MINIATURIZATION IN THE ORGANIC LABORATORY: ONE INSTITUTION'S EXPERIENCE

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ABSTRACT

The use of two styles of microscale equipment was evaluated by an organic laboratory section and the potential of the microscale method was investigated for possible adoption by the department. Laboratory manual suitability, additional student training, financial impact, equipment requirements, student experimental outcome, safety, and waste generation associated with the adoption of a microscale approach to laboratory were evaluated. As a result of this study, the department has adopted an integrated approach using both semi-microscale and microscale laboratory methods. The style of microscale equipment selected was the less expensive alternative using procedures most closely associated with those currently used for semi-microscale. No specialized laboratory manual was found to be required and little additional student training was necessary. The cost of equipping 15 microscale laboratory stations was approximately $3500. Microscale was found to have little negative impact on experimental results and product characterization except for liquid products. Laboratory safety, breakage, and waste management were impacted positively.

INTRODUCTION

Since the 1950's the solution volumes used in the sophomore organic laboratory have grown steadily smaller. Prior to the 1960's, solution volumes from 250mL to one liter were often used in organic laboratory preparations. Later, when converting to standard taper glassware kits, semi-microscale operations involving quantities between 25mL to 100mL became popular. In the contemporary organic laboratory, a further revolution is occurring in which microscale techniques regularly use volumes measured in microliters.

In a series of papers culminating in a 1985 publication, Mayo and coworkers (1985) introduced, on a national scale, the concept of microscale preparations in the undergraduate laboratory for the beginning organic course. The first edition of their book (Mayo, Pike,

and Butcher, 1986) placed the microscale undergraduate organic laboratory offering on a solid footing by providing an undergraduate laboratory manual specifically targeted for microscale techniques. In addition, adaptation of the microscale technique for the organic laboratory was facilitated with the commercial availability of a microscale organic kit matching the requirements of the laboratory manual.

In the spring 1990 term, the Augustana chemistry department initiated an investigation aimed at the possible adoption of a microscale program for the beginning organic chemistry course sequence. At that time there were two microscale kit types (Mayo and Williamson, see Table 1) to consider and several laboratory manuals that were oriented toward microscale experiments (Mayo et al., 1989; Pavia et al., 1990; Rodig et al., 1990; Williamson, 1987; and Williamson, 1989). While several of these texts contained only microscale experiments, some contained both microscale and semi-microscale experiments.

Table 1. Microscale kits, their suppliers, and approximate costs (1989).

Williamson Style Kits
Kontes; Vineland, NJ (microflex microware) >$135.26
Mayo, Pike, Butcher Style Kits
1. Ace Glass; Vineland, NJ (micro mini-ware) $206.00
2. Chemglass; Vineland, NJ (minum-ware) $176.00
3. Corning Glassworks; Corning, NY (micro-organic ware) >$175.00
4. Kimble; Vineland, NJ (Delta ware) >$219.00
5. Kontes; Vineland, NJ (threaded microware) $209.00

METHOD

The chemistry department deemed it desirable to gain some student and instructor experience with the microscale method before deciding to adopt microscale techniques on a course-wide basis.

The available texts and representative microscale kits were obtained for evaluation. Limited quantities of community equipment items that could be required for the microscale approach were also obtained for evaluation (for example: electronic balance having milligram sensitivity, calibrated pipet dispensers, centrifuges, heating sources, and syringes and accessories).

A small laboratory section from the second semester organic course was selected to become the evaluator for this technique. The students of this section were to repeat some of the experiments performed the first term and compare the old and new techniques and their experimental results.

The instructor would evaluate laboratory manual suitability and the level of training required to prepare the students to use this method. Experimental success (yields for preparative experiments) and student attitude (from the course evaluation forms) would also be assessed. Additionally, the financial, safety and waste disposal impacts of adoption of a microscale approach for the laboratory would be considered.

EXPERIMENTAL

Equipment: Half of the class was assigned to work with equipment from the Williamson-style kit and half from the Mayo-style kit. Heating source combinations used by the students included hot plates with aluminum heating blocks or sand-filled crystallizing dishes and 100mL heating mantles (regulated by a home-built dimmer switch control) filled with sand or glass wool. A centrifuge was provided for those students using Mayo-style kits, which required it for the Craig tube filtration operation.

Procedure: The students were first introduced to the microscale equipment by conducting assigned training exercises in which they calibrated a heating source, determined liquid density (using both a calibrated pipet dispenser and the pipet pump for volume measurement and an electronic balance for mass determination), and calibrated a capillary glass pipet to be used for later experiments.

After the introduction, students were expected to repeat four representative experiments they had completed in the first term, but at the microscale level. Two experiments involved isolation of a solid product, one liquid product, and the fourth fractional distillation. Students were furnished specific, detailed printed instructions for scaling down the quantities used in their laboratory manual (Lehman, 1988) for the first experiment. From then on, only general operational guidelines were supplied and the students were expected to calculate the quantities of starting materials required and modify the procedure, where necessary, for the remaining experiments.

