Redesign of a Grignard-Based Active Pharmaceutical Ingredient (API) Batch Synthesis to a Flow Process for the Preparation of Melitracen HCl

Redesign of a Grignard-Based Active Pharmaceutical Ingredient (API) Batch Synthesis to a Flow Process for the Preparation of Melitracen HCl

A Grignard-based batch process, for the preparation of Melitracen HCl, has been redesigned to fit a continuous reactor system. The Grignard addition is carried out at room temperature, with subsequent hydrolysis of the magnesium alkoxide intermediate followed by dehydration of the resulting alcohol. The product undergoes further workup by simple gravimetric phase separation and then crystallization with 2 M HCl in diethyl ether to afford pure Melitracen HCl. All steps in the laboratory setup were concatenated, and the setup was proven capable of producing a significant portion of the commercial quantities of Melitracen HCl. The flow setup profits from a reduced footprint, lower energy consumption, fewer synthetic steps, and reduced raw material usage compared to the batch process.

General information
Publication status: Published
Organisations: Department of Chemical and Biochemical Engineering, CHEC Research Centre, The Hempel Foundation Coatings Science and Technology Centre (CoaST), H. Lundbeck A/S
Corresponding author: Kiil, S.
Contributors: Pedersen, M. J., Skovby, T., Mealy, M. J., Dam-Johansen, K., Kiil, S.
Pages: 228–235
Publication date: 2018
Peer-reviewed: Yes

Publication information
Journal: Organic Process Research and Development
Volume: 22
Issue number: 2
ISSN (Print): 1083-6160
Ratings:
BFI (2018): BFI-level 1
Scopus rating (2018): CiteScore 3.27 SJR 1.243 SNIP 0.958
Web of Science (2018): Impact factor 3.327
Web of Science (2018): Indexed yes
Original language: English
Electronic versions:
Manuscript Reviewed.pdf. Embargo ended: 04/01/2019
DOIs:
10.1021/acs.oprd.7b00368
Source: Findit
Source ID: 2394862064
Research output: Contribution to journal › Journal article – Annual report year: 2018 › Research › peer-review