Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

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

**Mohamed Loubidi,[a]* Ahmed Benharref,[a] Lahcen El Ammari,[b] Mohamed Saadi[b] and Moha Berraho[a]**

[a]Laboratoire de Chimie Biomoleculaire, Substances Naturelles et Réactivité, URAC16, Faculté des Sciences Semlalia, BP 2390 Bd My Abdellah, 40000 Marrakech, Morocco, and [b]Laboratoire de Chimie du Solide Appliquée, Faculté des Sciences, Université Mohammed V-Agdal, BP 1014, Avenue Ibn Battouta, Rabat, Morocco
Correspondence e-mail: loubidim@gmail.com

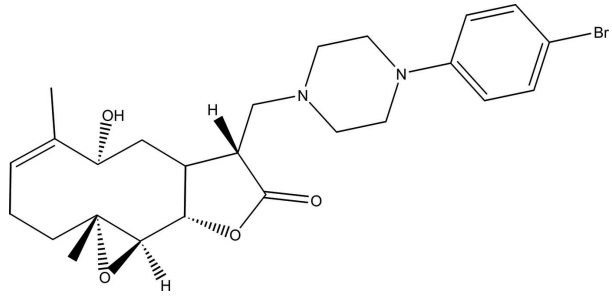
Received 17 March 2014; accepted 24 March 2014

Key indicators: single-crystal X-ray study; $T$ = 296 K; mean $\sigma$(C–C) = 0.003 Å; $R$ factor = 0.030; $wR$ factor = 0.076; data-to-parameter ratio = 20.2.

The title compound, $C_{25}H_{33}BrN_2O_4$, 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 was isolated from the chloroform extract of the aerial parts of *Anvillea radiata*. The molecule is built up from two fused five- and ten-membered rings with an additional epoxy ring system and a bromophenylpiperazine group as a substituent. The ten-membered ring adopts an approximate chair–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. An intramolecular O—H···N hydrogen bond stabilizes the molecular conformation. The crystal packing features C—H···O hydrogen bonds, which link the molecules into zigzag chains running along the $b$-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); Qureshi *et al.* (1990). For the reactivity of this sesquiterpene, see: Neukirch *et al.* (2003); Hwang *et al.* (2006); Neelakantan *et al.* (2009). For the synthetic procedure, see: Moumou *et al.* (2010). For conformational analysis, see: Cremer & Pople (1975)




## Experimental

### Crystal data

$C_{25}H_{33}BrN_2O_4$
$M_r$ = 505.44
Monoclinic, $P2_1$
$a$ = 9.6790 (4) Å
$b$ = 7.0710 (3) Å
$c$ = 17.3117 (7) Å
$\beta$ = 94.872 (2)°
$V$ = 1180.54 (8) Å$^3$
$Z$ = 2
Mo $K\alpha$ radiation
$\mu$ = 1.78 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)
$T_{min}$ = 0.634, $T_{max}$ = 0.746
14527 measured reflections
5899 independent reflections
5216 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.024

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.076
$S$ = 1.03
5899 reflections
292 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.44 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.44 e Å$^{-3}$
Absolute structure: Flack & Bernardinelli (2000), 2614 Friedel pairs
Absolute structure parameter: 0.007 (5)

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O4—H4···N1 | 0.82 | 2.18 | 2.995 (4) | 171 |
| C1—H1···O1$^{i}$ | 0.98 | 2.52 | 3.389 (3) | 148 |
| C15—H15$C$···O1$^{i}$ | 0.96 | 2.47 | 3.410 (3) | 167 |

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

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).

The authors thank the Unit of Support for Technical and Scientific Research (UATRS, CNRST) for the X-ray measurements.

Supporting information for this paper is available from the IUCr electronic archives (Reference: BT6970).