The following comparative results were obtained by the fifteen students for the experiments done in both semi-microscale (first yield value) and microscale (second yield value): Benzoic Acid: 2.7 $\pm$ 0.5g (88.6%); [1/30TH SCALE] 0.085 $\pm$ 0.01g (83.0%): Isoamyl Acetate: 9.5 $\pm$ 2.3g (48.7%); [1/20TH SCALE] 0.21 $\pm$ 0.16g (22%): Diels-Alder Adduct of Alpha-Phellandrene: 1.7 $\pm$ 0.9g (41%); [1/20TH SCALE] 0.16 $\pm$ 0.04g (38.6%): and Fractional Distillation (initial mixture cyclohexane/toluene ratio was unity yielding a first distillate fraction ratio [as reported by students from GC analysis]): 61%/31%; [1/21.5TH SCALE] 76%/24%

RESULTS AND DISCUSSION

The students assimilated the microscale techniques quite rapidly and formal experiments to introduce the microscale methods were not deemed necessary for full course implementation. The one exception to this observation was the desirability of encouraging students to conduct a practice distillation prior to experiments involving this technique in order to become familiar with the procedure.

It quickly became apparent that it was not desirable to limit student exposure to only microscale techniques, for several practical reasons. Future courses and graduate courses would not necessarily involve only microscale techniques, and since several operations differ significantly between these two scales (extraction, filtration [for one style of kit]), students should receive exposure to both. Current student equipment drawers contained a complete supply of semi-micro equipment and it did not make sense to declare this equipment obsolete and remove it at this stage.

The department has long used a laboratory manual (Lehman, 1988) that introduces technique as an incidental feature while experiments are performed rather than introduce techniques by fabricating a procedure to demonstrate techniques one at a time. Because the available texts having a microscale emphasis do not offer this option, and because this laboratory section had good experience scaling the experiments from their current laboratory manual, the department opted to continue to use the current manual. When using the current manual, detailed printed scaling instructions would be provided to the student for the first experiment to be reduced to microscale. Less specific instructions would be provided for the experiments to be performed thereafter.

The experimental results obtained by those students continuing on into the second semester of organic and who conducted these four experiments on both semi-microscale and microscale are shown in Table 2.

For the benzoic acid experiment, student yields were not found to be influenced by the style of equipment used nor did they differ substantially from the yields (when measured in percent) obtained by these same students one term earlier using the larger scale. Students had a difficult time determining the success of an experiment if the quantity of product was small. For instance, they considered an 88.6% yield for an experiment done at semi-microscale more successful than one done at microscale which yielded 83.0%. They seemed to equate a large rather than a small absolute quantity with a successful experiment, even though the yields, on a percentage basis, were nearly equivalent!

Table 2. Comparison of semi-microscale and microscale experimental results.

Product	Semi-microscale yield	Scale reduction	Microscale yield
Benzoic Acid	2.7 ± 0.5g [88.6%]	1/30	0.085 ± 0.01g [83.0%]
Isoamyl Acetate	9.5 ± 2.3g [48.7%]	1/20	0.21 ± 0.16g [22%]
Diels-Alder Adduct of alpha-phellandrene	1.7 ± 0.9g [41.0%]	1/20	0.16 ± 0.04g [38.6%]
Fractional Distillation* (cyclohexane/toluene ratio)	61%/31% GC analysis	1/21.5	76%/24% GC analysis

* Distillation pot cyclohexane/toluene ratio was unity.

Substantial differences were noted in the ease of filtration between the two kit styles. The Mayo-style kit, which used a Craig tube, involved a procedure very different from that used in the semi-microscale kit. It was more complex and required the availability of a centrifuge that would accommodate standard centrifuge tubes. Further, more than one student had difficulty with the procedure and one had the Craig tube shatter while centrifuging. The Williamson-style kit, on the other hand, involved equipment that was similar to that used in previous courses, only smaller in size. No difficulty was noted in the use of this style of equipment.

Several advantages of microscale preparation were noted. Student laboratory time was significantly shortened and two students who had laboratory spills or made procedural errors were able to start over and still complete the experiment within the allotted time. Secondly, laboratory spills were of less concern (from the safety viewpoint) because of the reduced quantities involved. Finally, the accumulation of student product was greatly reduced. The total obtained for this laboratory section was about as much as for one student doing the same experiment the previous term using the larger semi-microscale. The reduced volume of student product was also reflected in reduced spent solvent and solids generation and in about the same magnitude, greatly reducing solvent reclamation and waste disposal time and effort.

In the fractional distillation experiment, differences noted between the two kit styles included an unfamiliar method (Hickman still) and the necessity to withdraw samples by pipet as the distillation was

in progress (the Mayo-style equipment). A true fractionation was not possible with this kit style as the equipment in the kit allowed for only a one-step distillation. [An accessory spinning band kit now available produces good fractionation; however, it increases the cost of the equipment package.] The Williamson-style kit uses flexible synthetic connectors to construct a fractionation set-up closely similar to that normally encountered. Using the Williamson-style kit it was also possible to approximate the volume of distillate collected by a given temperature before removing the sample, while with the Hickman still this could only be done after the sample had been withdrawn by syringe or pipet. In subsequent experiments involving higher boiling substituted aromatic substances, the flexible connectors used in the Williamson-style kits were found to be seriously damaged during distillation. The Mayo-style kit connectors (ground glass and "O" ring seals) were not damaged. In both style kits our standard laboratory thermometers were usable; however, the thermometer size caused the microscale equipment to be ungainly and awkward to handle. For that reason, smaller thermometers were purchased for microscale use and are dispensed as community equipment.

