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# 9α-Hydroxy-12-{[4-(4-hydroxyphenyl)-piperazin-1-yl]methyl}-4,8-dimethyl-3,14-dioxatricyclo[9.3.0.0$^{2,4}$]tetradec-7-en-13-one

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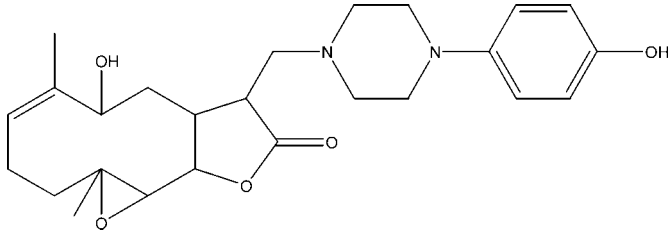
Key indicators: single-crystal X-ray study; $T$ = 296 K; mean $\sigma$(C–C) = 0.005 Å; disorder in main residue; $R$ factor = 0.044; $wR$ factor = 0.102; data-to-parameter ratio = 8.9.

The title compound, $C_{25}H_{34}N_2O_5$, was synthesized from 9α-hydroxyparthenolide (9α-hydroxy-4,8-dimethyl-12-methylen-3, 14-dioxa-tricyclo[9.3.0.0$^{2,4}$]tetradec-7-en-13-one), which in turn was isolated from the chloroform extract of the aerial parts of *Anvillea radiata*. The molecule comprises a ten-membered ring fused to a five-membered ring with an additional epoxy ring system fused to the ten-membered ring. The five-membered ring also carries a 4-hydroxyphenyl-piperazin-1-ylmethyl substituent. The ten-membered ring adopts an approximate chair–chair conformation, while the piperazine ring displays a chair conformation and the five-membered ring shows an envelope conformation with the C atom closest to the hydroxy group forming the flap. Two C atoms in the phenyl ring and the O atom of the hydroxyl group are disordered over two sites, with an occupancy ratio of 0.53 (5):0.47 (5). An intramolecular O—H···N hydrogen-bond stabilizes the molecular conformation. In the crystal, C—H···O hydrogen bonds link the molecules into zigzag chains running along the *a*-axis direction.

## Related literature

For background to the medicinal uses of the plant *Anvillea radiata*, see: Abdel Sattar *et al.* (1996); El Hassany *et al.* (2004). For the reactivity of this sesquiterpene, see: Hwang *et al.* (2006); Neelakantan *et al.* (2009). For a related synthetic procedure, see: Moumou *et al.* (2012). For conformational analysis, see: Cremer & Pople (1975).




## Experimental

### Crystal data

$C_{25}H_{34}N_2O_5$
$M_r$ = 442.54
Monoclinic, $C2$
$a$ = 29.880 (5) Å
$b$ = 6.841 (5) Å
$c$ = 11.999 (5) Å
$\beta$ = 102.307 (5)°
$V$ = 2396 (2) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.09 mm$^{-1}$
$T$ = 296 K
0.5 × 0.03 × 0.03 mm

### Data collection

Bruker X8 APEX Diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
$T_{min}$ = 0.639, $T_{max}$ = 0.747
13097 measured reflections
2868 independent reflections
1830 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.055

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.102
$S$ = 1.08
2868 reflections
322 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.14 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.14 e Å$^{-3}$

**Table 1**
Hydrogen-bond geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O3—H3···N1 | 0.82 | 2.22 | 3.030 (4) | 169 |
| C2—H2···O4$^{i}$ | 0.98 | 2.45 | 3.243 (4) | 138 |
| C4—H4$A$···O2$^{ii}$ | 0.97 | 2.43 | 3.315 (5) | 151 |

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

Data collection: *APEX2* (Bruker, 2009); cell refinement: *SAINT* (Bruker, 2009); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

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Supporting information for this paper is available from the IUCr electronic archives (Reference: SJ5394).

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# supporting information

*Acta Cryst.* (2014). E**70**, o530–o531 [doi:10.1107/S1600536814007430]

## 9$\alpha$-Hydroxy-12-{[4-(4-hydroxyphenyl)piperazin-1-yl]methyl}-4,8-dimethyl-3,14-dioxatricyclo[9.3.0.0$^{2,4}$]tetradec-7-en-13-one

