Conformational Analysis of AT_1 Antagonist Valsartan using 2D NMR Spectroscopy and Computational Analysis. Determination of Thermodynamic Parameters through Dynamic NMR Spectroscopy and Semi-empirical Calculations.

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Valsartan is an antihypertensive drug acting as an angiotensin II type I receptor blocker. Two distinct conformational diastereoisomers were observed at the ^{1}H NMR spectrum caused by the hindered rotation of its amide bond. The conformational properties of Valsartan were studied using a combination of 2D NMR spectroscopy and Computational Analysis. More spe-

cifically, intramolecular distances from 2D ROESY experiments were set as constraints for the calculation of the low energy conformers with the application of Computational Analysis. In order to estimate the Gibbs free energy of activation ($\Delta G^{\#}$) for the interconversion between the two conformations, it is necessary to know the rate constants of the equilibrium. These con-stant rates can be determined by dynamic NMR spectroscopy using 2D EXSY NMR experiments at different temperatures and various mixing times. Comparative theoretical studies are under progress using semi-empirical calculations.

VALSARTAN