## References


Abdel Sattar, E., Galal, A. M. & Mossa, J. S. (1996). *J. Nat. Prod.* **59**, 403–405.
Bruker (2009). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
El Hassany, B., El Hanbali, F., Akssira, M., Mellouki, F., Haidou, A. & Barero, A. F. (2004). *Fitoterapia*, **75**, 573–576.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.
Hwang, D.-R., Wu, Y.-S., Chang, C.-W., Lien, T.-W., Chen, W.-C., Tan, U.-K., Hsu, J. T. A. & Hsieh, H.-P. (2006). *Bioorg. Med. Chem.* **14**, 83–91.
Moumou, M., Akssira, M., El Ammari, L., Benharref, A. & Berraho, M. (2010). *Acta Cryst.* E**66**, o2395.
Neelakantan, S., Nasim, Sh., Guzman, M. L., Jordan, C. T. & Crooks, P. A. (2009). *Bioorg. Med. Chem. Lett.* **19**, 4346–4349.
Neukirch, H., Kaneider, N. C., Wiedermann, C. J., Guerriero, A. & D'Ambrosio, M. (2003). *Bioorg. Med. Chem.* **11**, 1503–1510.
Qureshi, S., Ageel, A. M., Al-Yahya, M. A., Tariq, M., Mossa, J. S. & Shah, A. H. (1990). *J. Ethnopharmacol.* **28**, 157–162.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.

# supporting information

*Acta Cryst.* (2014). E**70**, o497–o498 [doi:10.1107/S1600536814006473]

## 12-{[4-(4-Bromophenyl)piperazin-1-yl]methyl}-9$\alpha$-hydroxy-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

The natural sesquiterpene lactone 9$\alpha$-hydroxypartenolide is the main constituent of the chloroform extract of the aerial parts of *Anvillea radiata* (El Hassany *et al.*, 2004) and of *Anvillea garcini* (Abdel Sattar *et al.*, 1996). 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.*, 2010), in order to prepare products with a high added value that can be used in the pharmacological industry. In this context, we have treated 9$\alpha$-hydroxyparthenolide with an equivalent amount of 1- (4-bromophenyl)piperazine gives the title compound. The molecule contains a fused ring system and the bromophenyl-pyperazine group as a substituent to the lactone ring. The molecular structure (Fig. 1) shows the lactone ring to adopt an envelope conformation, as indicated by Cremer & Pople (1975) puckering parameters QT = 0.2525 (19) Å and $\varphi$2 = 259.3 (4)°. The ten-membered ring displays an approximate chair-chair-chair conformation, while the pyperazine ring has a perfect chair conformation with QT = 0.586 (2) Å, $\theta$ = 177.96 (18) and $\varphi$2 = 165 (4)°. In the crystal, C—H···O hydrogen bonding links the molecules to zigzag chains running along the b-axis (Table 1, Fig. 2). In addition, an intramolecular O4—H4···N1 hydrogen bond is also observed. Owing to the presence of a Br atom, the absolute configuration could be fully confirmed, by refining the Flack parameter (Flack & Bernardinelli, 2000) as C1(S), C2(R) C3(R), C8(R), C10(S) and C11(R).

### S2. Experimental

The mixture of 9?-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-bromophenyl-piperazine) in EtOH (20 ml) was stirred for twelve hours at room temperature. Then, the reaction was stopped by adding water (10 ml) and the solution was 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 mmol) of the title compound (yield: 79%). Recrystallization was performed from in 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$U_{eq}$(C$_{methyl}$, O). The torsion angles about the C-C$_{methyl}$ and C-O bonds were refined.

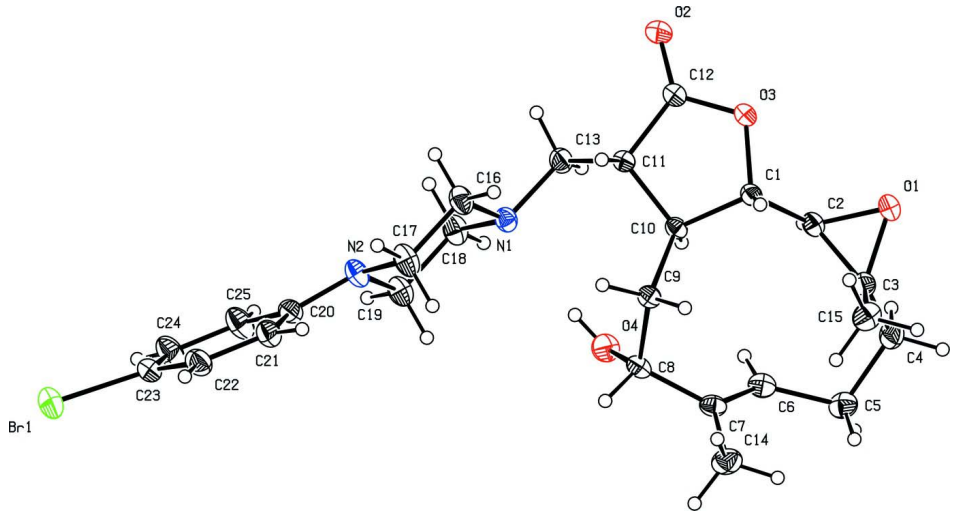



**Figure 1**

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.

