, respectively.

6. Synthesis and crystallization
Indoline-2,3-dione (0.1g, 0.0679 mmol) was taken up in 10 mL of acetone under stirring. Solid potassium carbonate (0.11 g, 0.815 mmol) was added in one portion. Then, the dark-colored suspension was raised to room temperature and stirred for a further 1 h. The appropriate 2-chloro-N-(2,6-dimethylphenyl)acetamide (0.119 g, 0.0679 mmol) and potassium iodide (0.05 g, 0.301 mmol) were added. Then, the reaction mixture was stirred at 353.15–373 K for 2 h until the reaction was complete, which was confirmed using TLC (ethyl acetate:hexane, 40:60). The resulting solid was filtered and recrystallized from ethanol to give title compound as colorless crystals. Yield: 64%; m.p. 527.15–529.15 K. FT–IR (ATR, \( \nu \), cm\(^{-1}\)) 3292 \( \nu \) (N—H amide), 1021 \( \nu \) (N—C amide), 1675 \( \nu \) (C=O amide), 1708 \( \nu \) (C=O lactam), 3073 \( \nu \) (C=H amine), 1175 \( \nu \) (C—N), 2952 \( \nu \) (C—H, CH\(_3\)), 3348 \( \delta \) ppm: 9.086 (s, 1H, NH); 7.011–7.338 (m, 7H, H\(_{\text{arom}}\)); 6.134 (s, 1H, OH); 3.16-4.52 (2d, 2H, CH\(_2\)); 2.03 (s, 6H, 2 CH\(_3\)); 1.97 (s, 3H, CH\(_3\)). 1\(^{3}\)C NMR (DMSO-d\(_6\)) \( \delta \) ppm: 207.448 (C=O), 177.126 (C=O lactam), 166.770 (C==O amide), 143.329; 135.794; 134.718; 131.196;

![Figure 4](image-url)

The Hirshfeld surface for the title molecule with three close neighbors added.

![Figure 5](image-url)

Fingerprint plots for the title molecule: (a) all contacts, (b) H\( \cdots \)H contacts, (c) O\( \cdots \)H/H\( \cdots \)C contacts and (d) C\( \cdots \)H/H\( \cdots \)C contacts.
Table 2
Experimental details.

| Crystal data | M, g/mol | Crystal system, space group | Temperature (K) | a, b, c (Å) | β (°) | V (Å³) | Z | Radiation type | μ (mm⁻¹) | Crystal size (mm) |
|--------------|----------|-----------------------------|----------------|-------------|-------|--------|---|----------------|----------|------------------|
| Chemical formula | C₂₁H₂₂N₂O₄ | Monoclinic, P2₁/c | 150 | 13.8608 (5), 8.8352 (3), 15.5411 (6) | 98.468 (1) | 1882.46 (12) | 4 | Mo Kα | 0.09 | 0.46 × 0.37 × 0.26 |

Data collection
Diffractometer | Bruker D8 QUEST PHOTON 3 | Tmax (K) | No. of measured, independent and observed [I > 2σ(I)] reflections | Rint, wR² | No. of parameters | H-atom treatment |
|----------------|--------------------------|----------|-----------------------------------------------------------------|-----------|-----------------|------------------|
|                |                          | 0.95, 0.98 | 101980, 6815, 5846                                               | 0.035     | 254             | H atoms treated by a mixture of independent and constrained refinement |

Refinement
R(F² > 2σ(F²)), wR(F²), S | 0.045, 0.129, 1.07 | No. of reflections | 6815 |
|--------------------------|-------------------|-------------------|---------|
| No. of parameters | 254                | H-atom treatment | H atoms treated by a mixture of independent and constrained refinement |
| Δρmax, Δρmin (e Å⁻³) | 0.42, −0.31        |                   |         |

Computer programs: APEX4 and SAINT (Bruker, 2021), SHELXT (Sheldrick, 2015a), SHELXL2018 (Sheldrick, 2015b), DIAMOND (Brandenburg & Putz, 2012) and SHELXTL (Sheldrick, 2008).

7. Refinement
Crystal data, data collection and structure refinement details are summarized in Table 2. Hydrogen atoms attached to carbon were included as riding contributions in idealized positions (C—H = 0.95–0.99 Å) with isotropic displacement parameters tied to those of the attached atoms [Uiso(H) = 1.2–1.5Ueq(C)]. Those attached to nitrogen and to oxygen were placed in locations derived from a difference map and refined with DFIX 0.91 0.01 and DFIX 0.84 0.01 instructions, respectively.

