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Cocrystals of the antimalarial drug 11-aza-artemisinin with three alkenoic acids of 1:1 or 2:1 stoichiometry

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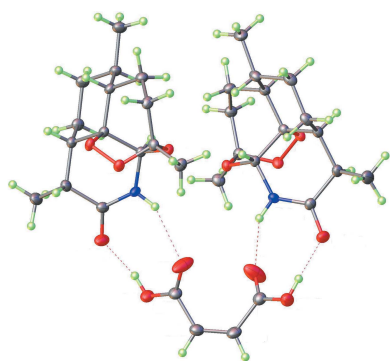
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The stoichiometry, X-ray structures and stability of four pharmaceutical cocrystals previously identified from liquid-assisted grinding (LAG) of 11-aza-artemisinin (11-Aza; systematic name: 1,5,9-trimethyl-14,15,16-trioxa-11-azatetracyclo[10.3.1.0^{4,13}.0^{8,13}]hexadecan-10-one) with *trans*-cinnamic (Cin), maleic (Mal) and fumaric (Fum) acids are herein reported. *trans*-Cinnamic acid, a mono acid, forms 1:1 cocrystal 11-Aza:Cin (**1**, C₁₅H₂₃NO₄·C₉H₈O₂). Maleic acid forms both 1:1 cocrystal 11-Aza:Mal (**2**, C₁₅H₂₃NO₄·C₄H₄O₄), in which one COOH group is involved in self-catenation, and 2:1 cocrystal 11-Aza₂:Mal (**3**, 2C₁₅H₂₃NO₄·C₄H₄O₄). Its isomer, fumaric acid, only affords 2:1 cocrystal 11-Aza₂:Fum (**4**). All cocrystal formation appears driven by acid–lactam *R*₂²(8) heterosynthons with short O–H...O=C hydrogen bonds [O...O = 2.56 (2) Å], augmented by weaker C=O...H–N contacts. Despite a better packing efficiency, cocrystal **3** is metastable with respect to **2**, probably due to a higher conformational energy for the maleic acid molecule in its structure. In each case, the microcrystalline powders from LAG were useful in providing seeding for the single-crystal growth.

1. Introduction

Artemisinins are a potent family of antimalarial drugs (Klayman, 1985). Commercial artemisinins, such as artesunate and artemether, break down to the active agent dihydro-artemisinin (DHA) (Haynes *et al.*, 2007a), which is neurotoxic and has been implicated in the mechanism of parasite resistance (Mbengue *et al.*, 2015). 11-Azaartemisinin (Torok & Ziffer, 1995) and its derivatives (Haynes *et al.*, 2007b) offer alternative medicines combining high antimalarial potency, better hydrolytic stability and lower neurotoxicity that avoid DHA as a breakdown product and so remain active against current drug-resistant parasitic strains (Harmse *et al.*, 2015, 2017). As an extension of this work, we have been examining the potential of 11-azaartemisinin (11-Aza) for cocrystal formulation, with a view to enhancing its solubility and solid-state stability with respect to the breakdown of its peroxide functionality. The facile preparation of 11-Aza in reasonable yield from its parent (Mekonnen & Ziffer, 1997; Haynes *et al.*, 2007b) allows for an in-depth study of its cocrystal formation.

Cocrystal formation between organic acids and amides is well established, primarily *via* a heteromolecular synthon between the two functionalities. This has been applied to the cocrystal engineering of important drugs, such as carbamazepine (Childs *et al.*, 2008; Li & Matzger, 2016). Recently, we reported the cocrystal formation of 11-Aza with various



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carboxylic acids (Nisar *et al.*, 2018) and again their formation appears driven by the formation of a robust lactam–acid $R_2^2(8)$ heterosynthon (Fig. 1). Four new cocrystal phases from the alkenoic acids *trans*-cinnamic acid (Cin), maleic acid (Mal) and fumaric acid (Fum) were indicated from powder X-ray diffraction patterns of liquid-assisted grinding (LAG) products, but proved less facile in yielding suitable single crystals. Suitable specimens have now been grown using the LAG-derived cocrystal powders to seed nucleation and the stoichiometries, crystal structures and properties of the four phases 11-Aza:Cin (**1**), 11-Aza:Mal (**2**), 11-Aza₂:Mal (**3**) and 11-Aza₂:Fum (**4**) (see Scheme 1) are reported herein.

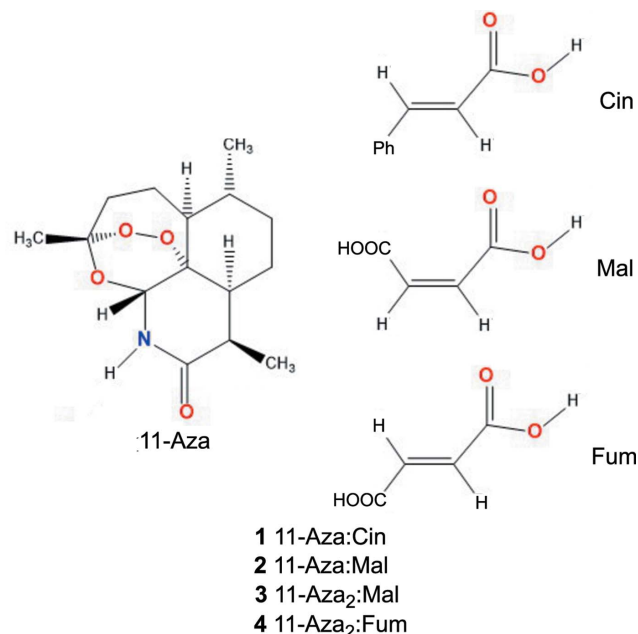
2. Experimental

2.1. Synthesis and crystallization

2.1.1. General procedure. Reagents and solvents used were of reagent grade (Sigma–Aldrich, Acros or TCI chemicals). 11-Aza was prepared according to the published method of Haynes *et al.* (2007b). All four new cocrystal phases, *i.e.* **1–4**, can be obtained in acceptable purity from liquid-assisted grinding (LAG), using a Tencan XQM-0.4A mini-planetary ball mill with zirconia vessels and media. A minimal amount of methanol (η factor = 0.2 ml g^{−1}) was used to accelerate the solid-state transformations, which took between 30 min and 2 h (Nisar *et al.*, 2018). The single crystals were grown by controlled evaporation at room temperature from methanolic solutions saturated with 11-Aza and containing excess acid to which a small amount of LAG-derived cocrystal powders were added to act as seeding nuclei for cocrystal growth and to suppress direct crystallization of the 11-Aza component itself. Elemental combustion analyses given below were carried out by Medac Ltd, Surrey, England.

2.1.2. 11-Aza:Cin, 1. 11-Azaartemisinin (140 mg, 0.5 mmol) and a slight excess of *trans*-cinnamic acid (80 mg, 0.55 mmol) were placed together in a vial and MeOH was added dropwise with shaking until all the solids were fully dissolved (*ca* 1.2 ml). The 0.4 M concentration represented the saturation

limit of 11-Aza in MeOH, though not for the acid. Micro-crystalline **1** (5 mg) derived from LAG was then added as seed nuclei. The vial was covered with Parafilm[®] punctured with pinholes to allow slow evaporation and left undisturbed. White plate-shaped crystals began to grow after a short time and were harvested after 2 d, filtered, washed with cold



Scheme 1

dioxane and dried, giving 45 mg of **1** (42% yield). A thin plate of dimensions 0.20 × 0.20 × 0.03 mm was selected for single-crystal X-ray diffraction. Elemental analysis found (calculated) for C₂₄H₃₁NO₆ (%): C 67.01 (67.11), H 7.23 (7.27), N 3.20 (3.26).

2.1.3. 11-Aza:Mal, 2. The preparation of **2** was the same as for **1**, but substituting maleic acid (58 mg, 0.5 mmol) and seeding with cocrystal powder **2** obtained from LAG of a 1:1 molar ratio of 11-Aza and maleic acid. The product was obtained after slow evaporation of the methanol to less than 50% of the original volume. Work-up produced colourless

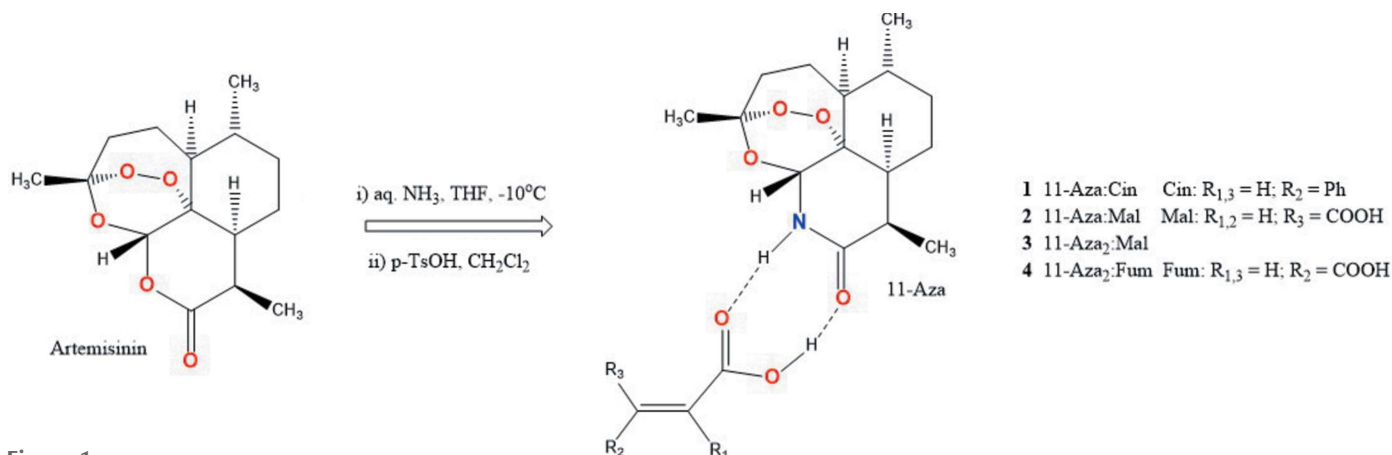


Figure 1

Synthetic scheme for the preparation of cocrystals **1–4**. The 2:1 cocrystals have a similar heterosynthon to a second 11-azaartemisinin *via* the R₂ or R₃ COOH group.

Table 1
Experimental details.

	1	2	3	4
Crystal data				
Chemical formula	C ₁₅ H ₂₃ NO ₄ ·C ₉ H ₈ O ₂	C ₁₅ H ₂₃ NO ₄ ·C ₄ H ₄ O ₄	2C ₁₅ H ₂₃ NO ₄ ·C ₄ H ₄ O ₄	2C ₁₅ H ₂₃ NO ₄ ·C ₄ H ₄ O ₄
<i>M_r</i>	429.50	397.41	678.76	678.76
Crystal system, space group	Triclinic, <i>P</i> 1	Orthorhombic, <i>P</i> 2 ₁ 2 ₁ 2 ₁	Orthorhombic, <i>P</i> 2 ₁ 2 ₁ 2 ₁	Monoclinic, <i>P</i> 2 ₁
Temperature (K)	100	100	100	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	9.5552 (4), 10.3175 (5), 11.9645 (6)	9.62162 (12), 10.40235 (11), 19.6935 (2)	9.7885 (1), 9.9965 (1), 33.7661 (4)	9.57929 (11), 10.05214 (16), 17.7765 (2)
α , β , γ (°)	91.085 (4), 110.515 (4), 93.998 (3)	90, 90, 90	90, 90, 90	90, 96.4731 (11), 90
<i>V</i> (Å ³)	1100.84 (9)	1971.08 (4)	3304.04 (6)	1700.82 (4)
<i>Z</i>	2	4	4	2
<i>D_x</i> (Mg m ^{−3})	1.296	1.339	1.365	1.325
Radiation type	Cu <i>K</i> α	Cu <i>K</i> α	Cu <i>K</i> α	Cu <i>K</i> α
μ (mm ^{−1})	0.76	0.88	0.86	0.83
Crystal size (mm)	0.20 × 0.20 × 0.03	0.40 × 0.40 × 0.35	0.20 × 0.20 × 0.10	0.40 × 0.15 × 0.12
Data collection				
Diffractometer		Rigaku SuperNova Dual Source diffractometer with an Atlas detector		
Absorption correction		Multi-scan (<i>CrysAlis PRO</i> ; Rigaku OD, 2015)		
<i>T_{min}</i> , <i>T_{max}</i>	0.934, 1.000	0.716, 1.000	0.973, 1.000	0.546, 1.000
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	16397, 7242, 6766	11105, 3504, 3466	9569, 5886, 5726	15361, 5657, 5564
<i>R_{int}</i>	0.032	0.019	0.021	0.024
(sin θ/λ) _{max} (Å ^{−1})	0.599	0.599	0.599	0.599
Refinement				
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.032, 0.077, 1.00	0.022, 0.056, 1.01	0.030, 0.075, 1.02	0.025, 0.066, 1.02
No. of reflections	7242	3504	5886	5657
No. of parameters	581	268	455	455
No. of restraints	3	0	0	1
H-atom treatment		H atoms treated by a mixture of independent and constrained refinement		
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ^{−3})	0.16, −0.18	0.18, −0.14	0.21, −0.18	0.15, −0.16
Absolute structure	Flack <i>x</i> determined using 2859 quotients [(<i>I</i> ⁺) − (<i>I</i> [−])]/[(<i>I</i> ⁺) + (<i>I</i> [−])] (Parsons <i>et al.</i> , 2013)	Flack <i>x</i> determined using 1483 quotients [(<i>I</i> ⁺) − (<i>I</i> [−])]/[(<i>I</i> ⁺) + (<i>I</i> [−])] (Parsons <i>et al.</i> , 2013)	Flack <i>x</i> determined using 2414 quotients [(<i>I</i> ⁺) − (<i>I</i> [−])]/[(<i>I</i> ⁺) + (<i>I</i> [−])] (Parsons <i>et al.</i> , 2013)	Flack <i>x</i> determined using 2330 quotients [(<i>I</i> ⁺) − (<i>I</i> [−])]/[(<i>I</i> ⁺) + (<i>I</i> [−])] (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	−0.05 (8)	−0.10 (4)	0.02 (7)	0.11 (6)

Computer programs: *CrysAlis PRO* (Rigaku OD, 2015), *SHELXS97* (Sheldrick, 2008), *SHELXL2014* (Sheldrick, 2015) and *OLEX2* (Dolomanov *et al.*, 2009; Borhuis *et al.*, 2009).

block-like crystals (35 mg) of **2** (35% yield). A specimen of dimensions 0.40 × 0.40 × 0.35 mm was selected for single-crystal X-ray diffraction. Elemental analysis found (calculated) for C₁₉H₂₇NO₈ (%): C 57.16 (57.42), H 6.77 (6.85), N 3.45 (3.52).

2.1.4. 11-Aza2:Mal, 3. The formation of single crystals of **3** can be directed by seeding with microcrystals of **3** formed by grinding a 2:1 molar stoichiometry of 11-Aza and maleic acid for *only 30 min*. Single crystals of **3** were formed by adding powdered **3** to a methanol solution formed by using the minimal amount of solvent to dissolve 11-Aza (0.5 mmol, 70 mg) and maleic acid (30 mg, 0.25 mmol). Suitable tablet-shaped specimens formed over a period of several days by Ostwald ripening and a crystal of approximate dimensions 0.2 × 0.2 × 0.1 mm was used for structure determination. However, after leaving the solutions to stand for several weeks, single crystals of **2** became the predominant solid phase, so harvesting should be carried out after 2 d. Elemental analysis found (calculated) for C₃₄H₅₀N₂O₁₂ (%): C 59.83 (60.16), H 7.36 (7.42), N 3.83 (4.13).

2.1.5. 11-Aza2:Fum, 4. The preparation of **4** was the same as for **1**, but substituting an excess of fumaric acid (30 mg,

0.25 mmol) and seeding with microcrystalline **4** obtained from a 2:1 ratio of 11-Aza and fumaric acid. The resulting white crystalline product was harvested as for **1** and dried, giving 52 mg of granular **4** (61% yield). A suitable colourless bar of dimensions 0.40 × 0.15 × 0.12 mm was selected for single-crystal X-ray diffraction. Elemental analysis found (calculated) for C₃₄H₅₀N₂O₁₂ (%): C 59.93 (60.16), H 7.33 (7.42), N 3.86 (4.13).

2.2. X-ray crystallography

Crystal data, data collection and structure refinement details are summarized in Table 1. Powder diffractograms were obtained on cocrystal powders at room temperature using Cu *K*α radiation using a PanAlytical X'Pert PRO diffractometer with a 1D X'celerator detector or a PanAlytical Aeris benchtop powder X-ray diffractometer. Single-crystal X-ray structure determinations of **1–4** were carried out at 100 K on a Rigaku Oxford Diffraction Supernova operating with a micro-focus Cu *K*α source and an Atlas detector, as reported previously (Wong *et al.*, 2017).

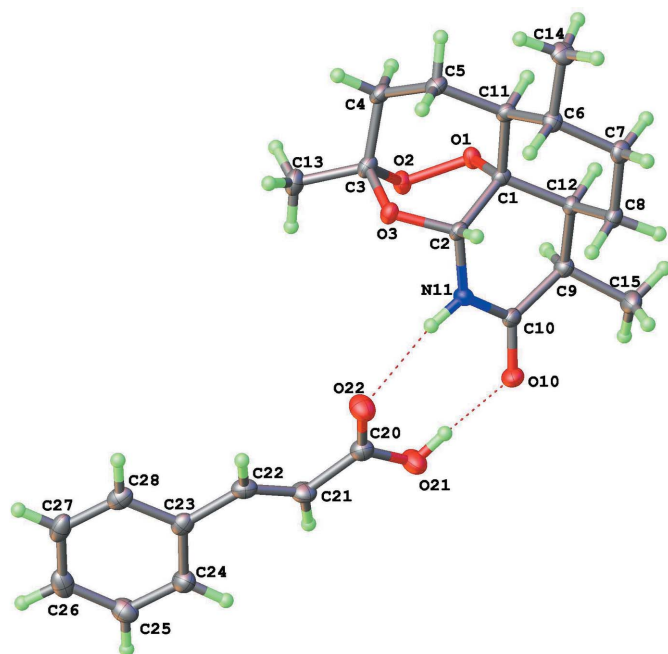


Figure 2
Displacement ellipsoid plot (50% probability) for 11-Aza:Cin, **1**, showing one molecular pair of the asymmetric unit.

Since the unit-cell origin is not defined in the space groups $P1$ or $P2_1$, overall restraints were applied to the atomic coordinates in structures **1** (x , y and z) and **4** (y). H atoms were placed geometrically and treated with riding constraints, and displacement parameters were derived from the C atoms to which they were attached. All CH and CH₂ groups had $U_{\text{iso}}(\text{H})$ values fixed at 1.2 times the U_{eq} value of the attached C atom. Methyl groups were idealized as freely rotating groups, with $U_{\text{iso}}(\text{H})$ values fixed at 1.5 times the U_{eq} value of the attached C atom. H atoms on N and O atoms of the lactam and acid groups were located in difference maps and were positionally refined with individual isotropic displacement parameters. All structures are enantiopure solids based on the incorporation of 11-Aza; the absolute structure parameters (Parsons *et al.*, 2013) of all three phases support the expected chirality.

2.3. Other characterization

$^1\text{H}\{^{13}\text{C}\}$ NMR spectra were recorded on a Bruker 400 MHz instrument to confirm the stoichiometry in the LAG-derived powders. Thermogravimetric analyses (TGA) were performed on a TA Instruments Q5000 SA thermogravimetric analyser. Details are available in the supporting information.

3. Results and discussion

3.1. Background and rationale

The development of pharmaceutical cocrystals as a method of improving drug formulation (Blagden *et al.*, 2014) has become a popular theme of crystal engineering, since a number of enhanced properties may result (Schultheiss &

Newman, 2009). The low aqueous solubility of the sesquiterpene artemisinins means they may be suitable targets for property enhancement by cocrystallization; however, screening of over 80 cocrystals with artemisinin itself yielded only two cocrystal products (Karki *et al.*, 2010).

Since 11-Aza is a lactam, we reasoned this may be more amenable to cocrystal formation, especially since amide–acid heterosynthons have been found in a number of cocrystal systems, notably including carbamazepine (Childs *et al.*, 2008). Recently, we reported that 11-Aza forms cocrystals with about 50% of 25 simple mono- and diacids screened, and the subsequent aqueous solubility of the resulting cocrystal typically improved in molarity by a factor of 3 (Nisar *et al.*, 2018). These 11-Aza–acid cocrystal phases were first identified by a liquid-assisted grinding (LAG) method (Trask & Jones, 2005). Full structural characterization was then carried out by single-crystal growth by either evaporation or solvent layer diffusion of a co-solution. The structures of seven cocrystals typically revealed an $R_2^2(8)$ heterosynthon was involved, with a short $\text{O}–\text{H} \cdots \text{O}=\text{C}$ hydrogen bond of around 2.60 Å from the acid to the keto O atom of the lactam (Nisar *et al.*, 2018). Furthermore, the specific volumes in the cocrystals at 100 K were all slightly contracted compared with those of the molecular components in the parent structures at the same temperature. The facile cocrystal formation supports the idea that when formed, such cocrystals are thermodynamically favoured at room temperature, consistent with the combination of stronger hydrogen bonding and more condensed solid phases. The failure to obtain cocrystals in the other half of cases presumably indicates that in these instances more energeti-

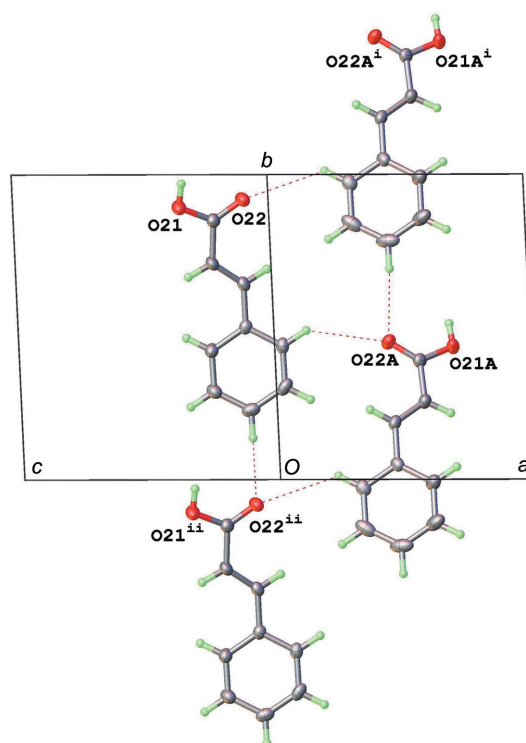


Figure 3
The packing of the cinnamic acid molecules in 11-Aza:Cin, **1**, viewed along [101] and showing the pseudo- 2_1 relationship along the b axis.

cally favourable packing arrangements than the parent structures cannot be found. The energetic driving forces for cocrystal formation have recently been discussed and found to be invariably thermodynamic, based on periodic DFT (density functional theory) calculations (Taylor & Day, 2018), where over 350 organic cocrystals were found on average to be 8 kJ mol^{-1} more stable than their coformers.

Although powder X-ray diffraction (PXRD) indicated that spontaneous cocrystal formation occurred for half the cases of the LAG experiments, solution-based single-crystal growth for these phases was not always facile due to the greatly differing solubility of the two components and the tendency for crystallization of 11-Aza in a number of systems. The cases of **1–4** were examined in more detail to attempt single-crystal formation by combining controlled evaporation with seeding from microcrystalline cocrystal powders previously obtained from LAG experiments.

3.2. Structure of 11-Aza:Cin, **1**

trans-Cinnamic acid (Cin) has been used as a cocrystal former with a number of amides, including its own amide derivative cinnamamide (Iwamoto & Kashino, 1990), and, since it is a GRAS (generally recognized as safe) compound, several notable pharmaceutical APIs (active pharmaceutical ingredients), such as isoniazid (Sarcevica *et al.*, 2013, 2014) have been prepared. Such amide cocrystals may exhibit $R_2^2(8)$ heterosynths, though not exclusively. For example, isonicotinamide–Cin cocrystals involve a pyridyl $\text{N} \cdots \text{HOOC}$ hydrogen bond (Aakeroy *et al.*, 2002) and in the Cin cocrystal with the API theophylline (Sarma & Saikia, 2014), a related but expanded $R_2^2(9)$ heterosynthon ring is found.