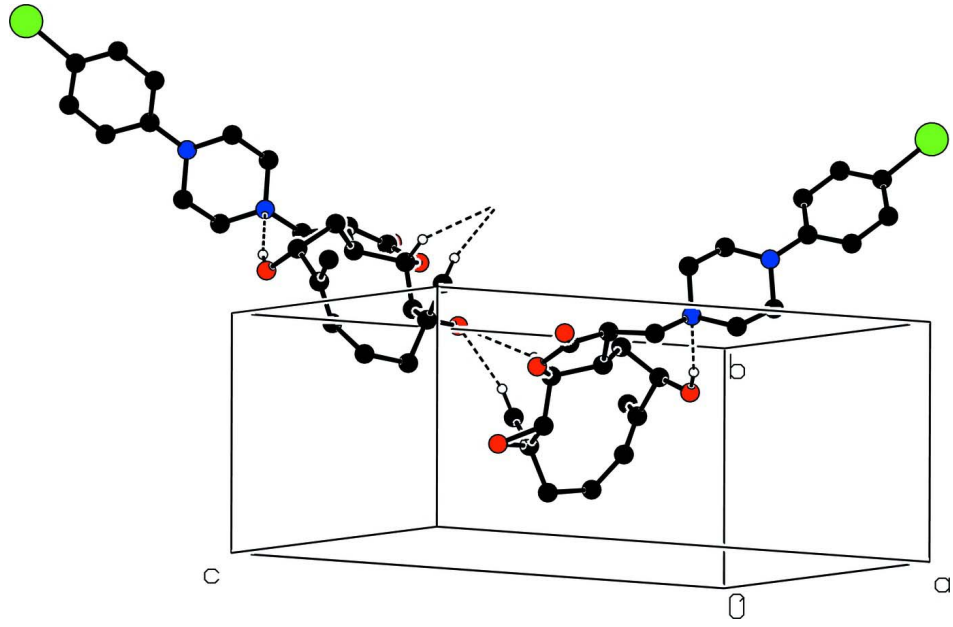



**Figure 2**

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

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

*Crystal data*

$C_{25}H_{33}BrN_2O_4$
$M_r$ = 505.44
Monoclinic, $P2_1$
Hall symbol: P 2yb
$a$ = 9.6790 (4) Å
$b$ = 7.0710 (3) Å

$c$ = 17.3117 (7) Å
$\beta$ = 94.872 (2)°
$V$ = 1180.54 (8) Å$^3$
$Z$ = 2
$F$(000) = 528
$D_x$ = 1.422 Mg m$^{-3}$
Mo $K\alpha$ radiation, $\lambda$ = 0.71073 Å

Cell parameters from 5899 reflections
$\theta$ = 2.4–28.7°
$\mu$ = 1.78 mm$^{-1}$
$T$ = 296 K
Box, 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)
$T_{min}$ = 0.634, $T_{max}$ = 0.746

14527 measured reflections
5899 independent reflections
5216 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.024
$\theta_{max}$ = 28.7°, $\theta_{min}$ = 2.4°
$h$ = −12→13
$k$ = −9→9
$l$ = −23→23

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.076
$S$ = 1.03
5899 reflections
292 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
$w = 1/[\sigma^2(F_o^2) + (0.0313P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.44 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.44 e Å$^{-3}$
Absolute structure: Flack & Bernardinelli (2000), 2614 Friedel pairs
Absolute structure parameter: 0.007 (5)

*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.

