



Crystal structure of 2,4-diamino-5-(4-hydroxy-3-methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile–dimethylformamide–water (1/1/1)

Nadia H. Metwally,^a Galal H. Elgemeie,^b El-shimaa S. M. Abd Al-latif^a and Peter G. Jones^{c*}

Received 8 March 2024

Accepted 19 March 2024

Edited by C. Schulzke, Universität Greifswald, Germany

Keywords: crystal structure; chromenopyridine; solvate; secondary interactions.

CCDC reference: 2341559

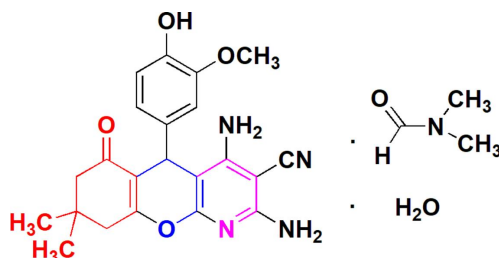
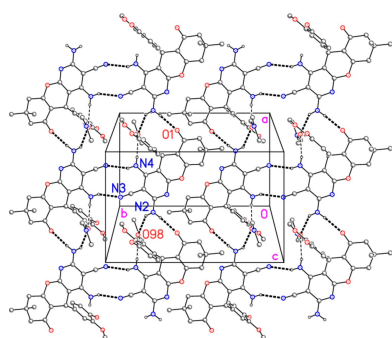
Supporting information: this article has supporting information at journals.iucr.org/e

^aChemistry Department, Faculty of Science, Cairo University, Giza, Egypt, ^bChemistry Department, Faculty of Science, Helwan University, Cairo, Egypt, and ^cInstitut für Anorganische und Analytische Chemie, Technische Universität Braunschweig, Hagenring 30, D-38106 Braunschweig, Germany. *Correspondence e-mail: p.jones@tu-braunschweig.de

In the structure of the title compound, $C_{22}H_{22}N_4O_4 \cdot C_3H_7NO \cdot H_2O$, the entire tricyclic system is approximately planar except for the carbon atom bearing the two methyl groups; the methoxyphenyl ring is approximately perpendicular to the tricycle. All seven potential hydrogen-bond donors take part in classical hydrogen bonds. The main molecule and the DMF combine to form broad ribbons parallel to the *a* axis and roughly parallel to the *ab* plane; the water molecules connect the residues in the third dimension.

1. Chemical context

Activated nitriles and α,β -unsaturated nitrile moieties are involved in a wide variety of natural plant products, drugs, colourants and agrochemicals (Fleming & Wang, 2003; Ahmed *et al.*, 2022); they also represent versatile starting materials for the synthesis of a wide variety of therapeutically important heterocycles (Zhang *et al.*, 2019; Metwally *et al.*, 2023). The generally accepted importance of these functions (Wang *et al.*, 2016; Hebishy *et al.*, 2023) is reflected in the investment of much effort to synthesize them (Zhang *et al.*, 2023; Elgemeie *et al.*, 1998*a,b*). Recently, we have reported several new methods for the synthesis of pharmaceutically relevant heterocycles utilizing activated nitriles and α,β -unsaturated nitriles as starting materials (*e.g.* Mohamed-Ezzat *et al.*, 2021). In this context, we and others have synthesized several condensed carbocyclic pyrans and carbocyclic pyridines using dimedone as the starting material (Hebishy *et al.*, 2022; Tu *et al.*, 2014).



The present investigation reports a new one-pot synthesis of condensed carbocyclic pyridines by the reaction of dimedone with enamino nitriles. It was found that 2-aminoprop-1-ene-1,1,3-tricarbonitrile (**1**) reacted with 4-hydroxy-3-methoxybenzaldehyde (**2**) and dimedone (**4**) in refluxing *n*-butanol containing catalytic amounts of trimethylamine to give the

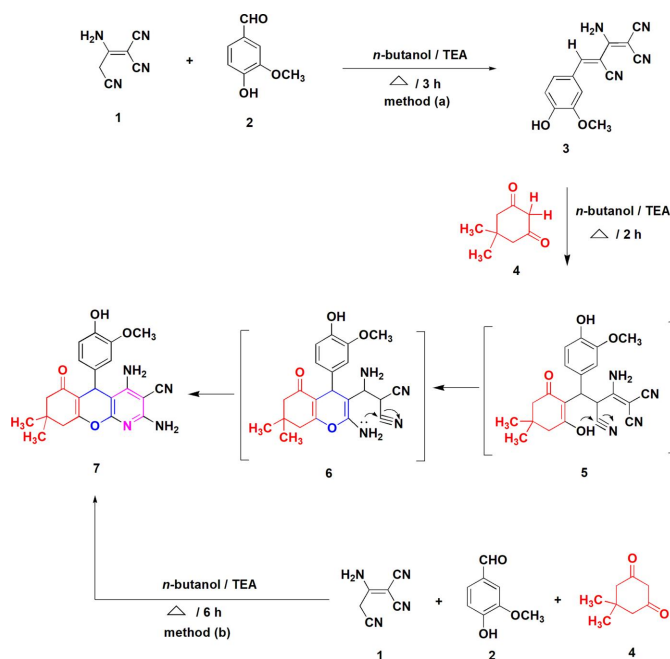


Figure 1
The reaction scheme for the synthesis of compound **7**.

corresponding condensed chromeno[2,3-*b*]pyridine-3-carbonitrile (**7**) (Fig. 1). The structure of **7** was confirmed on the basis of elemental analysis and spectroscopic studies (^1H NMR, IR and MS). We suggest that the formation mechanism of **7** from **1**, **2** and **4** involves a condensation reaction that consists of an initial Michael addition of the methylene group of the dimedone **4** to the double bond of intermediate **3** to give the next intermediate **5**, which then cyclizes to the condensed chromeno[2,3-*b*]pyridine-3-carbonitrile **7**. In order to establish the structure of the compound unambiguously, the crystal structure was determined and is presented here.

