Emil Fischer, His Personality, His Achievements, and His Scientific Progeny

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The 150th anniversary of the birth of Emil Fischer, coinciding with the centenary of his receiving the Nobel Prize in Chemistry – the second ever awarded – provides a welcome opportunity to highlight the paramount achievements of this towering figure of our science. By focussing his research on organic matter on which the living world is built – N-heterocycles, carbohydrates, tannins, proteins, and, finally, fats – he not only laid the foundations of organic chemistry and biochemistry as we know it today, but through the research education of 330 doctoral students and postdoctoral associates who flocked his laboratory from all over the world, he brought forth the succeeding generation of scientists.

1. Introduction

When we look at organic chemistry today and reflect on how it has developed over the last century, no other organic chemist has been more determining, focussed and inspiring than Emil Fischer (1852−1919) (Figures 1 and 2). He not only pioneered the scientific knowledge on which modern organic chemistry and much biochemistry is based, but also engendered the succeeding generation of scientists.

This year, the 150th anniversary of his birth coincides with the centennial of his receiving the 1902 Nobel Prize in Chemistry − the second ever awarded and the first in organic chemistry.[1] Hence we have a unique opportunity not only to appreciate this monumental scientific contributions with which he refocussed the thinking on organic chemistry back to its roots, the world of living Nature. The impact this had on the further development of organic chemistry and biochemistry has been treated extensively.[2−19] But it is also timely to remember his various other achievements, most notably his vital role as a mediator between science, industry, and government that led to the foundation of the Kaiser-Wilhelm- (today Max-Planck-) Society, and, not least, the indelible imprint his striking personality, his ideas, and his mode of conducting research left on his scientific progeny.

2. Fischer's Scientific Achievements

Fischer's impressive scientific œuvre, which made him the unique pioneering figure of his time in organic chemistry and biochemistry alike, is remarkable both in its variety of topics and its depth. Today, we marvel at his foresight in choosing his fields of research which were the basic structural and synthetic chemistry of purines, carbohydrates, polypeptides, and fats, i.e. the four kinds of organic matter on which the living world is built. In that, he tackled substances produced by living organisms which are constitu-

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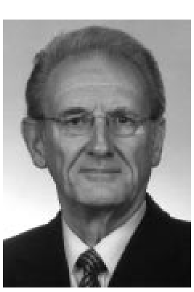

Frieder Lichtenthaler studied chemistry at the University of Heidelberg and received his doctorate there in 1959 with F. Cramer. After three postdoctoral years at the University of California, Berkeley, with H. O. L. Fischer − the only of Emil Fischer's three sons who survived World War I − he joined the faculty of the Technical University of Darmstadt, where he acquired his "Habilitation" in 1963, was appointed associate professor in 1968, and full professor in 1972. His research activities, documented in over 270 publications, comprise the generation of enantiopure building blocks from sugars, their use in the synthesis of oligosaccharides and complex non-carbohydrate natural products, molecular modelling of chemical and biological properties of sugars, and studies towards the utilization of carbohydrates as organic raw materials.

tionally repetitive and were then exceedingly difficult to study because of the lack of adequate methods for analysis, separation and synthesis. Thus, he differed markedly from the chemists of his time who were working on natural products and were occupied with the constitutional analyses and syntheses of easily crystallizable low-molecular-weight compounds. He steered the course of organic chemistry back to its origins, that is the task of studying the major substances of living organisms, thereby contributing greatly to the outlook of the next generation of organic chemists and biochemists.

The paramount achievements of Fischer's stellar career of 45 years are set out in his 600 or so experimental papers (*Abhandlungen mit experimentellem Inhalt*) and 20 lectures, which appeared, with very few exceptions, in *Ber. Dtsch. Chem. Ges.*, *Justus Liebigs Ann. Chem.*, *Hoppe-Seyler's Z. Physiol. Chem.* and *Sitzungsber. Preuß. Akad. Wiss.* They have been collected into a set of eight volumes,[26a−26h] each beginning with at least one comprehensive review, usually a detailed elaboration of a lecture.

