The Philosophy of Green Chemistry as Applied to the Microscale Inorganic Chemistry Laboratory

Zvi Szafran, Mono M. Singh, Ronald M. Pike*

Introduction

The advantages of using microscale chemistry in the laboratory are well known, especially in the area of Organic Chemistry (Mayo *et al.*, 1994). These include lower experiment costs, reduced exposure to potentially toxic materials, shorter reaction times, smaller waste disposal costs, and lower construction costs. These benefits are strongly applicable to the inorganic chemistry laboratory, where high chemical costs, toxicity issues and long reaction times often combine to ensure that many interesting experiments cannot be performed at all.

In addition, the growing emphasis in the academic sector on Green Chemistry also argues for the adoption of microscale methods. The simplest definition of Green Chemistry is "the use of chemistry techniques and methodologies that reduce or eliminate the use or generation of feedstocks, products, by-products, solvents, reagents, etc., that are hazardous to human health or the environment". (Anastas and Williamson, 1996). While more commonly being applied to industrial applications, the concepts of Green Chemistry should also be incorporated into laboratory pedagogy. The laboratory product, rather than being the industrial 10,000 lb/h of ethyl benzene, would be knowledge of a particular reaction mechanism. The application of Green Chemistry to this laboratory product would then be a modification of the reagents, solvents, experimental methodology and/or products to allow the gaining of this knowledge with the minimum hazard to human health or the environment.
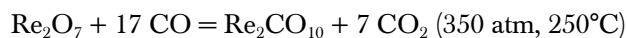
Several inorganic experiments (Szafran *et al.*, 1991) will be described to illustrate the advantages of conversion to the microscale level in development of a Green Inorganic Chemistry laboratory program.

## Modification of Reagents and Products

Metal carbonyls are one of the most important classes of organometallic compounds. They are usually prepared by the direct reaction of metals with carbon monoxide:

$$Fe + 5\ CO = Fe(CO)_5\ (200\ atm,\ 200°C)$$

or by the reduction of metal halides or oxides, again using carbon monoxide:

National Microscale Chemistry Center, Merrimack College.
315 Turnpike St. North Andover, MA 01845, USA.

$$Re_2O_7 + 17\ CO = Re_2CO_{10} + 7\ CO_2\ (350\ atm,\ 250°C)$$

These preparations are difficult to carry out in the instructional laboratory, due to the high toxicity of carbon monoxide, and the reaction conditions of high temperature and pressure. These laboratory hazards can be reduced considerably by a judicious choice of a metal system, allowing alternate reagents. Wilkinson's catalyst, $[RhCl(P(C_6H_5)_3)_3]$ is known to react with aldehydes or amides, abstracting a carbonyl group, resulting in the corresponding alkane or amine:

$$[RhCl(P(C_6H_5)_3)_3] + CH_3(CH_2)_5CHO =$$
$$trans\text{-}[Rh(CO)Cl(P(C_6H_5)_3)_2] + C_6H_{14} + P(C_6H_5)_3$$
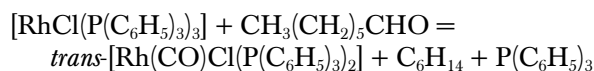
thus, resulting in the synthesis of a metal carbonyl. In the microscale experiment, $RhCl_3 \cdot xH_2O$ is reacted with triphenylphosphine and N,N-dimethylformamide (DMF) to form the metal carbonyl product:

$$RhCl_3 + 2\ (C_6H_5)_3P + HCON(CH_3)_2 =$$
$$trans\text{-}[Rh(CO)Cl(P(C_6H_5)_3)_2] + HN(CH_3)_2$$
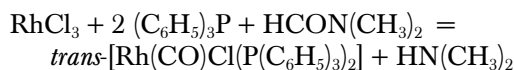
The reaction is readily carried out at reflux temperature (150°C) and atmospheric pressure, using a 10 mL roundbottom flask, microcondenser, and Hirsch funnel. While selection of the rhodium metal system would be prohibitively expensive at the standard laboratory scale (1g $RhCl_3 \cdot xH_2O$ costs $130 USD), the reaction can be easily carried out at the microscale level using 25-50 mg of rhodium chloride hydrate, resulting in a per student cost of $3-6 USD.

The product can then undergo oxidative addition (forming mer-$[Rh(CO)Cl_3\ (P(C_6H_5)_3)_2]$) or SO_2 adduct formation (forming $Rh(CO)ClSO_2\ (P(C_6H_5)_3)_2$), or be recycled to recover the rhodium.

In this way, microscale chemistry allows the Green Chemistry concept of feedstock substitution to be used, resulting in milder reaction conditions, and reduced environmental exposure.

Reduction of Exposure

One of the major advantages of microscale chemistry is the reduced quantity of chemicals−100 mg of solid, 1 mL of solvent are typical. Experiments can now be performed with materials that ordinarily are too expensive or might be considered too toxic to work with safely at the larger scale. The heavier elements within families are examples of such materials. Microscale chemistry therefore allows group

trends to be investigated more completely, using more than just the top triad of elements.

