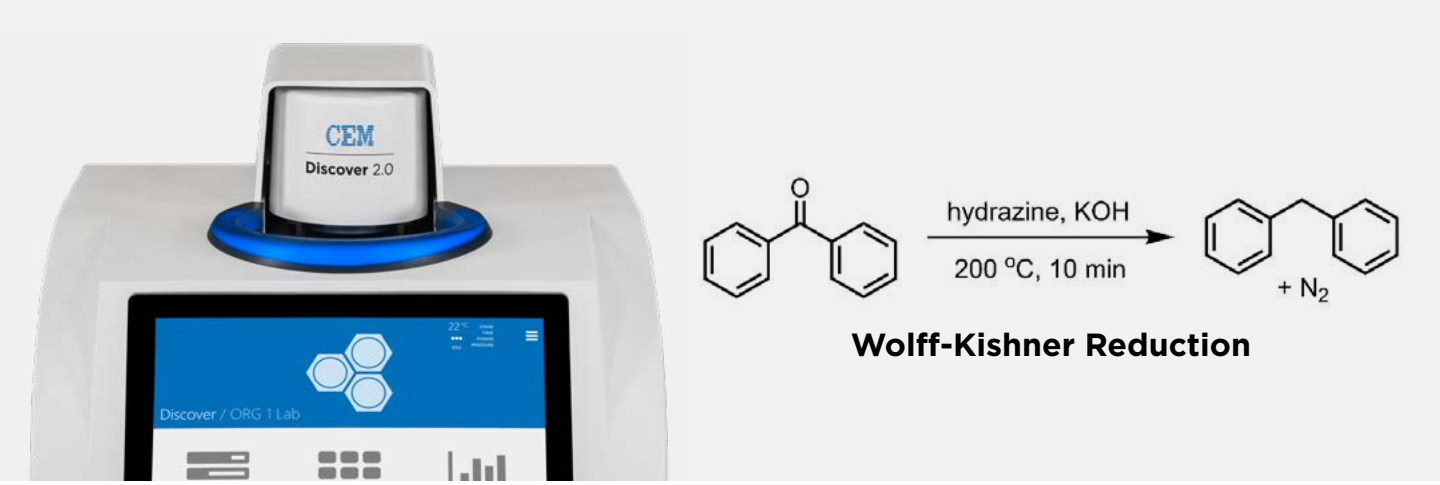
Microwave Reactions Generating a Gaseous Byproduct

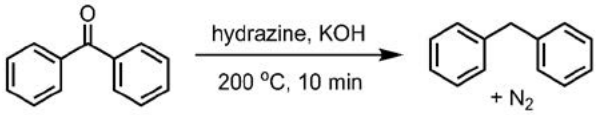


Introduction

The ability to perform high-temperature, high-pressure reactions in a safe and efficient manner is one of the greatest advantages offered by microwave reactors over conventional synthetic approaches. However, because reactor designs are largely based on this application alone, many laboratory microwaves lack the flexibility to release undesired pressure increases mid-reaction, and then continue the experiment uninterrupted. Any gaseous byproduct generated during the experiment must remain in the reaction vessel until experiment completion, which lessens reaction efficiency and increases chance for vessel failure. The Discover® 2.0, however, circumvents this limitation with its Activent pressure device, enabling seamless and customizable pressure release(s) throughout an experiment's duration.

To demonstrate the ability of the Discover 2.0 to release undesired gaseous byproducts, the Wolff-Kishner reduction was investigated. The Wolff-Kishner reduction of benzophenone (**Scheme 1**), a milder alternative to other methods of carbonyl reduction, deoxygenates ketones and aldehydes to their corresponding alkanes. By proceeding through the hydrazone (generated via condensation between hydrazine and the carbonyl compound), the compound is reduced through a loss of N_2 gas upon interaction with base.

Scheme 1. Wolff-Kishner reduction of benzophenone.



Conventionally, the Wolff-Kishner reduction must be performed in an open vessel to prevent nitrogen pressure build-up, which can decrease reaction efficiency and pose vessel failure risk. The Activent pressure device of the Discover 2.0, however, enables its safe and efficient performance under pressurized conditions.

Materials and Methods

Reagents

Benzophenone, diethylene glycol, 50–60% hydrazine hydrate solution, and potassium hydroxide were obtained from Sigma Aldrich (St. Louis, MO).

Procedure

Reaction Setup

A 35-mL vessel, equipped with a rare-earth stir bar, was charged with benzophenone (2.00 g, 11.0 mmol, 1.00 equiv.), 50–60% hydrazine hydrate solution (2.00 mL, 33.0 mmol, 3.0 equiv.), potassium hydroxide (1.23 g, 22.0 mmol, 2.0 equiv.), and di(ethylene glycol) (13.0 mL). (It is important to have a large, strong stir bar as di(ethylene glycol) is highly viscous.) Then, the vessel was sealed with a Teflon-lined silicon cap and placed in the Discover 2.0 microwave cavity, ready for microwave irradiation.

