Research Article

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A safe-at-home benzoin condensation from imitation almond extract

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Abstract: COVID-19 remote learning forced instructors to scramble for meaningful organic laboratory experiences safe enough to perform at home. While resources are available for laboratory experiments at home, organic synthesis suffers from issues involving safety, availabilities of reagents, difficulties measuring reagents, and difficulties analyzing products. We report a new take on the classic benzoin condensation using safe and commonly available reagents, capable of being setup with commonly available kitchen materials, and displaying visible and distinctive product. This experiment is aimed at reinforcing concepts of carbonyl chemistry in the undergraduate organic chemistry laboratory.

Keywords: at-home lab experiments; carbonyl chemistry; green chemistry; microwave-assisted organic synthesis; undergraduate organic chemistry

1 Introduction

We often take for granted basic laboratory equipment until it is no longer available. In COVID-19 quarantines, techniques as simple as measuring the mass of reagents became impossible for most students. The current literature has several undergraduate organic chemistry laboratory techniques safely performed at home (for example Easdon, 2020; Kelly, 2021; Orzolek & Kozlowski, 2021; Pitre et al., 2021), but has few actual syntheses, normally a cornerstone of organic curricula.

Our institution's decision to move online occurred late in the summer and our students are geographically dispersed, making delivery of materials directly to students impossible. Our supply options were limited to materials students had available at home or could readily find at a supermarket, and our measurement equipment was limited to those available in an American kitchen, which typically uses volumetric measurements and often does not include a scale.

The benzoin condensation, first reported in 1832 as a curious reaction catalyzed by the naturally occurring cyanide impurity within bitter almond oil (Wöhler & Liebig, 1832), is a biomimetic reaction, mimicking the "active aldehyde" chemistry promoted cellularly by thiamine pyrophosphate, vitamin B1. Appropriately, current literature often incorporates thiamine (Ault, 1983; Pavia et al., 2007) or thiazole containing analogues (Hanson, 1993; Stetter, 1976) in undergraduate laboratory experiments instead of cyanide, the latter reported as allowing a broader range of electrophiles including aliphatic aldehydes.

While thiazole has a pKa on the order of 2.5 (compared with hydrocyanic acid at 9.21), the use of strong bases to catalyze this reaction has persisted despite the competing Cannizzaro reaction (Hanson, 1993). This is surprising, as the reaction is thermodynamically controlled (Schowen et al., 1971) and, unlike the Cannizzaro reaction

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(Chenicek, 1939; Hunter, 1959; Richlin, 1945), has a rate independent of hydroxide or other base concentration (Wiberg, 1954).

We began rewriting our organic chemistry laboratory curriculum in 2018, with a focus on course content-relevant green chemistry drawing initially from Doxsee and Hutchison (2004) and the Guide to Green Chemistry Experiments for Undergraduate Organic Chemistry Laboratories generated collaboratively by Beyond Benign, My Green Labs, and MilliporeSigma (Beyond Benign and My Green Lab, 2018). While only a few of our experiments trace their roots back to these resources, both suggest a process of active learning at the center of many science education reform initiatives, including initiatives like the United States National Science Foundation-backed Course-based Undergraduate Research Experiences (CUREs; Bangera & Brownell, 2014) and the European Union-backed Student Active Learning in Science (SALiS; Kapanadze & Eilks, 2014). In our course structure, students exposed to the potential hazards of laboratory work are involved in the identification and reduction of those same hazards as a way to integrate the principles and practice of Green Chemistry (Anastas & Warner, 1998) into an organic chemistry course. Students are invited into that work in two ways – either as they perform the laboratory experiment alongside their peers or as independent research projects (Graham et al., 2014) focused on Green Chemistry objectives.

