# Tadeus Reichstein

(July 20, 1897 – August 1, 1996)

**Wloclawek – Kiev – Jena – Zurich**

Tadeus Reichstein was born on July 20, 1897 in Wloclawek (at the time in the Russian part of Poland) as the oldest of five sons of Jewish parents. His father's name was Isidor Reichstein. His mother, Gustava Brochmann, was descended from a respected Wloclawek family.

In those times, the Russians only allowed a small group of Polish Jews to attend the Technical Institute in St. Petersburg. Isidor Reichstein was extremely pleased to have been chosen for this honor. He hardly received any financial assistance, however, which meant that he could only pursue his studies through strict discipline and a frugal lifestyle. After a while he was able to earn some money by giving private tuition in mathematics and physics to the children of rich bourgeois families. Despite these difficult circumstances he was awarded a prize for his excellent scientific works. Upon completion of his education, Isidor moved to Kiev (in the Ukraine) where he set up his own business as an engineer specializing in sugar processing plants. His somewhat more solid financial basis now allowed him to get married.

In 1904, Tadeus Reichstein's youngest brother Paul was born, and the small flat in Kiev was becoming too crowded. As a result, Tadeus was sent to live with his aunt who was married to a pharmacist. Even though he was only eight years old, he took great interest in his uncle's pharmacy. He was allowed to make pills and syrups, mix plasters and assist in numerous other tasks in the pharmacy. Tadeus Reichstein explained to the author of this text in 1988 that he was absolutely certain it was this childhood experience that later prompted him to study chemistry, as he wanted to gain a deeper understanding of the processes which had so fascinated him as a boy.

Back in his parents' flat, he converted his bedroom into a laboratory and tried, together with a friend, to transform iron shavings into gold by means of chemical reactions. This was his first excursion into the realm of alchemy.

The year 1905 witnessed horrific pogroms against Russia's Jewish population. Little Tadeus heard the screams of the victims in the streets and saw the wounded and the

dead lying in their own blood. Tadeus Reichstein was never to forget this scene of terror. Having never seen blood before, he later remembered that apart from being shocked, he was also very interested in what he had seen.

The recurrent eruptions of anti-Semitic violence persuaded Isidor Reichstein that his children were no longer safe and that the family therefore had to leave Russia. He decided to emigrate to Switzerland. On their way through Germany, the family left Tadeus in a residential school in Jena. Since it was a renowned boy's boarding school, Isidor Reichstein hoped that it would secure a good future for his son. The flat in Zurich was too small in any case, all the more so as numerous relatives who were also fleeing from anti-Semitic violence had to be put up.

As he later said himself, the two years spent in the German boarding school were hell for Tadeus Reichstein. He loathed the military atmosphere of the Prussian institution where flogging even for very minor instances of disobedience was commonplace. Being small and thin for his age – the smallest boy in his class – he was understandably unable to keep up with the others during the daily outdoor hikes. Out of sheer exhaustion, he would often collapse, something that would trigger a fit of Teutonic rage in his teacher: he used to beat little Tadeus black and blue with a cane, until the boy was unable to walk at all.

Tadeus did not tell his parents anything about all that. Although aged only ten, he did not want to burden them even more and decided to endure the hardship until there would be room in Zurich for him too. Fortunately, Isidor Reichstein was able to acquire a house in the countryside just outside Zurich in 1907, so that Tadeus was able to return to his beloved family. He reflected later that it was from this moment on that his life was a happy one. Indeed, he was still a very cheerful person even in old age.

## Education and First Works

The Reichstein children did not go to school for the next seven years. Instead, they were taught at home together with a few friends. Taking the greatest care, Isidor himself instructed them in mathematics and physics. Other subjects were taught by visitors, while a young scientist replaced Isidor whenever he had to travel to Kiev. It can safely be assumed that it was this excellent private tuition that led to his enormous thirst for knowledge and his child-like ability to marvel at the wonders of life and nature and especially plants, traits that were to accompany Tadeus Reichstein throughout his long life of 99 years.

