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## L-Nebivololinium chloride dihydrate

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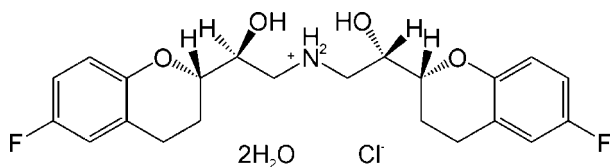
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Key indicators: single-crystal X-ray study;  $T = 291$  K; mean  $\sigma(\text{C}-\text{C}) = 0.005$  Å;  $R$  factor = 0.041;  $wR$  factor = 0.113; data-to-parameter ratio = 11.3.

The hydrochloride salt of chiral L-nebivolol {systematic name: (+)-(R,S,S,S)-bis[2-(6-fluoro-3,4-dihydro-2H-1-benzopyran-2-yl)-2-hydroxyethyl]ammonium chloride dihydrate},  $\text{C}_{22}\text{H}_{26}\text{F}_2\text{NO}_4^+ \cdot \text{Cl}^- \cdot 2\text{H}_2\text{O}$ , was obtained by chiral liquid chromatography as a dihydrate. The pyran rings adopt half-chair conformations. Hydrogen bonds between the cation, anions and water molecules contribute to the formation of layers parallel to the  $ac$  plane.

## Related literature

For related literature, see: Cini *et al.* (1990); van Lommen *et al.* (1990); Peeters *et al.* (1993); Tuchalski *et al.* (2006).



## Experimental

## Crystal data

 $\text{C}_{22}\text{H}_{26}\text{F}_2\text{NO}_4^+ \cdot \text{Cl}^- \cdot 2\text{H}_2\text{O}$  $M_r = 477.92$ Orthorhombic,  $P2_12_12_1$  $a = 4.8026$  (4) Å $b = 14.5781$  (12) Å $c = 33.261$  (3) Å $V = 2328.7$  (3) Å<sup>3</sup> $Z = 4$ Mo  $K\alpha$  radiation $\mu = 0.22$  mm<sup>-1</sup> $T = 291$  (2) K $0.60 \times 0.12 \times 0.09$  mm

## Data collection

Bruker SMART APEX CCD area-detector diffractometer

Absorption correction: multi-scan (SADABS; Bruker, 2001)

 $T_{\min} = 0.865$ ,  $T_{\max} = 0.981$ 

26222 measured reflections

3401 independent reflections

2857 reflections with  $I > 2\sigma(I)$  $R_{\text{int}} = 0.054$ 

## Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.041$  $wR(F^2) = 0.113$  $S = 1.05$ 

3401 reflections

301 parameters

6 restraints

H atoms treated by a mixture of independent and constrained refinement

 $\Delta\rho_{\max} = 0.33$  e Å<sup>-3</sup> $\Delta\rho_{\min} = -0.24$  e Å<sup>-3</sup>

Absolute structure: Flack (1983),

608 Friedel pairs

Flack parameter:  $-0.04$  (12)

Table 1

Hydrogen-bond geometry (Å, °).

| $D-H\cdots A$                                 | $D-H$    | $H\cdots A$ | $D\cdots A$ | $D-H\cdots A$ |
|-----------------------------------------------|----------|-------------|-------------|---------------|
| $\text{N1}-\text{H1}\cdots\text{O1W}^i$       | 0.90     | 2.12        | 2.794 (3)   | 131           |
| $\text{N1}-\text{H1}\cdots\text{O4}^{ii}$     | 0.90     | 2.37        | 3.056 (4)   | 133           |
| $\text{N1}-\text{H2}\cdots\text{O4}^{iii}$    | 0.90     | 2.19        | 3.061 (4)   | 162           |
| $\text{O4}-\text{H9}\cdots\text{Cl1}^i$       | 0.82     | 2.67        | 3.142 (2)   | 118           |
| $\text{O4}'-\text{H10}\cdots\text{O2W}^{ii}$  | 0.82     | 2.04        | 2.701 (4)   | 137           |
| $\text{O1W}-\text{H1B}\cdots\text{Cl1}$       | 0.89 (4) | 2.47 (4)    | 3.242 (2)   | 146 (4)       |
| $\text{O1W}-\text{H2B}\cdots\text{N1}^{iv}$   | 0.88 (3) | 2.47 (4)    | 2.794 (3)   | 102 (3)       |
| $\text{O2W}-\text{H1A}\cdots\text{Cl1}$       | 0.89 (4) | 2.29 (4)    | 3.175 (3)   | 175 (3)       |
| $\text{O2W}-\text{H2A}\cdots\text{Cl1}^{iii}$ | 0.88 (4) | 2.37 (4)    | 3.242 (3)   | 171 (3)       |
| $\text{C2}'-\text{H4}\cdots\text{O6}'$        | 0.97     | 2.26        | 2.708 (4)   | 107           |
| $\text{C2}-\text{H5}\cdots\text{O6}$          | 0.97     | 2.35        | 2.738 (4)   | 103           |
| $\text{C2}-\text{H6}\cdots\text{O6}^{ii}$     | 0.97     | 2.49        | 3.457 (4)   | 172           |
| $\text{Cl4}'-\text{H26}\cdots\text{F1}^v$     | 0.93     | 2.34        | 3.213 (5)   | 156           |

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

Data collection: SMART (Bruker, 2001); cell refinement: SAINT (Bruker, 2001); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEPIII (Burnett & Johnson, 1996); software used to prepare material for publication: SHELXTL (Bruker, 2001).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB2656).

