

# Methyl 2-acetamido-2-(4-hydroxy-2-methyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)-4-methylpentanoate

Hoong-Kun Fun,<sup>a,\*</sup> Ching Kheng Quah,<sup>a,§</sup> Kai Xu<sup>b</sup> and Yan Zhang<sup>b</sup>

<sup>a</sup>X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia, and <sup>b</sup>School of Chemistry and Chemical Engineering, Nanjing University, Nanjing, 210093, People's Republic of China  
Correspondence e-mail: hkfun@usm.my

Received 30 May 2011; accepted 14 June 2011

Key indicators: single-crystal X-ray study;  $T = 100$  K; mean  $\sigma(\text{C}-\text{C}) = 0.002$  Å;  $R$  factor = 0.024;  $wR$  factor = 0.059; data-to-parameter ratio = 10.6.

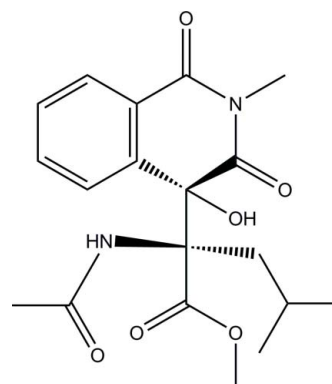
In the isoquinoline ring system of the title molecule,  $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_6$ , the  $N$ -heterocyclic ring is in a half-boat conformation. The molecular structure is stabilized by an intramolecular  $\text{O}-\text{H}\cdots\text{O}$  hydrogen bond, which generates an  $S(7)$  ring motif. In the crystal, molecules are linked via intermolecular bifurcated  $\text{N}-\text{H}\cdots(\text{O},\text{O})$  and weak  $\text{C}-\text{H}\cdots\text{O}$  hydrogen bonds into a three-dimensional network.

## Related literature

For general background to and the potential biological activity of title compound, see: Yu *et al.* (2010); Huang *et al.* (2011); Rao *et al.* (1995); Nagamitsu *et al.* (1996); Evans & Weber (1986); Heimgartner (1991); Rando (1975); Griesbeck *et al.* (2003); Zhang *et al.* (2004); Wang *et al.* (2010). For the stability of the temperature controller used in the data collection, see: Cosier & Glazer (1986). For standard bond-length data, see: Allen *et al.* (1987). For ring conformations, see: Cremer & Pople (1975). For related structures, see: Fun *et al.* (2011*a,b,c,d*). For hydrogen-bond motifs, see: Bernstein *et al.* (1995).

\* Thomson Reuters ResearcherID: A-3561-2009.

§ Thomson Reuters ResearcherID: A-5525-2009.



## Experimental

### Crystal data

$\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_6$   
 $M_r = 376.40$   
Monoclinic,  $Cc$   
 $a = 17.8256$  (15) Å  
 $b = 8.7584$  (6) Å  
 $c = 11.9182$  (8) Å  
 $\beta = 100.404$  (5)°

$V = 1830.1$  (2) Å<sup>3</sup>  
 $Z = 4$   
Cu  $K\alpha$  radiation  
 $\mu = 0.85$  mm<sup>-1</sup>  
 $T = 100$  K  
 $0.50 \times 0.15 \times 0.15$  mm

### Data collection

Bruker APEX DUO CCD area-detector diffractometer  
Absorption correction: multi-scan (SADABS; Bruker, 2009)  
 $T_{\min} = 0.678$ ,  $T_{\max} = 0.883$

18268 measured reflections  
2713 independent reflections  
2673 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.033$

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.024$   
 $wR(F^2) = 0.059$   
 $S = 1.05$   
2713 reflections  
257 parameters  
2 restraints

H atoms treated by a mixture of independent and constrained refinement  
 $\Delta\rho_{\max} = 0.11$  e Å<sup>-3</sup>  
 $\Delta\rho_{\min} = -0.14$  e Å<sup>-3</sup>  
Absolute structure: Flack (1983), 1204 Friedel pairs  
Flack parameter: 0.05 (13)

Table 1

Hydrogen-bond geometry (Å, °).

| $D-\text{H}\cdots A$                              | $D-\text{H}$ | $\text{H}\cdots A$ | $D\cdots A$ | $D-\text{H}\cdots A$ |
|---|--------------|--------------------|-------------|----------------------|
| $\text{N}2-\text{H}1\text{N}2\cdots\text{O}1^i$   | 0.92 (2)     | 2.511 (19)         | 3.3431 (17) | 150.3 (15)           |
| $\text{N}2-\text{H}1\text{N}2\cdots\text{O}3^i$   | 0.92 (2)     | 2.44 (2)           | 3.1675 (18) | 135.6 (16)           |
| $\text{O}3-\text{H}1\text{O}3\cdots\text{O}6$     | 0.86 (2)     | 1.83 (2)           | 2.6543 (16) | 160 (2)              |
| $\text{C}5-\text{H}5\text{A}\cdots\text{O}6^{ii}$ | 0.93         | 2.59               | 3.469 (2)   | 157                  |

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

Data collection: APEX2 (Bruker, 2009); cell refinement: SAINT (Bruker, 2009); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 2008); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL and PLATON (Spek, 2009).

