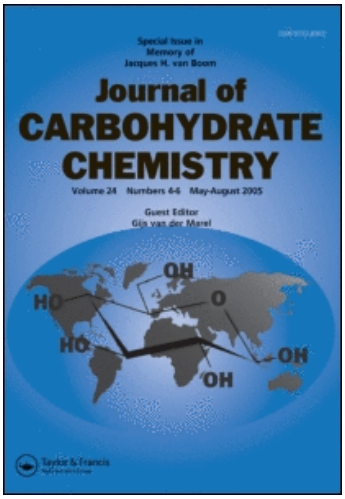

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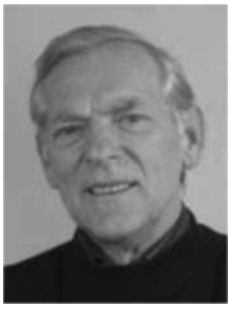

On July 31, 2004, Prof. Dr. Jacques H. van Boom, professor emeritus in Bio-organic Chemistry at the Leiden Institute of Chemistry and one of the most influential Dutch scientists of the last 25 years, died at the age of 67 after a short period of illness.

Jacques H. van Boom (1937) got his doctor's degree cum laude in 1968 at the University of Utrecht, with Professor Arens, on research led by Dr. Brandsma. After a period as postdoctoral researcher with Lord Todd at the University of Cambridge—for which he received a Ramsay Memorial Fellowship—he worked at Leiden University from 1970 as a researcher (1970–1975), a lecturer (1975–1978), and since 1978 as holder of the chair of Bio-organic Chemistry. In June 2002 he was given emeritus status at the age of 65 and was appointed as a research advisor to the Faculty of Mathematics and Natural Sciences.

Throughout his scientific career, Jacques van Boom devoted his skills as a bioorganic chemist to contribute to our understanding of processes revolving around what he liked to call the 'central dogma' in biology. Early on he realized the tremendous power of organic chemistry as a means to deepen our understanding of the complex biologic interactions that are at the basis of life. As the processes within the central dogma—transcription, translation, protein synthesis, and metabolite processing—all involve various biopolymers

and their interactions, the basic aim in his research was to prepare fragments of these and their synthetic analogs. In the selection of his research objectives he always felt that, rather than pursuing the synthesis of complex molecules, the prime objective of the organic chemist should be to create compounds with unique properties—properties that facilitate biophysical and biologic research and that cannot be obtained otherwise. In general, he followed a three-pronged strategy. First, he would select a specific process to which he would apply his synthetic skills. For this he assembled a wide international network of collaborators active in diverse biologic disciplines. Second, he would determine the synthetic technology required for the preparation of the target compounds. Since, in many cases, such methodology was not known at that time, at least not for general implementation, he and his research team ended up developing new methodologies themselves and have thus contributed to important general synthetic strategies. Third, the target compounds would be prepared in useful quantities and with high purity and evaluated in the proper context, and in collaboration with the aforementioned partners.

As the basic information of life is stored in DNA, Jacques van Boom started his independent research career with the pursuit of synthetic strategies toward DNA oligomers. Nowadays DNA synthesis is a highly standardized, automated process, and oligomers of up to a 100 nucleotides can be ordered from many companies. At the time Jacques van Boom became active in the field, in the middle of the ’70s, the successful synthesis of even small DNA oligomers entailed a tremendous scientific challenge. Jacques van Boom maintained a preeminent position in the area of DNA synthesis by the development of a series of new phosphorylation techniques, the most prominent of which is his modification of the phosphotriester method. With this ‘van Boom’s phosphotriester modification,’ it was, for the first time, possible to synthesize DNA fragments both on a large scale and in an automated, solid support fashion. Indeed, this method has been the method of choice for a number of years, up until the phosphoramidite methodology came to the forefront. The in-house strategy gave van Boom an important edge in the field, and he provided the scientific community in the ’70s and early ’80s with literally hundreds of synthetic oligomers, with which many exciting discoveries have been made. One highlight, achieved in collaboration with Alex Rich (Massachusetts Institute of Technology, Boston, USA), is the first single atom structure of a defined DNA duplex and the discovery, based on this, of Z-DNA as a new type of duplex DNA. Another highlight is the elucidation of the mode of action of the DNA-targeting antibiotic bleomycin, in collaboration with Sidney Hecht (University of Virginia, Charlottesville, USA).