**Mohamed Loubidi, Ahmed Benharref, Lahcen El Ammari, Mohamed Saadi and Moha Berraho**

### S1. Comment

Our work lies within the framework of the evaluation of medicinal plants and in particular, *Anvillea radiata*. The main constituent of the chloroform extract of the aerial parts of this plant is 9$\alpha$-hydroxypartenolide (Abdel Sattar *et al.*, 1996; El Hassany *et al.*, 2004). The reactivity of this sesquiterpene lactone and its derivatives has been the subject of several studies (Hwang *et al.*, 2006; Neelakantan *et al.*, 2009; Moumou *et al.*, 2012), in order to prepare high value added products for use in industrial pharmacology. In this work we present the crystal structure of the title compound (I). The molecule is built up from fused five-and ten-membered rings with the hydroxyphenyl-pyperazine group as a substituent. An additional epoxy ring system is also fused to the ten-membered ring at C2 and C3. The molecular structure of (I), Fig.1, shows the lactone ring to adopt an envelope conformation, as indicated by the Cremer & Pople (1975) puckering parameters QT = 0.208 (3) Å and $\varphi$2 = 248.2 (7)°. The ten-membered ring displays an approximate chair-chair conformation, while the pyperazine ring has a perfect chair conformation with QT = 0.572 (3) Å, $\theta$ = 176.9 (3) and $\varphi$2 = 184 (5)°. An intramolecular O4—H4···N1 hydrogen bond is observed. In the crystal, C—H···O hydrogen bonds link the molecules into zigzag chains running along the *a* axis (Table 1, Fig 1).

### S2. Experimental

A mixture of 9$\alpha$-hydoxypartenolide (9$\alpha$-hydroxy-4,8-dimethyl-12-methylene- 3,14-dioxatricyclo[9.3.0.0$^{2}$,$^{4}$]tetradec-7-en-13-one) (1 g, 3.8 mmol) and one equivalent of 1-(4-hydroxyphenyl-piperazine) in EtOH (20 ml) was stirred for twelve hours at room temperature. The reaction was stopped by adding water (10 ml) and the solution extracted with chloroform (3 *x* 20 ml). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to give 1.5 g (3.3 mmol) of the title compound (yield: 90%). Recrystallization was performed from ethyl acetate.

### S3. Refinement

All H atoms were fixed geometrically and treated as riding with C—H = 0.96 Å (methyl), 0.97 Å (methylene), 0.98 Å (methine) and O–H = 0.82 Å with $U_{iso}$(H) = 1.2$U_{eq}$ (methylene, methine) or $U_{iso}$(H) = 1.5$U_{eq}$ (methyl, OH). The O5, C22 and C21 atoms are disordered over two positions. The occupancy factors for these sites were refined and converged to the ratio 0.53 (5):0.47 (5). In the absence of significant anomalous scattering, the absolute configuration could not be reliably determined and any references to the Flack parameter were removed.

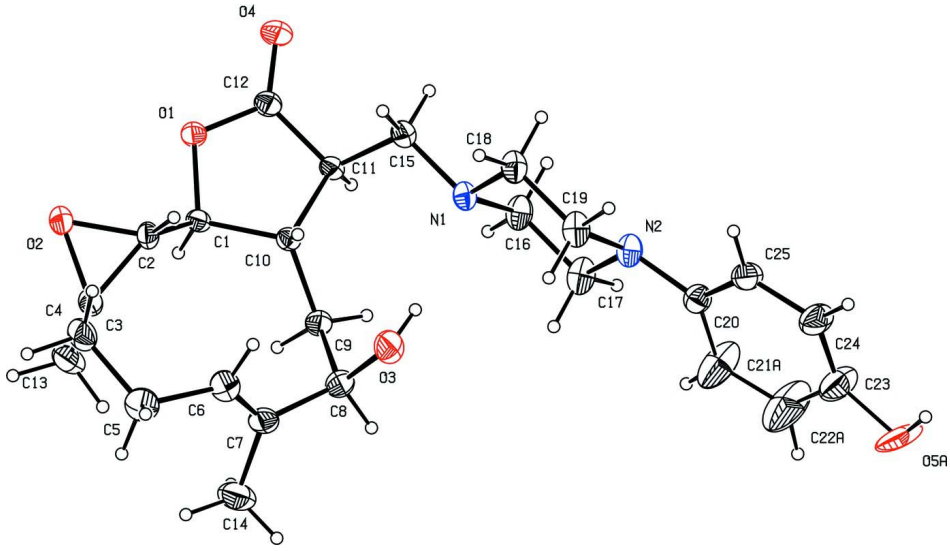


**Figure 1**

The molecular structure of the title compound with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. H atoms are represented as small spheres of arbitrary radii. For clarity only the major disorder components of the disordered C21 C22 and O5 atoms are shown.