## References

- Bruker (2001). SMART, SAINT, SADABS and SHELXTL. Bruker AXS Inc., Madison, Wisconsin, USA.
- Burnett, M. N. & Johnson, C. K. (1996). ORTEPIII. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
- Cini, M., Crotti, P. & Macchia, F. (1990). *Tetrahedron Lett.* **31**, 4661–4664.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Lommen, G. R. E. van, de Bruyn, M. F. L. & Schroven, M. F. J. (1990). *J. Pharm. Belg.* **45**, 355–360.
- Peeters, O. M., Bleton, N. M. & De Ranter, C. J. (1993). *Acta Cryst.* **C49**, 2154–2157.
- Sheldrick, G. M. (1997). SHELXS97 and SHELXL97. University of Göttingen, Germany.
- Tuchalski, G., Emmerling, F., Groger, K., Hänsicke, A., Nagel, T. & Reck, G. (2006). *J. Mol. Struct.* **800**, 28–44.

## supporting information

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## L-Nebivololinium chloride dihydrate

Gisbert Tuchalski, Andre Hänsicke, Günther Reck and Franziska Emmerling

## S1. Comment

*L*-Nebivolol is one enantiomer of the active pharmaceutical ingredient DL-nebivolol. DL-Nebivolol is a  $\beta$ -blocker of the third generation exhibiting a unique activity profile (van Lommen, *et al.*, 1990). Here we report the title compound, (I), the hydrochloride salt of *L*-nebivolol, obtained by chiral liquid chromatography.

The overall shape of the cation in (I) is strongly influenced by the conformation of the bridging C—C—N—C—C chain between the two benzopyran moieties. This conformation is stabilized by two intramolecular N—H $\cdots$ O hydrogen bonds, depicted in Figure 1. Two non-classical C—H $\cdots$ O intramolecular hydrogen bonds align the torsion angles C2—C3—C5—O6 and C2'—C3'—C5'—O6' in a synclinal (*sc*) arrangement. The length of the bridging chain defined by the distance between the carbon atoms C5 and C5' amounts to 7.434 (2) Å. O6 and O6' are in *cis*-position. The average C—N, C—C and C—O distances in the title compound (Fig. 1) are in good agreement with those in other nebivolol derivatives (Peeters *et al.*, 1993; Tuchalski *et al.*, 2006).

Figure 2 shows the packing in (I). Like in the other nebivolol isomers the molecular packing of l-nebivolol is directed by classical intermolecular hydrogen bonds. Nine unique hydrogen bonds between nitrogen and hydroxyl groups, nitrogen and water molecules, hydroxyl groups and water molecules, hydroxyl groups and chlorine as well as between water and chlorine can be observed (Table 1). Together, these result in layers propagating in (010).

## S2. Experimental

The title compound was synthesized by a subsequent ring-opening addition reaction (Cini *et al.*, 1990) of two different oxiran isomers with benzylamine leading to the individual benzyl-nebivolol isomers endowed with 4 chiral centers. The *L*-nebivolol isomer was isolated after hydrogenation and preparative chiral chromatography as its corresponding hydrochloride.

Colourless needles of (I) were grown by solvent evaporation from ethanol/ethyl acetate (1:1 *v/v*) at room temperature. NMR data:  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>),  $\delta$ (p.p.m.): 1.70 (1*H*, m); 1.77 (1*H*, m); 1.93 (1*H*, m); 2.11 (1*H*, m); 2.79 (4*H*, m); 3.05 (1*H*, m); 3.17 (1*H*, m); 3.22 (1*H*, m); 3.33 (1*H*, m); 3.89 (1*H*, m); 3.99 (1*H*, m); 3.99 (1*H*, m); 4.09 (1*H*, m); 5.75 (1*H*, d); 5.94 (1*H*, d); 6.76 (2*H*, dd); 6.91 (2*H*, m); 6.94 (2*H*, m); 8.63 (2*H*, broad)  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$ (p.p.m.): 22.1; 22.3; 23.4; 24.0; 49.4; 49.8; 67.3; 67.4; 76.7; 77.0; 113.6 (23.0); 113.6 (23.1); 115.2 (22.5); 115.3 (22.5); 117.3 (8.1); 117.3 (8.1); 123.6 (7.7); 123.7 (7.8); 150.0 (1.4); 150.4 (1.6); 155.8 (235.5); 155.9 (235.5);  $[\alpha]_D^{29} = -20.5^\circ$  (*c* = 1, THF/water = 4/1) chiral LC: 99.9 area-%

## S3. Refinement

The water H atoms were located in a difference map and their positions were freely refined with  $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$ .

The other hydrogen atoms were located in difference maps, repositioned with idealized geometry (C—H = 0.93–0.97 Å, N—H = 0.89 Å, O—H = 0.82 Å) and refined as riding with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{parent atom})$ .

