AJAY KUMAR BOSE

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AJAY KUMAR BOSE

(1925 – 2010)

Elected Fellow 1981

AJAY KUMAR BOSE, an internationally known organic chemist, expired on February 12, 2010. He lived a full life, one that was filled with achievements and honors. He was a dedicated teacher, a respected scientist, and a complete gentleman.

FAMILY BACKGROUND

Ajay Kumar Bose was born on February 12, 1925 at Silchar (Assam). He was the eldest amongst his eight brothers and sisters. His father, Dr Abinash Chandra Bose, was a respected Vedic Scholar and Professor of English Literature. His mother, Amita Kumari (Chanda) Bose, was a well known contributor of literary articles to Bengali magazines. Besides his mastery of English, Ajay was fluent in Marathi, Bengali, and Hindi. He also had a working knowledge of German and French. He was home schooled up to the age of eight. He received his BSc (1944) and MSc (1946) degrees from Allahabad University. He was always the top student in his class. In 1947 he joined the Massachusetts Institute of Technology (MIT) on a Govt. of India 'Overseas Scholarship'; he received his ScD degree in 1950 working under the supervision of Professor John C. Sheehan. He was an 'A' student in all courses that MIT required of doctoral students in Chemistry. His doctoral thesis dealt with a new synthesis of *beta*-lactams through the internal cyclization of substituted acetamidomalonates. In 1950-1951 he worked as a Fellow at Harvard University in Professor RB Woodward's laboratory. Ajay's topic of research at Harvard dealt with the synthesis of steroids. Prof. Woodward later received the Nobel Prize in chemistry. Ajay spent another year (1956-1957) as a Post-doctoral Research Associate in Charles C Price's laboratory in the University of Pennsylvania where he worked on the phthaloylation of amino acids under mild conditions that did not affect the stereochemistry of the chiral center.

After two years (1957-1959) as a research scientist in Upjohn Company, Kalamazoo, Michigan, Ajay joined the Stevens Institute of Technology as an Associate Professor in 1959 and retired from this Institute as a Professor in 2007.

PROFESSIONAL CAREER

Indian Institute of Technology, Kharagpur, India

Lecturer and Assistant Professor – 1951 – 1956

Stevens Institute of Technology, Hoboken, NJ, USA

- Associate Professor - 1959 - 1961
- Professor - 1961 – 1983
- George Meade Bond Professor - 1983 – 1996
- Professor - 1996 – 2007
- Emeritus Professor - 2007 - 2010

SCIENTIFIC CONTRIBUTIONS

Ajay was a dedicated scientist. He dealt with several areas of organic chemistry with distinction and left an indelible mark on each of them. During his six decades of active research career, he published approximately 300 scientific papers, guided 35 Ph. D. students and mentored about 100 post doctoral chemists from different parts of the world. He was the author of two books on the Chemistry of *beta*-lactams and related *beta*-lactam antibiotics. He also contributed several chapters to many edited books. He was a frequent lecturer in various national and international scientific meetings in this country and abroad.

It is difficult to summarize the voluminous work that he produced. He had assembled a dedicated group of workers from different parts of the world and provided them with 'state of the art' facilities. A list of publications emanating from his group is appended to this article; the list speaks for the variety of areas that he covered during his scientific investigations. Some of his major contributions are summarized below:

(a) Chemistry of beta-Lactams (Azetidin-2-ones)

In 1950, Ajay completed his doctoral dissertation, titled "A New Synthesis of *beta*-lactams" under the supervision of Prof. Sheehan at MIT. Since then, he carried out extensive research studies in this field, developing new syntheses of this heterocycle, 6-epi-penicillin and its various analogs. He was the plenary speaker at the 5th International Congress of Heterocyclic Chemistry, lecturing on "Cephalosporins, Penicillin and Other *beta*-lactams." Ajay and his coworkers published more than 110 research papers in the field of *beta*-lactam chemistry. No other academic or industrial laboratory has as many publications on *beta*-lactams, an important structural unit of penicillin. Ajay became an expert in the synthesis of *beta*-lactams and Penicillins, and a reaction (the Bose Reaction) is named after him; this reaction has been widely used to synthesize new types of penicillin related antibiotics. A high point of his career was reached in 1968 with his total synthesis of 6-epi Penicillin V Methyl Ester. The key reaction in this synthesis was the use of "Bose Reaction" (*beta*-lactam ring closure by the cyclo-addition of azidoacetyl chloride with an appropriately substituted thiazoline). This reaction has been widely used in other academic and industrial laboratories.