At the age of 17, Tadeus Reichstein entered the upper secondary school in Zurich where he pursued his interest in science subjects with great eagerness. Having been naturalized together with his four brothers in 1914, he was conscripted for military service as early as the first month after the outbreak of World War I. The situation in Europe at the time was catastrophic. The family got into major financial difficulties. No longer able to travel to Kiev, Isidor lost his business, his capital and his savings there. Worse still, his health deteriorated, he became bed-ridden and was never to recover fully. He died in the year 1931. His wife now had to do something to put food on the table for her family. So it came that the family home was converted into a boarding house. The boys now had to sleep in the arbor and do a lot of work to help their mother with the chores in the boarding house.

One of the guests that stayed with the family was to play a very special role in the life

of Tadeus Reichstein: it was a young woman from the Netherlands, Louise van Ufford, whom he married in 1927. Their daughter Ruth was born in 1933.

Having been dismissed from the army in the year 1916, Tadeus Reichstein was now able to complete his school education at the upper secondary school in Zurich. He then began reading chemistry at the ETHZ. After four years, Tadeus Reichstein passed his degree in chemical engineering with flying colors. Driven by the ardent wish finally to be able to support his family financially, he now wanted to find a well-paying job. Having compiled a list of 20 chemical companies, he went all over Zurich an its surrounding areas from morning till evening, visiting one company after another. No one wanted to hire him. He was rather depressed by the time he got back home, but one of his brothers greeted him with the news that someone wanted to talk to him on the telephone. The owner of one of the companies he had visited offered him 200 francs for a six-week job. The work was actually underpaid and wasn't in his field at all: he was asked to analyze wine samples. Nevertheless, Tadeus Reichstein immediately took it. He had never seen so much money in his life before.

Tadeus Reichstein soon discovered to his dismay that the way his boss generated revenues was by issuing certificates for wines of questionable quality, occasionally even for wines which had not been tested at all. He had little choice but to analyze the samples dutifully and to record excessive levels of sulphur dioxide, artificial colorings or contaminants so as to comply with the food safety regulations. What was then made of his findings was something he had no control over.

Fortunately, Tadeus Reichstein soon found a new position in a small company in Rorschach. The objective was to improve batteries for torches. He was able to solve the problem and was well paid for it. He was very pleased to be able to contribute 1000 francs towards his father's household budget. The elderly gentleman was touched to tears. Tadeus tried to comfort him by reminding him of all the good things that Isidor had done for the family.

Tadeus Reichstein spent a happy time in Rorschach. He joined the local swimming club, enjoyed sports, went on extensive bike tours and even took up mountaineering. All this was both physically and emotionally very good for him.

## Research

In 1921, Tadeus Reichstein began his doctorate under the supervision of Nobel laureate Hermann Staudinger. He saw his supervisor as a brilliant teacher of organic chemistry who knew how to create a stimulating and entertaining atmosphere for his 200 students. Practical laboratory skills were not Staudinger's forte, however. He is said to have had a predilection for strong reactions which were both fulminant and smelly.

At the same time, however, Tadeus Reichstein was able to work with Leopold Ruzicka in the cellar laboratory and benefit from the great practical skills of this poorly paid assistant of Staudinger's. Although Ruzicka was less gifted as a teacher of theoretical subjects, he developed brilliant working methods for the analysis of natural materials. His connection with Leopold Ruzicka was to have a profound impact on Tadeus Reichstein's entire subsequent career. Whereas he had originally planned to embark on a career in chemical engineering and certainly did not want to become a university teacher, he increasingly turned his attention to research as a result of

Ruzicka's influence.

On the basis of a plan drawn up by Staudinger, Tadeus Reichstein worked on the isolation of the volatile flavor components of roasted coffee for the German company Frank (Kathreiner's malt coffee) in a small laboratory in Albisrieden from 1922 to 1931. Together with his assistant and friend Joseph von Euw, he worked on this project for a total of nine years.