Phase-pure 11-Aza:Cin, **1**, is readily prepared from 11-Aza and *trans*-cinnamic acid by LAG as a fine microcrystalline powder, but sufficiently large single crystals for X-ray structure determination were only obtained after a number of attempts, including seeding, since the cocrystals typically formed very thin plates. A suitable specimen for crystal structure solution and refinement was finally found and gave an acceptable final discrepancy index $R_1 = 0.0315$ for the structure. The X-ray structure for **1** confirmed the expected 1:1 molecular stoichiometry. 11-Aza:Cin, **1**, was found to belong to the triclinic system; since 11-Aza is chiral, its incorporation requires the space group to be *P*1.

The unit-cell volume of $1100.8 \text{ \AA}^3$ indicates that two molecular pairs are found in each unit cell, which also comprises the asymmetric unit (*i.e.* both Z' and Z are 2). Fig. 2 shows one of the symmetry-independent molecular pairs, which are associated by a heterosynthon designated as $R_2^2(8)$ using the Etter graph-set notation (Etter *et al.*, 1990). These involve strong hydrogen bonds from the $\text{O21} \cdots \text{H21}$ group of the cinnamic acid to the lactam keto O10 atom of the 11-Aza molecules [$\text{O21} \cdots \text{O10} = 2.574(3) \text{ \AA}$ and $\text{O21A} \cdots \text{O10A} = 2.576(3) \text{ \AA}$]. These are augmented by a much weaker hydrogen bond from the $\text{N11} \cdots \text{H11}$ group to acid keto atom O22 . The $\text{N} \cdots \text{O}$ distances are $3.019(3)$ and $3.009(3) \text{ \AA}$ for the two molecular pairs. An overlay of the second molecular pair

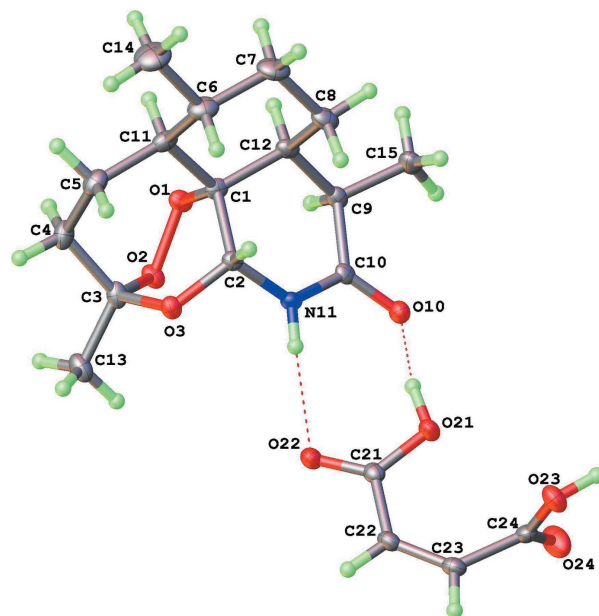


Figure 4
Displacement ellipsoid plot (50% probability) for 11-Aza:Mal, **2**, showing the heteromolecular $R_2^2(8)$ synthon.

(listed in the supplementary tables with suffix *A*) indicates a high level of geometric correspondence and so is not shown.

The carboxylic acid groups of the *trans*-cinnamic acid molecules are coplanar with the central $\text{C}=\text{C}$ double bonds; the torsion angle $\text{O22} \cdots \text{C21} \cdots \text{C22} \cdots \text{C23}$ is $0.0(5)^\circ$ [$2.8(5)^\circ$ for molecule *A*]. However, the phenyl rings are reasonably twisted from coplanarity with the alkene group, the $\text{C22} \cdots \text{C23} \cdots \text{C24} \cdots \text{C25}$ torsion angle being $20.3(4)^\circ$ [$22.8(4)^\circ$ for molecule *A*]. Both symmetry-independent cinnamic acid molecules have the same conformation, with the hydroxy O21 atom *anti* and the keto O22 atom *syn* with respect to the $\text{C}=\text{C}$

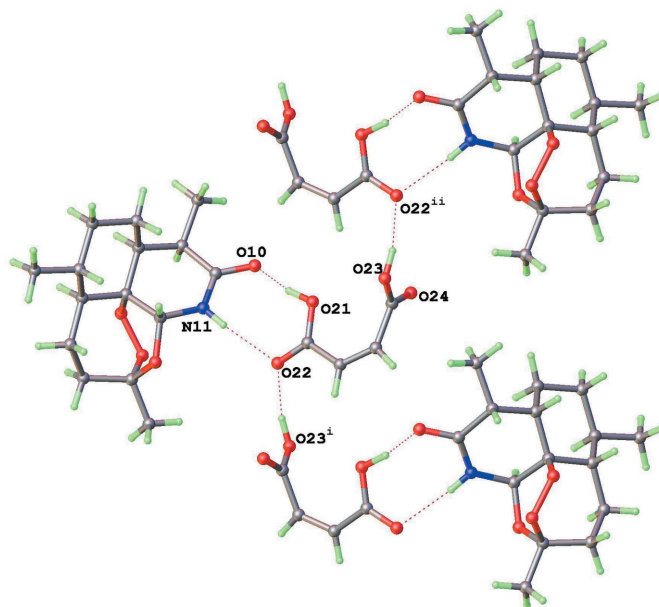


Figure 5
Screw-related molecular pairs for 11-Aza:Mal, **2**, showing the catenation of the maleic acid molecules.

double bond. Other key geometric parameters may be found in Tables S1–S4 of the supporting information.

Inspection of the packing for **1** indicates a pseudo- $P2_1$ relationship along the b axis for the independent molecular pairs, as illustrated in Fig. 3. The triclinic angles of $\alpha = 91.085$ (4)° and $\gamma = 93.998$ (3)° are considerably distorted from 90°, although a phase transition to monoclinic symmetry might be possible at higher temperature.

3.3. Structure of 11-Aza:Mal, **2**

Maleic acid is *cis*-butenedioic acid with a Z disposition of the acid groups about the central C=C bond. It has also been utilized in the cocrystal engineering of APIs, an example being the 1:1 cocrystal with the anti-HIV drug nevirapine (Caira *et al.*, 2012). The lactam functionality of this forms an $R_2^2(8)$ heterosynthon to one end of the maleic acid. Since maleic acid is a difunctional acid, a stoichiometry different to 11-Aza:Cin, **1**, might be anticipated. Two new cocrystal phases were formed from 11-Aza and maleic acid by LAG. The first came from a 1:1 reagent stoichiometry, whilst a different 2:1 phase could also be prepared by grinding with a stoichiometric excess of 11-Aza.

Attempts at single-crystal growth from solution typically required an excess of maleic acid in order to prevent precipitation of 11-Aza itself; however, the 2:1 phase was not formed. Eventually, a reasonably large block-like specimen was obtained of the 1:1 phase 11-Aza:Mal, **2**, based on seeding from powdered **2**. Cocrystals of **2** belong to the orthorhombic system with the space group $P2_12_12_1$. The crystal structure of **2** was solved and refined to $R_1 = 0.0220$ and includes one molecular pair per asymmetric unit, confirming the 1:1 molecular stoichiometry.

As expected, cocrystal **2** still retains the $R_2^2(8)$ heterosynthon found in **1** and the previous 11-Aza-acid cocrystals (Nisar *et al.*, 2018). As far as possible, an atomic labelling scheme corresponding to that for **1** has been used to assist comparison (see Table S1 in the supporting information) and the molecular pair of the asymmetric unit is shown in Fig. 4. Once again, the O21...O10 separation is very short [2.5428 (15) Å] and the N11...O22 distance is much longer [2.9118 (16) Å], though still shorter than the N(–H)...O distance found in 11-Aza itself of N11...O3' = 3.030 (5) Å (Nisar *et al.*, 2018).

Since maleic acid is difunctional, the other acid group is involved in forming hydrogen bonds to itself (Fig. 5). However, rather than forming homodimer rings of the $R_2^2(8)$ type, it is involved in self-catenation, which may be designated as $C(7)$ chains in the Etter graph-set notation, involving repetitively the atoms O22–C21–C22–C23–C24–O23–H23 along the backbone of each maleic acid molecule. The catenated O23–H23...O22 hydrogen bonds involve the screw-related molecules at $(-x + 1, y + \frac{1}{2}, -z + \frac{1}{2})$ along the b axis, with an O23...O22 separation of 2.6392 (15) Å.

The molecular conformation of the maleic acid once again has the C21 carboxylic acid group approximately coplanar with the C=C double bond. However, now the O22–C21–

C22–C23 torsion angle is 174.0 (2)°, meaning that the keto O22 atom is *anti* and the hydroxy O21 atom is *syn* with respect to the C=C double bond. Notably, the plane of the C24 carboxylic acid group is nearly perpendicular to the rest of the molecule, with a C22–C23–C24–O24 torsion angle of –80.7 (2)°.

3.4. Structure of 11-Aza₂:Mal, **3**

A suitable 2:1 maleic acid cocrystal was obtained with some difficulty since all attempts at growth from mixed 11-Aza-maleic acid solutions yielded the 1:1 phase. Grinding experiments clearly indicated that a second cocrystal phase existed in this system and solution ¹H NMR spectroscopy confirmed that the stoichiometry was 2:1. Larger crystals of the 1:1 phase, **2**, had been obtained using the ground powder as seed material by which to grow a larger single specimen by Ostwald ripening (Vorhees, 1985). In the case of 11-Aza₂:Mal, **3**, it was reasoned that starting with seeds of the 2:1 phase might afford sufficiently large single specimens of **3**, the growth of which would be in competition with dissolution and re-precipitation of **2**. In the event, addition of powdered phase **3** to saturated MeOH solutions allowed growth of sufficiently large single crystals after 2 d. After several weeks, growth of 1:1 cocrystals **2** was indeed also found.

Since the 2:1 form appeared metastable with respect to the 1:1 phase, it was of interest to compare their structures, especially given that **2** was not highly efficiently packed and was the only cocrystal we had examined to date with an expansion of specific volume compared to the parent compound phases. A small plate-like specimen of **3** was mounted and the structure determined with final $R_1 = 0.0296$. The crystal was confirmed to be the 2:1 phase, with $R_2^2(8)$ heterosynthons at each end of the maleic acid. The structure of the

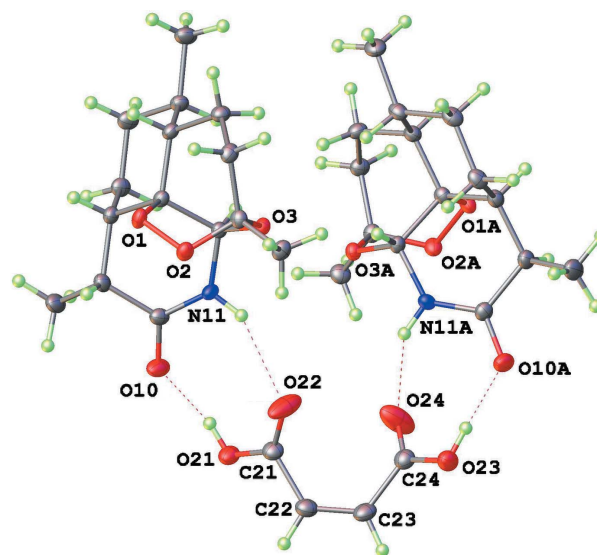


Figure 6
The molecular assembly of the asymmetric unit of 11-Aza₂:Mal, **3**, with pseudo-twofold symmetry. The second 11-Aza molecule has identical labels to the first, but with suffix A.

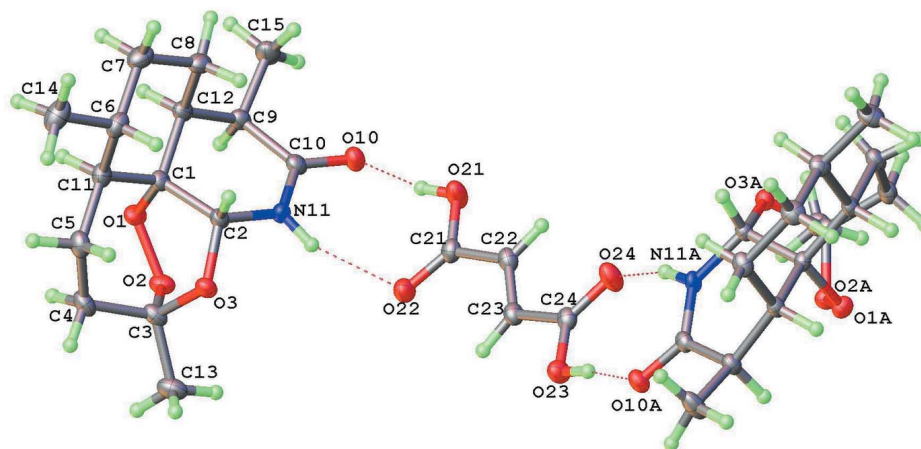


Figure 7

Displacement ellipsoid plot (50% probability) for asymmetric unit of 11-Aza₂:Fum, **4**. The atomic labelling for the second 11-azaartemisinin molecule has the same scheme, but with suffix *A*.

asymmetric unit in **3** is shown in Fig. 6 and comprises two 11-Aza and one maleic acid molecule arranged with a distorted twofold manner. The unit cell of **3** is orthorhombic in the space group $P2_12_12_1$, but with a pseudo-tetragonal arrangement. The *a* and *b* axes are metrically close [9.7885 (1) and 9.9965 (1) Å] and a similar packing is observed when the [100] and [010] directions are viewed. A room-temperature unit cell still showed significant, albeit smaller, differences between the *a*- and *b*-axis lengths. For tetragonal symmetry, a true crystallographic twofold axis would need to dissect the molecular assembly shown in Fig. 6, thus requiring a considerable molecular reorientation.

Several other notable features in the structure and packing can be seen compared to 1:1 phase **2**, in order to understand the origin of the metastability of **3**. Firstly, unlike the case of **2**, the packing has increased efficiency with a large net contraction, and secondly, the heterosynthons still contain very strong short O—H...O hydrogen bonds of 2.539 (2) and 2.548 (2) Å. These two features would seem to suggest that it should be **2** that is the metastable phase. However, a third and controlling issue is whether the molecular conformations found in the two phases are similar. In general, the molecular conformations of the 11-Aza molecules are highly constrained by their fused-ring systems and are essentially invariant between the parent compound and its various acid cocrystals. However, the structure of maleic acid in the parent acid and cocrystals **2** and **3** is much more variable.

In the parent compound, the carboxylic acid groups are both coplanar with the alkene group, thus promoting conjugation; however, one group is oriented to form a weaker intramolecular hydrogen bond to the other, so the hydrogen-bond energies in both cocrystals are favourable. In **2**, one COOH group of the maleic acid is coplanar with the alkene group, but the other is almost fully twisted (80°). This is apparently more stable, however, than having two half-twists of around 40° for each COOH group, as found in **3**, in which little stabilizing conjugation can occur.

The variable stoichiometry in cocrystals from such polyfunctional systems is not surprising. For example, in the

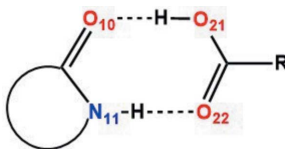
nicotinamide–fumaric acid system, both 1:1 and 1:2 cocrystals were obtained (Orola & Veidis, 2009), and in the carbamazepine–PABA system, several stoichiometries can be found, which notably did not greatly affect their solubility (Li & Matzger, 2016). Interestingly, in the caffeine–maleic acid cocrystal system, both 1:1 and 2:1 phases can be formed, again with the 1:1 form being more stable (Leyssens *et al.*, 2012). Although slightly different supramolecular synthons are involved in the caffeine cocrystals, the maleic acid conformations in the two phases are similar to the 11-Aza cases we report here.

3.5. Structure of 11-Aza₂:Fum, **4**

Fumaric acid is *trans*-butenedioic acid or the *E* isomer of maleic acid and is considerably more stable in the solid state. Once more it can form cocrystals with amides (Tothadi & Desiraju, 2012) and has been employed as a cocrystal former in the pharmaceutical formulation of amide-related compounds, such as carbamazepine (Rahim *et al.*, 2013), and the 1:1 cocrystal of acyclovir–fumaric acid (Yan *et al.*, 2013). Its density is 1.635 Mg m^{−3} and the melting/decomposition point a very high 287°C. This compares to the lower values of 1.59 Mg m^{−3} and 135°C for maleic acid. Accordingly, our expectation was that this inherent solid-state stability of the acid might prove problematic to its formation of cocrystals with 11-Aza. However, LAG experiments showed that a new PXRD pattern resulted after 2 h grinding in methanol.

Unlike maleic acid, the use of different reagent ratios of fumaric acid in the LAG experiments afforded only a single new phase, apparently with 2:1 stoichiometry, *i.e.* with two 11-Aza molecules per diacid. This 2:1 stoichiometry was the same as had been found previously by us for difunctional succinic, glutaric and pimelic acids (Nisar *et al.*, 2018). A single crystal of **4** with dimensions 0.40 × 0.15 × 0.12 mm was grown following our seeding procedure and was employed for single-crystal structure determination. Crystals of **4** belong to the monoclinic system with space group $P2_1$. Successful solution and refinement to $R_1 = 0.0254$ showed an asymmetric unit

Table 2

Geometry of lactam–acid $R_2^2(8)$ heterosynthons in **1–4**.


Cocrystal	O10...O21 (Å)	N11...O22 (Å)	Dihedral angle (°)
1	2.574 (3), 2.576 (3)	3.019 (3), 3.009 (3)	25.7 (2), 26.3 (2)
2	2.542 (2)	2.912 (2)	38.4 (2)
3	2.539 (2), 2.549 (2)	3.129 (3), 3.038 (3)	20.2 (2), 37.8 (2)
4	2.573 (2), 2.550 (2)	2.970 (2), 2.935 (2)	41.2 (2), 7.2 (2)

composed of two 11-Aza molecules and one fumaric acid molecule, confirming the 2:1 molecular stoichiometry (Fig. 7).

Each end of the fumaric acid molecule (atoms C21 and C24) is involved in symmetry-independent $R_2^2(8)$ heterosynthons to the two independent 11-Aza molecules, which are distinguished in the labelling scheme by suffix *A* for the second molecule, which is hydrogen bonded to the C24 carboxylic acid group. Unlike 2:1 maleic acid cocrystal **3**, the fumaric acid molecular conformation has both acid functionalities close to being coplanar with the central C=C bond. The hydroxy O21 and O23 atoms are *anti*, and the keto O22 and O24 atoms are *syn* with respect to the C=C double bond, which is the same as for cinnamic case **1**, but dissimilar to maleic acid cocrystal **2**. The hydrogen bonds of the $R_2^2(8)$ ring have short O...O distances of 2.573 (2) and 2.550 (2) Å, and long N...O distances of 2.970 (2) and 2.935 (2) Å, in keeping with the heterosynthons of the other cocrystals.

3.6. Geometry of heterosynthons

The key aspects of the geometry of the $R_2^2(8)$ heterosynthons found in **1–4** are summarized in Table 2. The O—H...O=C hydrogen bonds are very short intermolecular contacts and are slightly shorter than those found by us for saturated aliphatic acids, such as succinic, pimelic or L-malic. This presumably reflects the lower pK_a values of these alkenoic acids, which are more in line with benzoic and salicylic acid, which also have shorter O—H...O=C contacts. Short O—H...O=C distances below 2.50 Å have been found in $R_2^2(8)$ heterosynthons between fumaric and maleic acids with ureas (Jones *et al.*, 2014) and derivatives such as imidazolidin-2-one (Callea *et al.*, 2009). This can be attributed to the low

Table 4

Specific volumes for cocrystals **1–4** at 100 K.

Cocrystal	Acid Vol. ^a (Å ³)	Combined Vol. ^b (Å ³)	Cocrystal Vol. ^c (Å ³)	Diff. Specific Vol. ΔV (Å ³)
1 11-Aza:Cin	186.7	562.7	550.4	−12.3 (−2.2%)
2 11-Aza:Mal	115.7	491.7	492.8	+0.9 (+0.2%)
3 11-Aza ₂ :Mal	115.7	867.7	826.0	−41.7 (−4.8%)
4 11-Aza ₂ :Fum	113.3	865.3	850.4	−14.9 (−1.7%)

Notes: (a) acid volumes from unit cells measured at 100 K (see Table 3); (b) specific volume of 376.0 Å³ for 11-azaartemisinin at 100 K (Nisar *et al.*, 2018); (c) corresponding combined volume from cocrystal structures **1–4**.

pK_a values of the acids combined with the relatively high keto basicity in such nitrogen compounds.

The lactam N—H...O=C hydrogen bonds are much weaker and the N...O separations are more variable, but are usually around 2.9–3.0 Å. The hydrogen bonding in the heterosynthons appears to be a key driving force for cocrystal formation. The $R_2^2(8)$ heterosynthons have a nonplanar ring structure and the dihedral angles between the lactam NCO and acid OCO planes are listed in Table 2 and are typically 20–30°. This contrasts with the typical planar arrangement found in $R_2^2(8)$ homodimer synthons, as found involving two carboxylic acids.

In the structure of 11-Aza with other acids, we had found in each case a contraction in the specific volume of the cocrystal with respect to the parent coformers. The structures of **1–4** allow a similar determination to be made and details are given in Tables 3 and 4.

In Table 3, the unit cells of cocrystals **1–4** at 100 K are compared to those of the parent molecules. The crystal structures of 11-Aza (Nisar *et al.*, 2018) and *trans*-cinnamic acid (Howard *et al.*, 2009) at 100 K were determined previously. The maleic and fumaric acid unit cells were determined by us at 100 K (see supporting information) to assist the comparison of the specific volumes given in Table 4.

The results are reasonably consistent with those found by us for seven other 11-Aza–acid cocrystals, with a modest contraction in the cocrystals over the parent coformer crystals. In the case of **2**, however, a very slight (0.2%) expansion is found. As discussed above, much stronger hydrogen bonding in the cocrystal of **2** compared to 11-Aza and maleic acid still favours its formation. Surprisingly, the largest contraction, implying greater packing efficiency, is found for 11-Aza₂:Mal, **3**, which shows a contraction in volume of −4.8%. It appears that the large change in molecular conformation and the loss

Table 3

Unit cells for coformers and cocrystals **1–4**, all at 100 K.

Compound	<i>a</i>	<i>b</i>	<i>c</i>	α	β	γ	<i>V</i>	<i>Z</i>	Mol. Vol.	Reference
11-Azaartemisinin	11.718	11.718	9.487	90	90	120	1128.1	3	376.0	Nisar <i>et al.</i> (2018)
<i>trans</i> -Cinnamic acid	5.5504	17.5427	7.7161	90	96.30	90	746.78	4	186.7	Howard <i>et al.</i> (2009)
1 11-Aza:Cin	9.555	10.318	11.964	91.08	110.52	94.00	1100.8	2	550.4	This work
Maleic acid	6.934	10.061	7.481	90	117.53	90	462.8	4	115.7	This work
2 11-Aza:Mal	9.6216	10.4024	19.6935	90	90	90	1971.1	4	492.8	This work
3 11-Aza ₂ :Mal	9.7885	9.9965	33.766	90	90	90	3304.0	4	826.0	This work
Fumaric acid	7.612	14.870	6.446	90	111.30	90	680.0	6	113.3	This work
4 11-Aza ₂ :Fum	9.579	10.052	17.776	90	96.47	90	1700.8	2	850.4	This work

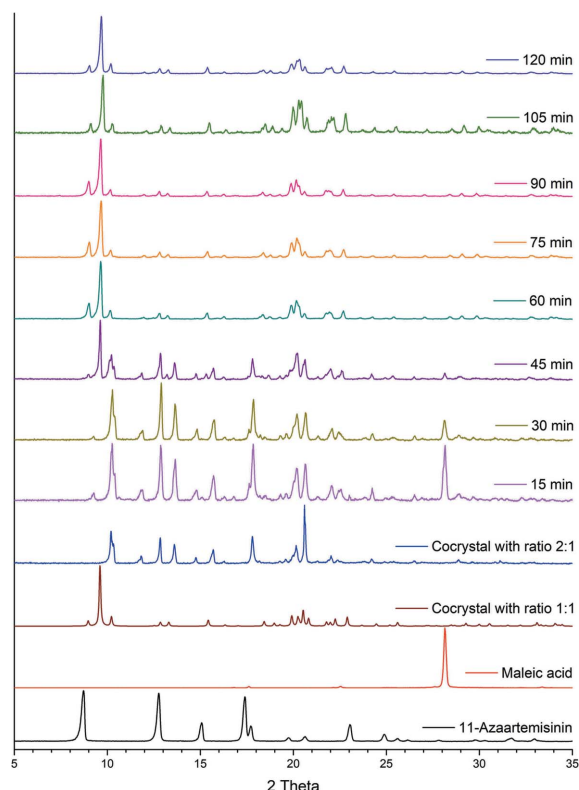


Figure 8
Experimental PXRD diffractograms of LAG products from grinding 11-Aza and maleic acid in a 1:1 ratio for different times *versus* patterns simulated from the starting and product phases.

of π -conjugation for the maleic acid molecule in the cococrystal of **3**, as compared to **2**, is the likely reason for the apparent metastability of the more efficiently packed 2:1 phase.