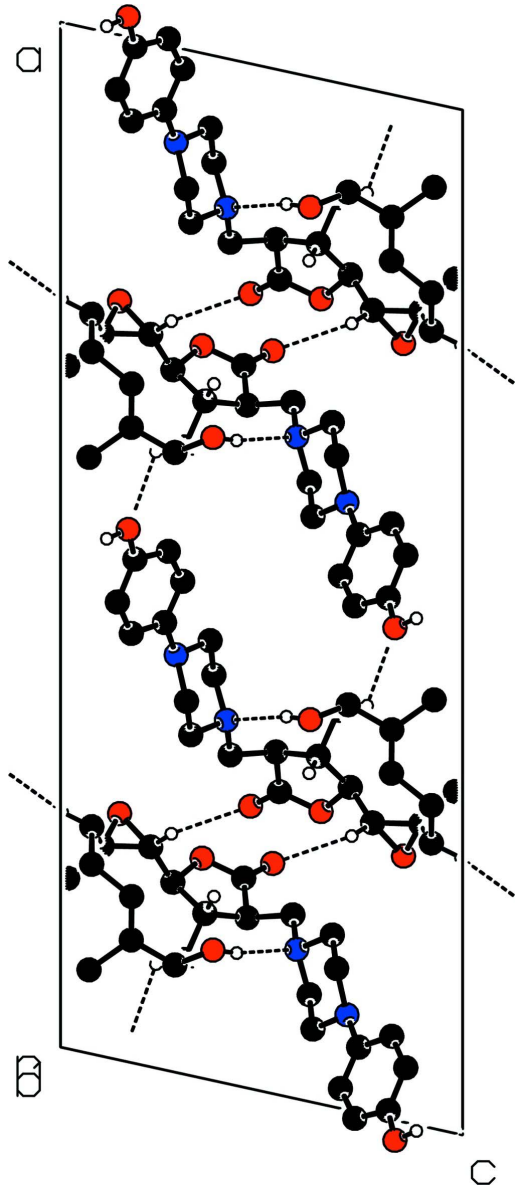


**Figure 2**

Packing view showing the C–H···O and O–H···N hydrogen bonds as dashed lines. H atoms not involved in hydrogen bonding and the atoms of the minor disorder component have been omitted for clarity.

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*Crystal data*

$C_{25}H_{34}N_2O_5$
$M_r$ = 442.54
Monoclinic, *C*2
Hall symbol: C 2y
*a* = 29.880 (5) Å
*b* = 6.841 (5) Å
*c* = 11.999 (5) Å
β = 102.307 (5)°
*V* = 2396 (2) Å$^3$
*Z* = 4
*F*(000) = 952
$D_x$ = 1.227 Mg m$^{-3}$
Mo *Kα* radiation, λ = 0.71073 Å
Cell parameters from 4801 reflections

$\theta$ = 2.5–27.1°
$\mu$ = 0.09 mm$^{-1}$
$T$ = 296 K

Needle, colourless
0.5 × 0.03 × 0.03 mm

*Data collection*

Bruker X8 APEX Diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
$\varphi$ and $\omega$ scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
$T_{min}$ = 0.639, $T_{max}$ = 0.747
13097 measured reflections

2868 independent reflections
1830 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.055
$\theta_{max}$ = 27.1°, $\theta_{min}$ = 2.5°
$h$ = −38→38
$k$ = −8→7
$l$ = −15→15

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.102
$S$ = 1.08
2868 reflections
322 parameters
1 restraint
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0408P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.14 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.14 e Å$^{-3}$
Extinction correction: *SHELXL*, $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0063 (6)

*Special details*

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

**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted $R$-factor $wR$ and goodness of fit $S$ are based on $F^2$, conventional $R$-factors $R$ are based on $F$, with $F$ set to zero for negative $F^2$. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating $R$-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. $R$-factors based on $F^2$ are statistically about twice as large as those based on $F$, and $R$- factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ | Occ. (<1) |
|---|---|---|---|---|---|
| C1 | 0.81526 (10) | 0.5109 (5) | 0.7206 (2) | 0.0388 (7) | |
| H1 | 0.8380 | 0.4421 | 0.7782 | 0.047* | |
| C2 | 0.78537 (10) | 0.6359 (5) | 0.7759 (2) | 0.0425 (7) | |
| H2 | 0.7681 | 0.7338 | 0.7245 | 0.051* | |
| C3 | 0.79457 (11) | 0.6940 (5) | 0.8964 (2) | 0.0478 (8) | |
| C4 | 0.77809 (13) | 0.8925 (6) | 0.9221 (3) | 0.0645 (10) | |
| H4A | 0.7699 | 0.8898 | 0.9961 | 0.077* | |
| H4B | 0.7508 | 0.9254 | 0.8655 | 0.077* | |
| C5 | 0.81482 (14) | 1.0505 (5) | 0.9224 (3) | 0.0687 (11) | |
| H5A | 0.8007 | 1.1787 | 0.9185 | 0.082* | |
| H5B | 0.8376 | 1.0428 | 0.9931 | 0.082* | |
| C6 | 0.83780 (13) | 1.0258 (5) | 0.8232 (3) | 0.0548 (9) | |

