

# Using Ozone in Organic Chemistry Lab: The Ozonolysis of Eugenol

Bruce M. Branan,\* Joshua T. Butcher, and Lawrence R. Olsen

Department of Chemistry, Asbury College, Wilmore, KY 40390; \*bbranan@asbury.edu

The ozonolysis of alkenes, a reaction that cleaves an alkene into two separate carbonyl groups, is a fundamental reaction covered in organic chemistry. It is ironic that such an important reaction is not included in most undergraduate labs, perhaps owing to the perceived difficulty and expense of generation and use of ozone, even though simple ozone generators have been known for some time (1–7). While a few of these generators are useful in reactions (8–10), their versatility is limited by the need for specialized glassware. An article in this *Journal* by Sponholtz, Walters, Tung, and BelBruno (11) offers a wonderful solution, providing instructions on the construction of a “simple and efficient ozone generator” that uses readily available equipment and is suitable for small-scale ozonolysis reactions. The low cost and simplicity of this device encouraged us to attempt construction of a similar device to be used in research projects and in an alkene-cleaving experiment in the organic chemistry lab. We have successfully built our own ozone generator for around \$350 using the same basic schematic as reported by BelBruno (11).

We utilize the ozone generator in our organic chemistry laboratory for cleaving the alkene of eugenol to an aldehyde. Eugenol is a natural component of cloves, with a structure that is pervasive in nature, similar to that of vanillin (vanilla), zingerone (ginger), isoeugenol (nutmeg), capsaicin (hot pepper), and curcumin (curry) (12), as well as many others (Figure 1). Our

students become familiar with eugenol as part of a separate lab exercise in which they steam distill it from cloves. (13). Other experiments involving eugenol have recently been reported in this *Journal*, including an olefin cross-metathesis experiment (14) and the study of eugenol’s antiseptic properties (15). In the ozonolysis of eugenol, students gain experience working at low temperatures ( $-78\text{ }^{\circ}\text{C}$ ) and participate in an exercise that simulates the drug discovery process (via the synthesis of a chemical derivative). Owing to the shorter length of this experiment than usual (ca. 2 hours) and the opportunity to work with 75,000 V of electricity, this experiment has been a successful addition to our second-semester organic chemistry labs.

## Ozone Generator

The design of the ozone generator is fairly simple, wherein oxygen gas flows through a region of high voltage to furnish a stream of gas composed of 3–4% ozone. The BelBruno apparatus (11) consists of two West condensers connected to allow oxygen to flow through the pathway normally taken by the water. With electrodes placed inside and outside the condensers (connected to the poles of a large transformer) and housed in a 6 in. PVC pipe capped at one end, the result is a small, but reliable ozone generator (Figure 2).

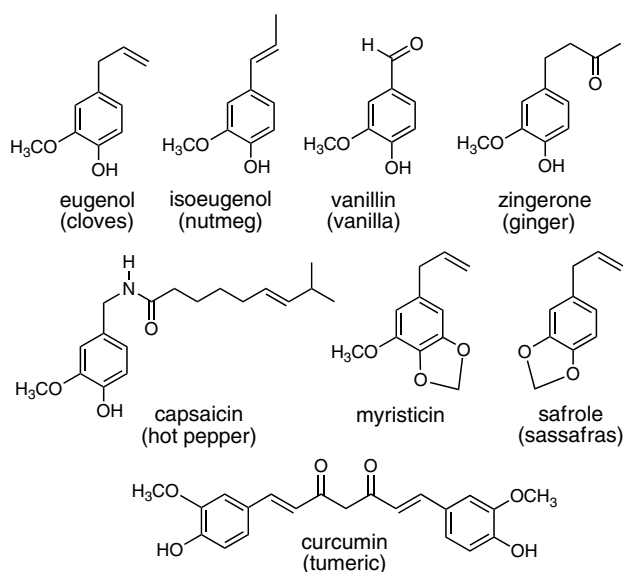


Figure 1. Eugenol and related compounds.

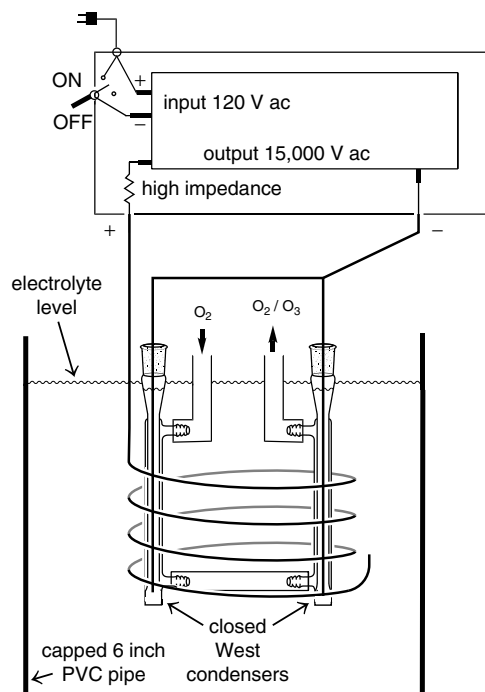


Figure 2. Schematic of the transformer and ozone generator (the insulation surrounding part of the Cu tubing is not shown).