In the early ’80s, at the pinnacle of his fame as a nucleic acid chemist, Jacques van Boom realized that for him to remain an important figure in bioorganic chemistry, a change from monodisciplinary research to multidisciplinary research was essential. He widened his horizon and tackled many synthetic

challenges involving the preparation of oligomeric fragments of the other biopolymers, peptides, and carbohydrates, but also hybrid structures thereof (nucleopeptides, glycosylated nucleotides) and compounds able to interfere with their biosynthetic assembly (enzyme inhibitors). Several highlights follow.

In collaboration with the Dutch biochemist Piet Borst (Netherlands Cancer Institute, Amsterdam, The Netherlands), a program aimed at the evaluation of the role of a specific glycosylated nucleobase, denominated J (beta-glucosylated 5-hydroxymethyl-deoxyuridine), as present in the genome of the human pathogen *Tryptanosoma brucei* (the causative of the African sleeping sickness), was started. Synthetic J and oligonucleotides of which J is a structural element proved to be invaluable in the generation of specific polyclonal antibodies. With these, not only detection of the presence of small amounts of *T. brucei* is possible, but also the presence of the J modification in other human pathogens of the *Kinetoplastida* family was discovered.

In collaboration with Eckard Wimmer (State University of New York, Stony Brook, USA), a breakthrough in our understanding of the replication mechanism of the poliovirus was achieved. Key to this study proved to be the accessibility of homogeneous uridylylated oligopeptide fragments. In itself, the chemical synthesis of peptide nucleic acid fragments of the complexity required for these studies, with the many synthetic hurdles that are caused by the incompatibility of standard peptide synthesis and nucleic acid synthesis protocols, represents a milestone in the oeuvre of Jacques van Boom and a hallmark in bioorganic chemistry.

An early highlight in the area of glycobiology comprises the development of a synthetic vaccine against *Haemophilus influenzae* type b (Hib), the causative of pneumonia and meningitis. Indeed, with this research executed in the end of the '80s and beginning of the '90s, van Boom proved to be far ahead of his time. In collaboration with the Dutch institute for environmental and health studies (RIVM), synthetic strategies for the preparation of oligomers of the Hib capsular polysaccharide were developed. With conjugates of these, and the immunogenic response they elicit, infant monkeys were protected successfully against Hib infections. At that time, the strategy was abandoned, primarily because there was no interest from industrial partners (who did not believe in the economic viability of synthetic vaccines) for further development. However, very recently a highly similar strategy has led to a successful synthetic conjugate vaccine against Hib, which is now applied in Cuba. (In fact, the synthetic strategy toward the synthetic oligosaccharide is essentially that reported by van Boom.)

Of more fundamental importance to the synthetic glycobiology community are the pioneering efforts in the assembly, on a solid support, of synthetic oligosaccharide fragments. The automated solid-phase synthesis of oligosaccharides and glycoconjugates of any desired length and nature, with the ease now

customary for oligonucleotide and oligopeptide synthesis, is one of the holy grails in contemporary organic chemistry. In recent years, many research groups have moved in this direction; however, we are far from solving this challenge. The first report that aims at solving this problem describes research by van Boom and coworkers on the use of polyethylene glycol as carrier in a solid-phase synthesis of a galactofuranose oligomer. This striking early example was carried out many years before other oligosaccharide synthesis groups dared to enter the arena of solid-phase-assisted oligosaccharide assembly.