When students engage alongside peers, multiple routes to the same product (i.e. reactions catalyzed by hydroxide, triethylamine, or carbonate) or multiple reactants using the same conditions (i.e. benzaldehyde, furfural, or butyraldehyde) are suggested in the laboratory, and students choose among routes. This allows students to engage experiments as inquiry by comparing results and generating laboratory discussion in collaboration with peers (Bybee, 2000), and follows best practices of involving students in active research (Bangera & Brownell, 2014; Carpi et al., 2017; Wilson et al. 2012). Student engagement around independent projects involves taking ownership to improve a single experiment. In both cases, students actively shape the laboratory curriculum for the following year by inquiry driven adoptions of sustainable practice in science and technology for hands-on laboratory work (Eilks, 2015).

Prior to the COVID-19 pandemic, we had been performing benzoin-type condensations for a furfural to furoin condensation, which is reported to be less sensitive to oxidation of the aldehyde (Pavia et al., 2007) and less erratic (Doxsee & Hutchison, 2004). As part of our inquiry-driven laboratory practice, we had also experimented with milder base systems and found that sodium carbonate in a 95 % ethanol solution predictably produced the condensation product. When our institution moved online due to the COVID-19 pandemic, we adapted our initial successes with mild bases to a procedure using imitation almond extract, vitamin B1 tablets, and catalytic baking soda.

Even under these mild conditions, we found that benzoin crystals were predictably formed over the course of 1–2 weeks when a small amount of solvent evaporation took place, allowing for the direct observation of product formation in an at-home setting.

Although the precipitating circumstances of the global pandemic have subsided, we report here a further optimized procedure (reaction scheme Figure 1) aimed at an undergraduate chemistry laboratory that tightens the timeline of crystal formation, minimizes inclusion of bicarbonate within crystals, and increases yield.

Figure 1: The materials needed for the experiment are imitation almond extract, vitamin B1 tablets, baking soda, a small glass container, and something to grind the B1 tablets up with.

2 The reaction

Starting from an existing procedure with modified base (Doxsee & Hutchison, 2004) we estimated the number of tablets of Vitamin B1 and the volume of baking soda (as we are located in the U.S., we presumed most students would not have a scale). For scaling base and vitamin B1 concentrations, we assumed a benzaldehyde concentration of less than 1 %, which we were later able to verify by NMR comparison. Our initial procedure was to grind up three 100 mg Vitamin B1 tablets and combine with 1 tsp of baking soda and a 1 oz bottle of imitation almond extract. The reaction was inverted in a closed container (we initially used a clean, closed glass spice container) and left to sit for approximately 2 weeks. Thin, white, needle-like crystals began to form in a yellowing solution (Figure 2). The yellow color is the result of a small amount of oxidation from the benzoin product to benzil, confirmed by TLC. Replicating this result in laboratory glassware required us to allow for a small amount of evaporation by covering loosely with aluminum foil punctured with pencil-sized holes rather than stoppering. Benzoin crystals were confirmed by TLC, IR and melting point (127 °C–130 °C compared to pure commercial benzoin at 129 °C–134 °C) in a laboratory with the understanding that only the visible crystals would be available for students at home (Figure 3).

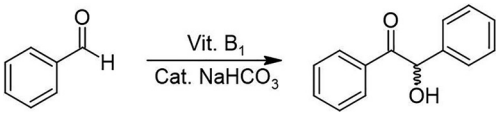

Figure 2: The classical benzoin condensation can be performed in mild conditions using vitamin B1 tablets and baking soda.

Figure 3: Fine, needle-like cystals readily form in the reaction solution. Small amounts of the yellow benzil oxidation product is visible in solution.

3 Minimizing background impurities from baking soda and vitamin B1 tablets

The initial conditions worked, but we hoped to limit the presence of insoluble binders in the vitamin B1 tablets and undissolved baking soda. We replicated the experiment with three 100 mg tablets of vitamin B1 and baking soda varied from a pinch to a tsp (Table 1). We found that using only a pinch of baking soda was sufficient to form observable crystals.