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

| | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| Br1 | 0.81297 (2) | 0.79383 (4) | −0.080172 (12) | 0.06016 (9) |
| O1 | 0.06025 (14) | −0.47571 (19) | 0.48432 (7) | 0.0400 (3) |
| O3 | 0.29861 (12) | −0.1832 (2) | 0.50486 (6) | 0.0367 (3) |
| O4 | 0.34442 (13) | −0.25359 (19) | 0.21350 (8) | 0.0418 (3) |
| H4 | 0.4035 | −0.1779 | 0.2306 | 0.063* |
| N1 | 0.53704 (14) | 0.0338 (2) | 0.29071 (8) | 0.0302 (3) |
| N2 | 0.63915 (15) | 0.2755 (2) | 0.17458 (8) | 0.0351 (3) |
| C1 | 0.20134 (15) | −0.2018 (3) | 0.43565 (8) | 0.0280 (3) |
| H1 | 0.1227 | −0.1152 | 0.4376 | 0.034* |
| O2 | 0.51010 (17) | −0.0713 (3) | 0.53716 (9) | 0.0637 (5) |
| C11 | 0.40639 (17) | −0.0352 (2) | 0.40481 (10) | 0.0301 (3) |
| H11 | 0.3778 | 0.0978 | 0.4024 | 0.036* |

| | | | | |
|---|---|---|---|---|
| C10 | 0.28736 (16) | −0.1544 (2) | 0.36682 (9) | 0.0257 (3) |
| H10 | 0.3270 | −0.2728 | 0.3492 | 0.031* |
| C2 | 0.15415 (18) | −0.4034 (2) | 0.43110 (10) | 0.0302 (3) |
| H2 | 0.2277 | −0.4925 | 0.4205 | 0.036* |
| C9 | 0.20719 (17) | −0.0612 (2) | 0.29633 (10) | 0.0275 (3) |
| H9A | 0.2462 | 0.0630 | 0.2885 | 0.033* |
| H9B | 0.1115 | −0.0439 | 0.3075 | 0.033* |
| C20 | 0.66722 (19) | 0.3843 (3) | 0.11021 (10) | 0.0333 (4) |
| C15 | −0.1053 (2) | −0.3330 (3) | 0.38362 (13) | 0.0416 (4) |
| H15A | −0.1899 | −0.3920 | 0.3961 | 0.062* |
| H15B | −0.1117 | −0.3022 | 0.3294 | 0.062* |
| H15C | −0.0903 | −0.2196 | 0.4136 | 0.062* |
| C8 | 0.21012 (17) | −0.1764 (2) | 0.22029 (9) | 0.0311 (3) |
| H8 | 0.1889 | −0.0899 | 0.1766 | 0.037* |
| C7 | 0.09765 (18) | −0.3259 (3) | 0.21770 (10) | 0.0315 (3) |
| C14 | −0.0380 (2) | −0.2547 (3) | 0.18031 (13) | 0.0460 (5) |
| H14A | −0.1099 | −0.3441 | 0.1886 | 0.069* |
| H14B | −0.0312 | −0.2393 | 0.1257 | 0.069* |
| H14C | −0.0595 | −0.1353 | 0.2027 | 0.069* |
| C3 | 0.01452 (19) | −0.4672 (2) | 0.40199 (10) | 0.0319 (4) |
| C16 | 0.5343 (2) | 0.2401 (3) | 0.29620 (11) | 0.0392 (4) |
| H16A | 0.6185 | 0.2834 | 0.3253 | 0.047* |
| H16B | 0.4563 | 0.2783 | 0.3242 | 0.047* |
| C17 | 0.5224 (2) | 0.3318 (3) | 0.21754 (11) | 0.0421 (5) |
| H17A | 0.4361 | 0.2940 | 0.1891 | 0.051* |
| H17B | 0.5215 | 0.4683 | 0.2233 | 0.051* |
| C5 | 0.0058 (2) | −0.6297 (2) | 0.27166 (12) | 0.0395 (4) |
| H5A | 0.0218 | −0.7510 | 0.2478 | 0.047* |
| H5B | −0.0839 | −0.5833 | 0.2507 | 0.047* |
| C6 | 0.1169 (2) | −0.4925 (2) | 0.25258 (10) | 0.0343 (4) |
| H6 | 0.2081 | −0.5278 | 0.2666 | 0.041* |
| C13 | 0.54475 (19) | −0.0520 (3) | 0.36882 (11) | 0.0364 (4) |
| H13A | 0.6166 | 0.0107 | 0.4020 | 0.044* |
| H13B | 0.5696 | −0.1844 | 0.3653 | 0.044* |
| C21 | 0.5923 (2) | 0.5468 (3) | 0.08862 (11) | 0.0379 (4) |
| H21 | 0.5133 | 0.5762 | 0.1133 | 0.046* |
| C22 | 0.6333 (2) | 0.6657 (3) | 0.03105 (11) | 0.0420 (4) |
| H22 | 0.5826 | 0.7745 | 0.0179 | 0.050* |
| C18 | 0.6578 (2) | −0.0185 (3) | 0.24953 (12) | 0.0387 (4) |
| H18A | 0.6627 | −0.1551 | 0.2451 | 0.046* |
| H18B | 0.7419 | 0.0249 | 0.2786 | 0.046* |
| C4 | 0.0055 (2) | −0.6550 (2) | 0.36027 (12) | 0.0398 (4) |
| H4A | −0.0788 | −0.7194 | 0.3717 | 0.048* |
| H4B | 0.0835 | −0.7333 | 0.3790 | 0.048* |
| C12 | 0.4169 (2) | −0.0961 (3) | 0.48858 (11) | 0.0389 (4) |
| C24 | 0.8214 (2) | 0.4589 (4) | 0.01092 (13) | 0.0514 (5) |
| H24 | 0.8976 | 0.4280 | −0.0158 | 0.062* |
| C23 | 0.7487 (2) | 0.6225 (3) | −0.00648 (11) | 0.0414 (4) |