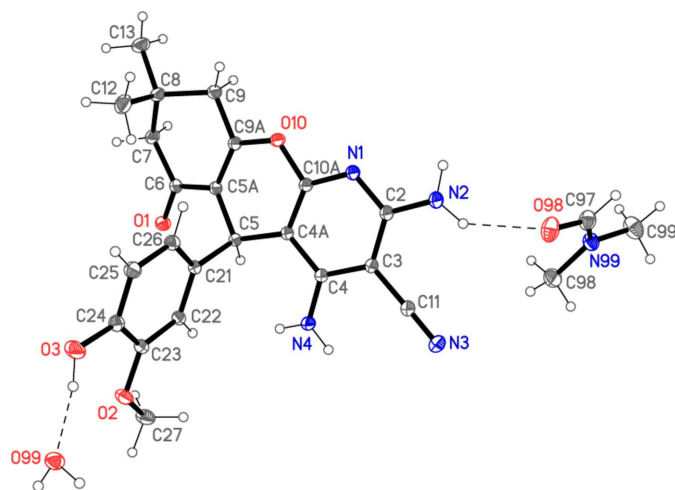


Figure 2
The structure of compound **7** (as its 1/1/1 adduct with DMF and water) in the crystal. Ellipsoids correspond to 50% probability levels. The dashed lines indicate hydrogen bonds.

Table 1
Selected geometric parameters (\AA , $^\circ$).

N1—C10A	1.3324 (7)	C9A—O10	1.3617 (7)
N1—C2	1.3399 (7)	O10—C10A	1.3783 (7)
C5A—C9A	1.3484 (8)		
C10A—N1—C2	117.21 (5)	C4A—C10A—O10	122.17 (5)
C10A—C4A—C5—C5A	11.45 (7)	C5—C5A—C9A—O10	5.67 (9)
C4A—C5—C5A—C9A	-14.61 (7)	C6—C5A—C9A—C9	5.77 (9)
C9A—C5A—C6—C7	-8.71 (8)	C8—C9—C9A—C5A	26.39 (9)
C5A—C6—C7—C8	-21.02 (8)	C5A—C9A—O10—C10A	8.25 (9)
C6—C7—C8—C9	50.42 (7)	C5—C4A—C10A—O10	0.48 (9)
C7—C8—C9—C9A	-51.84 (7)	C9A—O10—C10A—C4A	-11.26 (9)

2. Structural commentary

The structure of the product **7**, which crystallized from DMF as a 1/1/1 adduct with DMF and water, is shown in Fig. 2. Molecular dimensions, a selection of which are given in Table 1, may be regarded as normal (*e.g.* the double-bond length C5A=C9A). The pyridinic ring is planar, and its direct substituents also lie in the same plane (r.m.s. deviation of eleven atoms = 0.008 \AA); the angle between this plane and that of the methoxyphenyl ring is 77.86 (2) $^\circ$. The atoms C5A and C9A lie 0.317 (1) and 0.249 (1) \AA , respectively, out of the plane in the same direction. The central ring has the form of a flattened boat, with C5 and O10 lying 0.166 (1) and 0.101 (1) \AA , respectively, out of the plane of the other four atoms (r.m.s. deviation = 0.015 \AA). The third ring of the tricyclic system, formally related to cyclohexen-2-one, has the expected envelope form, in which the atom C8 lies 0.673 (1) \AA out of the plane of the other five atoms (r.m.s. deviation 0.029 \AA). Viewed from the side (Fig. 3), it can be seen that the entire tricyclic system is approximately planar (r.m.s. deviation 0.14 \AA) except for C8.

3. Supramolecular features

All seven of the potential hydrogen-bond donors do indeed take part in classical hydrogen bonds (Table 2), although the contact N4—H03...O98 is appreciably longer than the others, and O99—H07 is part of a three-centre system with N1 and the more distant O10 as acceptors. There is also one short linear contact involving a phenyl hydrogen, C22—H22...O98,

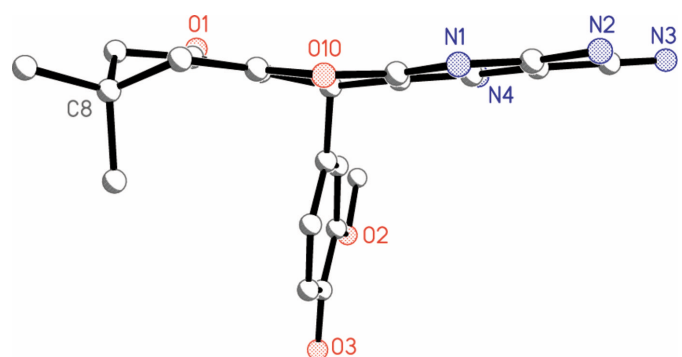


Figure 3
Side view of compound **7** (hydrogen atoms excluded).

Table 2
Hydrogen-bond geometry (Å, °).

<i>D</i> — <i>H</i> ··· <i>A</i>	<i>D</i> — <i>H</i>	<i>H</i> ··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> — <i>H</i> ··· <i>A</i>
N2—H01···O1 ⁱ	0.886 (13)	2.268 (13)	3.1492 (7)	173.6 (11)
N2—H02···O98	0.885 (13)	2.170 (13)	2.9167 (8)	141.8 (11)
N4—H03···O98 ⁱⁱ	0.836 (13)	2.590 (12)	3.2891 (8)	142.0 (11)
N4—H04···N3 ⁱⁱⁱ	0.863 (13)	2.237 (13)	3.0413 (8)	154.9 (12)
O3—H05···O99	0.879 (14)	1.816 (14)	2.6399 (7)	155.2 (12)
O99—H06···O1 ^{iv}	0.856 (14)	1.944 (14)	2.7944 (7)	172.0 (13)
O99—H07···N1 ^v	0.877 (14)	2.012 (14)	2.8699 (7)	165.5 (13)
O99—H07···O10 ^v	0.877 (14)	2.519 (14)	3.2180 (7)	137.2 (11)
C22—H22···O98 ⁱⁱ	0.95	2.39	3.3210 (8)	167

Symmetry codes: (i) $x - 1, y, z$; (ii) $x + 1, y, z$; (iii) $-x + 1, -y + 2, -z + 1$; (iv) $-x + \frac{1}{2}, y + \frac{1}{2}, -z + \frac{3}{2}$; (v) $-x + \frac{1}{2}, y + \frac{1}{2}, -z + \frac{3}{2}$.

which may be considered as a weak hydrogen bond; this is, however, not represented in the Figures for clarity reasons.

The molecules of **7** and the DMF combine to form broad ribbons parallel to the *a* axis (Fig. 4), in which inversion-symmetric $R_2^2(12)$ rings, based on the hydrogen bond N4—H04···N3, are prominent. The DMF molecules project above and below the planes of the ribbons. The water molecules connect the residues in the third dimension (Fig. 5). They accept one hydrogen bond and act as donor for three hydrogen bonds (counting both branches of the three-centre system).

4. Database survey

The search employed the routine ConQuest (Bruno *et al.*, 2002), part of Version 2022.3.0 of the Cambridge Database (Groom *et al.*, 2016).