| | | | | | |
|---|---|---|---|---|---|
| H6 | 0.8195 | 1.0503 | 0.7516 | 0.066* | |
| C7 | 0.88024 (13) | 0.9743 (5) | 0.8241 (3) | 0.0544 (9) | |
| C8 | 0.89540 (12) | 0.9174 (5) | 0.7157 (3) | 0.0545 (9) | |
| H8 | 0.9283 | 0.9432 | 0.7273 | 0.065* | |
| C9 | 0.88783 (10) | 0.6976 (5) | 0.6916 (2) | 0.0464 (8) | |
| H9A | 0.9070 | 0.6580 | 0.6397 | 0.056* | |
| H9B | 0.8985 | 0.6275 | 0.7625 | 0.056* | |
| C10 | 0.83879 (10) | 0.6316 (4) | 0.6409 (2) | 0.0369 (7) | |
| H10 | 0.8203 | 0.7490 | 0.6184 | 0.044* | |
| C11 | 0.83398 (10) | 0.5009 (5) | 0.5360 (2) | 0.0420 (7) | |
| H11 | 0.8624 | 0.4278 | 0.5393 | 0.050* | |
| C12 | 0.79599 (11) | 0.3623 (5) | 0.5444 (2) | 0.0452 (8) | |
| C13 | 0.83375 (13) | 0.6105 (6) | 0.9824 (2) | 0.0674 (11) | |
| H13A | 0.8596 | 0.6970 | 0.9913 | 0.101* | |
| H13B | 0.8419 | 0.4852 | 0.9566 | 0.101* | |
| H13C | 0.8249 | 0.5957 | 1.0542 | 0.101* | |
| C14 | 0.91847 (14) | 0.9532 (7) | 0.9290 (3) | 0.0855 (13) | |
| H14A | 0.9427 | 1.0427 | 0.9241 | 0.128* | |
| H14B | 0.9300 | 0.8218 | 0.9334 | 0.128* | |
| H14C | 0.9069 | 0.9817 | 0.9959 | 0.128* | |
| C15 | 0.82137 (11) | 0.6135 (5) | 0.4222 (2) | 0.0498 (8) | |
| H15A | 0.8201 | 0.5223 | 0.3597 | 0.060* | |
| H15B | 0.7911 | 0.6702 | 0.4150 | 0.060* | |
| C16 | 0.89578 (11) | 0.6953 (5) | 0.3813 (3) | 0.0574 (9) | |
| H16A | 0.8876 | 0.6275 | 0.3089 | 0.069* | |
| H16B | 0.9106 | 0.6023 | 0.4385 | 0.069* | |
| C17 | 0.92853 (12) | 0.8583 (6) | 0.3722 (3) | 0.0620 (10) | |
| H17A | 0.9380 | 0.9213 | 0.4459 | 0.074* | |
| H17B | 0.9556 | 0.8049 | 0.3508 | 0.074* | |
| C18 | 0.83255 (11) | 0.9076 (5) | 0.3240 (3) | 0.0559 (9) | |
| H18A | 0.8048 | 0.9589 | 0.3427 | 0.067* | |
| H18B | 0.8242 | 0.8397 | 0.2516 | 0.067* | |
| C19 | 0.86433 (12) | 1.0737 (5) | 0.3134 (3) | 0.0585 (10) | |
| H19A | 0.8494 | 1.1610 | 0.2531 | 0.070* | |
| H19B | 0.8709 | 1.1471 | 0.3841 | 0.070* | |
| C20 | 0.93639 (12) | 1.1478 (5) | 0.2585 (3) | 0.0524 (8) | |
| C21A | 0.9766 (11) | 1.167 (5) | 0.303 (2) | 0.103 (11) | 0.47 (5) |
| H21A | 0.9892 | 1.0838 | 0.3630 | 0.124* | 0.47 (5) |
| C22A | 1.0052 (11) | 1.307 (6) | 0.269 (3) | 0.184 (19) | 0.47 (5) |
| H22A | 1.0353 | 1.3161 | 0.3092 | 0.220* | 0.47 (5) |
| C21B | 0.9877 (9) | 1.150 (3) | 0.3049 (16) | 0.059 (4) | 0.53 (5) |
| H21B | 1.0010 | 1.0609 | 0.3605 | 0.071* | 0.53 (5) |
| C22B | 1.0145 (8) | 1.284 (2) | 0.2650 (12) | 0.066 (5) | 0.53 (5) |
| H22B | 1.0462 | 1.2840 | 0.2894 | 0.079* | 0.53 (5) |
| C23 | 0.99198 (17) | 1.4234 (8) | 0.1851 (4) | 0.0947 (15) | |
| C24 | 0.94645 (15) | 1.4229 (6) | 0.1412 (3) | 0.0817 (13) | |
| H24 | 0.9337 | 1.5159 | 0.0872 | 0.098* | |
| C25 | 0.91882 (13) | 1.2851 (6) | 0.1763 (3) | 0.0616 (10) | |