Acknowledgements
Author contributions are as follows. Conceptualization, YR and AA; methodology, YR; investigation, IN; theoretical calculations, JTM; writing (original draft), JMT and YR; writing (review and editing of the manuscript), YR; formal analysis, AA and YR; supervision, YR; crystal-structure determination and validation, JTM.

Funding information
JTM thanks Tulane University for support of the Tulane Crystallography Laboratory.

References
Allen, C. L. & Williams, J. M. J. (2011). Chem. Soc. Rev. 40, 3405–3415.
Beccalli, E. M., Broginni, G., Martinelli, M. & Sottocornola, S. (2007). Chem. Rev. 107, 5318–5365.
Becerra, D., Castillo, J., Insuasty, B., Cobo, J. & Glidewell, C. (2020). Acta Cryst. C76, 433–445.
Bekircan, O. & Bektas, H. (2008). Molecules, 13, 2126–2135.
Brandenburg, K. & Putz, H. (2012). DIAMOND. Crystal Impact GbR, Bonn, Germany.
Buker (2021). APEX4 and SAINT. Bruker AXS LLC, Madison, Wisconsin, USA.
Ding, Z., Zhou, M. & Zeng, C. (2020). Arch. Pharm. Chem. Life Sci. 353, 1900367–380.
Duan, Z., Han, J., Qian, P., Zhang, Z., Wang, Y. & Pan, Y. (2013). Org. Biomol. Chem. 11, 6456–6459.
Feng, L. S., Liu, M. L., Wang, B., Chai, Y., Hao, X. Q., Meng, S. & Guo, H. Y. (2010). Eur. J. Med. Chem. 45, 3407–3412.
Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). Acta Cryst. B72, 171–179.
Hu, Y. Q., Zhang, S., Xu, Z., Lv, Z. S., Liu, M. L. & Feng, L. S. (2017). Eur. J. Med. Chem. 141, 335–345.
Krause, L., Herbst-Irmer, R., Sheldrick, G. M. & Stalke, D. (2015). J. Appl. Cryst. 48, 3–10.
Liu, X.-W., Yang, J., Wang, G.-L., Gong, Y., Feng, T.-T., Liu, X.-L., Cao, Y., Zhou, Y. & Yuan, W.-C. (2018). J. Heterocycl. Chem. 55, 351–359.
Makaev, F. Z., Radul, O. M., Gđaniec, M., Malinovsky, S. T. & Gudima, A. P. (2006). Zh. Strukt. Khim. 47, 803.
Mathur, G. & Nain, S. (2014). Med. Chem. 4, 417–427.
Missioui, M., Lgaz, H., Guerrab, W., Lee, H., Ward, I., Mague, J. T., Ali, I. H., Essassi, E. M. & Ramli, Y. (2022a). J. Mol. Struct. 1253, 132132–143.
Missioui, M., Mortada, S., Guerrab, W., Serdaroglu, G., Kaya, S., Mague, J. T., Essassi, E. M., Faouzi, M. E. A. & Ramli, Y. (2021). J. Mol. Struct. 1239, 130484–494.
Missioui, M., Said, M. A., Demirtaş, G., Mague, J. T., Al-Sulami, A., Al-Kafif, N. S. & Ramli, Y. (2022b). Arab. J. Chem. 15, 103595–103613.
Missioui, M., Said, M. A., Demirtaş, G., Mague, J. T. & Ramli, Y. (2022c). J. Mol. Struct. 1247, 131420–433.
Nath, R., Pathania, S., Grover, G. & Akhtar, M. J. (2020). J. Mol. Struct. 1222, 128900–993.
Sheldrick, G. M. (2008). Acta Cryst. A64, 112–122.
Sheldrick, G. M. (2015a). Acta Cryst. A71, 3–8.
Sheldrick, G. M. (2015b). Acta Cryst. C71, 3–8.
Spackman, P. R., Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Jayatilaka, D. & Spackman, M. A. (2021). J. Appl. Cryst. 54, 1006–1011.
Tan, S. L., Jotani, M. M. & Tiekink, E. R. T. (2019). Acta Cryst. E75, 308–318.
Valeur, E. & Bradley, M. (2009). Chem. Soc. Rev. 38, 606–631.
Crystal structure and Hirshfeld surface analysis of N-(2,6-dimethylphenyl)-2-[3-hydroxy-2-oxo-3-(2-oxopropyl)indolin-1-yl]acetamide

Intissar Nchioua, Abdulsalam Alsubari, Joel T. Mague and Youssef Ramli

Computing details

Data collection: APEX4 (Bruker, 2021); cell refinement: SAINT (Bruker, 2021); data reduction: SAINT (Bruker, 2021); program(s) used to solve structure: SHELXT (Sheldrick, 2015a); program(s) used to refine structure: SHELXL2018/1 (Sheldrick, 2015b); molecular graphics: DIAMOND (Brandenburg & Putz, 2012); software used to prepare material for publication: SHELXTL (Sheldrick, 2008).