When we followed the instructions of the BelBruno article, we encountered some minor difficulties in obtaining pieces of equipment identical to that described. We could not locate the exact 20,000 V step-up transformer used, so we substituted a 15,000 V transformer we purchased from a local sign company. The sign company also supplied us with appropriately rated wire, insulated wire sleeve-tubing, and a metal box to house the transformer. The BelBruno instructions described the use of an Allied Electronics 120 V Repeat Cycle Timer (model 519-4005). However experience showed us that the use of this timer was not necessary, as concentrations of 3–6% ozone were realized without it. Finally, the BelBruno directions instructed to surround the two West condensers with copper mesh. We have found that using ordinary 0.25 in. copper tubing (of the same type used for the inner electrodes) twisted helix-like around the inside of the PVC container served just as well. The end of the wire from the transformer was simply crimped into one end of the copper tubing, which is then submerged into the electrolyte solution.

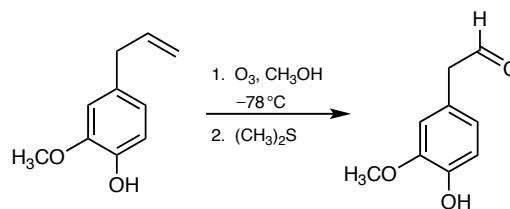
The ozone concentration was determined by bubbling the ozone/oxygen gas mixture through a solution of sodium iodide for one minute and then titrating with a standardized solution of sodium thiosulfate (16). With flow rates of ca. 30 mL min<sup>-1</sup> (measured by a bubble meter) at 293 K, we realized concentrations between 3–5% (vol/vol). When the flow rate was slower (15–17 mL min<sup>-1</sup>), the concentration increased to around 5–6%.

### Ozonolysis of Eugenol

A handout to students provides them with a fictitious scenario, the structures of eugenol and some related compounds, and the necessary experimental conditions (see the Supplemental Material<sup>(M)</sup>). Elemicin, a structural relative found in nutmeg, possesses hallucinogenic properties (17), yet only differs slightly from eugenol by having three methoxy groups, where eugenol has one methoxy group and one hydroxy group. Therefore, the purpose given to students for the experiment is to modify the *other* end of the eugenol structure, the end having the mono-substituted alkene, as part of a project aimed at evaluating the medicinal value of this new substance. One means of doing this is by ozone oxidation (Scheme I).

For this experiment students work in pairs and start the lab at 30 minute intervals. The scale of the experiment (200 mg of eugenol) enables the ozone treatment to be complete in 40 minutes, so students in line can have 10 minutes to prepare their reaction flasks with alkene and solvent. The generator is not turned off between groups. Instead, one flask is removed from the dry ice bath and another immediately replaces it. The tube supplying the ozone is simply transferred from the previous group to the next group. With the low cost of the ozone generators, two or three could be used in the lab at the same time. This would enable 24 students to complete the ozone addition in 2–3 hours.

The monosubstituted alkene of eugenol reacts cleanly with ozone to furnish an ozonide intermediate, which is reduced to an aldehyde using dimethyl sulfide. We have allowed one hour for this reduction, including time for the flask to warm back to room temperature. Solvent is removed by rotary evaporation,



Scheme I. Ozonolysis of eugenol.

and the residue is analyzed by IR and NMR spectroscopy. This experiment is conducted midway through the second semester, after students have covered alkene reactions and spectroscopy. Students must be able to make predictions about the product's identity and support these predictions with spectroscopic data, both from peak information present (aldehyde proton in <sup>1</sup>H NMR and carbonyl group in IR and <sup>13</sup>C NMR) and *not* present (alkene protons in <sup>1</sup>H NMR, reduced number of alkene signals in <sup>13</sup>C NMR). Students are also asked to calculate, based on a flow rate of 30 mL min<sup>-1</sup> and an ozone concentration of 3%, how long the reaction should take if every ozone molecule reacts. Students must remember, from general chemistry, how to use the ideal gas law,  $PV = nRT$ , to determine the volume of ozone needed, based on the moles of eugenol being reacted. Experimentally, the reaction is found to be complete (by NMR analysis of the product) in approximately the same time as predicted by this calculation (ca. 30–35 minutes).

Since no further purification is done before spectroscopic identification, *extraneous* signals appear in the <sup>1</sup>H NMR (2.5 ppm) and <sup>13</sup>C NMR (39.8 ppm) spectra. This generates some concern among students until they remember that residual DMSO is still present. Usually, reminding them of the mechanism, and referring them to *The Aldrich Library of <sup>13</sup>C and <sup>1</sup>HFT NMR Spectra* (18) enables them to solve this dilemma themselves. We have found that a short silica gel flash column (10% ethyl acetate in petroleum ether) is sufficient to provide clean samples of the product.

In this experiment students obtain high yields (the only product observed is the desired aldehyde). Online searching of the literature indicates that the product aldehyde, (4-hydroxy-3-methoxyphenyl)acetaldehyde (“homovanillin”), has not been studied extensively. However it has been synthesized (19), and its spectroscopic data are available for comparison purposes.

