

Synthesis of ‘Nereid’, a new phenol-free detergent to replace Triton X-100 in virus inactivation

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October 19, 2020

Abstract

In the 1980-ies, virus inactivation steps were implemented into the manufacturing of biopharmaceuticals in response to earlier unforeseen virus transmissions. The most effective inactivation process for lipid-enveloped viruses is the treatment by a combination of detergents, often including Triton X-100 (TX-100). Based on recent environmental concerns, the use of TX-100 in Europe will be ultimately banned, which forces the pharmaceutical industry, among others, to switch to an environmentally friendly alternative detergent with fully equivalent virus inactivation performance as TX-100. In this work, a structure-activity relationship study was conducted that ultimately led to the synthesis of several new detergents. One of them, named ‘Nereid’, displays inactivation activity fully equivalent to TX-100. The synthesis of this replacement candidate has been optimized to allow for the production of several kg of detergent at lab scale, to enable the required feasibility and comparison virus inactivation studies needed to support a potential future transition. The 3-step, chromatography-free synthesis process described herein uses inexpensive starting materials, has a robust and simple work-up, and allows production in a standard organic laboratory to deliver batches of several hundred grams with >99% purity.

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