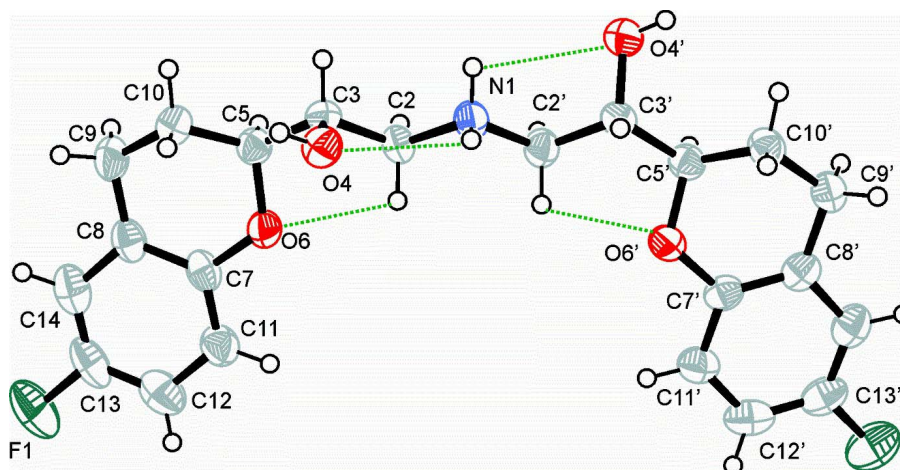


Figure 1

View of the molecular structure of (I) with 50% probability displacement ellipsoids for the non-hydrogen atoms.

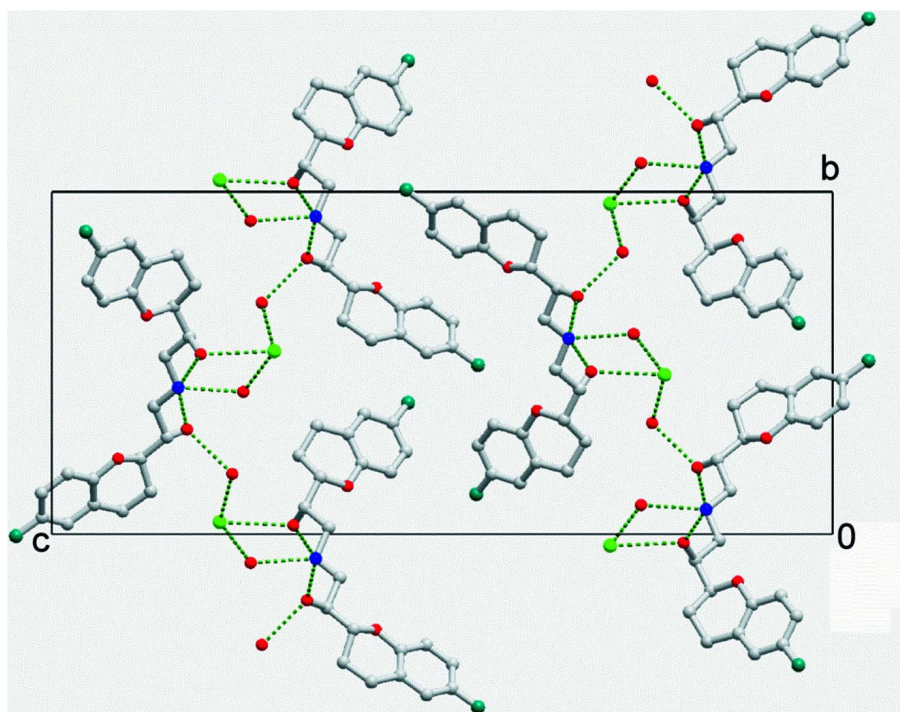


Figure 2

View of the layers array of (I), formed *via* hydrogen-bonding interactions (indicated by green lines).

**(+)-(R,S,S,S)-bis[2-(6-fluoro-3,4-dihydro-2H-1-benzopyran-2-yl)-2-yl hydroxyethyl]ammonium chloride dihydrate**

#### Crystal data

$C_{22}H_{26}F_2NO_4^+ \cdot Cl^- \cdot 2H_2O$

$M_r = 477.92$

Orthorhombic,  $P2_12_12_1$

Hall symbol: P 2ac 2ab

$a = 4.8026 (4) \text{ \AA}$

$b = 14.5781 (12) \text{ \AA}$

$c = 33.261 (3) \text{ \AA}$

$V = 2328.7 (3) \text{ \AA}^3$

$Z = 4$

$F(000) = 1008$

$D_x = 1.363 \text{ Mg m}^{-3}$   
 Mo  $K\alpha$  radiation,  $\lambda = 0.71069 \text{ \AA}$   
 Cell parameters from 120 reflections  
 $\theta = 1.2\text{--}25.4^\circ$

$\mu = 0.22 \text{ mm}^{-1}$   
 $T = 291 \text{ K}$   
 Needle, colourless  
 $0.60 \times 0.12 \times 0.09 \text{ mm}$

#### Data collection

APEX CCD area-detector  
 diffractometer  
 Radiation source: fine-focus sealed tube  
 Graphite monochromator  
 $\omega$ -scan  
 Absorption correction: multi-scan  
 (SADABS; Bruker, 2001)  
 $T_{\min} = 0.865$ ,  $T_{\max} = 0.981$

26222 measured reflections  
 3401 independent reflections  
 2857 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.054$   
 $\theta_{\max} = 26.4^\circ$ ,  $\theta_{\min} = 1.2^\circ$   
 $h = -6 \rightarrow 6$   
 $k = -18 \rightarrow 18$   
 $l = -41 \rightarrow 41$

#### Refinement

Refinement on  $F^2$   
 Least-squares matrix: full  
 $R[F^2 > 2\sigma(F^2)] = 0.041$   
 $wR(F^2) = 0.113$   
 $S = 1.05$   
 3401 reflections  
 301 parameters  
 6 restraints  
 Primary atom site location: structure-invariant  
 direct methods  
 Secondary atom site location: difference Fourier  
 map

Hydrogen site location: inferred from  
 neighbouring sites  
 H atoms treated by a mixture of independent  
 and constrained refinement  
 $w = 1/[\sigma^2(F_o^2) + (0.0545P)^2 + 0.978P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} = 0.004$   
 $\Delta\rho_{\max} = 0.33 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\min} = -0.24 \text{ e \AA}^{-3}$   
 Absolute structure: Flack (1983), xx Friedel  
 pairs  
 Absolute structure parameter:  $-0.04 (12)$

#### Special details

**Geometry.** All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'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  $F^2 > \sigma(F^2)$  is used only for calculating  $R$ -factors(gt) etc. and is not relevant to the choice of reflections for refinement.  $R$ -factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and  $R$ -factors based on ALL data will be even larger.