| | | | | | |
|---|---|---|---|---|---|
| H25 | 0.8876 | 1.2844 | 0.1440 | 0.074* | |
| N1 | 0.85421 (8) | 0.7703 (4) | 0.41259 (18) | 0.0446 (6) | |
| N2 | 0.90743 (9) | 1.0027 (4) | 0.2877 (2) | 0.0527 (7) | |
| O1 | 0.78550 (7) | 0.3726 (3) | 0.64797 (15) | 0.0455 (5) | |
| O2 | 0.75946 (8) | 0.5494 (4) | 0.85303 (16) | 0.0582 (7) | |
| O3 | 0.87276 (10) | 1.0320 (4) | 0.62102 (19) | 0.0689 (7) | |
| H3 | 0.8708 | 0.9690 | 0.5620 | 0.103* | |
| O4 | 0.77554 (8) | 0.2523 (4) | 0.47254 (18) | 0.0653 (7) | |
| O5A | 1.0188 (7) | 1.589 (4) | 0.174 (3) | 0.116 (8) | 0.47 (5) |
| H5A1 | 1.0053 | 1.6567 | 0.1208 | 0.173* | 0.47 (5) |
| O5B | 1.0186 (6) | 1.531 (3) | 0.1318 (16) | 0.080 (4) | 0.53 (5) |
| H5B1 | 1.0034 | 1.5704 | 0.0709 | 0.120* | 0.53 (5) |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C1 | 0.0456 (18) | 0.0352 (17) | 0.0330 (13) | −0.0035 (15) | 0.0025 (12) | −0.0011 (13) |
| C2 | 0.0496 (19) | 0.0439 (19) | 0.0364 (14) | −0.0019 (15) | 0.0147 (13) | 0.0051 (13) |
| C3 | 0.059 (2) | 0.0478 (19) | 0.0391 (15) | −0.0061 (18) | 0.0159 (15) | −0.0022 (15) |
| C4 | 0.075 (2) | 0.069 (3) | 0.0551 (19) | 0.004 (2) | 0.0274 (18) | −0.0153 (19) |
| C5 | 0.089 (3) | 0.044 (2) | 0.078 (2) | 0.003 (2) | 0.028 (2) | −0.0179 (18) |
| C6 | 0.080 (3) | 0.0266 (18) | 0.0600 (19) | 0.0035 (18) | 0.0194 (18) | −0.0011 (15) |
| C7 | 0.068 (2) | 0.040 (2) | 0.0543 (18) | −0.0102 (19) | 0.0107 (17) | −0.0105 (16) |
| C8 | 0.061 (2) | 0.044 (2) | 0.0589 (19) | −0.0102 (18) | 0.0134 (16) | −0.0023 (16) |
| C9 | 0.051 (2) | 0.042 (2) | 0.0467 (16) | −0.0034 (16) | 0.0113 (14) | −0.0057 (15) |
| C10 | 0.0417 (17) | 0.0323 (17) | 0.0363 (14) | −0.0004 (14) | 0.0075 (12) | −0.0029 (12) |
| C11 | 0.0441 (18) | 0.046 (2) | 0.0355 (14) | −0.0034 (16) | 0.0082 (12) | −0.0079 (14) |
| C12 | 0.050 (2) | 0.0412 (19) | 0.0432 (16) | 0.0006 (17) | 0.0074 (14) | −0.0051 (15) |
| C13 | 0.091 (3) | 0.062 (2) | 0.0424 (17) | −0.003 (2) | −0.0015 (17) | −0.0021 (16) |
| C14 | 0.084 (3) | 0.102 (4) | 0.065 (2) | −0.012 (3) | 0.003 (2) | −0.029 (2) |
| C15 | 0.052 (2) | 0.059 (2) | 0.0403 (15) | −0.0026 (18) | 0.0136 (14) | −0.0042 (15) |
| C16 | 0.056 (2) | 0.055 (2) | 0.068 (2) | 0.0122 (19) | 0.0284 (17) | 0.0078 (18) |
| C17 | 0.057 (2) | 0.056 (2) | 0.079 (2) | 0.018 (2) | 0.0284 (18) | 0.0184 (19) |
| C18 | 0.053 (2) | 0.065 (2) | 0.0532 (18) | 0.0101 (19) | 0.0180 (16) | 0.0112 (17) |
| C19 | 0.061 (2) | 0.057 (2) | 0.0636 (19) | 0.0196 (19) | 0.0258 (17) | 0.0146 (17) |
| C20 | 0.051 (2) | 0.051 (2) | 0.0564 (19) | 0.0008 (18) | 0.0149 (17) | 0.0001 (17) |
| C21A | 0.026 (12) | 0.111 (16) | 0.168 (17) | 0.010 (9) | 0.009 (8) | 0.088 (13) |
| C22A | 0.034 (10) | 0.23 (3) | 0.27 (3) | −0.002 (12) | −0.005 (11) | 0.13 (3) |
| C21B | 0.025 (9) | 0.062 (8) | 0.085 (8) | 0.017 (6) | 0.002 (5) | 0.015 (7) |
| C22B | 0.041 (7) | 0.049 (8) | 0.097 (9) | −0.011 (5) | −0.005 (5) | 0.022 (6) |
| C23 | 0.072 (3) | 0.087 (4) | 0.116 (4) | −0.027 (3) | −0.001 (3) | 0.033 (3) |
| C24 | 0.080 (3) | 0.077 (3) | 0.079 (2) | −0.025 (3) | −0.003 (2) | 0.025 (2) |
| C25 | 0.062 (2) | 0.058 (2) | 0.059 (2) | −0.010 (2) | 0.0006 (17) | 0.0061 (19) |
| N1 | 0.0462 (16) | 0.0481 (16) | 0.0422 (13) | 0.0059 (13) | 0.0156 (11) | 0.0046 (12) |
| N2 | 0.0531 (17) | 0.0512 (18) | 0.0590 (15) | 0.0100 (15) | 0.0233 (13) | 0.0086 (14) |
| O1 | 0.0577 (14) | 0.0379 (12) | 0.0422 (11) | −0.0094 (11) | 0.0136 (9) | −0.0071 (9) |
| O2 | 0.0718 (16) | 0.0643 (17) | 0.0440 (11) | −0.0185 (14) | 0.0245 (10) | −0.0059 (11) |
| O3 | 0.100 (2) | 0.0462 (15) | 0.0619 (13) | −0.0122 (15) | 0.0210 (14) | 0.0062 (12) |

