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Jaklová, Natalie
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N-alkylation of a lysergic acid derivative under PTC conditions in a continuous arrangement using sonication

Student: Mgr. Natalie Jaklová

Supervisor: Doc. Ing. Petr Klusoň, DSc.

Supervising Expert: Ing. Petr Stavárek, Ph.D.

This contribution focuses on the application of sonication to the synthesis of a methyl ester of the 1-methyl-10 α -methoxydihydrolysergic acid (MeLUME). The N-alkylation reaction takes place under phase transfer catalyzed conditions.^{1,2} The alkylation was performed in a continuous regime.³ This reaction in a batch reactor is included in the industry's production of the drug Nicergoline, prescribed to patients with Alzheimer's disease and dementia.⁴ The reaction proceeds in two immiscible phases, and to increase the space-time yield, the effect of sonication was examined. Sonication led to a more intensive renewal of the interfacial area and hence intensification of a mass transfer of reaction components through the interface. First experiments with sonication were in an apparatus with a FlowPlate microreactor (LONZA), where the sonication was applied to the outlet capillary, that represented as significant part of the reaction volume. The positive effect of sonication on the course of the reaction was observed. Therefore, the new reactor from static micromixers on a modular microreactor system was assembled. This reactor could be completely immersed into the sonication bath. However, the results achieved using this apparatus did not reach the values obtained from the previous measurements with the LONZA reactor. Based on the obtained knowledge, a new type of reactor consisting of a fluoropolymer (FEP) capillary was assembled. The results obtained after optimization of the reaction process in this reactor were comparable to those achieved in the LONZA reactor. The use of sonication for the N-alkylation reaction allowed for doubling of the amount of product synthesized while maintaining high conversion and selectivity.

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