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

|     | <i>x</i>   | <i>y</i>     | <i>z</i>    | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|-----|------------|--------------|-------------|----------------------------------|
| Cl1 | 0.7060 (2) | 0.96561 (9)  | 0.28493 (3) | 0.0826 (4)                       |
| O1W | 0.2063 (8) | 1.0846 (2)   | 0.24528 (8) | 0.0899 (10)                      |
| H1A | 0.348 (7)  | 0.866 (3)    | 0.2722 (19) | 0.135*                           |
| H1B | 0.348 (8)  | 1.075 (3)    | 0.2618 (13) | 0.135*                           |
| O2W | 0.2154 (7) | 0.8243 (2)   | 0.26894 (9) | 0.0772 (8)                       |
| H2A | 0.064 (6)  | 0.858 (3)    | 0.2719 (18) | 0.116*                           |
| H2B | 0.191 (10) | 1.0312 (17)  | 0.2332 (13) | 0.116*                           |
| N1  | 0.7326 (6) | 0.57169 (17) | 0.33807 (7) | 0.0461 (7)                       |
| H1  | 0.8475     | 0.5622       | 0.3171      | 0.069*                           |
| H2  | 0.5829     | 0.6026       | 0.3290      | 0.069*                           |

|      |             |              |              |             |
|------|-------------|--------------|--------------|-------------|
| C2'  | 0.8776 (7)  | 0.6276 (2)   | 0.36873 (9)  | 0.0435 (8)  |
| H3   | 1.0288      | 0.5918       | 0.3800       | 0.052*      |
| H4   | 0.7484      | 0.6414       | 0.3903       | 0.052*      |
| C2   | 0.6415 (7)  | 0.4814 (2)   | 0.35470 (9)  | 0.0397 (8)  |
| H5   | 0.5196      | 0.4920       | 0.3775       | 0.048*      |
| H6   | 0.8035      | 0.4483       | 0.3643       | 0.048*      |
| C3   | 0.4905 (7)  | 0.4230 (2)   | 0.32411 (9)  | 0.0390 (8)  |
| H7   | 0.6169      | 0.4092       | 0.3018       | 0.058*      |
| C3'  | 0.9940 (7)  | 0.7165 (2)   | 0.35241 (9)  | 0.0403 (8)  |
| H8   | 0.8498      | 0.7478       | 0.3367       | 0.048*      |
| O4   | 0.2600 (5)  | 0.47447 (14) | 0.30934 (6)  | 0.0449 (5)  |
| H9   | 0.1744      | 0.4437       | 0.2928       | 0.067*      |
| O4'  | 1.2211 (5)  | 0.69428 (15) | 0.32678 (6)  | 0.0508 (6)  |
| H10  | 1.2871      | 0.7415       | 0.3174       | 0.076*      |
| C5   | 0.3984 (7)  | 0.3337 (2)   | 0.34381 (9)  | 0.0403 (8)  |
| H11  | 0.5645      | 0.3008       | 0.3530       | 0.060*      |
| C5'  | 1.0904 (7)  | 0.7793 (2)   | 0.38644 (9)  | 0.0390 (8)  |
| H12  | 1.2551      | 0.7521       | 0.3991       | 0.047*      |
| O6   | 0.2381 (5)  | 0.36036 (13) | 0.37856 (6)  | 0.0455 (6)  |
| O6'  | 0.8676 (5)  | 0.78023 (15) | 0.41512 (6)  | 0.0473 (6)  |
| C7   | 0.0810 (7)  | 0.2942 (2)   | 0.39725 (9)  | 0.0421 (8)  |
| C7'  | 0.8967 (7)  | 0.8404 (2)   | 0.44712 (9)  | 0.0411 (8)  |
| C8   | 0.0283 (7)  | 0.2085 (2)   | 0.37968 (11) | 0.0457 (9)  |
| C8'  | 1.0804 (7)  | 0.9139 (2)   | 0.44601 (10) | 0.0431 (8)  |
| C9   | 0.1485 (8)  | 0.1844 (2)   | 0.33954 (11) | 0.0571 (10) |
| H13  | 0.0117      | 0.1508       | 0.3239       | 0.069*      |
| H14  | 0.3097      | 0.1452       | 0.3432       | 0.069*      |
| C9'  | 1.2565 (8)  | 0.9325 (2)   | 0.40927 (9)  | 0.0461 (8)  |
| H15  | 1.4495      | 0.9183       | 0.4152       | 0.055*      |
| H16  | 1.2451      | 0.9971       | 0.4025       | 0.055*      |
| C10  | 0.2340 (9)  | 0.2710 (2)   | 0.31677 (9)  | 0.0506 (9)  |
| H17  | 0.3460      | 0.2543       | 0.2936       | 0.061*      |
| H18  | 0.0692      | 0.3026       | 0.3072       | 0.061*      |
| C10' | 1.1607 (7)  | 0.8755 (2)   | 0.37343 (9)  | 0.0455 (8)  |
| H19  | 0.9982      | 0.9038       | 0.3614       | 0.055*      |
| H20  | 1.3072      | 0.8736       | 0.3534       | 0.055*      |
| C11  | −0.0325 (8) | 0.3188 (3)   | 0.43371 (10) | 0.0527 (9)  |
| H21  | 0.0097      | 0.3756       | 0.4449       | 0.063*      |
| C11' | 0.7255 (8)  | 0.8244 (2)   | 0.47963 (9)  | 0.0499 (9)  |
| H22  | 0.6006      | 0.7757       | 0.4791       | 0.060*      |
| C12  | −0.2092 (9) | 0.2592 (3)   | 0.45375 (12) | 0.0668 (11) |
| H23  | −0.2908     | 0.2753       | 0.4781       | 0.080*      |
| C12' | 0.7387 (9)  | 0.8806 (3)   | 0.51317 (10) | 0.0578 (10) |
| H24  | 0.6242      | 0.8707       | 0.5353       | 0.069*      |
| C13  | −0.2590 (9) | 0.1757 (3)   | 0.43632 (13) | 0.0660 (11) |
| C13' | 0.9266 (9)  | 0.9516 (3)   | 0.51263 (10) | 0.0581 (10) |
| C14  | −0.1492 (8) | 0.1495 (3)   | 0.40030 (13) | 0.0615 (11) |
| H25  | −0.1928     | 0.0924       | 0.3895       | 0.092*      |