| | | | | |
|---|---|---|---|---|
| C19 | 0.6466 (2) | 0.0693 (3) | 0.16953 (11) | 0.0383 (4) |
| H19A | 0.7265 | 0.0336 | 0.1427 | 0.046* |
| H19B | 0.5642 | 0.0220 | 0.1399 | 0.046* |
| C25 | 0.7808 (2) | 0.3408 (3) | 0.06823 (12) | 0.0471 (5) |
| H25 | 0.8299 | 0.2297 | 0.0793 | 0.057* |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| Br1 | 0.06273 (15) | 0.07268 (15) | 0.04532 (12) | −0.01813 (12) | 0.00605 (9) | 0.02022 (11) |
| O1 | 0.0448 (8) | 0.0446 (7) | 0.0312 (7) | −0.0100 (6) | 0.0071 (6) | 0.0077 (5) |
| O3 | 0.0389 (6) | 0.0481 (7) | 0.0232 (5) | −0.0105 (6) | 0.0036 (4) | 0.0038 (5) |
| O4 | 0.0341 (7) | 0.0539 (8) | 0.0390 (7) | 0.0043 (6) | 0.0129 (6) | −0.0079 (6) |
| N1 | 0.0268 (7) | 0.0342 (7) | 0.0301 (7) | 0.0026 (6) | 0.0059 (6) | 0.0041 (6) |
| N2 | 0.0405 (8) | 0.0358 (7) | 0.0306 (7) | 0.0071 (7) | 0.0129 (6) | 0.0049 (6) |
| C1 | 0.0287 (7) | 0.0316 (7) | 0.0241 (7) | −0.0003 (7) | 0.0043 (5) | 0.0015 (7) |
| O2 | 0.0577 (10) | 0.0973 (13) | 0.0334 (8) | −0.0328 (10) | −0.0125 (7) | 0.0183 (9) |
| C11 | 0.0295 (9) | 0.0359 (8) | 0.0245 (8) | −0.0029 (7) | 0.0003 (6) | 0.0029 (6) |
| C10 | 0.0262 (8) | 0.0286 (7) | 0.0227 (7) | 0.0038 (6) | 0.0043 (6) | 0.0011 (5) |
| C2 | 0.0328 (9) | 0.0299 (7) | 0.0283 (8) | 0.0024 (7) | 0.0045 (7) | 0.0058 (6) |
| C9 | 0.0280 (8) | 0.0271 (7) | 0.0274 (8) | 0.0050 (6) | 0.0014 (6) | 0.0022 (6) |
| C20 | 0.0325 (9) | 0.0395 (9) | 0.0281 (9) | 0.0016 (7) | 0.0033 (7) | 0.0017 (7) |
| C15 | 0.0328 (10) | 0.0442 (10) | 0.0484 (12) | 0.0042 (8) | 0.0058 (8) | −0.0078 (9) |
| C8 | 0.0338 (8) | 0.0362 (9) | 0.0232 (7) | 0.0060 (7) | 0.0028 (6) | 0.0036 (7) |
| C7 | 0.0332 (9) | 0.0361 (8) | 0.0252 (8) | 0.0059 (7) | 0.0015 (7) | −0.0057 (6) |
| C14 | 0.0394 (10) | 0.0482 (11) | 0.0478 (11) | 0.0022 (8) | −0.0109 (8) | 0.0045 (9) |
| C3 | 0.0338 (9) | 0.0315 (8) | 0.0310 (9) | −0.0022 (7) | 0.0065 (7) | 0.0005 (7) |
| C16 | 0.0476 (11) | 0.0376 (9) | 0.0346 (9) | 0.0001 (7) | 0.0158 (8) | −0.0007 (7) |
| C17 | 0.0503 (11) | 0.0362 (10) | 0.0428 (10) | 0.0128 (8) | 0.0219 (9) | 0.0053 (8) |
| C5 | 0.0468 (11) | 0.0280 (8) | 0.0428 (11) | 0.0010 (7) | −0.0005 (8) | −0.0059 (7) |
| C6 | 0.0372 (9) | 0.0337 (8) | 0.0321 (9) | 0.0074 (7) | 0.0035 (7) | −0.0058 (7) |
| C13 | 0.0274 (9) | 0.0472 (10) | 0.0343 (9) | −0.0015 (7) | 0.0016 (7) | 0.0097 (8) |
| C21 | 0.0371 (10) | 0.0421 (9) | 0.0353 (9) | 0.0033 (8) | 0.0073 (8) | 0.0044 (8) |
| C22 | 0.0491 (12) | 0.0412 (9) | 0.0353 (10) | 0.0011 (9) | 0.0019 (8) | 0.0077 (8) |
| C18 | 0.0330 (9) | 0.0410 (10) | 0.0435 (11) | 0.0087 (8) | 0.0119 (8) | 0.0073 (8) |
| C4 | 0.0444 (11) | 0.0303 (9) | 0.0447 (11) | −0.0045 (7) | 0.0047 (8) | 0.0019 (7) |
| C12 | 0.0408 (11) | 0.0483 (10) | 0.0273 (9) | −0.0103 (8) | 0.0003 (7) | 0.0050 (8) |
| C24 | 0.0478 (12) | 0.0690 (14) | 0.0397 (11) | 0.0096 (11) | 0.0177 (9) | 0.0107 (10) |
| C23 | 0.0443 (11) | 0.0519 (12) | 0.0275 (9) | −0.0110 (9) | −0.0005 (8) | 0.0069 (8) |
| C19 | 0.0432 (11) | 0.0365 (9) | 0.0374 (10) | 0.0094 (8) | 0.0161 (8) | 0.0013 (7) |
| C25 | 0.0480 (11) | 0.0559 (13) | 0.0396 (10) | 0.0154 (9) | 0.0160 (9) | 0.0120 (9) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| Br1—C23 | 1.9020 (19) | C8—H8 | 0.9800 |
| O1—C2 | 1.442 (2) | C7—C6 | 1.329 (3) |
| O1—C3 | 1.457 (2) | C7—C14 | 1.500 (3) |
| O3—C12 | 1.351 (2) | C14—H14A | 0.9600 |