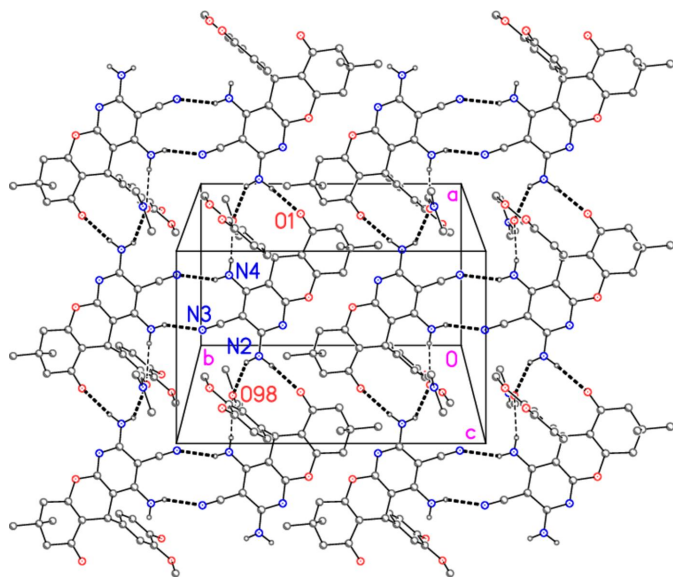


Figure 4
Packing diagram of compound **7** (including the DMF molecules, which are seen edge-on), showing two broad ribbons running vertically. The methoxyphenyl rings are reduced to the *ipso* atoms C21 for clarity. Hydrogen atoms not involved in hydrogen bonding are also omitted. View direction: perpendicular to the *ab* plane. Hydrogen bonds are shown as dashed lines (thin for the longer bonds N4—H03···O98, otherwise thick).

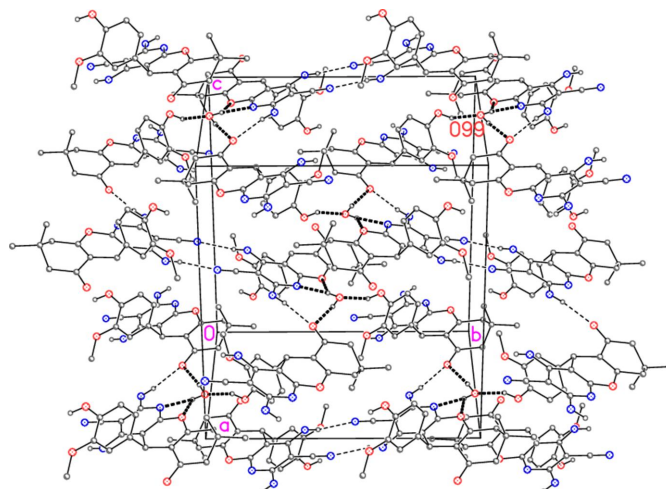


Figure 5
Packing diagram of compound **7**, with view direction approximately perpendicular to (101), showing the role of the water molecules. Hydrogen bonds involving these molecules are shown as thick dashed bonds, other hydrogen bonds as thin dashed bonds.

A search for the same tricyclic ring system gave only one hit, namely 8-(furan-2-yl)-12-(4-methoxyphenyl)-3,3,11-trimethyl-3,4,7,8,9,12-hexahydro-1*H*-chromeno[2,3-*b*]quinoline-1,10(2*H*)-dione (refcode EVANEW; Han *et al.*, 2015). This, however, has a further cyclohexanone-type ring fused to the pyridinic ring. In common with compound **7**, it bears two methyl groups at the atom corresponding to our C8, a keto function at C6 and an aromatic substituent (*p*-methoxyphenyl) at C5. The interplanar angle involving this ring is given as 83.7 (7)°.

A search for solvates with precisely one DMF and one water molecule (under the stringent conditions only organic, no disorder, no ionic compounds, no metals, all solvent H present) gave only 32 hits. We did not check for the plausibility of the water H atoms. The structures represented a broad distribution of organic compounds, *e.g.* during systematic studies of solvates of crown ethers [17,23-dibromo-18,22-dinitro-2,5,8,11,14-pentaoxa-26-azatetracyclo-(13.9.3.019,27.-021,25)heptacos-1(24),15,17,19 (27),21 (25),22-hexaene-20(26*H*)-one, refcode AMARAH; Huszthy *et al.*, 2003] or steroids [bis(17β-hydroxy-17α-methylandrostan-3,2-*c*)pyrazole, AVEQUO; Karpinska *et al.*, 2011]. Heterocyclic systems with groups likely to hydrogen bond were also well represented, *e.g.* 2'-amino-6'-ethyl-2,5'-dioxo-1,2,5',6'-tetrahydro-spiro[indole-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (MESVAL; Upadhyay *et al.*, 2023). Our own studies have shown that DMF is often a useful solvent for crystallization of heterocyclic compounds; as a hydrogen-bond acceptor, it has formed solvates with *N*-[2-amino-5-cyano-4-(methylsulfanyl)-6-oxopyrimidin-1(6*H*)-yl]-4-bromobenzenesulfonamide (WUSMUU; Elgemeie *et al.*, 2015) and *N*-[6-amino-5-(1,3-benzothiazol-2-yl)-3-cyano-4-(methylsulfanyl)-2-oxopyridin-1(2*H*)-yl]-4-methylbenzene-1-sulfonamide (ZELBUQ; Azzam *et al.*, 2017).

5. Synthesis and crystallization

Method A

A mixture of 2-aminoprop-1-ene-1,1,3-tricarbonitrile **1** (1.32 g, 0.01 mmol), 4-hydroxy-3-methoxybenzaldehyde **2** (1.52 g, 0.01 mmol) and a few drops of triethylamine in *n*-butanol (50 mL) was refluxed for 3 h. Then 5,5-dimethylcyclohexane-1,3-dione **4** (1.4 g, 0.01 mmol) was added and the mixture was refluxed for another 2 h. After cooling, the precipitate was collected by filtration and recrystallized from DMF. Yield 2.84 g (70%).

Method B

A mixture of 2-aminoprop-1-ene-1,1,3-tricarbonitrile **1** (1.32 g, 0.01 mmol), 4-hydroxy-3-methoxybenzaldehyde **2** (1.52 g, 0.01 mmol), 5,5-dimethylcyclohexane-1,3-dione **4** (1.4 g, 0.01 mmol) and few drops of triethylamine in *n*-butanol (5 ml) was refluxed for 6 h. After cooling, the precipitate was collected by filtration and recrystallized from DMF. Yield 3.04 g (75%).

