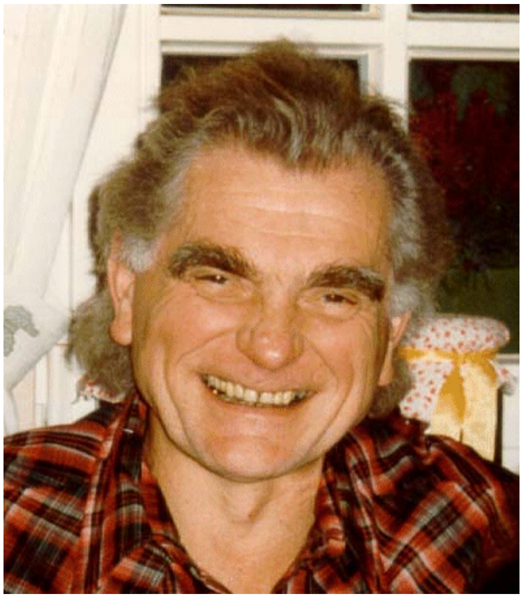
# Prof. Waldemar Adam

## A Tribute



Waldemar Adam was born July 26, 1937, in Alexanderdorf, Ukraine. He began his career in chemistry as a laboratory technician at the Cincinnati Chemical Works, received his B.Sc. in 1958 from the University of Illinois (under J.C. Martin) and his Ph.D. from MIT in 1961 (with F. D. Greene). He started his independent academic career in 1961 as Assistant Professor at the University of Puerto Rico, where he was promoted to Associate Professor in 1965 and to Full Professor in 1970. In 1980 he moved to the University of Würzburg to occupy the Chair of Organic Chemistry. After his formal retirement in October 2002, he moved back to Puerto Rico in April 2003. Presently, he holds a part-time appointment at the Department of Chemistry, University of Puerto Rico, Rio Piedras.

During his career he received numerous awards, honors and distinctions. Thus, he was A.P. Sloan Research Fellow, J.S. Guggenheim Fellow, NIH Career Development Fellow, NATO Senior Fellow, NSF Senior Fellow (India), JSPS Senior Fellow (Japan), INSA Senior Fellow (India), and Distinguished Visitor (University of Alberta). He obtained the Distinguished Scientist Award (Lion's Club of Puerto Rico), the Leonardo Igaravidez Award, the College of Chemists Award, the A. v. Humboldt - J. C. Mutis Award, the Japanese-German Research Award (JSPS, A. v. Humboldt-Foundation), the Theodor-Förster-Gedächtnisvorlesung (GDCh and Bunsen Society), the Iberdrola Visiting Professorship, and the Excellence in Teaching Award (ACS-PR Section). He also received the Dr. honoris causa from the University of São Paulo, Brazil, and he is a member of the Bavarian Academy of Sciences and the Brazilian Academy of Sciences.

He has been a visiting professor at the University of Zürich, Switzerland; SUNY-Buffalo, New York, University of São Paulo, Brazil; University of Puerto Rico, Marine Sciences, Mayaguez; Inter-American University, Hato Rey, Puerto Rico; University of Bari, Italy; Universidad de Concepción, Chile; University of Alberta, Canada; University of Krakow, Poland; University of Debrecen, Hungary; Polytechnical University of Valencia, Spain; Tulane University, University of New Orleans, USA; University of Miami, USA; University of Reims, France; University of Santiago, Spain; University of Bilbao, Spain; University of Ljubljana, Slovenia; and University "Mayor de San Andres" of La Paz, Bolivia.

## Research Interests

Waldemar Adam is well known for his significant contributions to physical organic chemistry, photochemistry and oxidation chemistry and his achievements are well documented in 975 publications. In particular, his research interests cover mechanistic organic chemistry, with an emphasis on peroxides, singlet oxygen, photochemistry, photobiology, chemiluminescence, bioluminescence, and synthetic / biomedical applications of metal-catalyzed and enzyme-catalyzed oxidation chemistry. Considering these different research interests, it is rather difficult to fit all of these activities in an all-embracing presentation. Having realized this problem himself, Waldemar Adam divided his whole research group into smaller subunits, the so-called "mini groups", which consisted of those coworkers that were engaged in the same research area. Since this subdivision turned out to be highly productive for his group, it will be used herein also to outline briefly the research activities of the Adam group, known as the AKA (Arbeitskreis Adam).

## Peroxides and Molecular Oxygen in Organic Synthesis

Presumably, most chemists tend to associate the name of Waldemar Adam with oxidation chemistry. Indeed, after a brief liaison with theoretical organic chemistry in the 1960s, he focused his attention on several aspects of synthetic oxidation chemistry. Thus, in his early years he was working on the synthesis of cyclic peroxides and he employed these highly reactive compounds for the preparation of unusual organic molecules (Review: *Angew. Chem., Int. Ed. Engl.*, **1974**, *13*, 619.). In the succeeding years oxidation chemistry was always an important part of his overall research efforts, and to date he is still active in this research area. The key reagents are molecular oxygen, hydrogen peroxide, or its derivatives such as hydroperoxides, perhydrates, peroxy acids, acyl peroxides, dioxiranes, dioxetanes, etc. He has used these results to understand the mechanisms of oxidation processes, and he employed this knowledge for selective, efficient and convenient synthetic transformations.

