Sieck Research Interests

Since the advent of systematic chemistry, synthetic organic chemists have been striving to develop the synthesis of some of the most complex, and generally rare biologically molecules. These molecules have many uses, with the most important being their utilization as drug therapies. Some of chemists' greatest achievements include the synthesis of penicillin, prostaglandins, and the cancer chemotherapeutic drug, taxol. Synthetic organic chemistry has evolved and developed the necessary expertise, skills and technologies that if given the appropriate resources and time a team of chemists can synthesize any molecular target they desire; though this may not be the greatest use of resources. To continue to improve the field of synthesis, chemists need to develop ways to increase their efficiency on multiple levels, including atom economy (how many molecules are wasted in a typical synthesis) and human economy (time needed to complete work).

So how can we increase our efficiency? Chemists choose to synthesize a number of different biologically important molecules with multiple degrees of difficulty. There are simple molecules that can be prepared utilizing a few atoms, and there are large complex molecular targets. The small molecule is structurally simple and typically straightforward, and can be completed in a short period of time. The larger more complex molecules, take much more time and effort. Figure A demonstrates this phenomenon. In general as the complexity of a molecular target increases so does the number of steps it takes to put it together. The ideal synthesis would be to construct these complex targets in a few short steps (red line). This may not always be possible, as for any given target the current technology or toolbox of reactions available prevents the chemist from developing this short streamlined synthesis. Currently the only way to make this complex target is through a long and impractical synthesis (blue line). How do we overcome this problem? One solution, and central theme of my research is the development of new and more efficient reactions.

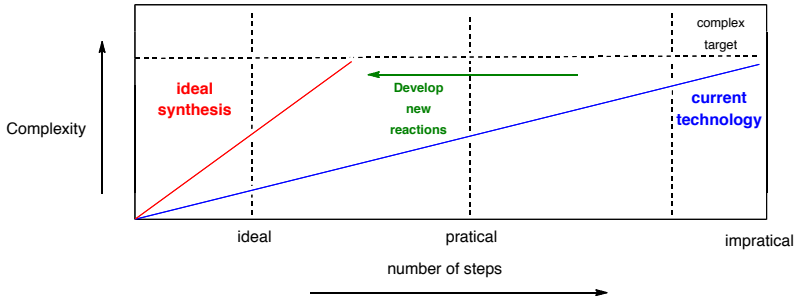

Figure A

One of the greatest challenges for synthetic chemists is the development of efficient, streamlined reaction processes towards useful chemical synthons, flexible building blocks. Chemistry relies on chemical commodities supplied by the petroleum industry. Today, more than ever, conservation of these natural resources is vital. Not only do chemical substrates we use for reactions in synthesis come from the petroleum feedstock, but so do the materials used to purify the products of such reactions (such as solvents and commodities used to carry out these procedures). By utilizing multi-component reactions, in which multiple transformations take place in a single reaction flask, we are able to generate complex chemical synthons necessary for many industries, while at the same time decreasing the number of purification steps and waste generated from such processes which in turn help preserve our natural petroleum resources.

This summer students in my lab have the choice of working on one of four projects. The first is the synthesis of a new class of phosphorus heterocycles known as thiol phosphonamidates. The second is the synthesis and characterization of chalcones via a microwave-irradiated aldol like condensation reaction. The third is the synthesis of secondary ketimines.

Synthesis of thiol phosphonamidates

Sulfur and phosphorous heterocycles have been shown to exhibit powerful biological activity. Ongoing research towards these heterocycles has been made significantly easier through the utilization of ring-closing metathesis.[1] We have begun to synthesize a new class of seven-member phosphorus heterocycles containing sulfur, and nitrogen to produce potentially biologically active molecules (Figure 1). We have successfully synthesized a general thiol phosphonamidate in high yield This summer we will focus on utilizing a variety of amino acids to produce substitution within the first nitrogen containing piece as shown in Figure 1.

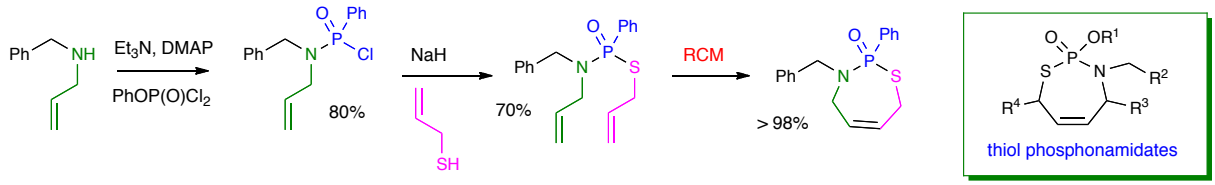

Figure 1: *Thiol phosphonamidates*

Synthesis of α-substituted chalcones

Recently we have developed an improved synthesis of α-substituted chalcones that utilizes microwave technology[2]. This project was spawned from our previous work with *N*-Acyl Nitrones. The chalcone, a fully conjugated bicyclic propenone, solicits extensive chemical study due to its ubiquity in nature and its potential for diversity-oriented synthesis (DOS).[3] As a common moiety in biologically active molecules, the chalcone has considerable agricultural, pharmaceutical, and synthetic application, as it composes essential building blocks of agrochemicals,[4] anticancer agents,[5] scavenging and chelating agents,[6] and various medicinal agents, including antiinflammatories[7] and PET scan imaging probes.[8] Thus, it is attractive to find facile and safe synthetic routes toward chalcones and chalcone derivatives, in order to produce more efficiently the biologically species. Despite the seemingly extensive exploration of chalcones and chalcone synthesis only a few studies have examined chalcone substitutions on the α,β-olefin.[9] Over the past 2 years we have developed an improved synthesis of α-substituted chalcones that utilizes microwave technology. We have utilized substituted benzoylacetonitriles and substituted aldehydes to produce an array (> 20) of crystalline α cyano-substituted chalcones in high yields (80-99%) with limited purification (Figure 2). We continue expand this methodology by investigation to various α-nitro and α-bromo substituted chalcones. Furthermore, we will continue to characterize these molecules via a number of spectroscopy methods. we will begin investigating the use of cyano chalcones for other synthetic applications.

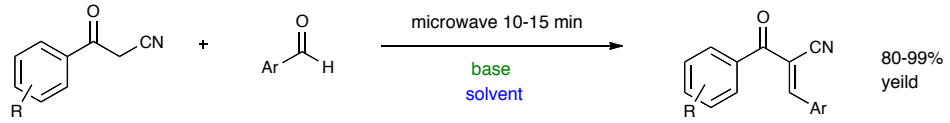

Figure 2: *cyano-substituted chalcones*

We continue to investigate the use of cyano chalcones for other synthetic applications including the synthesis of secondary ketimines. Other possible projects in the Seick lab include the synthesis of indoles and *N*-Acyl Nitrones.

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