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# Losartan potassium 3.5-hydrate, a new crystalline form

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**Key indicators**

Single-crystal X-ray study
$T$ = 295 K
Mean $\sigma$(C–C) = 0.004 Å
$R$ factor = 0.054
$wR$ factor = 0.124
Data-to-parameter ratio = 10.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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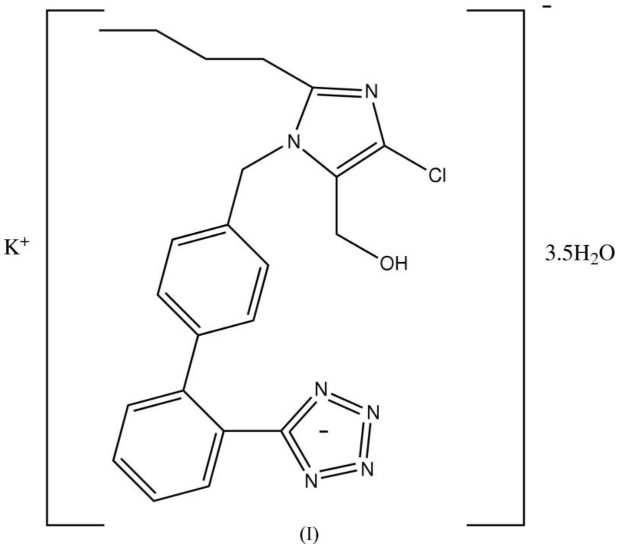
The asymmetric unit of the title compound, di-$\mu$-aqua-1:2$\kappa^4O$:$O$-triaqua-1$\kappa^3O$-dilosartanido-1$\kappa N$;2$\kappa^2N$,$N'$-dipotassium dihydrate, $[K_2(C_{22}H_{22}ClN_6O)_2(H_2O)_5]\cdot 2H_2O$, is composed of two losartan anions, two $K^+$ cations and seven water molecules. Some water molecules bridge the potassium ions linking the molecules to form an infinite chain. The two potassium ions have different environments; one is six-coordinated by three water O atoms and three tetrazole N atoms, whereas the other is five-coordinated by five water O atoms. Extensive hydrogen-bonding interactions lead to a three-dimensional structure.

## Comment

Losartan potassium is a potent and orally effective pharmaceutical product used for the treatment of arterial hypertension (Birkenhager & de Leeuw, 1999; Goa & Wagstaff, 1996; Gavras & Salerno, 1996). It is the prototype of a new class of antihypertensive agents, the angiotensin receptor antagonists. Two polymorphic modifications of the drug have been identified by spectroscopic (Raghavan *et al.*, 1993) and thermal (Wu *et al.*, 1993) studies, and the crystal structure of one polymorph has been reported (Fernandez *et al.*, 2002). We report here the crystal structure of a new losartan potassium hydrate, (I).



(I)

The asymmetric unit of (I) is composed of two losartan anions, two $K^+$ cations and seven water molecules (Fig. 1). The occurrence of water molecules greatly influences the coordination around potassium, which is different from that in the structure reported by Fernandez *et al.* (2002). One $K^+$ cation, K1, is six-coordinated by three water O atoms and three tetrazole N atoms, in which one tetrazole group serves as a bidentate ligand and another tetrazole group as a monodentate ligand, whereas the other K$^+$ cation, K2, is five-coordinated by five water O atoms (Fig. 2).

Three types of water molecules are present in the crystal structure of (I), *viz*. three bridging, two terminal and two uncoordinated water molecules.

Water atoms O53 and O54 bridge the K1$^+$ and K2$^+$ cations, resulting in a K1···K2 contact distance of 4.202 Å. Water atom O57 serves as a bridging ligand between K2···K1$^{i}$ [symmetry code: (i) $x + \frac{1}{2}$, $y$, $-z + \frac{1}{2}$], resulting in a contact distance of 4.486 Å between metal centres, thus forming an infinite chain (Fig. 2). This difference in coordination between K1 and K2 may explain the different $U_{eq}$ values. The six-coordinated central K1$^+$ ion has a lower $U_{eq}$ value compared to that of the five-coordinated K2$^+$ ion.