Orange crystals, yield 75%, m.p. 516–518 K. IR (KBr): ν_{\max} = 3448 (OH), 3351 (NH₂), 2204 (CN), 1662 (C=O) cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.00 (*s*, 3H, CH₃), 1.05 (*s*, 3H, CH₃), 2.43–2.52 (*m*, 4H, 2 CH₂), 3.66 (*s*, 3H, OCH₃), 4.75 (*s*, 1H, pyran-H), 6.38–6.42 (*m*, 5H, Ar-1H and 2 NH₂), 6.96 (*s*, 1H, Ar), 7.92 (*s*, 1H, Ar), 8.71 (*s*, 1H, OH) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 196.19 (C=O), 164.06 (O–C–N), 162.84 (C–O), 159.72 (C–NH₂), 157.22 (N=C–NH₂), 147.36 (C–OCH₃), 145.52 (C–OH), 135.72 (Ar–C), 120.37, 116.67 (Ar–CH), 115.07 (CN), 92.51 (C–CO), 72.13 (pyridine-C), 56.21 (C–CN), 50.68 (OCH₃), 33.29 (CH₂), 32.56 (CH₂), 29.32 (CH₃), 26.83 (CH₃) ppm. MS (70 eV, Fab mass, %): *m/z* = 406 (11%), 372 (9), 282 (100), 226 (33), 170 (11), 66 (9). Analysis calculated for C₂₂H₂₂N₄O₄ (406.16): C 65.01, H 5.46, N 13.78. Found: C 65.0, H 5.5, N 13.7%.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. Hydrogen atoms bonded to nitrogen or oxygen were refined freely. The methyl groups were included as an idealized rigid group allowed to rotate but not tip (command AFIX 137), with C–H = 0.99 Å and H–C–H = 109.5°. Other hydrogen atoms were included using a riding model starting from calculated positions (C–H_{methylene} = 0.99, C–H_{methine} = 1.00, C–H_{arom} = 0.95 Å). The *U*(H) values were fixed at 1.5 × *U*_{eq} of the parent carbon atoms for the methyl groups and 1.2 × *U*_{eq} for other hydrogens. Three reflections, with intensities clearly in error, were omitted. The largest peaks of residual electron density (max. 0.67 e Å⁻³) lie in the middle of bonds and thus do not give cause for concern.

Acknowledgements

The authors acknowledge support by the Open Access Publication Funds of the Technical University of Braunschweig.

Table 3

Experimental details.

Crystal data	
Chemical formula	C ₂₂ H ₂₂ N ₄ O ₄ ·C ₃ H ₇ NO·H ₂ O
<i>M_r</i>	497.55
Crystal system, space group	Monoclinic, <i>P</i> ₂ ₁ / <i>n</i>
Temperature (K)	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	9.9055 (2), 15.9600 (3), 16.4794 (4)
β (°)	106.344 (2)
<i>V</i> (Å ³)	2499.98 (10)
<i>Z</i>	4
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.10
Crystal size (mm)	0.2 × 0.2 × 0.1
Data collection	
Diffractometer	XtaLAB Synergy
Absorption correction	Multi-scan (<i>CrysAlis PRO</i> ; Rigaku OD, 2022)
<i>T</i> _{min} , <i>T</i> _{max}	0.735, 1.000
No. of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	210685, 13416, 11108
<i>R</i> _{int}	0.056
θ values (°)	θ_{\max} = 37.8, θ_{\min} = 2.2
(<i>sin</i> θ / λ) _{max} (Å ⁻¹)	0.862
Refinement	
$R[F^2 > 2\sigma(F^2)]$, <i>wR</i> (<i>F</i> ²), <i>S</i>	0.038, 0.114, 1.04
No. of reflections	13416
No. of parameters	358
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ⁻³)	0.67, -0.22

Computer programs: *CrysAlis PRO* (Rigaku OD, 2022), *SHELXT* (Sheldrick, 2015a), *SHELXL2019/3* (Sheldrick, 2015b) and *XP* (Bruker, 1998).

References

- Ahmed, E. A., Elgemeie, G. H. & Ahmed, K. A. (2022). *Pigm. Resin Technol.* **51**, 1–5.
- Azzam, R. A., Elgemeie, G. H., Elsayed, R. E. & Jones, P. G. (2017). *Acta Cryst.* **E73**, 1820–1822.
- Bruker (1998). *XP*. Bruker Analytical X-Ray Instruments, Madison, Wisconsin, USA.
- Bruno, I. J., Cole, J. C., Edgington, P. R., Kessler, M., Macrae, C. F., McCabe, P., Pearson, J. & Taylor, R. (2002). *Acta Cryst.* **B58**, 389–397.
- Elgemeie, G. E. H., Farag, D. S. & Jones, P. G. (1998a). *Acta Cryst.* **C54**, 1466–1468.
- Elgemeie, G. E. H., Fathy, N. M. & Jones, P. G. (1998b). *Acta Cryst.* **C54**, 1314–1316.
- Elgemeie, G. H., Mohamed, R. A., Hussein, H. A. & Jones, P. G. (2015). *Acta Cryst.* **E71**, 1322–1324.
- Fleming, F. F. & Wang, Q. Z. (2003). *Chem. Rev.* **103**, 2035–2078.
- Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* **B72**, 171–179.
- Han, G.-F., Zhao, L.-J., Chen, L.-Z., Du, J.-W. & Wang, Z.-X. (2015). *J. Heterocycl. Chem.* **52**, 1219–1225.
- Hebishy, A. M. S., Elgemeie, G. H., Ali, R. A. E. & Jones, P. G. (2022). *Acta Cryst.* **E78**, 638–641.
- Hebishy, A. M. S., Elgemeie, G. H., Gouda, L. M. & Jones, P. G. (2023). *Acta Cryst.* **E79**, 335–340.
- Huszthy, P., Vermes, B., Báthori, N. & Czugler, M. (2003). *Tetrahedron*, **59**, 9371–9377.
- Karpinska, J., Erxleben, A. & McArdle, P. (2011). *Cryst. Growth Des.* **11**, 2829–2838.
- Metwally, N. H., Elgemeie, G. H. & Fahmy, F. G. (2023). *ACS Omega*, **8**, 36636–36654.