| | | | |
|---|---|---|---|
| O3—C1 | 1.465 (2) | C14—H14B | 0.9600 |
| O4—C8 | 1.424 (2) | C14—H14C | 0.9600 |
| O4—H4 | 0.8200 | C3—C4 | 1.510 (3) |
| N1—C16 | 1.462 (3) | C16—C17 | 1.504 (3) |
| N1—C18 | 1.467 (2) | C16—H16A | 0.9700 |
| N1—C13 | 1.478 (2) | C16—H16B | 0.9700 |
| N2—C20 | 1.400 (2) | C17—H17A | 0.9700 |
| N2—C17 | 1.460 (2) | C17—H17B | 0.9700 |
| N2—C19 | 1.462 (3) | C5—C6 | 1.505 (3) |
| C1—C2 | 1.497 (3) | C5—C4 | 1.545 (3) |
| C1—C10 | 1.5473 (19) | C5—H5A | 0.9700 |
| C1—H1 | 0.9800 | C5—H5B | 0.9700 |
| O2—C12 | 1.193 (3) | C6—H6 | 0.9300 |
| C11—C12 | 1.508 (2) | C13—H13A | 0.9700 |
| C11—C13 | 1.529 (2) | C13—H13B | 0.9700 |
| C11—C10 | 1.530 (2) | C21—C22 | 1.387 (3) |
| C11—H11 | 0.9800 | C21—H21 | 0.9300 |
| C10—C9 | 1.538 (2) | C22—C23 | 1.374 (3) |
| C10—H10 | 0.9800 | C22—H22 | 0.9300 |
| C2—C3 | 1.473 (3) | C18—C19 | 1.513 (3) |
| C2—H2 | 0.9800 | C18—H18A | 0.9700 |
| C9—C8 | 1.550 (2) | C18—H18B | 0.9700 |
| C9—H9A | 0.9700 | C4—H4A | 0.9700 |
| C9—H9B | 0.9700 | C4—H4B | 0.9700 |
| C20—C21 | 1.393 (3) | C24—C23 | 1.373 (3) |
| C20—C25 | 1.402 (2) | C24—C25 | 1.379 (3) |
| C15—C3 | 1.511 (3) | C24—H24 | 0.9300 |
| C15—H15A | 0.9600 | C19—H19A | 0.9700 |
| C15—H15B | 0.9600 | C19—H19B | 0.9700 |
| C15—H15C | 0.9600 | C25—H25 | 0.9300 |
| C8—C7 | 1.516 (3) | | |

