

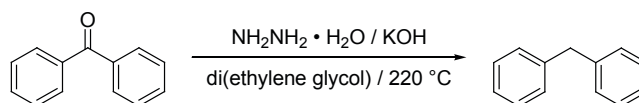
Microwave Reactions Generating a Gaseous Byproduct

Introduction

The ability to perform high temperature and pressure, sealed vessel reactions in a safe and efficient manner has long been an advantage of microwave reactors over conventional means. Because reactor design is often based on this application, the pressure monitoring devices that seal the reaction vessel do not have the ability to remove undesired gaseous products that can stall a reaction. This is **not** the case with the ActiVent pressure device, found on the CEM Discover SP

Procedure

The Wolff-Kishner reduction (Scheme 1) offers a mild method to deoxygenate carbonyl compounds to the corresponding alkane, as opposed to harsh methods requiring the use of dangerous metal reagents (Clemmensen reduction, etc). By proceeding through the hydrazone, the compound is reduced through a loss of N₂ to generate the desired alkane. Conventionally, this reaction must be performed in an open vessel as nitrogen build up in a closed vessel will stall the reaction and lead to low yields.



Scheme 1. One-pot Wolff-Kishner reduction of benzophenone

Since this reaction will generate a gas and uses a relatively high boiling solution (~150 °C), it is recommended to set the vessel release limits to 60 °C and 60 psi¹. Using a 35-mL microwave reaction vessel with rare earth stir bar², benzophenone (1.0 equiv; [0.75 M]), 50-60% hydrazine hydrate solution (3.0 equiv), and potassium hydroxide (2.0 equiv) were immersed in di(ethylene glycol)³. Because the benzophenone does not dissolve until the solution is warmed, a two stage method was used to first pre-heat the solution and begin hydrazone conversion, then heat the solution to reduction temperatures (Figure 1).

Method Name: Wolff-Kishner							
Delta Pressure:		25					
Properties							
Stage	Temp	Ramp Time	Hold Time	Pressure	Power	Overfl.	Stirring
1	80	20:00	01:00	300	300	Off	High
2	225	20:00	05:00	300	300	Off	High

Figure 1. Method parameters for two stage Wolff-Kishner reduction

After programming the pressure venting method (Pressure Stage 1: Delta Pressure = 25, PressureSP = 150, Times At SP = 100), the reaction vessel was capped and placed in the microwave attenuator. The reaction was started and heated according to the previously programmed method. Around 2:20 total time (mm:ss; 150 °C) the reaction began generating some pressure due to reflux, while within 30-40 seconds (~175 °C) a more rapid pressure increase resulting from nitrogen evolution was noted (Figure 2).

The ActiVent pressure device relieved the internal vessel pressure four times, venting only gas (25-50 psi per vent) while maintaining reaction volume despite maintaining a temperature above reflux for the solution. Additionally, after each vent the reaction vessel resealed and maintained pressure as if the cap had never opened. After six minutes total reaction time, rapid pressure evolution is seen to cease and a constant pressure is maintained until the reaction end. Following cooling, the reaction solution was diluted with diethyl ether and washed with saturated NH₄Cl, water, and brine, before drying the organic layer over MgSO₄. Following concentration in vacuo, the benzylbenzene product was furnished as a

colorless oil in a 96% yield.

Using the ActiVent pressure management system, microwave reactions that would otherwise stall due to over-pressurization or exceeding instrument limits can be performed with ease. The result is cleaner, faster chemistry that can take advantage of microwave heating.

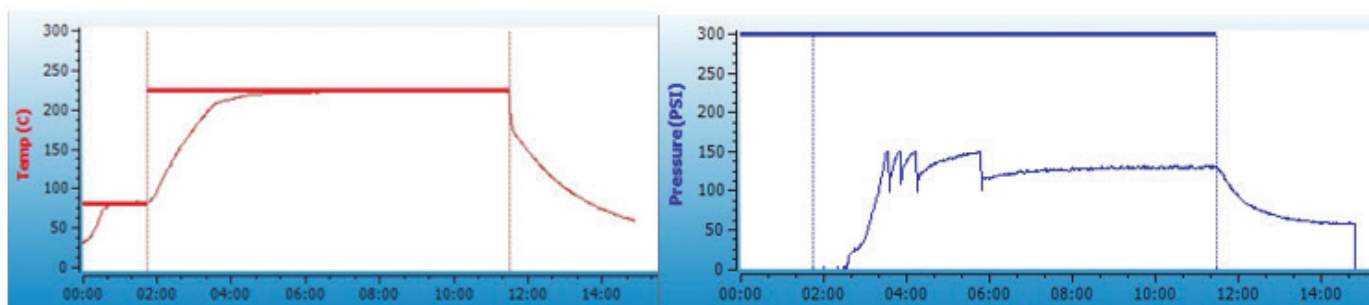


Figure 2. Temperature (left) and pressure (right) profiles of the Wolff-Kishner reduction

¹Since reactions that generate a gas in situ often have residual pressure after reaction completion, users have two options for pressure device release. One can either set higher pressure release limits, or manually release the pressure device by pressing the “stop” button after the reaction has sufficiently cooled below reflux.

²It is important to have a large, strong stir bar as the di(ethylene glycol) solution is highly viscous.

³The total reaction volume was approximately 15 mL.



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