HKF and CKQ thank Universiti Sains Malaysia for the Research University Grant (No. 1001/PFIZIK/811160). Financial support from the Ministry of Science and Tech-

nology of China of the Austria–China Cooperation project (2007DFA41590) is also acknowledged.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH5262).

## References

- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Bruker (2009). *APEX2, SAINT and SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
- Cosier, J. & Glazer, A. M. (1986). *J. Appl. Cryst.* **19**, 105–107.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Evans, D. A. & Weber, A. E. (1986). *J. Am. Chem. Soc.* **108**, 6757–6761.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Fun, H.-K., Quah, C. K., Huang, C. & Yu, H. (2011a). *Acta Cryst.* **E67**, o1271–o1272.
- Fun, H.-K., Quah, C. K., Huang, C. & Yu, H. (2011b). *Acta Cryst.* **E67**, o1273–o1274.
- Fun, H.-K., Quah, C. K., Huang, C. & Yu, H. (2011c). *Acta Cryst.* **E67**, o1311–o1312.
- Fun, H.-K., Quah, C. K., Huang, C. & Yu, H. (2011d). *Acta Cryst.* **E67**, o1340–o1341.
- Griesbeck, A. G., Bondock, S. & Lex, J. J. (2003). *Org. Chem.* **68**, 9899–9906.
- Heimgartner, H. (1991). *Angew. Chem. Int. Ed.* **30**, 238–265.
- Huang, C., Yu, H., Miao, Z., Zhou, J., Wang, S., Fun, H.-K., Xu, J. & Zhang, Y. (2011). *J. Org. Chem.* **9**, 3629–3631.
- Nagamitsu, T., Sunazuka, T., Tanaka, H., Omura, S., Sprengeler, P. A. & Smith, A. B. III (1996). *J. Am. Chem. Soc.* **118**, 3584–3590.
- Rando, R. R. (1975). *Acc. Chem. Res.* **8**, 281–288.
- Rao, A. V. R., Gurjar, M. K., Reddy, K. L. & Rao, A. S. (1995). *Chem. Rev.* **95**, 2135–2168.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Spek, A. L. (2009). *Acta Cryst.* **D65**, 148–155.
- Wang, L., Huang, Y. C., Liu, Y., Fun, H.-K., Zhang, Y. & Xu, J. H. (2010). *J. Org. Chem.* **75**, 7757–7768.
- Yu, H., Li, J., Kou, Z., Du, X., Wei, Y., Fun, H.-K., Xu, J. & Zhang, Y. (2010). *J. Org. Chem.* **75**, 2989–3001.
- Zhang, Y., Wang, L., Zhang, M., Fun, H.-K. & Xu, J.-X. (2004). *Org. Lett.* **6**, 4893–4895.

**supplementary materials**

*Acta Cryst.* (2011). E67, o1710-o1711 [ doi:10.1107/S1600536811022999 ]

## Methyl 2-acetamido-2-(4-hydroxy-2-methyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)-4-methylpentanoate

H.-K. Fun, C. K. Quah, K. Xu and Y. Zhang

### Comment

Photocycloaddition of isoquinoline-1,3,4-trione combined with following transformation of the photocycloadducts has become facile method to build various scaffold containing an isoquinoline moiety (Yu *et al.*, 2010; Huang *et al.*, 2011).  $\beta$ -Hydroxy-amino acids are important building blocks to constitute more complex natural products.  $\beta$ -Hydroxy tyrosine and  $\beta$ -hydroxy phenylalanine derivatives are found in the clinically important antibiotic glycopeptides vancomycin,  $\beta$ -hydroxy leucine is found in (+)-lactacystin, and E-2-butenyl-4,N-dimethyl-l-threonine is an essential part of cyclosporine (Rao *et al.*, 1995; Nagamitsu *et al.*, 1996; Evans *et al.*, 1986).  $\alpha,\alpha$ -Disubstituted amino acids represent a highly interesting class of non-proteinogenic amino acids, especially in view of their potential activity as enzyme inhibitors (Heimgartner, 1991; Rando, 1975). Many bioactive natural products contain  $\beta$ -hydroxy-amino acid or  $\alpha,\alpha$ -disubstituted amino acid and there has been intense interest to develop methodology to construct such moieties using photocycloadducts of oxazoles (Griesbeck *et al.*, 2003; Zhang *et al.*, 2004; Wang *et al.*, 2010). The title compound was derived from photocycloadducts of isoquinoline-1,3,4-trione and oxazoles. Due to the importance of  $\beta$ -hydroxy-amino acid derivatives, we report in this paper the crystal structure of the title compound.

In the title racemic compound, Fig. 1, the isoquinoline ring system (N1/C1-C9) is not completely planar, the *N*-heterocyclic ring (N1/C1-C3/C8/C9) being distorted towards a half-boat conformation with atom C9 deviating by 0.201 (2) Å from the mean plane through the remaining atoms, puckering parameters (Cremer & Pople, 1975)  $Q = 0.3038$  (17) Å,  $\Theta = 70.1$  (3)° and  $\phi = 110.6$  (3)°. Bond lengths (Allen *et al.*, 1987) and angles are within normal ranges and comparable to related structures (Fun *et al.*, 2011*a,b,c,d*). The molecular structure is stabilized by an intramolecular O3–H1O3 $\cdots$ O6 hydrogen bond (Table 1) which generates a *S*(7) ring motif (Fig. 1, Bernstein *et al.*, 1995).

