Professor Albert Padwa

A Tribute

Albert Padwa was born in New York City on October 3, 1937. He obtained both his B.A. and Ph.D. degrees from Columbia University studying the internal hydrogen transfer reactions of organo hypochlorites with Cheves Walling. After a NSF Postdoctoral Fellowship with Howard Zimmerman at the University of Wisconsin in 1962–1963 working in the area of organic photochemistry, he was appointed Assistant Professor of Chemistry at the Ohio State University in 1963. He moved to SUNY Buffalo in 1966 as an Associate Professor and was promoted to Full Professor in 1969. In 1979 he accepted the William Patterson Timmie Chair of Chemistry at Emory University.

Al has won a number of awards such as a Sloan Fellowship, a John S. Guggenheim Foundation Fellowship, an Alexander von Humboldt Senior Scientist Award, a NATO Fellowship, a Fulbright Hays Fellowship, the Southern Chemist Award of the Memphis Section of the ACS, the Stone Award of the ACS, the Herty Medal of the Southeast American Chemical Society, the Florida Award of the ACS, the Senior Scholar Award of the International Society of Heterocyclic Chemistry (1999) and the ACS Arthur C. Cope Scholar Award (2000). He was a Japan Society Promotion of Science (JSPS) Research Fellow (1984) and was named the Emory University Teacher/Scholar in 1988. He also has been a Humboldt Visiting Fellow at the University of Würzburg, Germany, a BASF Visiting Guest Professor at the University of

Kaiserslautern, Germany, a Visiting Professor at the University of Claude Bernard, France, a Visiting Professor at the University of Peking, China, the Rayson Huang Visiting Lecturer at the University of Hong Kong, a Guggenheim Visiting Professor at both the University of California at Los Angeles and Berkeley, and a Fulbright Hays Fellow at the Imperial College of Science in London.

He has been a member of the Editorial Board of the Journal of the American Chemical Society (1984–1987), the Journal of Organic Chemistry (1981–1985 and 1996–2000), Reviews of Chemical Intermediates (1976–1980), the Internet Journal of Chemistry (1997–present), and Organic Letters (1999–present). He has also has served on the Medicinal Chemistry NIH panel (1976–1980) and the ACS Petroleum Research Fund Advisory Board (1990–1992), and was the Chairman of the Gordon Conference on Heterocyclic Chemistry (1983). Al Padwa has been a Volume Editor for Organic Photochemistry (Vols. 4–11), Dipolar-Cycloaddition Chemistry, Synthetic Applications of Cycloadditions toward Heterocycles and Natural Products (Wiley), Comprehensive Heterocyclic Chemistry, Edition 2, and the Synthesis of Science, Vol. 27, series. He has served as an Alternate Councilor (1978–1985) as well as Chairman of the Organic Division of the ACS (1985–1986), and has been the President of the International Society of Heterocyclic Chemistry (1994–1996). More recently he was one of the distinguished Novartis Chemistry Lecturers in 2001.

Research Interests

Albert Padwa's early research was concentrated on the photochemical transformations of small-ring heterocycles. His work in the 60's and 70's was directed toward an understanding of the reaction mechanism associated with the photochemistry of epoxy-cyclopentenones, aryl-substituted pyrones, bicyclic aziridines, nitrogen- and sulfur bridged bicycles, and novel chromenes and isochromenes. Simultaneously with Huisgen, he was able to demonstrate that photolysis of the aziridine ring represents a convenient source of azomethine ylides. Al Padwa was one of the first to demonstrate that photochemical methods can be used to generate synthetically useful reactive intermediates derived from heterocyclic compounds. In particular, his group demonstrated that the photolysis of strained small-ring compounds can be used as a method for generating nitrile ylides, carbonyl ylides, vinyl carbenes and nitrenes. His studies dealing with the photochemistry of azirines established the involvement of the 1,1-stepwise cycloaddition reaction, whereby a nitrile ylide can behave as an imino carbene. His series of papers dealing with the intramolecular dipolar cycloaddition of substituted azirines led to a major development in the utilization of this reaction in total synthesis.