| | | | |
|---|---|---|---|
| C2—O1—C3 | 61.05 (11) | O1—C3—C15 | 113.30 (14) |
| C12—O3—C1 | 111.57 (12) | C2—C3—C15 | 123.01 (16) |
| C8—O4—H4 | 109.5 | C4—C3—C15 | 116.06 (17) |
| C16—N1—C18 | 107.64 (14) | N1—C16—C17 | 111.83 (16) |
| C16—N1—C13 | 110.47 (15) | N1—C16—H16A | 109.2 |
| C18—N1—C13 | 111.14 (14) | C17—C16—H16A | 109.2 |
| C20—N2—C17 | 117.81 (15) | N1—C16—H16B | 109.2 |
| C20—N2—C19 | 119.11 (14) | C17—C16—H16B | 109.2 |
| C17—N2—C19 | 110.26 (14) | H16A—C16—H16B | 107.9 |
| O3—C1—C2 | 107.50 (14) | N2—C17—C16 | 109.89 (15) |
| O3—C1—C10 | 105.06 (12) | N2—C17—H17A | 109.7 |
| C2—C1—C10 | 110.33 (13) | C16—C17—H17A | 109.7 |
| O3—C1—H1 | 111.2 | N2—C17—H17B | 109.7 |
| C2—C1—H1 | 111.2 | C16—C17—H17B | 109.7 |
| C10—C1—H1 | 111.2 | H17A—C17—H17B | 108.2 |
| C12—C11—C13 | 112.33 (15) | C6—C5—C4 | 110.75 (16) |

