

Acta Crystallographica Section E

Structure Reports

Online

ISSN 1600-5368

## 3-(2-Amino-1-methyl-4-oxo-4,5-dihydro-1H-imidazol-5-yl)-3-hydroxy-1-phenyl-indolin-2-one ethanol solvate

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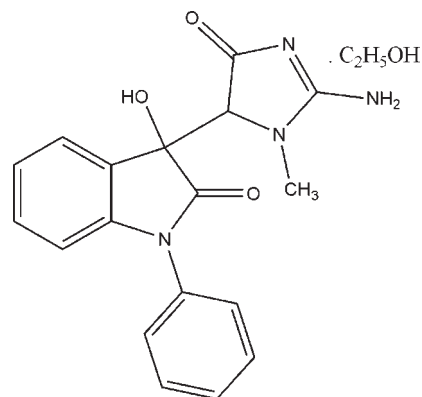
Received 18 August 2009; accepted 24 August 2009

 Key indicators: single-crystal X-ray study;  $T = 90$  K; mean  $\sigma(\text{C}-\text{C}) = 0.002$  Å;  $R$  factor = 0.037;  $wR$  factor = 0.098; data-to-parameter ratio = 12.8.

In the title compound,  $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}_3 \cdot \text{C}_2\text{H}_5\text{OH}$ , molecules are linked into chains by a series of intermolecular  $\text{N}-\text{H} \cdots \text{O}$ ,  $\text{N}-\text{H} \cdots \text{N}$  and  $\text{O}-\text{H} \cdots \text{O}$  hydrogen bonds which stabilize the crystal structure. The indole and creatinine units make a dihedral angle of  $56.45$  ( $4$ )°. The title compound has two chiral centres. The crystal structure indicates the compound is racemic ( $RR$  and  $SS$ ).

### Related literature

For the biological activity of isatin and its derivatives, see: Pandeya *et al.* (2005). The endogenous oxindoles 5-hydroxy-oxindole and isatin are antiproliferative and proapoptotic, see: Cane *et al.* (2000). For *in vitro* cytotoxicity evaluation of some substituted isatin derivatives, see: Vine *et al.* (2007). 2-Indol-3-yl-methylenequinuclidin-3-ols and NADPH oxidase activity has been reported by Sekhar *et al.* (2003), and novel substituted (*Z*)-2-(*N*-benzylindol-3-ylmethylene)quinuclidin-3-one and (*Z*)-( $\pm$ )-2-(*N*-benzylindol-3-ylmethylene)quinuclidin-3-ol derivatives as potent thermal sensitizing agents by Sonar *et al.* (2007). For the crystal and molecular structure of isatin, see: Frolova *et al.* (1988). For the structure of 3-(2-amino-1-methyl-4-oxo-4,5-dihydro-1H-imidazol-5-yl)-3-hydroxyindolin-2-one monohydrate, see: Penthala *et al.* (2009) and of 1,1'-diacetyl-3-hydroxy-2,2',3,3'-tetrahydro-3,3'-bi(1H-indole)-2,2'-dione, see: Usman *et al.* (2002). The aldol condensation enolate mechanism *via* a six-membered transition state has been described by Zimmerman & Traxler (1957).



### Experimental

#### Crystal data

 $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}_3 \cdot \text{C}_2\text{H}_6\text{O}$ 
 $M_r = 382.42$ 

 Triclinic,  $P\bar{1}$ 
 $a = 7.4912$  (1) Å

 $b = 11.0018$  (2) Å

 $c = 12.0835$  (2) Å

 $\alpha = 78.152$  (1)°

 $\beta = 74.413$  (1)°

 $\gamma = 74.090$  (1)°

 $V = 913.15$  (3) Å<sup>3</sup>
 $Z = 2$ 

 Cu  $K\alpha$  radiation

 $\mu = 0.82$  mm<sup>-1</sup>
 $T = 90$  K

 $0.11 \times 0.11 \times 0.08$  mm

#### Data collection

Bruker X8 Proteum diffractometer

Absorption correction: multi-scan

(SADABS in APEX2; Bruker, 2006)

 $T_{\min} = 0.828$ ,  $T_{\max} = 0.938$ 

13576 measured reflections

3294 independent reflections

 3126 reflections with  $I > 2\sigma(I)$ 
 $R_{\text{int}} = 0.035$ 

#### Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.037$ 
 $wR(F^2) = 0.098$ 
 $S = 1.07$ 

3294 reflections

258 parameters

H-atom parameters constrained

 $\Delta\rho_{\text{max}} = 0.37$  e Å<sup>-3</sup>
 $\Delta\rho_{\text{min}} = -0.41$  e Å<sup>-3</sup>
**Table 1**