N-(2,6-dimethylphenyl)-2-[3-hydroxy-2-oxo-3-(2-oxopropyl)indolin-1-yl]acetamide

Crystal data

C21H22N2O4
Mr = 366.40
Monoclinic, P2₁/c
a = 13.8608 (5) Å
b = 8.8352 (3) Å
c = 15.5411 (6) Å
β = 98.468 (1)°
V = 1882.46 (12) Å³
Z = 4

F(000) = 776
Dₐ = 1.293 Mg m⁻³
Mo Kα radiation, λ = 0.71073 Å
Cell parameters from 9714 reflections
θ = 3.0–32.6°
μ = 0.09 mm⁻¹
T = 150 K
Block, colourless

0.46 × 0.37 × 0.26 mm

Data collection

Bruker D8 QUEST PHOTON 3 diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 7.3910 pixels mm⁻¹
φ and ω scans
Absorption correction: numerical
(SADABS; Krause et al., 2015)

Tₘᵟᵣₐᵣᵱ = 0.95, Tₘᵞᵛᵩ = 0.98

Refinement

Refinement on F²
Least-squares matrix: full
R[F² > 2σ(F²)] = 0.045
wR(F²) = 0.129
S = 1.07
6815 reflections
254 parameters
0 restraints

Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement

w = 1/[σ(F²)² + (0.0697P)² + 0.4122P]
where P = (F² + 2Fc²)/3
(Δ/σ)_{max} = 0.001
Δρ_{max} = 0.42 \text{ e Å}^{-3}

Δρ_{min} = -0.31 \text{ e Å}^{-3}

**Special details**

**Experimental.** The diffraction data were obtained from 9 sets of frames, each of width 0.5° in ω or φ, collected with scan parameters determined by the "strategy" routine in APEX3. The scan time was 5 sec/frame.

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

**Refinement.** Refinement of F² against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F², conventional R-factors R are based on F, with F set to zero for negative F². The threshold expression of F² > 2σ(F²) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F² are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger. H-atoms attached to carbon were placed in calculated positions (C—H = 0.95 - 0.99 Å) and were included as riding contributions with isotropic displacement parameters 1.2 - 1.5 times those of the attached atoms. Those attached to nitrogen and to oxygen were placed in locations derived from a difference map and refined with DFIX 0.91 0.01 and DFIX 0.84 0.01 instructions, respectively.

**Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)**

|          | x      | y      | z      | U_{eq}/*U_{eq} |
|----------|--------|--------|--------|----------------|
| O1       | -0.01619 (5) | 0.15240 (7) | 0.58519 (4) | 0.02331 (13) |
| H1       | -0.0211 (11) | 0.0551 (17) | 0.5810 (10) | 0.035*        |
| O2       | 0.06628 (5)  | 0.15275 (7) | 0.41710 (4) | 0.02433 (13) |
| O3       | 0.27892 (5)  | 0.18850 (8) | 0.55047 (5) | 0.03248 (16) |
| O4       | 0.20771 (5)  | 0.56774 (9) | 0.30204 (4) | 0.02884 (15) |
| N1       | 0.10667 (5)  | 0.38567 (7) | 0.47826 (4) | 0.01780 (13) |
| N2       | 0.28454 (5)  | 0.43751 (9) | 0.41823 (5) | 0.02231 (14) |
| H2A      | 0.2780 (10)  | 0.3724 (17) | 0.4593 (10) | 0.035 (3)*    |
| C1       | 0.12285 (6)  | 0.44754 (8) | 0.56329 (5) | 0.01798 (14) |
| C2       | 0.14520 (7)  | 0.59580 (9) | 0.58717 (6) | 0.02279 (16) |
| H2       | 0.154105     | 0.670797   | 0.545243    | 0.027*        |
| C3       | 0.15409 (7)  | 0.63026 (10) | 0.67608 (6) | 0.02693 (17) |
| H3       | 0.169109     | 0.730952   | 0.694915    | 0.032*        |
| C4       | 0.14134 (7)  | 0.51983 (11) | 0.73723 (6) | 0.02757 (18) |
| H4       | 0.147813     | 0.545934   | 0.797102    | 0.033*        |
| C5       | 0.11902 (7)  | 0.37041 (10) | 0.71126 (5) | 0.02376 (16) |
| H5       | 0.110095     | 0.294882   | 0.752878    | 0.029*        |
| C6       | 0.11028 (6)  | 0.33536 (9) | 0.62380 (5) | 0.01846 (14) |
| C7       | 0.08199 (6)  | 0.18914 (8) | 0.57660 (5) | 0.01790 (14) |
| C8       | 0.08473 (6)  | 0.23521 (9) | 0.48075 (5) | 0.01807 (14) |
| C9       | 0.15003 (6)  | 0.05606 (9) | 0.60396 (5) | 0.02081 (15) |
| H9A      | 0.147274     | 0.032787   | 0.665866    | 0.025*        |
| H9B      | 0.125732     | -0.033851  | 0.569376    | 0.025*        |
| C10      | 0.25502 (6)  | 0.08274 (10) | 0.59283 (6) | 0.02231 (15) |
| C11      | 0.32861 (7)  | -0.02778 (12) | 0.63580 (7) | 0.0316 (2)    |
| H11A     | 0.307193     | -0.131044  | 0.619844    | 0.047*        |
| H11B     | 0.335063     | -0.015875  | 0.699085    | 0.047*        |
| H11C     | 0.391777     | -0.008787  | 0.616620    | 0.047*        |
### Atomic displacement parameters (Å²)

