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Microwave-Assisted Synthesis of a Natural Insecticide on Basic Montmorillonite K10 Clay

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Green Chemistry in the Undergraduate Organic Laboratory

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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* 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.

Experiment

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).[1] The reported synthesis of MDP is conducted under solvent-free conditions, on basic Montmorillonite K10 clay, K10–K$^+$, in a commercial microwave oven.[2,3] 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 reaction is carried out by simply combining the sesamol, aldehyde, and clay in a glass vial and exposing the mixture to microwave irradiation for ~5–8 min. The product is isolated from the clay by extraction with ethyl acetate, the resulting slurry filtered, and the filtrate concentrated by simple distillation or evaporation. The product may be analyzed by TLC, GC, GC–MS, IR, or

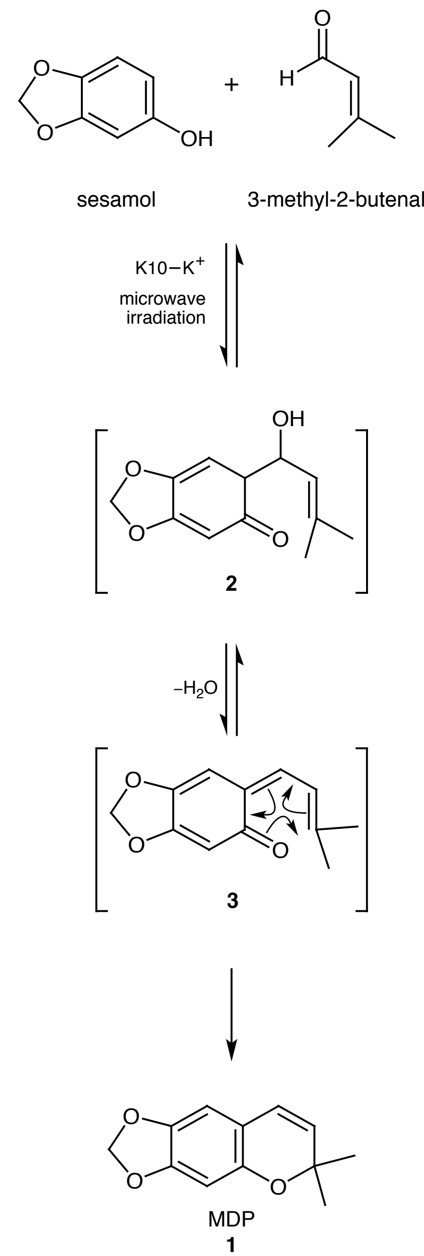

Figure 1. Synthesis of methylenedioxyprecocene (MDP, **1**).

NMR. Both the recovered clay and the ethyl acetate may be recycled.[4] More traditional methods for synthesizing chromene compounds like MDP employ higher temperatures, longer reaction times, or less environmentally friendly bases like pyridine *(21)* or titanium tetraethoxide *(22)*.

Hazards

General laboratory safety procedures, including wearing safety goggles and gloves, must be followed at all times. All experiments must be performed in a fume hood, and wearing a laboratory coat or apron is advised. Household microwave ovens are not designed to be spark or explosion proof and are not recommended for conducting chemical experiments that involve volatile organic compounds. However, the solventless conditions of the reported reaction most likely do not present a safety hazard. All chemicals involved in this experiment are considered hazardous and direct physical contact with them should be avoided. The following precautions should be observed: Potassium carbonate causes eye, skin, and respiratory tract irritation and may be harmful if swallowed. Sesamol is light sensitive and may cause eye, skin, respiratory, and digestive tract irritation. 3-Methyl-2-butenal causes eye, skin, and respiratory tract irritation and may be harmful if absorbed through the skin, inhaled, or swallowed. Sodium hydroxide is corrosive, causes eye and skin burns, and may cause severe respiratory or digestive tract irritation with possible burns. Ethyl acetate is a flammable liquid and vapor that causes eye irritation; breathing vapors may cause drowsiness and dizziness; it may cause respiratory tract irritation; prolonged or repeated contact causes defatting of the skin with irritation, dryness, and cracking.

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, and 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 quantity 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, 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; that is, 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.

