NOBEL LECTURES

CHEMISTRY

2001 – 2005

NOBEL LECTURES

INCLUDING PRESENTATION SPEECHES AND LAUREATES' BIOGRAPHIES

CHEMISTRY

2001–2005

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LITERATURE

PEACE

ECONOMIC SCIENCES

FOREWORD

Since 1901 the Nobel Foundation has published annually *Les Prix Nobel* with reports from the Nobel award ceremonies in Stockholm and Oslo as well as the biographies and Nobel lectures of the Nobel laureates. In order to make the lectures available for people with special interests in the different fields the Nobel Foundation gave Elsevier Publishing Company the right to publish in English the lectures for 1901–1970, which were published in 1964–1972 through the following volumes:

Physics 1901–1970	4 vols.
Chemistry 1901–1970	4 vols.
Physiology or Medicine 1901–1970	4 vols.
Literature 1901–1967	1 vol.
Peace 1901–1970	3 vols.

Thereafter, and until the year 2000, the Nobel Foundation has given World Scientific Publishing Company the right to bring the series up to date and also publish the Prize Lectures in Economics from the year 1969. Between the years 2001–2005, the Nobel Foundation has given World Scientific Publishing Company a publishing right through an agreement between Nobel Media AB and World Scientific Publishing Company.

The Nobel Foundation is very pleased that the intellectual and spiritual message to the world laid down in the laureates' lectures, thanks to the efforts of World Scientific, will reach new readers all over the world.

Michael Sohlman
Executive Director
Stockholm, April 2008

PREFACE

In the present volume the 2001–2005 Nobel Lectures in Chemistry, together with autobiographies, portraits of the laureates and the presentation speeches delivered at the awarding ceremonies, are published. This information has previously been published in *Les Prix Nobel* together with lectures in Physics, Physiology or Medicine, Literature, Peace and Economic Sciences (Alfred Nobel Memorial Prize). The intention is that this collection of lectures, together with the previous ones, will give an impression of the spectacular discoveries and improvements that have been made in chemistry. It should also serve as a source of inspiration.

In 1901 the first Nobel Prize in chemistry was awarded to J. H. van 't Hoff for the discovery of the laws of chemical dynamics and osmotic pressure in solutions. Another of his important contributions is the concept of the tetrahedral carbon, which is a basis for chiral chemistry. One hundred years later, in 2001, the progress in chiral organic synthesis was recognized by jointly awarding **W. S. Knowles** and **R. Noyori** "for their work on chirally catalyzed hydrogenation reactions" and **K. B. Sharpless** "for his work on chirally catalyzed oxidation reactions". Many of today's drugs are based on our knowledge of fields, where these laureates have made important discoveries; they are based on mirror images of molecules.

In 2002 the development of mass spectroscopy and NMR spectroscopy was in focus. The award was shared by **J. B. Fenn** and **K. Tanaka** "for their soft desorption ionisation methods for mass spectrometric analyses of biological macromolecules" and **K. Wüthrich** "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution". These methods give us new important knowledge about structures and dynamics of the molecules of life.

The 2003 prize recognized insights into the transportation of water and ions through biological membranes. **P. Agre** was awarded "for the discovery of water channels" and **R. MacKinnon** "for structural and mechanistic studies of ion channels". Their discoveries are about the mechanisms of the central life processes that control where, when, and how often ions and water are let into or out of the cells in our body.

The target for the 2004 prize was progress in the understanding of protein degradation in the cells. **A. Ciechanover**, **A. Hershko** and **I. Rose** were jointly awarded "for their discovery of ubiquitin-mediated protein degradation". Their discovery of a system for controlled protein degradation in cells has

fundamentally changed our way of thinking about protein degradation and is a basis for producing new medicines.

In 2005 advances of organic synthesis of carbon-carbon bonds were recognized. **Y. Chauvin**, **R. H. Grubbs** and **R. R. Schrock** were jointly awarded "for the development of the metathesis method in organic synthesis". Their discoveries have given us one of the most important methods for building organic molecules. It is among such molecules that we are finding new materials and new medicines.

Per Ahlberg

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WILLIAM S. KNOWLES and RYOJI NOYORI

"for their work on chirally catalysed hydrogenation reactions"

and the other half to

BARRY K. SHARPLESS

"for his work on chirally catalysed oxidation reactions"

THE NOBEL PRIZE IN CHEMISTRY

Speech by Professor Per Ahlberg of the Royal Swedish Academy of Sciences. Translation of the Swedish text.

Your Majesties, Your royal Highnesses, Honoured Nobel Laureates, Ladies and Gentlemen,

Science is exciting. At least I think so, along with everyone else here beside and behind me on this stage. As humans, we possess curiosity. With the aid of science we can discover answers – and surprises. That is exciting. But when I am going to explain something to a person who does not work with science, I hear: That may be interesting, but what is it good for? In the case of this year's Nobel Prize in Chemistry, I have no such problems. That is because it is very easy to answer the question. Many of today's drugs are based on our knowledge of fields where this year's Laureates have made important discoveries; they are based on mirror images of molecules.