3.7. LAG results in the 11-aza–maleic acid system

So far, the maleic acid system is the only one in which we have found evidence for two cococrystal phases with 11-azaartemisinin. We report herein a more detailed analysis of the LAG results in this system that support the contention that 2:1 is a metastable phase. In Fig. 8, plots of grinding with a 1:1 ratio over different times are shown. For a 1:1 ratio, 2:1 phase **3** is initially formed and all the 11-Aza is rapidly used up, but leaving some unreacted maleic acid solid. Phase **3** predominates for the first 30 min, but gradually the residual maleic acid peaks disappear and after 1 h and longer times essentially the phase-pure 1:1 phase **2** is obtained. If a 2:1 initial ratio is used, then once again the 2:1 phase is rapidly formed and this time it is phase pure. However, after 90 min and above, this starts to be contaminated with 1:1 phase **2**. No crystalline peaks for 11-Aza are observed, although the excess compound must be lost from phase **3**.

For completeness, the LAG results from the *trans*-cinnamic and fumaric acid systems are also presented in the supporting information, along with the ^1H NMR spectra, showing the integration of peaks from the various stoichiometric cococrystal solids.

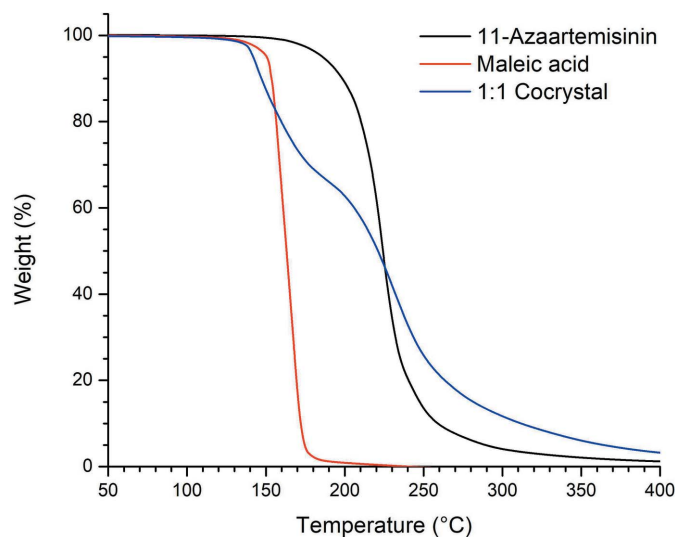


Figure 9
TGA overlay of 11-azaartemisinin, coformer (maleic acid) and cococrystal **2**, *i.e.* 11-Aza:Mal, heated at a rate of $10^\circ\text{C min}^{-1}$ under N_2 .

3.8. Properties of cococrystals 1–4

Some preliminary studies of the solubility of 11-Aza cococrystals with various acids has been carried out and typically a 2–3 $\times$ increase in molarity is found after 12 h stirring of the solution. Despite its high melting/decomposition temperature, fumaric acid has an aqueous solubility of 0.49 g/100 ml, 10 $\times$ less than its *cis* isomer maleic acid, but this is still considerably higher than 11-azaartemisinin. Regarding stability, the thermogravimetric analysis (TGA) of the cococrystals indicates that they are superior to existing artemisinin-based medicines (Haynes *et al.*, 2007*a*), much of which is due to the inherent stability of 11-Aza itself (Haynes *et al.*, 2007*b*), as shown in Fig. 9 for cococrystal **2**.

The antimalarial activity of 11-Aza and its sulfonyl derivatives, including against drug-resistant *plasmodium* strains and asexual parasitic stages, are highly promising (Harmse *et al.*, 2017). Related activity studies on these and other cococrystals of 11-Aza are currently under investigation and will be reported in the near future.

4. Conclusions

The facile and high-yield phase-pure synthesis of cococrystals of three alkenoic acids with 11-azaartemisinin was achieved by LAG and the microcrystalline powders formed were successful in seeding single-crystal growth. The resulting crystal structures of 11-Aza:Cin (**1**), 11-Aza:Mal (**2**), 11-Aza₂:Mal (**3**) and 11-Aza₂:Fum (**4**) show preserved $R_2^2(8)$ lactam–acid heterosynths. The conjugation of the alkene π -systems and the low $\text{p}K_a$ values of the acid lead to very short O–H $\cdots$ O hydrogen bonds, with values all well below 2.60 Å. The N–H $\cdots$ O hydrogen-bond components of the synths are weaker, but typically shorter than that found in 11-Aza itself. In most cases, the specific volume of the molecular cococrystals is contracted compared to the values for the parent

compounds measured at the same temperature. Interestingly, however, 11-Aza:Mal cocrystal **2** has a slight expansion in the specific volume (+0.2%) over its parent components, whereas 2:1 cocrystal 11-Aza₂:Mal **3** is greatly contracted (−4.8%). In spite of this, 1:1 form **2** is favoured over **3** either in grinding or solution crystallizations over longer time periods. The metastability of phase **3** may be due to a higher conformational energy for the maleic acid molecule in its structure.

Disclaimer

Any opinions, findings and conclusions, or recommendations expressed in this material are those of the authors and therefore the SA NRF does not accept any liability in regard thereto.

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References

- Aakeroy, C. B., Beatty, A. M. & Helfrich, B. A. (2002). *J. Am. Chem. Soc.* **124**, 14425–14432.
- Blagden, N., Coles, S. J. & Berry, D. J. (2014). *CrystEngComm*, **16**, 5753–5761.
- Bourhis, L. J., Dolomanov, O. V., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2015). *Acta Cryst.* **A71**, 59–75.
- Caira, M. R., Bourne, S. A., Samsodien, H., Engel, E., Liebenberg, W., Stieger, N. & Aucamp, M. (2012). *CrystEngComm*, **14**, 2541–2551.
- Callear, S. K., Hursthouse, M. B. & Threlfall, T. L. (2009). *CrystEngComm*, **11**, 1609–1614.
- Childs, S. L., Rodriguez-Hornedo, N., Reddy, L. S., Jayasankar, A., Maheshwari, C., McCausland, L., Shipplett, R. & Stahly, B. C. (2008). *CrystEngComm*, **10**, 856–864.
- Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
- Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* **B46**, 256–262.
- Harmse, R., Coertzen, D., Wong, H. N., Smit, F. J., van der Watt, M. E., Reader, J., Nondaba, S. H., Birkholz, L.-M., Haynes, R. K. & N'Da, D. (2017). *ChemMedChem*, **12**, 2086–2093.
- Harmse, R., Wong, H. N., Smit, F., Haynes, R. K. & N'Da, D. D. (2015). *Curr. Med. Chem.* **22**, 3607–3630.
- Haynes, R. K., Chan, H. W., Lung, C. M., Ng, N. C., Wong, H. N., Shek, L. Y., Williams, I. D., Gomes, M. F. & Cartwright, A. (2007a). *ChemMedChem*, **2**, 1448–1463.
- Haynes, R. K., Wong, H. N., Lee, K. W., Lung, C. M., Shek, L. Y., Williams, I. D., Croft, S. L., Vivas, L., Rattray, L., Stewart, L., Wong, V. K. W. & Ko, B. C. B. (2007b). *ChemMedChem*, **2**, 1464–1479.
- Howard, J. A. K., Mahon, M. F., Raithby, P. R. & Sparkes, H. A. (2009). *Acta Cryst.* **B65**, 230–237.
- Iwamoto, T. & Kashino, S. (1990). *Acta Cryst.* **C46**, 686–688.
- Jones, A. O. F., Leech, C. K., McIntyre, G. J., Wilson, C. C. & Thomas, L. H. (2014). *CrystEngComm*, **16**, 8177–8184.
- Karki, S., Friscic, T., Fabian, L. & Jones, W. (2010). *CrystEngComm*, **12**, 4038–4041.
- Klayman, D. L. (1985). *Science*, **228**, 1049–1055.
- Leyssens, T., Springuel, G., Montis, R., Candoni, N. & Veesler, S. (2012). *Cryst. Growth Des.* **12**, 1520–1530.
- Li, Z. & Matzger, A. J. (2016). *Mol. Pharm.* **13**, 990–995.
- Mbengue, A., Bhattacharjee, S., Pandharkar, T., Liu, H., Estiu, G., Stahelin, R. V., Rizk, S. S., Njimoh, D. L., Ryan, Y., Chotivanich, K., Nguon, C., Ghorbal, M., Lopez-Rubio, J.-J., Pfrender, M., Emrich, S., Mohandas, N., Dondorp, A. M., Wiest, O. & Haldar, K. (2015). *Nature*, **520**, 683–687.
- Mekonnen, B. & Ziffer, H. (1997). *Tetrahedron Lett.* **38**, 731–734.
- Nisar, M., Sung, H. H.-Y., Puschmann, H., Lakerveld, R., Haynes, R. K. & Williams, I. D. (2018). *CrystEngComm*, **20**, 1205–1219.
- Orola, L. & Veidis, M. V. (2009). *CrystEngComm*, **11**, 415–417.
- Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst.* **B69**, 249–259.
- Rahim, S. A., Hammond, R. B., Sheikh, A. Y. & Roberts, K. J. (2013). *CrystEngComm*, **15**, 3862–3873.
- Rigaku OD (2015). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, Oxfordshire, England.
- Sarcevic, I., Orola, L., Veidis, M. V. & Belyakov, S. (2014). *Acta Cryst.* **C70**, 392–395.
- Sarcevic, I., Orola, L., Veidis, M. V., Podjava, A. & Belyakov, S. (2013). *Cryst. Growth Des.* **13**, 1082–1090.
- Sarma, B. & Saikia, B. (2014). *CrystEngComm*, **16**, 4753–4765.
- Schultheiss, N. & Newman, A. (2009). *Cryst. Growth Des.* **9**, 2950–2967.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Sheldrick, G. M. (2015). *Acta Cryst.* **C71**, 3–8.
- Taylor, C. R. & Day, G. M. (2018). *Cryst. Growth Des.* **18**, 892–904.
- Torok, D. S. & Ziffer, H. (1995). *Tetrahedron Lett.* **36**, 829–832.
- Tothadi, S. & Desiraju, G. R. (2012). *Cryst. Growth Des.* **12**, 6188–6198.
- Trask, A. V. & Jones, W. (2005). *Top. Curr. Chem.* **254**, 41–70.
- Vorhees, P. W. (1985). *J. Stat. Phys.* **38**, 231–252.
- Wong, L. W. Y., Kan, J. W. H., Sung, H. H. Y. & Williams, I. D. (2017). *Acta Cryst.* **C73**, 625–631.
- Yan, Y., Chen, J. M. & Lu, T. B. (2013). *CrystEngComm*, **15**, 6457–6460.

supporting information

Acta Cryst. (2018). C74, 742-751 [https://doi.org/10.1107/S2053229618006320]

Cocrystals of the antimalarial drug 11-azartemisinin with three alkenoic acids of 1:1 or 2:1 stoichiometry

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Computing details

For all structures, data collection: *CrysAlis PRO* (Rigaku OD, 2015); cell refinement: *CrysAlis PRO* (Rigaku OD, 2015); data reduction: *CrysAlis PRO* (Rigaku OD, 2015); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

1,5,9-Trimethyl-14,15,16-trioxa-11-azatetracyclo[10.3.1.0^{4,13}.0^{8,13}]hexadecan-10-one-(2*E*)-3-Phenylprop-2-enoic acid (1/1) (madiha47cult)

Crystal data

C₁₅H₂₃NO₄·C₉H₈O₂

M_r = 429.50

Triclinic, *P*1

a = 9.5552 (4) Å

b = 10.3175 (5) Å

c = 11.9645 (6) Å

α = 91.085 (4)°

β = 110.515 (4)°

γ = 93.998 (3)°

V = 1100.84 (9) Å³

Z = 2

F(000) = 460

D_x = 1.296 Mg m⁻³

Cu *K*α radiation, λ = 1.54184 Å

Cell parameters from 8241 reflections

θ = 3.9–75.3°

μ = 0.76 mm⁻¹

T = 100 K

Plate, colourless

0.2 × 0.2 × 0.03 mm

Data collection

Rigaku SuperNova Dual Source

diffractometer with an Atlas detector

Radiation source: micro-focus sealed X-ray

tube, SuperNova (Cu) X-ray Source

Mirror monochromator

Detector resolution: 10.3577 pixels mm⁻¹

ω scans

Absorption correction: multi-scan

(*CrysAlis PRO*; Rigaku OD, 2015)

T_{min} = 0.934, *T_{max}* = 1.000

16397 measured reflections

7242 independent reflections

6766 reflections with *I* > 2σ(*I*)

R_{int} = 0.032

$\theta_{\max}$ = 67.5°, $\theta_{\min}$ = 4.0°

h = −11→11

k = −12→12

l = −14→14

Refinement

Refinement on *F*²

Least-squares matrix: full

R [*F*² > 2σ(*F*²)] = 0.032

wR(*F*²) = 0.077

S = 1.00

7242 reflections

581 parameters

3 restraints

Primary atom site location: structure-invariant
direct methods

Hydrogen site location: mixed
 H atoms treated by a mixture of independent
 and constrained refinement
 $w = 1/[\sigma^2(F_o^2) + (0.042P)^2 + 0.0075P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.16 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.18 \text{ e } \text{\AA}^{-3}$
 Absolute structure: Flack x determined using
 2859 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et*
al., 2013)
 Absolute structure parameter: -0.05 (8)

Special details

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.

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	0.92939 (18)	0.23922 (16)	0.90910 (15)	0.0179 (4)
O2	0.93313 (19)	0.10373 (16)	0.86936 (16)	0.0196 (4)
O3	0.83959 (18)	0.13856 (16)	0.66720 (15)	0.0181 (4)
O10	0.44598 (19)	0.11831 (17)	0.79596 (17)	0.0231 (4)
N11	0.6261 (2)	0.1556 (2)	0.71765 (19)	0.0178 (4)
H11	0.584 (3)	0.088 (3)	0.665 (3)	0.023 (8)*
C1	0.8452 (2)	0.3157 (2)	0.8100 (2)	0.0156 (5)
C2	0.7533 (2)	0.2275 (2)	0.7011 (2)	0.0162 (5)
H2	0.7124	0.2849	0.6326	0.019*
C3	0.9700 (3)	0.1068 (3)	0.7645 (2)	0.0199 (5)
C4	1.1033 (3)	0.2056 (2)	0.7772 (2)	0.0209 (5)
H4A	1.1661	0.2179	0.8628	0.025*
H4B	1.1652	0.1688	0.7351	0.025*
C5	1.0595 (3)	0.3376 (3)	0.7283 (2)	0.0204 (5)
H5A	1.0066	0.3259	0.6409	0.024*
H5B	1.1525	0.3942	0.7417	0.024*
C6	0.8854 (3)	0.5194 (2)	0.7022 (2)	0.0186 (5)
H6	0.8259	0.4804	0.6207	0.022*
C7	0.7788 (3)	0.5856 (2)	0.7506 (2)	0.0206 (5)
H7A	0.8381	0.6343	0.8264	0.025*
H7B	0.7257	0.6490	0.6928	0.025*
C8	0.6634 (3)	0.4898 (2)	0.7727 (2)	0.0199 (5)
H8A	0.5975	0.4463	0.6961	0.024*
H8B	0.6002	0.5373	0.8070	0.024*
C9	0.6359 (3)	0.2899 (2)	0.8923 (2)	0.0191 (5)
H9	0.7003	0.2458	0.9637	0.023*
C10	0.5617 (2)	0.1829 (2)	0.7963 (2)	0.0178 (5)
C11	0.9596 (3)	0.4090 (2)	0.7818 (2)	0.0170 (5)
H11B	1.0273	0.4513	0.8597	0.020*
C12	0.7417 (3)	0.3877 (2)	0.8588 (2)	0.0160 (5)
H12	0.8072	0.4358	0.9345	0.019*
C13	0.9972 (3)	-0.0316 (3)	0.7412 (3)	0.0254 (6)
H13A	0.9165	-0.0906	0.7490	0.038*

H13B	1.0935	−0.0525	0.7992	0.038*
H13C	0.9992	−0.0418	0.6601	0.038*
C14	1.0053 (3)	0.6191 (2)	0.6906 (3)	0.0251 (6)
H14A	1.0755	0.6477	0.7703	0.038*
H14B	0.9573	0.6941	0.6491	0.038*
H14C	1.0598	0.5792	0.6449	0.038*
C15	0.5199 (3)	0.3540 (3)	0.9310 (3)	0.0275 (6)
H15A	0.4472	0.3911	0.8618	0.041*
H15B	0.5703	0.4233	0.9920	0.041*
H15C	0.4677	0.2888	0.9642	0.041*
O1A	0.30814 (19)	0.69183 (16)	−0.03903 (15)	0.0186 (4)
O2A	0.30912 (19)	0.55827 (16)	0.00256 (16)	0.0188 (4)
O3A	0.39526 (18)	0.61595 (17)	0.20465 (15)	0.0180 (4)
O10A	0.7903 (2)	0.64839 (19)	0.08281 (18)	0.0258 (4)
N11A	0.6093 (2)	0.6674 (2)	0.15962 (19)	0.0179 (4)
H11A	0.651 (3)	0.607 (3)	0.213 (3)	0.023 (8)*
C1A	0.3856 (3)	0.7863 (2)	0.0603 (2)	0.0164 (5)
C2A	0.4764 (2)	0.7184 (2)	0.1714 (2)	0.0156 (5)
H2A	0.5116	0.7852	0.2392	0.019*
C3A	0.2687 (3)	0.5581 (2)	0.1054 (2)	0.0196 (5)
C4A	0.1311 (3)	0.6335 (2)	0.0908 (2)	0.0208 (5)
H4AA	0.0684	0.6309	0.0050	0.025*
H4AB	0.0711	0.5885	0.1334	0.025*
C5A	0.1666 (3)	0.7751 (3)	0.1370 (2)	0.0217 (5)
H5AA	0.2191	0.7767	0.2246	0.026*
H5AB	0.0707	0.8147	0.1221	0.026*
C6A	0.3256 (3)	0.9885 (2)	0.1586 (2)	0.0198 (5)
H6A	0.3835	0.9660	0.2422	0.024*
C7A	0.4308 (3)	1.0683 (2)	0.1120 (2)	0.0227 (6)
H7AA	0.4767	1.1444	0.1677	0.027*
H7AB	0.3720	1.1013	0.0337	0.027*
C8A	0.5556 (3)	0.9919 (2)	0.0976 (2)	0.0196 (5)
H8AA	0.6199	0.9640	0.1765	0.024*
H8AB	0.6189	1.0482	0.0650	0.024*
C9A	0.6023 (3)	0.7924 (2)	−0.0146 (2)	0.0195 (5)
H9A	0.5441	0.7368	−0.0878	0.023*
C10A	0.6747 (3)	0.6990 (2)	0.0810 (2)	0.0195 (5)
C11A	0.2621 (3)	0.8603 (2)	0.0832 (2)	0.0174 (5)
H11C	0.1933	0.8849	0.0034	0.021*
C12A	0.4872 (3)	0.8725 (2)	0.0131 (2)	0.0168 (5)
H12A	0.4218	0.9051	−0.0644	0.020*
C13A	0.2480 (3)	0.4165 (3)	0.1288 (3)	0.0236 (6)
H13D	0.3356	0.3728	0.1285	0.035*
H13E	0.1580	0.3761	0.0663	0.035*
H13F	0.2369	0.4086	0.2068	0.035*
C14A	0.1971 (3)	1.0681 (3)	0.1616 (3)	0.0254 (6)
H14D	0.1365	1.0885	0.0800	0.038*
H14E	0.2385	1.1491	0.2096	0.038*

H14F	0.1340	1.0175	0.1972	0.038*
C15A	0.7206 (3)	0.8741 (3)	−0.0468 (3)	0.0289 (6)
H15D	0.7862	0.9263	0.0237	0.043*
H15E	0.6712	0.9319	−0.1104	0.043*
H15F	0.7803	0.8167	−0.0747	0.043*
O21	0.3439 (2)	−0.1075 (2)	0.69320 (19)	0.0321 (5)
H21	0.375 (4)	−0.021 (4)	0.719 (3)	0.033 (9)*
O22	0.4631 (2)	−0.08116 (19)	0.56236 (19)	0.0302 (4)
C21	0.3923 (3)	−0.1499 (3)	0.6092 (3)	0.0241 (6)
C22	0.3549 (3)	−0.2909 (3)	0.5833 (3)	0.0255 (6)
H22	0.2991	−0.3361	0.6245	0.031*
C23	0.3953 (3)	−0.3579 (3)	0.5052 (2)	0.0228 (6)
H23	0.4416	−0.3098	0.4588	0.027*
C24	0.3750 (3)	−0.4995 (3)	0.4845 (2)	0.0214 (5)
C25	0.2707 (3)	−0.5764 (3)	0.5172 (3)	0.0259 (6)
H25	0.2044	−0.5358	0.5476	0.031*
C26	0.2623 (3)	−0.7104 (3)	0.5059 (3)	0.0284 (6)
H26	0.1913	−0.7611	0.5294	0.034*
C27	0.3575 (3)	−0.7713 (3)	0.4604 (3)	0.0285 (6)
H27	0.3532	−0.8635	0.4540	0.034*
C28	0.4586 (3)	−0.6963 (3)	0.4245 (2)	0.0279 (6)
H28	0.5223	−0.7374	0.3917	0.033*
C29	0.4677 (3)	−0.5616 (3)	0.4362 (2)	0.0238 (6)
H29	0.5375	−0.5112	0.4111	0.029*
O21A	0.8798 (2)	0.4353 (2)	0.1824 (2)	0.0307 (5)
H21A	0.852 (5)	0.523 (4)	0.157 (4)	0.053 (11)*
O22A	0.7572 (2)	0.4507 (2)	0.31047 (19)	0.0313 (5)
C21A	0.8306 (3)	0.3895 (3)	0.2653 (3)	0.0245 (6)
C22A	0.8714 (3)	0.2555 (3)	0.2932 (3)	0.0258 (6)
H22A	0.9327	0.2173	0.2562	0.031*
C23A	0.8256 (3)	0.1862 (3)	0.3683 (2)	0.0224 (6)
H23A	0.7725	0.2288	0.4102	0.027*
C24A	0.8507 (3)	0.0492 (3)	0.3915 (2)	0.0224 (6)
C25A	0.9668 (3)	−0.0103 (3)	0.3705 (3)	0.0304 (6)
H25A	1.0381	0.0409	0.3477	0.036*
C26A	0.9795 (4)	−0.1421 (3)	0.3823 (3)	0.0391 (8)
H26A	1.0587	−0.1809	0.3669	0.047*
C27A	0.8777 (4)	−0.2178 (3)	0.4163 (3)	0.0398 (8)
H27A	0.8851	−0.3090	0.4226	0.048*
C28A	0.7651 (4)	−0.1603 (3)	0.4412 (3)	0.0362 (7)
H28A	0.6962	−0.2118	0.4663	0.043*
C29A	0.7517 (3)	−0.0272 (3)	0.4298 (2)	0.0266 (6)
H29A	0.6746	0.0116	0.4482	0.032*

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0202 (8)	0.0152 (8)	0.0160 (9)	0.0040 (6)	0.0032 (7)	−0.0005 (7)

