Applied DoE Techniques in Industrial Environment: Optimization of a Nitration Step.

Luca Allievi, Jens Wutke, Michael Zengaffinen, Melina Koerber

Valsynthese SA (Fabrikstrasse 48, 3900 Brig, Switzerland)

Luca.Allievi@valsynthese.ch

Statistical techniques have been used in industrial chemistry environment since the early 20th century[1]. However, it was not until the introduction of Design of Experiments (DoE) techniques by Box and Wilson in the 1960s, that the chemical industry began to implement these methods as standard procedures for chemical process development (CPD) and quality control. Going through a Valsynthese typical industrial case, we will highlight the efficiency of this powerful DoE tool.

Valsynthese CDMO's core expertise is the development of dangerous, high-risk and energy-intensive industrial processes (technologies such as: Phosgenation, Hydrogenation, Oxidation, *etc*…), with a special focus on nitration technology – an area in which the company has many years of experience[2]. Among these, a specific nitration step was recently analyzed (*vide infra*), which proved to be economically not competitive due to the high amount of aqueous waste generated per kilogram of product.
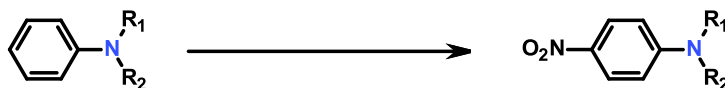
To overcome this drawback, a five-steps plan based on DoE techniques was developed and implemented:

1. Process analysis and first exploration, including the selection of the optimum nitrating agent.
2. DoE strategy set-up: objectives, factors/variables and responses definition, design selection.
3. Conducting experiments based on DoE plan.
4. Data analysis and best options selection.
5. Scale-up confirmation.

Our DoE-based laboratory development delivered, in a very short period, a more cost-effective and sustainable process. Scale-up batches are currently underway and validation of the process at industrial scale is foreseen for Q4 2025.

[1] S.A. Weissman, N.G. Anderson, *Org. Process Res. Dev.* **2015**, *19* (11), 1605–1633.
[2] For further information please see: https://www.valsynthese.ch/products/core-expertise