Another hallmark with fundamental implications is the discovery, also in the early '90s, of a set of activator systems that turn thioglycosides into effective donors for oligosaccharide assembly. At that time anomeric thioethers were regarded as suitable temporary protective groups because of their intrinsic stability toward many synthetic conditions. With the development of suitable thiophilic promoter systems, thioglycosides can now be employed as donor or acceptor in oligosaccharide synthesis, thereby markedly reducing the complexity of the synthesis of many oligosaccharides and glycoconjugates. The original report describing this advent is one of the most cited papers in modern carbohydrate chemistry, and the thioglycoside methodology is, with the possible exception of the trichloroacetimidate procedure, the most widely explored and applied strategy for the assembly of oligosaccharides and glycoconjugates, both in solution and on the solid support.

Jacques van Boom has reached his eminent position in bioorganic chemistry through a combination of utter dedication to research, complete confidence in his ability to recognize potential in his students, and his remarkable intuition in selecting his research objectives. His devotion to research was well known in the Netherlands, where he was famous for neglecting to be at institutional management meetings. To date, the term 'van Booming' describes not showing up at specific meetings, and on the rare occasions he did appear, a more-than-usual awareness of other colleagues present indicated that an important decision might be in the making. Jacques van Boom presided over both the intellectual and internal well-being of his pupils and did not shy away from menial tasks. He took it upon himself to distill most of the essential solvents that, apart from taking away this labor from his students, provided him with the necessary excuse to leave those board meetings he did get caught up in. Further, he presided over the preparation of coffee for the whole laboratory, and he regarded coffee making as a continuous extraction process, which required only the addition of some extra coffee beans at certain times.

Jacques van Boom has supervised more than 60 Ph.D. students and numerous postdoctoral fellows, many of which have reached eminent positions, both within the Netherlands and abroad, and both in academia and in industry. Roberto Crea, a postdoctoral fellow in the mid '70s, has had a major impact on the evolvement of Genentech as a leading Biotech

company by the establishment of an automated DNA synthesis facility. Peter Burgers, an early Ph.D. student, became interested in molecular biology in later years and is now professor at Washington University, St. Louis, USA. Geert-Jan Boons, Ph.D. student in the mid '80s, is professor in glycobiology in Athens, Georgia (USA). Stan van Boeckel, who defended his thesis in the beginning of the '80s, continued his career at the leading Dutch pharmaceutical company, Organon, where he became group leader at an early age. The highlight in his career is the development (together with Maurice Petitou) of the anticoagulating agent Arixtra (recently marketed), a synthetic heparin pentasaccharide. Jan de Rooij, another early Ph.D. student, ended his career as head of scientific research of the Dutch-British food giant Unilever. With Stan van Boeckel and Jan de Rooij, many other former students of Jacques van Boom found their way to the Dutch chemical and pharmaceutical industry, next to Organon and Unilever also Diosynth, Solvay Pharmaceuticals, Philips, Akzo Nobel, and DSM. Others have found employment at prominent Dutch research institutes, universities, and university hospitals, where they are active in many different research areas, not only in organic and bioorganic chemistry, but also in homogeneous catalysis, inorganic chemistry, and biochemistry. Thus, Jacques van Boom has made a large impact on chemistry-based scientific research both in the Netherlands and abroad.

Curriculum Vitae of Prof. Dr. J.H. van Boom

Date of Birth	May 14, 1937, Simpelveld
Scientific Career	1959: Propaedeuse Chemistry, University Utrecht 1965: Master of Science in Chemistry, University Utrecht 1968: Ph.D. (cum laude), University Utrecht Title thesis: Base catalyzed isomerisations and eliminations in four and six π-electron systems 1968–1969: Ramsey-Memorial Fellow with Prof. Lord Todd and Dr. C. B. Reese (Cambridge, England) 1970–1975: Scientific staff, Leiden University 1975–1978: Associate Professor in Organic Chemistry, Leiden University 1978–2002: Professor in Organic Chemistry, Leiden University 2002–2004: Scientific advisor, Faculty of Sciences, Leiden University
Awards	1975: Gold Medal of the Royal Dutch Chemical Society (KNCV) 1981: Fellow of the Royal Dutch Academy of Sciences (KNAW) 1985: Royal Shell Award 1999: Simon Stevin Master Award (STW) 2000: AKZO Nobel Science Award