We validated the three 100 mg tablets with a pinch of baking soda conditions by running our experiment with five different sources of (imitation) almond extract – McCormick Imitation Almond Extract, Badia Imitation Almond Extract, Shanks Imitation Almond Extract, Aldi's Almond Extract, and a vodka extract of locally grown peach pits. We were able to replicate the reaction with McCormick Imitation Almond Extract, but were not able to complete the reaction with other sources of benzaldehyde. Analysis by NMR (Bonjour et al., 2017) showed lower concentrations of benzaldehyde in solution in the other sources of benzaldehyde.

With only a pinch of baking soda, the bulk of the undissolved material prior to crystallization is the binder from the vitamin B1 tablets. We checked to see if we could reduce the vitamin B1 catalyst mass as well, and found that while all B1-containing conditions resulted in the crystallization of benzoin, the greatest observable crystallization occurred when using two 100 mg tablets (Table 2).

4 Length and yield

Seeking to establish length to crystallization and crystal yield, we preceded to test three sets of triplicate experiments prepared on different days. We switched from individual 1 oz. (30 mL) containers of imitation almond extract to using bulk imitation almond extract from the manufacturer. The crystallization occurred within 7–20 days, with average appearance at 14 days and a standard deviation of 7 days. Crude yield from the preparations was 0.22 g with a standard deviation of 0.08 g. While the yield is promising from such a dilute stock of benzaldehyde, the duration of the experiment seemed impractical. Microwave-assisted organic synthesis has been increasingly used as an accessible way to speed up reactions, making them more accessible to students in a shorter time window (Linkwitz et al., 2022). Literature precedent suggested that microwave catalysis of

Table 1: Benzoin condensation proceeds with minimal catalytic base.

Volume of baking soda (tsp)	Mass of baking soda (g)	Observable crystals
1	5.355	Yes
½	3.050	Yes
¼	1.818	Yes
Pinch	–	Yes

Table 2: Benzoin condensation proceeds best with 200 mg of Vitamin B1 within a range of productive concentrations.

Number of 100 mg Vit. B1 tablets	Observable crystals
3	Yes
2	Most
1	Yes
Pinch	Yes
None	No

thiamine-catalyzed benzoin type condensations in propylene glycol were able to give a wide variety of benzoin-type products in good yields (Bag et al., 2006). We tested whether we could accelerate this reaction by microwave. While higher power levels were prone to boil over, microwaving at minimal power level 1 on a 700 W microwave avoided boiling over for at least 2 min. Microwaving in the range from 30 s to 2 min reduced the days to crystallization to two days or less. We chose 1 min at power level 1 on a700 W microwave, replicating this experiment three times to give crystals withing 3 days with crude yield of 0.27 ± 0.03 g.

5 Vitamin B1 source

We wanted to confirm this experiment could worked across both Vitamin B1 tablet sources we tried, but met some initial trouble switching from Nature Made Vitamin B1 tablets to Now Vitamin B1 tablets. We first noticed that Now B1 was bubbly upon adding the bicarbonate, indicating the greater presence of acid. When we were not able to replicate the experiment with Now B1, we tested the pH of two Nature Made controls after reaction (pH 8.8) and the Now B1 after the experiment (pH 8.15 and pH 8.61). We also tested the pH of previous experiments, and found that over time, the B1 had a much larger impact on the solution pH, dropping down to 5.62 for Now B1, while Nature Made remained close to 7 (7.04). This matches the ingredients lists: Nature Made B1 contains basic carboxylates only – as croscarmellose sodium and magnesium stearate; while Now B1 contained a larger portion of stearic acid and a smaller portion vitamin B1.

We tested Now B1 at various baking soda concentrations to see if we could push the reaction towards crystallization by raising the pH. We found that adding additional baking soda allowed us to achieve similarly quick crystallizations (Table 3).

6 Final procedure

Acquire the following supplies available at a well-stocked supermarket:
- one 1 oz (30 mL) bottle McCormick® Imitation Almond Extract,
- one bottle of 100 mg Vitamin B1 tablets,
- a pinch of baking soda.

Crush 2 × 100 mg Vitamin B1 tablets and carefully combine with a 1 oz (30 mL) container of imitation almond extract or genuine almond extract in a microwave-safe container. It may be convenient to create a funnel out of a small piece of paper or a sticky note (Figure 4).