The crystal packing is stabilized by O—H···N and O—H···O hydrogen bonds (Table 1) involving some water H atoms.

The conformations of the two losartan anions are very similar. In both molecules, the tetrazole rings are affected by extensive electron delocalization. The rings are planar and the bond lengths within the rings range from 1.304 (4) to 1.350 (4) Å and from 1.313 (4) to 1.353 (4) Å for C1/N11/N12/N13/N14 and C23/N21/N22/N23/N24, respectively.

## Experimental

The title compound was obtained from the Laboratory of Microstructure in Zhejiang University. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a solution in a mixture of ethanol and water (4:1 *v*/*v*).

### *Crystal data*

$[K_2(C_{22}H_{22}ClN_6O)_2(H_2O)_5]\cdot 2H_2O$
$M_r = 1048.12$
Orthorhombic, *Pbca*
$a = 13.1389$ (3) Å
$b = 25.6885$ (5) Å
$c = 31.1822$ (7) Å
$V = 10524.6$ (4) Å$^3$
$Z = 8$
$D_x = 1.323$ Mg m$^{-3}$

Mo $K\alpha$ radiation
Cell parameters from 69404 reflections
$\theta = 1.3$–27.5°
$\mu = 0.34$ mm$^{-1}$
$T = 295$ (1) K
Block, colorless
0.40 × 0.28 × 0.22 mm

### *Data collection*

Rigaku R-AXIS RAPID diffractometer
$\omega$ scans
Absorption correction: multi-scan (*ABSCOR*; Higashi, 1995)
$T_{min} = 0.857$, $T_{max} = 0.927$
74477 measured reflections

11990 independent reflections
6573 reflections with $F^2 > 2\sigma(F^2)$
$R_{int} = 0.040$
$\theta_{max} = 27.5°$
$h = -16 \rightarrow 17$
$k = -33 \rightarrow 32$
$l = -40 \rightarrow 39$

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.124$
$S = 1.02$
6573 reflections
623 parameters
H-atom parameters constrained

$w = 1/[0.0012F_o^2 + 3\sigma(F_o^2) + 0.5]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.75$ e Å$^{-3}$
$\Delta\rho_{min} = -0.67$ e Å$^{-3}$
Extinction correction: Larson (1970)
Extinction coefficient: 3.9 (10) × 10$^2$

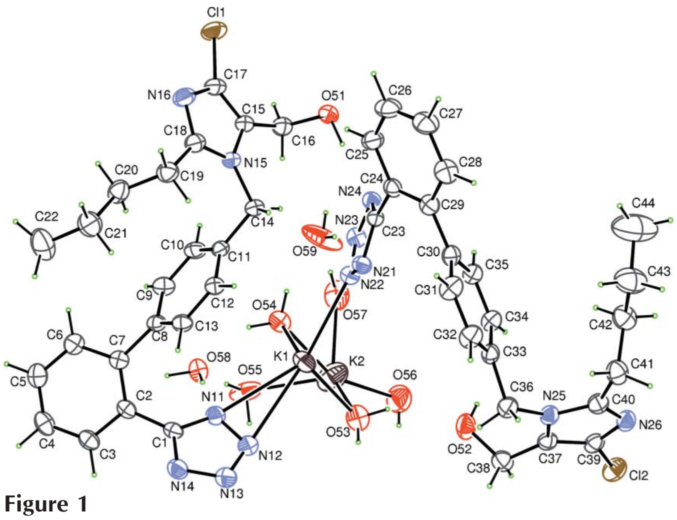


**Figure 1**
A view of the asymmetric unit of (I), showing the atom-numbering sheme, with displacement ellipsoids drawn at the 30% probability level.