(b) Microwave-induced Organic Reaction Enhancement

A new field of microwave chemistry was initiated by the publication of two seminal papers by Gedye and coworkers and by Giguere and his group in 1986. These two papers demonstrated that a variety of organic reactions could be completed in minutes instead of hours when conducted in sealed glass or Teflon vessels with microwave irradiation. Starting in 1990, Ajay and coworkers have published a series of significant papers in this field under the title of Microwave-induced Organic Reaction Enhancement (MORE) chemistry. This approach involves reactions in open vessels with a limited amount of polar solvents such as acetonitrile or dimethylformamide, in order to avoid any explosion. This facile methodology has been used for the synthesis of a variety of complex heterocycles of biological interest. The application of microwave techniques followed by mass spectroscopic analysis of samples provided rapid structure characterization of reaction products.

In 2006, Ajay reported a novel aspect of microwave-enhanced chemistry, "Cold microwave chemistry: synthesis using pre-cooled reagents." This technique provides selectively the information about the first intermediate in a multiple step reaction. Comparison of the normally conducted reaction and the one using cold-microwave technique can provide an insight into multiple-step reactions.

In the area of peptide biochemistry, the application of microwave-assisted reactions has been limited. Recently, Ajay co-authored several papers in collaboration with Dr. BN Pramanik, his former student now working for Merck and Co, on the use of microwave technology combined with mass spectrometry to accelerate the structural analysis of proteins and peptides. They demonstrated for the first time (2002) that using this novel approach, digestion of proteins occurred in minutes, in contrast to the hours required by conventional methods. This work is being used by scientists in academic and industrial laboratories throughout the world. These methods were further extended to the structural analysis of linear and cyclic peptides using Akabori hyrazinolysis reactions.

In brief, Ajay and his group had made significant contributions to new and important fields of research and trained several hundred students. His notable contributions were in the synthesis of biologically active molecules, introducing modifications in the use of spectral analysis to obtain rapid structural information, and the study of stereochemistry of a variety of natural products.

(c) Instrumentation and Techniques

Ajay had considerable interest in the use of modern instrumentation including mass spectrometry and nuclear magnetic resonance spectroscopy. In the area of mass spectrometry, he acquired one of the first high resolution magnetic sector mass spectrometer in the State of New Jersey in mid 1960s. He also implemented chemical

ionization mass spectrometry (CIMS) by the acquisition of a single stage quadrupole mass spectrometer in 1970 following its introduction, by Field and Munson in 1966. Ajay published a series of papers on the structural analysis of polar organic molecules and natural products (penicillins, cephalosporins, alkaloids, carbohydrates, steroids, peptides, lipids) using CIMS. One of the significant contributions is the use of salts such as ammonium chloride, ammonium carbonate, sodium chloride to form ammoniated and sodiated molecular ions. In many cases, the relative abundances of the molecular ions were enhanced significantly. This was the first report of the use of salts in mass spectrometry, (Anal. Biochemistry, 1978). This methodology has been widely used in FAB, PD, and ESI-MS techniques.

(d) Stereochemistry of Natural Products

Ajay was active in determining the stereochemistry of natural products. Using the principles of conformational analysis supported by spectral studies, he explored the conformation of carvomenthol;. verbenols, pinocampheols and pinocarveols. Tropane alkaloids, morphine alkaloids, rauwolscine, and alloyohimbine were also elaborated. Conformation of several terpenoids were also established on the basis of their dipole moments and proton NMR analysis using shift reagents.

He also explored the absolute configuration of monosaccharides using molecular rotation principles by assigning priorities to the substituents attached to chiral centers. Chemical transformations in conjunction with spectral data were extensively used to establish the absolute configuration of yohimbine; several indole, vinca, and cinchona alkaloids; as well as pimeric acid and its derivatives.