- Mohamed-Ezzat, R. A., Elgemeie, G. H. & Jones, P. G. (2021). *Acta Cryst.* **E77**, 547–550.
- Rigaku OD (2022). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, England.
- Sheldrick, G. M. (2015a). *Acta Cryst.* **C71**, 3–8.
- Sheldrick, G. M. (2015b). *Acta Cryst.* **A71**, 3–8.
- Tu, X., Fan, W., Hao, W., Jiang, B. & Tu, S. (2014). *ACS Comb. Sci.* **16**, 647–651.
- Upadhyay, D. B., Vala, R. M., Patel, S. G., Patel, P. J., Chi, C. & Patel, C. (2023). *J. Mol. Struct.* **1273**, 134305.
- Wang, C., Li, Y., Gong, M., Wu, Q., Zhang, J., Kim, J. K., Huang, M. & Wu, Y. (2016). *Org. Lett.* **18**, 4151–4153.
- Zhang, W., Yang, C., Zhang, Z., Li, X. & Cheng, J. (2019). *Org. Lett.* **21**, 4137–4142.
- Zhang, G., Zhang, C., Tian, Y. & Chen, F. (2023). *Org. Lett.* **25**, 917–922.

supporting information

Acta Cryst. (2024). E80, 396-400 [https://doi.org/10.1107/S2056989024002615]

Crystal structure of 2,4-diamino-5-(4-hydroxy-3-methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile–dimethylformamide–water (1/1/1)

Nadia H. Metwally, Galal H. Elgemeie, El-shimaa S. M. Abd Al-latif and Peter G. Jones

Computing details

2,4-Diamino-5-(4-hydroxy-3-methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile–dimethylformamide–water (1/1/1)

Crystal data

$C_{22}H_{22}N_4O_4 \cdot C_3H_7NO \cdot H_2O$

$M_r = 497.55$

Monoclinic, $P2_1/n$

$a = 9.9055$ (2) Å

$b = 15.9600$ (3) Å

$c = 16.4794$ (4) Å

$\beta = 106.344$ (2)°

$V = 2499.98$ (10) Å³

$Z = 4$

$F(000) = 1056$

$D_x = 1.322$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 76991 reflections

$\theta = 2.2$ – 39.6 °

$\mu = 0.10$ mm⁻¹

$T = 100$ K

Tablet, colourless

$0.2 \times 0.2 \times 0.1$ mm

Data collection

XtaLAB Synergy
diffractometer

Radiation source: micro-focus sealed X-ray
tube, PhotonJet (Mo) X-ray Source

Mirror monochromator

Detector resolution: 10.0000 pixels mm⁻¹

ω scans

Absorption correction: multi-scan
(CrysAlisPro; Rigaku OD, 2022)

$T_{\min} = 0.735$, $T_{\max} = 1.000$

210685 measured reflections

13416 independent reflections

11108 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.056$

$\theta_{\max} = 37.8$ °, $\theta_{\min} = 2.2$ °

$h = -17 \rightarrow 17$

$k = -27 \rightarrow 27$

$l = -28 \rightarrow 28$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.038$

$wR(F^2) = 0.114$

$S = 1.04$

13416 reflections

358 parameters

0 restraints

Primary atom site location: dual

Hydrogen site location: mixed

H atoms treated by a mixture of independent
and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0626P)^2 + 0.4082P]$

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

$(\Delta/\sigma)_{\max} = 0.001$

$\Delta\rho_{\max} = 0.67$ e Å⁻³

$\Delta\rho_{\min} = -0.22$ e Å⁻³

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.41040 (5)	0.66845 (3)	0.58286 (3)	0.01573 (8)
C2	0.35681 (6)	0.74408 (3)	0.55675 (4)	0.01397 (8)
N2	0.21622 (5)	0.75300 (4)	0.54244 (4)	0.01919 (9)
H01	0.1683 (13)	0.7091 (8)	0.5522 (8)	0.029 (3)*
H02	0.1692 (13)	0.7983 (8)	0.5197 (8)	0.032 (3)*
C3	0.44457 (6)	0.81052 (3)	0.54550 (3)	0.01332 (8)
C4	0.59114 (6)	0.79689 (3)	0.55989 (3)	0.01270 (8)
N4	0.67486 (5)	0.85813 (3)	0.54512 (4)	0.01630 (9)
H03	0.7612 (13)	0.8503 (8)	0.5540 (8)	0.030 (3)*
H04	0.6425 (14)	0.9076 (8)	0.5296 (8)	0.032 (3)*
C4A	0.64624 (5)	0.71688 (3)	0.58823 (3)	0.01254 (8)
C5	0.80070 (5)	0.69551 (3)	0.60532 (3)	0.01224 (8)
H5	0.832899	0.714157	0.555889	0.015*
C5A	0.81825 (6)	0.60167 (3)	0.61409 (3)	0.01306 (8)
C6	0.94969 (6)	0.56393 (3)	0.60992 (4)	0.01383 (8)
O1	1.03852 (5)	0.60592 (3)	0.58804 (3)	0.01802 (8)
C7	0.97538 (6)	0.47181 (4)	0.63057 (4)	0.01648 (9)
H7A	1.075931	0.463992	0.661303	0.020*
H7B	0.956598	0.440073	0.576928	0.020*
C8	0.88588 (6)	0.43440 (4)	0.68387 (4)	0.01705 (9)
C9	0.73204 (6)	0.45817 (4)	0.64135 (4)	0.01770 (10)
H9A	0.698047	0.427626	0.587129	0.021*
H9B	0.673250	0.441184	0.678188	0.021*
C9A	0.71700 (6)	0.55019 (3)	0.62522 (4)	0.01452 (9)
O10	0.58553 (5)	0.57747 (3)	0.62246 (3)	0.01756 (8)
C10A	0.54867 (6)	0.65861 (3)	0.59701 (4)	0.01403 (9)
C11	0.38620 (6)	0.89004 (4)	0.51709 (4)	0.01655 (9)
N3	0.34038 (7)	0.95535 (4)	0.49419 (5)	0.02514 (12)
C12	0.93212 (8)	0.46813 (5)	0.77471 (4)	0.02391 (12)
H12A	1.026948	0.447741	0.803183	0.036*
H12B	0.866481	0.448682	0.805418	0.036*
H12C	0.932458	0.529524	0.773538	0.036*
C13	0.90238 (8)	0.33896 (4)	0.68645 (6)	0.02501 (13)
H13A	0.867471	0.316360	0.629044	0.038*
H13B	0.848265	0.314956	0.722263	0.038*
H13C	1.001952	0.324471	0.709689	0.038*
C21	0.89109 (5)	0.73909 (3)	0.68486 (3)	0.01264 (8)
C22	0.98270 (6)	0.80413 (3)	0.67880 (3)	0.01367 (8)
H22	0.991495	0.819834	0.624914	0.016*
C23	1.06120 (6)	0.84614 (4)	0.75094 (4)	0.01489 (9)
O2	1.15118 (5)	0.91117 (3)	0.75031 (3)	0.01993 (9)
C24	1.05186 (6)	0.82200 (4)	0.83128 (4)	0.01673 (9)
O3	1.12872 (6)	0.85824 (4)	0.90394 (3)	0.02564 (11)
H05	1.1648 (14)	0.9072 (8)	0.8971 (8)	0.034 (3)*
C25	0.96244 (7)	0.75654 (4)	0.83672 (4)	0.01757 (10)

