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ABSTRACTS

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Experimental Observation of Hidden Conformations of Strychnine by NMR Spectroscopy

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Besides its high toxicity, strychnine possesses a very interesting structure (Figure 1) consisting of several cyclic fragments. Strychnine was first isolated in the beginning of the XIX century. Determination of its chemical structure after the first discovery required more than a century. The molecular structure of this molecule was obtained based on X-ray diffraction, residual dipolar couplings (RDC) and other methods. It seemed that the question of its molecular structure is finally solved; the molecule was regarded as rigid, without any conformational flexibility. However, Schmidt and co-authors [1] showed that the strychnine molecule can have different conformers. They arise due to the flexibility of the ring F. Later this suggestion was proved by Butts et al. [2]. After that another centre of conformational mobility was discovered, attributed to the ring C [3]. Moreover, molecular dynamics simulations allowed suggesting that there is also the third conformer [4].

We were interested in the question of the presence of minor conformers in solutions. In the present work we report on the existence of hidden conformers of the strychnine molecule in a number of solvents, analyse the literature data on molecular simulations, and compare them with an experiment.

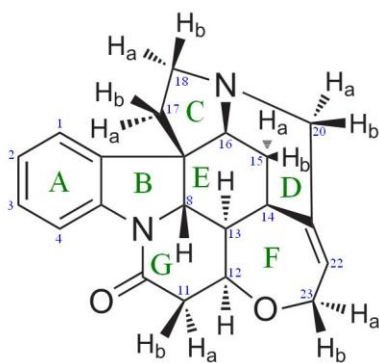


Figure 1. Molecular structure of strychnine

To solve this problem, we applied a complex NMR approach involving one- and two-dimensional methods (¹H, ¹³C, HSQC, NOESY). Nuclear Overhauser effect (NOE) spectroscopy [5, 6] was used to determine the conformer fractions. Thus, information on all hypothetical conformations of the strychnine molecule was obtained; structural peculiarities of the studied object were analysed experimentally, and distribution of the revealed conformations of the molecule in various organic solvents was found. Obtained information and additional calculations will help to shed light on the

mechanisms of formation of hidden strychnine conformers.

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