O2	0.0238 (9)	0.0156 (8)	0.0198 (9)	0.0046 (7)	0.0077 (7)	0.0005 (7)
O3	0.0175 (8)	0.0203 (9)	0.0169 (9)	0.0050 (7)	0.0062 (7)	−0.0007 (7)
O10	0.0192 (8)	0.0226 (9)	0.0303 (10)	−0.0013 (7)	0.0127 (8)	−0.0013 (8)
N11	0.0162 (9)	0.0182 (10)	0.0176 (10)	−0.0011 (8)	0.0050 (8)	−0.0019 (9)
C1	0.0133 (10)	0.0171 (12)	0.0159 (12)	0.0028 (9)	0.0041 (9)	0.0025 (10)
C2	0.0135 (10)	0.0181 (12)	0.0172 (12)	0.0034 (9)	0.0053 (9)	0.0013 (10)
C3	0.0183 (11)	0.0226 (13)	0.0206 (13)	0.0069 (10)	0.0079 (10)	0.0037 (10)
C4	0.0153 (11)	0.0242 (13)	0.0248 (14)	0.0042 (10)	0.0086 (10)	0.0011 (11)
C5	0.0167 (11)	0.0240 (13)	0.0225 (14)	0.0024 (9)	0.0093 (10)	0.0025 (10)
C6	0.0202 (12)	0.0175 (12)	0.0189 (12)	0.0030 (9)	0.0073 (10)	0.0031 (10)
C7	0.0221 (12)	0.0178 (12)	0.0224 (13)	0.0061 (10)	0.0076 (10)	0.0048 (10)
C8	0.0183 (11)	0.0194 (12)	0.0235 (13)	0.0056 (9)	0.0084 (10)	0.0009 (10)
C9	0.0183 (11)	0.0206 (12)	0.0195 (13)	0.0015 (9)	0.0080 (10)	−0.0007 (10)
C10	0.0151 (11)	0.0164 (12)	0.0219 (13)	0.0028 (9)	0.0063 (10)	0.0016 (10)
C11	0.0143 (11)	0.0191 (12)	0.0167 (12)	0.0023 (9)	0.0041 (9)	0.0008 (10)
C12	0.0159 (10)	0.0164 (11)	0.0169 (12)	0.0020 (9)	0.0072 (9)	−0.0005 (10)
C13	0.0274 (13)	0.0232 (14)	0.0282 (15)	0.0090 (10)	0.0117 (11)	0.0012 (11)
C14	0.0275 (13)	0.0187 (13)	0.0299 (15)	−0.0005 (10)	0.0115 (11)	0.0062 (11)
C15	0.0264 (13)	0.0266 (14)	0.0349 (16)	−0.0007 (11)	0.0185 (12)	−0.0060 (12)
O1A	0.0225 (8)	0.0158 (8)	0.0154 (9)	0.0020 (7)	0.0042 (7)	0.0003 (7)
O2A	0.0230 (8)	0.0137 (8)	0.0200 (9)	0.0023 (6)	0.0076 (7)	0.0012 (7)
O3A	0.0165 (8)	0.0191 (8)	0.0179 (9)	−0.0010 (6)	0.0056 (7)	0.0022 (7)
O10A	0.0205 (9)	0.0256 (9)	0.0369 (11)	0.0081 (7)	0.0155 (8)	0.0090 (8)
N11A	0.0146 (9)	0.0191 (10)	0.0196 (11)	0.0052 (8)	0.0046 (8)	0.0056 (9)
C1A	0.0153 (10)	0.0178 (12)	0.0149 (11)	0.0015 (9)	0.0037 (9)	−0.0013 (10)
C2A	0.0145 (11)	0.0168 (12)	0.0160 (12)	0.0009 (9)	0.0060 (9)	0.0025 (9)
C3A	0.0158 (11)	0.0220 (13)	0.0196 (13)	0.0002 (9)	0.0045 (10)	0.0008 (10)
C4A	0.0156 (11)	0.0214 (13)	0.0257 (14)	0.0009 (9)	0.0078 (10)	0.0030 (11)
C5A	0.0187 (11)	0.0217 (13)	0.0266 (14)	0.0040 (9)	0.0101 (10)	0.0003 (11)
C6A	0.0215 (12)	0.0182 (12)	0.0196 (12)	0.0031 (9)	0.0070 (10)	0.0003 (10)
C7A	0.0271 (13)	0.0173 (12)	0.0234 (14)	0.0021 (10)	0.0087 (11)	0.0005 (10)
C8A	0.0197 (12)	0.0178 (12)	0.0224 (13)	−0.0008 (9)	0.0091 (10)	0.0019 (10)
C9A	0.0197 (12)	0.0201 (12)	0.0208 (13)	0.0041 (10)	0.0091 (10)	0.0047 (10)
C10A	0.0174 (11)	0.0186 (12)	0.0230 (13)	0.0006 (9)	0.0077 (10)	0.0010 (10)
C11A	0.0163 (11)	0.0174 (12)	0.0181 (12)	0.0041 (9)	0.0051 (9)	0.0016 (10)
C12A	0.0189 (11)	0.0170 (12)	0.0155 (12)	0.0021 (9)	0.0070 (9)	0.0021 (10)
C13A	0.0221 (12)	0.0198 (13)	0.0276 (14)	0.0004 (10)	0.0073 (11)	0.0029 (11)
C14A	0.0313 (14)	0.0212 (13)	0.0273 (14)	0.0073 (11)	0.0138 (12)	−0.0003 (11)
C15A	0.0297 (14)	0.0271 (14)	0.0399 (17)	0.0081 (11)	0.0230 (13)	0.0129 (12)
O21	0.0354 (11)	0.0267 (11)	0.0385 (12)	−0.0072 (8)	0.0206 (9)	−0.0075 (9)
O22	0.0379 (11)	0.0247 (10)	0.0326 (11)	−0.0033 (8)	0.0192 (9)	0.0004 (9)
C21	0.0202 (12)	0.0253 (14)	0.0263 (14)	0.0009 (10)	0.0078 (11)	0.0004 (11)
C22	0.0243 (13)	0.0244 (14)	0.0297 (15)	−0.0040 (10)	0.0129 (11)	0.0018 (11)
C23	0.0185 (12)	0.0265 (14)	0.0223 (14)	−0.0011 (10)	0.0062 (11)	0.0039 (11)
C24	0.0191 (11)	0.0272 (14)	0.0165 (12)	0.0046 (10)	0.0040 (10)	0.0018 (10)
C25	0.0245 (13)	0.0269 (15)	0.0273 (15)	0.0001 (11)	0.0110 (11)	−0.0026 (12)
C26	0.0330 (15)	0.0264 (14)	0.0255 (15)	−0.0039 (11)	0.0111 (12)	0.0015 (12)
C27	0.0339 (14)	0.0236 (14)	0.0215 (14)	0.0076 (11)	0.0009 (11)	0.0000 (11)

C28	0.0254 (13)	0.0364 (16)	0.0208 (14)	0.0139 (11)	0.0047 (11)	−0.0005 (12)
C29	0.0198 (12)	0.0342 (15)	0.0169 (13)	0.0034 (10)	0.0055 (10)	0.0022 (11)
O21A	0.0329 (10)	0.0290 (11)	0.0409 (12)	0.0123 (8)	0.0238 (9)	0.0148 (9)
O22A	0.0369 (11)	0.0286 (11)	0.0368 (12)	0.0122 (9)	0.0213 (9)	0.0077 (9)
C21A	0.0181 (12)	0.0260 (14)	0.0289 (15)	0.0024 (10)	0.0076 (11)	0.0013 (11)
C22A	0.0264 (13)	0.0270 (14)	0.0282 (15)	0.0067 (10)	0.0141 (11)	0.0034 (11)
C23A	0.0179 (12)	0.0271 (14)	0.0216 (13)	0.0036 (10)	0.0061 (10)	−0.0015 (11)
C24A	0.0250 (13)	0.0254 (14)	0.0155 (12)	−0.0013 (10)	0.0063 (10)	0.0004 (10)
C25A	0.0374 (16)	0.0302 (15)	0.0284 (16)	0.0097 (12)	0.0162 (13)	0.0059 (12)
C26A	0.058 (2)	0.0341 (17)	0.0297 (16)	0.0186 (15)	0.0187 (15)	0.0044 (13)
C27A	0.066 (2)	0.0233 (15)	0.0205 (15)	0.0045 (14)	0.0036 (15)	0.0007 (12)
C28A	0.0427 (17)	0.0352 (17)	0.0198 (15)	−0.0128 (13)	0.0000 (13)	0.0062 (12)
C29A	0.0247 (13)	0.0337 (15)	0.0166 (13)	−0.0026 (11)	0.0025 (10)	0.0013 (11)

Geometric parameters (Å, °)

O1—O2	1.475 (2)	C5A—H5AB	0.9900
O1—C1	1.460 (3)	C5A—C11A	1.530 (4)
O2—C3	1.418 (3)	C6A—H6A	1.0000
O3—C2	1.418 (3)	C6A—C7A	1.514 (4)
O3—C3	1.439 (3)	C6A—C11A	1.547 (3)
O10—C10	1.249 (3)	C6A—C14A	1.535 (3)
N11—H11	0.90 (3)	C7A—H7AA	0.9900
N11—C2	1.455 (3)	C7A—H7AB	0.9900
N11—C10	1.328 (3)	C7A—C8A	1.531 (3)
C1—C2	1.530 (3)	C8A—H8AA	0.9900
C1—C11	1.536 (3)	C8A—H8AB	0.9900
C1—C12	1.536 (3)	C8A—C12A	1.531 (3)
C2—H2	1.0000	C9A—H9A	1.0000
C3—C4	1.536 (3)	C9A—C10A	1.515 (4)
C3—C13	1.508 (3)	C9A—C12A	1.541 (3)
C4—H4A	0.9900	C9A—C15A	1.524 (4)
C4—H4B	0.9900	C11A—H11C	1.0000
C4—C5	1.520 (4)	C12A—H12A	1.0000
C5—H5A	0.9900	C13A—H13D	0.9800
C5—H5B	0.9900	C13A—H13E	0.9800
C5—C11	1.541 (3)	C13A—H13F	0.9800
C6—H6	1.0000	C14A—H14D	0.9800
C6—C7	1.529 (3)	C14A—H14E	0.9800
C6—C11	1.545 (3)	C14A—H14F	0.9800
C6—C14	1.530 (4)	C15A—H15D	0.9800
C7—H7A	0.9900	C15A—H15E	0.9800
C7—H7B	0.9900	C15A—H15F	0.9800
C7—C8	1.525 (4)	O21—H21	0.93 (4)
C8—H8A	0.9900	O21—C21	1.324 (3)
C8—H8B	0.9900	O22—C21	1.220 (4)
C8—C12	1.530 (4)	C21—C22	1.474 (4)
C9—H9	1.0000	C22—H22	0.9500

C9—C10	1.520 (3)	C22—C23	1.329 (4)
C9—C12	1.536 (4)	C23—H23	0.9500
C9—C15	1.528 (3)	C23—C24	1.465 (4)
C11—H11B	1.0000	C24—C25	1.396 (4)
C12—H12	1.0000	C24—C29	1.398 (4)
C13—H13A	0.9800	C25—H25	0.9500
C13—H13B	0.9800	C25—C26	1.381 (4)
C13—H13C	0.9800	C26—H26	0.9500
C14—H14A	0.9800	C26—C27	1.389 (4)
C14—H14B	0.9800	C27—H27	0.9500
C14—H14C	0.9800	C27—C28	1.384 (4)
C15—H15A	0.9800	C28—H28	0.9500
C15—H15B	0.9800	C28—C29	1.388 (4)
C15—H15C	0.9800	C29—H29	0.9500
O1A—O2A	1.473 (2)	O21A—H21A	0.98 (4)
O1A—C1A	1.466 (3)	O21A—C21A	1.319 (4)
O2A—C3A	1.413 (3)	O22A—C21A	1.224 (3)
O3A—C2A	1.413 (3)	C21A—C22A	1.475 (4)
O3A—C3A	1.447 (3)	C22A—H22A	0.9500
O10A—C10A	1.248 (3)	C22A—C23A	1.328 (4)
N11A—H11A	0.90 (3)	C23A—H23A	0.9500
N11A—C2A	1.458 (3)	C23A—C24A	1.465 (4)
N11A—C10A	1.333 (4)	C24A—C25A	1.399 (4)
C1A—C2A	1.524 (3)	C24A—C29A	1.393 (4)
C1A—C11A	1.548 (3)	C25A—H25A	0.9500
C1A—C12A	1.528 (4)	C25A—C26A	1.379 (4)
C2A—H2A	1.0000	C26A—H26A	0.9500
C3A—C4A	1.533 (3)	C26A—C27A	1.381 (5)
C3A—C13A	1.505 (4)	C27A—H27A	0.9500
C4A—H4AA	0.9900	C27A—C28A	1.381 (5)
C4A—H4AB	0.9900	C28A—H28A	0.9500
C4A—C5A	1.524 (3)	C28A—C29A	1.392 (4)
C5A—H5AA	0.9900	C29A—H29A	0.9500
C1—O1—O2	111.60 (16)	C5A—C4A—H4AA	108.6
C3—O2—O1	107.83 (17)	C5A—C4A—H4AB	108.6
C2—O3—C3	113.49 (18)	C4A—C5A—H5AA	108.2
C2—N11—H11	115 (2)	C4A—C5A—H5AB	108.2
C10—N11—H11	117 (2)	C4A—C5A—C11A	116.3 (2)
C10—N11—C2	127.4 (2)	H5AA—C5A—H5AB	107.4
O1—C1—C2	110.92 (19)	C11A—C5A—H5AA	108.2
O1—C1—C11	107.09 (17)	C11A—C5A—H5AB	108.2
O1—C1—C12	104.17 (19)	C7A—C6A—H6A	108.1
C2—C1—C11	111.3 (2)	C7A—C6A—C11A	111.8 (2)
C2—C1—C12	110.68 (18)	C7A—C6A—C14A	110.4 (2)
C11—C1—C12	112.40 (19)	C11A—C6A—H6A	108.1
O3—C2—N11	108.92 (19)	C14A—C6A—H6A	108.1
O3—C2—C1	113.32 (18)	C14A—C6A—C11A	110.1 (2)

O3—C2—H2	107.3	C6A—C7A—H7AA	108.9
N11—C2—C1	112.5 (2)	C6A—C7A—H7AB	108.9
N11—C2—H2	107.3	C6A—C7A—C8A	113.4 (2)
C1—C2—H2	107.3	H7AA—C7A—H7AB	107.7
O2—C3—O3	108.00 (19)	C8A—C7A—H7AA	108.9
O2—C3—C4	112.4 (2)	C8A—C7A—H7AB	108.9
O2—C3—C13	104.8 (2)	C7A—C8A—H8AA	109.7
O3—C3—C4	110.2 (2)	C7A—C8A—H8AB	109.7
O3—C3—C13	107.2 (2)	C7A—C8A—C12A	109.8 (2)
C13—C3—C4	113.9 (2)	H8AA—C8A—H8AB	108.2
C3—C4—H4A	108.6	C12A—C8A—H8AA	109.7
C3—C4—H4B	108.6	C12A—C8A—H8AB	109.7
H4A—C4—H4B	107.6	C10A—C9A—H9A	105.8
C5—C4—C3	114.4 (2)	C10A—C9A—C12A	113.8 (2)
C5—C4—H4A	108.6	C10A—C9A—C15A	110.9 (2)
C5—C4—H4B	108.6	C12A—C9A—H9A	105.8
C4—C5—H5A	108.3	C15A—C9A—H9A	105.8
C4—C5—H5B	108.3	C15A—C9A—C12A	114.0 (2)
C4—C5—C11	116.1 (2)	O10A—C10A—N11A	120.7 (2)
H5A—C5—H5B	107.4	O10A—C10A—C9A	120.3 (2)
C11—C5—H5A	108.3	N11A—C10A—C9A	119.0 (2)
C11—C5—H5B	108.3	C1A—C11A—H11C	106.7
C7—C6—H6	108.1	C5A—C11A—C1A	112.5 (2)
C7—C6—C11	111.5 (2)	C5A—C11A—C6A	111.4 (2)
C7—C6—C14	110.5 (2)	C5A—C11A—H11C	106.7
C11—C6—H6	108.1	C6A—C11A—C1A	112.39 (19)
C14—C6—H6	108.1	C6A—C11A—H11C	106.7
C14—C6—C11	110.3 (2)	C1A—C12A—C8A	110.5 (2)
C6—C7—H7A	109.0	C1A—C12A—C9A	110.8 (2)
C6—C7—H7B	109.0	C1A—C12A—H12A	106.9
H7A—C7—H7B	107.8	C8A—C12A—C9A	114.6 (2)
C8—C7—C6	113.0 (2)	C8A—C12A—H12A	106.9
C8—C7—H7A	109.0	C9A—C12A—H12A	106.9
C8—C7—H7B	109.0	C3A—C13A—H13D	109.5
C7—C8—H8A	109.6	C3A—C13A—H13E	109.5
C7—C8—H8B	109.6	C3A—C13A—H13F	109.5
C7—C8—C12	110.37 (19)	H13D—C13A—H13E	109.5
H8A—C8—H8B	108.1	H13D—C13A—H13F	109.5
C12—C8—H8A	109.6	H13E—C13A—H13F	109.5
C12—C8—H8B	109.6	C6A—C14A—H14D	109.5
C10—C9—H9	106.1	C6A—C14A—H14E	109.5
C10—C9—C12	113.3 (2)	C6A—C14A—H14F	109.5
C10—C9—C15	111.1 (2)	H14D—C14A—H14E	109.5
C12—C9—H9	106.1	H14D—C14A—H14F	109.5
C15—C9—H9	106.1	H14E—C14A—H14F	109.5
C15—C9—C12	113.4 (2)	C9A—C15A—H15D	109.5
O10—C10—N11	121.1 (2)	C9A—C15A—H15E	109.5
O10—C10—C9	119.9 (2)	C9A—C15A—H15F	109.5

N11—C10—C9	118.9 (2)	H15D—C15A—H15E	109.5
C1—C11—C5	112.6 (2)	H15D—C15A—H15F	109.5
C1—C11—C6	112.55 (19)	H15E—C15A—H15F	109.5
C1—C11—H11B	106.7	C21—O21—H21	115 (2)
C5—C11—C6	111.1 (2)	O21—C21—C22	111.4 (2)
C5—C11—H11B	106.7	O22—C21—O21	123.9 (2)
C6—C11—H11B	106.7	O22—C21—C22	124.6 (3)
C1—C12—H12	106.9	C21—C22—H22	118.4
C8—C12—C1	110.7 (2)	C23—C22—C21	123.3 (3)
C8—C12—C9	114.8 (2)	C23—C22—H22	118.4
C8—C12—H12	106.9	C22—C23—H23	117.1
C9—C12—C1	110.25 (19)	C22—C23—C24	125.8 (3)
C9—C12—H12	106.9	C24—C23—H23	117.1
C3—C13—H13A	109.5	C25—C24—C23	122.2 (2)
C3—C13—H13B	109.5	C25—C24—C29	118.2 (2)
C3—C13—H13C	109.5	C29—C24—C23	119.5 (3)
H13A—C13—H13B	109.5	C24—C25—H25	119.5
H13A—C13—H13C	109.5	C26—C25—C24	121.1 (3)
H13B—C13—H13C	109.5	C26—C25—H25	119.5
C6—C14—H14A	109.5	C25—C26—H26	119.9
C6—C14—H14B	109.5	C25—C26—C27	120.2 (3)
C6—C14—H14C	109.5	C27—C26—H26	119.9
H14A—C14—H14B	109.5	C26—C27—H27	120.3
H14A—C14—H14C	109.5	C28—C27—C26	119.4 (3)
H14B—C14—H14C	109.5	C28—C27—H27	120.3
C9—C15—H15A	109.5	C27—C28—H28	119.7
C9—C15—H15B	109.5	C27—C28—C29	120.5 (3)
C9—C15—H15C	109.5	C29—C28—H28	119.7
H15A—C15—H15B	109.5	C24—C29—H29	119.8
H15A—C15—H15C	109.5	C28—C29—C24	120.5 (3)
H15B—C15—H15C	109.5	C28—C29—H29	119.8
C1A—O1A—O2A	111.33 (17)	C21A—O21A—H21A	116 (2)
C3A—O2A—O1A	108.75 (16)	O21A—C21A—C22A	111.6 (2)
C2A—O3A—C3A	113.09 (19)	O22A—C21A—O21A	123.5 (3)
C2A—N11A—H11A	115 (2)	O22A—C21A—C22A	124.9 (3)
C10A—N11A—H11A	117.7 (19)	C21A—C22A—H22A	118.8
C10A—N11A—C2A	127.8 (2)	C23A—C22A—C21A	122.5 (2)
O1A—C1A—C2A	111.0 (2)	C23A—C22A—H22A	118.8
O1A—C1A—C11A	106.24 (18)	C22A—C23A—H23A	117.5
O1A—C1A—C12A	103.84 (19)	C22A—C23A—C24A	125.1 (2)
C2A—C1A—C11A	111.1 (2)	C24A—C23A—H23A	117.5
C2A—C1A—C12A	111.35 (19)	C25A—C24A—C23A	122.2 (3)
C12A—C1A—C11A	113.0 (2)	C29A—C24A—C23A	119.5 (2)
O3A—C2A—N11A	107.88 (19)	C29A—C24A—C25A	118.2 (3)
O3A—C2A—C1A	114.55 (18)	C24A—C25A—H25A	119.5
O3A—C2A—H2A	107.3	C26A—C25A—C24A	121.1 (3)
N11A—C2A—C1A	112.2 (2)	C26A—C25A—H25A	119.5
N11A—C2A—H2A	107.3	C25A—C26A—H26A	119.9

C1A—C2A—H2A	107.3	C25A—C26A—C27A	120.3 (3)
O2A—C3A—O3A	108.09 (19)	C27A—C26A—H26A	119.9
O2A—C3A—C4A	112.7 (2)	C26A—C27A—H27A	120.2
O2A—C3A—C13A	104.8 (2)	C28A—C27A—C26A	119.5 (3)
O3A—C3A—C4A	109.4 (2)	C28A—C27A—H27A	120.2
O3A—C3A—C13A	107.5 (2)	C27A—C28A—H28A	119.7
C13A—C3A—C4A	114.0 (2)	C27A—C28A—C29A	120.5 (3)
C3A—C4A—H4AA	108.6	C29A—C28A—H28A	119.7
C3A—C4A—H4AB	108.6	C24A—C29A—H29A	119.8
H4AA—C4A—H4AB	107.5	C28A—C29A—C24A	120.3 (3)
C5A—C4A—C3A	114.8 (2)	C28A—C29A—H29A	119.8
O1—O2—C3—O3	−75.1 (2)	O3A—C3A—C4A—C5A	26.2 (3)
O1—O2—C3—C4	46.6 (2)	C1A—O1A—O2A—C3A	46.3 (2)
O1—O2—C3—C13	170.81 (17)	C2A—O3A—C3A—O2A	35.7 (2)
O1—C1—C2—O3	−52.4 (3)	C2A—O3A—C3A—C4A	−87.5 (2)
O1—C1—C2—N11	71.7 (2)	C2A—O3A—C3A—C13A	148.2 (2)
O1—C1—C11—C5	68.4 (2)	C2A—N11A—C10A—O10A	178.8 (2)
O1—C1—C11—C6	−165.09 (18)	C2A—N11A—C10A—C9A	−4.2 (4)
O1—C1—C12—C8	170.72 (18)	C2A—C1A—C11A—C5A	−50.8 (3)
O1—C1—C12—C9	−61.1 (2)	C2A—C1A—C11A—C6A	76.0 (3)
O2—O1—C1—C2	14.0 (2)	C2A—C1A—C12A—C8A	−70.7 (2)
O2—O1—C1—C11	−107.65 (19)	C2A—C1A—C12A—C9A	57.3 (2)
O2—O1—C1—C12	133.08 (17)	C3A—O3A—C2A—N11A	−100.5 (2)
O2—C3—C4—C5	−95.7 (3)	C3A—O3A—C2A—C1A	25.3 (3)
O3—C3—C4—C5	24.8 (3)	C3A—C4A—C5A—C11A	57.1 (3)
C1—O1—O2—C3	46.7 (2)	C4A—C5A—C11A—C1A	−37.5 (3)
C2—O3—C3—O2	35.4 (3)	C4A—C5A—C11A—C6A	−164.8 (2)
C2—O3—C3—C4	−87.7 (2)	C6A—C7A—C8A—C12A	57.8 (3)
C2—O3—C3—C13	147.9 (2)	C7A—C6A—C11A—C1A	47.8 (3)
C2—N11—C10—O10	174.9 (2)	C7A—C6A—C11A—C5A	175.2 (2)
C2—N11—C10—C9	−8.5 (4)	C7A—C8A—C12A—C1A	−57.8 (3)
C2—C1—C11—C5	−53.0 (3)	C7A—C8A—C12A—C9A	176.3 (2)
C2—C1—C11—C6	73.5 (2)	C10A—N11A—C2A—O3A	144.2 (2)
C2—C1—C12—C8	−70.0 (3)	C10A—N11A—C2A—C1A	17.2 (3)
C2—C1—C12—C9	58.2 (3)	C10A—C9A—C12A—C1A	−44.1 (3)
C3—O3—C2—N11	−99.8 (2)	C10A—C9A—C12A—C8A	81.7 (3)
C3—O3—C2—C1	26.3 (3)	C11A—C1A—C2A—O3A	66.6 (2)
C3—C4—C5—C11	57.2 (3)	C11A—C1A—C2A—N11A	−169.95 (19)
C4—C5—C11—C1	−36.1 (3)	C11A—C1A—C12A—C8A	55.1 (3)
C4—C5—C11—C6	−163.4 (2)	C11A—C1A—C12A—C9A	−176.89 (19)
C6—C7—C8—C12	57.0 (3)	C11A—C6A—C7A—C8A	−52.7 (3)
C7—C6—C11—C1	49.3 (3)	C12A—C1A—C2A—O3A	−166.54 (19)
C7—C6—C11—C5	176.62 (19)	C12A—C1A—C2A—N11A	−43.1 (3)
C7—C8—C12—C1	−57.2 (2)	C12A—C1A—C11A—C5A	−176.75 (19)
C7—C8—C12—C9	177.2 (2)	C12A—C1A—C11A—C6A	−50.0 (3)
C10—N11—C2—O3	145.9 (2)	C12A—C9A—C10A—O10A	−165.2 (2)
C10—N11—C2—C1	19.4 (3)	C12A—C9A—C10A—N11A	17.8 (3)