|      |             |              |              |            |
|------|-------------|--------------|--------------|------------|
| C14' | 1.0930 (8)  | 0.9700 (3)   | 0.48011 (10) | 0.0551 (9) |
| H26  | 1.2141      | 1.0198       | 0.4807       | 0.066*     |
| F1   | −0.4347 (6) | 0.11636 (19) | 0.45634 (9)  | 0.1020 (9) |
| F1'  | 0.9452 (7)  | 1.00610 (18) | 0.54589 (7)  | 0.0957 (9) |

*Atomic displacement parameters (Å<sup>2</sup>)*

|      | $U^{11}$    | $U^{22}$    | $U^{33}$    | $U^{12}$     | $U^{13}$     | $U^{23}$     |
|------|-------------|-------------|-------------|--------------|--------------|--------------|
| Cl1  | 0.0593 (7)  | 0.1298 (10) | 0.0587 (6)  | −0.0099 (7)  | −0.0044 (5)  | 0.0150 (6)   |
| O1W  | 0.098 (3)   | 0.120 (3)   | 0.0524 (17) | 0.013 (2)    | −0.0059 (17) | −0.0197 (17) |
| O2W  | 0.0740 (19) | 0.095 (2)   | 0.0626 (16) | −0.0110 (18) | 0.0067 (18)  | 0.0175 (16)  |
| N1   | 0.0506 (17) | 0.0464 (15) | 0.0414 (14) | −0.0137 (15) | 0.0035 (14)  | −0.0038 (13) |
| C2'  | 0.0459 (19) | 0.0432 (19) | 0.0414 (18) | −0.0070 (16) | −0.0018 (16) | −0.0028 (15) |
| C2   | 0.0390 (18) | 0.0357 (17) | 0.0444 (17) | −0.0061 (15) | 0.0004 (15)  | 0.0030 (14)  |
| C3   | 0.0357 (18) | 0.0401 (17) | 0.0411 (17) | 0.0007 (16)  | 0.0039 (15)  | −0.0046 (15) |
| C3'  | 0.0384 (18) | 0.0422 (18) | 0.0403 (17) | −0.0039 (16) | 0.0044 (15)  | 0.0003 (15)  |
| O4   | 0.0432 (12) | 0.0465 (13) | 0.0450 (12) | 0.0013 (13)  | −0.0060 (12) | −0.0019 (10) |
| O4'  | 0.0512 (14) | 0.0442 (12) | 0.0569 (13) | −0.0016 (12) | 0.0125 (13)  | −0.0022 (11) |
| C5   | 0.0404 (18) | 0.0349 (17) | 0.0456 (18) | 0.0003 (15)  | 0.0008 (17)  | −0.0006 (15) |
| C5'  | 0.0348 (17) | 0.0430 (19) | 0.0393 (17) | −0.0010 (15) | −0.0008 (15) | 0.0007 (15)  |
| O6   | 0.0562 (14) | 0.0394 (12) | 0.0410 (11) | −0.0112 (12) | 0.0060 (12)  | −0.0027 (10) |
| O6'  | 0.0437 (13) | 0.0532 (14) | 0.0449 (12) | −0.0116 (11) | 0.0076 (11)  | −0.0069 (11) |
| C7   | 0.0403 (18) | 0.044 (2)   | 0.0424 (19) | −0.0079 (17) | −0.0072 (16) | 0.0112 (16)  |
| C7'  | 0.0400 (19) | 0.0469 (19) | 0.0365 (17) | 0.0051 (17)  | −0.0033 (16) | −0.0046 (15) |
| C8   | 0.0412 (19) | 0.0370 (18) | 0.059 (2)   | −0.0038 (17) | −0.0063 (17) | 0.0082 (17)  |
| C8'  | 0.0386 (19) | 0.0441 (19) | 0.0467 (19) | 0.0081 (17)  | −0.0071 (16) | −0.0029 (16) |
| C9   | 0.060 (3)   | 0.0351 (18) | 0.076 (3)   | −0.0089 (18) | 0.005 (2)    | −0.0075 (18) |
| C9'  | 0.0445 (19) | 0.0416 (18) | 0.0522 (19) | −0.0056 (18) | −0.0005 (18) | 0.0015 (16)  |
| C10  | 0.056 (2)   | 0.046 (2)   | 0.0500 (19) | −0.008 (2)   | 0.003 (2)    | −0.0102 (16) |
| C10' | 0.049 (2)   | 0.0463 (19) | 0.0408 (18) | −0.0076 (16) | −0.0002 (16) | 0.0044 (15)  |
| C11  | 0.058 (2)   | 0.055 (2)   | 0.045 (2)   | −0.012 (2)   | 0.0019 (19)  | 0.0034 (18)  |
| C11' | 0.051 (2)   | 0.055 (2)   | 0.0446 (19) | 0.0013 (19)  | 0.0068 (18)  | 0.0017 (16)  |
| C12  | 0.060 (3)   | 0.078 (3)   | 0.062 (2)   | −0.011 (2)   | 0.007 (2)    | 0.016 (2)    |
| C12' | 0.058 (2)   | 0.072 (2)   | 0.0435 (19) | 0.016 (2)    | 0.0081 (19)  | 0.0023 (19)  |
| C13  | 0.055 (2)   | 0.060 (2)   | 0.084 (3)   | −0.020 (2)   | 0.001 (2)    | 0.027 (2)    |
| C13' | 0.068 (3)   | 0.065 (3)   | 0.041 (2)   | 0.008 (2)    | −0.001 (2)   | −0.0143 (19) |
| C14  | 0.054 (2)   | 0.048 (2)   | 0.082 (3)   | −0.0118 (19) | −0.008 (2)   | 0.009 (2)    |
| C14' | 0.059 (2)   | 0.051 (2)   | 0.056 (2)   | −0.002 (2)   | −0.007 (2)   | −0.0113 (18) |
| F1   | 0.090 (2)   | 0.0920 (18) | 0.124 (2)   | −0.0404 (17) | 0.0217 (17)  | 0.0312 (17)  |
| F1'  | 0.124 (2)   | 0.1009 (19) | 0.0617 (14) | −0.0078 (18) | 0.0089 (15)  | −0.0367 (14) |

