Biomedical Polyhedral Borane Chemistry

The traditional use of organic chemistry as the mainstay of all aspects of contemporary biomedical chemistry has provided truly miraculous results. However, advances in the closely related area of aromatic polyhedral borane chemistry (polyhedral ions, carboranes, metallacarboranes, metallaboranes and other heteroatom derivatives) has now provided the basic discoveries necessary for the assembly of a totally new set of biomedically unique structures and reactions for immediate use. Thus, while some polyhedral borane derivatives may be employed across the wide spectrum of biomedicine in much the same way as organic compounds, the former species present unusual chemical, biochemical and physical properties which provide enhanced and often unique performance. More importantly, totally new biomedical applications as well as novel solutions to old problems emerge. In short, polyhedral borane chemistry provides an additional set of opportunities to assist medical science by utilizing a surrogate for carbon chemistry. Notable biomedical applications of this emerging chemistry impinge upon such representative topics as positron emission tomography (PET), enzyme impervious agents for radioimaging and radiotherapy, new drug delivery agents for targeting the cell nucleus, use of the cytotoxic boron-10 neutron capture reaction for cancer (BNCT) and arthritis (BNCS) therapies, new drug and diagnostic agent delivery vehicles based upon multivalent cell-targeted unimolecular nanoparticles (closomers and liposomes) and the design and synthesis of catabolism-proof structural modules for incorporation in new pharmaceuticals. These and other related topics are presently under investigation in the Hawthorne Laboratory. An example of the continuing development of one such subject which involves tumor imaging is presented immediately below.

Metallacarboranes and Related Species as Radionuclide Carriers for Antibody- Mediated Tumor Diagnosis and Therapy

Metallacarboranes derived from the transition metals represent a large family of aromatic borane derivatives which, when equipped with a radiometal, are potentially useful in radioimaging and radiotherapy of tumors. The radiometallacarborane may be localized in tumor by a tumor cell-selective antibody molecule to which it is attached or by other means (biomolecule, liposome). A particular advantage of radiometallacarboranes in these applications is their extraordinarily great kninetic stability and invisibility to enzyme systems which normally degrade organic radiometal carriers (chelates) with release of the radiometal in an unwanted way. The space-filling model shown below is a representation of a radiometallacarborane utilizing a generalized Co^{3+} nucleus and the Venus Flytrap ligand system which is, in turn, connected to a tumor-selective antibody. Use of ^{55}Co, a positron emitter, is under investigation for application as a positron emission tomography (PET) agent. PET is extraordinarily useful in diagnosis. Other radioimaging systems based upon the invincibility of aromatic boranes to enzyme attack involve simple radioiodination of the ubiquitous *nido*-7,8-$C_2B_9H_{12}^-$ ion and its derivatives. This is a facile process and the iodine remains fixed to the boron atom to which it is bound. These and other useful systems are described in M. Frederick Hawthorne and Andreas Maderna, "Applications of Radiolabeled Boron Clusters to the Diagnosis and Boron Neutron Capture Therapy of Cancer," *Chem. Rev.*, *99*, 3421 (**1999**). The use of radionuclides which emit alpha or beta particles would be useful as therapeutic agents against cancer and work of this type is also underway.

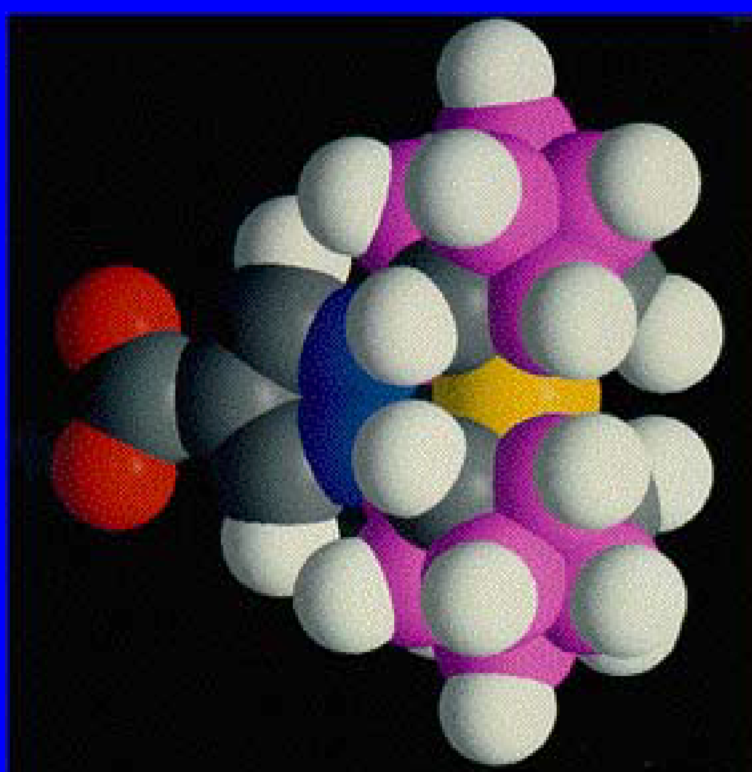

Figure 1. The Co complex of the Venus Flytrap ligand carrying a carboxyl group for conjugation with a biomolecule such as an IgG monoclonal antibody targeted for cancer cells.

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