The connection with Joseph von Euw proved very productive and developed into a collaboration and friendship that was to last for some fifty years. Von Euw was actually a precision mechanic by training which meant that he first had to familiarize himself with the ins and outs of chemistry. But he soon got accustomed to handling the sensitive substances and even constructed most devices and apparatuses himself. Chromatographic methods were still unknown at the time and the analysis of very small quantities of complex mixtures of unstable products posed major problems. However, by means of fractional distillation, isolation of the various pH values and finally crystallization and derivatization, the required results were ultimately obtained nevertheless. Although Staudinger published all these findings as part of his own patents, Reichstein was at least able to publish his newly found reactions of heterocyclic components (furans and pyrroles) under his own name in the journal Helvetica Chimica Acta.

Upon completion of the works in Albisrieden, Leopold Ruzicka succeeded in persuading Reichstein to become an assistant at the Institute of Organic Chemistry of the ETHZ and seriously to consider an academic career.

## Vitamin C

It was only after two years at the ETH that Reichstein became titular professor, before eventually being appointed associate professor. The group of doctoral and post-doctoral students he soon assembled increasingly permitted him to invest his enormous energy in his research. Since he was particularly interested in substances that both played an important role and had great potential in medicine, he chose vitamins as his field of specialization.

The aim at the time was to find a way to synthesize vitamin C artificially. As a starting material, a sugar, L-sorbose was to be used. Although this substance was known, it was not available on the market. What to do? It was a known fact that there were strains of bacteria that could transform sorbitol into L-sorbose. It was generally assumed that the bacteria in question were the slime-producing microorganisms found in mother of vinegar. Reichstein immediately came up with the idea of trying it that way. However, many tests with mould cultures failed. No sorbose was produced. Inspired by a nineteenth-century research dissertation, Tadeus Reichstein at once devised a new experiment. Glasses containing a watery sorbitol solution, yeast, and a small quantity of vinegar (the pH value must be around 5 to ensure that no other bacteria grow) were put outdoors for a few days. When the glasses were taken back inside, three of them still contained sorbitol. However, three others contained a deposit of white crystals. As the analysis showed, the deposit consisted of the sugar so urgently needed: pure L-sorbose.

What had happened? Responsible for the transformation was a strain of bacteria that

was later to be called Acetobacter suboxydans. In one of the glasses, a dead fruit fly was floating in the liquid. On one of its legs, L-sorbose crystals had grown. Evidently, a colony of precisely this type of bacteria had been on the fly's leg.

No time was lost in cultivating the bacteria, and after only a few days, 100 grams of pure sorbose had been produced. The rest went according to plan. Together with his doctoral student R. Oppenauer, Reichstein was able to continue the process of synthesis, acetylation and oxidation, until all of a sudden it was possible to produce synthetic vitamin C in a way that had great commercial potential.

What seems so simple and elegant in retrospect also involved a great deal of hard work, however. The heavy workload in the laboratory, the unavailability of methods for the analysis and control of intermediate steps that are now taken for granted (no chromatography, no spectrometry), and the competition from research teams who were working on the same problem in other countries all meant that Tadeus Reichstein and his colleagues were under enormous pressure. But the result justified all the hard work. Tadeus Reichstein now held the patent for the only commercially profitable method of producing vitamin C. The laboratory's financial future was secure for the next few years, since the patent, which Tadeus Reichstein had made available to the company Hoffmann-La Roche, yielded substantial revenues.

It is impressive to think that Reichstein's ingenious synthesis technique has not changed to this day and that many thousands of tons of vitamin C are still produced by this method every year.

Many were surprised that Reichstein was not awarded the Nobel Prize for this discovery. The interface between chemistry, biology and medicine was his great passion. His original idea of including a microbiological component in organic synthesis meant that he was far ahead of his times (biotechnology). Many reasons could be found why his great scientific achievement was not awarded the highest accolade. One is that trouble was now brewing in the world.

## Basel and the Pharmaceutical Institute in the Totengässlein

All of a sudden, there were insurmountable administrative obstacles at the ETH in Zurich. In the late thirties, it was not possible for a Polish Jew to be appointed full professor (irrespective of the fact that he was actually a Swiss citizen who had been in the Swiss Army during the First World War). Reichstein had to leave Ruzicka's laboratory in Zurich. It must be emphasized in this connection that Tadeus Reichstein always saw himself as Swiss and that he loved Switzerland which he saw as his homeland. It should also be pointed out that Reichstein was a very tolerant but completely unreligious man.