H25	0.955884	0.739310	0.890663	0.021*
C26	0.88214 (6)	0.71565 (4)	0.76446 (4)	0.01552 (9)
H26	0.820851	0.671449	0.769635	0.019*
C27	1.16872 (8)	0.93355 (4)	0.67030 (4)	0.02151 (11)
H27A	1.077008	0.947598	0.631269	0.032*
H27B	1.209836	0.886314	0.647569	0.032*
H27C	1.231375	0.982140	0.676969	0.032*
C97	-0.12972 (7)	0.83937 (4)	0.40895 (4)	0.02086 (11)
H97	-0.220125	0.819639	0.409112	0.025*
C98	0.02521 (8)	0.88437 (5)	0.32596 (5)	0.02539 (13)
H98A	0.082462	0.904757	0.380990	0.038*
H98B	0.008664	0.930221	0.284779	0.038*
H98C	0.074841	0.838697	0.306776	0.038*
O98	-0.04221 (6)	0.84926 (4)	0.47838 (3)	0.02704 (11)
N99	-0.10846 (6)	0.85392 (4)	0.33387 (3)	0.01883 (9)
C99	-0.21966 (8)	0.83914 (6)	0.25620 (5)	0.02841 (14)
H99A	-0.193276	0.792258	0.225408	0.043*
H99B	-0.233445	0.889604	0.220932	0.043*
H99C	-0.307232	0.825602	0.269909	0.043*
O99	1.23412 (5)	1.01108 (3)	0.92936 (3)	0.02037 (9)
H06	1.3078 (14)	1.0356 (8)	0.9237 (8)	0.033 (3)*
H07	1.1765 (15)	1.0538 (9)	0.9237 (9)	0.039 (3)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.01093 (17)	0.01421 (18)	0.0225 (2)	0.00127 (14)	0.00540 (16)	0.00266 (15)
C2	0.01156 (19)	0.0146 (2)	0.0158 (2)	0.00106 (15)	0.00391 (16)	0.00067 (16)
N2	0.01142 (19)	0.0177 (2)	0.0285 (3)	0.00216 (16)	0.00582 (17)	0.00442 (18)
C3	0.01208 (19)	0.01273 (19)	0.0148 (2)	0.00120 (15)	0.00318 (15)	0.00130 (15)
C4	0.01184 (19)	0.01280 (19)	0.01307 (19)	0.00009 (15)	0.00285 (15)	0.00058 (15)
N4	0.01292 (18)	0.01354 (18)	0.0221 (2)	-0.00014 (15)	0.00446 (16)	0.00403 (16)
C4A	0.01060 (18)	0.01223 (18)	0.01442 (19)	0.00021 (14)	0.00292 (15)	0.00092 (15)
C5	0.01039 (18)	0.01210 (18)	0.01403 (19)	-0.00016 (14)	0.00309 (15)	0.00053 (15)
C5A	0.01084 (18)	0.01237 (18)	0.0157 (2)	0.00037 (15)	0.00333 (15)	0.00069 (15)
C6	0.01133 (19)	0.0143 (2)	0.0155 (2)	0.00046 (15)	0.00311 (16)	0.00048 (16)
O1	0.01310 (17)	0.01693 (18)	0.0254 (2)	-0.00010 (14)	0.00763 (15)	0.00243 (15)
C7	0.0139 (2)	0.0144 (2)	0.0213 (2)	0.00266 (16)	0.00530 (18)	0.00277 (17)
C8	0.0144 (2)	0.0142 (2)	0.0224 (2)	0.00181 (17)	0.00503 (18)	0.00436 (18)
C9	0.0133 (2)	0.0129 (2)	0.0266 (3)	0.00028 (16)	0.00501 (19)	0.00304 (18)
C9A	0.01132 (19)	0.01308 (19)	0.0190 (2)	0.00082 (15)	0.00398 (16)	0.00187 (16)
O10	0.01171 (16)	0.01288 (16)	0.0291 (2)	0.00140 (13)	0.00737 (15)	0.00510 (15)
C10A	0.01180 (19)	0.01265 (19)	0.0178 (2)	0.00074 (15)	0.00446 (16)	0.00174 (16)
C11	0.0130 (2)	0.0159 (2)	0.0198 (2)	0.00068 (16)	0.00297 (17)	0.00216 (17)
N3	0.0186 (2)	0.0177 (2)	0.0366 (3)	0.00268 (18)	0.0038 (2)	0.0075 (2)
C12	0.0241 (3)	0.0267 (3)	0.0200 (3)	0.0026 (2)	0.0046 (2)	0.0068 (2)
C13	0.0210 (3)	0.0150 (2)	0.0396 (4)	0.0037 (2)	0.0094 (3)	0.0076 (2)
C21	0.01090 (18)	0.01291 (19)	0.01364 (19)	-0.00027 (15)	0.00269 (15)	0.00041 (15)

C22	0.01250 (19)	0.0141 (2)	0.01379 (19)	-0.00121 (15)	0.00278 (15)	0.00045 (15)
C23	0.0142 (2)	0.0144 (2)	0.0151 (2)	-0.00214 (16)	0.00256 (16)	0.00023 (16)
O2	0.0216 (2)	0.01943 (19)	0.01761 (18)	-0.00873 (16)	0.00363 (15)	-0.00127 (15)
C24	0.0180 (2)	0.0169 (2)	0.0136 (2)	-0.00189 (18)	0.00167 (17)	-0.00018 (17)
O3	0.0343 (3)	0.0243 (2)	0.01417 (18)	-0.0115 (2)	0.00005 (18)	-0.00124 (16)
C25	0.0201 (2)	0.0185 (2)	0.0137 (2)	-0.00243 (19)	0.00417 (18)	0.00106 (17)
C26	0.0154 (2)	0.0158 (2)	0.0153 (2)	-0.00179 (17)	0.00414 (17)	0.00110 (16)
C27	0.0242 (3)	0.0197 (2)	0.0215 (3)	-0.0072 (2)	0.0078 (2)	-0.0002 (2)
C97	0.0195 (2)	0.0257 (3)	0.0172 (2)	0.0028 (2)	0.0049 (2)	0.0038 (2)
C98	0.0200 (3)	0.0277 (3)	0.0303 (3)	-0.0008 (2)	0.0100 (2)	0.0045 (2)
O98	0.0258 (2)	0.0361 (3)	0.0163 (2)	0.0069 (2)	0.00111 (17)	0.00401 (18)
N99	0.0165 (2)	0.0236 (2)	0.0159 (2)	-0.00074 (17)	0.00382 (16)	0.00215 (17)
C99	0.0252 (3)	0.0405 (4)	0.0169 (3)	-0.0059 (3)	0.0015 (2)	-0.0013 (2)
O99	0.01655 (19)	0.01737 (19)	0.0278 (2)	-0.00084 (15)	0.00723 (17)	-0.00182 (16)

