ABSTRACT/KEYWORDS:

# Green Chemistry in the Undergraduate Organic Laboratory: Microwave-Assisted Synthesis of a Natural Insecticide on Basic Montmorillonite K10 Clay

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## Abstract

A microwave-assisted, one-pot synthesis of a naturally occurring insecticide on basic Montmorillonite K10 is described. The reaction is suitable for incorporation into the undergraduate organic chemistry laboratory course and represents a practical example of green chemistry. The described synthesis employs naturally benign, base-washed Montmorillonite K10 clay as a heterogeneous catalyst, is carried out under solvent-free conditions in a commercial-grade microwave oven, and features several interesting mechanistic considerations, including an electrophilic aromatic addition, dehydration, and intramolecular hetero-Diels Alder cyclization.

*Keywords:* Organic chemistry; Synthesis; Green chemistry; Second-year undergraduate; Spectroscopy; Laboratory instruction**.**

LAB SUMMARY:

# Green Chemistry in the Undergraduate Organic Laboratory: Microwave-Assisted Synthesis of a Natural Insecticide on Basic Montmorillonite K10 Clay

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Green chemistry—the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances[1]—is a topic of emerging importance and one that is well suited for incorporation into the modern undergraduate organic laboratory curriculum. In recent years a number of reports concerning green chemistry and education have appeared in this *Journal*,[1-4] and growing numbers of relevant laboratory experiments appropriate for the undergraduate chemistry curriculum have emerged.[5-12] In the words of *Chemical & Engineering News's* Editor-in-chief, Rudy M. Baum, "green" has indeed gone "mainstream,"[13] and so it becomes increasingly relevant that young chemists be exposed to alternative, environmentally friendlier methods for carrying out reactions of traditional importance.

Application of naturally benign substances like Montmorillonite clays as catalysts for chemical reactions constitutes an exciting component of green chemistry.[14,15] The use of microwave irradiation to promote faster and cleaner chemical reactions is also an important component of green chemistry, especially when used in combination with clays

and other solvent-free conditions.[16-19] Here we report a simple, one-pot, solvent-free synthesis of methylenedioxyprecocene (MDP, **1**), a natural insecticide with anti-juvenile hormone activity in some insects.[20] The reported synthesis, a clay-catalyzed, microwave-assisted condensation of sesamol with 3-methyl-2-butenal (Figure 1), is appropriate for incorporation into the undergraduate organic laboratory curriculum and constitutes a unique example of green chemistry in action.

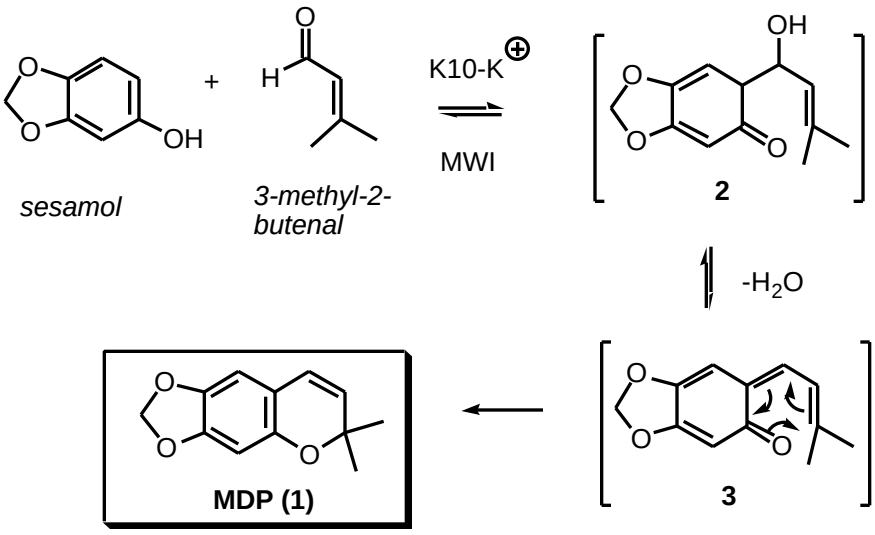


**Figure 1.** Synthesis of methylenedioxyprecocene (MDP, **1**)

## Discussion

In the most general sense, clays are a type of fine-grained earth, primarily composed of aluminum and silicate minerals.[15] Montmorillonite clays are thought to have formed from volcanic ash during the Jurassic and later periods, and were named for the location of their discovery, Montmorillon, France, in the 1800s. These clays are now

mined from regions all over the world, including Europe, Africa, Asia, South and North America, with U.S. mines in Florida, Georgia, Illinois and Texas. Montmorillonite clays have a wide variety of uses, including as catalysts for a broad range of chemical reactions.[14,15]