Examine the ingredients list on your B1 source. If all the binders indicate salts (i.e. croscarmellose sodium, magnesium stearate), add one pinch of baking soda. If some of the binders indicate acid (i.e. stearic acid), add 3 pinches of baking soda.

Invert (closed) or stir thoroughly to mix. Microwave at power level 1 for 60 s. Power was set on a 700 W microwave – adjust power level and time to microwave power proportionally. Monitor closely to prevent boil-overs.

Table 3: Additional baking soda can account for Vitamin B1 reagent differences.

Amount of baking soda (pinches)	Days to crystallization
2	3
3	2
4	2

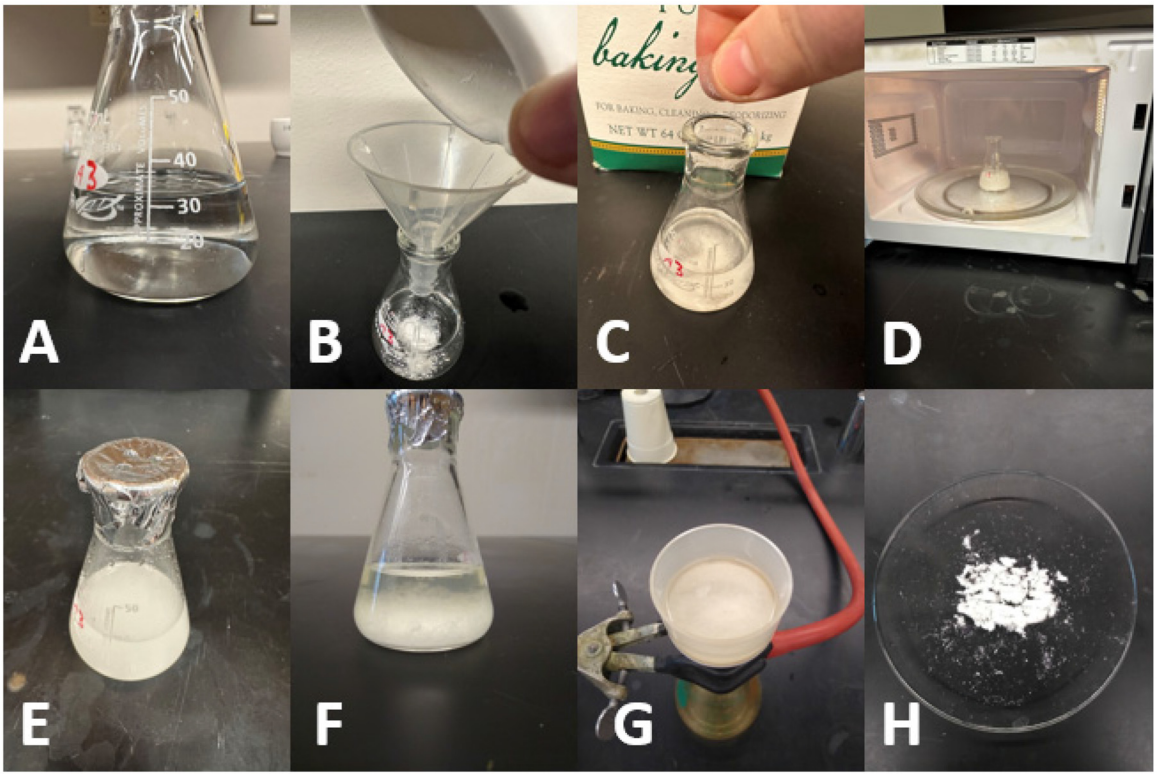

Figure 4: The steps for the final procedure. A. Measure out 30 mL (1 oz) of McCormick Imitation Almond Extract. B. Add 2 crushed up 100 mg vitamin B1 tablets. C. Add a pinch of baking soda and gently shake to mix. D. Microwave at power level 1 for 60 s (700 W microwave). E. Cover with aluminum foil with holes poked in it and gently shake to mix. F. Wait 2–3 days for crystals to appear. G. Pour into filter to separate crystals from solution. H. Retrieve crystals and let them dry.