Hydrogen-bond geometry (Å, °).

| $D-\text{H} \cdots A$                                             | $D-\text{H}$ | $\text{H} \cdots A$ | $D \cdots A$ | $D-\text{H} \cdots A$ |
|-------------------------------------------------------------------|--------------|---------------------|--------------|-----------------------|
| $\text{O}2-\text{H}2 \cdots \text{O}1\text{S}$                    | 0.84         | 2.19                | 2.9579 (14)  | 152                   |
| $\text{O}2-\text{H}2 \cdots \text{O}3^{\text{i}}$                 | 0.84         | 2.58                | 3.2440 (12)  | 137                   |
| $\text{N}3-\text{H}3\text{A} \cdots \text{O}1^{\text{ii}}$        | 0.88         | 2.02                | 2.8898 (13)  | 169                   |
| $\text{N}3-\text{H}3\text{B} \cdots \text{N}2^{\text{iii}}$       | 0.88         | 2.06                | 2.9391 (15)  | 174                   |
| $\text{O}1\text{S}-\text{H}1\text{S} \cdots \text{O}3^{\text{i}}$ | 0.84         | 1.89                | 2.7048 (13)  | 162                   |

 Symmetry codes: (i)  $x + 1, y, z$ ; (ii)  $-x + 1, -y, -z$ ; (iii)  $-x, -y, -z$ .

Data collection: APEX2 (Bruker, 2006); cell refinement: SAINT (Bruker, 2006); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: XP in SHELXTL (Sheldrick, 2008); software used to prepare material for publication: SHELXL97 and local procedures.

This investigation was supported by NIH/National Cancer Institute grant PO1 CA104457 (PAC) and by NSF MRI grant CHE 0319176 (SP).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HG2557).

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**supplementary materials**

*Acta Cryst.* (2009). E65, o2439-o2440 [ doi:10.1107/S1600536809033881 ]

### 3-(2-Amino-1-methyl-4-oxo-4,5-dihydro-1*H*-imidazol-5-yl)-3-hydroxy-1-phenylindolin-2-one ethanol solvate

N. R. Penthala, T. R. Y. Reddy, S. Parkin and P. A. Crooks

#### Comment

1*H*-Indole-2,3-diones (isatins) are versatile molecules that display diverse biological activities, (Pandeya *et al.*, 2005), including anticancer activity. (Cane *et al.*, 2000 and Vine *et al.*, 2007). Based on the results of earlier work on radiosensitizers such as (*Z*)-2-(*N*-benzylindol-3-ylmethylene)quinuclidin-3-one and (*Z*)-(±)-2-(*N*-benzylindol-3-ylmethylene) quinuclidin-3-ol derivatives (Sekhar *et al.*, 2003; Sonar *et al.*, 2007), we have carried out the design, synthesis and structural analysis of a series of 3-(2-amino-1-methyl-4-oxo-4,5-dihydro-1*H*-imidazol-5-yl)-3-hydroxyindolin-2-one analogs with different substituents on the indole moiety. This X-ray analysis of the title compound was performed to confirm the stereochemistry of the molecule and to obtain detailed information on the conformation of the molecule, which may be useful in structure-activity relationship (SAR) analysis. The title compound was prepared by the aldol condensation of *N*-phenylindol-2,3-dione (*N*-phenyl isatin) with 2-amino-1-methyl-1*H*-imidazol-4(5*H*)-one (creatinine) in the presence of sodium acetate in acetic acid under microwave irradiation. The compound was crystallized from ethyl alcohol. This aldol condensation reaction proceeds by the formation of the *E*-enolate, as per the Zimmerman-Traxler model (Zimmerman & Traxler, 1957), which favors anti products, and leads to the formation of a racemic compound (equimolar *RR* and *SS* enantiomers). The molecular structure and the atom-numbering scheme are shown in Fig.1. The isatin ring is planar (r.m.s. deviation = 0.00342 (10) Å) with bond distances and angles comparable with those previously reported for other isatin derivatives (Frolova *et al.*, 1988; Usman, *et al.*, 2002 and Penthala *et al.* 2009). The indole and creatinine moieties make a dihedral angle of 56.45 (4)°. Intermolecular N—H⋯O and O—H⋯N hydrogen bonds stabilize the crystal structure and form a supramolecular aggregation.