|    | $U^{11}$  | $U^{22}$  | $U^{33}$  | $U^{12}$  | $U^{13}$  | $U^{23}$  |
|----|-----------|-----------|-----------|-----------|-----------|-----------|
| O1 | 0.0214 (3) | 0.0181 (3) | 0.0320 (3) | −0.0025 (2) | 0.0089 (2) | 0.0019 (2) |
| O2 | 0.0324 (3) | 0.0196 (3) | 0.0212 (3) | −0.0036 (2) | 0.0045 (2) | −0.0041 (2) |
| O3 | 0.0261 (3) | 0.0303 (3) | 0.0419 (4) | −0.0001 (3) | 0.0079 (3) | 0.0139 (3) |
| O4 | 0.0303 (3) | 0.0361 (4) | 0.0206 (3) | 0.0004 (3) | 0.0053 (2) | 0.0107 (2) |
| N1 | 0.0230 (3) | 0.0147 (3) | 0.0162 (3) | −0.0012 (2) | 0.0045 (2) | 0.0007 (2) |
| N2 | 0.0221 (3) | 0.0242 (3) | 0.0213 (3) | 0.0006 (2) | 0.0051 (2) | 0.0069 (2) |
| C1 | 0.0214 (3) | 0.0153 (3) | 0.0178 (3) | −0.0010 (2) | 0.0045 (2) | −0.0007 (2) |
| C2 | 0.0296 (4) | 0.0157 (3) | 0.0237 (3) | −0.0032 (3) | 0.0062 (3) | −0.0013 (3) |
| C3 | 0.0348 (4) | 0.0198 (4) | 0.0266 (4) | −0.0037 (3) | 0.0057 (3) | −0.0062 (3) |
| C4 | 0.0356 (5) | 0.0269 (4) | 0.0203 (3) | −0.0020 (3) | 0.0044 (3) | −0.0053 (3) |
| C5 | 0.0311 (4) | 0.0226 (4) | 0.0179 (3) | −0.0012 (3) | 0.0049 (3) | 0.0008 (3) |
| C6 | 0.0226 (3) | 0.0153 (3) | 0.0179 (3) | −0.0010 (2) | 0.0044 (2) | −0.0002 (2) |
| C7 | 0.0206 (3) | 0.0145 (3) | 0.0193 (3) | −0.0019 (2) | 0.0050 (2) | 0.0012 (2) |
| C8 | 0.0196 (3) | 0.0155 (3) | 0.0193 (3) | −0.0005 (2) | 0.0037 (2) | −0.0005 (2) |
| C9 | 0.0235 (3) | 0.0157 (3) | 0.0236 (3) | 0.0004 (3) | 0.0045 (3) | 0.0029 (3) |
| C10| 0.0236 (3) | 0.0200 (3) | 0.0236 (3) | 0.0015 (3) | 0.0044 (3) | 0.0010 (3) |
| C11| 0.0271 (4) | 0.0310 (4) | 0.0374 (5) | 0.0081 (3) | 0.0072 (3) | 0.0093 (4) |
| C12| 0.0228 (3) | 0.0196 (3) | 0.0180 (3) | 0.0010 (3) | 0.0043 (3) | 0.0041 (2) |
| C13| 0.0237 (3) | 0.0186 (3) | 0.0173 (3) | −0.0003 (3) | 0.0044 (3) | 0.0011 (2) |
| C14| 0.0215 (3) | 0.0354 (5) | 0.0230 (4) | −0.0008 (3) | 0.0034 (3) | 0.0095 (3) |
| C15| 0.0299 (4) | 0.0478 (6) | 0.0334 (5) | 0.0128 (4) | 0.0102 (4) | 0.0136 (4) |
| C16| 0.0342 (5) | 0.0853 (11) | 0.0517 (7) | 0.0270 (6) | 0.0199 (5) | 0.0313 (7) |
| C17| 0.0237 (5) | 0.1103 (14) | 0.0668 (9) | 0.0030 (7) | 0.0118 (5) | 0.0503 (10) |
C18 0.0323 (5) 0.0797 (10) 0.0591 (8) −0.0212 (6) −0.0020 (5) 0.0332 (8)
C19 0.0328 (5) 0.0454 (6) 0.0342 (5) −0.0131 (4) −0.0010 (4) 0.0135 (4)
C20 0.0586 (8) 0.0398 (6) 0.0598 (8) 0.0159 (6) 0.0215 (7) −0.0014 (6)
C21 0.0691 (9) 0.0350 (6) 0.0522 (7) −0.0196 (6) 0.0019 (6) −0.0015 (5)