In the crystal structure, Fig. 2, molecules are linked *via* intermolecular N2–H1N2 $\cdots$ O1<sup>i</sup>, N2–H1N2 $\cdots$ O3<sup>i</sup> and weak C5–H5A $\cdots$ O6<sup>ii</sup> hydrogen bonds (Table 1) into a three-dimensional network.

### Experimental

The title compound was the main product from the acid-catalyzed transformation of the photocycloadducts of isoquinoline-1,3,4-trione and 4-isobutyl-5-methoxy-2-methyloxazole. The compound was purified by flash column chromatography with ethyl acetate/petroleum ether (1:5) as eluents. X-ray quality crystals of the title compound were obtained from slow evaporation of an acetone and petroleum ether solution (1:8) of the title compound, *m.p.* 425–427 K.

### Refinement

Atoms H1N2 and H1O3 were located in a difference Fourier map and refined freely [N2–H1N2 = 0.92 (2) Å, O3–H1O3 = 0.86 (2) Å]. The remaining H atoms were positioned geometrically and refined using a riding model with C–H = 0.93

## supplementary materials

- 0.97 Å and  $U_{\text{iso}}(\text{H}) = 1.2$  or  $1.5 U_{\text{eq}}(\text{C})$ . A rotating-group model was applied for the methyl groups. The highest residual electron density peak is located at 0.20 Å from H16B and the deepest hole is located at 0.78 Å from C9.

### Figures

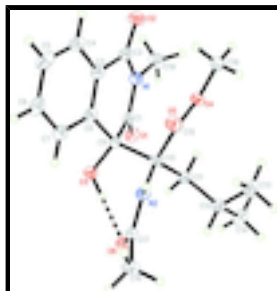


Fig. 1. The molecular structure of the title compound showing 50% probability displacement ellipsoids for non-H atoms. Intramolecular hydrogen bond is shown as dashed line.

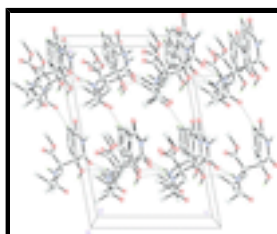


Fig. 2. Part of the crystal structure of the title compound, viewed along the *b* axis. H atoms not involved in hydrogen bonds (dashed lines) have been omitted for clarity.

### Methyl 2-acetamido-2-(4-hydroxy-2-methyl-1,3-dioxo- 1,2,3,4-tetrahydroisoquinolin-4-yl)-4-methylpentanoate

#### Crystal data

$\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_6$

$M_r = 376.40$

Monoclinic, *Cc*

Hall symbol: C -2yc

$a = 17.8256$  (15) Å

$b = 8.7584$  (6) Å

$c = 11.9182$  (8) Å

$\beta = 100.404$  (5)°

$V = 1830.1$  (2) Å<sup>3</sup>

$Z = 4$

$F(000) = 800$

$D_x = 1.366$  Mg m<sup>-3</sup>

Cu *K*α radiation,  $\lambda = 1.54178$  Å

Cell parameters from 9888 reflections

$\theta = 5.1$ – $64.2$ °

$\mu = 0.85$  mm<sup>-1</sup>

$T = 100$  K

Needle, colourless

$0.50 \times 0.15 \times 0.15$  mm

#### Data collection

Bruker APEX DUO CCD area-detector diffractometer

Radiation source: fine-focus sealed tube graphite

$\varphi$  and  $\omega$  scans

Absorption correction: multi-scan (*SADABS*; Bruker, 2009)

$T_{\text{min}} = 0.678$ ,  $T_{\text{max}} = 0.883$

18268 measured reflections

2713 independent reflections

2673 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.033$

$\theta_{\text{max}} = 64.7$ °,  $\theta_{\text{min}} = 5.1$ °

$h = -20 \rightarrow 20$

$k = -9 \rightarrow 10$

$l = -12 \rightarrow 13$

*Refinement*

|  |  |
|--|--|
| Refinement on $F^2$  | Secondary atom site location: difference Fourier map                               |
| Least-squares matrix: full                                     | Hydrogen site location: inferred from neighbouring sites                           |
| $R[F^2 > 2\sigma(F^2)] = 0.024$                                | H atoms treated by a mixture of independent and constrained refinement             |
| $wR(F^2) = 0.059$  | $w = 1/[\sigma^2(F_o^2) + (0.0319P)^2 + 0.7184P]$                                  |
| $S = 1.05$   | where $P = (F_o^2 + 2F_c^2)/3$   |
| 2713 reflections   | $(\Delta/\sigma)_{\max} < 0.001$   |
| 257 parameters   | $\Delta\rho_{\max} = 0.11 \text{ e } \text{\AA}^{-3}$                              |
| 2 restraints   | $\Delta\rho_{\min} = -0.14 \text{ e } \text{\AA}^{-3}$                             |
| Primary atom site location: structure-invariant direct methods | Absolute structure: Flack (1983), 1204 Friedel pairs<br>Flack parameter: 0.05 (13) |

*Special details*

**Experimental.** The crystal was placed in the cold stream of an Oxford Cryosystems Cobra open-flow nitrogen cryostat (Cosier & Glazer, 1986) operating at 100.0 (1) K.

