ABSTRACT

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Title of Thesis **Synthesis of carboxyxanthone derivatives as building blocks for enantiomeric pure compounds. Synthesis and structure elucidation of xanthone derivative (XD) 2-carboxy-6-methoxyxanthone (XD-2)**

The importance of xanthone derivatives is considerable. They possess large variety of biological and pharmacological activities. Many of them proved to be important building blocks for synthesis of new compounds.

Chirality is a fundamental property of biological systems and reflects the underlying asymmetry of matter. Almost one-third of all drug sales worldwide are chiral compounds and the authorities recommend that the chiral drugs should be saled in pure enantiomeric forms because enantiomers may differ both quantitatively and qualitatively in their biological activities. At one extreme, one enantiomer may be devoid of any biological activity; at the other extreme, both enantiomers may have qualitatively different biological activities. Enantiomers also differ in bioavailability – one enantiomer can be more bioavailable than the other, also the volume of distribution is different for *levo* and *dextro* enantiomer.

The synthesis of the xanthone derivative (XD) 2-carboxy-6-methoxyxanthone was a six-step reaction:

1. Synthesis of dimethyl 4-bromoisophthalate by Fisher esterification.
2. *N*,*N*-Dimethylglycine-promoted Ullmann condensation of dimethyl 4-bromoiso-phthalate with 3-methoxyphenol to get dimethyl 4-(3'-methoxyphenoxy) isophthalate.
3. Hydrolysis of dimethyl 4-(3'-methoxyphenoxy)isophthalate to obtain 4-(3'-methoxyphenoxy)isophthalic acid.
4. Synthesis of 2-carboxy-6-methoxyxanthone and 2-carboxy-8-methoxyxanthone by an intramolecular acylation.
5. Esterification of 2-carboxy-6-methoxyxanthone and 2-carboxy-8-methoxy-xanthone.
6. Hydrolysis of methyl 6-methoxyxanthone-2-carboxylate to obtain 2-carboxy-6-methoxyxanthone.

2-Carboxy-6-methoxyxanthone was used as a building block for synthesis of an enantiomerically pure compound, namely *N*-[(1*R*)-1-(hydroxymethyl)-2-methylpropyl]-6-methoxyxanthone-2-carboxamide by a coupling reaction with the amino alcohol D-valinol.

Almost all the synthesized compounds were structurally elucidated by different spectroscopic methods: ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) and by Infrared Spectroscopy (IR).