Microscale Organic Chemistry Laboratory: Good News for Biologists, Too

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Introduction

The microscale laboratory technique is an important new development in undergraduate organic chemistry education. This new approach was pioneered by Dana Mayo and Ronald Pike at Bowdoin College and Kenneth Williamson at Mount Holyoke College, who started using "microscale" in their instructional labs about 1981. Since the publication of their laboratory texts (1,2), many chemistry departments have changed from a "macro" to a "micro" approach. Symposia and workshops are being held (3), and new microscale experiments are frequently found in the literature.

This essay outlines what microscale is and why chemists are excited about it. I know the dangers of bringing up a "non-biological" topic in the Bioscience, but I hope that you (and the editors) will indulge me this once, because microscale is likely to have a significant impact on biology education.

Even though the changeover to microscale will be a decision for chemists to make, biology faculty should also be aware of what is happening and should encourage their chemistry colleagues. Biology majors who take organic chemistry will benefit from microscale, and I think we will see the positive effects extending into our programs in biochemistry, microbiology, and cell biology.

What is "Microscale"?

The essence of microscale is just what the name implies: all reactions and purifications are done on a scale 10 to 1000 times smaller than usual. Where the traditional organic lab uses grams, microscale uses milligrams.

Students in microscale labs feel that their health is better protected, and they enjoy the lab more and learn more readily.

Two examples will serve to illustrate this. Consider first the oxidation of cyclohexanol to cyclohexanone, a common reaction in organic laboratory texts. Typically, students react 15 g of cyclohexanol with 15 g of sodium dichromate dihydrate (4) and analyze the products by gas chromatography (GC) and infrared spectroscopy (IR). But with microscale only 0.1 g are used. Why synthesize 10 g when 0.1 g is more than enough for analysis?

Second, consider the isolation of a natural product, caffeine. Typically, 25 g of tea leaves are extracted to purify 0.3 g of caffeine (4, 5). However, in the microscale lab only 1 g is extracted -- less than the contents of a single tea bag (1, 2).
After purification by sublimation, 15 mg of highly pure caffeine is obtained -- enough for an IR spectrum and melting point determination. On this scale, the caffeine from a single Excedrin tablet can be extracted and analyzed (2)!

**Microscale Techniques**

A 10 to 1000 fold reduction in the amount of material has profound implications. To start with, it demands different experimental techniques and different equipment.

For example, small quantities of liquids must be handled in conical vials (0.1 - 1.0 ml volume), and they must be transferred with a syringe, Pasteur pipette, or automatic delivery pipette. They cannot be poured! For solids, microspatulas and a balance with milligram accuracy are required.

In some cases, microscale uses scaled down versions of ordinary organic laboratory glassware, but in most cases the equipment is quite different (6). Reactions are carried out in tubes or conical vials in sand baths instead of in round-bottomed flasks on heating mantles. Conical centrifuge tubes and Pasteur pipettes replace separatory funnels for extractions. Hickman stills are used for distillation (1), and Craig tubes for recrystallization (3).

For characterization of compounds, microscale relies heavily on the GC, IR spectrometer, Abbe refractometer, and an oil-bath capillary melting point apparatus. (The latter can also be used to determine boiling points with only 3 - 4 microliters of a liquid (7).) Bench top centrifuges and hot plate-magnetic stirrers are essential equipment, and preparative GC is increasingly used.

Microscale continues to evolve, and part of the excitement of it is the continuing flow of new ideas and techniques (8-10).

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**What are the Advantages?**

By switching to microscale, chemistry departments can improve teaching, improve laboratory health and safety, and at the same time save money!

The original motivation of Mayo and Pike was to improve laboratory air quality without a costly upgrade of the ventilation system (1), and they succeeded admirably. Smells are not a problem in the microscale lab, because reduction in the amount of starting material leads to a corresponding reduction in volatile organic solvents.

Microscale has numerous other advantages as well (1, 2, 11). Smaller quantities of chemicals and solvents mean lower costs for supplies, reduced student contact with toxic substances, lower threat to safety from explosion or fire, and less chemical waste to be disposed of. Moreover, the microscale glassware appears to be more durable, leading to lower breakage costs.

Most importantly there are pedagogic advantages. Many of the microscale operations take less time (12), so that students can do more and learn to solve more lab puzzles. The teacher can afford to let students learn from their mistakes, because hazards are reduced and because there is time for the unsuccessful experiment to be repeated.

It is also possible to expand the variety and sophistication of the lab activities. Experiments can be conducted which would be too hazardous or expensive on a

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larger scale, such as the condensation of benzaldehyde using a cyanide catalyst (1), and starting materials can be used which are not available commercially (11). Micro-techniques for analysis of gases open up entirely new possibilities (1).

**Improvements in Learning**

Perhaps the question in the back of your mind is, can sophomore college students do it? They can, and indeed they thrive on it. With microscale, students gain the greatest ability to handle lab materials in the shortest period of time.

Mayo and Pike report that when test and control laboratory groups were compared, the entire range of the class performed better using microscale (1). Other teachers who have tried microscale report similar outcomes (3). Students in microscale sections appear to master details and procedures more effectively and perform "significantly better in upper level work" (1).

Students in microscale labs also feel that their health is better protected, and they enjoy the lab more and learn more readily (3). They gain in dexterity and have a greater sense of accomplishment and self-confidence.

The benefits of microscale are perhaps greatest for biology and biochemistry majors. Because microscale borrows techniques which have been standard in biochemistry for years, the skills and experience which the sophomore student gains will be more useful to his later upper level work than the skills taught in the traditional organic lab.

One potential disadvantage of microscale is that students might not learn to use conventional equipment. This problem could be circumvented by including a few "macro" experiments in the microscale lab. However, it is generally easier to learn to scale up than to scale down. It is probably much more important that the students learn to work precisely.

**Conclusions**

Microscale has tremendous advantages for students in sophomore level organic chemistry. It can be a great boon to both biology and chemistry students and give them better preparation for biochemistry and other upper level courses.

The biggest obstacle to converting from traditional organic lab to microscale (other than faculty inertia) is the initial investment in instruments, glassware, and other equipment. However, in the long run it more than pays for itself (13).

Perhaps the most important aspect of microscale is the opportunity it affords for teaching safety and environmental awareness. Chemists must teach, by their example, responsible attitudes toward the handling and disposal of hazardous substances (14,15), because some of our students will be the industrial chemists of the future. As Wendy Walton has written, "If we want the next generation to deal with hazardous waste appropriately... then we must teach them" (14). Converting to microscale is one of the best ways to deal with the problem of chemical wastes in academic labs (16).

In conclusion, microscale is an important step in the right direction, and one that ought to be encouraged.

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References

6. Glassware for microscale is available from Ace Glass, Kontes, and others, but many experiments can be done without special glassware. (3)