Today, the essence of these prodigious achievements has not only entered the textbooks of organic chemistry but also those of biochemistry. Accordingly, a detailed exposition appears unnecessary here, as accounts of Fischer's major research contributions are readily available, such as on the unravelment of the sugar configurations,[11,13,27] his conventions for projecting stereoformulas into a plane,[28] or the lock-and-key analogy for the specificity of enzyme action,[14−16] which has provided generations of scientists with their mental image of molecular recognition processes. Nonetheless, a brief overview of the sequence of Fischer's research work would seem to be appropriate.

Fischer's scientific work began 1873 in Baeyer's laboratory at Straßburg with his investigations of triphenylmethane dyes which was the subject of his dissertation.[21] He continued this work in Munich together with his cousin Otto Fischer,[20] resulting from 1876 onwards in 14 joint publications,[29] which the two young men, although only in their twenties, were allowed to publish on their own. The absence of any acknowledgment to their teacher attests both to their independence and to Baeyer's apparent esteem and encouragment towards his gifted pupils. Apart from this work, Emil Fischer, while in Munich, exploited the chemistry of phenylhydrazine which he had accidentally discovered in 1874, while still in Straßburg;[30] he prepared the phenylhydrazones of the common aliphatic and aromatic aldehydes[31] and also elaborated the indole synthesis, which has come to bear his name.[32]

For nearly ten years he does not appear to have recognized the tremendous value of the phenylhydryazine for the characterization and identification of carbonyl compounds, until, in 1884, he eventually applied it to the sugars, thereby entering new territory into which few had ventured before him. By means of an ingenious series of systematically planned experiments and brilliant reasoning, along with some serendipity, Fischer unravelled their configurations within the course of seven years.[33] This brilliant synthetic and analytical work, and the manner in which he applied and further developed the van't Hoff−Le Bel theory for elucidating the stereochemical relationships of the sugars stands out as the pinnacle of his career. A hundred years ago, on the occasion of the Nobel Prize being awarded to him, the President of the Royal Swedish Academy of Sciences in his presentation speech expressed his appreciation in the following words:[1]

''The specific type of research which has characterized organic chemistry during the final decades of the nineteenth century attained its zenith of development and its finest form in Fischer's studies of sugars and purines. From the experimental point of view they are unsurpassed.''

Emil Fischer was born on 9 October 1852 in Euskirchen, a small town near Bonn. He was the youngest of eight children, two of whom had already died. The female dominance of his five older sisters was balanced by five male cousins living next to the trading house *Gebrüder Fischer*, which specialized in experimental dyeing and wool-spinning and was owned by his father and two of his uncles. After attending elementary school in Euskirchen and secondary schools (*Gymnasium*) at Wetzlar and Bonn, he obtained his *Abitur* in 1869, at the age of 17, when he was apprenticed to his brother-in-law, a timber merchant, as his father wanted him to enter the family business. This occupation proved uncongenial and, at 19, he was finally allowed to follow his inclination to study mathematics, physics, and chemistry at the University of Bonn, where he and his cousin Otto Fischer[20] commenced in the summer of 1871. Unimpressed by the lectures of Kekulé, Zincke, and Kundt (physics), the two cousins moved, a year later, to the newly established University of Straßburg. Here they came under the influence of Adolf Baeyer, who fired their enthusiasm for organic chemistry. Both young men joined his group and, at the age of 22 (in 1874) obtained their Dr. phil. degrees under his guidance for work on the structures of phthaleins, newly discovered (E. F.[21]), and the action of chloral on toluene (O. F.). In the same year, Emil Fischer was appointed assistant instructor in the organic laboratory course, where, by chance, by meticulous observation, and by keen perception, he turned a student's faulty experiment into his own first great discovery, phenylhydrazine. When, in mid-1875, Baeyer moved to Munich as successor to Justus von Liebig, both Fischers joined him. There, Emil continued his work on the hydrazines, which became the basis of his *Habilitation* (1876), carried out extensive investigations on rosaniline dyes with his cousin Otto, and also started work on purines. In 1879, he was appointed Associate Professor of Analytical Chemistry, as successor to Volhard.[22] In the same year, he was offered the Chair of Chemistry at Aachen which he refused; but in 1882 he accepted an invitation from the University of Erlangen to succeed again Volhard. There he was much preoccupied with the conversion of phenylhydrazine into N-heterocycles. In 1885, he again moved, this time to the University of Würzburg, at first continuing his work on purines, but then entering the at the time quite desolate state of carbohydrate chemistry. Within the unbelievably short span of seven years he solved the perplexing problem of the sugar configurations − work that in 1902 was recognized with the Nobel Prize in Chemistry, the second ever awarded. In 1892, on the death of A. W. von Hofmann,[23] Fischer, after some initial reluctance, accepted the invitation to become his successor in Berlin; so by the age of 40 he achieved the most coveted academic position in chemistry that Wilhelminian Germany had to offer, which he filled with ever increasing distinction until his death in 1919.

