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An Integrated Synthesis Laboratory for the Sophomore Year

Integration of the various areas of chemistry through laboratory experience has been attempted in a variety of ways (*1–5*). We wish to report on an integrated synthesis laboratory for sophomores as part of a laboratory sequence required for the chemistry major.

This synthesis laboratory is a two-semester long sequence for which students register separate from the lecture course taken at the same time. Students registering for these laboratory courses have had general chemistry and are required to have concurrent or prior registration in the sophomore organic course. The laboratory is scheduled for one afternoon per week (4 hr) during a 13-week semester and is taught by faculty members assisted by junior or senior chemistry majors. The student assistants are used to help supervise the laboratory, to aid in instrument operation and instruction, and to assist in grading. During 1973–74, these courses were taught to 135 students in five sections during the first semester and to 110 students in the same number of sections during the second semester. One laboratory is used solely for these courses. The department has available two infrared and two visible-ultraviolet spectrophotometers and a JEOL-C60-HL nuclear magnetic resonance spectrometer. These are shared by the students in the synthesis courses with students in other upperclass courses. Students operate the instruments themselves with the exception of the nmr spectrometer; the faculty member or the student assistant obtains nmr spectra for the students. Special equipment in the laboratory includes two hot tube furnaces, four dc power supplies, an Abbé refractometer, two polarimeters, two glc instruments, and a kit of ball and socket ground glassware in each desk. Equipment such as vacuum pumps, stirring motors, additional ground glassware, and dry bags are available for the special project experiments.

Students are asked to purchase two laboratory manuals (*6, 7*) which serve to acquaint them with the theory associated with the experimental techniques and as a source of instructions for experiments performed. Each experiment assigned is accompanied by a set of "student notes" prepared by the instructor which enlarges upon some of the experimental directions given, explains in detail the chemistry, especially the mechanism, associated with each experiment and gives helpful hints and cautions when necessary. In addition, written material is distributed on areas such as spectroscopy, chromatography, and optical activity, and includes specific instructions for the operation of the instruments used.

Each laboratory period is begun with a short pre-lab discussion. The orientation to the principles is given one week ahead and laboratory tips about the experiment on the day the experiment is performed. We have settled upon a system requiring a written pre-lab report covering items such as important reactions and side reactions, purification steps, and pertinent physical constant data which is due before the experiment may be started. Recording of data as the experiment is performed is done in the laboratory notebook which is checked periodically. No post-lab reports are required.

One of the problems encountered in a laboratory such as this is to supply enough special laboratory equipment for all students in large laboratory sections. We have solved this problem by assigning a number of experiments as a block on a rotating basis. For instance, the preparation of anhydrous chromium chloride and potassium peroxydisulfate require special equipment which is available to us in limited numbers. By dovetailing these two experiments with the resolution of $Co(en)_3^{3+}$ and the dehydration of 4-methyl-2-pentanol, the limited number of hot tube furnaces and power supplies proves to be no problem. The students at times find it frustrating to be thinking about and doing more than one experiment at a time. However, the close simulation of this process to the type of planning that must take place in any research laboratory if efficient use of time is to be realized makes this a very useful experience.

Basic to the decision to make an integrated synthesis sequence part of the laboratory offerings, instead of the traditionally divided organic and inorganic laboratories, is the belief that all synthetic chemists need a background in the same basic techniques and theory. Using the syntheses of both organic and inorganic compounds as the means of education in the skills necessary for synthetic work allows for more efficient use of time and for a chance to break down in the students' minds the artificial categorization of compounds into these two traditional areas of chemistry.

Table 1. Outline of Compounds Synthesized

Semester I
1. Decane-1-d
2. 4-Methyl-1-pentene, 4-methyl-2-pentene, 2-methyl-2-pentene, and 2-methyl-1-pentene
3. Anhydrous $CrCl_3$
4. 3-Hydroxy-3-methyl-2-butanone
5. Styrene and polystyrene
6. Stereoisomers of $Co(en)_3^{3+}$
7. $K_2S_2O_8$
8. Acetylferrocene

Semester II
1. *cis*-4-Cyclohexene-1,2-dicarboxylic anhydride
2. *n*-Butyl bromide
3. *trans*-Stilbene
4. 2-Chloronaphthalene
5. *trans*-Benzalacetophenone
6. $Cr(OH_2)_6^{3+}$, $CrCl(OH_2)_5^{2+}$, and $CrCl_2(OH_2)_4^{+}$
7. $[Co(NH_3)_5Cl]Cl_2$ and $[Co(NH_3)_4CO_3]NO_3$
8. Special projects[a]

[a] See Table 3 for a listing of projects.

Table 2. Outline of Techniques

Separation and Purification	Purity and Structure Determination
1. Distillation	1. Melting point
a. Fractional	2. Boiling point
b. Steam	3. Refractive index
c. Vacuum	4. Specific rotation
2. Crystallization	5. Glc
3. Extraction	6. Infrared
4. Chromatography	a. Pure liquid
a. Thin layer	b. Solution
b. Dry column	c. Mull
c. Glc	7. Visible-Ultraviolet
d. Ion exchange	8. Nuclear magnetic resonance
5. Chemical resolution	

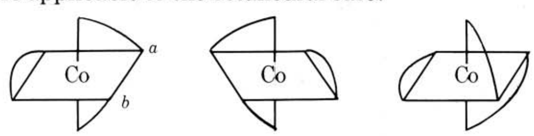
This paper was presented at the Conference on Laboratory Instruction in Chemistry, sponsored by IUPAC, held at Rensselaer Polytechnic Institute, June 10–12, 1974.