*Geometric parameters (Å, °)*

|         |           |          |           |
|---------|-----------|----------|-----------|
| O1W—H1B | 0.89 (4)  | C7—C8    | 1.402 (5) |
| O1W—H2B | 0.88 (3)  | C7'—C11' | 1.378 (5) |
| O2W—H1A | 0.89 (4)  | C7'—C8'  | 1.388 (5) |
| O2W—H2A | 0.92 (5)  | C8—C14   | 1.391 (5) |
| N1—C2'  | 1.479 (4) | C8—C9    | 1.496 (5) |

|             |           |              |           |
|-------------|-----------|--------------|-----------|
| N1—C2       | 1.493 (4) | C8'—C14'     | 1.400 (5) |
| N1—H1       | 0.9000    | C8'—C9'      | 1.511 (5) |
| N1—H2       | 0.9000    | C9—C10       | 1.528 (5) |
| C2'—C3'     | 1.512 (4) | C9—H13       | 0.9700    |
| C2'—H3      | 0.9700    | C9—H14       | 0.9700    |
| C2'—H4      | 0.9700    | C9'—C10'     | 1.525 (4) |
| C2—C3       | 1.512 (4) | C9'—H15      | 0.9700    |
| C2—H5       | 0.9700    | C9'—H16      | 0.9700    |
| C2—H6       | 0.9700    | C10—H17      | 0.9700    |
| C3—O4       | 1.424 (4) | C10—H18      | 0.9700    |
| C3—C5       | 1.524 (4) | C10'—H19     | 0.9700    |
| C3—H7       | 0.9800    | C10'—H20     | 0.9700    |
| C3'—O4'     | 1.422 (4) | C11—C12      | 1.385 (5) |
| C3'—C5'     | 1.528 (4) | C11—H21      | 0.9300    |
| C3'—H8      | 0.9800    | C11'—C12'    | 1.386 (5) |
| O4—H9       | 0.8200    | C11'—H22     | 0.9300    |
| O4'—H10     | 0.8200    | C12—C13      | 1.370 (6) |
| C5—O6       | 1.442 (4) | C12—H23      | 0.9300    |
| C5—C10      | 1.506 (5) | C12'—C13'    | 1.372 (5) |
| C5—H11      | 0.9800    | C12'—H24     | 0.9300    |
| C5'—O6'     | 1.434 (4) | C13—C14      | 1.363 (6) |
| C5'—C10'    | 1.505 (4) | C13—F1       | 1.379 (4) |
| C5'—H12     | 0.9800    | C13'—C14'    | 1.371 (5) |
| O6—C7       | 1.373 (4) | C13'—F1'     | 1.365 (4) |
| O6'—C7'     | 1.386 (4) | C14—H25      | 0.9300    |
| C7—C11      | 1.377 (5) | C14'—H26     | 0.9300    |
| H1B—O1W—H2B | 102 (4)   | C14—C8—C7    | 117.1 (3) |
| H1A—O2W—H2A | 101 (4)   | C14—C8—C9    | 122.1 (3) |
| C2'—N1—C2   | 111.6 (2) | C7—C8—C9     | 120.7 (3) |
| C2'—N1—H1   | 109.3     | C7'—C8'—C14' | 117.2 (3) |
| C2—N1—H1    | 109.3     | C7'—C8'—C9'  | 121.1 (3) |
| C2'—N1—H2   | 109.3     | C14'—C8'—C9' | 121.7 (3) |
| C2—N1—H2    | 109.3     | C8—C9—C10    | 110.6 (3) |
| H1—N1—H2    | 108.0     | C8—C9—H13    | 109.5     |
| N1—C2'—C3'  | 113.5 (3) | C10—C9—H13   | 109.5     |
| N1—C2'—H3   | 108.9     | C8—C9—H14    | 109.5     |
| C3'—C2'—H3  | 108.9     | C10—C9—H14   | 109.5     |
| N1—C2'—H4   | 108.9     | H13—C9—H14   | 108.1     |
| C3'—C2'—H4  | 108.9     | C8'—C9'—C10' | 111.4 (3) |
| H3—C2'—H4   | 107.7     | C8'—C9'—H15  | 109.3     |
| N1—C2—C3    | 112.8 (2) | C10'—C9'—H15 | 109.3     |
| N1—C2—H5    | 109.0     | C8'—C9'—H16  | 109.3     |
| C3—C2—H5    | 109.0     | C10'—C9'—H16 | 109.3     |
| N1—C2—H6    | 109.0     | H15—C9'—H16  | 108.0     |
| C3—C2—H6    | 109.0     | C5—C10—C9    | 110.3 (3) |
| H5—C2—H6    | 107.8     | C5—C10—H17   | 109.6     |
| O4—C3—C2    | 108.0 (2) | C9—C10—H17   | 109.6     |