After microwaving, cover with aluminum foil or other loose cover and poke thrice with a pencil or pen to create ~1/4 inch diameter holes to facilitate evaporation. Leave container aside for 2–3 days for solid to crystallize. A yellow tint at surface of crystals represents a small amount of oxidation from benzoin to benzil. Crystals may be recovered by filtering through coffee paper at home or via vacuum filtration with a Büchner funnel in the lab.

7 Laboratory adaptation for other aldehyde sources

The procedure given above can be modified to illustrate the same green chemistry principles with a wide variety of laboratory aldehydes, including naturally sourced furfural (Adams & Voorhees, 1921) with the following procedure we use in our own lab. It is our practice to have several students run experiments using a successful protocol from the prior year, while others alter either reactant or conditions.

Grind up 1 NatureMade® 100 mg Vitamin B1 tablet (0.3 mmol) and combine with 0.75 mL (0.87 g, 9 mmol) of furfural (or the same amount (in moles) of another aldehyde) in 2 mL of 95 % ethanol in a 10 mL Erlenmeyer flask. Add 0.5 mL of saturated sodium bicarbonate. Microwave in a 700 W countertop microwave for 1 min at power level 1. Remove and cover the reaction with aluminum foil. Carefully record observations. Let the reaction run in the hood until next week. In the next lab period, cool the mixture in an ice-water bath, collect the product on a filter with a Hirsch funnel, and wash it first with 3 separate 1-mL portions of ice-cold ethanol.

Obtain a crude yield and a melting point tube of the crude. Recrystallize the crude product from 95 % ethanol. Report final yield (mass and percent yield) and melting point range of final product. Obtain an IR spectra and record the significant peaks intensities and locations in your notebook.

8 Conclusions

The traditional benzoin condensation is an accessible experiment with safe, inexpensive, and readily available materials. Because only the benzaldehyde is stoichiometric, limitations with home measuring equipment are avoided. Common sense substitutions of base and catalyst were optimized, and adaptions to readily available home equipment led to an experiment that could be performed quickly, with visible product in less than 3 days.

While the experiment as written can be performed to demonstrate carbonyl and umpolung chemistry covered in organic chemistry courses, the simplicity of this experiment allows for application and extension anywhere from high school chemistry, general chemistry, or organic chemistry. High school and college general chemistry-level investigations could investigate alternative imitation almond extract sources and their benzaldehyde concentrations by NMR (Bonjour et al., 2017). Students could also evaluate solvent polarity effects on the precipitation equilibrium that drives the reaction through measured additions of table salt or rubbing alcohol.

The variability of readily available imitation almond extracts and vitamin B1 sources invites inquiry through side-by-side comparisons and discussions within specific geographic areas, which could vary from purely exploratory at lower levels, to investigations of pH in food and product science (see our discussion on stabilizers in B1 sources), or as we use it as a useful lens for mechanistic insights in an organic chemistry class.

While the initial premise for our research was to create a synthetic protocol safe and robust enough for at home engagement, the findings of this study can be generalized to make safer laboratory experiments. Moreover, the mild conditions and self-precipitating product suggest that these conditions might be appropriate for a wider range of benzoin condensation products than the existing laboratory experiments. Accordingly, we have already begun expanding the scope of this protocol to use similar conditions with a wider range of laboratory-sourced aldehydes such as the anisaldehydes and short aliphatic aldehydes; and investigating the use of bicarbonate as a base in other laboratory experiments.

Attention to Green Chemistry principles in our traditional laboratory curriculum allowed us to think creatively in the crucible of the COVID-19 pandemic towards developing new laboratory experiments. The increasingly broad field of Green Chemistry literature serves as fertile ground for similar student-focused investigations towards at-home applications. Simultaneously, the milder conditions required for at-home syntheses may offer new opportunities for safer reagents, waste reduction, and reaction selectivity.

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