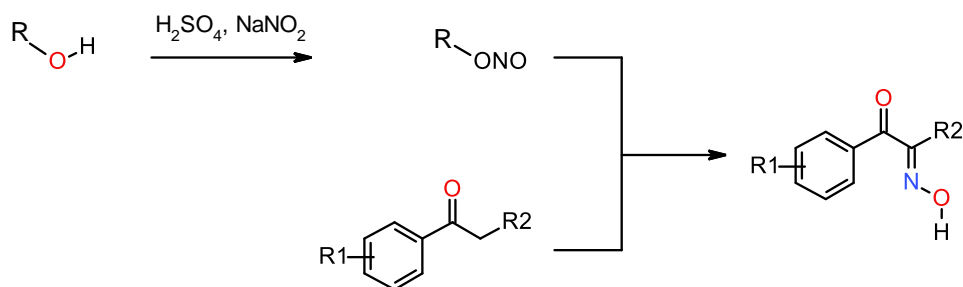


A PILOT PLANT VALIDATION EXPERIENCE AND THE DEVELOPMENT FOR AN ALTERNATIVE INDUSTRIAL SCALE-UP

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ABSTRACT



The α -oxidation of ketones using **alkyl nitrites** to the corresponding **1,2-ketoximes**, followed by a reduction, is a straightforward strategy to obtain **1,2-amino alcohols**; such compounds are building blocks for the preparation of different Active Pharmaceutical Ingredients (API).

The use of alkyl nitrites on industrial scale, however, presents some issues related to both **safety** and **quality**.

Dipharma successfully **validated**, on **pilot plant** scale, a process that relies on such oxidation obtaining \approx 30 Kg of a 1,2-ketoxime intermediate. However, in planning a potential scale-up, we had to carefully consider how to handle such chemistry on an industrial scale. One possible solution identified is the implementation of a system for the **continuous** production of alkyl nitrites, and their immediate use in ketone nitrosation.

In collaboration with our sister company, **BIAZZI**, we proceed to study such possibility. We divided our work into two different phases: **discovery** and **development**. During the discovery phase, the reactions and the unit operations necessary for the selected transformations were screened and identified. After having identified the best conditions, we tested them on different substrates, proving the general applicability and reliability of the **continuous** set up. During the development, the attention was focused on a single substrate and the best technology for the scale up was selected. In this phase the parameters needed for the design of an industrial plant were also collected and the procedure for **start up**, **shut down** and **hold** were identified.