**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  $F^2$  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 ( $\text{\AA}^2$ )*

|     | <i>x</i>     | <i>y</i>     | <i>z</i>     | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|-----|--------------|--------------|--------------|----------------------------------|
| O1  | 0.81985 (6)  | 0.74615 (13) | 1.04040 (10) | 0.0229 (3)                       |
| O2  | 1.05834 (6)  | 0.65801 (14) | 0.97375 (10) | 0.0302 (3)                       |
| O3  | 0.76692 (6)  | 0.48621 (12) | 0.94001 (10) | 0.0204 (2)                       |
| O4  | 0.91523 (6)  | 0.77211 (12) | 0.76247 (9)  | 0.0193 (2)                       |
| O5  | 0.89019 (6)  | 0.56633 (12) | 0.65074 (9)  | 0.0204 (2)                       |
| O6  | 0.64674 (6)  | 0.52211 (12) | 0.77471 (10) | 0.0223 (3)                       |
| N1  | 0.93918 (7)  | 0.70763 (15) | 1.00450 (11) | 0.0206 (3)                       |
| N2  | 0.75643 (7)  | 0.51865 (14) | 0.70247 (12) | 0.0171 (3)                       |
| C1  | 0.86194 (9)  | 0.67556 (17) | 0.99008 (14) | 0.0188 (3)                       |
| C2  | 0.99257 (9)  | 0.61559 (19) | 0.96548 (14) | 0.0222 (4)                       |
| C3  | 0.96586 (9)  | 0.46387 (18) | 0.91865 (14) | 0.0200 (3)                       |
| C4  | 1.02036 (9)  | 0.3555 (2)   | 0.90385 (14) | 0.0253 (4)                       |
| H4A | 1.0719       | 0.3803       | 0.9194       | 0.030*                           |
| C5  | 0.99735 (10) | 0.2104 (2)   | 0.86574 (15) | 0.0285 (4)                       |

## supplementary materials

|      |              |              |              |            |
|------|--------------|--------------|--------------|------------|
| H5A  | 1.0334       | 0.1376       | 0.8550       | 0.034*     |
| C6   | 0.92023 (10) | 0.17437 (19) | 0.84364 (15) | 0.0259 (4) |
| H6A  | 0.9049       | 0.0765       | 0.8192       | 0.031*     |
| C7   | 0.86576 (9)  | 0.28210 (18) | 0.85750 (14) | 0.0217 (3) |
| H7A  | 0.8143       | 0.2565       | 0.8424       | 0.026*     |
| C8   | 0.88811 (8)  | 0.42821 (18) | 0.89389 (13) | 0.0181 (3) |
| C9   | 0.82982 (8)  | 0.55120 (17) | 0.90207 (14) | 0.0174 (3) |
| C10  | 0.80278 (8)  | 0.62935 (17) | 0.77805 (14) | 0.0167 (3) |
| C11  | 0.76008 (9)  | 0.78137 (17) | 0.78789 (13) | 0.0180 (3) |
| H11A | 0.7260       | 0.7664       | 0.8419       | 0.022*     |
| H11B | 0.7974       | 0.8574       | 0.8201       | 0.022*     |
| C12  | 0.71318 (9)  | 0.84730 (17) | 0.67768 (15) | 0.0217 (3) |
| H12A | 0.6734       | 0.7732       | 0.6477       | 0.026*     |
| C13  | 0.75969 (10) | 0.8792 (2)   | 0.58470 (15) | 0.0285 (4) |
| H13A | 0.7803       | 0.7852       | 0.5620       | 0.043*     |
| H13B | 0.8006       | 0.9479       | 0.6135       | 0.043*     |
| H13C | 0.7274       | 0.9246       | 0.5201       | 0.043*     |
| C14  | 0.67409 (10) | 0.9933 (2)   | 0.70714 (17) | 0.0306 (4) |
| H14A | 0.6414       | 1.0315       | 0.6401       | 0.046*     |
| H14B | 0.7120       | 1.0686       | 0.7352       | 0.046*     |
| H14C | 0.6443       | 0.9716       | 0.7647       | 0.046*     |
| C15  | 0.87344 (8)  | 0.65099 (17) | 0.72155 (14) | 0.0165 (3) |
| C16  | 0.98383 (9)  | 0.79217 (19) | 0.71419 (15) | 0.0230 (4) |
| H16A | 1.0110       | 0.8807       | 0.7472       | 0.035*     |
| H16B | 0.9701       | 0.8053       | 0.6331       | 0.035*     |
| H16C | 1.0158       | 0.7037       | 0.7304       | 0.035*     |
| C17  | 0.68252 (8)  | 0.48575 (17) | 0.69911 (14) | 0.0179 (3) |
| C18  | 0.64504 (9)  | 0.40140 (19) | 0.59393 (15) | 0.0248 (4) |
| H18A | 0.6056       | 0.3365       | 0.6124       | 0.037*     |
| H18B | 0.6824       | 0.3404       | 0.5657       | 0.037*     |
| H18C | 0.6232       | 0.4734       | 0.5365       | 0.037*     |
| C19  | 0.96743 (10) | 0.84909 (19) | 1.06333 (17) | 0.0300 (4) |
| H19A | 0.9273       | 0.8958       | 1.0952       | 0.045*     |
| H19B | 0.9839       | 0.9179       | 1.0100       | 0.045*     |
| H19C | 1.0096       | 0.8261       | 1.1233       | 0.045*     |
| H1N2 | 0.7798 (11)  | 0.479 (2)    | 0.6459 (18)  | 0.025 (5)* |
| H1O3 | 0.7237 (13)  | 0.510 (2)    | 0.8986 (18)  | 0.037 (6)* |