In contrast to Zurich, the situation in Basel was different at the time. The combination of a social democratic government and strong liberal forces within the parliament (called "red Basel" by outsiders and "social Basel" by insiders) led to a prevailing mood of anti-Fascism and extreme skepticism with regard to the Third Reich, both among the population and in political circles. In part, this political climate was probably due to Basel's geographical location: the proximity to the international borders provoked a reaction. In addition, individual personalities shaped the world of Basel at the time. The Director of Education, legendary social democrat Fritz Hauser, deserves mention as does the liberal President of the Grand Council (and editor-in-chief of the

Basler Nachrichten) Albert Oeri-Preiswerk.

It was thanks to Hauser that Reichstein was offered the Chair of Pharmacy at the University of Basel. He accepted and thus became Head of the Pharmaceutical Institute of the University of Basel, a position he held from 1938 to 1950. He soon succeeded in his task of modernizing the Institute in order to bring it up to international standards. He was totally wrapped up in his research and later reflected that the 12 years spent at the Pharmaceutical Institute in Basel were, despite the catastrophe into which the whole of Europe plunged in this time, were the most fruitful and happiest years of his life.

Of course Reichstein had taken his closest research assistant, Joseph von Euw, to Basel with him, and he soon assembled a small group of students and assistants. The new field of activity were adrenal cortical hormones. Reichstein had begun to study these substances as early as 1934, i.e. when he was still at the ETHZ. Together with his group, Reichstein isolated about 30 chemically very similar corticosteroids which were, however, very different in terms of their biological effects. The team even succeeded in creating a crystalline representation for most of the corticosteroids. The so-called Substance E – universally known as cortisone today – was one of them. These substances perform a wide range of biological functions: they control sugar metabolism, they play an important role in the development of nerve and heart muscle cells, they are sexual hormones, and they influence the entire immune system. It is hardly surprising, then, that their isolation and identification was an extremely important undertaking. But what a difficult task. Only those experienced in the chemistry of natural products can fully appreciate how incredibly difficult it can be to separate substances of high chemical affinity which only exist in very small quantities among a great multitude of organic materials. From more than a ton of slaughter waste (bovine adrenal glands) these substances were eventually extracted in quantities of milligrams.

If it is borne in mind that these substances form mixed crystals and remembered that modern chromatographic methods did not exist as yet, one begins to wonder why Reichstein did not despair at the task. Other groups abroad were working on the same problem, and this led to a race against time. However, the aims were achieved: the substances were isolated and the results published. Together with his American rivals (Hench und Kendall) Tadeus Reichstein was awarded the Nobel Prize for Medicine in 1950. In his speech given on the occasion of the award ceremony, Reichstein expressed his gratitude to his rivals (and co-laureates) for their mutual support. He said that he owed his Nobel Prize entirely to them, since it was only due to their work that the biological significance of these substances became known – with all the public attention that this entailed worldwide.

Once again, the possibility of (semi-)synthetic production – of cortisone in particular – was the result of his research. The starting materials were bile pigments and plant material from Africa (so-called Strophantus types). As early as 1947, Reichstein had sent two of his assistants on an expedition to Africa for months on end to look for suitable starting materials. For already during the war, a race for the potential botanic sources of steroids – especially for those with an oxygen function in position 11 – had begun. It was hoped that industrial production of this new substance class would not only yield huge financial profits but, for a while, even that it might help win the war.

## The Institute of Organic Chemistry

In 1948, the Head of the Institute of Organic Chemistry died unexpectedly, and Reichstein was asked whether he would like to take up the position. He did not want to turn down the offer. As a result, he was, for four years until 1952, in charge of both institutes at the same time. However, as he later said, he would have much preferred to stay in his old institution in the Totengässlein to continue with his research projects. The chemical institute had to be substantially extended and modernized. For two years, Reichstein had to work particularly hard in order to convince the Grand Council of the importance and adequacy of the project. He was to succeed. His strong conviction that the entire city of Basel would ultimately benefit from the fruits of chemical research eventually prevailed and has, from today's point of view, undoubtedly been confirmed.