Figure 1. Photograph of the Baeyer group in 1878 at the laboratory of the University of Munich (room for combustion analysis), with inscriptions from Fischer's hand;[24] in the center Adolf Baeyer, to his right the 25-year-old Emil Fischer, in a peaked cap and strikingly self-confident three years after his doctorate; to the left Jacob Volhard[22] who was in charge of the analytical devision in Baeyer's institute, and whose successor Fischer was to become in Munich a year later (1879), and at the University of Erlangen in 1882; sitting left to Volhard Fischer's cousin Otto Fischer,[20] with whom he did extensive work on rosaniline dyes;[29] between Baeyer and Volhard stands Wilhelm Koenigs who in 1900, together with his doctoral student Eduard Knorr, discovered the Ag_2CO_3-induced glycosidation of aceto-bromoglucose,[25] known today as the Koenigs-Knorr reaction

This classical work was not the only great service Fischer rendered to chemistry, since later he returned to the work he had started in 1882 in Munich on purines, which led to the general classification of this class of substances[26b] and, subsequently, to the synthesis of the first nucleosides.[34]

When the fundamental work in one field was done, Fischer moved on to a new one. In 1899 he started working on proteins and, during the succeeding ten years, the efforts of his large research group were mainly directed towards the study of amino acids, peptides and polypeptides, culminating in the formidable synthesis of an octadecapeptide composed of 15 glycyl and three leucyl units.[35] The success of these activities, which brought the proteins into the orbit of respectable organic chemistry, fell short of his aims which went much further. Indeed a passage from a letter to A. von Baeyer, written at the end of 1905, reads:[36]

"My entire yearning is directed toward the synthesis of the first enzyme. If its preparation falls into my lap with the synthesis of a natural protein material, I consider my mission fulfilled."

So, around 1910, when his work on the proteins ceased because of insurmountable experimental difficulties at the time − only eight publications out of the total of 147 on this subject appeared thereafter[26f] − he initiated another sustained and successful research program on lichens and tannins which he termed depsides.[26g] In the final years of his life he turned to the synthesis of glycerides,[37] thus adding the fats to the classes of chemical constituents of biological systems, purines, carbohydrates, and proteins, that he had studied in the 45 years of his scientific career.

3. Fischer's Personality and Working Style

Apart from his autobiography,[38] written in 1918 but published posthumously in 1922, which covers his life only up to about 1905, the number of writings about Fischer is legion.[1−19,39−51] The most valuable are the extensive Hoesch biography[6] and accounts by Ludwig Knorr (1919[2]), Martin O. Forster (1920[5]), Max Bergmann