| | | | | | | |
|---|---|---|---|---|---|---|
| O4 | 0.0738 (17) | 0.0670 (17) | 0.0549 (13) | −0.0186 (14) | 0.0136 (12) | −0.0250 (12) |
| O5A | 0.090 (7) | 0.087 (11) | 0.138 (16) | −0.065 (8) | −0.048 (9) | 0.047 (10) |
| O5B | 0.066 (5) | 0.084 (9) | 0.080 (6) | −0.054 (5) | −0.010 (5) | 0.029 (6) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| C1—O1 | 1.454 (3) | C15—N1 | 1.475 (4) |
| C1—C2 | 1.490 (4) | C15—H15A | 0.9700 |
| C1—C10 | 1.542 (4) | C15—H15B | 0.9700 |
| C1—H1 | 0.9800 | C16—N1 | 1.464 (4) |
| C2—O2 | 1.454 (3) | C16—C17 | 1.503 (5) |
| C2—C3 | 1.468 (4) | C16—H16A | 0.9700 |
| C2—H2 | 0.9800 | C16—H16B | 0.9700 |
| C3—O2 | 1.455 (4) | C17—N2 | 1.459 (4) |
| C3—C13 | 1.499 (4) | C17—H17A | 0.9700 |
| C3—C4 | 1.499 (5) | C17—H17B | 0.9700 |
| C4—C5 | 1.540 (5) | C18—N1 | 1.462 (4) |
| C4—H4A | 0.9700 | C18—C19 | 1.504 (5) |
| C4—H4B | 0.9700 | C18—H18A | 0.9700 |
| C5—C6 | 1.505 (5) | C18—H18B | 0.9700 |
| C5—H5A | 0.9700 | C19—N2 | 1.469 (4) |
| C5—H5B | 0.9700 | C19—H19A | 0.9700 |
| C6—C7 | 1.314 (5) | C19—H19B | 0.9700 |
| C6—H6 | 0.9300 | C20—C21A | 1.21 (3) |
| C7—C14 | 1.516 (5) | C20—C25 | 1.381 (5) |
| C7—C8 | 1.516 (4) | C20—N2 | 1.409 (4) |
| C8—O3 | 1.426 (4) | C20—C21B | 1.52 (3) |
| C8—C9 | 1.539 (5) | C21A—C22A | 1.41 (4) |
| C8—H8 | 0.9800 | C21A—H21A | 0.9300 |
| C9—C10 | 1.530 (4) | C22A—C23 | 1.27 (3) |
| C9—H9A | 0.9700 | C22A—H22A | 0.9300 |
| C9—H9B | 0.9700 | C21B—C22B | 1.37 (3) |
| C10—C11 | 1.526 (4) | C21B—H21B | 0.9300 |
| C10—H10 | 0.9800 | C22B—C23 | 1.415 (18) |
| C11—C12 | 1.499 (4) | C22B—H22B | 0.9300 |
| C11—C15 | 1.543 (4) | C23—O5B | 1.340 (15) |
| C11—H11 | 0.9800 | C23—C24 | 1.350 (6) |
| C12—O4 | 1.208 (3) | C23—O5A | 1.411 (17) |
| C12—O1 | 1.347 (3) | C24—C25 | 1.377 (5) |
| C13—H13A | 0.9600 | C24—H24 | 0.9300 |
| C13—H13B | 0.9600 | C25—H25 | 0.9300 |
| C13—H13C | 0.9600 | O3—H3 | 0.8200 |
| C14—H14A | 0.9600 | O5A—H5A1 | 0.8200 |
| C14—H14B | 0.9600 | O5B—H5B1 | 0.8200 |
| C14—H14C | 0.9600 | | |
| | | | |
| O1—C1—C2 | 107.0 (2) | N1—C15—C11 | 113.0 (2) |
| O1—C1—C10 | 106.13 (18) | N1—C15—H15A | 109.0 |

