1. **Nucleic Acid Chemistry**

We are developing new ways to investigate DNA and RNA structure. The method involves synthesizing nucleoside analogues that contain a probe group. IR and NMR spectroscopy is then employed to study the local environment around the probe which has been incorporated into DNA. Probes investigated so far include nitrile (CN) and azide (N$_3$) groups (Figure 1). The vibrational Stark effect can be used to measure the electric field if the Stark tuning rate of the probe is known. We have therefore collaborated with the Boxer group at Stanford to determine the tuning rate of a number of IR probes.$^1$ We are now collaborating with Scott Brewer in our department to further investigate the solvent and temperature dependence of the IR absorption band of several of these probe-containing nucleosides. An important part of this collaboration is modeling our experimental results utilizing DFT calculations.

![Figure 1. Nucleoside Analogues Containing Nitrile (CN) and Azide (N$_3$) Vibrational Probes.](image)

In order to use NMR spectroscopy to investigate DNA we are incorporating an $^{15}$N or $^{13}$C label into the nitrile group. In this way we can investigate the solvent and temperature dependence of $^{15}$N-NMR and $^{13}$C-NMR chemical shifts of the probe. These results will be compared to the IR peak shifts we observed and to DFT NMR shift calculations.

These nucleoside projects are an outgrowth of our earlier work on silatranyl- and germatranyl-nucleosides.$^{2-4}$ These atranes were designed to be transition state analogues for phosphoryl transfer reactions.

We gratefully acknowledge past support for our nucleoside research from the National Science Foundation and Research Corporation.
2. Molecular Knot Chemistry

Another project in our group involves the synthesis of molecular knots. This work involves a novel Thread & Cut method for knot formation. Synthetic targets include the world's smallest trefoil knot, the first non-DNA figure eight knot, and a polyethylene trefoil knot (Figure 2). The current published record for the smallest knot is an 80-atom trefoil prepared by the Sauvage group in France. Our small knot targets range in size from 63 to 78 backbone atoms. The figure eight knot is a particularly attractive target because of its unusual stereochemistry – it is a topological rubber glove. If successful, the figure eight knot produced will be only the second example of a chemically achiral molecule with this property. Finally, the polyethylene trefoil knot target is of interest because we can compare its polymer properties to that of linear and cyclic polyethylene. Further background about this aspect of our work is given below in a description aimed at a general audience.

Figure 2. a. Size limits on the trefoil, b. A figure eight knot, c. A polyethylene trefoil knot.

We gratefully acknowledge past support for our molecular knot research from Research Corporation and Franklin & Marshall College.

Why synthesize molecular knots?
Long, linear objects spontaneously form knots. Examples include electrical cords, hair, and molecules such as DNA and polymers. How do knots affect the structure of a material? A knot is known to weaken a rope and when stretched the breaking point is always at the entrance to the knot. Theoretical calculations suggest that the same is true of knotted polymer molecules, but this has never been tested experimentally. Furthermore, calculations strongly suggest that minute quantities of knots spontaneously form when polymers such as polyethylene are synthesized. Polyethylene is perhaps the most important plastic with an annual production of 40 million tons. Milk bottles, grocery bags, and pipes are made of polyethylene. The goal of one of our projects is to prepare a knotted version of a polyethylene molecule and test its
Thus, the knowledge gained in this work may eventually address the issue of why some grocery bags weaken and split open.

Polyethylene comes in different forms, but the basic structure is a long linear chain of carbon atoms, each with two hydrogen atoms attached. Recently, Noble Laureate Bob Grubbs of Caltech prepared and patented a cyclic version of polyethylene.7 This version has unusual properties that may prove useful. In terms of knotted polyethylene, this molecule is a chemical Holy Grail. Frisch and Wasserman8 first discussed it in 1961 and as recently as 1999 Sauvage et al. stated that, "the properties of a pure polymethylene knotted ring should be fascinating, although the synthesis of such a compound seems to be presently out of reach."9

3. References (undergraduate coauthors denoted with an asterisk*)