#### Experimental

A mixture of *N*-phenyl isatin (1 mmol), creatinine (1.1 mmol) and sodium acetate (1.2 mmol) in acetic acid (1 ml) was irradiated in a domestic microwave oven for 30 sec with intermittent cooling every 5 sec. The reaction mixture was allowed to cool to room temperature, 10 ml of saturated sodium bicarbonate solution was added and the mixture was stirred for 10 minutes. The precipitate thus obtained was collected by filtration, washed with cold water and dried to afford the crude product. Crystallization from ethyl alcohol gave a white crystalline product of 3-(2-amino-1-methyl-4-oxo-4,5-dihydro-1*H*-imidazol-5-yl)-3-hydroxy-1-phenylindolin-2-one ethanolate which was suitable for X-ray analysis. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.25 (*s*, 3H), 4.22 (*s*, 1H), 6.62 (*s*, 1H, OH), 6.64–6.65 (*d*, *J*=2.4 Hz, 1H), 7.00–7.03 (*t*, *J*=7.5 Hz, 1H), 7.17–7.23 (*m*, 2H), 7.44–7.47 (*m*, 4H), 7.55–7.57 (*d*, *J*=7.5 Hz, 1H), 7.60 (*bs*, 2H, NH<sub>2</sub>) p.p.m.; <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 33.02, 70.60, 76.26, 108.92, 122.74, 124.38, 126.95, 127.10, 128.13, 129.60, 129.86, 134.40, 143.93, 171.90, 174.09, 182.53 p.p.m..

#### Refinement

H atoms were found in difference Fourier maps and subsequently placed in idealized positions with constrained distances of 0.98 Å (RCH<sub>3</sub>), 0.99 Å (R<sub>2</sub>CH<sub>2</sub>), 1.00 Å (R<sub>3</sub>CH), 0.95 Å (C<sub>Ar</sub>H), 0.84 Å (O—H), 0.88 Å (N—H), and with *U*<sub>iso</sub>(H) values set to either 1.2*U*<sub>eq</sub> or 1.5*U*<sub>eq</sub> (RCH<sub>3</sub>, OH) of the attached atom.

## Figures

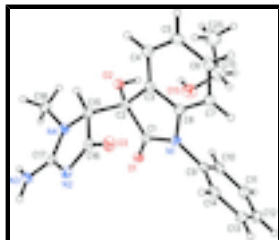


Fig. 1. A view of the molecule with the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

## 3-(2-Amino-1-methyl-4-oxo-4,5-dihydro-1H-imidazol-5-yl)-3-hydroxy-1-phenylindolin-2-one ethanol solvate

### Crystal data

$C_{18}H_{16}N_4O_3 \cdot C_2H_6O$

$M_r = 382.42$

Triclinic,  $P\bar{1}$

Hall symbol: -P 1

$a = 7.4912(1) \text{ \AA}$

$b = 11.0018(2) \text{ \AA}$

$c = 12.0835(2) \text{ \AA}$

$\alpha = 78.152(1)^\circ$

$\beta = 74.413(1)^\circ$

$\gamma = 74.090(1)^\circ$

$V = 913.15(3) \text{ \AA}^3$

$Z = 2$

$F_{000} = 404$

$D_x = 1.391 \text{ Mg m}^{-3}$

Cu  $K\alpha$  radiation,  $\lambda = 1.54178 \text{ \AA}$

Cell parameters from 9955 reflections

$\theta = 3.8\text{--}68.3^\circ$

$\mu = 0.82 \text{ mm}^{-1}$

$T = 90 \text{ K}$

Block, colourless

$0.11 \times 0.11 \times 0.08 \text{ mm}$

### Data collection

Bruker X8 Proteum  
diffractometer

Radiation source: fine-focus rotating anode

Monochromator: graded multilayer optics

Detector resolution: 5.6 pixels  $\text{mm}^{-1}$

$T = 90 \text{ K}$

$\varphi$  and  $\omega$  scans

Absorption correction: multi-scan  
(SADABS in APEX2; Bruker, 2006)

$T_{\min} = 0.828$ ,  $T_{\max} = 0.938$

13576 measured reflections

3294 independent reflections

3126 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.035$

$\theta_{\max} = 68.3^\circ$

$\theta_{\min} = 3.8^\circ$

$h = -9 \rightarrow 9$

$k = -13 \rightarrow 10$

$l = -14 \rightarrow 14$

### Refinement

Refinement on  $F^2$

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.037$

Hydrogen site location: inferred from neighbouring sites

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0501P)^2 + 0.3708P]$

where  $P = (F_o^2 + 2F_c^2)/3$

|                                                                |                                                                                                                 |
|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| $wR(F^2) = 0.098$                                              | $(\Delta/\sigma)_{\max} < 0.001$                                                                                |
| $S = 1.07$                                                     | $\Delta\rho_{\max} = 0.37 \text{ e } \text{\AA}^{-3}$                                                           |
| 3294 reflections                                               | $\Delta\rho_{\min} = -0.41 \text{ e } \text{\AA}^{-3}$                                                          |
| 258 parameters                                                 | Extinction correction: SHELXL97 (Sheldrick, 2008),<br>$F_c^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$ |
| Primary atom site location: structure-invariant direct methods | Extinction coefficient: 0.0068 (7)                                                                              |
| 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  $F^2 > 2\sigma(F^2)$  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 ( $\text{\AA}^2$ )

