STRUCTURE AND ANALGESIC ACTIVITY OF *N*-BENZYL-4-HYDROXY-1-METHYL-2,2-DIOXO-1*H*-2Λ^6,1-BENZOTHIAZINE-3-CARBOXAMIDE CONFORMERS

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While studying *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carbox-amide (**1**) crystal modifications described before and producing a high analgesic effect, it was found that this compound can form two pseudo-enantiomeric forms **A** and **B** (see Figure), which are mirror images of each other. This fact seems interesting as there is no stereogenic atom in the original molecule. Besides, analgesic properties of form **A** are about four times as high as those of enantiomer **B**, which fact has stimulated further studies of benzylamide **1** new conformers.

In order to obtain and then test pharmocologically any possible new conformers of the feasible analgesic benzylamide **1** its 4-*O*-Sodium salt was synthesized using two methods. X-Ray diffraction study made it possible to determine that depending on the chosen synthesis conditions the above-mentioned compound forms either monosolvate with methanol (**2**) or monohydrate (**3**), where organic anion exists in the form of three different conformers (**C-D** or **E**, respectively).

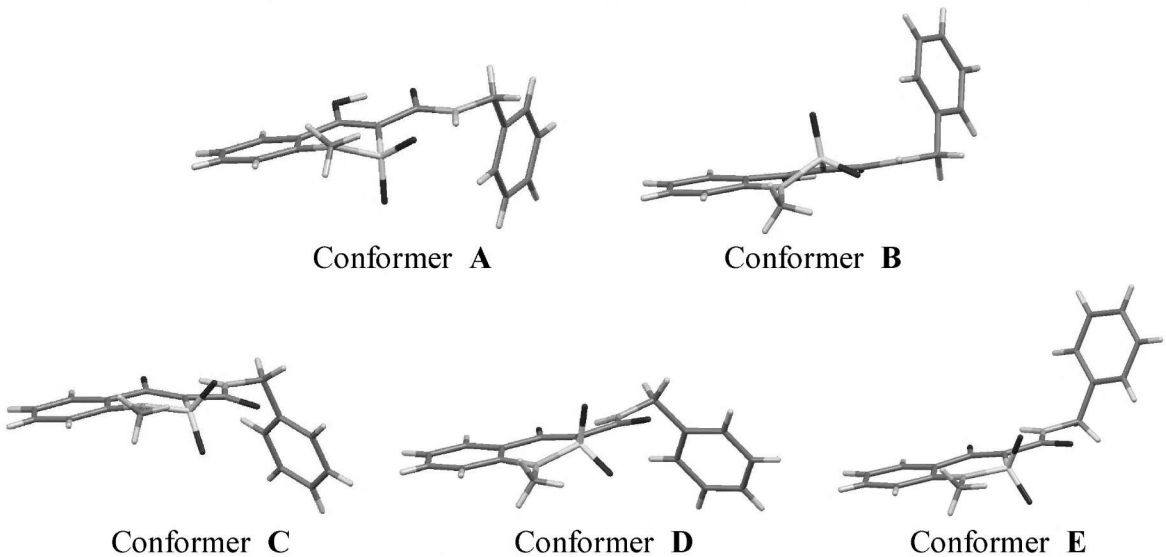

Figure. Highly (**A**) and low-active (**B**) conformers of benzylamide **1**; highly (**C**) and low-active (**D**) conformers of Sodium salt methanol solvate **2**; low-active conformer **E** of Sodium salt hydrate **3**.

Pharmacological testing of the two forms of the original *N*-benzylamide **1** and of the two solvates of its Sodium salt (**2** and **3**) was performed simultaneously under the same conditions and in equimolar doses. Comparison of the results obtained while studying the peculiarities of the conformers **A-E** spatial structure and biological properties revealed an important structure-action relationship. It was in particular shown that the intensity of analgesic effect of different conformers *N*-benzylamide **1** may change considerably: while low-active conformers are comparable with Piroxicam, highly active conformer is more than twice as effective as Meloxicam.