Conclusions

We recently reported a detailed investigation of the clay-catalyzed condensation of sesamol and other phenols with 3-methyl-2-butenal to give MDP and other chromenes *(23)*. The experimental procedure for the synthesis of MDP outlined in this report is slightly modified for convenient execution in a typical undergraduate organic chemistry laboratory. This synthesis affords students a firsthand experience in the green synthesis of a physiologically active compound, using nontraditional technology that minimizes the use and generation of hazardous substances.

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[W]Supplemental Material

Instructions for the students, notes for the instructor, and spectral data are available in this issue of *JCE Online.*

Notes

1. The basic Montmorillonite K10 clay (K10-K^+) may either be prepared ahead of time by the laboratory instructor or teaching assistant or included as part of the experiment. Prior preparation is recommended to save time in labs that run for only three hours.
2. When conducting the experiment in a lab of 20 or more students, the reaction mixtures may be irradiated all at once or in several smaller batches.
3. If a microwave oven is not available, the reaction also proceeds well, though much more slowly, in a conventional oven (or oil/sand bath) at 110 °C for ~1 h.
4. The clay may be recycled after use by washing with methanol, then washing with saturated aqueous K_2CO_3, filtering, and drying in an oven at 110 °C for 1–2 h.

Literature Cited

1. Kirchhoff, M. M. *J. Chem. Educ.* **2001,** *78,* 1577.
2. Hjeressen, D. L.; Schutt, D. L.; Boese, J. M *J. Chem. Educ.* **2000,** *77,* 1543.
3. Singh, M. M.; Szafran, Z.; Pike, R. M. *J. Chem. Educ.* **1999,** *76,* 1684.
4. Collins, T. J. *J. Chem. Educ.* **1995,** *72,* 965.
5. Leung, S. H.; Angel, S. A. *J. Chem. Educ.* **2004,** *81,* 1492.
6. Seen, A. J. *J. Chem. Educ.* **2004,** *81,* 383.
7. Uffelman, E. S.; Doherty, J. R.; Schulze, C.; Burke, A. L.; Bonnema, K. R.; Watson, T. T.; Lee, D. W., III. *J. Chem. Educ.* **2004,** *81,* 325.
8. Uffelman, E. S.; Doherty, J. R.; Schulze, C.; Burke, A. L.; Bonnema, K. R.; Watson, T. T.; Lee, D. W., III. *J. Chem. Educ.* **2004,** *81,* 182.
9. Pohl, N.; Clague, A.; Schwarz, K. *J. Chem. Educ.* **2002,** *79,* 727.
10. Reed, S. M.; Hutchison, J. E. *J. Chem. Educ.* **2000,** *77,* 1627.
11. Angeles, E.; Ramírez, A.; Martínez, I.; Moreno, E. *J. Chem. Educ.* **1994,** *71,* 533.
12. Helsen, J. *J. Chem. Educ.* **1982,** *59,* 1063.
13. Baum, R. M. *Chem. Eng. News* **2003,** *81* (Sep 29), 3.
14. Lasszlo, P. *Science* **1987,** *235,* 1473, and references therein.
15. Nagendrappa, G. *Resonance* **2002,** 64.
16. Lindström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001,** *57,* 9225.
17. Perreux, L.; Loupy, A. *Tetrahedron* **2001,** *57,* 9199.
18. Giguere, R. J.; Bray, T. L.; Duncan, S. M. *Tetrahedron Lett.* **1986,** *27,* 4945.
19. Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986,** *27,* 279.
20. Brooks, G. T.; Pratt, G. E.; Jennings, R. C. *Nature* **1979,** *281,* 570.
21. North, J. T.; Kronenthal, D. R.; Pullockaran, A. J.; Real, S. D.; Chem, H. Y. *J. Org. Chem.* **1995,** *60,* 3397.
22. Sartori, G.; Casiraghi, G.; Bolzoni, L.; Casnati, G. *J. Org. Chem.* **1979,** *44,* 803.
23. Dintzner, M. R.; Lyons, T. W.; Akroush, M. H.; Wucka, P.; Rzepka, A. T. *Synlett* **2005,** *5,* 785.