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Synthesis of beta-propiolactone by *in situ* catalytic interaction of formaldehyde with ketene

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COVID-19 (coronavirus infection 2019) is a potentially severe acute respiratory infection caused by the SARS-CoV-2 coronavirus. The most effective method to combat COVID-19 is vaccination. Currently, a number of vaccines have been developed to prevent COVID-19, among which a special place is occupied by the inactivated vaccines, which are obtained by chemical inactivation of the virus. An important condition for the effectiveness of vaccines is the choice of the inactivator and optimal conditions for inactivation, which makes it possible to deprive the virus of infectivity while maintaining its immunogenic properties in a maximal degree.

In the practice of developing inactivated vaccines the most widely used are chemical inactivators applied in the production of licensed viral vaccines. The choice of inactivation method is based on the mechanism of action of the inactivator and the properties of the virus to be inactivated.

Beta-propiolactone is a promising inactivator of COVID-19 featuring the strongest biocidal effect. The effectiveness of beta-propiolactone is associated with the complete destruction of the virus RNA within a maximum of two days, while inactivation occurs under physiological conditions, i.e. without temperature rise. Currently, despite the high demand for beta-propiolactone, it is not produced in Russia. At the same time, the market value of 1 kg of beta-propiolactone costs about 100 thousand rubles. Pharmaceutical companies and research centers are forced to purchase imported reagents for research and development of vaccines. In this regard, the need to develop a domestic technology for the production of beta-propiolactone is of particular relevance.

We have developed a laboratory method to synthesize beta-propiolactone by catalytic interaction of formaldehyde with ketene generated *in situ*. $BF_3O(C_2H_5)_2$, $AlCl_3$, $ZnCl_2$ and their mixtures in various ratios were chosen as the catalyst. It was shown that the use of catalyst mixtures significantly increases the yield of beta-propiolactone compared to individual ones. The developed method makes it possible to obtain a product with a purity of up to 98%.

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