| | | | |
|---|---|---|---|
| C2—C1—C10 | 111.3 (2) | C11—C15—H15A | 109.0 |
| O1—C1—H1 | 110.7 | N1—C15—H15B | 109.0 |
| C2—C1—H1 | 110.7 | C11—C15—H15B | 109.0 |
| C10—C1—H1 | 110.7 | H15A—C15—H15B | 107.8 |
| O2—C2—C3 | 59.74 (17) | N1—C16—C17 | 111.1 (3) |
| O2—C2—C1 | 120.0 (3) | N1—C16—H16A | 109.4 |
| C3—C2—C1 | 126.1 (3) | C17—C16—H16A | 109.4 |
| O2—C2—H2 | 113.5 | N1—C16—H16B | 109.4 |
| C3—C2—H2 | 113.5 | C17—C16—H16B | 109.4 |
| C1—C2—H2 | 113.5 | H16A—C16—H16B | 108.0 |
| O2—C3—C2 | 59.63 (18) | N2—C17—C16 | 111.2 (3) |
| O2—C3—C13 | 112.6 (3) | N2—C17—H17A | 109.4 |
| C2—C3—C13 | 122.0 (3) | C16—C17—H17A | 109.4 |
| O2—C3—C4 | 116.5 (3) | N2—C17—H17B | 109.4 |
| C2—C3—C4 | 116.6 (3) | C16—C17—H17B | 109.4 |
| C13—C3—C4 | 116.5 (3) | H17A—C17—H17B | 108.0 |
| C3—C4—C5 | 111.8 (3) | N1—C18—C19 | 111.0 (3) |
| C3—C4—H4A | 109.3 | N1—C18—H18A | 109.4 |
| C5—C4—H4A | 109.3 | C19—C18—H18A | 109.4 |
| C3—C4—H4B | 109.3 | N1—C18—H18B | 109.4 |
| C5—C4—H4B | 109.3 | C19—C18—H18B | 109.4 |
| H4A—C4—H4B | 107.9 | H18A—C18—H18B | 108.0 |
| C6—C5—C4 | 111.4 (3) | N2—C19—C18 | 111.5 (3) |
| C6—C5—H5A | 109.4 | N2—C19—H19A | 109.3 |
| C4—C5—H5A | 109.4 | C18—C19—H19A | 109.3 |
| C6—C5—H5B | 109.4 | N2—C19—H19B | 109.3 |
| C4—C5—H5B | 109.4 | C18—C19—H19B | 109.3 |
| H5A—C5—H5B | 108.0 | H19A—C19—H19B | 108.0 |
| C7—C6—C5 | 128.8 (3) | C21A—C20—C25 | 115.6 (14) |
| C7—C6—H6 | 115.6 | C21A—C20—N2 | 124.6 (14) |
| C5—C6—H6 | 115.6 | C25—C20—N2 | 119.8 (3) |
| C6—C7—C14 | 126.0 (3) | C21A—C20—C21B | 7 (2) |
| C6—C7—C8 | 121.7 (3) | C25—C20—C21B | 117.1 (10) |
| C14—C7—C8 | 112.2 (3) | N2—C20—C21B | 122.9 (10) |
| O3—C8—C7 | 111.4 (3) | C20—C21A—C22A | 123 (2) |
| O3—C8—C9 | 111.2 (3) | C20—C21A—H21A | 118.3 |
| C7—C8—C9 | 110.7 (3) | C22A—C21A—H21A | 118.3 |
| O3—C8—H8 | 107.8 | C23—C22A—C21A | 124 (2) |
| C7—C8—H8 | 107.8 | C23—C22A—H22A | 118.2 |
| C9—C8—H8 | 107.8 | C21A—C22A—H22A | 118.2 |
| C10—C9—C8 | 116.9 (3) | C22B—C21B—C20 | 120.0 (17) |
| C10—C9—H9A | 108.1 | C22B—C21B—H21B | 120.0 |
| C8—C9—H9A | 108.1 | C20—C21B—H21B | 120.0 |
| C10—C9—H9B | 108.1 | C21B—C22B—C23 | 117.2 (17) |
| C8—C9—H9B | 108.1 | C21B—C22B—H22B | 121.4 |
| H9A—C9—H9B | 107.3 | C23—C22B—H22B | 121.4 |
| C11—C10—C9 | 114.5 (2) | C22A—C23—O5B | 127.0 (17) |
| C11—C10—C1 | 102.9 (2) | C22A—C23—C24 | 115.0 (15) |