This year's Nobel Prize in Chemistry concerns molecules that occur in two forms that are mirror images of each other. Such molecules are called *"chiral"* after the Greek word *cheir* meaning hand. Our hands are *chiral* – our right hand is a mirror image of our left hand – like most of life's molecules. In our cells we find only one of these forms. This is true, for example, of enzymes, antibodies, hormones and DNA.

Thus the enzymes in our cells are chiral, as are other receptors that play an important part in cell machinery. This means that they prefer to bind to one of the mirror image forms. The two forms of a chiral molecule often have totally different effects on cells. For example, the receptors in our nose are sensitive to mirror symmetry. One form of the substance *limonene smells like lemons,* while its mirror image smells like oranges. Most drugs consist of chiral molecules, and often only one of the mirror image forms is of interest. The other form may even be harmful. This was the case, for example, with the drug thalidomide, which was given in the 1960s to pregnant women. One mirror image form helped against nausea, while the other one – as it was discovered too late – could cause fetal damage.

It is obviously important to be able to produce each of the forms, as pure as possible. When producing compounds in the laboratory, ordinarily the result is equal quantities of both mirror image forms. This year's Nobel Laureates in Chemistry have developed chiral catalysts in order to produce only one of the forms. A catalyst is a substance that speeds up reactions without itself being consumed.

In 1968 William Knowles was the first who was able to demonstrate that chirally catalyzed hydrogenation was feasible. It was a timely discovery that immediately inspired many researchers. Knowles quickly applied his own ba-

sic research and that of others to create an industrial synthesis of the drug L-DOPA, which is used in the treatment of Parkinson's disease. Millions of patients have gained relief by using this medicine, including my own father, who suffered severely from this disease.

The man who led the further development resulting in today's more selective and general chiral hydrogenation catalysts was Ryoji Noyori. A single one of his catalyst molecules can yield millions of product molecules. His methods have gained very large practical importance, especially in industrial production of various antibiotics, for example. An important and, today, unfortunately highly newsworthy application.

Barry Sharpless has developed chiral catalysts for another important type of reactions – oxidations. His chirally catalyzed epoxidation and dihydroxylation reactions have given us new possibilities for also building complex molecules. They have gained very broad use, especially in industry, for example in producing medicines against ulcers and high blood pressure, two of our most serious health problems.

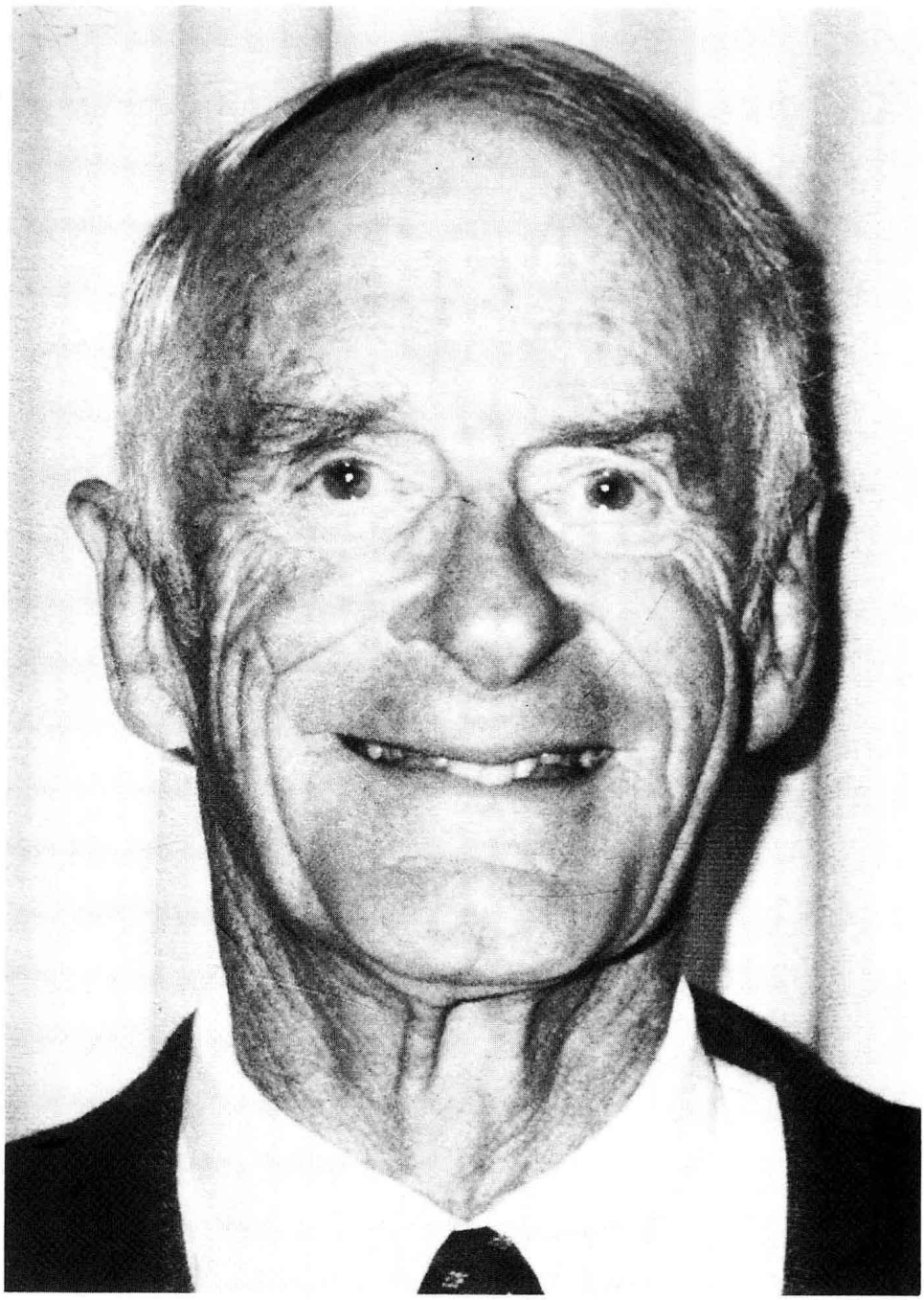
I have focused especially on the industrial role of the Laureates' discoveries, but they also constitute extremely important tools in academic research, thereby contributing to more rapid advances in research – not only in chemistry but also in materials science, biology and medicine.

