Microscale Organic Laboratory

I: An Approach to Improving Air Quality in Instructional Laboratories

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Increased awareness of the significance of low gas phase concentrations of commonly used chemicals in instructional laboratories has been reflected in previous articles on lab safety (*1–4*).

In moving toward cleaner laboratory air, it is likely that many institutions have been guided by the occupational exposure standards established by the Occupational Safety and Health Administration (*5*). In one case (*4*), an institution has adopted as policy the maintenance of air quality based on the Permissible Exposure Level (PEL) applied to 15-min averaging times.

Judging by the literature and a brief survey (*6*), academic institutions have improved air quality in instructional laboratories in two ways: (1) the amount of hood space and ventilation per student has been increased to reduce concentrations in the breathing zone, and (2) some materials have been completely eliminated from use (benzene is a common example). While there seems to be much room for the improvement of air quality through these two approaches, each one also comes with limitations and drawbacks. Increased ventilation can result in a costly retrofit project for many buildings. Expanded hood space may create visual obstructions and lead to greatly increased noise levels. Where there is a large heating or cooling load during the academic year the above modifications may also result in a considerable increase in operating expense for the conditioning of make up air. A principal disadvantage to the substitution of less hazardous materials is that substitutes may not be available which allow the program to achieve its educational objectives. As an extreme example, the exclusive use of water phase reactions presents a limited and unrealistic experience for organic students.

This paper and the following paper present preliminary reports on a third possible approach to the improvement of air quality which we have termed the microscale approach. This approach modifies the experimental techniques used by the students in order to minimize laboratory emissions. We have initiated this program on a trial basis in our sophomore chemistry laboratory where, for example, we now carry out experiments in organic synthesis at a much smaller scale than is commonly employed. Thus, where students formerly worked with about 10–50 g of starting material and 50–500 g of solvent, they may now work with 10–150 mg of reactant and 1–10 g of solvent. The small quantities of material utilized in the Bowdoin program results in a significant improvement of air quality in addition to presenting a number of other benefits to the teaching laboratory (to be discussed in Part II).

Characterization of Air Quality

The concentration of a contaminant in an enclosed space, such as a laboratory, is a function of two important parameters: (1) the rates of emission from various processes in the laboratory; and (2) the dilution of emissions in the room. Dilution in turn depends on dispersion within the room and ventilation/exhaust from the room. Since sources of emissions will be expected to occur only at isolated points, the personal exposure will depend on where the receptor is located and on the mixing processes.

Air quality in enclosed spaces has often been treated by a mass balance approach for a completely or partially mixed reactor (see Turk (*7*), Esmen (*8*), and also several more general treatments on indoor air quality (*9, 10*)). A ventilation model may be described for our purposes by the following equation.

$$V dc/dt = G(t) - kQc + kQc' \tag{1}$$

The concentration in the room is c and c' is the background concentration of the contaminant in question. V is the room volume, $G(t)$ is the emission rate, Q is the volume rate of removal of air from the room, and k is a dimensionless empirical term known as the mixing factor. This relationship assumes that there is no recirculation of partially filtered air. For the present we are interested in only the steady state solution to eqn. (1).

$$c = G/kQ + c' \tag{2}$$

As has been noted by Esmen (*8*), values of k will depend on the size and shape of the room and on the locations of sources and receptors. In this empirical approach, for a given room, receptors close to the source will tend to be associated with small k values and remote receptors will have larger k values. The case of the well-mixed room is represented by $k = 1$. Drivas, et al. (*11*) and Ishizu (*12*) have obtained k values ranging from 0.3 to 0.7 in selected cases. Since there is no reason to feel that k values may be transferred from other studies, we have conducted two types of measurements which bear on the characterization of mixing in the laboratory. One series of measurements has been devoted to the determination of a dispersion constant (not the same as the mixing factor described above) for indoor air spaces in the absence of ventilation. This work is described in detail elsewhere (*13*). For present purposes it is enough to know that the worst case dispersion constant (slow mixing) leads to a mixing factor in the range 0.3–0.5 for our large instructional laboratories.

In the second type of experiment we have measured steady state concentrations of a tracer in our laboratory while the ventilation was in use. The tracer used was acetaldehyde at a concentration about 1% of the TLV of 180 mg/m^3. The vapor concentration was determined by the sensitive colorimetric method described by Hauser and Cummings (*14*). The acetaldehyde concentration was measured at seven locations in the laboratory ranging from 1 to 14 m from the source in a room 19.2 m long. During sampling, the doors to the laboratory were generally closed but no attempt was made to limit the movement of the three or four people associated with the project.

Thirty 1-h average concentrations were obtained for the 6 h in which the experiment was conducted. We experienced some difficulties with low collection efficiencies during one 3-h period, but assuming that the collection efficiency was the same for each sampler, the minimum ratio of the smallest concentration to the largest concentration for a given hour was 0.53.