In addition to being environmentally benign and reducing the amount of waste that is generated from chemical laboratories, there are other incentives for using clays in the undergraduate laboratory curriculum. Clays are commercially available and very inexpensive (Montmorillonite K10 is available from Aldrich Chemical Co. for less than $0.03 per gram!), as well as extremely easy to use and safe to handle. Use of clays as catalysts allows them to be recycled, which further increases their economic efficiency. Furthermore, reactions that are catalyzed by clay are very easy to "work-up;" since the clay does not dissolve in the reaction medium (solvent) it must simply be filtered away when the reaction is complete. Alternatively, reactions can often be carried out on clay without any solvent at all, in which case products are isolated by extracting the clay with a suitable solvent when the reaction is complete.

The use of microwave irradiation (in ordinary household microwave ovens) as an energy source for speeding up chemical reactions is another important development in green chemistry. Reactions that proceed in a matter of hours or days when heated by conventional means have been shown to go to completion in several minutes when

exposed to microwaves.[16-19] Speeding up a chemical reaction to this extent is not only much more energy and time efficient, but often also results in cleaner processes—i.e. the development of unwanted byproducts that may form when a reaction is heated for extended periods of time are reduced or eliminated completely. The combination of conducting chemical reactions using clay catalysts and microwave irradiation promises to contribute even more substantially to the progress of green chemistry.

In its natural form, Montmorillonite K10 clay is Brønsted acidic, but it can be easily made basic by washing with a saturated aqueous basic solution (potassium carbonate for instance). The reported synthesis of MDP (**1**) is conducted under solvent-free conditions, on basic Montmorillonite K10 clay, in a commercial microwave oven. The synthesis of MDP (**1**), outlined in Figure 1, involves electrophilic addition of 3-methyl-2-butenal to sesamol to give intermediate **2**, followed by dehydration to give **3** and subsequent intramolecular hetero-Diels Alder cyclization. The product is isolated from the clay by extraction into methylene chloride, the resulting slurry filtered and the filtrate concentrated by simple distillation or evaporation. Both the recovered clay and the methylene chloride may be recycled. More traditional methods for synthesizing chromene compounds like MDP employ higher temperatures, longer reaction times, and/or less environmentally friendly bases like pyridine[21] or titanium tetraethoxide.[22]

## Conclusions

We recently reported a detailed investigation of the clay-catalyzed condensation of sesamol with 3-methyl-2-butenal to give MDP (**1**).[23] The experimental procedure for the synthesis of **1** outlined in this report is slightly modified for convenient execution in a typical undergraduate organic chemistry laboratory. This synthesis affords students a first-hand experience in the green synthesis of a physiologically active compound, using somewhat nontraditional technology: clay as a catalyst and microwave irradiation as an energy source.

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LAB DOCUMENTATION:

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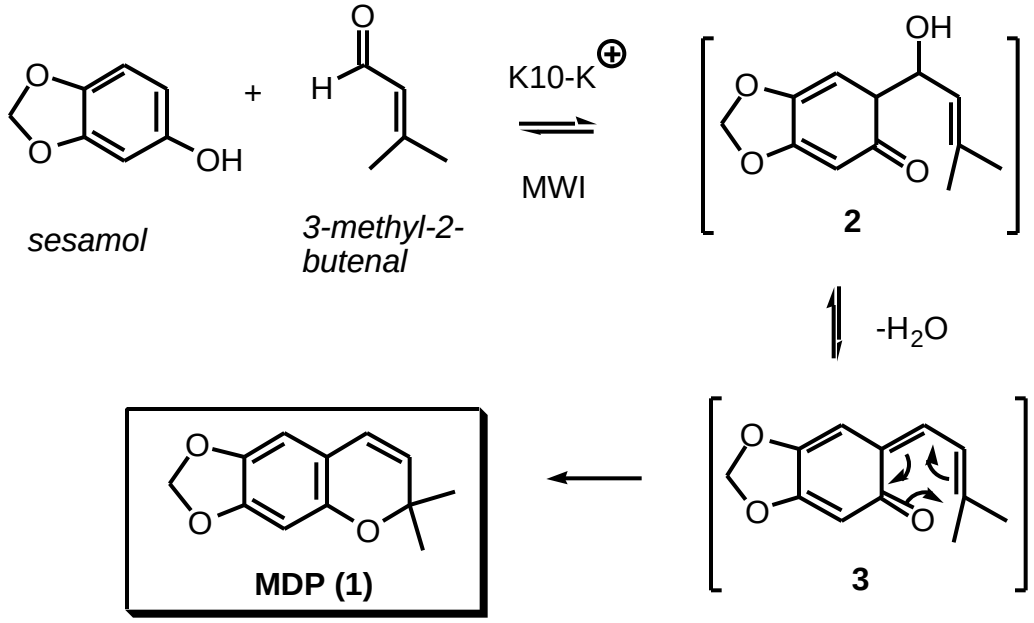
**Special Chemical Needs:** Montmorillonite K10 clay, saturated aqueous Potassium Carbonate, Acetone, Sesamol, 3-methyl-2-butenal, Methylene chloride, Methanol, Sodium Hydroxide, Magnesium Sulfate, Hydrochloric Acid