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

|    | $U^{11}$   | $U^{22}$   | $U^{33}$   | $U^{12}$    | $U^{13}$    | $U^{23}$    |
|----|------------|------------|------------|-------------|-------------|-------------|
| O1 | 0.0255 (6) | 0.0248 (6) | 0.0184 (7) | 0.0040 (4)  | 0.0040 (5)  | -0.0020 (5) |
| O2 | 0.0178 (6) | 0.0408 (7) | 0.0299 (8) | -0.0067 (5) | -0.0013 (5) | 0.0021 (6)  |
| O3 | 0.0173 (5) | 0.0267 (6) | 0.0173 (7) | -0.0020 (4) | 0.0036 (5)  | 0.0027 (5)  |
| O4 | 0.0171 (5) | 0.0208 (5) | 0.0201 (7) | -0.0039 (4) | 0.0033 (4)  | -0.0013 (5) |
| O5 | 0.0191 (5) | 0.0237 (5) | 0.0188 (7) | -0.0013 (4) | 0.0046 (4)  | -0.0021 (5) |
| O6 | 0.0177 (5) | 0.0279 (6) | 0.0215 (7) | -0.0011 (4) | 0.0045 (5)  | -0.0014 (5) |
| N1 | 0.0220 (7) | 0.0223 (7) | 0.0162 (8) | -0.0040 (5) | -0.0003 (5) | 0.0005 (6)  |

|     |             |             |             |             |             |             |
|-----|-------------|-------------|-------------|-------------|-------------|-------------|
| N2  | 0.0163 (7)  | 0.0188 (7)  | 0.0161 (8)  | -0.0006 (5) | 0.0026 (6)  | -0.0022 (5) |
| C1  | 0.0221 (8)  | 0.0190 (7)  | 0.0143 (9)  | 0.0005 (6)  | 0.0004 (6)  | 0.0044 (6)  |
| C2  | 0.0195 (8)  | 0.0310 (9)  | 0.0143 (9)  | -0.0008 (6) | -0.0019 (6) | 0.0057 (7)  |
| C3  | 0.0206 (8)  | 0.0281 (8)  | 0.0112 (9)  | 0.0010 (6)  | 0.0024 (6)  | 0.0038 (7)  |
| C4  | 0.0210 (8)  | 0.0383 (10) | 0.0163 (10) | 0.0049 (7)  | 0.0027 (7)  | 0.0045 (7)  |
| C5  | 0.0322 (10) | 0.0339 (10) | 0.0193 (11) | 0.0139 (7)  | 0.0042 (7)  | 0.0002 (7)  |
| C6  | 0.0352 (10) | 0.0242 (9)  | 0.0168 (10) | 0.0055 (7)  | 0.0009 (7)  | 0.0007 (7)  |
| C7  | 0.0248 (8)  | 0.0246 (8)  | 0.0151 (9)  | 0.0009 (7)  | 0.0021 (6)  | -0.0002 (7) |
| C8  | 0.0210 (8)  | 0.0239 (8)  | 0.0095 (9)  | 0.0021 (6)  | 0.0030 (6)  | 0.0028 (6)  |
| C9  | 0.0167 (7)  | 0.0204 (8)  | 0.0149 (9)  | -0.0010 (6) | 0.0025 (6)  | 0.0017 (6)  |
| C10 | 0.0161 (7)  | 0.0196 (7)  | 0.0130 (9)  | -0.0030 (6) | -0.0007 (6) | -0.0009 (6) |
| C11 | 0.0159 (7)  | 0.0216 (8)  | 0.0163 (9)  | 0.0001 (6)  | 0.0025 (6)  | 0.0005 (6)  |
| C12 | 0.0204 (7)  | 0.0219 (8)  | 0.0207 (10) | -0.0012 (6) | -0.0015 (6) | 0.0013 (7)  |
| C13 | 0.0318 (9)  | 0.0316 (9)  | 0.0212 (10) | 0.0051 (7)  | 0.0022 (7)  | 0.0070 (8)  |
| C14 | 0.0318 (9)  | 0.0302 (9)  | 0.0280 (12) | 0.0085 (7)  | 0.0002 (8)  | 0.0036 (8)  |
| C15 | 0.0156 (7)  | 0.0191 (8)  | 0.0134 (9)  | -0.0003 (6) | -0.0010 (6) | 0.0030 (6)  |
| C16 | 0.0190 (8)  | 0.0264 (8)  | 0.0238 (10) | -0.0048 (6) | 0.0043 (7)  | 0.0010 (7)  |
| C17 | 0.0165 (7)  | 0.0178 (7)  | 0.0191 (10) | -0.0003 (6) | 0.0018 (6)  | 0.0013 (6)  |
| C18 | 0.0178 (8)  | 0.0319 (9)  | 0.0241 (10) | -0.0055 (7) | 0.0024 (7)  | -0.0034 (8) |
| C19 | 0.0364 (10) | 0.0282 (9)  | 0.0235 (10) | -0.0103 (7) | 0.0004 (8)  | -0.0038 (8) |