Method Programming

A two-step Ramp to Temperature method (**Figure 1**) was programmed for the Wolff-Kishner reduction of benzophenone. During the first step, the reaction mixture was heated to 80 °C over a 2-minute period and held for 2 minutes (to assist

with benzophenone dissolution and begin hydrazone conversion). Then, the reaction mixture was heated to 200 °C over a 5-minute period and held for 10 minutes. The Activent pressure venting parameters (**Figure 2**) were set to: Pressure SP = 175, Times at SP = 100, and Delta Pressure = 25, and ensured that any pressure generated above 175 psi was released.

Figure 1. Ramp to Temperature microwave method details for the Wolff-Kishner reduction of benzophenone.

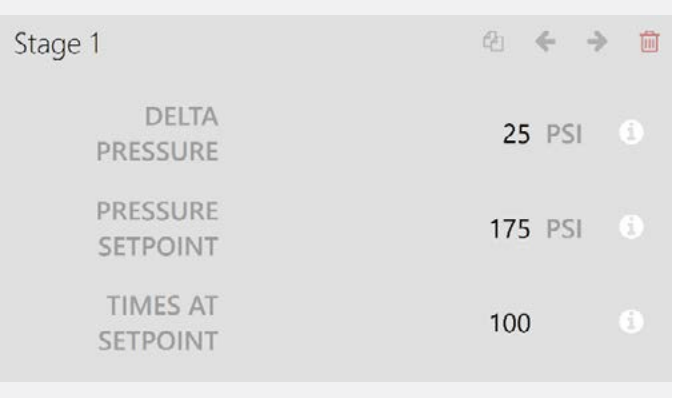


Figure 2. Pressure venting programming details for the Wolff-Kishner Reduction of benzophenone.

Note: Because this reaction generates a gaseous byproduct and uses a moderately high-boiling solution, it is recommended to set the vessel release limits to 60 °C and 60 psi. To do this, navigate to: Settings/Discover 2.0/Release Limit Settings, and change the release limits. Alternatively, the vessel can be manually released by pressing the "Stop" button once the vessel contents have sufficiently cooled.

Reaction Work Up

Upon cooling, the reaction solution was diluted with diethyl ether (50 mL), and washed sequentially with sat. aq. NH_4Cl (50 mL), water (50 mL), and sat. aq. NaCl (50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated.

Results and Discussion

During the first heating stage, the target temperature (80 °C) was reached within 2 minutes and then maintained for 2 minutes, allowing full dissolution of benzophenone. Then the solution was heated to 200 °C, reaching the target temperature within 5 minutes, and held at 200 °C for 10 minutes. While heating to 200 °C, increased internal vessel pressure is observed, signifying the generation of N_2 byproduct. The pressure was relieved by the Activent pressure device eight times, removing N_2 byproduct (25–40 psi) with each vent. After the eighth Activent pressure release, N_2 generation slowed and a constant internal vessel pressure was maintained until completion of heating (**Figure 3**). Upon vessel cooling and reaction work up, benzylbenzene was isolated as a colorless oil in 96% yield (1.78g, 10.6 mmol).

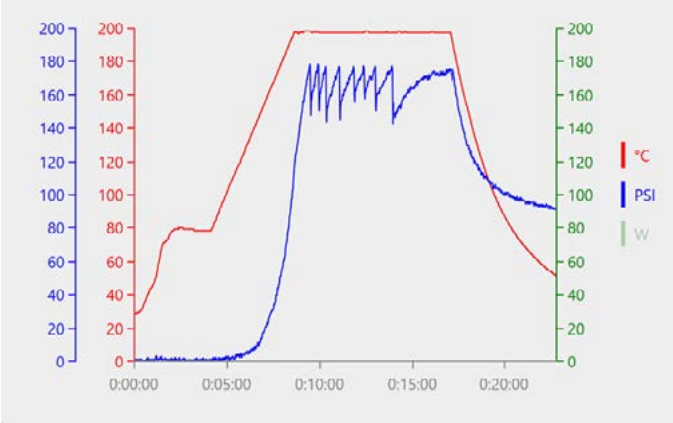


Figure 3. Discover 2.0 temperature and pressure profiles for the Wolff-Kishner reduction of benzophenone.

Conclusion

The Wolff-Kishner reduction of benzophenone was completed in the Discover 2.0 in under 20 minutes, yielding benzylbenzene in 96% yield. Though gaseous N_2 byproduct was generated, the Activent pressure device was able to relieve the internal vessel pressure repeatedly, resealing the reaction vessel as though the cap had never opened after each release.

The Discover 2.0 is capable of performing closed-vessel, gas-generating experiments safely and with ease, due to the Activent pressure device's vent-and-reseal technology. The Activent pressure device circumvents issues typically encountered with gas-generating reactions performed in closed vessels, such as decreased reaction efficiency and increased chance of vessel failure. The result is safer, cleaner, and faster chemistry with the advantages of microwave heating.

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