|     | $x$           | $y$          | $z$          | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|-----|---------------|--------------|--------------|----------------------------------|
| O1  | 0.37921 (12)  | 0.08545 (8)  | 0.23487 (7)  | 0.0188 (2)                       |
| N1  | 0.16513 (14)  | 0.24923 (9)  | 0.32617 (8)  | 0.0159 (2)                       |
| C1  | 0.29249 (17)  | 0.19721 (11) | 0.23418 (10) | 0.0161 (3)                       |
| O2  | 0.50070 (12)  | 0.30752 (8)  | 0.07786 (7)  | 0.0202 (2)                       |
| H2  | 0.5529        | 0.3158       | 0.1284       | 0.030*                           |
| N2  | 0.03753 (14)  | 0.13607 (10) | 0.04645 (8)  | 0.0174 (2)                       |
| C2  | 0.30826 (17)  | 0.30455 (11) | 0.12863 (10) | 0.0173 (3)                       |
| O3  | -0.10708 (12) | 0.31235 (9)  | 0.14096 (8)  | 0.0232 (2)                       |
| N3  | 0.26263 (14)  | 0.00056 (10) | -0.07643 (9) | 0.0185 (2)                       |
| H3A | 0.3780        | -0.0201      | -0.1202      | 0.022*                           |
| H3B | 0.1798        | -0.0454      | -0.0697      | 0.022*                           |
| C3  | 0.18841 (17)  | 0.42116 (12) | 0.18239 (10) | 0.0178 (3)                       |
| N4  | 0.33379 (14)  | 0.17486 (10) | -0.02748 (8) | 0.0175 (2)                       |
| C4  | 0.15762 (18)  | 0.54854 (12) | 0.13580 (11) | 0.0210 (3)                       |
| H4  | 0.2148        | 0.5746       | 0.0573       | 0.025*                           |
| C5  | 0.04026 (19)  | 0.63828 (12) | 0.20688 (11) | 0.0222 (3)                       |
| H5  | 0.0180        | 0.7266       | 0.1768       | 0.027*                           |
| C6  | -0.04402 (18) | 0.59920 (12) | 0.32105 (11) | 0.0212 (3)                       |
| H6  | -0.1239       | 0.6615       | 0.3680       | 0.025*                           |
| C7  | -0.01412 (17) | 0.47040 (12) | 0.36854 (10) | 0.0183 (3)                       |
| H7  | -0.0728       | 0.4437       | 0.4465       | 0.022*                           |
| C8  | 0.10411 (17)  | 0.38371 (11) | 0.29745 (10) | 0.0168 (3)                       |
| C9  | 0.12524 (17)  | 0.18231 (11) | 0.44190 (10) | 0.0161 (3)                       |
| C10 | 0.27258 (18)  | 0.12805 (11) | 0.49893 (11) | 0.0192 (3)                       |
| H10 | 0.3994        | 0.1339       | 0.4615       | 0.023*                           |

