5.2: Reagant Concepts

Major Concepts

The opportunity to do chemistry by means of, for example, a fixed substrate is very much in keeping with the concepts that we are learning. We explored the functionality and power of packed-bed columns that do chemistry normally done in solution with dissolved solutes. A packed-bed reactor can provide a source of protons, ions, or other chemicals that can affect chemistry. An ion-exchange system can perform ion metathesis, i.e., substitute the anion (X^{-m}) in dilute salt system $(M^{+n})_m(X^{-m})_n$ for the anion enriched on the packed bed. Shown below is an example of the process of interest. The solute (a mixture of proteins) is loaded onto the exchanger and subsequently adsorbs to the carboxymethyl anion substrate (a porogen). This process is typically characterized as a facile equilibrium process in which the protein mixture can replace the sodium cations. UV absorbance can follow the overall displacement as shown in the graph at the lower right (1^{st}: Mes anion peak; 2^{nd} and 3^{rd} peaks are the desired protein chloride substance).

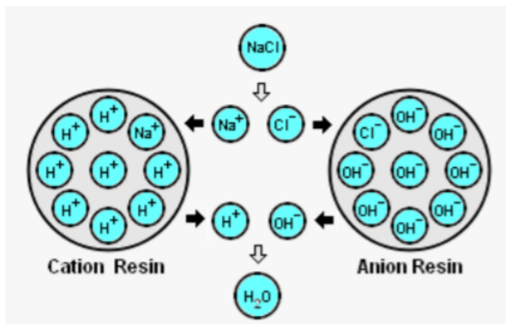

Figure 5.2.1: Shown is a simplified representation of the way metathesis occurs on cation and anion exchanging beds. The steps of the process are replacing the sodium cations for the positively charged hydrogens while simultaneously the chloride is replaced by the negatively charged hydroxides to lead to water. http://www.pharmaguideline.com/2014/09/mixed-bed-ion-exchanger-inpurified-water- system.html

Replacing Hazardous Substances

A common misconception in chemistry is that we should be vigilant only when we know we are working with a hazardous compound. In fact, all substances should be treated with the level of respect that they deserve. Even salt can be an irritant when used incorrectly. The most importance criteria to consider in the evaluation of the hazards of substances are the following:

- **Efficacy:** the alternative must carry out desired transformation with comparable or superior efficiency
- **Safety:** the alternative reagent should display reduced volatility, flammability, toxicity, and/or reactivity, as well as increased stability
- **Environmental impacts:** the alternative reagent should represent a reduced environmental impact

Each of the above three criteria may be used in the assessment of a compound with respect to hazard level. Obviously, efficacy must be emphasized or else there is no need to go any further with the replacement.

Inorganic and Organic Supports

Supports or scaffolds or templates represent a fixed medium for the express purpose of a targeted transformation. We will use the following paper (shown are title, authors, and abstract) for our discussion in this part of the chapter.

“Paper-immobilized enzyme as a green microstructured catalyst” Hirotaka Koga, Takuya Kitaokabc and Akira Isogaia; DOI: 10.1039/c2jm30759f

The facile and direct introduction of methacryloxy groups into cellulose paper was carried out using a silane coupling technique, leading to the improvement of hydrophobicity and both dry and wet physical strengths of the paper. Immobilization of lipase enzymes onto the methacrylate- modified paper was then accomplished, possibly due to hydrophobic interaction. The as-prepared immobilized lipase on methacrylatemodified paper possessed paper-specific practical utility. During a batch process for the nonaqueous transesterification between 1 phenylethanol and vinyl acetate to produce 1- phenylethylacetate, the paperimmobilized lipase showed high catalytic activity, selectivity and reusability, suggesting that the methacryloxy groups introduced into the cellulose paper played a key role in the hyperactivation of lipases. In addition, a higher productivity of 1-phenylethylacetate was achieved in a continuous flow reaction system than in the batch system, indicating that the interconnected porous microstructure of *the paper provided favorable flow paths for the reactant solution. Thus, the paper-immobilized enzyme is expected to offer a green catalytic material for the effective production of useful chemicals.*

What we note in this “paper” is the “smart” exploitation of paper as a porous microreaction chamber (interconnected paths) for a transesterification reaction between 1-phenylethanol and vinyl acetate to produce 1-Phenylethylacetate, as shown below:

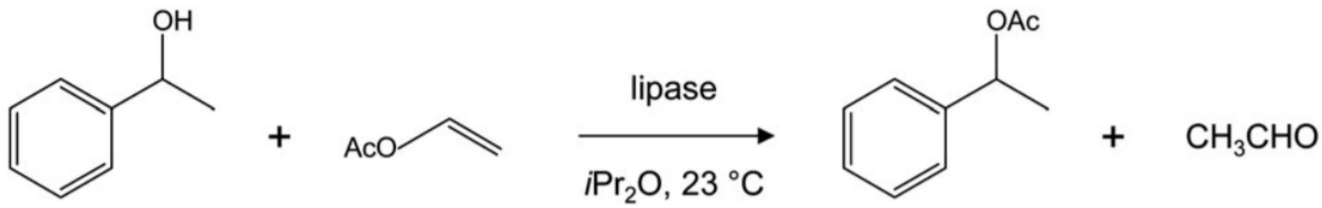

Figure 5.2.2: The reaction of interest (transesterification) on a solid support (cellulosic paper) between 1 phenylethanol and vinyl acetate that leads to the production of 1- phenylethylacetate. Reproduced from “Paper-immobilized enzyme as a green microstructured catalyst” Hirotaka Koga, Takuya Kitaokabc and Akira Isogaia; DOI: 10.1039/c2jm30759f

This research effort explores the opportunity to catalyze reactions of interest using natural catalysts (enzymes). In this case, lipase-catalyzed reactions (e.g., esterification, transesterification, aminolysis, acylation, and thio-transesterification) that can be carried out in nonaqueous media have been examined in the synthesis of many useful chemicals for food, cosmetic, pharmaceutical and biodiesel.

However, lipases are typically unstable in nonaqueous media due to aggregation, denaturation, or some other form of deactivation. Enzymes are often immobilized on supporting materials (silica, ceramics, carbon, resins) to provide reusability, isolation advantages, and stability in nonaqueous media. Their study offered a number of advantages for the use of this green system including the asymmetry of the final productcomposition:

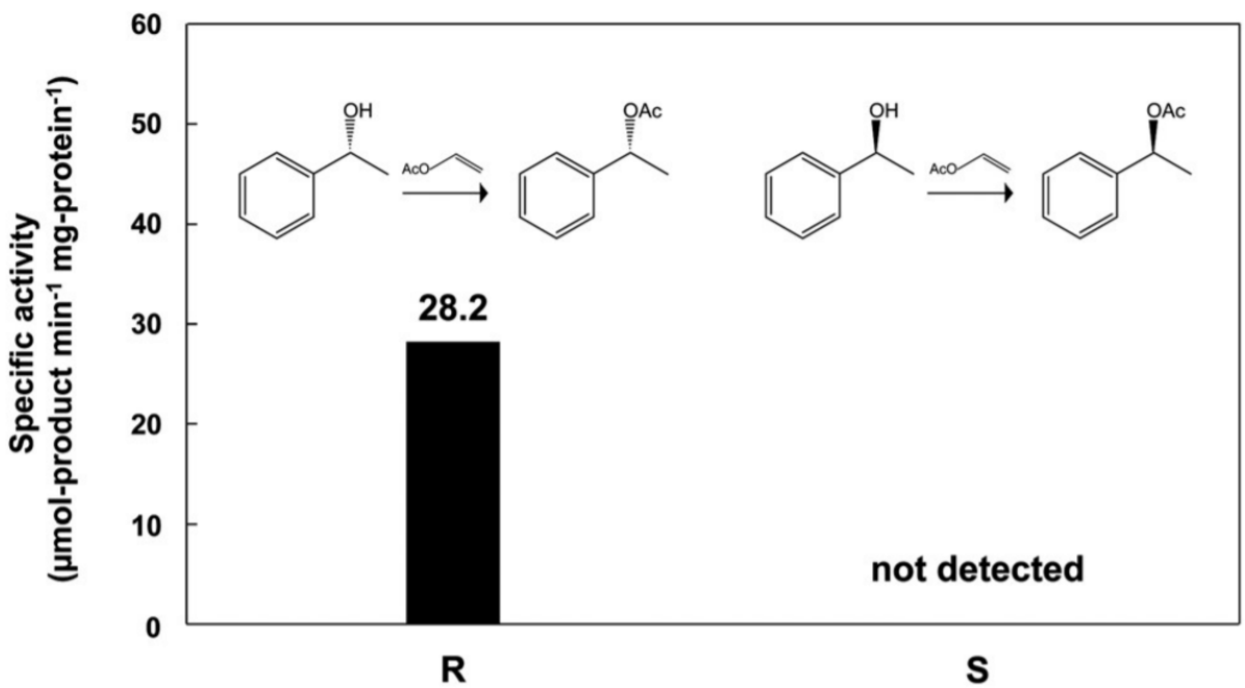

Figure 5.2.3: Enantioselectivity of immobilized lipase on methacrylate-modified Cellulose Whatman paper. Reaction temperature = 23 °C; stirring rate =150 rpm. Reproduced from “Paperimmobilized enzyme as a green microstructured catalyst” Hirotaka Koga, Takuya Kitaokabc and Akira Isogaia, DOI: 10.1039/c2jm30759f

Figure 5-3 shows that the paper-based system encourages the formation of the “R” enantiomer as opposed to the S (non-detected). Such a finding signals the value of a simple, facile, and highly conserved approach to an enantioselective and high yield (50%, 5 hrs.).