C10—C9—C12—C1	−47.0 (3)	C13A—C3A—C4A—C5A	146.5 (2)
C10—C9—C12—C8	78.9 (3)	C14A—C6A—C7A—C8A	−175.7 (2)
C11—C1—C2—O3	66.7 (3)	C14A—C6A—C11A—C1A	171.0 (2)
C11—C1—C2—N11	−169.17 (18)	C14A—C6A—C11A—C5A	−61.7 (3)
C11—C1—C12—C8	55.1 (2)	C15A—C9A—C10A—O10A	−35.1 (3)
C11—C1—C12—C9	−176.72 (19)	C15A—C9A—C10A—N11A	147.9 (2)
C11—C6—C7—C8	−52.7 (3)	C15A—C9A—C12A—C1A	−172.6 (2)
C12—C1—C2—O3	−167.5 (2)	C15A—C9A—C12A—C8A	−46.8 (3)
C12—C1—C2—N11	−43.4 (3)	O21—C21—C22—C23	−177.7 (3)
C12—C1—C11—C5	−177.76 (19)	O22—C21—C22—C23	0.0 (5)
C12—C1—C11—C6	−51.3 (3)	C21—C22—C23—C24	173.5 (2)
C12—C9—C10—O10	−161.0 (2)	C22—C23—C24—C25	20.3 (4)
C12—C9—C10—N11	22.3 (3)	C22—C23—C24—C29	−156.2 (3)
C13—C3—C4—C5	145.4 (2)	C23—C24—C25—C26	−174.5 (3)
C14—C6—C7—C8	−175.8 (2)	C23—C24—C29—C28	174.8 (2)
C14—C6—C11—C1	172.5 (2)	C24—C25—C26—C27	−0.6 (4)
C14—C6—C11—C5	−60.2 (3)	C25—C24—C29—C28	−1.8 (4)
C15—C9—C10—O10	−32.0 (3)	C25—C26—C27—C28	−1.2 (4)
C15—C9—C10—N11	151.3 (2)	C26—C27—C28—C29	1.4 (4)
C15—C9—C12—C1	−174.8 (2)	C27—C28—C29—C24	0.1 (4)
C15—C9—C12—C8	−48.9 (3)	C29—C24—C25—C26	2.1 (4)
O1A—O2A—C3A—O3A	−74.7 (2)	O21A—C21A—C22A—C23A	−175.5 (3)
O1A—O2A—C3A—C4A	46.4 (2)	O22A—C21A—C22A—C23A	2.8 (4)
O1A—O2A—C3A—C13A	170.94 (16)	C21A—C22A—C23A—C24A	174.2 (2)
O1A—C1A—C2A—O3A	−51.4 (3)	C22A—C23A—C24A—C25A	22.8 (4)
O1A—C1A—C2A—N11A	72.1 (2)	C22A—C23A—C24A—C29A	−153.7 (3)
O1A—C1A—C11A—C5A	70.0 (3)	C23A—C24A—C25A—C26A	−173.8 (3)
O1A—C1A—C11A—C6A	−163.2 (2)	C23A—C24A—C29A—C28A	173.8 (3)
O1A—C1A—C12A—C8A	169.77 (19)	C24A—C25A—C26A—C27A	−0.6 (5)
O1A—C1A—C12A—C9A	−62.2 (2)	C25A—C24A—C29A—C28A	−2.9 (4)
O2A—O1A—C1A—C2A	13.6 (2)	C25A—C26A—C27A—C28A	−1.5 (5)
O2A—O1A—C1A—C11A	−107.2 (2)	C26A—C27A—C28A—C29A	1.4 (4)
O2A—O1A—C1A—C12A	133.40 (17)	C27A—C28A—C29A—C24A	0.9 (4)
O2A—C3A—C4A—C5A	−94.2 (3)	C29A—C24A—C25A—C26A	2.8 (4)

Hydrogen-bond geometry ($\text{\AA}$, $^\circ$)

$D\cdots A$	$D\cdots H$	$H\cdots A$	$D\cdots A$	$D\cdots H\cdots A$
N11—H11 $\cdots$ O22	0.90 (3)	2.13 (3)	3.019 (3)	169 (3)
N11A—H11A $\cdots$ O22A	0.90 (3)	2.12 (3)	3.009 (3)	169 (3)
O21—H21 $\cdots$ O10	0.93 (4)	1.66 (4)	2.574 (3)	167 (3)
O21A—H21A $\cdots$ O10A	0.98 (4)	1.61 (4)	2.576 (3)	166 (4)

1,5,9-Trimethyl-14,15,16-trioxa-11-azatetracyclo[10.3.1.0^{4,13}.0^{8,13}]hexadecan-10-one-*cis*-butenedioic acid (1/1)
(madiha29cult)

Crystal data

C₁₅H₂₃NO₄·C₄H₄O₄
 $M_r = 397.41$
 Orthorhombic, $P2_12_12_1$
 $a = 9.62162$ (12) Å
 $b = 10.40235$ (11) Å
 $c = 19.6935$ (2) Å
 $V = 1971.08$ (4) Å³
 $Z = 4$
 $F(000) = 848$

$D_x = 1.339$ Mg m⁻³
 Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
 Cell parameters from 8948 reflections
 $\theta = 4.5\text{--}75.6^\circ$
 $\mu = 0.88$ mm⁻¹
 $T = 100$ K
 Block, colourless
 $0.4 \times 0.4 \times 0.35$ mm

Data collection

Rigaku SuperNova Dual Source
 diffractometer with an Atlas detector
 Radiation source: micro-focus sealed X-ray
 tube, SuperNova (Cu) X-ray Source
 Mirror monochromator
 Detector resolution: 10.3577 pixels mm⁻¹
 ω scans
 Absorption correction: multi-scan
 (CrysAlis PRO; Rigaku OD, 2015)

$T_{\min} = 0.716$, $T_{\max} = 1.000$
 11105 measured reflections
 3504 independent reflections
 3466 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.019$
 $\theta_{\max} = 67.5^\circ$, $\theta_{\min} = 5.1^\circ$
 $h = -11 \rightarrow 11$
 $k = -12 \rightarrow 12$
 $l = -23 \rightarrow 20$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.022$
 $wR(F^2) = 0.056$
 $S = 1.01$
 3504 reflections
 268 parameters
 0 restraints
 Primary atom site location: structure-invariant
 direct methods
 Hydrogen site location: mixed

H atoms treated by a mixture of independent
 and constrained refinement
 $w = 1/[\sigma^2(F_o^2) + (0.032P)^2 + 0.2852P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.18$ e Å⁻³
 $\Delta\rho_{\min} = -0.14$ e Å⁻³
 Absolute structure: Flack x determined using
 1483 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
 Absolute structure parameter: -0.10 (4)

Special details

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.

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.13170 (10)	0.26302 (10)	0.57995 (5)	0.0174 (2)
O2	0.12539 (10)	0.13681 (10)	0.54588 (5)	0.0179 (2)
O3	0.36214 (10)	0.11255 (10)	0.53420 (5)	0.0166 (2)
O10	0.25079 (11)	0.40482 (10)	0.37164 (5)	0.0192 (2)
N11	0.32147 (12)	0.27619 (12)	0.45656 (6)	0.0156 (2)
H11	0.351 (2)	0.224 (2)	0.4254 (10)	0.024 (5)*

C1	0.27190 (15)	0.31804 (14)	0.57780 (7)	0.0156 (3)
C2	0.36156 (15)	0.24771 (13)	0.52617 (7)	0.0147 (3)
H2	0.4593	0.2783	0.5323	0.018*
C3	0.24132 (15)	0.06274 (14)	0.56756 (8)	0.0182 (3)
C4	0.25854 (17)	0.06638 (15)	0.64479 (8)	0.0223 (3)
H4A	0.1671	0.0849	0.6656	0.027*
H4B	0.2882	−0.0197	0.6606	0.027*
C5	0.36331 (17)	0.16579 (16)	0.66992 (8)	0.0228 (3)
H5A	0.4562	0.1421	0.6523	0.027*
H5B	0.3675	0.1607	0.7201	0.027*
C6	0.46439 (17)	0.38974 (17)	0.65924 (8)	0.0263 (4)
H6	0.5390	0.3542	0.6293	0.032*
C7	0.43671 (19)	0.52849 (17)	0.63734 (9)	0.0296 (4)
H7A	0.3678	0.5674	0.6685	0.035*
H7B	0.5239	0.5785	0.6410	0.035*
C8	0.38249 (16)	0.53724 (15)	0.56482 (9)	0.0231 (3)
H8A	0.4539	0.5044	0.5331	0.028*
H8B	0.3640	0.6283	0.5533	0.028*
C9	0.18497 (15)	0.46594 (14)	0.48504 (8)	0.0168 (3)
H9	0.0892	0.4296	0.4895	0.020*
C10	0.25789 (14)	0.38138 (13)	0.43396 (7)	0.0148 (3)
C11	0.33353 (16)	0.30612 (15)	0.64984 (7)	0.0202 (3)
H11A	0.2618	0.3393	0.6822	0.024*
C12	0.24835 (15)	0.45867 (14)	0.55666 (7)	0.0175 (3)
H12	0.1785	0.4957	0.5888	0.021*
C13	0.21698 (17)	−0.07039 (14)	0.53893 (9)	0.0238 (3)
H13A	0.1929	−0.0638	0.4907	0.036*
H13B	0.1406	−0.1117	0.5636	0.036*
H13C	0.3017	−0.1219	0.5440	0.036*
C14	0.5169 (2)	0.3851 (2)	0.73242 (9)	0.0398 (5)
H14A	0.4421	0.4113	0.7633	0.060*
H14B	0.5959	0.4437	0.7375	0.060*
H14C	0.5462	0.2973	0.7434	0.060*
C15	0.16500 (18)	0.60305 (15)	0.45888 (8)	0.0245 (3)
H15A	0.2560	0.6424	0.4506	0.037*
H15B	0.1144	0.6536	0.4928	0.037*
H15C	0.1118	0.6011	0.4165	0.037*
O21	0.40673 (12)	0.29370 (10)	0.28549 (6)	0.0214 (2)
H21	0.347 (3)	0.327 (3)	0.3188 (14)	0.055 (7)*
O22	0.36344 (12)	0.10985 (10)	0.33941 (5)	0.0226 (2)
O23	0.66564 (12)	0.36037 (11)	0.18037 (6)	0.0251 (2)
H23	0.650 (3)	0.443 (2)	0.1681 (12)	0.045 (6)*
O24	0.46072 (14)	0.31992 (12)	0.13105 (7)	0.0345 (3)
C21	0.42193 (16)	0.17039 (14)	0.29387 (7)	0.0174 (3)
C22	0.51583 (16)	0.10315 (14)	0.24596 (8)	0.0190 (3)
H22	0.5347	0.0153	0.2553	0.023*
C23	0.57634 (16)	0.15295 (14)	0.19137 (7)	0.0191 (3)
H23A	0.6371	0.0982	0.1667	0.023*

C24	0.55830 (17)	0.28680 (15)	0.16494 (7)	0.0191 (3)
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Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0117 (5)	0.0174 (5)	0.0230 (5)	−0.0015 (4)	0.0026 (4)	−0.0019 (4)
O2	0.0136 (5)	0.0152 (5)	0.0248 (5)	−0.0008 (4)	−0.0037 (4)	0.0004 (4)
O3	0.0133 (5)	0.0161 (5)	0.0203 (5)	0.0012 (4)	0.0016 (4)	0.0016 (4)
O10	0.0224 (6)	0.0164 (5)	0.0189 (5)	0.0015 (4)	0.0005 (4)	0.0015 (4)
N11	0.0155 (6)	0.0145 (5)	0.0169 (6)	0.0017 (5)	0.0018 (5)	−0.0024 (5)
C1	0.0096 (6)	0.0199 (7)	0.0173 (7)	−0.0017 (5)	0.0018 (5)	−0.0018 (6)
C2	0.0118 (6)	0.0163 (7)	0.0158 (6)	0.0000 (6)	0.0003 (5)	−0.0011 (5)
C3	0.0116 (7)	0.0189 (7)	0.0241 (7)	0.0000 (6)	−0.0014 (6)	0.0063 (6)
C4	0.0183 (8)	0.0263 (8)	0.0223 (7)	−0.0020 (6)	0.0001 (6)	0.0080 (6)
C5	0.0198 (7)	0.0310 (8)	0.0177 (6)	−0.0011 (7)	−0.0026 (6)	0.0016 (6)
C6	0.0217 (8)	0.0323 (9)	0.0250 (8)	−0.0039 (7)	−0.0048 (6)	−0.0087 (7)
C7	0.0284 (9)	0.0261 (8)	0.0341 (9)	−0.0059 (7)	−0.0039 (7)	−0.0125 (7)
C8	0.0195 (7)	0.0185 (7)	0.0313 (8)	−0.0042 (6)	0.0024 (7)	−0.0055 (6)
C9	0.0133 (7)	0.0155 (7)	0.0217 (7)	0.0014 (6)	0.0032 (6)	0.0003 (6)
C10	0.0112 (6)	0.0133 (6)	0.0199 (7)	−0.0033 (5)	0.0012 (5)	−0.0002 (5)
C11	0.0174 (7)	0.0267 (8)	0.0165 (7)	−0.0012 (6)	0.0013 (6)	−0.0037 (6)
C12	0.0150 (7)	0.0165 (7)	0.0210 (7)	0.0003 (6)	0.0033 (6)	−0.0038 (5)
C13	0.0217 (8)	0.0170 (7)	0.0328 (9)	−0.0003 (6)	−0.0051 (7)	0.0043 (6)
C14	0.0399 (11)	0.0489 (12)	0.0308 (9)	−0.0073 (10)	−0.0131 (8)	−0.0106 (9)
C15	0.0300 (8)	0.0169 (7)	0.0267 (7)	0.0052 (6)	0.0072 (7)	−0.0003 (6)
O21	0.0283 (6)	0.0132 (5)	0.0228 (5)	0.0028 (4)	0.0055 (4)	0.0004 (4)
O22	0.0318 (6)	0.0145 (5)	0.0216 (5)	−0.0010 (5)	0.0043 (4)	−0.0010 (4)
O23	0.0264 (6)	0.0154 (5)	0.0336 (6)	0.0006 (5)	−0.0014 (5)	0.0023 (5)
O24	0.0421 (8)	0.0253 (6)	0.0361 (6)	0.0010 (6)	−0.0190 (6)	0.0040 (5)
C21	0.0195 (7)	0.0154 (7)	0.0174 (7)	−0.0011 (6)	−0.0038 (6)	−0.0014 (5)
C22	0.0230 (8)	0.0125 (7)	0.0215 (7)	0.0017 (6)	−0.0024 (6)	−0.0024 (6)
C23	0.0213 (7)	0.0152 (7)	0.0208 (7)	0.0014 (6)	−0.0014 (6)	−0.0046 (6)
C24	0.0263 (8)	0.0175 (7)	0.0133 (6)	0.0019 (6)	0.0012 (6)	−0.0026 (5)

Geometric parameters ($\text{\AA}$, $^\circ$)

O1—O2	1.4757 (14)	C8—H8B	0.9900
O1—C1	1.4660 (17)	C8—C12	1.536 (2)
O2—C3	1.4213 (17)	C9—H9	1.0000
O3—C2	1.4149 (17)	C9—C10	1.5091 (19)
O3—C3	1.4323 (17)	C9—C12	1.538 (2)
O10—C10	1.2532 (18)	C9—C15	1.529 (2)
N11—H11	0.87 (2)	C11—H11A	1.0000
N11—C2	1.4546 (18)	C12—H12	1.0000
N11—C10	1.3303 (19)	C13—H13A	0.9800
C1—C2	1.5209 (19)	C13—H13B	0.9800
C1—C11	1.543 (2)	C13—H13C	0.9800
C1—C12	1.538 (2)	C14—H14A	0.9800

C2—H2	1.0000	C14—H14B	0.9800
C3—C4	1.530 (2)	C14—H14C	0.9800
C3—C13	1.513 (2)	C15—H15A	0.9800
C4—H4A	0.9900	C15—H15B	0.9800
C4—H4B	0.9900	C15—H15C	0.9800
C4—C5	1.527 (2)	O21—H21	0.94 (3)
C5—H5A	0.9900	O21—C21	1.3015 (19)
C5—H5B	0.9900	O22—C21	1.2320 (19)
C5—C11	1.539 (2)	O23—H23	0.90 (2)
C6—H6	1.0000	O23—C24	1.321 (2)
C6—C7	1.530 (2)	O24—C24	1.202 (2)
C6—C11	1.542 (2)	C21—C22	1.482 (2)
C6—C14	1.528 (2)	C22—H22	0.9500
C7—H7A	0.9900	C22—C23	1.328 (2)
C7—H7B	0.9900	C23—H23A	0.9500
C7—C8	1.523 (2)	C23—C24	1.497 (2)
C8—H8A	0.9900		
C1—O1—O2	111.84 (9)	C10—C9—H9	105.5
C3—O2—O1	108.27 (10)	C10—C9—C12	113.46 (12)
C2—O3—C3	114.05 (10)	C10—C9—C15	112.19 (12)
C2—N11—H11	116.8 (13)	C12—C9—H9	105.5
C10—N11—H11	115.5 (13)	C15—C9—H9	105.5
C10—N11—C2	127.20 (12)	C15—C9—C12	113.86 (12)
O1—C1—C2	110.70 (11)	O10—C10—N11	120.84 (13)
O1—C1—C11	107.20 (11)	O10—C10—C9	120.93 (12)
O1—C1—C12	104.10 (11)	N11—C10—C9	118.06 (12)
C2—C1—C11	110.99 (12)	C1—C11—H11A	107.0
C2—C1—C12	111.11 (11)	C5—C11—C1	112.58 (12)
C12—C1—C11	112.47 (12)	C5—C11—C6	110.63 (13)
O3—C2—N11	107.98 (11)	C5—C11—H11A	107.0
O3—C2—C1	113.92 (11)	C6—C11—C1	112.27 (12)
O3—C2—H2	107.4	C6—C11—H11A	107.0
N11—C2—C1	112.44 (12)	C1—C12—C9	110.69 (11)
N11—C2—H2	107.4	C1—C12—H12	107.1
C1—C2—H2	107.4	C8—C12—C1	110.73 (12)
O2—C3—O3	107.64 (11)	C8—C12—C9	113.76 (13)
O2—C3—C4	111.72 (12)	C8—C12—H12	107.1
O2—C3—C13	105.23 (12)	C9—C12—H12	107.1
O3—C3—C4	111.04 (12)	C3—C13—H13A	109.5
O3—C3—C13	106.61 (12)	C3—C13—H13B	109.5
C13—C3—C4	114.18 (13)	C3—C13—H13C	109.5
C3—C4—H4A	108.7	H13A—C13—H13B	109.5
C3—C4—H4B	108.7	H13A—C13—H13C	109.5
H4A—C4—H4B	107.6	H13B—C13—H13C	109.5
C5—C4—C3	114.23 (13)	C6—C14—H14A	109.5
C5—C4—H4A	108.7	C6—C14—H14B	109.5
C5—C4—H4B	108.7	C6—C14—H14C	109.5

C4—C5—H5A	108.3	H14A—C14—H14B	109.5
C4—C5—H5B	108.3	H14A—C14—H14C	109.5
C4—C5—C11	115.87 (13)	H14B—C14—H14C	109.5
H5A—C5—H5B	107.4	C9—C15—H15A	109.5
C11—C5—H5A	108.3	C9—C15—H15B	109.5
C11—C5—H5B	108.3	C9—C15—H15C	109.5
C7—C6—H6	107.9	H15A—C15—H15B	109.5
C7—C6—C11	110.88 (14)	H15A—C15—H15C	109.5
C11—C6—H6	107.9	H15B—C15—H15C	109.5
C14—C6—H6	107.9	C21—O21—H21	110.2 (16)
C14—C6—C7	110.69 (15)	C24—O23—H23	111.1 (16)
C14—C6—C11	111.42 (14)	O21—C21—C22	116.94 (13)
C6—C7—H7A	109.1	O22—C21—O21	123.01 (14)
C6—C7—H7B	109.1	O22—C21—C22	120.05 (14)
H7A—C7—H7B	107.9	C21—C22—H22	116.6
C8—C7—C6	112.35 (13)	C23—C22—C21	126.77 (14)
C8—C7—H7A	109.1	C23—C22—H22	116.6
C8—C7—H7B	109.1	C22—C23—H23A	116.8
C7—C8—H8A	109.5	C22—C23—C24	126.43 (14)
C7—C8—H8B	109.5	C24—C23—H23A	116.8
C7—C8—C12	110.74 (14)	O23—C24—C23	111.61 (13)
H8A—C8—H8B	108.1	O24—C24—O23	124.91 (14)
C12—C8—H8A	109.5	O24—C24—C23	123.38 (14)
C12—C8—H8B	109.5		
O1—O2—C3—O3	−74.51 (13)	C7—C6—C11—C5	178.29 (13)
O1—O2—C3—C4	47.64 (14)	C7—C8—C12—C1	−56.21 (16)
O1—O2—C3—C13	172.07 (11)	C7—C8—C12—C9	178.39 (13)
O1—C1—C2—O3	−51.62 (15)	C10—N11—C2—O3	152.17 (13)
O1—C1—C2—N11	71.65 (14)	C10—N11—C2—C1	25.64 (19)
O1—C1—C11—C5	68.73 (15)	C10—C9—C12—C1	−47.19 (16)
O1—C1—C11—C6	−165.63 (12)	C10—C9—C12—C8	78.24 (15)
O1—C1—C12—C8	169.41 (11)	C11—C1—C2—O3	67.29 (15)
O1—C1—C12—C9	−63.48 (14)	C11—C1—C2—N11	−169.43 (12)
O2—O1—C1—C2	14.64 (14)	C11—C1—C12—C8	53.70 (15)
O2—O1—C1—C11	−106.54 (11)	C11—C1—C12—C9	−179.19 (12)
O2—O1—C1—C12	134.10 (10)	C11—C6—C7—C8	−55.12 (18)
O2—C3—C4—C5	−96.54 (15)	C12—C1—C2—O3	−166.77 (11)
O3—C3—C4—C5	23.64 (18)	C12—C1—C2—N11	−43.50 (15)
C1—O1—O2—C3	45.45 (13)	C12—C1—C11—C5	−177.44 (12)
C2—O3—C3—O2	36.57 (15)	C12—C1—C11—C6	−51.81 (16)
C2—O3—C3—C4	−86.00 (14)	C12—C9—C10—O10	−157.01 (13)
C2—O3—C3—C13	149.06 (11)	C12—C9—C10—N11	27.73 (18)
C2—N11—C10—O10	167.29 (13)	C13—C3—C4—C5	144.20 (14)
C2—N11—C10—C9	−17.5 (2)	C14—C6—C7—C8	−179.31 (15)
C2—C1—C11—C5	−52.27 (16)	C14—C6—C11—C1	175.37 (14)
C2—C1—C11—C6	73.37 (16)	C14—C6—C11—C5	−57.94 (18)
C2—C1—C12—C8	−71.41 (15)	C15—C9—C10—O10	−26.22 (19)