| | | | |
|---|---|---|---|
| C9—C10—C1 | 115.9 (2) | O5B—C23—C24 | 117.8 (8) |
| C11—C10—H10 | 107.7 | C22A—C23—O5A | 119.3 (17) |
| C9—C10—H10 | 107.7 | O5B—C23—O5A | 26.9 (13) |
| C1—C10—H10 | 107.7 | C24—C23—O5A | 120.6 (10) |
| C12—C11—C10 | 104.8 (2) | C22A—C23—C22B | 13 (2) |
| C12—C11—C15 | 109.2 (2) | O5B—C23—C22B | 116.5 (12) |
| C10—C11—C15 | 113.6 (3) | C24—C23—C22B | 123.9 (9) |
| C12—C11—H11 | 109.7 | O5A—C23—C22B | 114.0 (11) |
| C10—C11—H11 | 109.7 | C23—C24—C25 | 120.2 (4) |
| C15—C11—H11 | 109.7 | C23—C24—H24 | 119.9 |
| O4—C12—O1 | 120.6 (3) | C25—C24—H24 | 119.9 |
| O4—C12—C11 | 128.4 (3) | C24—C25—C20 | 121.5 (4) |
| O1—C12—C11 | 110.9 (2) | C24—C25—H25 | 119.3 |
| C3—C13—H13A | 109.5 | C20—C25—H25 | 119.3 |
| C3—C13—H13B | 109.5 | C18—N1—C16 | 107.9 (2) |
| H13A—C13—H13B | 109.5 | C18—N1—C15 | 109.0 (2) |
| C3—C13—H13C | 109.5 | C16—N1—C15 | 112.3 (3) |
| H13A—C13—H13C | 109.5 | C20—N2—C17 | 116.9 (3) |
| H13B—C13—H13C | 109.5 | C20—N2—C19 | 115.6 (3) |
| C7—C14—H14A | 109.5 | C17—N2—C19 | 110.2 (2) |
| C7—C14—H14B | 109.5 | C12—O1—C1 | 110.8 (2) |
| H14A—C14—H14B | 109.5 | C2—O2—C3 | 60.63 (18) |
| C7—C14—H14C | 109.5 | C8—O3—H3 | 109.5 |
| H14A—C14—H14C | 109.5 | C23—O5A—H5A1 | 109.5 |
| H14B—C14—H14C | 109.5 | C23—O5B—H5B1 | 109.5 |

*Hydrogen-bond geometry (Å, º)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O3—H3···N1 | 0.82 | 2.22 | 3.030 (4) | 169 |
| C2—H2···O4$^{i}$ | 0.98 | 2.45 | 3.243 (4) | 138 |
| C4—H4*A*···O2$^{ii}$ | 0.97 | 2.43 | 3.315 (5) | 151 |

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