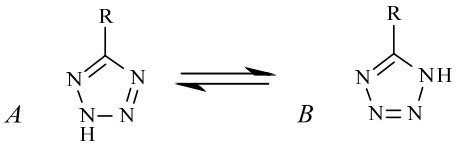
P22

# Crystal and Molecular Structure of Irbesartan Sesquihydrochloride Hydroxonium Sesquihydrate

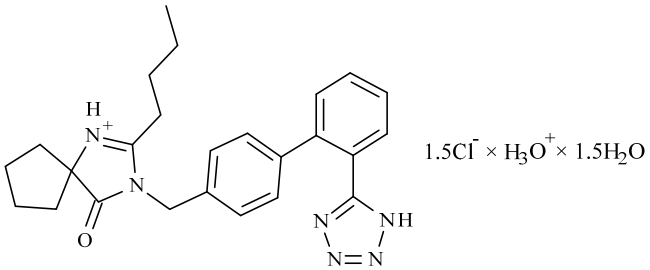
Dmitrijs Stepanovs
*Latvian Institute of Organic Synthesis, Aizkraukles Str. 21, Riga, LV-1006, Latvia*
*e-mail: d_stepanovs@osi.lv*

Irbesartan, 2-butyl-3-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl]-1,3-diaza-spiro[4.4]non-1-en-4-one, $C_{25}H_{28}N_6O$, is an antihypertensive agent that inhibits the renin-angiotensin system by selectively blocking the $AT_1$ subtype of receptors [1, 2]. Irbesartan in a solid state was found to exist in two distinct crystal forms (*A* and *B*). It provides a rare example of desmotropy [3], since monosubstituted tetrazole ring can undergo a tautomeric process according to Scheme 1 [4].



Scheme 1. Tautomeric process of the monosubstituted tetrazole ring (3*H*- and 2*H*-tetrazoles, *A* and *B* respectively)

Up to now, there are three crystal forms described in the literature, namely, irbesartan base [4], irbesartan hydrochloride 1.69-hydrate [5] and irbesartan hydrobromide sesquihydrate [2], all of them contain tetrazole ring form *B*. Present research describes irbesartan sesquihydrochloride hydroxonium sesquihydrate, obtained by recrystallization of irbesartan form *B* from the mixture of dimethyl sulfoxide and hydrochloric acid (Scheme 2).



$1.5Cl^- \times H_3O^+ \times 1.5H_2O$

**Scheme 2.** Molecular structure of the title compound

The title compound, $C_{25}H_{29}N_6O^+ \cdot 1.5Cl^- \cdot H_3O^+ \cdot 1.5H_2O$, crystallizes in the orthorhombic system, space group $Pbn2_1$ with the unit cell parameters $a$ = 12.3596(1), b = 15.4862(2), $c$ = 28.3389(3) Å, Z = 4, V = 5424.16(10) Å$^3$. Structure contains 2*H*-tetrazole ring, as in form *B*. The structure was solved by direct methods and refined anisotropically on $F^2$ values using Shelxl-97 [6]. Final $R(F)$ = 0.054 and $wR(F^2)$ = 0.110.

ORTEP-III drawing of the title compound is shown in Figure 1. The asymmetric unit consists of two irbesartan cations, three chloride anions, two hydroxonium cations (both contain one hydrogen atom with occupation factor equal to 0.5) and three water molecules. The overall conformation of irbesartan fragment is similar to that of the neutral molecule of form *B* [4] and known salt forms [2] and [5].

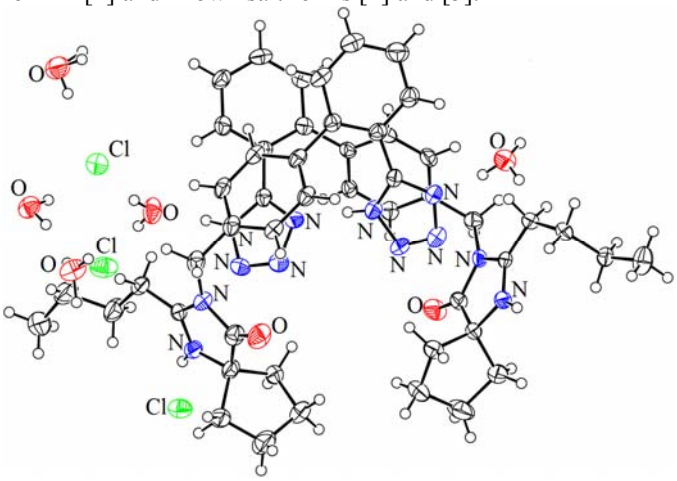


**Figure 1.** The crystal structure of the title compound, showing 50% probability ellipsoids for non-hydrogen atoms

The crystal structure has networks of hydrogen bonds, which link $Cl^-$, $H_3O^+$, water molecules and irbesartan cations into infinite chains. Irbesartan cations are connected by hydrogen bond of N–H···N type and form dimmers. Irbesartan cations are also connected to one of the hydroxonium anion by O–H···N and to water molecule by N–H···O hydrogen bonds. By means of hydrogen bonds O–H···Cl chloride anions are connected to water molecules and hydroxonium ions making infinite chains.

In both irbesartan cations the dihedral angles formed by the planes of two benzene rings are 48.9 and 49.7°, whereas the angles between the tetrazole plane and that of the adjacent benzene ring are 39.7 and 40.9° respectively.

*Supervisor: Dr.phys. A.Mishnev.*

## References

[1] Shakya, K.S., Al-Hiar, Y.M., Alhamami, O.M.O. *J. Chromatogr. B.* **2007**, *848*, 245-250.
[2] Wang, L., Zhou, L.N., Bao, Y., Wang J.K., *Acta Crystallogr. E*, **2007**, *63*, o4933.
[3] Lempert, K., Nyitrai, J., Zauer, K., Kalman, A., Argay, Gy., Duisenberg, A.J.M., Sohar, P. *Tetrahedron*. **1973**, *22*, 3565-3569.
[4] Bocskei, Z., Simon, K., Rao, R., Caron, A., Rodger, C.A., Bauer, M. *Acta Crystallogr. C*. **1998**, *54*, 808-810.
[5] Bartolucci, G., Bruni, B., Di Vaira, M., Giannellini, V. *Acta Crystallogr. E*, **2007**, *63*, o1529-o1531.
[6] Sheldrick, G.M. *Acta Crystallogr. A*. **2008**, *64*, 112-122.