Geometric parameters (Å, º)

| Bond | Distance (Å) | Angle (º) |
|------|--------------|-----------|
| O1—C7 | 1.4242 (10) | C9—H9B 0.9900 |
| O1—H1 | 0.864 (15) | C10—C11 1.4965 (13) |
| O2—C8 | 1.2248 (9) | C11—H11A 0.9800 |
| O3—C10 | 1.2167 (11) | C11—H11B 0.9800 |
| O4—C13 | 1.2266 (10) | C11—H11C 0.9800 |
| N1—C8 | 1.3655 (10) | C12—C13 1.5187 (11) |
| N1—C1 | 1.4170 (10) | C12—C13 1.5900 (15) |
| N1—C12 | 1.4450 (10) | C12—C13 1.5900 (15) |
| N2—C13 | 1.3467 (11) | C13—C14 1.3956 (15) |
| N2—C14 | 1.4329 (11) | C13—C14 1.4005 (15) |
| N2—H2A | 0.874 (15) | C13—C14 1.4005 (15) |
| C2—C1 | 1.3840 (11) | C15—C16 1.3956 (15) |
| C2—H2 | 0.9500 | C15—C16 1.3956 (15) |
| C3—C2 | 1.3913 (13) | C16—H16 0.9500 |
| C3—C4 | 1.4017 (13) | C16—H16 0.9500 |
| C4—C3 | 0.9500 | C17—C18 1.370 (3) |
| C4—H4 | 0.9500 | C17—C18 1.370 (3) |
| C5—C4 | 1.3818 (11) | C18—H18 0.9500 |
| C5—H5 | 0.9500 | C18—H18 0.9500 |
| C6—C5 | 1.5087 (11) | C19—C21 1.499 (2) |
| C6—H6 | 0.9500 | C19—C21 1.499 (2) |
| C7—C6 | 1.5279 (11) | C20—H20A 0.9800 |
| C7—C9 | 1.5501 (11) | C20—H20A 0.9800 |
| C9—C10 | 1.5091 (12) | C20—H20B 0.9800 |
| C9—H9A | 0.9900 |