## supplementary materials

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|      |               |              |               |            |
|------|---------------|--------------|---------------|------------|
| C11  | 0.2316 (2)    | 0.06493 (12) | 0.61182 (11)  | 0.0233 (3) |
| H11  | 0.3312        | 0.0268       | 0.6516        | 0.028*     |
| C12  | 0.0459 (2)    | 0.05757 (12) | 0.66629 (11)  | 0.0247 (3) |
| H12  | 0.0185        | 0.0150       | 0.7435        | 0.030*     |
| C13  | -0.10000 (19) | 0.11217 (12) | 0.60827 (11)  | 0.0233 (3) |
| H13  | -0.2271       | 0.1071       | 0.6460        | 0.028*     |
| C14  | -0.06071 (18) | 0.17416 (12) | 0.49517 (11)  | 0.0195 (3) |
| H14  | -0.1599       | 0.2105       | 0.4548        | 0.023*     |
| C15  | 0.22403 (17)  | 0.28338 (11) | 0.03230 (10)  | 0.0173 (3) |
| H15  | 0.2094        | 0.3626       | -0.0256       | 0.021*     |
| C16  | 0.03012 (17)  | 0.24701 (12) | 0.08034 (10)  | 0.0175 (3) |
| C17  | 0.21402 (17)  | 0.09987 (11) | -0.02122 (10) | 0.0162 (3) |
| C18  | 0.49912 (18)  | 0.18208 (12) | -0.12386 (10) | 0.0207 (3) |
| H18A | 0.5813        | 0.0964       | -0.1304       | 0.031*     |
| H18B | 0.5707        | 0.2375       | -0.1096       | 0.031*     |
| H18C | 0.4562        | 0.2172       | -0.1962       | 0.031*     |
| O1S  | 0.57472 (13)  | 0.29564 (10) | 0.30873 (9)   | 0.0304 (3) |
| H1S  | 0.6853        | 0.2952       | 0.2685        | 0.046*     |
| C1S  | 0.5142 (2)    | 0.39650 (15) | 0.37674 (14)  | 0.0336 (3) |
| H1S1 | 0.5991        | 0.3811       | 0.4309        | 0.040*     |
| H1S2 | 0.3837        | 0.3965       | 0.4237        | 0.040*     |
| C2S  | 0.5151 (2)    | 0.52356 (16) | 0.30585 (16)  | 0.0413 (4) |
| H2S1 | 0.6444        | 0.5248       | 0.2601        | 0.062*     |
| H2S2 | 0.4729        | 0.5894       | 0.3570        | 0.062*     |
| H2S3 | 0.4285        | 0.5405       | 0.2535        | 0.062*     |

### Atomic displacement parameters ( $\text{\AA}^2$ )

|     | $U^{11}$   | $U^{22}$   | $U^{33}$   | $U^{12}$    | $U^{13}$    | $U^{23}$    |
|-----|------------|------------|------------|-------------|-------------|-------------|
| O1  | 0.0220 (4) | 0.0146 (4) | 0.0180 (4) | -0.0041 (3) | -0.0011 (3) | -0.0034 (3) |
| N1  | 0.0206 (5) | 0.0124 (5) | 0.0138 (5) | -0.0041 (4) | -0.0026 (4) | -0.0012 (4) |
| C1  | 0.0187 (6) | 0.0160 (6) | 0.0152 (6) | -0.0067 (5) | -0.0032 (5) | -0.0030 (4) |
| O2  | 0.0216 (5) | 0.0249 (5) | 0.0171 (4) | -0.0115 (4) | -0.0028 (3) | -0.0033 (3) |
| N2  | 0.0185 (5) | 0.0188 (5) | 0.0149 (5) | -0.0057 (4) | -0.0020 (4) | -0.0028 (4) |
| C2  | 0.0216 (6) | 0.0160 (6) | 0.0145 (6) | -0.0076 (5) | -0.0020 (5) | -0.0016 (5) |
| O3  | 0.0225 (5) | 0.0246 (5) | 0.0212 (5) | -0.0051 (4) | 0.0000 (4)  | -0.0080 (4) |
| N3  | 0.0177 (5) | 0.0193 (5) | 0.0199 (5) | -0.0067 (4) | -0.0011 (4) | -0.0068 (4) |
| C3  | 0.0231 (6) | 0.0168 (6) | 0.0160 (6) | -0.0068 (5) | -0.0061 (5) | -0.0026 (5) |
| N4  | 0.0191 (5) | 0.0193 (5) | 0.0151 (5) | -0.0075 (4) | 0.0000 (4)  | -0.0056 (4) |
| C4  | 0.0289 (7) | 0.0183 (6) | 0.0182 (6) | -0.0084 (5) | -0.0086 (5) | 0.0002 (5)  |
| C5  | 0.0306 (7) | 0.0136 (6) | 0.0253 (7) | -0.0054 (5) | -0.0126 (5) | -0.0003 (5) |
| C6  | 0.0253 (6) | 0.0173 (6) | 0.0234 (6) | -0.0017 (5) | -0.0096 (5) | -0.0068 (5) |
| C7  | 0.0220 (6) | 0.0179 (6) | 0.0165 (6) | -0.0048 (5) | -0.0061 (5) | -0.0033 (5) |
| C8  | 0.0215 (6) | 0.0140 (6) | 0.0173 (6) | -0.0058 (5) | -0.0071 (5) | -0.0017 (4) |
| C9  | 0.0236 (6) | 0.0110 (5) | 0.0131 (6) | -0.0043 (4) | -0.0017 (5) | -0.0028 (4) |
| C10 | 0.0230 (6) | 0.0150 (6) | 0.0188 (6) | -0.0033 (5) | -0.0032 (5) | -0.0042 (5) |
| C11 | 0.0337 (7) | 0.0156 (6) | 0.0194 (6) | -0.0009 (5) | -0.0089 (5) | -0.0024 (5) |
| C12 | 0.0409 (8) | 0.0152 (6) | 0.0154 (6) | -0.0078 (5) | -0.0014 (5) | -0.0011 (5) |