Alfred Nobel himself focused on the utilitarian aspect of science when he wrote in his will that the prize should be awarded to those who "shall have conferred the greatest benefit on mankind." Thus this year's Nobel Prize in Chemistry not only makes it easy to answer what science is good for, but is also a prize entirely in the spirit of Alfred Nobel.

Dear Dr. Knowles, Dr. Noyori and Dr. Sharpless,

I have briefly described your discoveries and improvements. The beneficial consequences of your achievements to mankind are already plentiful and will certainly be amplified by the work of your numerous followers in the field of chiral catalysis.

On behalf of the Royal Swedish Academy of Sciences, I wish to convey our warmest congratulations and ask you to step forward to receive the Nobel Prize from the hands of His Majesty the King.



William S. Knowles

WILLIAM S. KNOWLES

I was born in Taunton, Massachusetts on June 1, 1917, but I actually grew up in nearby New Bedford. My family background was heavily slanted toward business and seafaring matters. I can't think of any relatives that ever went into science. My family gave me the best in education. To my father, business was the highest calling, but to my mother, medicine was the top profession. She would probably have gone to medical school if she had been born in a more enlightened era.

I went to boarding school at Berkshire in western Massachusetts, definitely the most beautiful part of the state. I'll never forget the fall colors on the Berkshires. In those days I was terrible at athletics and never made a team, but quite easily led my class in academics. I was particularly good at math and science. I also got a good lesson in New England thrift. To get free ice for our physics experiments we had to wait until it snowed.

On graduating, I was easily admitted to Harvard. In that era all one had to do was pass the College Board exams. If any one in my family went to college that was where he went. My father spent a year there and quit to go into the textile business. At this point I was strongly advised that I was too young socially to go to college so I took a second senior year at Andover, another boarding school. At that time many students did this. At Andover I took my first chemistry course from a teacher named Bushy Graham and was fascinated by the subject. I remember him trying to explain Avagadro's number and his discussion of the dangers of hydrogen and oxygen. At the end of the year, I took a competitive exam and won my first prize, the $50 Boylston prize in chemistry.

That summer I took a cruise on a 75-foot schooner with no engine, sailing from Gloucester, Massachusetts to Norway. We sailed around the Baltic ending up at Stockholm. I didn't think of it at the time, but we spent most of three weeks on the north Atlantic with no contact at all with the outside world. Today one is always in touch with home base even if you go to the South Pole or the Moon. Memories of this sailing trip have always been vivid. On one instance we were mistakenly arrested in Tallin, Estonia and got a ride in the paddy wagon. Later we were released without comment. Little did I think that one day years later I would be returning to Stockholm to share the Nobel Prize in Chemistry.

At Harvard I majored in chemistry with a strong inclination toward math. I took the minimum of humanities. I was told I'd be a natural for physical chemistry but taking organic with Louis Fieser changed my mind. It was there I got my introduction to optical isomerism and the tetrahedral carbon atom. At