|                  |            |                   |            |
|------------------|------------|-------------------|------------|
| O4—C3—C5         | 111.9 (3)  | C5—C10—H18        | 109.6      |
| C2—C3—C5         | 109.3 (2)  | C9—C10—H18        | 109.6      |
| O4—C3—H7         | 109.2      | H17—C10—H18       | 108.1      |
| C2—C3—H7         | 109.2      | C5'—C10'—C9'      | 110.5 (3)  |
| C5—C3—H7         | 109.2      | C5'—C10'—H19      | 109.5      |
| O4'—C3'—C2'      | 107.7 (3)  | C9'—C10'—H19      | 109.5      |
| O4'—C3'—C5'      | 110.4 (3)  | C5'—C10'—H20      | 109.5      |
| C2'—C3'—C5'      | 111.1 (2)  | C9'—C10'—H20      | 109.5      |
| O4'—C3'—H8       | 109.2      | H19—C10'—H20      | 108.1      |
| C2'—C3'—H8       | 109.2      | C7—C11—C12        | 120.2 (3)  |
| C5'—C3'—H8       | 109.2      | C7—C11—H21        | 119.9      |
| C3—O4—H9         | 109.5      | C12—C11—H21       | 119.9      |
| C3'—O4'—H10      | 109.5      | C7'—C11'—C12'     | 120.3 (4)  |
| O6—C5—C10        | 111.3 (3)  | C7'—C11'—H22      | 119.9      |
| O6—C5—C3         | 105.6 (2)  | C12'—C11'—H22     | 119.9      |
| C10—C5—C3        | 114.5 (3)  | C13—C12—C11       | 117.5 (4)  |
| O6—C5—H11        | 108.4      | C13—C12—H23       | 121.3      |
| C10—C5—H11       | 108.4      | C11—C12—H23       | 121.3      |
| C3—C5—H11        | 108.4      | C13'—C12'—C11'    | 117.7 (4)  |
| O6'—C5'—C10'     | 110.5 (3)  | C13'—C12'—H24     | 121.1      |
| O6'—C5'—C3'      | 105.8 (2)  | C11'—C12'—H24     | 121.1      |
| C10'—C5'—C3'     | 114.4 (3)  | C14—C13—C12       | 123.5 (4)  |
| O6'—C5'—H12      | 108.7      | C14—C13—F1        | 119.1 (4)  |
| C10'—C5'—H12     | 108.7      | C12—C13—F1        | 117.4 (4)  |
| C3'—C5'—H12      | 108.7      | C14'—C13'—F1'     | 119.1 (4)  |
| C7—O6—C5         | 117.8 (2)  | C14'—C13'—C12'    | 122.7 (3)  |
| C7'—O6'—C5'      | 116.2 (2)  | F1'—C13'—C12'     | 118.1 (3)  |
| O6—C7—C11        | 115.7 (3)  | C13—C14—C8        | 119.9 (4)  |
| O6—C7—C8         | 122.4 (3)  | C13—C14—H25       | 120.1      |
| C11—C7—C8        | 121.8 (3)  | C8—C14—H25        | 120.1      |
| C11'—C7'—O6'     | 115.8 (3)  | C13'—C14'—C8'     | 120.0 (4)  |
| C11'—C7'—C8'     | 122.0 (3)  | C13'—C14'—H26     | 120.0      |
| O6'—C7'—C8'      | 122.1 (3)  | C8'—C14'—H26      | 120.0      |
| C2—N1—C2'—C3'    | 175.4 (3)  | O6'—C7'—C8'—C9'   | 0.8 (5)    |
| C2'—N1—C2—C3     | 179.6 (3)  | C14—C8—C9—C10     | 157.4 (4)  |
| N1—C2—C3—O4      | -56.6 (3)  | C7—C8—C9—C10      | -19.6 (5)  |
| N1—C2—C3—C5      | -178.5 (3) | C7'—C8'—C9'—C10'  | 11.8 (4)   |
| N1—C2'—C3'—O4'   | -70.0 (4)  | C14'—C8'—C9'—C10' | -167.6 (3) |
| N1—C2'—C3'—C5'   | 169.0 (3)  | O6—C5—C10—C9      | -59.5 (4)  |
| O4—C3—C5—O6      | -64.8 (3)  | C3—C5—C10—C9      | -179.1 (3) |
| C2—C3—C5—O6      | 54.8 (3)   | C8—C9—C10—C5      | 47.3 (4)   |
| O4—C3—C5—C10     | 58.0 (4)   | O6'—C5'—C10'—C9'  | 61.2 (4)   |
| C2—C3—C5—C10     | 177.5 (3)  | C3'—C5'—C10'—C9'  | -179.6 (3) |
| O4'—C3'—C5'—O6'  | -167.0 (2) | C8'—C9'—C10'—C5'  | -41.4 (4)  |
| C2'—C3'—C5'—O6'  | -47.6 (3)  | O6—C7—C11—C12     | 175.8 (3)  |
| O4'—C3'—C5'—C10' | 71.1 (4)   | C8—C7—C11—C12     | -1.5 (5)   |
| C2'—C3'—C5'—C10' | -169.5 (3) | O6'—C7'—C11'—C12' | 179.9 (3)  |