### Experimental Procedure

To a *tared* 25 mL round-bottomed flask equipped with a magnetic stir bar was added eugenol (ca. 0.20 grams, or around 10 pipet drops, 1.3 mmol) and methanol (15 mL). A Claisen adapter was added, and this mixture was cooled in a dry ice/acetone bath. A tube supplying ozone (ca. 3% in ozone) was attached through the top of the Claisen adapter, and ozone was bubbled into the rapidly stirred mixture at a rate of 30 mL per minute for 40 minutes. During this time, the IR and NMR (<sup>1</sup>H and <sup>13</sup>C) spectra for eugenol were obtained. After 40 minutes, the stream of ozone and the cooling bath were removed, and di-

methyl sulfide (ca. 0.2 grams, 20 drops from a pipet) was added. The mixture was stirred and warmed to room temperature over the course of 1 hour. The solvent was removed by rotary evaporation, followed by at least 5 minutes of high vacuum. A typical yield of unpurified product was 0.25 g, with samples contaminated with ca. 0.05 g DMSO.

IR (neat,  $\text{cm}^{-1}$ ): 3426, 1722.

$^1\text{H}$  NMR (60 MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 9.72 (t, 1H,  $J = 2.44$  Hz); 7.04–6.66 (m, 3H); 5.92 (s, 1H); 3.89 (3, 3H); 3.61 (d, 2H,  $J = 2.44$  Hz).

$^{13}\text{C}$  NMR (15 MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 199.87, 147.25, 145.11, 123.12, 122.13, 115.11, 112.45, 55.63, and 49.68.

## Hazards

Ozone is a toxic, irritating gas that may cause chronic respiratory problems. The high voltages involved should be isolated from any nearby solvents. Dimethyl sulfide and dimethyl sulfoxide are toxic and skin irritants. The health effects of all compounds used in this experiment have not been thoroughly tested, so their use should be limited to within a fume hood while wearing gloves.

## Conclusion

A convenient ozonolysis experiment for the undergraduate organic chemistry laboratory has been developed. Eugenol's alkene is easily converted in good yields into an aldehyde using ozone produced by the inexpensive ozone generator reported by Sponholtz, Walters, Tung, and BelBruno (11), and the product is identified by students via IR and NMR spectroscopy. The experiment demonstrates the drug discovery process by enabling students to synthesize a chemical derivative of a known natural compound.

## <sup>w</sup>Supplemental Material

A student handout (containing the scenario and experimental procedure), NMR and IR spectra, and step-by-step instructions (with pictures and photos) for building the ozone generator are available in this issue of *JCE Online*.

## Literature Cited

1. Maxwell, M. *J. Chem. Educ.* **1928**, *5*, 1493.
2. Lisk, G. M. *J. Chem. Educ.* **1931**, *8*, 2429.
3. Lisk, G. M. *J. Chem. Educ.* **1932**, *9*, 2099.
4. Uhrig, K. *J. Chem. Educ.* **1945**, *22*, 582.
5. Ransford, J. E. *J. Chem. Educ.* **1951**, *28*, 477.
6. Andrews, A. C.; Mickel, B. L.; Klassen, K. C. *J. Chem. Educ.* **1955**, *32*, 154.
7. Rubin, M. B. *J. Chem. Educ.* **1964**, *41*, 388.
8. Bonner, W. A. *J. Chem. Educ.* **1953**, *30*, 452.
9. Whaley, T. P. *J. Chem. Educ.* **1957**, *34*, 94.
10. Dardin, V. J. *J. Chem. Educ.* **1966**, *43*, 439.
11. Sponholtz, D. J.; Walters, M. A.; Tung, J.; BelBruno, J. J. *J. Chem. Educ.* **1999**, *76*, 1712.
12. Curcumin has recently been found to be active against many types of cancer. See King, A. G. *J. Chem. Educ.* **2006**, *83*, 347–348.
13. Lehman, J. W. *Operational Organic Chemistry*, 3rd ed.; Prentice Hall: Upper Saddle River, NJ, 1999; pp 81–87.
14. Taber, D. F.; Frankowski, K. J. *J. Chem. Educ.* **2006**, *83*, 283.
15. Miles, W. H.; Smiley, P. M. *J. Chem. Educ.* **2002**, *79*, 90.
16. Harris, D. C. *Quantitative Chemical Analysis*, 7th ed.; W. H. Freeman and Co.; New York, 2007; pp 340–343.
17. Le Couteur, P.; Burrenson, J. *Napoleon's Buttons*; Penguin: New York, 2003.
18. *The Aldrich Library of  $^{13}\text{C}$  and  $^1\text{H}$  FT NMR Spectra*; Pouchert, C. J., Behnke, J., Eds.; Aldrich Chemical Company: Milwaukee, WI, 1993.
19. (a) Fukuda, H.; Tetsu, M.; Kitazume, T. *Tetrahedron* **1996**, *52*, 157–164. (b) Challis, A. A.; Clemo, G. R. *J. Chem. Soc.* **1947**, 1692–1694.