C2—C1—C12—C9	55.71 (15)	C15—C9—C10—N11	158.53 (13)
C3—O3—C2—N11	−100.94 (13)	C15—C9—C12—C1	−177.15 (12)
C3—O3—C2—C1	24.72 (16)	C15—C9—C12—C8	−51.72 (17)
C3—C4—C5—C11	58.32 (18)	O21—C21—C22—C23	−6.8 (2)
C4—C5—C11—C1	−36.84 (18)	O22—C21—C22—C23	173.89 (16)
C4—C5—C11—C6	−163.36 (13)	C21—C22—C23—C24	−2.5 (3)
C6—C7—C8—C12	57.80 (18)	C22—C23—C24—O23	102.65 (19)
C7—C6—C11—C1	51.59 (17)	C22—C23—C24—O24	−80.7 (2)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H $\cdots$ <i>A</i>	<i>D</i> —H	H $\cdots$ <i>A</i>	<i>D</i> $\cdots$ <i>A</i>	<i>D</i> —H $\cdots$ <i>A</i>
N11—H11 $\cdots$ O22	0.87 (2)	2.07 (2)	2.9118 (16)	163.0 (19)
O21—H21 $\cdots$ O10	0.94 (3)	1.61 (3)	2.5428 (15)	172 (3)
O23—H23 $\cdots$ O22 ⁱ	0.90 (2)	1.75 (2)	2.6392 (15)	168 (2)

Symmetry code: (i) $-x+1, y+1/2, -z+1/2$.**1,5,9-Trimethyl-14,15,16-trioxo-11-azatetracyclo[10.3.1.0^{4,13}.0^{8,13}]hexadecan-10-one-*cis*-butenedioic acid (2/1) (madiha55cult)***Crystal data*2C₁₅H₂₃NO₄·C₄H₄O₄*M_r* = 678.76Orthorhombic, *P*2₁2₁2₁*a* = 9.7885 (1) Å*b* = 9.9965 (1) Å*c* = 33.7661 (4) Å*V* = 3304.04 (6) Å³*Z* = 4*F*(000) = 1456*D_x* = 1.365 Mg m^{−3}Cu *Kα* radiation, *λ* = 1.54178 Å

Cell parameters from 7193 reflections

θ = 4.6–75.4°*μ* = 0.86 mm^{−1}*T* = 100 K

Block, colourless

0.2 × 0.2 × 0.1 mm

Data collection

Rigaku SuperNova Dual Source

diffractometer with an Atlas detector

Radiation source: micro-focus sealed X-ray

tube, SuperNova (Cu) X-ray Source

Mirror monochromator

Detector resolution: 10.3577 pixels mm^{−1}*ω* scans

Absorption correction: multi-scan

(CrysAlis PRO; Rigaku OD, 2015)

T_{min} = 0.973, *T_{max}* = 1.000

9569 measured reflections

5886 independent reflections

5726 reflections with *I* > 2σ(*I*)*R_{int}* = 0.021*θ_{max}* = 67.5°, *θ_{min}* = 4.6°*h* = −10→11*k* = −8→11*l* = −40→28*Refinement*Refinement on *F*²

Least-squares matrix: full

R [*F*² > 2σ(*F*²)] = 0.030*wR*(*F*²) = 0.075*S* = 1.02

5886 reflections

455 parameters

0 restraints

Primary atom site location: structure-invariant
direct methods

Hydrogen site location: mixed

H atoms treated by a mixture of independent
and constrained refinement*w* = 1/[σ²(*F_o*²) + (0.040*P*)² + 0.6791*P*]where *P* = (*F_o*² + 2*F_c*²)/3(Δ/σ)_{max} < 0.001Δρ_{max} = 0.21 e Å^{−3}

$$\Delta\rho_{\min} = -0.18 \text{ e } \text{\AA}^{-3}$$

Absolute structure: Flack x determined using
2414 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)

Absolute structure parameter: 0.02 (7)

Special details

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.4239 (2)	0.5209 (2)	0.45667 (6)	0.0152 (4)
N1	0.58735 (18)	0.35610 (17)	0.42840 (5)	0.0168 (4)
H1	0.659 (3)	0.339 (3)	0.4132 (8)	0.023 (6)*
O1	0.49755 (14)	0.55528 (15)	0.49297 (4)	0.0181 (3)
C2	0.5224 (2)	0.4865 (2)	0.42312 (6)	0.0147 (4)
H2	0.4673	0.4816	0.3982	0.018*
O2	0.64369 (14)	0.57876 (15)	0.48525 (4)	0.0184 (3)
C3	0.6543 (2)	0.6633 (2)	0.45172 (6)	0.0172 (4)
O3	0.62388 (14)	0.58492 (14)	0.41716 (4)	0.0151 (3)
C4	0.5584 (2)	0.7841 (2)	0.45467 (6)	0.0196 (4)
H4A	0.5412	0.8033	0.4830	0.024*
H4B	0.6049	0.8630	0.4432	0.024*
C5	0.4210 (2)	0.7655 (2)	0.43375 (6)	0.0196 (4)
H5A	0.4383	0.7606	0.4049	0.024*
H5B	0.3652	0.8465	0.4386	0.024*
C6	0.2285 (2)	0.6074 (2)	0.41371 (6)	0.0189 (4)
H6	0.2782	0.5820	0.3889	0.023*
C7	0.1432 (2)	0.4876 (2)	0.42687 (7)	0.0226 (5)
H7A	0.0896	0.5124	0.4506	0.027*
H7B	0.0782	0.4637	0.4056	0.027*
C8	0.2318 (2)	0.3664 (2)	0.43645 (7)	0.0205 (4)
H8A	0.2798	0.3367	0.4122	0.025*
H8B	0.1731	0.2920	0.4456	0.025*
C9	0.4291 (2)	0.2821 (2)	0.48027 (6)	0.0207 (4)
H9	0.4758	0.3093	0.5054	0.025*
C10	0.5412 (2)	0.2546 (2)	0.45075 (7)	0.0192 (4)
O10	0.59364 (17)	0.14148 (15)	0.44918 (6)	0.0297 (4)
C11	0.3358 (2)	0.6430 (2)	0.44559 (6)	0.0171 (4)
H11	0.2839	0.6685	0.4700	0.020*
C12	0.3369 (2)	0.4000 (2)	0.46856 (6)	0.0176 (4)
H12	0.2845	0.4263	0.4928	0.021*
C13	0.8037 (2)	0.6988 (2)	0.44857 (7)	0.0210 (4)
H13A	0.8587	0.6170	0.4495	0.031*
H13B	0.8291	0.7574	0.4707	0.031*
H13C	0.8203	0.7453	0.4235	0.031*

C14	0.1366 (2)	0.7271 (2)	0.40429 (7)	0.0260 (5)
H14A	0.0974	0.7621	0.4289	0.039*
H14B	0.0628	0.6987	0.3866	0.039*
H14C	0.1907	0.7971	0.3914	0.039*
C15	0.3503 (2)	0.1538 (2)	0.48994 (8)	0.0294 (5)
H15A	0.2783	0.1738	0.5092	0.044*
H15B	0.4131	0.0874	0.5011	0.044*
H15C	0.3091	0.1182	0.4657	0.044*
C1A	0.7189 (2)	0.6715 (2)	0.29446 (6)	0.0154 (4)
N1A	0.89184 (18)	0.51898 (18)	0.32339 (5)	0.0174 (4)
H1A	0.907 (3)	0.443 (3)	0.3348 (8)	0.027 (7)*
O1A	0.69096 (15)	0.59186 (14)	0.25893 (4)	0.0178 (3)
C2A	0.7575 (2)	0.5804 (2)	0.32907 (6)	0.0149 (4)
H2A	0.7626	0.6373	0.3534	0.018*
O2A	0.67404 (15)	0.44902 (14)	0.26854 (4)	0.0184 (3)
C3A	0.5861 (2)	0.4382 (2)	0.30168 (6)	0.0171 (4)
O3A	0.66195 (14)	0.47756 (14)	0.33643 (4)	0.0155 (3)
C4A	0.4578 (2)	0.5243 (2)	0.29709 (6)	0.0196 (4)
H4AA	0.3794	0.4760	0.3089	0.023*
H4AB	0.4386	0.5361	0.2685	0.023*
C5A	0.4683 (2)	0.6625 (2)	0.31641 (6)	0.0193 (4)
H5AA	0.4753	0.6499	0.3454	0.023*
H5AB	0.3820	0.7112	0.3112	0.023*
C6A	0.6120 (2)	0.8667 (2)	0.33295 (6)	0.0196 (4)
H6A	0.6333	0.8262	0.3593	0.024*
C7A	0.7344 (2)	0.9519 (2)	0.32033 (7)	0.0222 (4)
H7AA	0.7122	0.9986	0.2953	0.027*
H7AB	0.7518	1.0208	0.3408	0.027*
C8A	0.8629 (2)	0.8693 (2)	0.31446 (6)	0.0208 (4)
H8AA	0.8888	0.8263	0.3398	0.025*
H8AB	0.9389	0.9283	0.3061	0.025*
C9A	0.9652 (2)	0.6773 (2)	0.27198 (6)	0.0207 (4)
H9A	0.9449	0.6376	0.2454	0.025*
C10A	0.9912 (2)	0.5600 (2)	0.29921 (6)	0.0187 (4)
O10A	1.10277 (15)	0.50020 (16)	0.29724 (5)	0.0264 (3)
C11A	0.5873 (2)	0.7514 (2)	0.30313 (6)	0.0173 (4)
H11A	0.5590	0.7939	0.2776	0.021*
C12A	0.8391 (2)	0.7614 (2)	0.28285 (6)	0.0185 (4)
H12A	0.8111	0.8094	0.2582	0.022*
C13A	0.5593 (2)	0.2902 (2)	0.30643 (7)	0.0220 (4)
H13D	0.6459	0.2412	0.3048	0.033*
H13E	0.4980	0.2598	0.2853	0.033*
H13F	0.5168	0.2737	0.3322	0.033*
C14A	0.4847 (2)	0.9543 (2)	0.33759 (7)	0.0258 (5)
H14D	0.4583	0.9903	0.3117	0.039*
H14E	0.5047	1.0282	0.3558	0.039*
H14F	0.4097	0.9004	0.3483	0.039*
C15A	1.0957 (2)	0.7599 (3)	0.26655 (8)	0.0313 (5)

H15D	1.0776	0.8345	0.2485	0.047*
H15E	1.1677	0.7030	0.2554	0.047*
H15F	1.1254	0.7948	0.2923	0.047*
C21	0.9037 (2)	0.1337 (2)	0.41140 (7)	0.0223 (5)
O21	0.81182 (17)	0.04403 (16)	0.42055 (5)	0.0269 (4)
H21	0.732 (4)	0.086 (3)	0.4277 (10)	0.043 (9)*
C22	1.0388 (2)	0.0711 (2)	0.40218 (7)	0.0249 (5)
H22	1.0694	0.0006	0.4188	0.030*
O22	0.8829 (2)	0.25272 (18)	0.41105 (8)	0.0525 (6)
C23	1.1185 (2)	0.1070 (2)	0.37251 (7)	0.0260 (5)
H23A	1.2037	0.0628	0.3692	0.031*
O23	1.18129 (17)	0.29587 (18)	0.33620 (5)	0.0305 (4)
H23	1.149 (4)	0.365 (4)	0.3219 (10)	0.050 (10)*
C24	1.0798 (2)	0.2144 (2)	0.34383 (7)	0.0239 (5)
O24	0.9674 (2)	0.2250 (2)	0.32975 (7)	0.0515 (6)

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0135 (9)	0.0177 (10)	0.0146 (9)	0.0002 (8)	0.0003 (7)	−0.0005 (7)
N1	0.0141 (8)	0.0145 (8)	0.0218 (9)	0.0010 (7)	0.0042 (7)	−0.0001 (7)
O1	0.0139 (7)	0.0260 (8)	0.0143 (6)	−0.0018 (6)	0.0023 (5)	−0.0003 (6)
C2	0.0129 (9)	0.0150 (9)	0.0161 (9)	−0.0014 (8)	0.0007 (8)	0.0008 (7)
O2	0.0129 (7)	0.0242 (7)	0.0181 (7)	−0.0014 (6)	−0.0004 (6)	0.0011 (6)
C3	0.0187 (10)	0.0186 (10)	0.0143 (9)	−0.0015 (8)	−0.0005 (8)	−0.0017 (8)
O3	0.0152 (7)	0.0144 (7)	0.0159 (6)	−0.0018 (5)	0.0024 (5)	−0.0006 (5)
C4	0.0195 (10)	0.0161 (10)	0.0233 (10)	−0.0034 (8)	0.0035 (8)	−0.0024 (8)
C5	0.0185 (10)	0.0160 (10)	0.0244 (10)	0.0020 (8)	0.0014 (9)	0.0000 (8)
C6	0.0149 (10)	0.0196 (10)	0.0222 (10)	0.0014 (8)	−0.0004 (8)	0.0024 (8)
C7	0.0149 (10)	0.0228 (11)	0.0301 (11)	−0.0021 (9)	−0.0021 (9)	0.0014 (9)
C8	0.0154 (10)	0.0188 (11)	0.0273 (11)	−0.0037 (8)	0.0001 (9)	0.0020 (8)
C9	0.0179 (10)	0.0202 (11)	0.0240 (10)	−0.0012 (9)	0.0019 (9)	0.0069 (8)
C10	0.0147 (10)	0.0160 (10)	0.0269 (11)	−0.0009 (8)	−0.0008 (8)	0.0023 (8)
O10	0.0227 (8)	0.0153 (7)	0.0513 (10)	0.0012 (7)	0.0085 (8)	0.0070 (7)
C11	0.0145 (9)	0.0173 (10)	0.0194 (9)	0.0015 (8)	0.0029 (8)	−0.0005 (8)
C12	0.0151 (9)	0.0181 (10)	0.0197 (9)	−0.0006 (8)	0.0033 (8)	0.0022 (8)
C13	0.0164 (10)	0.0230 (10)	0.0234 (10)	−0.0024 (9)	0.0010 (8)	−0.0025 (9)
C14	0.0176 (11)	0.0240 (12)	0.0364 (13)	0.0032 (9)	−0.0012 (9)	0.0070 (9)
C15	0.0234 (11)	0.0227 (11)	0.0421 (13)	0.0011 (9)	0.0077 (10)	0.0138 (10)
C1A	0.0164 (9)	0.0164 (10)	0.0133 (9)	−0.0004 (8)	−0.0013 (7)	−0.0002 (8)
N1A	0.0154 (8)	0.0165 (9)	0.0205 (8)	0.0008 (7)	−0.0011 (7)	0.0044 (7)
O1A	0.0243 (8)	0.0146 (7)	0.0144 (6)	−0.0018 (6)	−0.0004 (6)	0.0011 (5)
C2A	0.0132 (9)	0.0159 (9)	0.0156 (9)	−0.0022 (8)	0.0005 (7)	0.0000 (7)
O2A	0.0230 (7)	0.0133 (7)	0.0189 (7)	0.0001 (6)	0.0031 (6)	−0.0010 (5)
C3A	0.0170 (9)	0.0180 (10)	0.0164 (9)	−0.0024 (8)	−0.0001 (8)	−0.0013 (8)
O3A	0.0156 (7)	0.0160 (7)	0.0150 (6)	−0.0024 (6)	0.0008 (6)	0.0009 (5)
C4A	0.0154 (9)	0.0187 (10)	0.0247 (10)	−0.0017 (8)	−0.0010 (8)	0.0007 (9)
C5A	0.0158 (10)	0.0170 (10)	0.0251 (10)	0.0022 (8)	0.0013 (8)	−0.0003 (8)

C6A	0.0257 (11)	0.0148 (9)	0.0183 (9)	0.0023 (9)	−0.0005 (8)	0.0006 (8)
C7A	0.0270 (11)	0.0156 (10)	0.0239 (10)	−0.0026 (9)	−0.0035 (9)	0.0005 (8)
C8A	0.0210 (11)	0.0171 (10)	0.0243 (10)	−0.0052 (8)	−0.0036 (9)	0.0032 (8)
C9A	0.0160 (10)	0.0225 (11)	0.0237 (10)	−0.0014 (9)	0.0028 (8)	0.0055 (9)
C10A	0.0142 (9)	0.0209 (10)	0.0209 (10)	−0.0022 (8)	0.0000 (8)	0.0007 (8)
O10A	0.0163 (7)	0.0251 (8)	0.0379 (9)	0.0018 (6)	0.0054 (7)	0.0069 (7)
C11A	0.0177 (10)	0.0159 (9)	0.0183 (10)	0.0007 (8)	−0.0010 (8)	0.0020 (8)
C12A	0.0175 (10)	0.0181 (10)	0.0198 (10)	−0.0015 (8)	0.0005 (8)	0.0039 (8)
C13A	0.0239 (11)	0.0161 (10)	0.0260 (11)	−0.0029 (8)	−0.0007 (9)	−0.0002 (8)
C14A	0.0303 (12)	0.0186 (10)	0.0286 (11)	0.0070 (10)	0.0049 (10)	−0.0004 (9)
C15A	0.0193 (11)	0.0320 (13)	0.0425 (14)	−0.0009 (10)	0.0066 (10)	0.0147 (11)
C21	0.0237 (11)	0.0166 (11)	0.0266 (11)	0.0010 (9)	0.0011 (9)	−0.0019 (8)
O21	0.0254 (8)	0.0179 (8)	0.0374 (9)	0.0021 (7)	0.0077 (7)	0.0029 (7)
C22	0.0242 (11)	0.0187 (11)	0.0320 (12)	0.0021 (9)	−0.0007 (9)	0.0022 (9)
O22	0.0307 (10)	0.0173 (9)	0.1096 (19)	−0.0012 (8)	0.0240 (11)	−0.0065 (10)
C23	0.0235 (11)	0.0185 (10)	0.0360 (12)	0.0040 (9)	0.0038 (9)	−0.0023 (9)
O23	0.0208 (8)	0.0320 (9)	0.0387 (9)	0.0013 (7)	0.0046 (7)	0.0118 (8)
C24	0.0240 (11)	0.0216 (11)	0.0261 (11)	0.0007 (9)	0.0025 (9)	−0.0022 (9)
O24	0.0399 (12)	0.0398 (11)	0.0748 (15)	−0.0180 (9)	−0.0261 (11)	0.0239 (11)

Geometric parameters (Å, °)

C1—O1	1.463 (2)	N1A—C10A	1.334 (3)
C1—C2	1.527 (3)	O1A—O2A	1.474 (2)
C1—C11	1.541 (3)	C2A—H2A	1.0000
C1—C12	1.532 (3)	C2A—O3A	1.412 (2)
N1—H1	0.89 (3)	O2A—C3A	1.416 (2)
N1—C2	1.461 (3)	C3A—O3A	1.443 (2)
N1—C10	1.342 (3)	C3A—C4A	1.531 (3)
O1—O2	1.4728 (19)	C3A—C13A	1.511 (3)
C2—H2	1.0000	C4A—H4AA	0.9900
C2—O3	1.413 (2)	C4A—H4AB	0.9900
O2—C3	1.417 (2)	C4A—C5A	1.531 (3)
C3—O3	1.437 (2)	C5A—H5AA	0.9900
C3—C4	1.533 (3)	C5A—H5AB	0.9900
C3—C13	1.508 (3)	C5A—C11A	1.533 (3)
C4—H4A	0.9900	C6A—H6A	1.0000
C4—H4B	0.9900	C6A—C7A	1.531 (3)
C4—C5	1.530 (3)	C6A—C11A	1.549 (3)
C5—H5A	0.9900	C6A—C14A	1.530 (3)
C5—H5B	0.9900	C7A—H7AA	0.9900
C5—C11	1.535 (3)	C7A—H7AB	0.9900
C6—H6	1.0000	C7A—C8A	1.518 (3)
C6—C7	1.526 (3)	C8A—H8AA	0.9900
C6—C11	1.546 (3)	C8A—H8AB	0.9900
C6—C14	1.531 (3)	C8A—C12A	1.535 (3)
C7—H7A	0.9900	C9A—H9A	1.0000
C7—H7B	0.9900	C9A—C10A	1.511 (3)

C7—C8	1.524 (3)	C9A—C12A	1.538 (3)
C8—H8A	0.9900	C9A—C15A	1.533 (3)
C8—H8B	0.9900	C10A—O10A	1.247 (3)
C8—C12	1.531 (3)	C11A—H11A	1.0000
C9—H9	1.0000	C12A—H12A	1.0000
C9—C10	1.508 (3)	C13A—H13D	0.9800
C9—C12	1.537 (3)	C13A—H13E	0.9800
C9—C15	1.531 (3)	C13A—H13F	0.9800
C10—O10	1.243 (3)	C14A—H14D	0.9800
C11—H11	1.0000	C14A—H14E	0.9800
C12—H12	1.0000	C14A—H14F	0.9800
C13—H13A	0.9800	C15A—H15D	0.9800
C13—H13B	0.9800	C15A—H15E	0.9800
C13—H13C	0.9800	C15A—H15F	0.9800
C14—H14A	0.9800	C21—O21	1.307 (3)
C14—H14B	0.9800	C21—C22	1.496 (3)
C14—H14C	0.9800	C21—O22	1.207 (3)
C15—H15A	0.9800	O21—H21	0.92 (4)
C15—H15B	0.9800	C22—H22	0.9500
C15—H15C	0.9800	C22—C23	1.319 (3)
C1A—O1A	1.465 (2)	C23—H23A	0.9500
C1A—C2A	1.529 (3)	C23—C24	1.495 (3)
C1A—C11A	1.544 (3)	O23—H23	0.90 (4)
C1A—C12A	1.532 (3)	O23—C24	1.310 (3)
N1A—H1A	0.87 (3)	C24—O24	1.204 (3)
N1A—C2A	1.464 (3)		
O1—C1—C2	111.31 (15)	C10A—N1A—H1A	114.9 (19)
O1—C1—C11	107.05 (16)	C10A—N1A—C2A	127.28 (18)
O1—C1—C12	103.88 (15)	C1A—O1A—O2A	111.52 (13)
C2—C1—C11	110.59 (16)	C1A—C2A—H2A	107.6
C2—C1—C12	111.58 (17)	N1A—C2A—C1A	111.82 (16)
C12—C1—C11	112.16 (16)	N1A—C2A—H2A	107.6
C2—N1—H1	116.6 (18)	O3A—C2A—C1A	113.83 (16)
C10—N1—H1	116.4 (18)	O3A—C2A—N1A	108.21 (16)
C10—N1—C2	126.60 (18)	O3A—C2A—H2A	107.6
C1—O1—O2	111.58 (13)	C3A—O2A—O1A	108.45 (13)
C1—C2—H2	107.1	O2A—C3A—O3A	108.01 (15)
N1—C2—C1	112.66 (16)	O2A—C3A—C4A	112.07 (17)
N1—C2—H2	107.1	O2A—C3A—C13A	105.33 (16)
O3—C2—C1	113.14 (16)	O3A—C3A—C4A	110.54 (16)
O3—C2—N1	109.43 (15)	O3A—C3A—C13A	105.66 (16)
O3—C2—H2	107.1	C13A—C3A—C4A	114.77 (18)
C3—O2—O1	107.94 (13)	C2A—O3A—C3A	113.35 (14)
O2—C3—O3	107.97 (15)	C3A—C4A—H4AA	108.7
O2—C3—C4	111.88 (16)	C3A—C4A—H4AB	108.7
O2—C3—C13	105.56 (17)	C3A—C4A—C5A	114.17 (17)
O3—C3—C4	110.80 (17)	H4AA—C4A—H4AB	107.6