Geometric parameters (Å, °)

N1—C10A	1.3324 (7)	C12—H12B	0.9800
N1—C2	1.3399 (7)	C12—H12C	0.9800
C2—N2	1.3529 (8)	C13—H13A	0.9800
C2—C3	1.4160 (8)	C13—H13B	0.9800
N2—H01	0.886 (13)	C13—H13C	0.9800
N2—H02	0.885 (13)	C21—C26	1.3907 (8)
C3—C11	1.4183 (8)	C21—C22	1.4007 (8)
C3—C4	1.4204 (8)	C22—C23	1.3954 (8)
C4—N4	1.3476 (7)	C22—H22	0.9500
C4—C4A	1.4154 (7)	C23—O2	1.3700 (7)
N4—H03	0.836 (13)	C23—C24	1.4068 (8)
N4—H04	0.863 (13)	O2—C27	1.4230 (8)
C4A—C10A	1.3779 (8)	C24—O3	1.3545 (8)
C4A—C5	1.5146 (7)	C24—C25	1.3888 (9)
C5—C5A	1.5101 (7)	O3—H05	0.879 (14)
C5—C21	1.5308 (8)	C25—C26	1.3941 (8)
C5—H5	1.0000	C25—H25	0.9500
C5A—C9A	1.3484 (8)	C26—H26	0.9500
C5A—C6	1.4535 (8)	C27—H27A	0.9800
C6—O1	1.2377 (7)	C27—H27B	0.9800
C6—C7	1.5145 (8)	C27—H27C	0.9800
C7—C8	1.5337 (9)	C97—O98	1.2359 (8)
C7—H7A	0.9900	C97—N99	1.3326 (9)
C7—H7B	0.9900	C97—H97	0.9500
C8—C13	1.5313 (9)	C98—N99	1.4503 (9)
C8—C12	1.5345 (10)	C98—H98A	0.9800
C8—C9	1.5349 (8)	C98—H98B	0.9800
C9—C9A	1.4925 (8)	C98—H98C	0.9800
C9—H9A	0.9900	N99—C99	1.4538 (9)
C9—H9B	0.9900	C99—H99A	0.9800
C9A—O10	1.3617 (7)	C99—H99B	0.9800

O10—C10A	1.3783 (7)	C99—H99C	0.9800
C11—N3	1.1570 (8)	O99—H06	0.856 (14)
C12—H12A	0.9800	O99—H07	0.877 (14)
C10A—N1—C2	117.21 (5)	C8—C12—H12A	109.5
N1—C2—N2	116.49 (5)	C8—C12—H12B	109.5
N1—C2—C3	120.95 (5)	H12A—C12—H12B	109.5
N2—C2—C3	122.56 (5)	C8—C12—H12C	109.5
C2—N2—H01	117.6 (8)	H12A—C12—H12C	109.5
C2—N2—H02	123.6 (8)	H12B—C12—H12C	109.5
H01—N2—H02	118.6 (11)	C8—C13—H13A	109.5
C2—C3—C11	120.33 (5)	C8—C13—H13B	109.5
C2—C3—C4	119.98 (5)	H13A—C13—H13B	109.5
C11—C3—C4	119.65 (5)	C8—C13—H13C	109.5
N4—C4—C4A	120.95 (5)	H13A—C13—H13C	109.5
N4—C4—C3	120.71 (5)	H13B—C13—H13C	109.5
C4A—C4—C3	118.32 (5)	C26—C21—C22	118.77 (5)
C4—N4—H03	120.8 (9)	C26—C21—C5	120.55 (5)
C4—N4—H04	121.4 (9)	C22—C21—C5	120.68 (5)
H03—N4—H04	117.7 (12)	C23—C22—C21	120.81 (5)
C10A—C4A—C4	115.27 (5)	C23—C22—H22	119.6
C10A—C4A—C5	122.02 (5)	C21—C22—H22	119.6
C4—C4A—C5	122.69 (5)	O2—C23—C22	124.42 (5)
C5A—C5—C4A	108.92 (4)	O2—C23—C24	115.46 (5)
C5A—C5—C21	110.17 (4)	C22—C23—C24	120.12 (5)
C4A—C5—C21	111.95 (4)	C23—O2—C27	116.52 (5)
C5A—C5—H5	108.6	O3—C24—C25	118.31 (5)
C4A—C5—H5	108.6	O3—C24—C23	123.06 (6)
C21—C5—H5	108.6	C25—C24—C23	118.61 (5)
C9A—C5A—C6	117.67 (5)	C24—O3—H05	114.5 (9)
C9A—C5A—C5	123.19 (5)	C24—C25—C26	121.20 (5)
C6—C5A—C5	119.14 (5)	C24—C25—H25	119.4
O1—C6—C5A	120.61 (5)	C26—C25—H25	119.4
O1—C6—C7	120.18 (5)	C21—C26—C25	120.48 (5)
C5A—C6—C7	119.19 (5)	C21—C26—H26	119.8
C6—C7—C8	114.77 (5)	C25—C26—H26	119.8
C6—C7—H7A	108.6	O2—C27—H27A	109.5
C8—C7—H7A	108.6	O2—C27—H27B	109.5
C6—C7—H7B	108.6	H27A—C27—H27B	109.5
C8—C7—H7B	108.6	O2—C27—H27C	109.5
H7A—C7—H7B	107.6	H27A—C27—H27C	109.5
C13—C8—C7	109.19 (5)	H27B—C27—H27C	109.5
C13—C8—C12	108.77 (6)	O98—C97—N99	125.77 (7)
C7—C8—C12	111.11 (5)	O98—C97—H97	117.1
C13—C8—C9	110.06 (5)	N99—C97—H97	117.1
C7—C8—C9	107.58 (5)	N99—C98—H98A	109.5
C12—C8—C9	110.12 (5)	N99—C98—H98B	109.5
C9A—C9—C8	111.17 (5)	H98A—C98—H98B	109.5