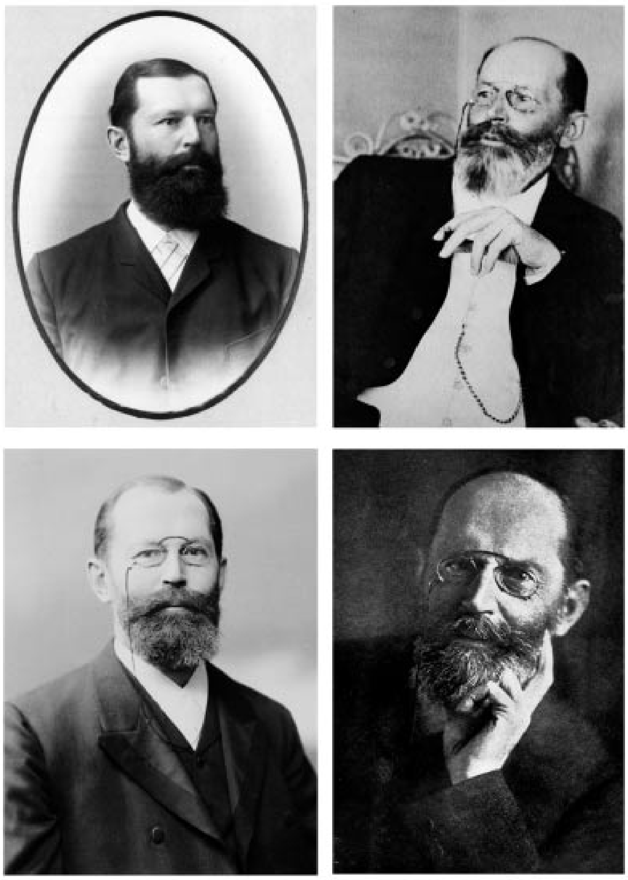

Figure 2. Emil Fischer at 37 (top left), 50 (bottom left), at the celebration of his 60th birthday (top right) and around 1915[24]

(1930[7]), Burkhardt Helferich (1953[8]), and Karl Freudenberg (1966[11]), all of whom received their doctorates under Fischer in Erlangen (L. K.), Würzburg (M. O. F.), and Berlin. As an authentic picture of Fischer's personality and of the way in which he succeeded in his monumental achievements is best obtained from accounts of those who were associated with him over a longer period or knew him well, thus some of their recollections are cited below.

''The salient quality of his life was unswerving singleness of purpose as a researcher. He possessed a remarkable memory and, despite his constant ailments – caused by phenylhydrazine and mercury poisoning – a superhuman capacity for sustained work'' (Forster[5]).

''Phenomenal keenness of mind and flash-like comprehension were characteristic of Emil Fischer. Mere indications sufficed to grasp the entire matter in its uttermost significance. He could have taken any other profession, he would have excelled in it'' (Harries[39]).

''His amazing successes are particularly startling due to the fact, that they required a minimum of theoretical presuppositions, and reached their goal by logical application of the suppositions available, and by the skilful execution of the experiments'' (Bergmann[7]).

''Very early, he developed his characteristic manner of working. He worked with many selected co-workers, subordinating each individual problem to the clearly envisaged general goal, and, thus, worked out the whole. Unlike his teacher Baeyer, who might be compared to the leader of a reconnaissance patrol with a trained eye for the terrain and the possibilities of the pathways, Emil Fischer was the clever tactician who proceeded on a broad front, here gaining ground very quickly, there holding back cautiously, until what lay behind was all safely in his possession. He knew how to make good use of the great advantages of the research programs required for doctoral candidates at German universities. Teamwork, as he developed it, demands a superior leader. It was magnificent to work under his direction and yet independently; as a research instructor, he blazed the trail for the generations succeeding him'' (Freudenberg[11]).

''Physically commanding, his authority rested on the solid foundation of natural dignity unmarred by self-assertion. The brisk, upright carriage marked the man of action; the glowing eyes revealed his attitude of constant, keen inquiry; the impatience with trivialities was one aspect of his dominating, steadfast control of essentials. With ordinary human perception, it was impossible for anyone to escape his contagious enthusiasm, and yet all the time the master did not obscure the man, for although his daily demeanour was tinged with severity, his heart when revealed was deeply kind, and, in circumstances of relaxation, joyous'' (Forster[5]).

A glimpse of the atmosphere in the Berlin institute (Figure 3) has been provided by the American physician James B. Herrick, who worked with him in 1905:[52]

Figure 3. Emil Fischer around the turn of the century in his "Privatlaboratorium" at the University of Berlin;[24] the somewhat unusual laboratory stool he inherited from his predecessor, August Wilhelm von Hofmann, who, in 1865, brought it to Berlin on his move from the Royal College of Chemistry, London

"He was modest, kindly, always the gentleman. Twice a day he made the rounds, moving quietly from desk to desk inspecting the work, always seeming interested, criticizing, helpfully suggesting. He had the faculty of seeing quickly where one's trouble lay. So gentle in manner was he that one scarcely realized that he was a good executive commanding officer".

On the other hand, in the recollection of Bergmann:[7]

"Fischer was reticent with his co-workers when he gave them instructions for the conduct of experiments or when he himself did laboratory work in their presence. Then, an indication of the purpose and goal and expected outcome of the experiment was either not given or stated very incompletely".