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Emission Measurements

The emissions from selected unit processes were measured using propionaldehyde (bp 49°) and isobutyraldehyde (bp 61°) to simulate volatile solvents. The selected unit processes (such as liquid-liquid extraction with a separatory funnel) were carried out in a large metal duct which captured all emissions and through which the air flow rate could be measured. The air flow through the duct was typically 5.4 m^3/min. At the downstream end of the duct a small aliquot of the air was sampled with the aldehyde samplers. The duct system has been used for other work and has been described previously (*15*). The amount of aldehyde in the sampler was determined photometrically using appropriate standard curves. The amount of material emitted by the unit process was obtained by multiplying the amount in the sampler by the ratio of duct flow rate to the sampling rate. We also evaluated the collection efficiency for the aldehydes by injecting known amounts into a glass U-tube placed ahead of two or three samplers in series. A rough measure of the efficiency was obtained by examining the ratio of aldehyde in the first sampler to aldehyde in all samplers. By this test, the efficiency for acetaldehyde was greater than 90% at room temperature and the efficiency for propionaldehyde was 78%. The results for isobutyraldehyde ranged from 29% to 82% and an average value of 56% is used in this report.

The four unit processes selected for preliminary evaluation were typical of those seen in conventional organic chemistry laboratories in terms of quantities and apparatus used. The results of our preliminary measurements are shown in Table 1. The multiple entries indicate amounts obtained by separate samplers, not results from separate runs of the processes. The values shown here are intended to indicate the range and magnitudes of emissions to be expected from a very small set of processes. Bayer (*1*, *4*) has described emissions of methylene chloride from reflux and liquid-liquid extractions and some values for other emission studies. Although the details of the liquid-liquid extraction steps may be different, methylene chloride emissions reported by Bayer are higher by an order of magnitude than those obtained for isobutyraldehyde in the present study. Much of the difference may result from a vapor pressure effect.

Application to Air Quality

The emission results may be combined with the laboratory mixing measurements to obtain estimates of concentrations to be expected from selected unit processes. A mixing factor of 0.3 would seem to add a reasonable element of conservat to eqn. (2) for our laboratory for the purposes of these es mates. Some results are summarized in Table 2. Selected u processes are indicated on the left and the resulting stea state concentrations on the right. We have assumed a section of 30 students for some of the processes. For t present, we have not weighted the concentrations to obt an exposure value for the 8-h period for which the TLV is tended.

It may be seen in Table 2 that there are certain substan for which quantities used will have to be greatly limited a which may only be used in properly operating hoods. For i stance, a single open bottle of a liquid with a volatility simil to propionaldehyde should not be allowed for any substan with a TLV less than 1.8 mg/m^3. The results given in Tab 2 only apply to the room in which the tests were made or similar rooms. Care should be exercised in extrapolating the results to other situations.

There are a number of choices available for predicting a quality in other laboratories. In one method the effecti mixing time, V/kQ, may be measured by the dynamic metho as for example in Drivas (*11*), Ishizu (*12*), and Bayer (*4*). Th steady state concentration may then be obtained from eq (2) and the room volume. In the second method the worst cas value for the dispersion constant (*13*) may be combined wit the ventilation rate to obtain an estimate of the range o concentrations in the room.

Ventilation rates are not commonly measured in instruc tional laboratories even though they are not very difficult t make. These measurements yield a number of benefits. Sen sitive thermoelectric air velocity meters are available for less than $1000 which can produce reliable measurements of ve locities in the 100 ft/min range. Descriptions of methods fo measuring ventilation rates are available (American Confer ence of Governmental Industrial Hygienists (16)). These measurements are not only useful for air quality consider ations, as described above, but also are useful for evaluating hood performance and maintaining the proper openings o hood doors.

Discussion

Our preliminary studies indicate some of the materials and processes which must be restricted in an instructional laboratory. For instance, open transfers of liquids having a volatility similar to propionaldehyde should not be permitted for liquids having a vapor TLV less than 20 mg/m^3. There is a similar limit on the use of liquids such as isobutyraldehyde for which there is a likelihood of two spills per hour. If one considers the additive effects of these two processes, the upper TLV limit for a compound used under these circumstances is 40 mg/m^3.

We plan to expand our emission measurements to include other normal scale processes and microscale processes. We also expect to measure vapor concentrations in the laboratory. These measurements should enable us to determine materials and practices which can safely be used in the laboratory. We are confident that methods readily availabale for liquid transfer at the microscale (syringes and micropipets, for instance) can greatly reduce emissions of volatile liquids. While we have not considered hazards associated with skin contact, explosion, or fire, these risks should also be reduced as a by-

Table 1. Emissions from Unit Processes

Process	Emission
1. Liquid transfer[a]	
a. 10 transfers of propionaldehyde in 8.17 min	2.72 g, 2.53 g
b. 5 transfers of propionaldehyde in 3.8 min	0.69 g, 0.62 g
c. 10 transfers of isobutyraldehyde in 5.13 min	1.54 g
2. Open bottle[b]	
Propionaldehyde for 21.33 min	0.19 g, 0.18 g
3. Isobutyraldehdye spill[c]	3.86 g, 2.46 g
4. Liquid-liquid extraction[d]	
3 isobutyraldehyde-water extractions	0.70 g, 0.57 g

[a] About 5 mL was transferred from a reagent bottle to a test tube, filling the tube to an arbitrary mark. Then the test tube was emptied back into the reagent bottle. The reagent bottle was allowed to stand open and the used test tubes remained in the rack until the end of the run.