In selecting experiments to be performed in this laboratory (Table 1), we were guided by the following considerations

1) The basic skills involved in the separation and purification of products must be illustrated and developed (Table 2).
2) Modern methods of analysis for purity and of structure determination must be represented (Table 2).
3) Classic examples of important synthetic reactions should be a part of the students' experience.

Obviously, only the preparation of certain organometallic type compounds provides a truly integrative synthesis. However, the exclusive use of experiments involving this type of preparation represents an unbalanced introduction to synthesis so we chose to employ a number of experiments in which the products are easily identifiable according to traditional definitions. We chose rather to emphasize the integrative aspects involved in the techniques employed and the design necessary for a successful synthesis. Some of our experiments proved to be more successful than others in promoting integrative thinking on the part of the students and we are seeking to strengthen or replace those which we find are not as strong in this respect.

Perhaps the most successful experiment from an integrative viewpoint is the synthesis and resolution of $Co(en)_3^{3+}$. The separation of the enantiomers by chemical resolution using barium tartrate is accomplished with a minimal investment of time spent in crystallizations and the idea that configurational isomerism is not limited to compounds of carbon is clearly illustrated. In addition, the optically pure form can be readily racemized. While the mechanism by which such racemization occurs is unknown, the observation may be made that the Fischer transformation, which states that the interchanging of any two groups on a chiral carbon atom gives the enantiomer, is here applicable to the octahedral case.



I II III

The interchanging of the two groups at ligand sites *a* and *b* on I results in III which is identical with II, the mirror image of I, by a rotation of 180° about a vertical axis.

The preparation of acetylferrocene proved to be another successful integrative experiment. The use of ferrocene instead of the classical aromatic system such as benzene in a Friedel-Crafts reaction emphasizes the aromatic character associated with this type of organometallic based on the $4n + 2\pi$ election system stabilized by the metal-π bond interaction. Dry column chromatography provides a rapid separation of products, and the nmr spectra obtained are useful in demonstrating spin-spin splitting and in qualitatively estimating the percentage of diacetylferrocene present in the isolated acetylferrocene.

Few students obtain any experience with the use of electrochemistry in syntheses even though it is quite widely used commercially. The preparation of potassium peroxydisulfate serves to illustrate the utility of this process as a synthetic method. This experiment also allows for the demonstration of the importance of overvoltage to the success of electrolytic preparations. The nature of the electrode surface, the effect of temperature and current density, and the importance of a high concentration of reactant to overvoltage and hence to the success of the experiment is clearly shown. An added advantage of this preparation is that the students gain experience with one of the strongest oxidizing agents known.

The last five weeks of the second semester are allotted to a synthesis project selected from among a listing of suggested ones (see Table 3). These involve multi-step syntheses and the need to modify existing directions. This is an extremely well-liked and successful portion of the laboratory. Students are required to report the results of their projects in the form of a journal article. Instruction in the organization and writing style of a research paper is given and preliminary drafts are read and criticized by the instructors before the final draft is prepared. Some students felt that for persons not planning a career in chemistry the paper is unnecessary, but the majority considered it to be a worthwhile experience.

Table 3. Outline of Special Projects

1.	2-Carboethoxycyclopentanone
2.	Malonic ester and acetoacetic ester syntheses
3.	Amineboranes and halogenated amineboranes
4.	Dicyclopropyl ketone
5.	2-Alkylcycloalkanones via enamines
6.	Diols via photochemical reactions of ketones
7.	Benzoins via thiamine catalysis
8.	$[Co(en)_2mal]Br$ and $[Co(en)_2BHA]Cl$
9.	$[(C_6H_5)_3PCl]$ $[SbCl_6]$ and mesitylene tricarbonylmolybdenum(0)
10.	Tetraethyltin and dichlorodiethyltin

The laboratory overall is highly successful based on the performances and the reactions of the students on questionnaires. This is particularly pleasing to us as the majority of students in the class are oriented toward professional school, mainly medicine, and generally have a rather low opinion of the necessity of laboratory work. One notable example is that of the student who remarked, "It was for the most part fun; a lot of bitterness I had had about chemistry was removed." The bases of its acceptance by students appear to be

1) Synthetic chemistry is generally liked by students more than other types of laboratory activity. The excitement of "making compounds" seems to be an important factor in maintaining interest in the laboratory.
2) The courses provide an excellent milieu for the introduction of spectrophotometric techniques and other experimental methods.
3) A steady progression of independence in the laboratory is realized culminating in the special project. Students apparently feel they grow and become more comfortable in this type of laboratory experience.
4) The area of synthesis is integrated. Students begin to think more in terms of the problems associated with preparing a compound than with what kind of compound is being prepared.

It is difficult to judge how effectively thinking about chemistry is changed from a compartmental view to a unified one. One example serves to illustrate the potential which a laboratory like this has in achieving this, however. In the identification of $[Co(NH_3)_5Cl]$ Cl and $[Co(NH_3)_4CO_3]$ NO_3 by infrared spectroscopy, many students were both surprised and pleased to learn that the ammine and carbonato stretching frequencies are found in the regions associated with amines and carbonyl compounds! It appears that small incidents like this provide a steady atmosphere of decompartmentalization and a positive reinforcement of the idea that chemistry is really a unified whole and not a series of subdisciplines.

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