O3—C3—C13	105.81 (16)	C5A—C4A—H4AA	108.7
C13—C3—C4	114.40 (18)	C5A—C4A—H4AB	108.7
C2—O3—C3	114.21 (15)	C4A—C5A—H5AA	108.1
C3—C4—H4A	108.7	C4A—C5A—H5AB	108.1
C3—C4—H4B	108.7	C4A—C5A—C11A	116.71 (17)
H4A—C4—H4B	107.6	H5AA—C5A—H5AB	107.3
C5—C4—C3	114.40 (17)	C11A—C5A—H5AA	108.1
C5—C4—H4A	108.7	C11A—C5A—H5AB	108.1
C5—C4—H4B	108.7	C7A—C6A—H6A	108.1
C4—C5—H5A	108.0	C7A—C6A—C11A	110.79 (17)
C4—C5—H5B	108.0	C11A—C6A—H6A	108.1
C4—C5—C11	117.00 (18)	C14A—C6A—H6A	108.1
H5A—C5—H5B	107.3	C14A—C6A—C7A	110.33 (17)
C11—C5—H5A	108.0	C14A—C6A—C11A	111.42 (18)
C11—C5—H5B	108.0	C6A—C7A—H7AA	109.1
C7—C6—H6	108.1	C6A—C7A—H7AB	109.1
C7—C6—C11	110.47 (17)	H7AA—C7A—H7AB	107.8
C7—C6—C14	110.66 (18)	C8A—C7A—C6A	112.46 (17)
C11—C6—H6	108.1	C8A—C7A—H7AA	109.1
C14—C6—H6	108.1	C8A—C7A—H7AB	109.1
C14—C6—C11	111.34 (18)	C7A—C8A—H8AA	109.6
C6—C7—H7A	109.2	C7A—C8A—H8AB	109.6
C6—C7—H7B	109.2	C7A—C8A—C12A	110.32 (18)
H7A—C7—H7B	107.9	H8AA—C8A—H8AB	108.1
C8—C7—C6	111.98 (17)	C12A—C8A—H8AA	109.6
C8—C7—H7A	109.2	C12A—C8A—H8AB	109.6
C8—C7—H7B	109.2	C10A—C9A—H9A	105.8
C7—C8—H8A	109.4	C10A—C9A—C12A	114.48 (17)
C7—C8—H8B	109.4	C10A—C9A—C15A	110.49 (18)
C7—C8—C12	110.98 (18)	C12A—C9A—H9A	105.8
H8A—C8—H8B	108.0	C15A—C9A—H9A	105.8
C12—C8—H8A	109.4	C15A—C9A—C12A	113.76 (18)
C12—C8—H8B	109.4	N1A—C10A—C9A	119.20 (18)
C10—C9—H9	106.1	O10A—C10A—N1A	121.5 (2)
C10—C9—C12	113.39 (17)	O10A—C10A—C9A	119.17 (18)
C10—C9—C15	110.83 (19)	C1A—C11A—C6A	112.24 (17)
C12—C9—H9	106.1	C1A—C11A—H11A	106.7
C15—C9—H9	106.1	C5A—C11A—C1A	112.92 (16)
C15—C9—C12	113.64 (18)	C5A—C11A—C6A	111.09 (17)
N1—C10—C9	118.63 (19)	C5A—C11A—H11A	106.7
O10—C10—N1	121.7 (2)	C6A—C11A—H11A	106.7
O10—C10—C9	119.59 (19)	C1A—C12A—C8A	110.55 (17)
C1—C11—C6	111.53 (17)	C1A—C12A—C9A	110.87 (17)
C1—C11—H11	106.7	C1A—C12A—H12A	106.5
C5—C11—C1	113.03 (17)	C8A—C12A—C9A	115.35 (18)
C5—C11—C6	111.83 (17)	C8A—C12A—H12A	106.5
C5—C11—H11	106.7	C9A—C12A—H12A	106.5
C6—C11—H11	106.7	C3A—C13A—H13D	109.5

C1—C12—C9	110.22 (16)	C3A—C13A—H13E	109.5
C1—C12—H12	107.0	C3A—C13A—H13F	109.5
C8—C12—C1	111.15 (17)	H13D—C13A—H13E	109.5
C8—C12—C9	114.11 (18)	H13D—C13A—H13F	109.5
C8—C12—H12	107.0	H13E—C13A—H13F	109.5
C9—C12—H12	107.0	C6A—C14A—H14D	109.5
C3—C13—H13A	109.5	C6A—C14A—H14E	109.5
C3—C13—H13B	109.5	C6A—C14A—H14F	109.5
C3—C13—H13C	109.5	H14D—C14A—H14E	109.5
H13A—C13—H13B	109.5	H14D—C14A—H14F	109.5
H13A—C13—H13C	109.5	H14E—C14A—H14F	109.5
H13B—C13—H13C	109.5	C9A—C15A—H15D	109.5
C6—C14—H14A	109.5	C9A—C15A—H15E	109.5
C6—C14—H14B	109.5	C9A—C15A—H15F	109.5
C6—C14—H14C	109.5	H15D—C15A—H15E	109.5
H14A—C14—H14B	109.5	H15D—C15A—H15F	109.5
H14A—C14—H14C	109.5	H15E—C15A—H15F	109.5
H14B—C14—H14C	109.5	O21—C21—C22	111.73 (18)
C9—C15—H15A	109.5	O22—C21—O21	124.2 (2)
C9—C15—H15B	109.5	O22—C21—C22	124.0 (2)
C9—C15—H15C	109.5	C21—O21—H21	109 (2)
H15A—C15—H15B	109.5	C21—C22—H22	117.7
H15A—C15—H15C	109.5	C23—C22—C21	124.5 (2)
H15B—C15—H15C	109.5	C23—C22—H22	117.7
O1A—C1A—C2A	110.42 (15)	C22—C23—H23A	118.7
O1A—C1A—C11A	106.30 (16)	C22—C23—C24	122.5 (2)
O1A—C1A—C12A	104.63 (16)	C24—C23—H23A	118.7
C2A—C1A—C11A	111.69 (17)	C24—O23—H23	108 (2)
C2A—C1A—C12A	110.80 (16)	O23—C24—C23	112.5 (2)
C12A—C1A—C11A	112.66 (16)	O24—C24—C23	123.4 (2)
C2A—N1A—H1A	117.5 (19)	O24—C24—O23	124.1 (2)
C1—O1—O2—C3	46.72 (19)	O1A—C1A—C2A—N1A	70.0 (2)
C1—C2—O3—C3	25.7 (2)	O1A—C1A—C2A—O3A	−53.0 (2)
N1—C2—O3—C3	−100.77 (18)	O1A—C1A—C11A—C5A	68.3 (2)
O1—C1—C2—N1	73.3 (2)	O1A—C1A—C11A—C6A	−165.18 (15)
O1—C1—C2—O3	−51.5 (2)	O1A—C1A—C12A—C8A	169.36 (16)
O1—C1—C11—C5	66.4 (2)	O1A—C1A—C12A—C9A	−61.4 (2)
O1—C1—C11—C6	−166.56 (15)	O1A—O2A—C3A—O3A	−74.51 (18)
O1—C1—C12—C8	169.06 (16)	O1A—O2A—C3A—C4A	47.5 (2)
O1—C1—C12—C9	−63.4 (2)	O1A—O2A—C3A—C13A	172.94 (15)
O1—O2—C3—O3	−74.63 (18)	C2A—C1A—O1A—O2A	14.2 (2)
O1—O2—C3—C4	47.5 (2)	C2A—C1A—C11A—C5A	−52.2 (2)
O1—O2—C3—C13	172.56 (15)	C2A—C1A—C11A—C6A	74.3 (2)
C2—C1—O1—O2	13.5 (2)	C2A—C1A—C12A—C8A	−71.6 (2)
C2—C1—C11—C5	−55.0 (2)	C2A—C1A—C12A—C9A	57.6 (2)
C2—C1—C11—C6	72.0 (2)	C2A—N1A—C10A—C9A	−4.3 (3)
C2—C1—C12—C8	−70.9 (2)	C2A—N1A—C10A—O10A	179.03 (19)

C2—C1—C12—C9	56.6 (2)	O2A—C3A—O3A—C2A	34.5 (2)
C2—N1—C10—C9	−14.0 (3)	O2A—C3A—C4A—C5A	−95.0 (2)
C2—N1—C10—O10	170.1 (2)	C3A—C4A—C5A—C11A	56.3 (2)
O2—C3—O3—C2	35.3 (2)	O3A—C3A—C4A—C5A	25.6 (2)
O2—C3—C4—C5	−95.3 (2)	C4A—C3A—O3A—C2A	−88.48 (19)
C3—C4—C5—C11	55.0 (2)	C4A—C5A—C11A—C1A	−35.8 (3)
O3—C3—C4—C5	25.2 (2)	C4A—C5A—C11A—C6A	−162.93 (17)
C4—C3—O3—C2	−87.49 (19)	C6A—C7A—C8A—C12A	58.8 (2)
C4—C5—C11—C1	−33.3 (3)	C7A—C6A—C11A—C1A	50.4 (2)
C4—C5—C11—C6	−160.11 (17)	C7A—C6A—C11A—C5A	177.83 (17)
C6—C7—C8—C12	57.4 (2)	C7A—C8A—C12A—C1A	−57.5 (2)
C7—C6—C11—C1	53.8 (2)	C7A—C8A—C12A—C9A	175.75 (17)
C7—C6—C11—C5	−178.55 (18)	C10A—N1A—C2A—C1A	19.6 (3)
C7—C8—C12—C1	−55.4 (2)	C10A—N1A—C2A—O3A	145.8 (2)
C7—C8—C12—C9	179.25 (17)	C10A—C9A—C12A—C1A	−42.3 (2)
C10—N1—C2—C1	21.6 (3)	C10A—C9A—C12A—C8A	84.3 (2)
C10—N1—C2—O3	148.36 (19)	C11A—C1A—O1A—O2A	−107.15 (16)
C10—C9—C12—C1	−48.4 (2)	C11A—C1A—C2A—N1A	−171.92 (16)
C10—C9—C12—C8	77.5 (2)	C11A—C1A—C2A—O3A	65.1 (2)
C11—C1—O1—O2	−107.45 (16)	C11A—C1A—C12A—C8A	54.3 (2)
C11—C1—C2—N1	−167.84 (16)	C11A—C1A—C12A—C9A	−176.46 (16)
C11—C1—C2—O3	67.4 (2)	C11A—C6A—C7A—C8A	−54.9 (2)
C11—C1—C12—C8	53.8 (2)	C12A—C1A—O1A—O2A	133.43 (15)
C11—C1—C12—C9	−178.66 (16)	C12A—C1A—C2A—N1A	−45.4 (2)
C11—C6—C7—C8	−56.3 (2)	C12A—C1A—C2A—O3A	−168.44 (16)
C12—C1—O1—O2	133.72 (15)	C12A—C1A—C11A—C5A	−177.65 (17)
C12—C1—C2—N1	−42.2 (2)	C12A—C1A—C11A—C6A	−51.2 (2)
C12—C1—C2—O3	−167.02 (16)	C12A—C9A—C10A—N1A	15.7 (3)
C12—C1—C11—C5	179.76 (16)	C12A—C9A—C10A—O10A	−167.51 (19)
C12—C1—C11—C6	−53.2 (2)	C13A—C3A—O3A—C2A	146.79 (17)
C12—C9—C10—N1	27.2 (3)	C13A—C3A—C4A—C5A	144.95 (18)
C12—C9—C10—O10	−156.8 (2)	C14A—C6A—C7A—C8A	−178.81 (18)
C13—C3—O3—C2	147.99 (16)	C14A—C6A—C11A—C1A	173.60 (17)
C13—C3—C4—C5	144.73 (18)	C14A—C6A—C11A—C5A	−58.9 (2)
C14—C6—C7—C8	179.95 (18)	C15A—C9A—C10A—N1A	145.8 (2)
C14—C6—C11—C1	177.17 (17)	C15A—C9A—C10A—O10A	−37.5 (3)
C14—C6—C11—C5	−55.2 (2)	C15A—C9A—C12A—C1A	−170.66 (18)
C15—C9—C10—N1	156.3 (2)	C15A—C9A—C12A—C8A	−44.1 (3)
C15—C9—C10—O10	−27.6 (3)	C21—C22—C23—C24	−1.4 (4)
C15—C9—C12—C1	−176.15 (18)	O21—C21—C22—C23	137.4 (2)
C15—C9—C12—C8	−50.3 (3)	C22—C23—C24—O23	136.1 (2)
C1A—O1A—O2A—C3A	46.43 (19)	C22—C23—C24—O24	−43.3 (4)
C1A—C2A—O3A—C3A	27.3 (2)	O22—C21—C22—C23	−43.8 (4)
N1A—C2A—O3A—C3A	−97.71 (18)		

Hydrogen-bond geometry (Å, °)

<i>D</i> —H $\cdots$ <i>A</i>	<i>D</i> —H	H $\cdots$ <i>A</i>	<i>D</i> $\cdots$ <i>A</i>	<i>D</i> —H $\cdots$ <i>A</i>
N1—H1 $\cdots$ O22	0.89 (3)	2.36 (3)	3.128 (3)	146 (2)
N1A—H1A $\cdots$ O24	0.87 (3)	2.26 (3)	3.038 (3)	149 (2)
O21—H21 $\cdots$ O10	0.92 (4)	1.63 (4)	2.539 (2)	167 (3)
O23—H23 $\cdots$ O10A	0.90 (4)	1.65 (4)	2.548 (2)	174 (4)

1,5,9-Trimethyl-14,15,16-trioxa-11-azatetracyclo[10.3.1.0^{4,13}.0^{8,13}]hexadecan-10-one-(2*E*)-but-2-enedioic acid (1/1) (madiha46cult)

Crystal data

2C₁₅H₂₃NO₄·C₄H₄O₄*M_r* = 678.76Monoclinic, *P*2₁*a* = 9.57929 (11) Å*b* = 10.05214 (16) Å*c* = 17.7765 (2) Å β = 96.4731 (11)°*V* = 1700.82 (4) Å³*Z* = 2*F*(000) = 728*D_x* = 1.325 Mg m⁻³Cu *K*α radiation, λ = 1.54184 Å

Cell parameters from 10873 reflections

 θ = 4.6–75.5° μ = 0.83 mm⁻¹*T* = 100 K

Block, colourless

0.4 × 0.15 × 0.12 mm

Data collection

Rigaku SuperNova Dual Source

diffractometer with an Atlas detector

Radiation source: micro-focus sealed X-ray tube, SuperNova (Cu) X-ray Source

Mirror monochromator

Detector resolution: 10.3577 pixels mm⁻¹ ω scans

Absorption correction: multi-scan

(CrysAlis PRO; Rigaku OD, 2015)

*T*_{min} = 0.546, *T*_{max} = 1.000

15361 measured reflections

5657 independent reflections

5564 reflections with *I* > 2σ(*I*)*R*_{int} = 0.024 $\theta_{\max}$ = 67.5°, $\theta_{\min}$ = 4.7°*h* = −11→11*k* = −10→12*l* = −21→20

Refinement

Refinement on *F*²

Least-squares matrix: full

R [*F*² > 2σ(*F*²)] = 0.025*wR*(*F*²) = 0.066*S* = 1.02

5657 reflections

455 parameters

1 restraint

Primary atom site location: structure-invariant direct methods

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

 $w = 1/[\sigma^2(F_o^2) + (0.0392P)^2 + 0.2051P]$ where $P = (F_o^2 + 2F_c^2)/3$ (Δ/σ)_{max} < 0.001Δρ_{max} = 0.15 e Å⁻³Δρ_{min} = −0.16 e Å⁻³Absolute structure: Flack *x* determined using2330 quotients [(*I*+)−(*I*−)]/[(*I*+) + (*I*−)] (Parsons *et al.*, 2013)

Absolute structure parameter: 0.11 (6)

Special details

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.

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	−0.14705 (13)	0.01930 (15)	0.43814 (7)	0.0210 (3)
O2	−0.16249 (13)	0.00003 (15)	0.51896 (7)	0.0223 (3)
O3	−0.14576 (13)	0.22260 (14)	0.55118 (7)	0.0203 (3)
O10	0.30392 (13)	0.09722 (15)	0.52817 (7)	0.0229 (3)
N11	0.08612 (15)	0.17835 (18)	0.53053 (9)	0.0185 (3)
H11	0.112 (2)	0.205 (3)	0.5749 (14)	0.026 (6)*
C1	−0.10110 (18)	0.1537 (2)	0.42303 (10)	0.0181 (4)
C2	−0.04967 (17)	0.2267 (2)	0.49631 (10)	0.0177 (4)
H2	−0.0373	0.3223	0.4830	0.021*
C3	−0.23863 (18)	0.1106 (2)	0.54311 (11)	0.0218 (4)
C4	−0.36889 (18)	0.1414 (2)	0.48717 (12)	0.0263 (5)
H4A	−0.3982	0.0591	0.4591	0.032*
H4B	−0.4466	0.1682	0.5162	0.032*
C5	−0.34649 (19)	0.2507 (2)	0.43025 (11)	0.0255 (4)
H5A	−0.3277	0.3350	0.4584	0.031*
H5B	−0.4352	0.2624	0.3965	0.031*
C6	−0.1824 (2)	0.3593 (2)	0.34533 (11)	0.0246 (4)
H6	−0.1477	0.4208	0.3876	0.029*
C7	−0.0624 (2)	0.3357 (2)	0.29766 (11)	0.0282 (5)
H7A	−0.0311	0.4223	0.2791	0.034*
H7B	−0.0973	0.2814	0.2530	0.034*
C8	0.0629 (2)	0.2655 (2)	0.34086 (11)	0.0241 (4)
H8A	0.1045	0.3235	0.3825	0.029*
H8B	0.1353	0.2490	0.3064	0.029*
C9	0.14019 (19)	0.0564 (2)	0.41805 (10)	0.0197 (4)
H9	0.1029	−0.0345	0.4270	0.024*
C10	0.18336 (18)	0.1151 (2)	0.49567 (10)	0.0193 (4)
C11	−0.22729 (19)	0.2280 (2)	0.38059 (11)	0.0218 (4)
H11A	−0.2659	0.1695	0.3377	0.026*
C12	0.01905 (18)	0.1331 (2)	0.37367 (10)	0.0197 (4)
H12	−0.0184	0.0758	0.3300	0.024*
C13	−0.2729 (2)	0.0746 (2)	0.62168 (12)	0.0300 (5)
H13A	−0.1869	0.0468	0.6528	0.045*
H13B	−0.3411	0.0016	0.6182	0.045*
H13C	−0.3129	0.1523	0.6448	0.045*
C14	−0.3053 (2)	0.4275 (3)	0.29779 (13)	0.0332 (5)
H14A	−0.2709	0.5058	0.2727	0.050*
H14B	−0.3755	0.4551	0.3307	0.050*
H14C	−0.3482	0.3653	0.2595	0.050*
C15	0.2678 (2)	0.0359 (2)	0.37455 (12)	0.0291 (5)
H15A	0.3157	0.1211	0.3699	0.044*
H15B	0.2366	0.0009	0.3240	0.044*
H15C	0.3326	−0.0275	0.4019	0.044*
O1A	0.81813 (12)	0.99691 (14)	0.98122 (6)	0.0179 (3)
O2A	0.83624 (13)	0.85557 (14)	0.96239 (7)	0.0189 (3)

O3A	0.81395 (12)	0.88511 (13)	0.83245 (7)	0.0164 (3)
O10A	0.38942 (12)	0.88100 (14)	0.91775 (7)	0.0208 (3)
N11A	0.58533 (15)	0.91491 (18)	0.86173 (9)	0.0170 (3)
H11B	0.569 (2)	0.839 (3)	0.8393 (13)	0.025 (6)*
C1A	0.76808 (17)	1.07386 (19)	0.91388 (9)	0.0149 (4)
C2A	0.71516 (17)	0.98276 (19)	0.84849 (10)	0.0153 (4)
H2A	0.6944	1.0393	0.8023	0.018*
C3A	0.90985 (18)	0.8486 (2)	0.89763 (10)	0.0184 (4)
C4A	1.03800 (18)	0.9410 (2)	0.90419 (11)	0.0216 (4)
H4AA	1.0711	0.9538	0.9585	0.026*
H4AB	1.1144	0.8967	0.8805	0.026*
C5A	1.01141 (18)	1.0771 (2)	0.86762 (11)	0.0206 (4)
H5AA	0.9911	1.0641	0.8123	0.025*
H5AB	1.0993	1.1294	0.8765	0.025*
C6A	0.84479 (19)	1.2720 (2)	0.83779 (10)	0.0199 (4)
H6A	0.8106	1.2293	0.7883	0.024*
C7A	0.7233 (2)	1.3519 (2)	0.86383 (11)	0.0236 (4)
H7AA	0.6907	1.4181	0.8244	0.028*
H7AB	0.7570	1.4010	0.9107	0.028*
C8A	0.59940 (19)	1.2629 (2)	0.87903 (11)	0.0215 (4)
H8AA	0.5242	1.3181	0.8969	0.026*
H8AB	0.5607	1.2185	0.8315	0.026*
C9A	0.53028 (18)	1.0664 (2)	0.96248 (10)	0.0184 (4)
H9A	0.5681	1.0283	1.0126	0.022*
C10A	0.49670 (17)	0.9490 (2)	0.91108 (10)	0.0174 (4)
C11A	0.89160 (17)	1.1607 (2)	0.89452 (10)	0.0172 (4)
H11C	0.9309	1.2052	0.9426	0.021*
C12A	0.64707 (17)	1.1581 (2)	0.93868 (10)	0.0168 (4)
H12A	0.6862	1.2075	0.9852	0.020*
C13A	0.9415 (2)	0.7027 (2)	0.88912 (11)	0.0230 (4)
H13D	0.8566	0.6505	0.8941	0.035*
H13E	1.0160	0.6760	0.9286	0.035*
H13F	0.9724	0.6869	0.8392	0.035*
C14A	0.9675 (2)	1.3635 (2)	0.82478 (12)	0.0271 (4)
H14D	1.0121	1.3962	0.8736	0.041*
H14E	0.9326	1.4390	0.7932	0.041*
H14F	1.0365	1.3138	0.7992	0.041*
C15A	0.39547 (19)	1.1407 (2)	0.97620 (13)	0.0294 (5)
H15D	0.3515	1.1778	0.9283	0.044*
H15E	0.4186	1.2130	1.0125	0.044*
H15F	0.3302	1.0789	0.9966	0.044*
O21	0.41238 (14)	0.26565 (17)	0.62699 (8)	0.0286 (3)
H21	0.368 (4)	0.205 (4)	0.595 (2)	0.084 (12)*
O22	0.21229 (13)	0.27193 (16)	0.68154 (8)	0.0249 (3)
O23	0.31017 (14)	0.65994 (15)	0.85688 (8)	0.0237 (3)
H23	0.352 (3)	0.742 (4)	0.8795 (19)	0.067 (10)*
O24	0.51070 (13)	0.64800 (15)	0.80351 (8)	0.0290 (3)
C21	0.32987 (18)	0.3129 (2)	0.67523 (11)	0.0210 (4)

C22	0.39656 (19)	0.4253 (2)	0.72062 (11)	0.0215 (4)
H22	0.4866	0.4556	0.7107	0.026*
C23	0.33419 (19)	0.4837 (2)	0.77402 (10)	0.0201 (4)
H23A	0.2487	0.4482	0.7878	0.024*
C24	0.39572 (18)	0.6052 (2)	0.81339 (10)	0.0201 (4)