| Bond | Distance (Å) | Angle (º) |
|------|--------------|-----------|
| C7—O1—H1 | 106.6 (10) | C10—C11—H11B 109.5 |
| C8—N1—C1 | 110.76 (6) | H11A—C11—H11B 109.5 |
| C8—N1—C12 | 123.77 (7) | C10—C11—H11C 109.5 |
| C1—N1—C12 | 125.35 (6) | H11A—C11—H11C 109.5 |
| C13—N2—C14 | 120.85 (7) | H11B—C11—H11C 109.5 |
| C13—N2—H2A | 120.0 (9) | N1—C12—C13 116.66 (7) |
| C14—N2—H2A | 118.0 (9) | N1—C12—C13 116.66 (7) |
| C2—C1—C6 | 122.48 (7) | C13—C12—H12A 108.1 |
| C2—C1—N1 | 127.85 (7) | N1—C12—H12B 108.1 |
| C6—C1—N1 | 109.65 (6) | C13—C12—H12B 108.1 |
| C1—C2—C3 | 116.96 (8) | H12A—C12—H12B 107.3 |
| C1—C2—H2 | 121.5 | O4—C13—N2 123.73 (8) |
| C3—C2—H2 | 121.5 | O4—C13—C12 118.34 (7) |
| C4—C3—C2 | 121.27 (8) | N2—C13—C12 117.91 (7) |
| Bond Lengths (Å) | Bond Angle (°) |
|------------------|----------------|
| C4—C3—H3        | 119.4          |
| C2—C3—H3        | 119.4          |
| C3—C4—C5        | 120.58 (8)     |
| C3—C4—H4        | 119.7          |
| C5—C4—H4        | 119.7          |
| C6—C5—C4        | 118.55 (8)     |
| C6—C5—H5        | 120.7          |
| C4—C5—H5        | 120.7          |
| C5—C6—C1        | 120.16 (7)     |
| C5—C6—C7        | 130.47 (7)     |
| C1—C6—C7        | 109.27 (7)     |
| O1—C7—C9        | 116.90 (7)     |
| O1—C7—C8        | 107.99 (6)     |
| C8—N1—C1—C2     | −178.96 (8)    |
| N8—N1—C1—C2     | −2.79 (13)     |
| C8—N1—C1—C6     | −0.65 (9)      |
| C12—N1—C1—C6    | 175.53 (7)     |
| C6—C1—C2—C3     | −0.55 (13)     |
| N1—C1—C2—C3     | 177.57 (8)     |
| C1—C2—C3—C4     | 0.25 (14)      |
| C2—C3—C4—C5     | −0.08 (15)     |
| C3—C4—C5—C6     | 0.18 (14)      |
| C4—C5—C6—C1     | −0.47 (13)     |
| C4—C5—C6—C7     | −176.29 (8)    |
| C2—C1—C6—C5     | 0.68 (13)      |
| N1—C1—C6—C5     | −177.74 (7)    |
| C2—C1—C6—C7     | 177.32 (7)     |
| N1—C1—C6—C7     | −1.11 (9)      |
| C5—C6—C7—O1     | 64.33 (11)     |
| C1—C6—C7—O1     | −111.85 (7)    |
C5—C6—C7—C9  −61.13 (12)  C19—C14—C15—C20  179.24 (11)
C1—C6—C7—C9  122.69 (7)  N2—C14—C15—C20  −1.49 (15)
C5—C6—C7—C8  178.34 (9)  C14—C15—C16—C17  1.46 (18)
C1—C6—C7—C8  2.16 (8)  C20—C15—C16—C17  −178.06 (13)
C1—N1—C8—O2  179.22 (8)  C15—C16—C17—C18  −1.3 (2)
C12—N1—C8—O2  2.97 (12)  C16—C17—C18—C19  −0.1 (2)
C1—N1—C8—C7  2.07 (9)  C17—C18—C19—C14  1.18 (18)
C12—N1—C8—C7  −174.18 (7)  C17—C18—C19—C21  −178.97 (13)
O1—C7—C8—O2  −64.57 (10)  C15—C14—C19—C18  −1.01 (15)
C6—C7—C8—O2  −179.67 (8)  C15—C14—C19—C21  179.15 (11)
C9—C7—C8—O2  57.64 (10)  C15—C14—C19—C21  179.15 (11)
O1—C7—C8—N1  112.55 (7)  N2—C14—C19—C21  −0.12 (15)

Hydrogen-bond geometry (Å, °)

\[
\begin{array}{cccc}
D—H···A & D—H & H···A & D···A & D—H···A \\
O1—H1···O2^i & 0.864 (15) & 1.942 (15) & 2.7829 (9) & 164.1 (14) \\
N2—H2A···O3 & 0.874 (15) & 2.154 (15) & 3.0193 (10) & 170.3 (13) \\
C3—H3···O4^ii & 0.95 & 2.44 & 3.3280 (12) & 155 \\
C9—H9A···O4^iii & 0.99 & 2.33 & 3.2537 (11) & 154 \\
C11—H11B···O4^iii & 0.98 & 2.59 & 3.2988 (12) & 129 \\
C12—H12A···O1^iv & 0.99 & 2.60 & 3.5835 (11) & 173 \\
\end{array}
\]

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