*Geometric parameters (Å, °)*

|         |             |          |           |
|---------|-------------|----------|-----------|
| O1—C1   | 1.211 (2)   | C8—C9    | 1.512 (2) |
| O2—C2   | 1.217 (2)   | C9—C10   | 1.621 (2) |
| O3—C9   | 1.4032 (19) | C10—C15  | 1.543 (2) |
| O3—H1O3 | 0.86 (2)    | C10—C11  | 1.549 (2) |
| O4—C15  | 1.3368 (18) | C11—C12  | 1.537 (2) |
| O4—C16  | 1.4531 (18) | C11—H11A | 0.9700    |
| O5—C15  | 1.201 (2)   | C11—H11B | 0.9700    |
| O6—C17  | 1.236 (2)   | C12—C13  | 1.525 (3) |
| N1—C1   | 1.3851 (19) | C12—C14  | 1.527 (2) |
| N1—C2   | 1.390 (2)   | C12—H12A | 0.9800    |
| N1—C19  | 1.467 (2)   | C13—H13A | 0.9600    |
| N2—C17  | 1.3420 (19) | C13—H13B | 0.9600    |
| N2—C10  | 1.4715 (19) | C13—H13C | 0.9600    |
| N2—H1N2 | 0.92 (2)    | C14—H14A | 0.9600    |
| C1—C9   | 1.548 (2)   | C14—H14B | 0.9600    |
| C2—C3   | 1.486 (2)   | C14—H14C | 0.9600    |
| C3—C4   | 1.392 (2)   | C16—H16A | 0.9600    |
| C3—C8   | 1.399 (2)   | C16—H16B | 0.9600    |
| C4—C5   | 1.386 (3)   | C16—H16C | 0.9600    |
| C4—H4A  | 0.9300      | C17—C18  | 1.504 (2) |
| C5—C6   | 1.389 (3)   | C18—H18A | 0.9600    |
| C5—H5A  | 0.9300      | C18—H18B | 0.9600    |
| C6—C7   | 1.385 (2)   | C18—H18C | 0.9600    |
| C6—H6A  | 0.9300      | C19—H19A | 0.9600    |
| C7—C8   | 1.386 (2)   | C19—H19B | 0.9600    |
| C7—H7A  | 0.9300      | C19—H19C | 0.9600    |