**Safety:** Safety goggles, gloves, and a laboratory coat or apron should be worn at all times. All experiments must be performed in a fume hood. All chemicals should be considered hazardous and direct physical contact with them must be avoided. If exposed, immediately flush skin with water for at least 10 min, while contaminated clothing is removed. Do not ingest or taste any chemicals under any circumstances.

## Student Instructions

**Prelaboratory:** Search the literature and find the references related to the synthesis of methylenedioxyprecocene. Read the references and understand the mechanism pertaining to the synthetic route shown below:




*sesamol*

*3-methyl-2-butenal*

**Experimental Procedure:**

*Synthesis of methylenedioxyprecocene* (**1**)

Using a balance, weigh out 500 mg of Montmorillonite K10 clay. Transfer the clay to a 50 mL Erlenmeyer flask. Using a graduated cylinder measure out 10 mL of saturated aqueous $K_2CO_3$ and add it to the flask containing the clay. Add a magnetic stir bar to the aqueous clay mixture and stir for approximately 30 min at room temperature. Meanwhile set up a vacuum filtration apparatus (side-arm Erlenmeyer flask, filter adapter, Büchner funnel with filter paper; connect the side arm of the Erlenmeyer to an aspirator via vacuum tubing). Remove the magnetic stir bar, swirl the aqueous basic clay

mixture and collect the clay by vacuum filtration. Allow the clay to dry in the Buchner funnel for several minutes, then transfer it to a clean watch glass, spread it out with a spatula and allow it to dry in an oven at 110 °C for a period of 1 h. Carefully remove the hot, basic clay from the oven and allow it to cool to room temperature on the watch glass in a desiccator. While the clay is cooling, weigh out the sesamol (138 mg, 1 mmol) and add it to a disposable scintillation vial. Using a micropipet draw up the 3-methyl-2-butenal (106 μL, 1.1 mmol) and add it to the vial with the sesamol. Gently tap the vial to allow the sesamol to dissolve. To the resulting dark solution add all of the cool, dry clay and carefully distribute the mixture evenly using a metal spatula. Place the vial in the center of the carousel platform of a household grade microwave oven, cover the vial with a watch glass or other flat piece of glass, and microwave for a period of 10 minutes (several samples may be microwaved at once). Let the reaction mixture cool to room temperature. Then add about 5 mL of methylene chloride and gently swirl the vial. Separate the clay from the organic solution by vacuum filtration. Rinse the clay with two successive 5-mL portions of methylene chloride and two 5-mL portions of methanol. GC-MS analysis may be done at this point on a small aliquot of the crude product mixture. Transfer the filtrate to a 250-mL separatory funnel and wash successively with 2 N NaOH (2 x 10 mL), water (1 x 10 mL) and saturated aqueous NaCl (1 x 10 mL). Save the combined aqueous washings to recover unreacted starting material later. Dry the

organic phase over $MgSO_4$. Remove the drying agent by vacuum filtration, and transfer the filtrate to a tared 25-mL round-bottom flask. Set up a simple distillation apparatus and carefully distill off the methylene chloride (the distillate can be saved and reused). Residual methylene chloride may be removed by gently blowing a stream of air over the crude product until mass is constant. Weigh the flask containing the crude methylenedioxyprecocene product and calculate a percent yield. Analyze the product by GC-MS, IR, and/or NMR spectroscopy. Assess the purity of your product and interpret all data. If desired, acidify the saved aqueous washings with 2M HCl and extract with ethyl acetate (2 x 25 mL). Dry over $MgSO_4$, filter and concentrate. Re-calculate your percent yield of **1** based on recovered starting material.