An example of such an experiment is in the investigation of the thermal properties of the Group IIA oxalate hydrates. These are prepared in the following manner:

$$MgO, CaCO_3, SrCO_3, BaCO_3 + HCl + (NH_4)_2C_2O_4 = MC_2O_4 \cdot xH_2O$$
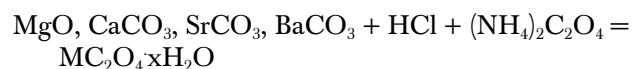
Normally, one would be reluctant to work with larger quantities of strontium or barium salts, but at the microscale level the reactions are carried out using only 25 mg of the starting compound. When analyzed by thermogravimetric analysis, the percentages of water are found to be approximately 22% (Mg), 12% (Ca), 11% (Sr) and 3.4% (Ba), corresponding to the magnesium oxalate being a dihydrate, calcium a monohydrate, strontium a monohydrate, and barium being a half hydrate.

More importantly, the thermal properties relating to decomposition of the group can be investigated. Oxalate hydrates decompose in three steps:

1. Loss of water to form the anhydride
   $MC_2O_4 \cdot xH_2O = MC_2O_4$ (anh) $+ xH_2O$
2. Loss of CO to form carbonate $MC_2O_4 = MCO_3 + CO$
3. Loss of CO_2 to form oxide $MCO_3 = MO + CO_2$

The temperatures at which these reactions occur show interesting periodic trends. The midpoint temperature for reaction 1 is 210°C (Mg), 208°C (Ca), 163°C (Sr) and 141°C (Ba), showing that the water of hydration is less tightly held as the metal cation gets larger. This is reasonable, as the charge/size ratio of the metal declines down the family, making the metal less polarizing. The midpoint temperature for reaction 2 shows no such trend, and remains nearly constant: 502°C (Mg), 519°C (Ca), 510°C (Sr) and 515°C (Ba). This is because the second decomposition is a function of the thermal stability of oxalate ion, which is not strongly correlated to the metal to which the oxalate is bonded. Finally, the midpoint temperature for reaction 3 is 502°C (Mg, lost simultaneously with CO), 806°C (Ca), 923°C (Sr) and 1100°C (Ba). Since carbonate is a soft ligand, one would expect it to be most strongly bonded to the softest metal. The softest metal would also be least favorable to form a stable lattice with the hard oxide ion.

This experiment also illustrates that modern analytical methods, such as thermogravimetric analysis, are inherently microtechniques, requiring only a few mg of material for analysis. From a Green Chemistry perspective, the product (which can be viewed as either the metal oxalate or as the knowledge of the thermochemical periodic trends) can be accomplished with extremely low exposures to the heavy metals.

Altered Solvents and Reaction Times

In Green Chemistry, one is not only concerned with the reagent and product, but also with solvents, byproducts, and other materials not incorporated directly into the product. Use of different solvents or reducing the quantity of solvent can sometimes have many beneficial effects-better laboratory air quality, lessened exposure to potentially toxic organics, reduced risk of fire or explosion, etc.

Microscale Chemistry reverses a trend that has occurred over the past 100 years toward using *more* solvent in laboratory reactions, to a level of 1 mL, on average. The larger surface area relative to bulk at the microscale level also gives a mass transfer advantage, leading to shortened reaction times. Typically, a microscale experiment can be performed in about 50% of the time required for a standard laboratory preparation.

An experiment that illustrates all these points is the synthesis of hexakis (4-nitrophenoxy)cyclotriphosphazene, a flame retardant material. The original synthesis (Bornstein, 1985) involved the preparation of potassium 4-nitrophenoxide from 4-nitrophenol and KOH in absolute ethanol. This was reacted with hexachlorotriphosphazene in xylene, using tetra-*n*-butylammonium bromide as a phase transfer catalyst:

$$(NPCl_2)_3 + 6\ KOC_6H_4NO_2 = [NP(OC_6H_4NO_2)_2]_3$$

Using a different solvent system (4 mL of THF replacing the xylene) and conversion to the microscale level reduced the time necessary for this experiment from the reported 16 hours of reaction time to 3.5 hours.

Conclusion

As can be seen from the above experiments, microscale chemistry and Green Chemistry coordinate with each other in a mutually beneficial manner, resulting in an enhanced inorganic laboratory program. ◪

References

Mayo, DW; Pike, RM; Butcher, SS; Trumper, PK *Microscale Organic Chemistry*, 3rd Edition, Wiley, New York, 1994.

Anastas, PT and Williamson, TC, *Green Chemistry. Designing Chemistry for the Environment*, ACS Symposium Series #626, American Chemical Society, Washington, DC, 1996, p. 2.

Experiments are fully described in Szafran, Z; Pike, RM; Singh, MM, *Microscale Inorganic Chemistry*, Wiley, New York, 1991.

Bornstein, J; Macaione, DP; Bergquist, PR, *Inorg. Chem.*, 1985, *24*, 625.