## supplementary materials

---

|              |             |               |              |
|--------------|-------------|---------------|--------------|
| C9—O3—H1O3   | 113.6 (14)  | C10—C11—H11A  | 108.0        |
| C15—O4—C16   | 113.89 (13) | C12—C11—H11B  | 108.0        |
| C1—N1—C2     | 124.49 (13) | C10—C11—H11B  | 108.0        |
| C1—N1—C19    | 118.57 (13) | H11A—C11—H11B | 107.2        |
| C2—N1—C19    | 116.93 (13) | C13—C12—C14   | 110.13 (14)  |
| C17—N2—C10   | 126.82 (13) | C13—C12—C11   | 114.00 (13)  |
| C17—N2—H1N2  | 117.8 (12)  | C14—C12—C11   | 108.57 (14)  |
| C10—N2—H1N2  | 114.8 (12)  | C13—C12—H12A  | 108.0        |
| O1—C1—N1     | 121.72 (14) | C14—C12—H12A  | 108.0        |
| O1—C1—C9     | 120.54 (14) | C11—C12—H12A  | 108.0        |
| N1—C1—C9     | 117.67 (13) | C12—C13—H13A  | 109.5        |
| O2—C2—N1     | 120.25 (15) | C12—C13—H13B  | 109.5        |
| O2—C2—C3     | 122.84 (15) | H13A—C13—H13B | 109.5        |
| N1—C2—C3     | 116.87 (13) | C12—C13—H13C  | 109.5        |
| C4—C3—C8     | 120.56 (15) | H13A—C13—H13C | 109.5        |
| C4—C3—C2     | 118.28 (14) | H13B—C13—H13C | 109.5        |
| C8—C3—C2     | 121.12 (14) | C12—C14—H14A  | 109.5        |
| C5—C4—C3     | 119.65 (16) | C12—C14—H14B  | 109.5        |
| C5—C4—H4A    | 120.2       | H14A—C14—H14B | 109.5        |
| C3—C4—H4A    | 120.2       | C12—C14—H14C  | 109.5        |
| C4—C5—C6     | 119.64 (16) | H14A—C14—H14C | 109.5        |
| C4—C5—H5A    | 120.2       | H14B—C14—H14C | 109.5        |
| C6—C5—H5A    | 120.2       | O5—C15—O4     | 123.60 (14)  |
| C7—C6—C5     | 120.92 (16) | O5—C15—C10    | 123.84 (13)  |
| C7—C6—H6A    | 119.5       | O4—C15—C10    | 112.54 (13)  |
| C5—C6—H6A    | 119.5       | O4—C16—H16A   | 109.5        |
| C6—C7—C8     | 119.87 (15) | O4—C16—H16B   | 109.5        |
| C6—C7—H7A    | 120.1       | H16A—C16—H16B | 109.5        |
| C8—C7—H7A    | 120.1       | O4—C16—H16C   | 109.5        |
| C7—C8—C3     | 119.33 (14) | H16A—C16—H16C | 109.5        |
| C7—C8—C9     | 121.04 (13) | H16B—C16—H16C | 109.5        |
| C3—C8—C9     | 119.57 (14) | O6—C17—N2     | 123.78 (14)  |
| O3—C9—C8     | 109.28 (12) | O6—C17—C18    | 121.61 (13)  |
| O3—C9—C1     | 106.64 (13) | N2—C17—C18    | 114.60 (14)  |
| C8—C9—C1     | 111.74 (12) | C17—C18—H18A  | 109.5        |
| O3—C9—C10    | 109.99 (12) | C17—C18—H18B  | 109.5        |
| C8—C9—C10    | 109.67 (13) | H18A—C18—H18B | 109.5        |
| C1—C9—C10    | 109.47 (12) | C17—C18—H18C  | 109.5        |
| N2—C10—C15   | 103.07 (12) | H18A—C18—H18C | 109.5        |
| N2—C10—C11   | 112.55 (12) | H18B—C18—H18C | 109.5        |
| C15—C10—C11  | 112.23 (12) | N1—C19—H19A   | 109.5        |
| N2—C10—C9    | 108.76 (12) | N1—C19—H19B   | 109.5        |
| C15—C10—C9   | 108.54 (11) | H19A—C19—H19B | 109.5        |
| C11—C10—C9   | 111.30 (13) | N1—C19—H19C   | 109.5        |
| C12—C11—C10  | 117.22 (13) | H19A—C19—H19C | 109.5        |
| C12—C11—H11A | 108.0       | H19B—C19—H19C | 109.5        |
| C2—N1—C1—O1  | 168.38 (15) | O1—C1—C9—C8   | -151.28 (14) |
| C19—N1—C1—O1 | -12.6 (2)   | N1—C1—C9—C8   | 31.84 (19)   |
| C2—N1—C1—C9  | -14.8 (2)   | O1—C1—C9—C10  | 87.02 (17)   |

|              |              |                 |              |
|--------------|--------------|-----------------|--------------|
| C19—N1—C1—C9 | 164.27 (14)  | N1—C1—C9—C10    | -89.86 (15)  |
| C1—N1—C2—O2  | 174.17 (15)  | C17—N2—C10—C15  | -164.63 (14) |
| C19—N1—C2—O2 | -4.9 (2)     | C17—N2—C10—C11  | -43.5 (2)    |
| C1—N1—C2—C3  | -8.2 (2)     | C17—N2—C10—C9   | 80.31 (18)   |
| C19—N1—C2—C3 | 172.78 (14)  | O3—C9—C10—N2    | -49.92 (16)  |
| O2—C2—C3—C4  | 12.4 (2)     | C8—C9—C10—N2    | 70.29 (15)   |
| N1—C2—C3—C4  | -165.20 (15) | C1—C9—C10—N2    | -166.77 (12) |
| O2—C2—C3—C8  | -169.92 (15) | O3—C9—C10—C15   | -161.37 (12) |
| N1—C2—C3—C8  | 12.5 (2)     | C8—C9—C10—C15   | -41.16 (16)  |
| C8—C3—C4—C5  | -0.9 (2)     | C1—C9—C10—C15   | 81.77 (14)   |
| C2—C3—C4—C5  | 176.79 (16)  | O3—C9—C10—C11   | 74.64 (15)   |
| C3—C4—C5—C6  | -0.5 (3)     | C8—C9—C10—C11   | -165.15 (12) |
| C4—C5—C6—C7  | 1.0 (3)      | C1—C9—C10—C11   | -42.22 (16)  |
| C5—C6—C7—C8  | 0.0 (3)      | N2—C10—C11—C12  | -42.05 (18)  |
| C6—C7—C8—C3  | -1.4 (2)     | C15—C10—C11—C12 | 73.68 (17)   |
| C6—C7—C8—C9  | 175.79 (15)  | C9—C10—C11—C12  | -164.44 (12) |
| C4—C3—C8—C7  | 1.9 (2)      | C10—C11—C12—C13 | -58.65 (18)  |
| C2—C3—C8—C7  | -175.74 (15) | C10—C11—C12—C14 | 178.18 (13)  |
| C4—C3—C8—C9  | -175.38 (15) | C16—O4—C15—O5   | -0.5 (2)     |
| C2—C3—C8—C9  | 7.0 (2)      | C16—O4—C15—C10  | 177.71 (12)  |
| C7—C8—C9—O3  | 37.1 (2)     | N2—C10—C15—O5   | -15.55 (19)  |
| C3—C8—C9—O3  | -145.72 (14) | C11—C10—C15—O5  | -136.90 (15) |
| C7—C8—C9—C1  | 154.86 (15)  | C9—C10—C15—O5   | 99.66 (17)   |
| C3—C8—C9—C1  | -27.9 (2)    | N2—C10—C15—O4   | 166.23 (12)  |
| C7—C8—C9—C10 | -83.55 (17)  | C11—C10—C15—O4  | 44.89 (17)   |
| C3—C8—C9—C10 | 93.64 (17)   | C9—C10—C15—O4   | -78.55 (14)  |
| O1—C1—C9—O3  | -31.9 (2)    | C10—N2—C17—O6   | -15.0 (2)    |
| N1—C1—C9—O3  | 151.20 (13)  | C10—N2—C17—C18  | 164.21 (14)  |