These facets of life in Fischer's Berlin institute may be balanced by the testimony of Richard Willstätter, 20 years younger than Fischer, but also from the Baeyer school. In 1911, while holding the chair of chemistry at the Swiss Federal Institute (ETH), Zürich, Willstätter had turned down the offer of the directorship of the Kaiser-Wilhelm-Institute for Chemistry in Berlin-Dahlem, yet was persuaded by Fischer who visited him in Zürich to change his mind ("the reverence for the great man played a role when I complied"):[53a]

"Emil Fischer ruled his laboratory with absolute authority. The princely man who gathered about him most of the doctoral students and other young investigators overshadowed everyone in greatness, spirit, and scientific insight ... He was the unequalled classic, the master of organic-chemical research in analytical and synthetic direction."

Another principal feature of Fischer's personality was his pronounced aversion to any sort of theoretical speculation. Although "his keen intellect was aboundingly endowed towards the speculative side, his critical disposition towards anything that transgressed what could be proved experimentally prevented him from communicating speculations in either word or script".[7] A few examples illustrate this attitude.

Referring to the question still controversial in 1914 on the ring sizes of the fructose and glucose portions of sucrose and how these sugars are linked, Fischer, who had established the basis of carbohydrate chemistry, clearly stated his position:

"We know nothing definite on the mode, how the fructose residue is linked in cane sugar, thus leaving huge room for speculation. I, however, gladly renounce to use it."[54]

A pertinent example is the Fischer lock-and-key analogy of 1894, used alongside his studies on the fermentability of the sugars by yeast. Towards the end of his famous paper of 1894 on the "Influence of the Sugar Configuration on the Action of Enzymes",[55] he simply illustrates the results he had obtained by using a pictorial analogy:

"To use a picture I would like to say that enzyme and glucoside have to fit together like lock and key in order to exert a chemical effect on each other."

That this rather incidentally used metaphor was immediately taken up, not only by organic and physiological chemists but by medical researchers in particular, obviously surprised Fischer. Paul Ehrlich, for example, introduced it from 1897 onwards into the then young discipline of immunology through his so-called "side-chain theory of immunity", which was elaborated in great detail.[56] As this greatly transgressed what could be proved experimentally, Fischer already felt in 1898 that he had to state the scope of his analogy:

"As there must be a similarity in the molecular configuration between the enzymes and their object of attack, if reaction is to take place, I have used the image of lock and key to make this thought more perspicuous. I am far from placing this hypothesis side by side with the established theories of our science, and readily admit that it can only be thoroughly tested when we are able to isolate the enzymes in a pure state and thus investigate their configuration."[57]

While Ehrlich had brought the lock-and-key concept from the realm of chemical reactions in solution to reactions on the cell surface, others extended it to cell-cell interactions (e.g. Lillie to fertilization[58]) to try to explain phenomena which were much too complex to yield to rationalization or comprehension at that time. These theories from Ehrlich, Lillie, and others who thought along similar lines,[59] yielded conflicting experimental evidence. Fischer's lock-and-key analogy, however, still stands in the annals of science, over a 100 years later, as a most fertile concept, because it was unspecified in its details, and thus left ample room for the imagination of chemists, biologists, and medical researchers alike.

Fischer's refusal to make theoretical speculations was even imposed on his co-workers, with a printed guide for the conduct of experiments, regularly presented to the older students and to his assistants. This document contained the unequivocal directive:

"You are urgently warned against allowing yourself to be influenced in any way by theories or by other preconceived notions in the observation of phenomena, the performance of analyses, and other determinations."[7]

In literary style Fischer's papers are uncompromisingly ascetic. Each subject is pursued from a deeply perceived, superior point of view, and the treatment, although complete, is so concise that a concluding summary of the results is unnecessary. Usually though, in a sentence or two, a clear indication is given at the end of the paper of what has to be done next.

This terse style of writing which undoubtedly was adopted by many of his scientific progeny, can be traced back to his first publication on the accidental discovery of phenylhydrazine in 1875.[30] This paper is unusual in several respects: First, Baeyer, allowed him to publish it independently without even an acknowledgment to his teacher, attesting to the high esteem Baeyer had for his gifted pupil. Secondly, the paper is formulated in an unusually concise, clear style and written in the first person:

"I have again taken up experiments on the reduction of diazo compounds. ... I arrived at a class of well-characterized bases, for which I propose the name hydrazine compounds." [30a]

A rather self-confident statement for a young chemist of 23 who had just received his doctorate, and the more so, since the parent compound, hydrazine, was to be discovered only twelve years later.[60] Reading today Fischer's paper of 1875 which − unknowingly at the time of its publication − contained the key for his later elucidation of the sugar configurations,[13,27] engenders the sensation of sitting at the modest source of what was to become a mighty river within the next 45 years.