Among the most remarkable contributions along these lines are detailed studies of the chemiluminescence of 1,2-dioxetanes (Review: *Bull. Soc. Chim. Belg.*, **1984**, *93*, 605), peroxylactones (Monograph: Chemical and Biological Generation of Excited States, Adam, W.; Cilento, G., Eds.; Academic Press: New York 1982), as well as singlet-oxygen chemiluminescence (Review: *Chem. Rev.*, **2005**, *105*, 3371). This work helped to lay the mechanistic foundation for understanding the details of chemiluminescence (and bioluminescence), and he provided the essential knowledge for the development of the chemiand bioluminescent assays that nowadays constitute valuable commercial tools in analytical medicine.

One of the permanent members of the Adam group is singlet oxygen, produced either by photosensitization or by chemical reactions. Waldemar Adam demonstrated that selective oxidation reactions such as [4+2] and [2+2] cycloadditions, ene reactions, and hetero-atom oxidations, may be performed with singlet oxygen. In particular, the ene reaction (Schenk reaction) was explored most extensively (Review: *Angew. Chem., Int. Ed. Engl.*, **1996**, *35*, 477). Thus, efficient syntheses of optically active building blocks and natural products were developed from simple olefins and the crucial factors were assessed which allow these reactions to proceed with high stereoselectivity. Most recently, attempts have been made to generate "chiral" singlet oxygen through the thermal retro-cleavage of optically active arene endoperoxides in order to perform asymmetric oxyfunctionalizations directly, but time ran out for him!

Along with singlet oxygen, the most versatile reagent used by the AKA was dimethyldioxirane or DMD for short (Review: *Org. React.*, **2002**, *61*, 219). Although the oxidizing activity of DMD had been established, it was the AKA that demonstrated in detail its value and its remarkable usefulness in Organic Synthesis. For example, DMD was used for the oxyfunctionalization of a large variety of electron-rich and electron-poor substrates, which includes epoxidations (π bonds), hydroxylations (σ bonds) and hetero-atom oxidations (lone pairs). Notably, the AKA improved the synthesis of DMD, and the corresponding manuscript is still his most cited publication (*Chem. Ber.*, **1991**, *124*, 2377). Recently, enantioselective oxidations, especially epoxidations, were achieved through the use of optically active ketones with $C_2$ symmetry (Review: *Synlett*, **2005**, 1047).

During the last decade, Waldemar Adam has also ventured into developing analogous sulfur-atom transfer reactions, a most challenging objective. These studies were initiated by the discovery that certain thioozonides episulfidize diastereoselectively strained olefins to give the corresponding thiiranes. A more convenient direct episulfidation route employs the photoinduced activation of sulfines (thione oxides) in the presence of strained olefins, in which sulfur-atom transfers in up to 90% yields were achieved.

The enophilic similarity between triazoline-3,5-diones (TADs) and singlet oxygen allowed the AKA to extend the scope of the ene reaction. Thus, nitrogen functionalities could be introduced efficiently by the ene reaction of the TADs with appropriate olefins. Moreover, the use of chiral auxiliaries permitted asymmetric azetation through steric control. Most recently, nitrosoarenes (ArNO) have been employed to introduce nitrogen functionalities into olefins through the ene reaction (Review: *Chem. Rev.*, **2003**, *103*, 4131).

## Photochemical Generation and Mechanistic Elucidation of Reaction Intermediates

In the last 25 years, azoalkanes played an important role in the AKA, especially their propensity to denitrogenate upon irradiation or heating. Originally the denitrogenation of azoalkanes was used for the independent generation of diradicals that were proposed as intermediates in the di-π-methane rearrangement. In the following studies, however, numerous azoalkane derivatives were synthesized and used extensively as precursor molecules to generate short-lived radical intermediates as well as persistent radical species. Thus, transient singlet and/or triplet localized (mainly 1,3-cyclopentanediyl type) and cross-conjugated (trimethylenemethane non-Kekulé type) diradicals and polyradicals were produced, whose chemical, physical and spectral (absorption, fluorescence, phosphorescence) properties were studied in detail by experimental and theoretical methods. Notably, the persistent diradicals, which are easily available by this method, allowed the determination of zero-field splitting parameters ($D$ and $E$) that provide valuable information about the electronic structure of these unpaired electron species. With this approach, Waldemar Adam established a new and useful experimental parameter that may be used to evaluate substituent effects in spin delocalization and radical stabilization (Review: *Adv. Photochem.*, **1998**, *24*, 205).

