

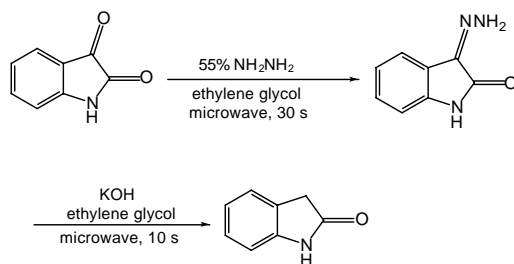
Microwave-Assisted Wolff–Kishner Reduction Reaction

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Wolff–Kishner reduction is described in most introductory organic textbooks. However, the reaction is rarely included in undergraduate organic laboratory textbooks. Wolff–Kishner reduction of carbonyl groups is usually conducted with hydrazine hydrate in the presence of a strong base at elevated temperatures (about 200 °C) for hours. Soriano reported a simple Wolff–Kishner reduction of isatin under mild condition (1). However, this method still required a 3- to 4-h laboratory period and the base, sodium ethoxide, had to be freshly prepared—which presents a potential danger for inexperienced chemists. Our undergraduate organic laboratory is scheduled for 2 h and 50 min, which includes 10 min of lab quiz and about 30 min of lab lecture. Therefore, the traditional Wolff–Kishner reaction cannot be carried out in our student laboratory or in most of the undergraduate organic laboratories in the U.S.A.

There have been reports (2–4) of significant decreases in reaction time for organic reactions carried out in household microwave ovens. However, Wolff–Kishner reduction reactions in microwave ovens have never been reported in the literature. The following reaction investigated in our laboratory gives the Wolff–Kishner reduction product of high purity in a very short period of time without a complicated workup. The two-step reaction is summarized by the following equation:



The two-step syntheses described here offer several advantages:

- Very short reaction time with no need for special microscale glassware.

- Mild experimental conditions. (Hot oil baths and heating mantles are not required.)
- Reagents easy to handle. (Students do not need to prepare sodium ethoxide from sodium metal and absolute ethanol.)

Procedure

The microwave oven used was a Panasonic model NN5505A (850 watt).

Isatin (0.25 g, 1.7 mmol), 55% hydrazine (0.30 g, 0.425 mmol) and ethylene glycol (1 mL) were added to a 50-mL beaker. The mixture was shaken gently to ensure proper mixing. The beaker was then covered with a watch glass and irradiated in the microwave oven at medium power for 30 s. After the beaker was removed from the oven and cooled to room temperature, the mixture was further cooled in an ice bath for 5 min. The yellow powders were collected in a suction flask, washed with cold ethanol (2 × 0.5 mL), and air dried. Yield: 0.223 g (81.5%); mp: 219–221 °C (lit. 219 °C); *R*_f: .36 (hexane:ethyl acetate 1:1).

A 50-mL beaker containing 0.5 mL of ethylene glycol and potassium hydroxide (62 mg, 1.1 mmol) was irradiated in the microwave oven for 10 s to dissolve the base. Isatin 3-hydrazone (58.5 mg, 0.36 mmol) was then added to the beaker and irradiated in the microwave oven for 10 s. The beaker was removed from the oven and cooled to room temperature. The brown solution was then diluted with 1 mL of deionized water, acidified with 6 M HCl until pH = 2, and extracted with diethyl ether (3 × 1.5 mL). The ether solution was dried with anhydrous sodium sulfate and evaporated in a hood to give a yellow solid. The solid was recrystallized from 0.7 mL of deionized water to yield 15.5 mg (32.4%) of oxindole as white needles, mp: 125–128 °C (lit. 125–127 °C).

Literature Cited

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