|     |            |            |             |             |             |             |
|-----|------------|------------|-------------|-------------|-------------|-------------|
| C13 | 0.0280 (7) | 0.0191 (6) | 0.0206 (6)  | -0.0099 (5) | 0.0044 (5)  | -0.0053 (5) |
| C14 | 0.0221 (6) | 0.0162 (6) | 0.0203 (6)  | -0.0047 (5) | -0.0032 (5) | -0.0043 (5) |
| C15 | 0.0216 (6) | 0.0165 (6) | 0.0140 (6)  | -0.0060 (5) | -0.0023 (5) | -0.0029 (4) |
| C16 | 0.0201 (6) | 0.0190 (6) | 0.0130 (5)  | -0.0053 (5) | -0.0032 (5) | -0.0014 (4) |
| C17 | 0.0186 (6) | 0.0179 (6) | 0.0126 (5)  | -0.0056 (5) | -0.0039 (4) | -0.0005 (4) |
| C18 | 0.0218 (6) | 0.0246 (6) | 0.0164 (6)  | -0.0099 (5) | 0.0011 (5)  | -0.0054 (5) |
| O1S | 0.0213 (5) | 0.0303 (5) | 0.0384 (6)  | -0.0077 (4) | -0.0007 (4) | -0.0078 (4) |
| C1S | 0.0254 (7) | 0.0339 (8) | 0.0426 (9)  | -0.0049 (6) | -0.0067 (6) | -0.0115 (7) |
| C2S | 0.0424 (9) | 0.0358 (9) | 0.0530 (10) | -0.0102 (7) | -0.0231 (8) | -0.0044 (7) |

*Geometric parameters (Å, °)*

|            |             |             |             |
|------------|-------------|-------------|-------------|
| O1—C1      | 1.2226 (15) | C7—C8       | 1.3770 (17) |
| N1—C1      | 1.3658 (15) | C7—H7       | 0.9500      |
| N1—C8      | 1.4220 (15) | C9—C14      | 1.3876 (18) |
| N1—C9      | 1.4353 (15) | C9—C10      | 1.3886 (18) |
| C1—C2      | 1.5531 (16) | C10—C11     | 1.3929 (18) |
| O2—C2      | 1.4136 (15) | C10—H10     | 0.9500      |
| O2—H2      | 0.8400      | C11—C12     | 1.386 (2)   |
| N2—C16     | 1.3477 (16) | C11—H11     | 0.9500      |
| N2—C17     | 1.3562 (15) | C12—C13     | 1.388 (2)   |
| C2—C3      | 1.5071 (17) | C12—H12     | 0.9500      |
| C2—C15     | 1.5472 (16) | C13—C14     | 1.3895 (18) |
| O3—C16     | 1.2314 (15) | C13—H13     | 0.9500      |
| N3—C17     | 1.3123 (16) | C14—H14     | 0.9500      |
| N3—H3A     | 0.8800      | C15—C16     | 1.5419 (17) |
| N3—H3B     | 0.8800      | C15—H15     | 1.0000      |
| C3—C4      | 1.3794 (17) | C18—H18A    | 0.9800      |
| C3—C8      | 1.3918 (17) | C18—H18B    | 0.9800      |
| N4—C17     | 1.3546 (16) | C18—H18C    | 0.9800      |
| N4—C15     | 1.4560 (15) | O1S—C1S     | 1.4181 (18) |
| N4—C18     | 1.4621 (15) | O1S—H1S     | 0.8400      |
| C4—C5      | 1.3972 (18) | C1S—C2S     | 1.483 (2)   |
| C4—H4      | 0.9500      | C1S—H1S1    | 0.9900      |
| C5—C6      | 1.3870 (19) | C1S—H1S2    | 0.9900      |
| C5—H5      | 0.9500      | C2S—H2S1    | 0.9800      |
| C6—C7      | 1.3960 (18) | C2S—H2S2    | 0.9800      |
| C6—H6      | 0.9500      | C2S—H2S3    | 0.9800      |
| C1—N1—C8   | 110.74 (10) | C12—C11—C10 | 120.23 (12) |
| C1—N1—C9   | 124.57 (10) | C12—C11—H11 | 119.9       |
| C8—N1—C9   | 123.74 (10) | C10—C11—H11 | 119.9       |
| O1—C1—N1   | 125.87 (11) | C11—C12—C13 | 120.17 (12) |
| O1—C1—C2   | 125.91 (10) | C11—C12—H12 | 119.9       |
| N1—C1—C2   | 108.21 (10) | C13—C12—H12 | 119.9       |
| C2—O2—H2   | 109.5       | C12—C13—C14 | 120.17 (12) |
| C16—N2—C17 | 106.75 (10) | C12—C13—H13 | 119.9       |
| O2—C2—C3   | 115.27 (10) | C14—C13—H13 | 119.9       |
| O2—C2—C15  | 106.63 (9)  | C9—C14—C13  | 119.20 (12) |
| C3—C2—C15  | 110.59 (10) | C9—C14—H14  | 120.4       |