The Institute of Organic Chemistry was rebuilt from the ground up. It was Reichstein's vision as well as his energy and effectiveness that ensured the success of the complete reconstruction and reorganization of the institute. Unlike many of his academic colleagues, he did not shy away from administrative tasks and was determined to create an outstanding teaching and research institution.

His endeavors were crowned with success. Hundreds of scientists worked at the institute over the subsequent decades pursuing research at an international level.

## Personality

Reichstein was far ahead of his time in more than one respect. Thus he accepted women as scientists and colleagues as a matter of course and without any reservations. His leadership style as the head of both academic and administrative units was characterized not by dictatorial authority but rather by his great ability to motivate others. His enthusiasm for new possibilities and methods, his curiosity for the processes of nature, but also his cheerful personality were all contagious qualities. He was not only a brilliant teacher but showed great psychological skills as the head of his institute and great empathy in his interactions with his subordinates.

## Plants and Butterflies

Throughout his life, Tadeus Reichstein had a great passion for plants. On a practical level, he loved cultivating plants, especially ferns, but here too his interests ranged widely. He himself repeatedly said that he had inherited his aptitude for gardening from his mother. His garden on Weissensteinstrasse in the Bruderholz area in Basel is still vividly remembered by many as a botanical paradise and so is his garden in Agarone in the Ticino region where he owned a summer cottage. Reichstein combined an emotional attachment to the world of plants with a scientific approach to understanding plant development.

Plant substances always interested Reichstein. Apart from his works on the flavoring substances in coffee, his wine analyses, and his research on vitamins, this interest manifested itself in his botanical and phytochemical work on plant substances which was to contribute to a semi-synthetic production of corticosteroids, as mentioned above. There were many other subjects to which Reichstein turned his attention, however, for example steroid glycosides which have cardiotonic properties. It was this interest which later led him to an entirely new field of activity, namely the isolation of steroid glycosides from insects. The fact that these substances are found in insects was not

known at all until the sixties. Together with Miriam Rothschild, Reichstein published a series of articles about more than 20 cardenolides which were not only found in the famous monarch butterflies, but also in grasshoppers and many other insects.

Already in the late fifties, Reichstein began to take an interest in ferns. Following his retirement in 1967, his scientific work, which he was to continue to the end of his life, increasingly focused on this subject. At the age of 75, he said that he wanted to abandon his research in organic chemistry in order to dedicate himself entirely to ferns. He explained that the scientific literature in the field of organic chemistry had become too vast for him, so that he hardly had time to read even the titles of all the publications anymore. He added that he preferred to work with live material only in future.

The systematics, chemotaxonomy, cytology and micromorphology of ferns – those were now to become the subjects of his scientific work. Reichstein soon built up yet another international network of scientists and specialists. It was very lucky that Reichstein had found such an ideal field of work for his long retirement. After all, he worked longer as a scientist after he retired than many of his colleagues did all their lives. On the one hand, he had his work in the garden and greenhouse, on the other hand his scientific work. After his retirement, he published more than 100 works on the subject of ferns.

## Memory of a Great Scientist

Tadeus Reichstein died in 1996 at the age of 99. Also advanced in years, his beloved wife Louise had died a few years before him. When he was 95, he once said that he had the impression of having lived too long already. He also pointed out, however, that he needed at least three more years in order to complete his botanical publications.

In the course of his life, Tadeus Reichstein worked on many different subjects. He became an internationally renowned authority in all his various fields. Apart from the Nobel Prize and the Copley Medal, Tadeus Reichstein received more than 50 honors and prizes – not in one, but in many different fields.

Evidently, it was not only his intellectual capacity and the effectiveness of his scientific approach that led to the astonishing diversity of his work. Tadeus Reichstein was also an extraordinary human being. He had the ability to immerse himself deeply in a subject without narrowing his horizon in the process. This ability not only gave him rare cognitive powers, but it was also a precondition for his development into a non-fanatic yet highly motivated scientist as well as a great human being.