In a joint project with Prof. MMD Bokadia of Ujjain University the structure and stereochemistry of Lyratol, a new C-10 alcohol from *Cyathocline lyrata*, was established in Ajay's laboratory using NMR data. Optical Rotatory Dispersion and Circular Dichroism were also used to establish the configuration of some tetralones. Ajay also collaborated with Dr. Harkishan Singh in establishing the structure of some heterosteroids synthesized via the Schmidt Reaction on cholestanone derivatives.

(e) Biosynthetic Studies

Another area of investigation that attracted Ajay's attraction was the biosynthesis of natural products. His approach was primarily based upon the incorporation of stable isotopes, such as C-13, N-15, and/or D in the natural products and study them using NMR and mass spectrometry. This obviated the use of radio-active isotopes that required special handling and extraordinary laboratory facilities but provided comparable results. Using this methodology he investigated such sensitive molecules as gliotoxin. This cyclodipeptide incorporates a disulfide bridge in the heterocyclic ring. Using stable isotopically labelled phenylalanine and serine, Ajay

proved that these amino acids were incorporated in the gliotoxin molecule. He proved that the methylenedioxy carbon in phlebiarubrone was supplied by the labelled amino acid precursors. The terpene biosynthesis was also reinvestigated using stable isotope precursors. Because he made extensive contributions to the biosynthesis of natural products by using non-invasive techniques, he was invited to serve as a Consultant to the Human Reproduction Unit of the World Health Organization.

SPECIAL PROGRAMMES

(a) UPTAM Programme

One of Ajay's favorite programmes that he instituted at Stevens in 1972 and continued till his retirement was the UPTAM (Undergraduate Projects in Technology and Medicine) programme. This summer programme was designed to attract superior science students and initiate them to chemical and medical research so that they are sufficiently motivated to compete in graduate schools, medical schools, and in industry. This programme proved to be highly successful. All alumni who participated in this programme either entered top graduate schools or medical schools in different parts of the country. Several of the participants continued with their projects during the academic year without any monetary compensation. This way they could complete their undergraduate theses. Their diplomas mentioned the award of the degree 'with Thesis'.

In course of time this programme was expanded with funding from the National Science Foundation, industry, and some philanthropic organizations. The mentoring of the participants was undertaken by Stevens's faculty, professors at neighbouring Medical Schools, and scientists at interested research organizations.

Later this programme was expanded to include talented local high school students. Enterprising science teachers worked with them in the laboratory. Trained teachers were permitted to borrow the equipment from Stevens, under 'equipment of the month club' scheme, for use in their laboratories.

The projects selected for the participants were such that the students could finish them in a day and would be helpful in their science classes. The impact of these programmes is difficult to measure, but they undoubtedly touched the lives of many young student.

(b) Chemical Biology Enhancement Programme

Ajay was the Founder and Director of the Chemical Biology Enhancement Programme at Stevens, a programme that received a one million dollars grant (1988–1993) through a country-wide competition sponsored by the Howard Hughes Medical Institute. This programme was used to develop courses and research for popularizing the study of Chemical Biology. Since then, it has become customary for

most of the students at Stevens, who are interested in careers in biomedical field, to major in Chemical Biology.

(c) Bioactive Substances from the Indian Ocean

From 1984 to 1991, Ajay was the American Principal Investigator of a two million dollar collaborative Indo-US Project on "Bioactive Substances from the Indian Ocean". Central Drug Research Institute, Lucknow, Bose Institute, Calcutta, and Regional Research Laboratory, Goa were the participating laboratories from India. This programme was directed towards a search for novel anti-cancer and anti-viral compounds from marine natural products. This project was formally approved after direct contact between Ajay and the then Prime Minister of India, Mrs. Indira Gandhi.

(d) Cooperative programme with Polish Academy of Sciences

The Polish Academy of Sciences invited collaboration between their Institute of Organic Chemistry in Warsaw and Ajay's group at Stevens Institute of Technology. At the suggestion of the National Research Council of the National Academy of Sciences (USA), Ajay visited Poland in May 1990 and developed plans for collaborative research in the *beta*-lactam field. In 1994 and 1995, Ajay and several of his colleagues lectured at various Institutes in Poland, bringing newly emerging technology (*e.g.* chemometrics, neural networks, microwave-induced enhancement of chemical reactions, as well as *beta*-lactam chemistry) to the attention of Polish chemists. A number of scientists and students from Poland spent time at Stevens in an exchange programme under this plan.