| | | | |
|---|---|---|---|
| C12—C11—C10 | 104.05 (13) | C6—C5—H5A | 109.5 |
| C13—C11—C10 | 115.82 (14) | C4—C5—H5A | 109.5 |
| C12—C11—H11 | 108.1 | C6—C5—H5B | 109.5 |
| C13—C11—H11 | 108.1 | C4—C5—H5B | 109.5 |
| C10—C11—H11 | 108.1 | H5A—C5—H5B | 108.1 |
| C11—C10—C9 | 114.56 (13) | C7—C6—C5 | 126.55 (18) |
| C11—C10—C1 | 102.89 (13) | C7—C6—H6 | 116.7 |
| C9—C10—C1 | 115.83 (13) | C5—C6—H6 | 116.7 |
| C11—C10—H10 | 107.7 | N1—C13—C11 | 111.29 (14) |
| C9—C10—H10 | 107.7 | N1—C13—H13A | 109.4 |
| C1—C10—H10 | 107.7 | C11—C13—H13A | 109.4 |
| O1—C2—C3 | 59.99 (11) | N1—C13—H13B | 109.4 |
| O1—C2—C1 | 120.69 (14) | C11—C13—H13B | 109.4 |
| C3—C2—C1 | 125.25 (15) | H13A—C13—H13B | 108.0 |
| O1—C2—H2 | 113.5 | C22—C21—C20 | 121.23 (17) |
| C3—C2—H2 | 113.5 | C22—C21—H21 | 119.4 |
| C1—C2—H2 | 113.5 | C20—C21—H21 | 119.4 |
| C10—C9—C8 | 113.85 (13) | C23—C22—C21 | 119.91 (19) |
| C10—C9—H9A | 108.8 | C23—C22—H22 | 120.0 |
| C8—C9—H9A | 108.8 | C21—C22—H22 | 120.0 |
| C10—C9—H9B | 108.8 | N1—C18—C19 | 110.06 (15) |
| C8—C9—H9B | 108.8 | N1—C18—H18A | 109.6 |
| H9A—C9—H9B | 107.7 | C19—C18—H18A | 109.6 |
| C21—C20—N2 | 122.36 (15) | N1—C18—H18B | 109.6 |
| C21—C20—C25 | 117.07 (17) | C19—C18—H18B | 109.6 |
| N2—C20—C25 | 120.38 (16) | H18A—C18—H18B | 108.2 |
| C3—C15—H15A | 109.5 | C3—C4—C5 | 111.61 (15) |
| C3—C15—H15B | 109.5 | C3—C4—H4A | 109.3 |
| H15A—C15—H15B | 109.5 | C5—C4—H4A | 109.3 |
| C3—C15—H15C | 109.5 | C3—C4—H4B | 109.3 |
| H15A—C15—H15C | 109.5 | C5—C4—H4B | 109.3 |
| H15B—C15—H15C | 109.5 | H4A—C4—H4B | 108.0 |
| O4—C8—C7 | 112.85 (15) | O2—C12—O3 | 121.57 (17) |
| O4—C8—C9 | 110.74 (14) | O2—C12—C11 | 128.41 (17) |
| C7—C8—C9 | 109.07 (12) | O3—C12—C11 | 109.99 (16) |
| O4—C8—H8 | 108.0 | C23—C24—C25 | 119.72 (18) |
| C7—C8—H8 | 108.0 | C23—C24—H24 | 120.1 |
| C9—C8—H8 | 108.0 | C25—C24—H24 | 120.1 |
| C6—C7—C14 | 125.23 (18) | C24—C23—C22 | 120.37 (18) |
| C6—C7—C8 | 122.16 (17) | C24—C23—Br1 | 119.54 (15) |
| C14—C7—C8 | 112.24 (16) | C22—C23—Br1 | 120.05 (16) |
| C7—C14—H14A | 109.5 | N2—C19—C18 | 110.77 (16) |
| C7—C14—H14B | 109.5 | N2—C19—H19A | 109.5 |
| H14A—C14—H14B | 109.5 | C18—C19—H19A | 109.5 |
| C7—C14—H14C | 109.5 | N2—C19—H19B | 109.5 |
| H14A—C14—H14C | 109.5 | C18—C19—H19B | 109.5 |
| H14B—C14—H14C | 109.5 | H19A—C19—H19B | 108.1 |
| O1—C3—C2 | 58.95 (11) | C24—C25—C20 | 121.58 (19) |

| | | | |
|---|---|---|---|
| O1—C3—C4 | 115.59 (15) | C24—C25—H25 | 119.2 |
| C2—C3—C4 | 116.57 (15) | C20—C25—H25 | 119.2 |

*Hydrogen-bond geometry (Å, º)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O4—H4···N1 | 0.82 | 2.18 | 2.995 (4) | 171 |
| C1—H1···O1$^{i}$ | 0.98 | 2.52 | 3.389 (3) | 148 |
| C15—H15*C*···O1$^{i}$ | 0.96 | 2.47 | 3.410 (3) | 167 |

Symmetry code: (i) −*x*, *y*+1/2, −*z*+1.