„Conformation and chiroptical properties of cisoid enones"

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Within the dissertation I was studying chiroptical properties of compounds containing *cis*-enone chromophore in their structure. One of my goals was to verify the range of applicability of known helicity rules created for this group of compounds. Another objective was to explain the source of recognized exceptions to the rules. In the course of realisation of this dissertation I tried to determine how high is the confidence level of absolute configuration determination by helicity rules. Due to the known limitations, the question arose whether the determining of the absolute configuration using the existing rules of electronic circular dichroism (ECD) should be replaced by theoretical analysis which consists of a comparison of the experimental and theoretical curves.

To explain the above doubts, I made a detailed analysis of the cisoid enone derivatives involving different classes of compounds. Model compounds were examined both experimentally and theoretically by means of molecular mechanics and TD-DFT method. The research included a chromophore located both in five and six membered rings, isolated and substituted in the immediate vicinity of the enone. Based on the results obtained I tried to formulate a new, universal helicity rule working for all classes of compounds containing the *cis*-enone chromophore. However, extended circular dichroism study supported by theoretical methods did not lead to the development of the general rule applicable to all α,β-unsaturated ketones and an unequivocal explanation of the sources of existing exceptions. I was able to find correlation between the torsion angle "b" and a sign of the Cotton effect around 330 nm only for enones with keto group in five-membered ring. This correlation does not work however, for derivatives with keto chromophore located in six-membered ring. The results of these studies clearly show that the shape and character of diagnostic Cotton effects depend on both geometries outside of immediate surroundings of the chromophore and electronic effects.

Detailed studies for determining the relationship between the structure and the chiroptical properties of the *cis*-enones required having a wide variety of model compounds. Upon closer inspection of XIII IChO PAN team resources, I found it expedient to synthesize steroid derivatives with another six-membered ring fitted to the A ring of the steroid skeleton and substituted enones in α position both to the carbonyl group and the double bond. I also synthesized *cis*-enones with more flexible structure starting from abietic acid. In a few cases, I used ECD and VCD spectroscopy to determine the absolute configuration of obtained derivatives. By doing so I proved that two complementary techniques of circular dichroism spectroscopy are extremely useful tool in stereochemical analysis. Such approach is particularly important in situations where other commonly used methods, such as NMR and X-ray structural analysis, fail or when it is impossible to use them effectively.

In view of these results, it appears that application of the helicity rules to determine the absolute configuration of cisoid-enones will be probably stopped. These rules, of course, will support the stereochemical study but the main way of determining the absolute configuration by chiroptical methods will be a combined experimental-theoretical analysis. This is closely

connected with the continuous development of theoretical chemistry and allows for the most accurate calculation of the ECD spectra. An important conclusion of my thesis is that the theoretical support of the experiment is necessary to reliably assign stereochemistry. On the other hand, however, the need for a very careful approach to the calculation should be emphasized, with a particular focus on the conformational analysis. Otherwise, the theoretical analysis carried out unquestioningly can lead to incorrect results.