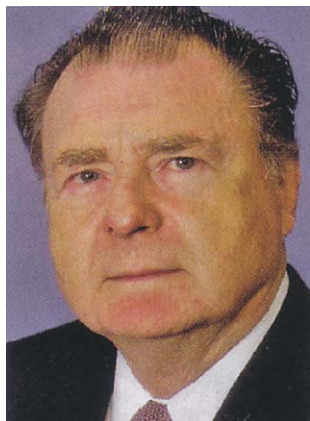


### Laudation for Professor Richard Heck\*



Richard Heck was born in 1931 in Springfield, MA. At the age of eight, Dick moved with his parents to Los Angeles, CA. He believes that his interest in chemistry was initiated by the vivid colors and abundant fragrances of flowers in their garden. He entered the University of California at Los Angeles (UCLA) where he obtained B.S. (1952) and Ph.D. (1954) degrees.

His graduate research was carried out with Saul Winstein, studying neighboring (anchimeric) group assistance in the solvolysis of arylsulfonates. A NSF post-doctoral fellowship award took him to the ETH in Zurich to work with Nobel Laureate Vladimir Prelog on the solvolysis of medium-sized cycloalkyl arylsulfonates. In 1955, Dick Heck returned to the Winstein laboratories to carry out further studies on neighboring group effects, an area which is now covered in organic textbooks.

In 1989, after a remarkable and productive career, Dick Heck became Emeritus Professor at the University of Delaware and retired to Florida with his wife, Soccoro. In 2005, he was recipient of the Wallace Carothers Award, and in 2006, received the Herbert C. Brown Award for Creative Research in Synthetic Methods from the American Chemical Society, his first major award. In the same year, he also returned to the bench to pursue one of his first loves, cobalt chemistry, as Visiting Professor at Queen's University (*vide infra*).

#### Vita chimica

The strong physical organic chemistry background undoubtedly influenced the decision at Hercules Powder Co. (subsequently Hercules, Inc.), Wilmington, DE to hire the twenty-five year old Dick Heck in 1956. His first projects dealt with the formation of crystalline polymers from monomeric vinyl ethers. After about two years, his supervisor, Dr. David Breslow advised him to "do something with transition metals." The first study concerned the hydroformylation reaction for which, in due course, he suggested a mechanistic rationalization. Today, this is regarded as the first correct mechanism

proposed for a transition-metal-catalyzed reaction. With this understanding, Dick Heck undertook systematic studies of organocobalt carbonyl complexes, which resulted in the preparation of a variety of new complexes (including the first characterized  $\pi$ -allyl cobalt complex) and the discovery of new reactions with carbon monoxide, alkenes, dienes, epoxides, and unsaturated carbonyl compounds. These studies provided the basis for clarification of many other unexplained transition-metal-catalyzed reactions of the time. A brief foray into nickel carbonyl complexes also led to an appreciation of their analogous reactivity to the cobalt carbonyls.

As narrated by Dick in the personal *Account* in this *Synlett* issue, a discussion with Pat Henry, who was working in a lab next door on the commercially important  $\text{PdCl}_2$ -catalyzed Wacker process, led to the discovery of the new C–C bond-forming reaction which we know today as the Heck reaction. With perceptive structural and mechanistic insight, he found that, in the very first exciting experiment, stoichiometric combination of  $\text{PdCl}_2$  with  $\text{PhHgCl}$  under one atmosphere of ethylene, resulted in a rapid absorption of 1 equiv of ethylene (gas buret) and the formation of a black solution from which styrene was isolated in high yield. Thereby, the door was opened to systematic studies in which reactions with carbon monoxide, alkenes, dienes, and alkynes were demonstrated. Of great synthetic significance, recalling that carbanionic C–C bond-forming methodology was primarily in use at this time, was the compatibility of this process with almost all common organic functional groups.

Despite the dictum of the day that "anything could be mercurated", the toxicity and the expense of mercurials, as well as the stoichiometric requirement of expensive palladium, combined to prohibit further development of this reaction. However, reports on the successful formation of halo(aryl)palladium–phosphine complexes changed this perspective. They suggested to Dick, after he moved to the University of Delaware in 1971, that these intermediates could replace the arylmercurial– $\text{PdCl}_2$  combination. Most significantly, he reasoned that, by the addition of certain bases to quench the hydrogen halide generated in the reaction, a catalytic process would result. The discovery, disclosed in 1972, set the panorama for systematic studies on the application of this reaction in organic synthesis including, in addition to reactions with alkenes, dienes, and trienes and the first intramolecular versions, carbonylative esterification and amination processes.

In addition to the discovery of the Heck reaction, Dick and his students also discovered, in the ensuing years, two other very useful palladium-catalyzed C–C bond-forming reactions, of alkynes and of vinylboronic acids. The alkyne coupling reaction was disclosed by the Heck group in 1975. Later that same year, Sonogashira, citing Heck's work, reported that inclusion of copper resulted in an accelerated reaction. A single Heck paper, also published in 1975, briefly described the coupling of vinylboronic acids with acrylates (Dieck, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083). This may be considered as a harbinger of the venerable Suzuki reaction.