(e) Visiting Scientists Programme

Securing funds from the industry, Ajay established a 'Visiting Scientists Programme' in the Department of Chemistry at Stevens. In this programme, eminent scientists from different institutions were invited to spend a semester in the Chemistry department. They were required to give special lectures in the field of their expertise and participate in research projects if they so choose. Some of the renowned scientists who participated in this programme were: Dr. Max Tishler (USA), Dr. UK Pandit (Holland), Drs. Nityanand and Sukhdev (India), Dr. JD Bu'lock (England), Dr. Ahmed Mustafa (Egypt), and Dr. S Oae (Japan) to name a few. This programme was immensely successful and was heavily attended by scientists from the neighbouring industry as well as by research personnel from Stevens.

AWARDS AND HONOURS

Professor Bose received many awards as a teacher as well as a scientist. Some of them are listed below:

1968 Ottens Research Award for the 'Total Synthesis of Penicillin' [illegible] Institute of Technology (SIT).

1981 Elected Fellow of the Indian National Science Academy.

Davis Research Award for the synthesis of *beta* - Lactam Antibiotics. (SIT)

1983 Appointed to the George Meade Bond Chair in Chemistry. (SIT)

1987 The first Henry Morgan Distinguished Teacher Award. (SIT)

1989 Faculty Recognition Award of the State of New Jersey.

1990 New Jersey Professor of the Year Award (Council for the Advancement and Support of Education and the Carnegie Foundation of Education)

Outstanding Achievement Award of the Federation of India America Association.

1992 New Jersey State Senate resolution in recognition of contribution to science and education. Citation: "...for the academic alliance between Stevens Institute and the inner-city schools of Union City, New Jersey with 93% minority student population.'

Jess H. Davis Research Award for Microwave-induced Organic Reaction Enhancement Chemistry. (SIT)

1995 Ranbaxy Science Foundation Award for Research Excellence in Pharmaceutical Sciences. This award was for new methods developed for the efficient synthesis of pharmaceuticals.

1997 Catalyst Award of the Chemical Manufacturers Association.

National Award for excellence in chemistry teaching.

Camille and Henry Dreyfus Foundation Award (to encourage disadvantaged students to enter chemical sciences) of the American Chemical Society.

1999 United States Presidential Award for excellence in Science, Mathematics, and Engineering Mentoring.

Certificate of 'Special Congressional Recognition for outstanding and invaluable service to the community'.

2006 Recipient of Life Time Achievement Award of the Indian Chemical Society.

2007 Emeritus Professor of Chemistry (SIT).

Membership in Academic and Scientific Organizations

American Association for the Advancement of Science (since 2004)

Indian National Science Academy (since 1981)

New York Academy of Science (since 1970)

Sigma Xi Research Honor Society (since 1950)

American Chemical Society (since 1950)

Counselor of the North Jersey Section of American Chemical Society (1964–1970)

American Chemical Society Lecture (several times)

New Jersey Academy of Science (Chairman of several Lecture Sessions)

Education Committee of the New Jersey Health Science Group

External Review Committee of the University of Medicine and Dentistry of New Jersey (for 12 years)

Editorial Board of the Journal of Heterocyclic Chemistry (for two years)

Because his health was failing, Ajay took retirement from Stevens in 2007 and settled in Easton, Pennsylvania. In spite of his handicap, he continued to help his former students in their research problems and to edit their manuscripts. Discussion of chemistry and reading of chemical literature were one means for his relaxation. He enjoyed horseback riding and Indian cooking. For diversion he occasionally engaged himself in gardening, especially flowers.

Professor Bose is survived by his two brothers Ashish and Arvinda (Oru) and sister Anubha; wife Margaret (at the end of this year they would have celebrated their 60th wedding anniversary); sons Ryan, Ranjan, Rajendra; daughters Indrani, Indira, Krishna; and twelve grandchildren.

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