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0235 (6)	0.0186 (8)	0.0215 (6)	−0.0056 (5)	0.0051 (5)	−0.0009 (5)
O2	0.0237 (6)	0.0209 (8)	0.0236 (6)	0.0012 (6)	0.0083 (5)	0.0030 (6)
O3	0.0169 (6)	0.0227 (8)	0.0223 (6)	−0.0005 (5)	0.0060 (5)	−0.0026 (6)
O10	0.0167 (6)	0.0259 (8)	0.0260 (7)	−0.0004 (5)	0.0018 (5)	−0.0051 (6)
N11	0.0161 (7)	0.0234 (9)	0.0158 (8)	−0.0013 (6)	0.0011 (6)	−0.0042 (6)
C1	0.0174 (8)	0.0165 (10)	0.0202 (9)	−0.0041 (7)	0.0016 (7)	−0.0006 (8)
C2	0.0145 (8)	0.0195 (11)	0.0194 (8)	−0.0009 (7)	0.0028 (7)	−0.0013 (8)
C3	0.0181 (8)	0.0180 (11)	0.0306 (10)	−0.0008 (8)	0.0083 (7)	0.0000 (8)
C4	0.0158 (8)	0.0275 (13)	0.0361 (11)	−0.0023 (8)	0.0049 (8)	−0.0009 (9)
C5	0.0178 (9)	0.0262 (12)	0.0315 (10)	0.0014 (8)	−0.0019 (7)	−0.0016 (9)
C6	0.0299 (10)	0.0217 (11)	0.0210 (9)	−0.0001 (9)	−0.0024 (8)	−0.0013 (8)
C7	0.0370 (11)	0.0268 (13)	0.0207 (9)	−0.0029 (9)	0.0030 (8)	0.0027 (9)
C8	0.0268 (9)	0.0246 (11)	0.0216 (9)	−0.0058 (8)	0.0060 (7)	0.0010 (8)
C9	0.0186 (8)	0.0196 (11)	0.0217 (9)	−0.0016 (7)	0.0053 (7)	−0.0045 (8)
C10	0.0178 (8)	0.0180 (11)	0.0228 (9)	−0.0040 (7)	0.0049 (7)	−0.0012 (8)
C11	0.0207 (9)	0.0209 (11)	0.0228 (9)	−0.0012 (8)	−0.0023 (7)	−0.0025 (8)
C12	0.0204 (8)	0.0202 (11)	0.0188 (9)	−0.0041 (7)	0.0035 (7)	−0.0039 (7)
C13	0.0282 (10)	0.0294 (13)	0.0348 (11)	0.0036 (9)	0.0146 (8)	0.0036 (10)
C14	0.0425 (12)	0.0256 (13)	0.0287 (10)	0.0069 (10)	−0.0076 (9)	−0.0017 (9)
C15	0.0236 (10)	0.0375 (14)	0.0274 (10)	0.0005 (9)	0.0081 (8)	−0.0092 (9)
O1A	0.0212 (6)	0.0142 (7)	0.0180 (6)	0.0022 (5)	0.0005 (5)	−0.0022 (5)
O2A	0.0221 (6)	0.0139 (7)	0.0210 (6)	0.0024 (5)	0.0039 (5)	−0.0007 (5)
O3A	0.0147 (6)	0.0157 (7)	0.0187 (6)	0.0018 (5)	0.0013 (5)	−0.0022 (5)
O10A	0.0157 (6)	0.0193 (8)	0.0279 (7)	−0.0028 (5)	0.0042 (5)	−0.0018 (6)
N11A	0.0143 (7)	0.0155 (9)	0.0209 (7)	−0.0023 (6)	0.0002 (6)	−0.0043 (7)
C1A	0.0142 (8)	0.0141 (10)	0.0158 (8)	0.0006 (7)	−0.0011 (6)	−0.0005 (7)
C2A	0.0126 (8)	0.0143 (10)	0.0193 (8)	−0.0010 (7)	0.0029 (6)	−0.0004 (7)
C3A	0.0153 (8)	0.0208 (11)	0.0191 (9)	0.0035 (7)	0.0013 (7)	0.0015 (8)
C4A	0.0143 (8)	0.0241 (11)	0.0260 (9)	0.0026 (7)	0.0012 (7)	−0.0032 (8)
C5A	0.0154 (8)	0.0203 (11)	0.0266 (9)	−0.0026 (7)	0.0042 (7)	−0.0037 (8)
C6A	0.0216 (9)	0.0157 (10)	0.0227 (9)	−0.0032 (8)	0.0035 (7)	−0.0004 (8)
C7A	0.0258 (10)	0.0158 (11)	0.0292 (10)	0.0011 (8)	0.0033 (8)	0.0023 (8)
C8A	0.0171 (8)	0.0179 (11)	0.0289 (9)	0.0023 (7)	0.0008 (7)	−0.0005 (8)
C9A	0.0147 (8)	0.0178 (11)	0.0231 (9)	−0.0018 (7)	0.0035 (7)	−0.0021 (8)
C10A	0.0124 (8)	0.0187 (11)	0.0206 (8)	0.0010 (7)	0.0001 (6)	0.0026 (7)
C11A	0.0148 (8)	0.0151 (10)	0.0219 (9)	−0.0031 (7)	0.0025 (7)	−0.0032 (8)
C12A	0.0139 (8)	0.0160 (10)	0.0205 (8)	−0.0008 (7)	0.0020 (6)	−0.0027 (7)
C13A	0.0228 (9)	0.0193 (11)	0.0275 (9)	0.0043 (8)	0.0048 (7)	0.0000 (8)
C14A	0.0282 (10)	0.0192 (11)	0.0356 (11)	−0.0053 (8)	0.0104 (8)	0.0011 (9)

C15A	0.0176 (9)	0.0266 (13)	0.0458 (12)	−0.0031 (8)	0.0113 (8)	−0.0116 (10)
O21	0.0190 (7)	0.0322 (9)	0.0349 (8)	−0.0021 (6)	0.0041 (6)	−0.0135 (7)
O22	0.0225 (7)	0.0272 (8)	0.0249 (6)	−0.0041 (6)	0.0026 (5)	−0.0047 (6)
O23	0.0232 (6)	0.0233 (8)	0.0251 (7)	−0.0049 (6)	0.0053 (5)	−0.0051 (6)
O24	0.0198 (7)	0.0248 (9)	0.0430 (8)	−0.0036 (6)	0.0061 (6)	−0.0099 (7)
C21	0.0191 (9)	0.0208 (11)	0.0222 (9)	0.0013 (8)	−0.0017 (7)	−0.0007 (8)
C22	0.0175 (8)	0.0199 (11)	0.0265 (9)	−0.0012 (8)	−0.0008 (7)	0.0016 (8)
C23	0.0187 (8)	0.0180 (11)	0.0229 (9)	−0.0026 (7)	0.0000 (7)	0.0024 (8)
C24	0.0188 (9)	0.0186 (11)	0.0220 (9)	0.0006 (7)	−0.0017 (7)	0.0028 (7)

Geometric parameters (Å, °)

O1—O2	1.4735 (18)	N11A—H11B	0.87 (3)
O1—C1	1.456 (2)	N11A—C2A	1.461 (2)
O2—C3	1.422 (2)	N11A—C10A	1.332 (2)
O3—C2	1.415 (2)	C1A—C2A	1.521 (2)
O3—C3	1.432 (2)	C1A—C11A	1.540 (2)
O10—C10	1.245 (2)	C1A—C12A	1.540 (2)
N11—H11	0.84 (3)	C2A—H2A	1.0000
N11—C2	1.456 (2)	C3A—C4A	1.533 (3)
N11—C10	1.337 (2)	C3A—C13A	1.508 (3)
C1—C2	1.527 (2)	C4A—H4AA	0.9900
C1—C11	1.543 (3)	C4A—H4AB	0.9900
C1—C12	1.538 (2)	C4A—C5A	1.524 (3)
C2—H2	1.0000	C5A—H5AA	0.9900
C3—C4	1.537 (3)	C5A—H5AB	0.9900
C3—C13	1.514 (3)	C5A—C11A	1.541 (2)
C4—H4A	0.9900	C6A—H6A	1.0000
C4—H4B	0.9900	C6A—C7A	1.529 (3)
C4—C5	1.525 (3)	C6A—C11A	1.539 (3)
C5—H5A	0.9900	C6A—C14A	1.531 (3)
C5—H5B	0.9900	C7A—H7AA	0.9900
C5—C11	1.537 (3)	C7A—H7AB	0.9900
C6—H6	1.0000	C7A—C8A	1.534 (3)
C6—C7	1.522 (3)	C8A—H8AA	0.9900
C6—C11	1.543 (3)	C8A—H8AB	0.9900
C6—C14	1.532 (3)	C8A—C12A	1.528 (3)
C7—H7A	0.9900	C9A—H9A	1.0000
C7—H7B	0.9900	C9A—C10A	1.505 (3)
C7—C8	1.523 (3)	C9A—C12A	1.545 (2)
C8—H8A	0.9900	C9A—C15A	1.535 (2)
C8—H8B	0.9900	C11A—H11C	1.0000
C8—C12	1.531 (3)	C12A—H12A	1.0000
C9—H9	1.0000	C13A—H13D	0.9800
C9—C10	1.515 (3)	C13A—H13E	0.9800
C9—C12	1.535 (3)	C13A—H13F	0.9800
C9—C15	1.532 (2)	C14A—H14D	0.9800
C11—H11A	1.0000	C14A—H14E	0.9800

C12—H12	1.0000	C14A—H14F	0.9800
C13—H13A	0.9800	C15A—H15D	0.9800
C13—H13B	0.9800	C15A—H15E	0.9800
C13—H13C	0.9800	C15A—H15F	0.9800
C14—H14A	0.9800	O21—H21	0.91 (4)
C14—H14B	0.9800	O21—C21	1.319 (2)
C14—H14C	0.9800	O22—C21	1.216 (2)
C15—H15A	0.9800	O23—H23	0.98 (4)
C15—H15B	0.9800	O23—C24	1.310 (2)
C15—H15C	0.9800	O24—C24	1.214 (2)
O1A—O2A	1.4744 (19)	C21—C22	1.490 (3)
O1A—C1A	1.460 (2)	C22—H22	0.9500
O2A—C3A	1.418 (2)	C22—C23	1.316 (3)
O3A—C2A	1.415 (2)	C23—H23A	0.9500
O3A—C3A	1.443 (2)	C23—C24	1.495 (3)
O10A—C10A	1.251 (2)		
C1—O1—O2	111.57 (13)	O1A—C1A—C11A	107.08 (13)
C3—O2—O1	107.64 (13)	O1A—C1A—C12A	104.18 (13)
C2—O3—C3	113.52 (14)	C2A—C1A—C11A	111.62 (14)
C2—N11—H11	116.2 (16)	C2A—C1A—C12A	110.68 (13)
C10—N11—H11	115.8 (16)	C12A—C1A—C11A	112.00 (15)
C10—N11—C2	126.99 (16)	O3A—C2A—N11A	108.03 (15)
O1—C1—C2	111.33 (15)	O3A—C2A—C1A	113.51 (13)
O1—C1—C11	107.62 (14)	O3A—C2A—H2A	107.7
O1—C1—C12	103.95 (15)	N11A—C2A—C1A	111.98 (14)
C2—C1—C11	110.12 (16)	N11A—C2A—H2A	107.7
C2—C1—C12	111.19 (14)	C1A—C2A—H2A	107.7
C12—C1—C11	112.44 (15)	O2A—C3A—O3A	108.03 (13)
O3—C2—N11	108.79 (14)	O2A—C3A—C4A	112.05 (15)
O3—C2—C1	113.66 (14)	O2A—C3A—C13A	104.69 (15)
O3—C2—H2	107.2	O3A—C3A—C4A	109.80 (15)
N11—C2—C1	112.51 (15)	O3A—C3A—C13A	106.48 (16)
N11—C2—H2	107.2	C13A—C3A—C4A	115.37 (15)
C1—C2—H2	107.2	C3A—C4A—H4AA	108.6
O2—C3—O3	108.10 (13)	C3A—C4A—H4AB	108.6
O2—C3—C4	111.66 (16)	H4AA—C4A—H4AB	107.6
O2—C3—C13	105.32 (16)	C5A—C4A—C3A	114.69 (14)
O3—C3—C4	110.84 (16)	C5A—C4A—H4AA	108.6
O3—C3—C13	106.97 (17)	C5A—C4A—H4AB	108.6
C13—C3—C4	113.61 (16)	C4A—C5A—H5AA	108.1
C3—C4—H4A	108.7	C4A—C5A—H5AB	108.1
C3—C4—H4B	108.7	C4A—C5A—C11A	116.83 (15)
H4A—C4—H4B	107.6	H5AA—C5A—H5AB	107.3
C5—C4—C3	114.21 (15)	C11A—C5A—H5AA	108.1
C5—C4—H4A	108.7	C11A—C5A—H5AB	108.1
C5—C4—H4B	108.7	C7A—C6A—H6A	107.8
C4—C5—H5A	108.2	C7A—C6A—C11A	111.06 (15)

C4—C5—H5B	108.2	C7A—C6A—C14A	110.75 (17)
C4—C5—C11	116.33 (18)	C11A—C6A—H6A	107.8
H5A—C5—H5B	107.4	C14A—C6A—H6A	107.8
C11—C5—H5A	108.2	C14A—C6A—C11A	111.34 (15)
C11—C5—H5B	108.2	C6A—C7A—H7AA	109.2
C7—C6—H6	107.9	C6A—C7A—H7AB	109.2
C7—C6—C11	110.80 (18)	C6A—C7A—C8A	112.18 (17)
C7—C6—C14	110.16 (17)	H7AA—C7A—H7AB	107.9
C11—C6—H6	107.9	C8A—C7A—H7AA	109.2
C14—C6—H6	107.9	C8A—C7A—H7AB	109.2
C14—C6—C11	112.00 (17)	C7A—C8A—H8AA	109.6
C6—C7—H7A	108.9	C7A—C8A—H8AB	109.6
C6—C7—H7B	108.9	H8AA—C8A—H8AB	108.1
C6—C7—C8	113.15 (16)	C12A—C8A—C7A	110.35 (15)
H7A—C7—H7B	107.8	C12A—C8A—H8AA	109.6
C8—C7—H7A	108.9	C12A—C8A—H8AB	109.6
C8—C7—H7B	108.9	C10A—C9A—H9A	105.8
C7—C8—H8A	109.4	C10A—C9A—C12A	114.43 (15)
C7—C8—H8B	109.4	C10A—C9A—C15A	110.62 (15)
C7—C8—C12	111.15 (16)	C12A—C9A—H9A	105.8
H8A—C8—H8B	108.0	C15A—C9A—H9A	105.8
C12—C8—H8A	109.4	C15A—C9A—C12A	113.64 (16)
C12—C8—H8B	109.4	O10A—C10A—N11A	120.89 (18)
C10—C9—H9	106.1	O10A—C10A—C9A	119.50 (16)
C10—C9—C12	112.67 (16)	N11A—C10A—C9A	119.52 (16)
C10—C9—C15	111.14 (15)	C1A—C11A—C5A	112.24 (16)
C12—C9—H9	106.1	C1A—C11A—H11C	106.7
C15—C9—H9	106.1	C5A—C11A—H11C	106.7
C15—C9—C12	114.07 (16)	C6A—C11A—C1A	112.58 (15)
O10—C10—N11	120.80 (17)	C6A—C11A—C5A	111.42 (15)
O10—C10—C9	120.69 (16)	C6A—C11A—H11C	106.7
N11—C10—C9	118.35 (16)	C1A—C12A—C9A	109.99 (15)
C1—C11—H11A	106.9	C1A—C12A—H12A	106.6
C5—C11—C1	112.49 (16)	C8A—C12A—C1A	110.88 (15)
C5—C11—C6	111.45 (17)	C8A—C12A—C9A	115.63 (15)
C5—C11—H11A	106.9	C8A—C12A—H12A	106.6
C6—C11—C1	111.93 (15)	C9A—C12A—H12A	106.6
C6—C11—H11A	106.9	C3A—C13A—H13D	109.5
C1—C12—H12	107.1	C3A—C13A—H13E	109.5
C8—C12—C1	110.77 (16)	C3A—C13A—H13F	109.5
C8—C12—C9	114.12 (15)	H13D—C13A—H13E	109.5
C8—C12—H12	107.1	H13D—C13A—H13F	109.5
C9—C12—C1	110.22 (15)	H13E—C13A—H13F	109.5
C9—C12—H12	107.1	C6A—C14A—H14D	109.5
C3—C13—H13A	109.5	C6A—C14A—H14E	109.5
C3—C13—H13B	109.5	C6A—C14A—H14F	109.5
C3—C13—H13C	109.5	H14D—C14A—H14E	109.5
H13A—C13—H13B	109.5	H14D—C14A—H14F	109.5

H13A—C13—H13C	109.5	H14E—C14A—H14F	109.5
H13B—C13—H13C	109.5	C9A—C15A—H15D	109.5
C6—C14—H14A	109.5	C9A—C15A—H15E	109.5
C6—C14—H14B	109.5	C9A—C15A—H15F	109.5
C6—C14—H14C	109.5	H15D—C15A—H15E	109.5
H14A—C14—H14B	109.5	H15D—C15A—H15F	109.5
H14A—C14—H14C	109.5	H15E—C15A—H15F	109.5
H14B—C14—H14C	109.5	C21—O21—H21	112 (2)
C9—C15—H15A	109.5	C24—O23—H23	109.9 (19)
C9—C15—H15B	109.5	O21—C21—C22	111.93 (16)
C9—C15—H15C	109.5	O22—C21—O21	124.56 (19)
H15A—C15—H15B	109.5	O22—C21—C22	123.49 (17)
H15A—C15—H15C	109.5	C21—C22—H22	119.1
H15B—C15—H15C	109.5	C23—C22—C21	121.83 (17)
C1A—O1A—O2A	111.13 (12)	C23—C22—H22	119.1
C3A—O2A—O1A	108.31 (13)	C22—C23—H23A	119.5
C2A—O3A—C3A	113.24 (13)	C22—C23—C24	121.02 (17)
C2A—N11A—H11B	116.6 (15)	C24—C23—H23A	119.5
C10A—N11A—H11B	115.8 (15)	O23—C24—C23	112.32 (16)
C10A—N11A—C2A	127.12 (17)	O24—C24—O23	125.09 (19)
O1A—C1A—C2A	110.98 (15)	O24—C24—C23	122.57 (17)
O1—O2—C3—O3	−75.33 (16)	O1A—C1A—C2A—O3A	−53.41 (18)
O1—O2—C3—C4	46.84 (18)	O1A—C1A—C2A—N11A	69.25 (17)
O1—O2—C3—C13	170.59 (14)	O1A—C1A—C11A—C5A	67.91 (18)
O1—C1—C2—O3	−51.2 (2)	O1A—C1A—C11A—C6A	−165.41 (14)
O1—C1—C2—N11	72.98 (18)	O1A—C1A—C12A—C8A	169.96 (15)
O1—C1—C11—C5	67.0 (2)	O1A—C1A—C12A—C9A	−60.88 (17)
O1—C1—C11—C6	−166.59 (14)	O2A—O1A—C1A—C2A	14.00 (17)
O1—C1—C12—C8	170.02 (14)	O2A—O1A—C1A—C11A	−108.05 (14)
O1—C1—C12—C9	−62.71 (17)	O2A—O1A—C1A—C12A	133.15 (13)
O2—O1—C1—C2	13.05 (18)	O2A—C3A—C4A—C5A	−94.82 (19)
O2—O1—C1—C11	−107.72 (14)	O3A—C3A—C4A—C5A	25.2 (2)
O2—O1—C1—C12	132.84 (13)	C1A—O1A—O2A—C3A	46.89 (16)
O2—C3—C4—C5	−96.5 (2)	C2A—O3A—C3A—O2A	33.9 (2)
O3—C3—C4—C5	24.1 (2)	C2A—O3A—C3A—C4A	−88.58 (17)
C1—O1—O2—C3	46.95 (16)	C2A—O3A—C3A—C13A	145.87 (15)
C2—O3—C3—O2	36.03 (19)	C2A—N11A—C10A—O10A	−178.97 (16)
C2—O3—C3—C4	−86.64 (18)	C2A—N11A—C10A—C9A	−2.4 (3)
C2—O3—C3—C13	149.01 (16)	C2A—C1A—C11A—C5A	−53.7 (2)
C2—N11—C10—O10	168.54 (19)	C2A—C1A—C11A—C6A	72.94 (19)
C2—N11—C10—C9	−16.1 (3)	C2A—C1A—C12A—C8A	−70.70 (19)
C2—C1—C11—C5	−54.5 (2)	C2A—C1A—C12A—C9A	58.46 (19)
C2—C1—C11—C6	71.88 (19)	C3A—O3A—C2A—N11A	−96.98 (16)
C2—C1—C12—C8	−70.09 (19)	C3A—O3A—C2A—C1A	27.8 (2)
C2—C1—C12—C9	57.2 (2)	C3A—C4A—C5A—C11A	56.1 (2)
C3—O3—C2—N11	−101.04 (17)	C4A—C5A—C11A—C1A	−34.7 (2)
C3—O3—C2—C1	25.2 (2)	C4A—C5A—C11A—C6A	−161.99 (15)

C3—C4—C5—C11	57.3 (2)	C6A—C7A—C8A—C12A	57.9 (2)
C4—C5—C11—C1	−34.6 (2)	C7A—C6A—C11A—C1A	51.3 (2)
C4—C5—C11—C6	−161.27 (16)	C7A—C6A—C11A—C5A	178.43 (15)
C6—C7—C8—C12	56.4 (2)	C7A—C8A—C12A—C1A	−57.1 (2)
C7—C6—C11—C1	51.9 (2)	C7A—C8A—C12A—C9A	176.83 (16)
C7—C6—C11—C5	178.85 (16)	C10A—N11A—C2A—O3A	144.14 (17)
C7—C8—C12—C1	−55.0 (2)	C10A—N11A—C2A—C1A	18.4 (2)
C7—C8—C12—C9	179.94 (16)	C10A—C9A—C12A—C1A	−42.5 (2)
C10—N11—C2—O3	149.75 (18)	C10A—C9A—C12A—C8A	84.0 (2)
C10—N11—C2—C1	22.9 (3)	C11A—C1A—C2A—O3A	65.96 (19)
C10—C9—C12—C1	−49.7 (2)	C11A—C1A—C2A—N11A	−171.38 (14)
C10—C9—C12—C8	75.73 (19)	C11A—C1A—C12A—C8A	54.57 (19)
C11—C1—C2—O3	68.1 (2)	C11A—C1A—C12A—C9A	−176.28 (14)
C11—C1—C2—N11	−167.73 (14)	C11A—C6A—C7A—C8A	−54.6 (2)
C11—C1—C12—C8	53.9 (2)	C12A—C1A—C2A—O3A	−168.57 (14)
C11—C1—C12—C9	−178.82 (16)	C12A—C1A—C2A—N11A	−45.9 (2)
C11—C6—C7—C8	−54.4 (2)	C12A—C1A—C11A—C5A	−178.48 (14)
C12—C1—C2—O3	−166.63 (16)	C12A—C1A—C11A—C6A	−51.8 (2)
C12—C1—C2—N11	−42.4 (2)	C12A—C9A—C10A—O10A	−168.40 (16)
C12—C1—C11—C5	−179.11 (16)	C12A—C9A—C10A—N11A	14.9 (2)
C12—C1—C11—C6	−52.7 (2)	C13A—C3A—C4A—C5A	145.53 (16)
C12—C9—C10—O10	−155.53 (18)	C14A—C6A—C7A—C8A	−178.81 (16)
C12—C9—C10—N11	29.1 (2)	C14A—C6A—C11A—C1A	175.24 (15)
C13—C3—C4—C5	144.58 (19)	C14A—C6A—C11A—C5A	−57.7 (2)
C14—C6—C7—C8	−178.86 (18)	C15A—C9A—C10A—O10A	−38.5 (2)
C14—C6—C11—C1	175.34 (16)	C15A—C9A—C10A—N11A	144.86 (18)
C14—C6—C11—C5	−57.7 (2)	C15A—C9A—C12A—C1A	−170.95 (15)
C15—C9—C10—O10	−26.1 (3)	C15A—C9A—C12A—C8A	−44.4 (2)
C15—C9—C10—N11	158.55 (18)	O21—C21—C22—C23	−177.50 (19)
C15—C9—C12—C1	−177.59 (16)	O22—C21—C22—C23	3.6 (3)
C15—C9—C12—C8	−52.2 (2)	C21—C22—C23—C24	−173.53 (17)
O1A—O2A—C3A—O3A	−74.54 (16)	C22—C23—C24—O23	171.06 (18)
O1A—O2A—C3A—C4A	46.53 (17)	C22—C23—C24—O24	−7.1 (3)
O1A—O2A—C3A—C13A	172.27 (13)		

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>
N11—H11...O22	0.84 (3)	2.14 (3)	2.970 (2)	170 (2)
N11A—H11B...O24	0.87 (3)	2.08 (3)	2.935 (2)	169 (2)
O21—H21...O10	0.91 (4)	1.67 (4)	2.573 (2)	172 (4)
O23—H23...O10A	0.98 (4)	1.58 (4)	2.550 (2)	169 (3)