### Impact

Those who can fast-backward to the 1970s recall that enolate chemistry dominated the teaching and practice of C–C bond formation; those encountering the Heck reaction perhaps considered it a curiosity and certainly viewed palladium as an exotic metal. Thus the importance of this reaction grew slowly on the synthetic organic community. In 1982, Heck was able to write an *Organic Reactions* chapter that covered all the known instances in just 45 pages. By 2002, applications had grown to the extent that the *Organic Reactions* chapter of Larry Overman, limited to the *intramolecular* Heck reaction, required 377 pages. The current impact of the Heck discovery is clearly seen by plugging in the term as a full-text search in SciFinder which leads to 1298 hits for the 2000–2005 and 424 for the 2005–2006 (February) periods.

Today, the Heck reaction is an essential concept and tool for every organic chemist. Organopalladium chemistry has been propelled into a position of paramount importance by its operational simplicity, unprecedented functional group compatibility, and wide applicability. From material science to enantioselective synthesis of natural products, nearly every sub-discipline of modern organic chemistry has benefited from the advances in the field of organopalladium chemistry. Although Dick Heck expressed surprise recently (“when I began, I never thought that it would become important”), his work may be considered as a forerunner for a variety of other Pd-catalyzed couplings, including those with boronic acids (Suzuki), organotin (Stille), organonickel compounds (Kumada–Corriu), organozinc (Negishi), and organosilanes (Hiyama) as well as with alcohols and amines. Undergraduates see the Heck reaction in class and laboratory, medicinal and process chemists practice it. Industrial palladium-catalyzed reactions are run on ton scales for the manufacture of fine chemicals, fragrances, crop protection agents, and pharmaceuticals.

Of the reactions developed by Dick Heck, the greatest societal impact has been from the Pd-mediated coupling of an alkyne with an aryl halide. This is the reaction that was used to couple fluorescent dyes to DNA bases, allowing the automation of DNA sequencing and the elucidation of the human genome. In the same context, his initial work motivated hundreds of researchers to investigate the potential of palladium catalysts in their own work. The result is an unusually magnificent legacy of significant contributions to chemistry and society.

Before Dick Heck, *all* organometallic C–C bond formation was stoichiometric. To us, being impressed by this current catalytic organometallic transformation or that is like being taken by the dazzle on a wave, while not giving credit to the wind that moved the water. The contributions of Dick Heck provided the spark and laid the foundation for the metal-catalyzed coupling reactions that are central to organic synthesis as it is practiced today.

### Epilogue

In 2004, during a casual conversation, Dick Heck said “you know, I would like to go into the lab and follow up on some of my cobalt chemistry... that is, if it has not been done!” Fortunately, an opportunity for Dick to work in the Department of Chemistry, Queen's University was arranged. Students working in the same laboratory overcame their awe and worked alongside him and attempted desperately to arrive before his normal 8 a.m. starting time. Observing Dick Heck in the laboratory during the past six months has reinforced the view of a dedicated scientist interested in making observations, examining the results, whether failed or successful, and deducing the next step to take. Fifteen years after retirement and 45 years after opening the door to organocobalt chemistry, Dick entered the lab again, made the complexes, measured their IR spectra (“you get all of the information you need”), obtained, via assistance of eager students, NMR and HRMS data, interpreted them, and took the next step. The compounds and the lab notes are available for the student who is inspired and eager to stand on his shoulders and, as is common in the time lapses of scientific discovery, to take the next step in cobalt chemistry.

Together with the chemists of the 65 contributions to this *Synlett* Special Issue, Peter Vollhardt and all of the Editors, Susanne Haak and her Thieme team, we celebrate this occasion, long overdue, of your fundamental discoveries for chemical synthesis.

*Qui vivat atque floreat ad plurimos annos*

\* Based, in part, on discussions with Dick Heck, the beautifully concise review by Ei-ichi Negishi (*J. Organomet. Chem.* **1999**, *576*, xv), and the insightful comments of Tom Stevenson, Dupont Crop Protection, and William Nugent, Bristol-Myers Squibb, each of whom we acknowledge with deep gratitude.

Douglass Taber, University of Delaware  
Victor Snieckus, Queen's University

To the contributors and readers of *Synlett*.

It is indeed an honor to have a special issue of *Synlett* dedicated to you. Of course, much of the credit and honor should go to my students who contributed substantially to my research.

When I retired from the University of Delaware in 1988, it was unclear what would develop from the early results in palladium catalysis. My expectations have been more than fulfilled as shown by the many subsequent reports of others as exemplified by articles in this issue of *Synlett*. There appears to be no end in sight for what can be done with palladium.

One can only speculate as to how much more useful chemistry of the other transition metals remains to be discovered but undoubtedly there, also, is much more.

Surely, the articles in this volume will give the readers new ideas on this subject to think about.

Richard J. Heck

June 5, 2006

Kingston, Ontario, Canada