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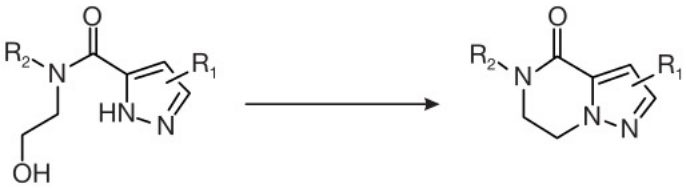
Phoenix Flow Reactor: Your Solution To Dead End Chemistry. Application #1.

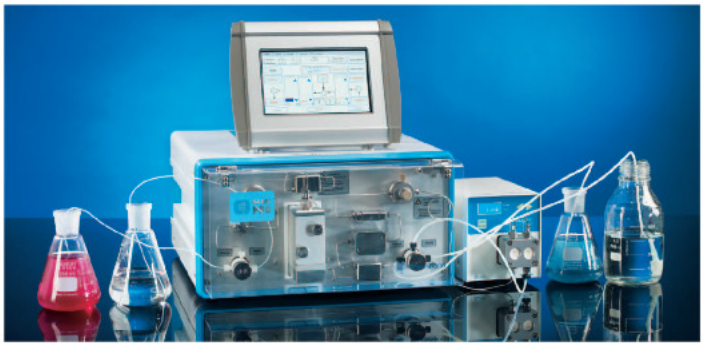
INTRODUCTION

Today's chemistry reaction space is severely restricted by conventional laboratory equipment. Chemists do not have too many options when it comes to temperature and pressure accessibility. Chemists are under pressure to synthesize new compounds, develop new processes, increase yields on existing processes, and decrease time to market at the same time. However, working in a conventional chemical space with the same equipment does not facilitate this. ThalesNano's Phoenix Flow Reactor is designed to overcome this problem by offering chemists a versatile solution that can extend their chemistry capability significantly. The continuous-flow reactor can fit either a fix bed reactor for heterogeneous catalyst/reagent chemistry or a coil for homogeneous reactions up to 450 °C and 100 bar safely. The aim of this application note is to show an example of where utilizing the Phoenix Flow Reactor has led to a successful reaction after a failure using batch methods.

MITSUNOBU TYPE SYNTHESIS

The below reaction was performed first in batch using T3P, as a green alternative of the Mitsunobu synthesis. The reaction failed using either the general conditions of the Mitsunobu or traditional batch heating, so we tried to perform the reaction in the Phoenix Flow Reactor to see if we could obtain a successful reaction with flow.





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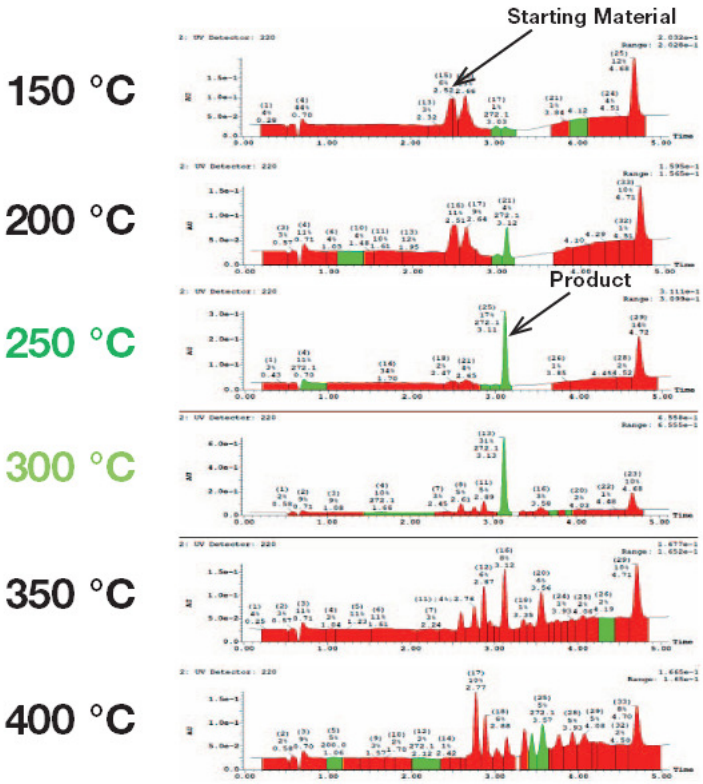
RESULTS AND DISCUSSION

During the optimization process we found the optimum temperature was 300 °C. Below 300 °C, the reaction only yielded starting material, while above 300 °C the compound decomposed. Reaction optimization took less than 3 hours and it resulted in the desired product WITH 65% yield.



EXPERIMENTAL PROTOCOL

0.01 M of starting material was dissolved in THF in the presence of T3P (14 equ., 50% in THF). The pressure of the reaction (80 bar), the liquid flow rate (1 mL/min) and the temperature (300 °C) of the 8 mL loop were set on the H-Cube Pro user interface. After pushing the Start button on the touch screen, the system automatically started the pumping of pure solvent while the pressure and temperature parameters reached steady state.

Then the reagent mixture was pumped into the Phoenix Flow Reactor and product was collected at the outlet of the H-Cube Pro. The product was purified by evaporation, followed by column chromatography. After grinding and filtration, the final product was isolated in 65% yield.

SUMMARY

We have presented an easy and practical way of performing a Mitsunobu type reaction which was not possible using standard conditions in batch. The reaction mixture was easy to workup and the desired product was formed with a 65% yield. In addition to the rapid optimization and excellent result of the reaction, the described also showed other advantages.

Waste prevention: Using a low boiling point solvent (THF) at high temperatures, the removal process of the solvent from the reaction mixture is much easier compared to high boiling point solvents and speeds up the isolation of the final product.

Less hazardous chemical syntheses and designing safer chemicals, solvents and auxiliaries: The presented synthesis uses T3P instead of DEAD, which is quite dangerous and explodes upon heating. Also the synthesis requires the presence of only 1 additive.

ThalesNano Nanotechnology Inc.
Zahony u. 7.
H-1031 Budapest
Hungary
Tel.: +36 1 880 8500
Fax: +36 1 880 8501
E-mail: sales@thalesnano.com

US Office ThalesNano
50 S. Penn St. Suite B-2
Hatboro
PA. 19040
USA
Phone: +1 732 274 3388
E-mail: USAsales@thalesnano.com

www.thalesnano.com