The separation achieved by microscale was not outstanding, but it was slightly better than the semi-microscale using a column packed with a steel sponge. Unfortunately, the student results were not separated by kit style so the results from each style of kit could not be compared.

In the isoamyl acetate preparation, a reflux, extraction, liquid drying and final product distillation procedure were carried out. While no particular differences were noted between the two styles of kit, the percentage yields were lower than those for the larger scale experiment done the first term. The reasons for this are twofold. Firstly, the reduction in scale was probably too large. Acceptable results have since been obtained by doing a 1/10th scale reduction. Secondly, at the time, the students could not control their heat sources properly as they were using large hot plates and the condensers and receivers were too close to the hot plate and had no heat shields. Product often failed to condense properly under this condition and was lost as vapor.

The final experiment involved preparation of a solid from a liquid mixture by forming its solid maleic anhydride adduct, filtering, and recrystallizing the adduct. The students were allowed to select their own method of filtration. All selected the method used in the Williamson-style kit. The percentage yields obtained in this experiment were essentially the same as those obtained earlier by the class using semi-microscale methods.

The methods used to characterize semi-microscale products [mp, bp, index of refraction, infrared and GC] were applicable to microscale preparations as well, although the several drops of liquid needed for refractive index proved a challenge for those with low yields.

At the end of the term students were asked to comment upon their microscale laboratory experience on the formal course evaluation. Most of the comments were favorable, some were neutral, while one or two preferred the larger scale.

As a result of our evaluative work and based upon the results from the trials with student workers in this organic laboratory section, the department selected an integrated semi-microscale and microscale laboratory program for both large and small sections of the beginning organic course in the fall of 1990. The use of the current text was continued, supplemented with oral/written instructions, as required, for the experiments to be done in microscale.

The department chose to purchase enough Williamson-style microscale kits to allow students to share between sections. This kit was selected because of its lower cost, ease of use, and similarity to the equipment normally used in larger scale organic laboratory operations. Occasional replacement of the flexible connectors in this kit, easily damaged by high-boiling aromatic compounds, would be tolerated as a departmental expense. Because the microscale glassware has thick walls relative to its size, it is more rugged and less susceptible to breakage. With one exception, breakage of microscale equipment was rare. Students trying to clean small flasks sometimes broke them by trying to force test tube brushes through their narrow necks. This problem was solved by using pipe cleaners bent to fit the inside shape of the flask bulb.

The department took this opportunity to convert completely to non-flame sources for heating in the organic laboratory. Sufficient 100mL heating mantles were obtained for each laboratory station. Glass wool was supplied for encasing smaller vessels to distribute heat more evenly. The department purchased components to fabricate a power controller for the mantles; they included an electrical box and face plate, wall outlet, dimmer switch and electrical chord and plug. A summer student assistant assembled the controllers. This expense, of course, would not normally be associated with microscale conversion for laboratories already using flameless heating sources.

For measuring mass, electronic balances (one balance/15 students) sensitive to 1mg up to 40g capacity [and 0.01g sensitivity beyond that mass and to a capacity of 400g] were obtained. To protect the balances from laboratory air currents, a large clear plastic hood

was constructed from rigid plastic sheets and a plastic glue obtained from a hobby shop. The student summer assistant also assembled the hoods.

Plastic, one-piece, disposable dropping pipets were issued to students. The students calibrated the pipets using water, the new electronic balances, and a black marking pen. For more sophisticated microscale volumetric measurements, an assortment of sizes of pipet pumps and measuring volumetric pipets were purchased to be used as community equipment.

The approximate equipment cost per 15 student stations was $3,500 [15 kits and microscale thermometers, one electronic balance, ten 2 and 10mL pipet pumps, twelve 1 and 2ml measuring pipets, box of disposable, polyethylene dropping pipets]. The 100mL heating mantles and home-built controls were not included.

After the introduction of the integrated microscale program in the fall of 1990, the following benefits were verified. The odors caused by the more volatile products or starting materials in the laboratory were greatly reduced, fire and spill hazards from solvents were reduced, the amount of student product and recovered solvents and materials for consideration to declare as waste were reduced, the amount of time required to complete a given experiment was shortened, the cost of starting materials and solvents declined, and the breakage cost was reduced.

The introduction of microscale techniques into the organic laboratory is a relatively new enterprise. Those wishing to keep current with this trend might wish to subscribe to a specialized newsletter now available on that topic: *Smaller Is Better: The Newsletter of Microscale Organic Chemistry Programs*, Department of Chemistry, Bowdoin College, Brunswick, Maine 04011.

The department is positive about its new integrated semi-microscale/microscale organic laboratory program and the program is well on the way to becoming established in the department.

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