



AMT TN-02

Slurry Handling Within the Coflore® ACR - Case Study 1



Introduction

The Coflore® Agitated Cell Reactor (ACR) is a multipurpose flow reactor designed for laboratory and small scale manufacturing duties. By separating the flow channel into a series of discrete cells with independent dynamic mixers, it offers plug flow, low pressure drop and good mixing over a much wider range of operating conditions than PFRs or static mixers. It can also handle materials that would block a micro reactor and is capable of handling 3-phase solid-liquid-gas reactions.

Gorin, B, *et al.*, of Apotex Pharma have published work on the “Continuous Flow Process for Reductive Deoxygenation of ω -Chloro ketone in the Synthesis of Vilazodone” in the journal OPR&D (DOI: 10.1021/acs.oprd.8b00145). This work involves successful handling of a slurry solution within the Coflore® ACR.

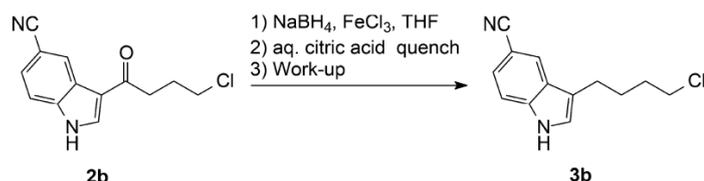


Figure 1: Reaction scheme for the reductive deoxygenation of compound 2b

Experimental Work

The publication describes a reductive deoxygenation of a vilazodone precursor, compound 2b, carried out in the Coflore® ACR (Figure 1). Compound 2b was introduced into ACR cell 1 as a 23.5% w/v slurry (20 g of Compound 2b suspended in 68 mL of THF, 85 mL total suspension volume), along with a solution of FeCl_3 . NaBH_4 in tetraglyme was added at ACR cell 2 at which point hydrogen gas evolution is observed. NaBH_4 in tetraglyme was further added at ACR cell 6 and the reaction mixture exited the ACR from cell 10 (Figure 2).

Conclusion

The authors stated that “the benefit of a continuous flow process to the synthesis of [a vilazodone precursor] intermediate is unmistakable. The limitations of controlling the exotherm in a batch reaction are now successfully overcome by conducting the reaction in a continuous flow CSTR setting that is also able to handle heterogeneous mixtures”. The authors also noted that the continuous flow process reduced the generation of a key dimeric impurity, and improved the yield of the desired product.

This publication gives a clear example of the Coflore® ACR’s ability to handle solid suspensions in flow. In this example, a 23.5% w/v slurry was successfully pumped through the ACR cell block. Successful handling of hydrogen gas evolution within the system was also achieved, showing that the Coflore® ACR can handle a 3-phase, solid-liquid-gas reactive system.

Acknowledgments

AM Technology thank the authors of this publication for their work. The full publication is linked to on the [AMT website here](#).

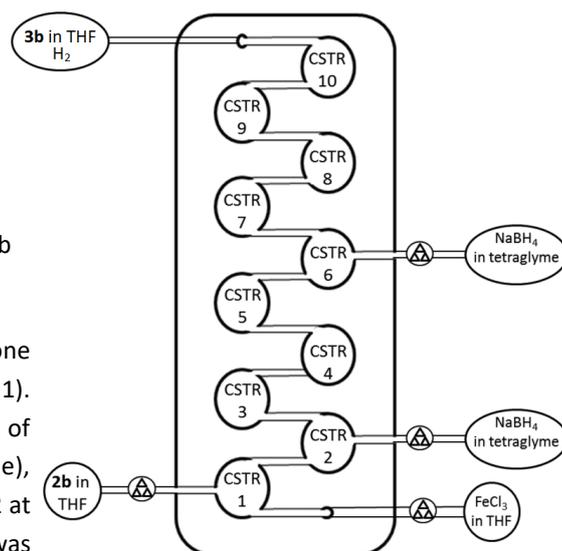


Figure 2 : ACR Cell Block Layout with Reagent Injection Sites Shown