|                   |            |                     |            |
|-------------------|------------|---------------------|------------|
| C10—C5—O6—C7      | 41.9 (4)   | C8'—C7'—C11'—C12'   | −2.0 (5)   |
| C3—C5—O6—C7       | 166.7 (3)  | C7—C11—C12—C13      | 1.5 (6)    |
| C10'—C5'—O6'—C7'  | −49.5 (4)  | C7'—C11'—C12'—C13'  | −0.1 (5)   |
| C3'—C5'—O6'—C7'   | −173.9 (2) | C11—C12—C13—C14     | −1.4 (7)   |
| C5—O6—C7—C11      | 170.0 (3)  | C11—C12—C13—F1      | 179.9 (3)  |
| C5—O6—C7—C8       | −12.7 (4)  | C11'—C12'—C13'—C14' | 1.9 (6)    |
| C5'—O6'—C7'—C11'  | −163.3 (3) | C11'—C12'—C13'—F1'  | −178.6 (3) |
| C5'—O6'—C7'—C8'   | 18.7 (4)   | C12—C13—C14—C8      | 1.3 (7)    |
| O6—C7—C8—C14      | −175.8 (3) | F1—C13—C14—C8       | 180.0 (3)  |
| C11—C7—C8—C14     | 1.3 (5)    | C7—C8—C14—C13       | −1.2 (5)   |
| O6—C7—C8—C9       | 1.4 (5)    | C9—C8—C14—C13       | −178.3 (4) |
| C11—C7—C8—C9      | 178.5 (3)  | F1'—C13'—C14'—C8'   | 178.8 (3)  |
| C11'—C7'—C8'—C14' | 2.2 (5)    | C12'—C13'—C14'—C8'  | −1.7 (6)   |
| O6'—C7'—C8'—C14'  | −179.8 (3) | C7'—C8'—C14'—C13'   | −0.4 (5)   |
| C11'—C7'—C8'—C9'  | −177.2 (3) | C9'—C8'—C14'—C13'   | 179.0 (3)  |

## 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> |
|------------------------------------------------|-------------|---------------|-----------------------|-------------------------|
| N1—H1...O1 <i>W</i> <sup>i</sup>               | 0.90        | 2.12          | 2.794 (3)             | 131                     |
| N1—H1...O4 <sup>ii</sup>                       | 0.90        | 2.37          | 3.056 (4)             | 133                     |
| N1—H2...O4 <sup>iii</sup>                      | 0.90        | 2.19          | 3.061 (4)             | 162                     |
| O4—H9...C11 <sup>i</sup>                       | 0.82        | 2.67          | 3.142 (2)             | 118                     |
| O4'—H10...O2 <i>W</i> <sup>ii</sup>            | 0.82        | 2.04          | 2.701 (4)             | 137                     |
| O1 <i>W</i> —H1 <i>B</i> ...C11                | 0.89 (4)    | 2.47 (4)      | 3.242 (2)             | 146 (4)                 |
| O1 <i>W</i> —H2 <i>B</i> ...N1 <sup>iv</sup>   | 0.88 (3)    | 2.47 (4)      | 2.794 (3)             | 102 (3)                 |
| O2 <i>W</i> —H1 <i>A</i> ...C11                | 0.89 (4)    | 2.29 (4)      | 3.175 (3)             | 175 (3)                 |
| O2 <i>W</i> —H2 <i>A</i> ...C11 <sup>iii</sup> | 0.88 (4)    | 2.37 (4)      | 3.242 (3)             | 171 (3)                 |
| C2'—H4...O6'                                   | 0.97        | 2.26          | 2.708 (4)             | 107                     |
| C2—H5...O6                                     | 0.97        | 2.35          | 2.738 (4)             | 103                     |
| C2—H6...O6 <sup>ii</sup>                       | 0.97        | 2.49          | 3.457 (4)             | 172                     |
| C14'—H26...F1 <sup>v</sup>                     | 0.93        | 2.34          | 3.213 (5)             | 156                     |

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