## supplementary materials

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|              |              |                 |              |
|--------------|--------------|-----------------|--------------|
| O2—C2—C1     | 111.04 (9)   | C13—C14—H14     | 120.4        |
| C3—C2—C1     | 101.86 (9)   | N4—C15—C16      | 100.87 (9)   |
| C15—C2—C1    | 111.52 (9)   | N4—C15—C2       | 114.64 (10)  |
| C17—N3—H3A   | 120.0        | C16—C15—C2      | 112.68 (9)   |
| C17—N3—H3B   | 120.0        | N4—C15—H15      | 109.4        |
| H3A—N3—H3B   | 120.0        | C16—C15—H15     | 109.4        |
| C4—C3—C8     | 120.49 (11)  | C2—C15—H15      | 109.4        |
| C4—C3—C2     | 130.40 (11)  | O3—C16—N2       | 127.04 (11)  |
| C8—C3—C2     | 109.10 (10)  | O3—C16—C15      | 123.08 (11)  |
| C17—N4—C15   | 107.56 (10)  | N2—C16—C15      | 109.88 (10)  |
| C17—N4—C18   | 122.36 (10)  | N3—C17—N4       | 123.26 (11)  |
| C15—N4—C18   | 122.80 (10)  | N3—C17—N2       | 122.16 (11)  |
| C3—C4—C5     | 118.36 (11)  | N4—C17—N2       | 114.58 (10)  |
| C3—C4—H4     | 120.8        | N4—C18—H18A     | 109.5        |
| C5—C4—H4     | 120.8        | N4—C18—H18B     | 109.5        |
| C6—C5—C4     | 120.40 (11)  | H18A—C18—H18B   | 109.5        |
| C6—C5—H5     | 119.8        | N4—C18—H18C     | 109.5        |
| C4—C5—H5     | 119.8        | H18A—C18—H18C   | 109.5        |
| C5—C6—C7     | 121.51 (12)  | H18B—C18—H18C   | 109.5        |
| C5—C6—H6     | 119.2        | C1S—O1S—H1S     | 109.5        |
| C7—C6—H6     | 119.2        | O1S—C1S—C2S     | 112.92 (14)  |
| C8—C7—C6     | 117.14 (11)  | O1S—C1S—H1S1    | 109.0        |
| C8—C7—H7     | 121.4        | C2S—C1S—H1S1    | 109.0        |
| C6—C7—H7     | 121.4        | O1S—C1S—H1S2    | 109.0        |
| C7—C8—C3     | 122.10 (11)  | C2S—C1S—H1S2    | 109.0        |
| C7—C8—N1     | 128.13 (11)  | H1S1—C1S—H1S2   | 107.8        |
| C3—C8—N1     | 109.73 (10)  | C1S—C2S—H2S1    | 109.5        |
| C14—C9—C10   | 121.20 (11)  | C1S—C2S—H2S2    | 109.5        |
| C14—C9—N1    | 119.23 (11)  | H2S1—C2S—H2S2   | 109.5        |
| C10—C9—N1    | 119.56 (11)  | C1S—C2S—H2S3    | 109.5        |
| C9—C10—C11   | 119.02 (12)  | H2S1—C2S—H2S3   | 109.5        |
| C9—C10—H10   | 120.5        | H2S2—C2S—H2S3   | 109.5        |
| C11—C10—H10  | 120.5        |                 |              |
| C8—N1—C1—O1  | 174.88 (11)  | C1—N1—C9—C10    | 57.36 (16)   |
| C9—N1—C1—O1  | 5.70 (19)    | C8—N1—C9—C10    | -110.45 (13) |
| C8—N1—C1—C2  | -5.06 (13)   | C14—C9—C10—C11  | -0.27 (18)   |
| C9—N1—C1—C2  | -174.24 (10) | N1—C9—C10—C11   | 179.09 (10)  |
| O1—C1—C2—O2  | -50.77 (15)  | C9—C10—C11—C12  | -0.49 (18)   |
| N1—C1—C2—O2  | 129.18 (10)  | C10—C11—C12—C13 | 0.53 (19)    |
| O1—C1—C2—C3  | -174.02 (12) | C11—C12—C13—C14 | 0.19 (19)    |
| N1—C1—C2—C3  | 5.93 (12)    | C10—C9—C14—C13  | 0.99 (18)    |
| O1—C1—C2—C15 | 68.01 (15)   | N1—C9—C14—C13   | -178.38 (11) |
| N1—C1—C2—C15 | -112.05 (11) | C12—C13—C14—C9  | -0.94 (18)   |
| O2—C2—C3—C4  | 53.97 (17)   | C17—N4—C15—C16  | 4.68 (12)    |
| C15—C2—C3—C4 | -67.06 (16)  | C18—N4—C15—C16  | 155.35 (10)  |
| C1—C2—C3—C4  | 174.30 (13)  | C17—N4—C15—C2   | 126.01 (10)  |
| O2—C2—C3—C8  | -125.10 (11) | C18—N4—C15—C2   | -83.31 (13)  |
| C15—C2—C3—C8 | 113.87 (11)  | O2—C2—C15—N4    | 52.11 (12)   |
| C1—C2—C3—C8  | -4.77 (12)   | C3—C2—C15—N4    | 178.14 (9)   |

