THE NEWSMAGAZINE OF THE CHEMICAL WORLD

CHEMISTRY HIGHLIGHTS 2002

December 16, 2002

Volume 80, Number 50

CENEAR 80 50 pp. 40-41

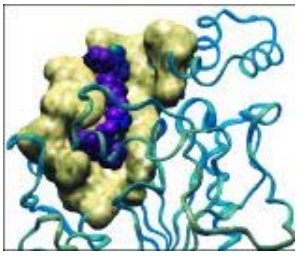
ISSN 0009-2347

BIOCHEMISTRY

STU BORMAN, C&EN WASHINGTON

Stephen D. Kinrade and Ashley Gillson of Lakehead University, Thunder Bay, Ontario, and Christopher T. G. Knight of the University of Illinois,Urbana-Champaign (UIUC), found the first direct evidence for production of an organosilicate complex by a living system, a diatom [*J. Chem. Soc., Dalton Trans.*, **2002**, 307; C&EN, Feb. 11, page 27]. They believe the discovery could jumpstart a new field: silicon biochemistry.

K. Barry Sharpless of Scripps and coworkers devised in situ click chemistry--the use of biological or supramolecular recognition sites as templates to promote selective reactions--and used the technique to identify the most powerful inhibitor of the enzyme acetylcholinesterase ever found [*Angew. Chem. Int. Ed.*, **41**, 1053 (2002); C&EN, Feb. 11, page 29].



CLICK Model of inhibitor (purple) in the active site of acetylcholinesterase, similar to an inhibitor found experimentally by Sharpless and coworkers using in situ click chemistry. SCRIPPS RESEARCH INSTITUTE

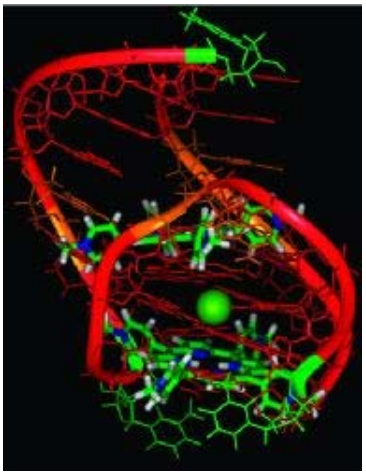
Using nuclear magnetic resonance (NMR) relaxation techniques, Dorothee Kern of Brandeis University and coworkers for the first time detected motions of an enzyme's amino acid residues during an enzyme-catalyzed reaction [*Science*, **295**, 1520 (2002); C&EN, Feb. 25, page 9].

Only a handful of naturally occurring fluorinated compounds have been identified, and how they are biosynthesized has been a mystery. David O'Hagan of the University of St. Andrews, Scotland, and coworkers helped solve that puzzle this year by identifying the first-known fluorinase enzyme [*Nature*, **416**, 279 (2002); C&EN, March 25, page 11].

Using chemical genetics--a technique in which small organic molecules are used to determine protein mechanisms and functions and identify

useful forms of bioactivity--Stuart L. Schreiber of Harvard University and coworkers discovered a previously unknown glucose signaling pathway in yeast that may be related to a human diabetes-related pathway [*Nature*, **416**, 653 (2002); C&EN, April 15, page 15].

A "Trp-cage miniprotein"--a 20-residue peptide that folds into a 3-D conformation as if it were a larger protein--was designed and characterized by Niels H. Andersen and coworkers at the University of Washington, Seattle [*Nat. Struct. Biol.*, **9**, 425 (2002); C&EN, April 29, page 24]. A second group found the observed fold could be reproduced by molecular dynamics [*J. Am. Chem. Soc.*, **124**, 11258 (2002)], and a third found that the miniprotein folds in only four microseconds--making it the fastest folding proteinlike system known
[*J. Am. Chem. Soc.*, **124**, 12952 (2002)].



QUAD **The first direct evidence for a G-quadruplex (shown) in a human gene was found by Hurley and coworkers.**
HARIPRASAD VANKAYALAPATI/U OF ARIZONA

Proximity ligation, a technique that uses polymerase chain reaction to identify and quantitate proteins, was developed by Ulf Landegren and coworkers at Uppsala University, Sweden [*Nat. Biotechnol.*, **20**, 473 (2002); C&EN, May 6, page 43]. They used it to detect a few tens of zeptomoles (40×10^{-21} mol) of platelet-derived growth factor.

Floyd E. Romesberg, Peter G. Schultz and coworkers at Scripps used directed evolution to convert DNA polymerases--which normally catalyze DNA synthesis--into mutant enzymes that efficiently catalyze RNA synthesis instead [*Proc. Natl. Acad. Sci. USA*, **99**, 6597 (2002); C&EN, May 20, page 37].

There were believed to be just 20 genetically encoded amino acids in mammalian cells, with a few organisms also using a 21st. But Joseph A. Krzycki, Michael K. Chan, and coworkers at Ohio State University discovered a 22nd (l-pyrrolysine) in a methane-producing microbe [*Science*, **296**, 1459 and 1462 (2002); C&EN, May 27, page 13].

The first ribozymes that catalyze the joining of RNA to protein were developed by David P. Bartel's group at the Whitehead Institute for Biomedical Research, Cambridge, Mass. [*Proc. Natl. Acad. Sci. USA*, **99**, 9154 (2002); C&EN, June 24, page 31].

A group led by Hiroaki Suga of the State University of New York, Buffalo (SUNY Buffalo), devised an efficient and inexpensive new route to nonnatural proteins [*Nat. Biotechnol.*, **20**, 723 (2002); C&EN, July 1, page 21]. A ribozyme they developed catalyzes transfer of nonnatural amino acids from donor molecules to specific tRNAs, which can then incorporate the amino acids into proteins.

The mechanism by which bacteria biosynthesize enediynes like C-1027 and calicheamicin has been uncertain, but Ben Shen and Jon S. Thorson of the University of Wisconsin, Chris M. Farnet of Ecopia Biosciences, Montreal, and coworkers showed that the enediyne cores of both drugs are biosynthesized by a common polyketide pathway [*Science*, 297, 1170 and 1173 (2002); C&EN, Aug. 19, page 12].

The first direct evidence for a G-quadruplex (a boxlike DNA conformation) in a human gene was obtained by Laurence H. Hurley and coworkers at the University of Arizona, Tucson [*Proc. Natl. Acad. Sci. USA*, **99**, 11593 (2002); C&EN, Sept. 2, page 9]. The study helps confirm quadruplexes as valid targets for drug design.

Bruce A. Garetz of Polytechnic University, Brooklyn; Allan S. Myerson of Illinois Institute of Technology, Chicago; and coworkers found that polarized laser radiation can be used to direct amino acid crystallization toward one polymorphic form over another [*Phys. Rev. Lett.*, **89**, 175501 (2002); C&EN, Oct. 21, page 16].

Ketone groups incorporated biosynthetically into bacterial cell walls provide chemically reactive sites for surface attachment of a range of nonnatural compounds [*J. Am. Chem. Soc.*, **124**, 9018 (2002); C&EN, Aug. 5, page 11]. The technique, developed by Shin-Ichiro Nishimura of Hokkaido University, Sapporo, Japan, and coworkers, has implications for vaccine design and studies of bacterial surface interactions.

And nanocircles of synthetic DNA that mimic the enzyme telomerase's ability to lengthen telomeres (chromosome end-caps) were developed by Eric T. Kool of Stanford and coworkers [*Proc. Natl. Acad. Sci. USA*, **99**, 15953 (2002); C&EN, Nov. 25, page 18]. The nanocircles could make it possible to grow long-lived normal human cell lines for research.

Top