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> |
|---------------------------|-------------|---------------|-----------------------|-------------------------|
| N2—H1N2...O1 <sup>i</sup> | 0.92 (2)    | 2.511 (19)    | 3.3431 (17)           | 150.3 (15)              |
| N2—H1N2...O3 <sup>i</sup> | 0.92 (2)    | 2.44 (2)      | 3.1675 (18)           | 135.6 (16)              |
| O3—H1O3...O6              | 0.86 (2)    | 1.83 (2)      | 2.6543 (16)           | 160 (2)                 |
| C5—H5A...O6 <sup>ii</sup> | 0.93        | 2.59          | 3.469 (2)             | 157                     |

Symmetry codes: (i)  $x, -y+1, z-1/2$ ; (ii)  $x+1/2, y-1/2, z$ .

Fig. 1

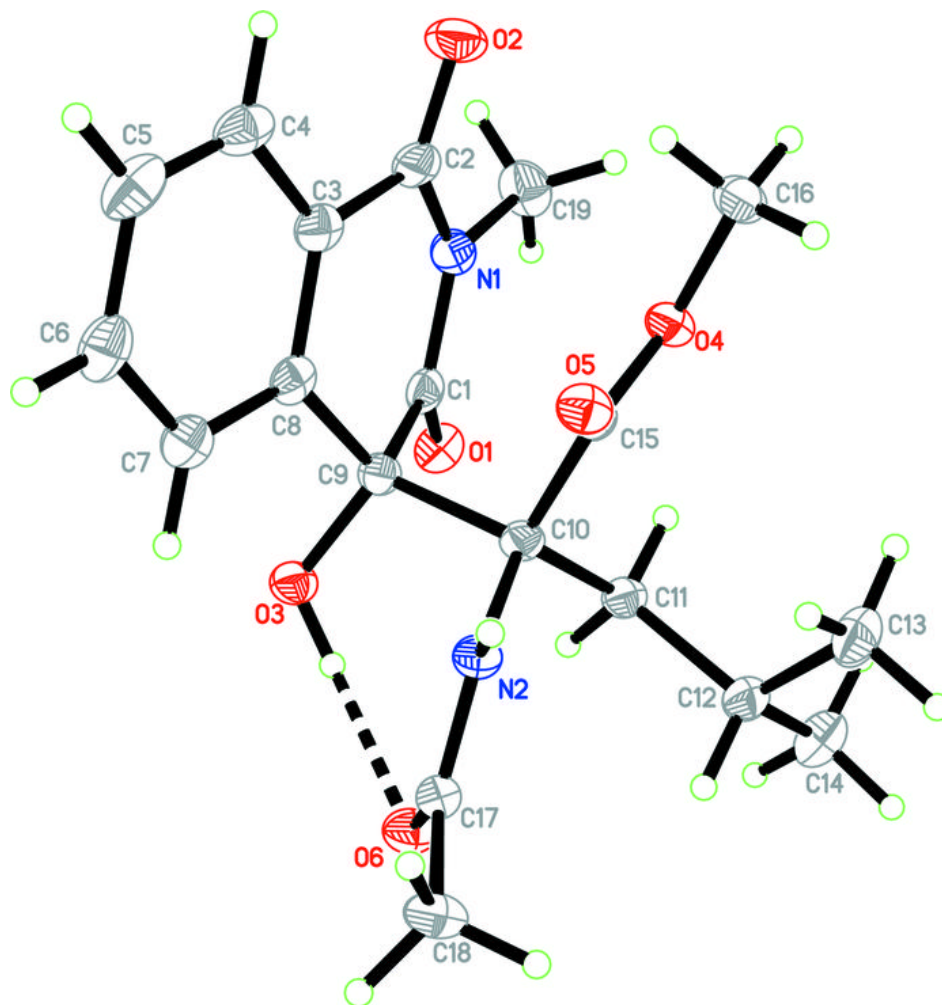


Fig. 2