|              |              |                |              |
|--------------|--------------|----------------|--------------|
| C8—C3—C4—C5  | 0.01 (18)    | C1—C2—C15—N4   | -69.27 (13)  |
| C2—C3—C4—C5  | -178.97 (12) | O2—C2—C15—C16  | 166.73 (9)   |
| C3—C4—C5—C6  | -0.60 (19)   | C3—C2—C15—C16  | -67.24 (13)  |
| C4—C5—C6—C7  | 0.32 (19)    | C1—C2—C15—C16  | 45.36 (13)   |
| C5—C6—C7—C8  | 0.56 (18)    | C17—N2—C16—O3  | 178.51 (12)  |
| C6—C7—C8—C3  | -1.17 (18)   | C17—N2—C16—C15 | -1.87 (13)   |
| C6—C7—C8—N1  | 176.39 (11)  | N4—C15—C16—O3  | 177.90 (11)  |
| C4—C3—C8—C7  | 0.91 (19)    | C2—C15—C16—O3  | 55.19 (15)   |
| C2—C3—C8—C7  | -179.91 (11) | N4—C15—C16—N2  | -1.74 (12)   |
| C4—C3—C8—N1  | -177.05 (11) | C2—C15—C16—N2  | -124.45 (11) |
| C2—C3—C8—N1  | 2.13 (14)    | C15—N4—C17—N3  | 172.92 (11)  |
| C1—N1—C8—C7  | -175.84 (12) | C18—N4—C17—N3  | 22.09 (18)   |
| C9—N1—C8—C7  | -6.55 (19)   | C15—N4—C17—N2  | -6.58 (13)   |
| C1—N1—C8—C3  | 1.96 (14)    | C18—N4—C17—N2  | -157.41 (11) |
| C9—N1—C8—C3  | 171.25 (11)  | C16—N2—C17—N3  | -174.16 (11) |
| C1—N1—C9—C14 | -123.26 (13) | C16—N2—C17—N4  | 5.35 (14)    |
| C8—N1—C9—C14 | 68.92 (15)   |                |              |

Hydrogen-bond geometry (Å, °)

| <i>D</i> —H... <i>A</i>    | <i>D</i> —H | H... <i>A</i> | <i>D</i> ... <i>A</i> | <i>D</i> —H... <i>A</i> |
|----------------------------|-------------|---------------|-----------------------|-------------------------|
| O2—H2...O1S                | 0.84        | 2.19          | 2.9579 (14)           | 152                     |
| O2—H2...O3 <sup>i</sup>    | 0.84        | 2.58          | 3.2440 (12)           | 137                     |
| N3—H3A...O1 <sup>ii</sup>  | 0.88        | 2.02          | 2.8898 (13)           | 169                     |
| N3—H3B...N2 <sup>iii</sup> | 0.88        | 2.06          | 2.9391 (15)           | 174                     |
| O1S—H1S...O3 <sup>i</sup>  | 0.84        | 1.89          | 2.7048 (13)           | 162                     |

Symmetry codes: (i)  $x+1, y, z$ ; (ii)  $-x+1, -y, -z$ ; (iii)  $-x, -y, -z$ .

Fig. 1