[b] A small narrow-necked bottle was allowed to stand in the duct with the cap off.

[c] About 5 mL of isobutyraldehyde was spilled onto an enameled tray with an area of about 0.2 m^2. After about 15 s, the aldehyde was wiped up with paper towels which were removed from the duct. Sampling was terminated about 80 s after mop-up was complete. (This is the length of time required for air at the spill site to reach the samplers.)

[d] 25 mL of water and 10 mL of isobutyraldehyde were added to a clean separatory funnel. The funnel was stoppered and shaken vigorously and vented. The shaking and venting cycle was done three times and then the liquids were carefully separated into 50-mL Erlenmeyer flasks. This entire process was repeated twice while the samplers were running to simulate three extractions. The Erlenmeyer flasks were not capped between runs.

Table 2. Concentrations Resulting from Selected Sources

Source		Concentration
1. Open bottle of propionaldehyde	8.7 mg/min	1.8 mg/m^3
2. 30 propionaldehyde transfers/h	100 mg/min	20 mg/m^3
3. 30 isobutyraldehyde separatory cycles/h	110 mg/min	22 mg/m^3
4. 15 isobutyraldehyde spills/h	800 mg/min	160 mg/m^3

Assumed values: Q (ventilation rate) = 16.5 m^3/min
k (mixing factor) = 0.3

product of the microscale technique.

The approach outlined in this and the following paper is not intended to be a subtitute for adequate laboratory ventilation or for carrying out certain manipulations in properly operating hoods. We do feel that the concept offers the potential for increasing laboratory safety while lowering capital investment, energy use, material costs and indicates an avenue which other chemistry departments may wish to explore.

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II: The Benefits Derived from Conversion to the Program and Representative Experiments

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Part I presented a preliminary study of the emissions from selected processes and the mixing of these emissions within the laboratory atmosphere (*1*). This paper describes the reduction to practice of microscale laboratory procedures and outlines benefits derived from this approach to improving laboratory air quality. In order to illustrate the style and scale of the laboratory experiments which may be incorporated into such a program two representative examples are given in detail in the discussion.

We are currently in the process of developing and testing a wide variety of experiments at the microscale level. These exercises will eventually provide the core of a laboratory text. We are also in the process of evaluating the reduction of harmful emissions from these microexperiments (*1*). The results of this latter work and an illustrated discussion of the microtechniques involved will be incorporated in an instructor's manual to accompany the new student text.

Microscale Organic Laboratory Experiments

Two reaction sequences which have been reduced to practice in our laboratory program are described. These experiments represent a variety of introductory transformations ranging from the classical to the rarely performed. In all cases the quantity of starting material does not exceed 150 mg.

The compelling arguments for undertaking the microapproach are as follows: (1) reduction of the scale of *starting material* by 100-fold (nearly 1000-fold in certain cases) leads to a parallel reduction in *organic solvents* required for these experiments. This contraction from the usual level (50–500 g) of solvent/student/experiment reduces the demands on the laboratory ventilation system (*1*); (2) regardless of the quality of a laboratory atmosphere, microscale reactions simply reduce student contact with toxic materials of all types; (3) the threat to laboratory safety from explosion or fire is largely eliminated; (4) the cost of chemicals parallels the 100- to 1000-fold reduction in use; (5) conversely, the very large reduction in chemical costs presents an opportunity to expand the available variety of experiments. Until the introduction of the microscale reactions, elimination of experiments based on cost has been a recurring theme over the past few years in this laboratory, and it appears that the complete elimination of the undergraduate introductory organic laboratory at many institutions is a likely response to advancing budgets; (6) the option of being able locally to synthesize adequate supplies of reagents and starting materials, not commercially available, for use in a particular experiment, is an additional bonus of the microapproach. If a relatively simple synthesis of the materials is available in the literature, a *multiple year supply* can usually be obtained from a *single synthetic preparation* (see experiment B: Preparation of an Aromatic Nitrile); (7) in our experience microglassware (Ace Glass, Inc.) (2) is considerably more durable than macro- or semimicro-ground glass equipment. This stability translates into lower laboratory breakage costs and, thus, is welcome news to students, whose costs for organic chemistry are already very high. It should be emphasized that, while commercially available microglassware kits (2) are attractive for programs undertaking full conversion to this scale of experimentation, many of the microscale experiments can be carried out utilizing ordinary organic laboratory equipment. For example, the Cannizzaro reaction described below can be run quite satisfactorily employing two 10 × 75-mm test tubes and one 12-mL centrifuge tube plus a Pasteur pipet (which can function both as a separatory funnel and as a means to transfer solutions); and finally, (8) we perceive a significant pedagogic advantage in this laboratory concept at the sophomore level. For example, the close relationship of the techniques required to those of analytical chemistry reinforces parallel laboratory programs at this stage

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