
NIH

Johnston

AIDS VACCINE TRIALS HALTED

INFECTIOUS DISEASES: Lack of efficacy leads NIH and Merck to stop testing

RESEARCHERS HAVE VOWED to push on after clinical trials of a leading HIV vaccine candidate were halted because an independent monitoring board found that the vaccine is ineffective. The vaccine is made by Merck & Co., which was funding the clinical trials along with NIH's National Institute of Allergy & Infectious Diseases (NIAID).

The Merck vaccine, known as V520, was considered one of the most promising in development. "We share the disappointment of the research and HIV communities," said Peter S. Kim, president of Merck Research Laboratories, when disclosing the outcome. "Sadly, developing an effective AIDS vaccine remains one of the most challenging tasks facing modern medicine." Groups including the International AIDS Vaccine Initiative and the AIDS Vaccine Advocacy Coalition expressed similar views but encouraged researchers to keep working.

"It's important that we not equate the failure of one product with failure of a concept," says Margaret I. Johnston, director of the vaccine research program in NIAID's AIDS Division. Several classes of vaccines are in development, and V520 is among about 30 individual vaccines being studied. Instead, Johnston says, it's prudent to learn from the Merck trial to improve future studies. According to Kim, Merck will look at the trial data closely and share them with other vaccine efforts.

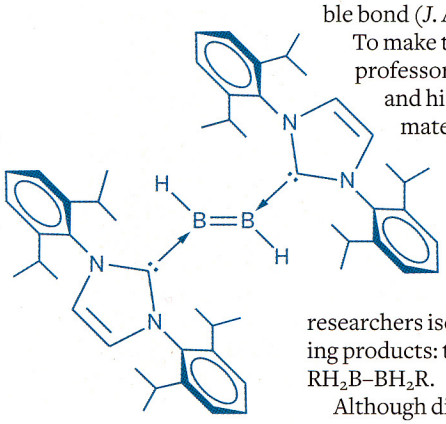
V520 consists of *gag*, *pol*, and *nef* HIV genes delivered in a type 5 adenovirus vector. Designed to stimulate a CD8 T-cell-based immune response, the vaccine didn't prevent infection or reduce the amount of virus in people who did become infected. In 2003, VaxGen, a now nearly defunct South San Francisco-based biotechnology company, reported that its subunit vaccine, using the gp120 HIV surface protein to generate an antibody response, failed to show efficacy in Phase III trials.

Researchers continue to take a variety of tacks to generate T-cell, antibody, or combined responses. "Antibody vaccine approaches are an absolute top priority," Johnston says. "Most people believe we will need a broadly neutralizing antibody to prevent infection. No one ever considered that these T-cell vaccines would be a final goal, but maybe an interim measure until we crack the antibody problem."—ANN THAYER

NEUTRAL DIBORENE IS A FIRST

MAIN-GROUP CHEMISTRY: Unexpected compound's boron-boron double bond confirmed by calculations

A TEAM LED BY Gregory H. Robinson was trying to make a compound with a boron-boron triple bond using solution-phase chemistry. That didn't quite work out. But they got something else that will shed some light on multiple bonding: the first stable, neutral compound containing a boron-boron double bond (*J. Am. Chem. Soc.*, DOI: 10.1021/ja075932i).



To make this "diborene," Robinson, a chemistry professor at the University of Georgia, Athens, and his coworkers synthesized a new starting material: $RBBr_3$, in which R is a bulky N-heterocyclic carbene ligand. The chemists treated this compound with a reducing agent (potassium graphite, KC_8) in diethyl ether, hoping to make RB≡BR. But instead, the potassium liberated hydrogens from the solvent, and the researchers isolated two crystalline hydrogen-containing products: the diborene RHB=BHR and the diborane $RH_2B–BH_2R$.

Although dianions containing a B=B bond have been reported by other groups, no one previously had been able to get two boron atoms to form a double bond in a stable, neutral molecule.

It's "a major development in the chemistry of the main-group elements," comments inorganic chemist Alan H. Cowley of the University of Texas, Austin. Chemist Jerry L. Atwood of the University of Missouri, Columbia, agrees, noting that "this is the type of fundamental discovery that will find its way very quickly into textbooks."

The neutral diborene's B=B bond distance is 1.560 Å—considerably shorter than the single boron-boron bond in the corresponding diborane $RH_2B–BH_2R$ and also shorter than the B–B distance in some dianions that purportedly contain a strong B–B π bond, the Georgia researchers note.

The doubly bonded nature of the diborene's B=B bond is supported by theoretical studies carried out by Robinson's chemistry department colleagues R. Bruce King, Henry F. Schaefer III, and Paul v. R. Schleyer.

The carbene ligands are key to the diborene's B=B bond, Robinson points out. The divalent carbon atom of each carbene donates its two free electrons to form a carbon-boron bond, allowing the boron's three valence electrons to form a bond to hydrogen and a σ and a π bond to the other boron.

As far as making a stable boron-boron triple bond is concerned, that's still on Robinson's "to do" list. After all, the only molecule known with a bond of this type had to be prepared at cryogenic temperatures in a frozen argon matrix.—RON DAGANI