Our two main research interests are vitamin B\textsubscript{12} and the B\textsubscript{12}-dependent enzyme reactions and the bioinorganic chemistry of vanadium complexes. This year our research efforts have become more medicinally focused, which is reflected by the change in the name of our group. Of the \sim\textsubscript{15} vitamin B\textsubscript{12}-dependent enzyme reactions known, two of these reactions, involving methionine synthase and methylmalonyl-CoA mutase, occur in humans. In the former reaction, the vitamin B\textsubscript{12} derivative methylcobalamin is an intermediate in the methylation of homocysteine by methyl-tetrahydrofolate. A current “hot topic” in the medical literature is the recently demonstrated relationship between high serum levels of homocysteine and a greatly increased risk of strokes or heart attacks. In addition, there is increasing evidence that individuals with high serum levels of homocysteine are more likely to develop neurological disorders. This year we have begun to collaborate with Dr Andrew McCaddon and his research team in Wales, who are interested in the relationship between aberrant B\textsubscript{12} metabolism and Alzheimer’s disease.

Last year we decided to embark upon a completely new area of research for us: vanadium chemistry. This is finally beginning to pay off, and we now have some exciting results concerning the types of complexes formed between vanadium(III) and carboxylates. This is discussed in more detail below.

This year has also been one of much change with respect to personnel. In January, Dr Robert Doyle from Trinity College, University of Dublin, took up a one-year postdoctoral position, and in March, Dr Fiona Fry from Monash University took up a similar position. Dr Ling Xia left us in March to take up a postdoctoral position in the GlaxoSmithKline research team. Sam Brodie from Massey University, New Zealand, joined us for ten weeks on a summer vacation scholarship from November 2001–February 2002.

In July, Dr Brasch travelled to Europe and gave invited lectures at the University of Sheffield and the Inorganic Coordination Chemistry Conference (ICCC) in Heidelberg, Germany. Recently, Dr Brasch accepted a tenure-track appointment at the Department of Chemistry, Kent State University, USA, commencing in January 2003.

Using Vitamin B\textsubscript{12} as a Drug Carrier

Targeted drug delivery, as opposed to systemic delivery, can dramatically increase drug efficacy while minimizing the side effects associated with administering high doses of drugs in a non-strategic manner. Targeted delivery requires loading drugs onto molecular vehicles. This requires that the drug be directly conjugated to, for example, targeting proteins, vitamins, cytokines or antibodies. Vitamin B\textsubscript{12} and its derivatives have very efficient intestinal absorption and cellular uptake mechanisms. Vitamin B\textsubscript{12}/peptide and vitamin B\textsubscript{12}/protein bioconjugates have already been shown to have applications in the uptake of both peptides and proteins administered orally. Over the past year we have synthesised a number of vitamin B\textsubscript{12} bioconjugates for the enhanced transportation of drugs. (with R.P. Doyle)
Further Investigations on the Reaction between Methylcobalamin and Cyanide

We have re-investigated the cause of the $^1$H NMR spectroscopy chemical shift changes observed for the reaction between methylcobalamin and cyanide and found that cyanide actually binds at the lower (axial) site of methylcobalamin, rather than simply forming an association complex. (with S.J. Brodie, A.G. Cregan, and R. van Eldik [U. Erlangen-Nuremberg, Germany])

Determination of Activation Parameters for the Reaction between Coenzyme B$_{12}$ and Cyanide

The mechanism of the reaction between coenzyme B$_{12}$ and cyanide has been a topic of much discussion in the B$_{12}$ literature over several decades. Recently we proposed a mechanism in which a water molecule plays an important role in assisting Co-C heterolytic bond cleavage. Determining activation parameters for Co-C heterolysis provides us with a novel way to further probe our proposed mechanism for this process, and confirmed that a solvent molecule is indeed involved in the transition state of Co-C bond cleavage. (with A.G. Cregan, and M.S.A. Hamza, R. van Eldik [U. Erlangen-Nuremberg, Germany])

Studies on the Interactions of Vanadium(III) with Acetate

Ascidians of the suborder Phlebobranchia are small marine animals that sequester vanadium(V) from seawater and reduce it to vanadium(III). How or why these creatures accumulate this metal ion is unknown. In addition, the chemistry of vanadium(III) itself, especially in aqueous systems, is poorly defined compared with that of vanadium in the more stable oxidation states of +4 and +5. Our studies of vanadium(III) complexes have commenced with the acetate ligand, since it is used as a buffer in the isolation of compounds from ascidian blood cells, in addition to being a simple model for amino acids. X-ray diffraction studies of V(III)-acetato complexes isolated from aqueous solution have to date shown that at least two cationic complexes are formed. The first compound is a tetranuclear species with a ratio of acetate:vanadium of 1:1, while the second salt isolated shows an acetate:vanadium ratio of 2:1, with a trinuclear core. A titration study by $^1$H NMR spectroscopy clearly demonstrates the presence of a 2:1 species in solution, as well as the existence of a second species with a lower acetate:vanadium(III) ratio. (with A.J. Edwards, F.H. Fry)