C9A—C9—H9A	109.4	N99—C98—H98C	109.5
C8—C9—H9A	109.4	H98A—C98—H98C	109.5
C9A—C9—H9B	109.4	H98B—C98—H98C	109.5
C8—C9—H9B	109.4	C97—N99—C98	121.91 (6)
H9A—C9—H9B	108.0	C97—N99—C99	120.70 (6)
C5A—C9A—O10	122.79 (5)	C98—N99—C99	117.39 (6)
C5A—C9A—C9	125.66 (5)	N99—C99—H99A	109.5
O10—C9A—C9	111.55 (5)	N99—C99—H99B	109.5
C9A—O10—C10A	118.66 (5)	H99A—C99—H99B	109.5
N1—C10A—C4A	128.24 (5)	N99—C99—H99C	109.5
N1—C10A—O10	109.59 (5)	H99A—C99—H99C	109.5
C4A—C10A—O10	122.17 (5)	H99B—C99—H99C	109.5
N3—C11—C3	179.08 (6)	H06—O99—H07	100.5 (12)
C10A—N1—C2—N2	179.82 (6)	C6—C5A—C9A—C9	5.77 (9)
C10A—N1—C2—C3	-0.47 (9)	C5—C5A—C9A—C9	-174.65 (6)
N1—C2—C3—C11	179.43 (6)	C8—C9—C9A—C5A	26.39 (9)
N2—C2—C3—C11	-0.88 (9)	C8—C9—C9A—O10	-153.90 (5)
N1—C2—C3—C4	1.58 (8)	C5A—C9A—O10—C10A	8.25 (9)
N2—C2—C3—C4	-178.73 (6)	C9—C9A—O10—C10A	-171.47 (5)
C2—C3—C4—N4	176.42 (5)	C2—N1—C10A—C4A	-0.02 (9)
C11—C3—C4—N4	-1.44 (8)	C2—N1—C10A—O10	-179.40 (5)
C2—C3—C4—C4A	-2.14 (8)	C4—C4A—C10A—N1	-0.56 (9)
C11—C3—C4—C4A	180.00 (5)	C5—C4A—C10A—N1	-178.82 (6)
N4—C4—C4A—C10A	-176.96 (5)	C4—C4A—C10A—O10	178.74 (5)
C3—C4—C4A—C10A	1.60 (8)	C5—C4A—C10A—O10	0.48 (9)
N4—C4—C4A—C5	1.29 (8)	C9A—O10—C10A—N1	168.16 (5)
C3—C4—C4A—C5	179.84 (5)	C9A—O10—C10A—C4A	-11.26 (9)
C10A—C4A—C5—C5A	11.45 (7)	C5A—C5—C21—C26	-52.13 (7)
C4—C4A—C5—C5A	-166.67 (5)	C4A—C5—C21—C26	69.23 (6)
C10A—C4A—C5—C21	-110.63 (6)	C5A—C5—C21—C22	128.86 (5)
C4—C4A—C5—C21	71.24 (6)	C4A—C5—C21—C22	-109.79 (6)
C4A—C5—C5A—C9A	-14.61 (7)	C26—C21—C22—C23	-1.52 (8)
C21—C5—C5A—C9A	108.55 (6)	C5—C21—C22—C23	177.51 (5)
C4A—C5—C5A—C6	164.97 (5)	C21—C22—C23—O2	-178.88 (5)
C21—C5—C5A—C6	-71.88 (6)	C21—C22—C23—C24	1.67 (9)
C9A—C5A—C6—O1	169.75 (6)	C22—C23—O2—C27	-3.02 (9)
C5—C5A—C6—O1	-9.86 (8)	C24—C23—O2—C27	176.45 (6)
C9A—C5A—C6—C7	-8.71 (8)	O2—C23—C24—O3	-1.81 (9)
C5—C5A—C6—C7	171.68 (5)	C22—C23—C24—O3	177.69 (6)
O1—C6—C7—C8	160.51 (6)	O2—C23—C24—C25	179.90 (6)
C5A—C6—C7—C8	-21.02 (8)	C22—C23—C24—C25	-0.60 (9)
C6—C7—C8—C13	169.85 (5)	O3—C24—C25—C26	-178.96 (6)
C6—C7—C8—C12	-70.19 (7)	C23—C24—C25—C26	-0.59 (9)
C6—C7—C8—C9	50.42 (7)	C22—C21—C26—C25	0.33 (9)
C13—C8—C9—C9A	-170.71 (6)	C5—C21—C26—C25	-178.70 (5)
C7—C8—C9—C9A	-51.84 (7)	C24—C25—C26—C21	0.73 (9)
C12—C8—C9—C9A	69.39 (7)	O98—C97—N99—C98	-0.18 (11)

C6—C5A—C9A—O10	-173.91 (5)	O98—C97—N99—C99	179.44 (7)
C5—C5A—C9A—O10	5.67 (9)		

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—H01...O1 ⁱ	0.886 (13)	2.268 (13)	3.1492 (7)	173.6 (11)
N2—H02...O98	0.885 (13)	2.170 (13)	2.9167 (8)	141.8 (11)
N4—H03...O98 ⁱⁱ	0.836 (13)	2.590 (12)	3.2891 (8)	142.0 (11)
N4—H04...N3 ⁱⁱⁱ	0.863 (13)	2.237 (13)	3.0413 (8)	154.9 (12)
O3—H05...O99	0.879 (14)	1.816 (14)	2.6399 (7)	155.2 (12)
O99—H06...O1 ^{iv}	0.856 (14)	1.944 (14)	2.7944 (7)	172.0 (13)
O99—H07...N1 ^v	0.877 (14)	2.012 (14)	2.8699 (7)	165.5 (13)
O99—H07...O10 ^v	0.877 (14)	2.519 (14)	3.2180 (7)	137.2 (11)
C22—H22...O98 ⁱⁱ	0.95	2.39	3.3210 (8)	167

Symmetry codes: (i) $x-1, y, z$; (ii) $x+1, y, z$; (iii) $-x+1, -y+2, -z+1$; (iv) $-x+5/2, y+1/2, -z+3/2$; (v) $-x+3/2, y+1/2, -z+3/2$.