Most of the above studies were performed prior to 1980 and established his ability to contribute work of importance to the areas of photochemistry, reaction mechanisms, and the chemistry of reactive intermediates derived from heterocycles. However, he is probably best known for his work in the area of heterocyclic cycloaddition chemistry which was initiated in the late 70's. His book on "*Dipolar Cycloaddition Chemistry*" published in 1984 has been heavily cited and represents the most authoritative source in the field. His research program in this area involves a broadly based study of the chemistry of a variety of dipoles. These include azomethine ylides, nitrile ylides, nitrilimines, nitrile oxides, diazo compounds, azides, nitrones, and more recently carbonyl ylides. Through his efforts it has become apparent that the 1,3-dipolar cycloaddition reaction represents an extremely important method for the preparation of five-membered heterocyclic rings. His research group has also been extensively involved in the development of new methods for the formation of 1,3-dipoles and their utilization in synthesis. Some of the new methods used involve the desilylation of methoxysilyl-amines to generate unstabilized azomethine ylides, addition of hydroxylamines to alkynes to produce nitrones, ring opening of oxaziridines, extrusion of carbon dioxide from nitrogen heterocycles, and the addition of carbenes to nitriles and ketones. There was an intense study in his laboratory using nitrone cycloadditions to allenes as a method for generating alkaloid precursors. The base-induced rearrangement of 5-nitro-isoxazolidines was developed as a novel method for producing lactams. Silyl- substituted thioimidates were used as nitrile ylide equivalents. A variety of cycloalkenones was generated from the intramolecular cyclopropanation reaction of furanyl diazoketones. Higher-order dipolar cycloaddition processes were studied in some detail.

Ylide formation as a result of carbene interaction with an unshared electron pair of a heteroatom represents a major contribution to organic synthetic methodology. Very little was known about the interaction of metal carbenoids with carbonyl groups before Padwa's work in this area. His 1988–1998 series of papers in *The Journal of the American Society* and *The Journal of Organic Chemistry* established the importance of this method for the synthesis of a wide variety of heterocycles and alkaloids. After having demonstrated the scope and generality of the process, Padwa also applied the tandem cycloaddition reaction to the synthesis of a variety of natural products. His work in this area has shown that the reaction of diazoketones with transition metals such as rhodium(II) carboxylates represents a particularly powerful method for generating synthetically useful electrophilic hetero-carbene complexes. Through a series of papers in the early to mid 90's he has illustrated that the cyclization reactions of diazo-alkynyl substituted ketones represent a powerful method for preparing many complex heterocycles. More recently, he has extended this method toward the generation of isomünchnones, which represent an under-utilized class of mesoionic compounds. These dipoles were produced via a metal-catalyzed cyclization of a series of diazoimides, which when treated with Rh(II) catalysts, undergo the tandem cyclization–cycloaddition process in extremely high yield. Through the use of this protocol he has been able to provide a very short and convergent synthesis of a variety of alkaloids. His group demonstrated that the isomünchnone class of mesoionic compounds offers the possibility of constructing several uniquely different heterocyclic systems from a common intermediate. A similar application using thio-isomünchnones has also been carried out and represents another important method for use in the total synthesis of alkaloids. Some of the early work is summarized in a 1991 *Accounts of Chemical Research* article and in recent *Chemical Reviews* and *Tetrahedron* review articles. His research with mesoionics has been extended to related 1,4-dipoles which were found to undergo smooth internal cycloaddition reactions to generate a variety of novel heterocycles which have great potential for alkaloid synthesis. Intimately tied to his efforts on the synthesis of heterocyclic compounds is his development and subsequent implementation of new synthetic methodologies or synthetic strategies involving tandem processes. His recent investigations dealing with the tandem- Pummerer reaction have added new dimensions to synthetic organic chemistry and have made it possible to prepare many alkaloids in a highly convergent manner. A particularly interesting application of the method involves a triple-cascade reaction of an easily assembled amidosulfoxide to create the spirocyclic skeleton of the *erythrina* alkaloid family. Most recently, his group has been using the intramolecular Diels-Alder reaction of aminofurans to prepare a variety of novel and biologically interesting azapolycyclic ring systems. Along the way he has not missed opportunities to expand his findings and thus has also discovered new chemistry with great synthetic possibilities, especially in the heterocyclic arena.

Besides his love for chemistry and heterocycles, Al finds time to spend with his family and is an avid runner and mountain climber. More details of his scientific and other endeavors can be found on Al's website: http://euch6f.chem.emory.edu/info.html.

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