**Table 1**
Selected bond lengths (Å).

| | | | |
|---|---|---|---|
| K1—O53 | 2.860 (3) | K2—O57 | 2.682 (4) |
| K1—O54 | 2.746 (3) | O51—C16 | 1.430 (4) |
| K1—O57$^{i}$ | 2.804 (3) | O52—C38 | 1.415 (4) |
| K1—N11 | 2.921 (3) | N15—C18 | 1.350 (4) |
| K1—N12 | 2.884 (3) | N16—C17 | 1.359 (5) |
| K1—N22 | 2.804 (3) | N25—C40 | 1.363 (4) |
| K2—O53 | 2.693 (4) | C7—C8 | 1.499 (4) |
| K2—O54 | 2.830 (3) | C29—C30 | 1.476 (5) |
| K2—O55 | 2.798 (4) | C37—C39 | 1.350 (5) |
| K2—O56 | 2.728 (4) | | |

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

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

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O51—H511···N24 | 0.99 | 1.88 | 2.863 (3) | 176 |
| O54—H541···O59 | 0.92 | 1.92 | 2.789 (5) | 159 |
| O54—H542···O58 | 0.93 | 1.96 | 2.792 (4) | 149 |
| O55—H551···O58 | 0.96 | 1.84 | 2.790 (4) | 169 |
| O57—H571···O59 | 0.91 | 2.06 | 2.919 (5) | 158 |
| O59—H591···N23 | 0.95 | 1.91 | 2.854 (5) | 176 |
| O52—H521···N14$^{ii}$ | 0.97 | 1.80 | 2.740 (4) | 162 |
| O53—H531···N13$^{ii}$ | 0.90 | 2.03 | 2.897 (4) | 160 |
| O53—H532···O56$^{i}$ | 0.87 | 2.19 | 3.030 (5) | 162 |
| O55—H552···N16$^{iii}$ | 0.96 | 1.87 | 2.766 (4) | 154 |
| O56—H561···O51$^{iv}$ | 0.96 | 2.21 | 2.858 (4) | 124 |
| O58—H582···N26$^{v}$ | 0.96 | 1.85 | 2.804 (4) | 173 |
| O59—H592···N21$^{ii}$ | 0.92 | 1.93 | 2.830 (4) | 166 |

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

H atoms of the hydroxy group and water molecules were located in a difference Fourier map and included in the refinement based on the as-found bond lengths, but riding on the O atoms to which they are bonded. Their isotropic displacement paramenters were initially refined and then fixed in the final stage. All other H atoms were placed in calculated positions, with C—H = 0.96–0.98 Å, and included in the refinement with a riding model, with $U_{iso}(H) = 1.2U_{eq}$(carrier atom).

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SHELXS97* (Alto-

*Acta Cryst.* (2005). E**61**, m1686–m1688 Hu *et al.* • $[K_2(C_{22}H_{22}ClN_6O)_2(H_2O)_5]\cdot 2H_2O$ **m1687**

mare *et al.*, 1999); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *CrystalStructure*.

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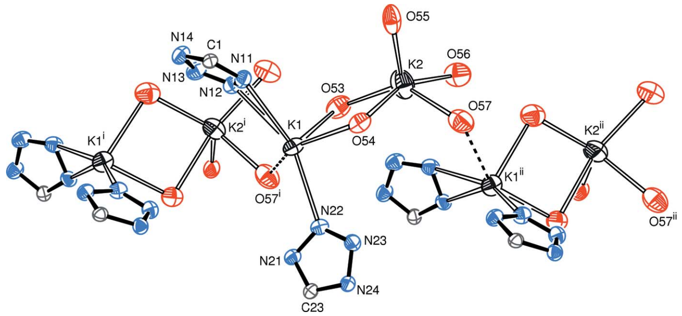

**Figure 2**

The infinite chain generated by the bridging water molecules [symmetry codes: (i) $x - \frac{1}{2}, y, -z + \frac{1}{2}$; (ii) $x + \frac{1}{2}, y, -z + \frac{1}{2}$].

**m1688** Hu *et al.* • $[K_2(C_{22}H_{22}ClN_6O)_2(H_2O)_5]\cdot 2H_2O$ *Acta Cryst.* (2005). E**61**, m1686–m1688