Moreover, the strained reaction products that result from denitrogenation of diazabicylo[2.2.1]heptane, namely housane derivatives, were also used for the generation of intermediate radical anions or radical cations. By means of photochemical (PET) and chemical (CET) electron transfer, radical cations were produced to elucidate their chemical fate and to assess their physical and spectral properties (Review: *Chem. Soc. Rev.*, **1999**, *28*, 359).

The double inversion of 2,3-diazabicyclo[2.2.1]heptene(DBH)-type azoalkanes upon thermal and photochemical denitrogenation constitutes a unique stereoselective process, under much mechanistic dispute for almost four decades. The work of Waldemar Adam's group on this intriguing phenomenon serves as an example *par excellence* of harnessing the structural variation of the DBH-type substrate and the change of medium properties such as viscosity and polarity to diagnose a complex reaction mechanism. These combined experimental efforts, supported by computational studies, have disclosed a stepwise mechanism of the nitrogen extrusion. Thus, thanks to the work by the AKA during the last few years, the mechanism of this perplexing photochemical denitrogenation of DBH-type azoalkanes is now well understood. Although this problem is specific, the focus in resolving its mechanistic complexities is *general* and, thus, may be applied to the investigation of other intricate reaction mechanisms. Indeed, this all-embracing approach has been utilized by the AKA in the studies on stereochemical memory, to demonstrate the importance of Curtin-Hammett behavior in radical-cation rearrangements. The potential of this straightforward methodology is invaluable for further studies on stereo- and regioselective processes, as well as for elucidating intramolecular motions in enzymatic reactions and molecular machines and motors (Review: *Acc. Chem. Res.*, **2003**, *36*, 571).

## Mechanistic Aspects of Activation and Preparative Applications of Organic Metal- and Enzyme-Catalyzed Stereoselective Reactions

In the 1980s Waldemar Adam extended his expertise to metal-catalyzed oxidation reactions. He rapidly discovered that chemo-, regio- and stereoselective catalytic oxidations of a variety of substrates may be performed with the help of peroxy-, peroxo- and oxo- complexes with the appropriate transition metal. The most recent efforts in this project concern the challenge of mimicking asymmetric catalytic oxyfunctionalizations akin to biological processes. Important advances and contributions were made by using reactions such as the Sharpless-Katsuki epoxidation of allylic alcohols by tartrate-assisted titanium peroxy complexes, the Jacobsen-Katsuki epoxidation of unfunctionalized olefins by salen-type manganese oxo complexes, or selective oxidations with Herrmann's methyltrioxorhenium diperoxo complex (Review: *J. Organomet. Chem.*, **2002**, *661*, 3). In addition to these homogeneous catalytic oxidations, zeolites were employed to perform catalytic selective oxyfunctionalization in the confined spaces of the cavities under heterogenous conditions. As pointed out earlier, the metal-catalyzed oxidations were used to mimic biological oxidation processes; consequently, the chemical work was complemented with enzyme-catalyzed oxidation reactions (Review: *J. Organomet. Chem.*, **2002**, *661*, 17). Indeed, even whole bacteria and fungi were used as "chemical factories" for enantioselective synthesis!

## Genotoxicity of Excited States and Reactive Oxygen Species

It should be emphasized that Waldemar Adam never hesitated to explore new research areas and that he always used his expertise for interdisciplinary activities. His insatiable drive for the New is best documented in his photobiological research that he started already at the University of Puerto Rico (UPR) at the end of the 1970s. For this purpose, he employed triplet-excited carbonyl compounds (derived from dioxetanes) and reactive oxygen species, in particular oxygen-centered radicals, generated either photochemically or thermally. These reactive intermediates were used for deliberate DNA damage, to unravel in detail the complex reaction mechanisms responsible for DNA damage. Notably, these results have helped to understand the diverse pathways in oxygen-dependent metabolism (oxidative stress) such as mutagenesis, carcinogenesis, and aging.

Waldemar has always led his group, the "AKA", with an outstanding ability to organize. He has passed his remarkable dedication to chemistry and science on to his coworkers, and he encouraged them to be curious and to follow (and defend) their own ideas even at an early stage of their careers. He worked hard with his associates on each project and he expected and appreciated hard work from his group members. He never requested from anyone *to work more*, but encouraged them *to try harder*. In fact, the latter became the work slogan of the AKA, namely “Try harder!”. Socially, he considered the AKA as a big family, and he insisted on gregarious awareness by all members of his group. Unquestionably, Waldemar enjoyed each academic and each festive event. Certainly, anyone who has had the great pleasure of attending AKA parties, in particular the birthday celebrations, will never forget the experience!

For more information on Waldemar Adam's prolific research activities, consult his homepage at http://www-organik.chemie.uni-wuerzburg.de/ak_adam/index-de.html. Should you ask Waldemar Adam, which of his umpteen scientific contributions he considers to be his *highlight*, he will, without hesitation, enthusiastically claim it to be the synthesis of the first α-peroxy lactone in 1972 at UPR (Adam and Liu, *J. Am. Chem. Soc.* **1972**, *94*, 2849)!

Heiko Ihmels, University of Siegen; March 2006