

CORNING

Advanced-Flow™ Reactors



Accelerating Reactions Working Under Pressure

Application Note #4

Issued: February 2018

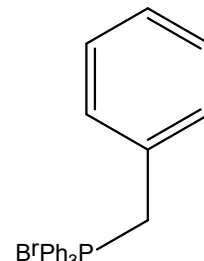
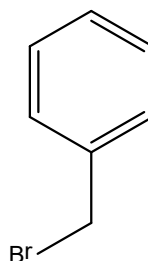
Setup: Corning® Lab Reactor with one module

Model Reaction: Formation of Wittig salt

Adapted to flow from J. Med. Chem. 2012, 55, 5760-5773

PPh_3

+



Analytics: Conversion by $^1\text{H-NMR}$

Safety:

Make sure you have read the MSDS of the chemicals and the safety notes in the Lab Reactor Manual.

Feed Preparation:

- Feed 1: 1.71g (0.1 mol) of benzyl bromide (CAS 100-39-0) are dissolved in 100 ml Ethanol.
- Feed 2: 2.62g (0.1 mol) Triphenylphosphine (CAS 603-35-0) are dissolved in 100 ml Ethanol.

Flow experiment:

The solutions are pumped with similar flow rates (e.g. 1 ml/min per pump) through the module. The flow rates and temperature can be varied in order to optimize conversion.

Hint: Increase the pressure of back pressure regulator when bubbles are observed in the module.

Cleaning: Replace both feed solutions with Ethanol and pump @ 1 ml/min for at least 20 min.

Results:

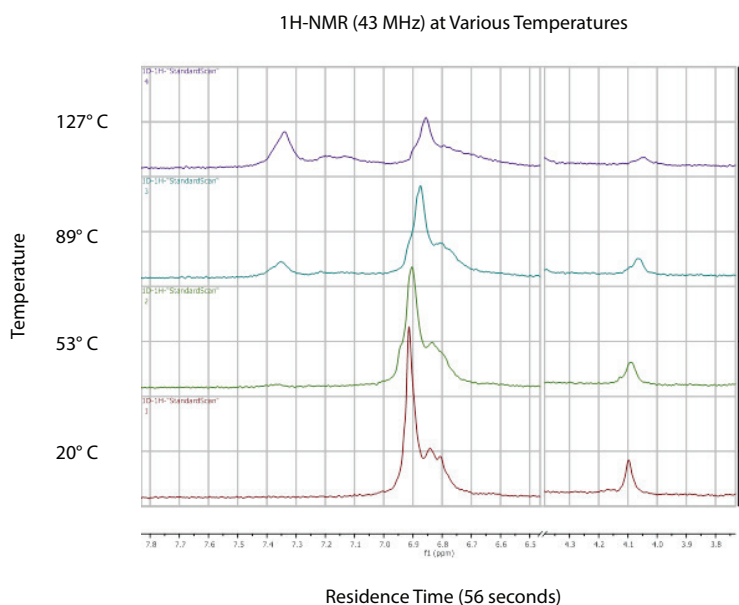
Depending on your flow rates and temperature more or less conversion will be observed.

$^1\text{H-NMR}$ (43 MHz) at various temperature

Best results are obtained @ 125 °C and 168 s residence time,

Conclusion:

In flow chemistry you are not limited to the boiling point. The system is closed, so pressures up to 18 bar are standard. This allows you to speed up your reaction by going at higher temperature than usual. But be aware that higher temperatures can also favor side reactions.



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Tips & Tricks

Safety: Solvents above boiling point under pressure will partially evaporate after the backpressure regulator, this can lead to clogging. Ideally the solution should be below boiling point @ atmospheric pressure before flowing through the backpressure regulator.

Calculated boiling points in °C for selected pure solvents:

Note: Solvent mixtures can have higher or lower boiling points.

Solvent	1 bar (°C)	16 bar (°C)	Solvent	1 bar (°C)	16 bar (°C)
Acetone	56	167	Dichloromethane	40	149
Ethanol	78	171	Diethyl ether	35	144
Methanol	65	156	Pentane	36	150
Isopropanol	83	176	Heptane	98	230
Water	100	201	THF	66	185
Toluene	110	247	Tetralin	207	375

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To learn more visit: corning.com/reactors
reactors@corning.com | reactor.asia@corning.com