Of the nearly 600 experimental papers that were to follow, 185 appeared under his sole authorship, giving credit therein to the co-worker(s) only by an acknowledgment. For example, the two co-workers Dr. W. Axthausen and Dr. H. Tappen who performed the tremendous experimental work in the formidable synthesis of an octadecapeptide, are merely thanked "for their valuable help" in the last sentence of the paper.[61] Even more curious in this context, a total of 92 papers were published under the sole authorship of his doctoral students, representing limited extracts from their dissertations with elaborate experimental details, but scant discussion. Each paper, inevitably, bore the introductory phrase "On the instigation of Professor Emil Fischer I have investigated ...".

4. Fischer and the Chemical Industry

Fischer's probably greatest and most direct contribution to chemical industry lies in the stream of young chemists passing regularly from his laboratory to the factories, men soundly trained in the methods of systematic inquiry and inspired by the imposing example of their teacher which had established their devotion to chemistry. Fischer's personal relationship to the chemical industry was initiated by the interest the tar-dye factories had in his early work with his cousin Otto on fuchsine and rosaniline dyes[29] which had generated a demand for his expertise to such an extent, that at the relatively young age of 31 − he just had resumed his professorship at the University of Erlangen − the Badische Anilin- und Soda-Fabrik (BASF) offered him the position of director of research, in succession to Heinrich Caro. But Fischer declined the offer despite a most attractive salary for that time (1883) of 100000 marks,[40] because − in his own words[38a] − "full freedom in scientific research was more appealing to me. However, I accepted the invitation for a three-week stay, in which I was shown the entire factory and took the opportunity to use the technical laboratory for methylating large amounts of uric acid", which were needed for further investigations in the purine series. The same attitude prevailed much later in his life, e.g. in February 1919, when Bayer Leverkusen wanted to elect him to its board. His response was unequivocal, as he wrote in a letter to Carl Duisberg:[62]

"Prussian jurisdiction prohibits to be a member of a profit-oriented enterprise while still being in office. Although there are some exceptions, it is better that I still be considered as a sort of confidant between administrative authorities and industry."

An industrial connection with Farbwerke Hoechst emerged from a product, dimethyl-phenyl-pyrazolinone, which was prepared by his then assistant Ludwig Knorr from phenylhydrazine and ethyl acetoacetate and subsequent methylation. It proved to have excellent analgesic and antipyretic properties and was marketed by Hoechst under the name antipyrine. Various analogues of similar activity, such as the highly successful pyramidone, were subsequently developed by Knorr and the Hoechst laboratories.

A highly profitable industrial involvement originated in 1902 from Fischer's joint work on diethyl barbituric acid with J. von Mering, Professor of Medicine at Halle University.[63] This substance proved to be a highly effective soporific that Fischer used successfully even on himself.[64] After obtaining the patent rights,[65] diethylbarbituric acid was first produced by Merck at Darmstadt, and then, from 1904 onwards, jointly with Bayer Leverkusen, becoming under the name veronal (or barbital) one of the most valuable hypnotics. In later joint research with von Mering (1907) calcium iodobehenate ("sajodin"), a tasteless iodine source readily tolerated by the organism, was manufactered by the Bayer and Hoechst companies. Another pharmaceutical line began in 1913, when Fischer collaborated with G. Klemperer, chief physician of the Moabit Hospital in Berlin and cancer expert,[66] in the evaluation of certain arsino- and seleno-behenolates which he had prepared as carcinoma remedies.[67] One of these, "Elarson" was marketed by Bayer's Elberfeld factory.

Fischer's intense interaction with the chemical industry is documented in great detail by his immense correspondence with essentially all of the major companies in Germany and their principal leaders. The Emil Fischer Papers[68] contain 181 letters from Carl Duisberg, (covering the years 1895−1919), from Farbenfabriken Bayer (271), Hoechst (50), Boehringer Mannheim (116), BASF (54), Merck Darmstadt (33), and various others, their content delineating the multifaceted interrelationships between academe and the chemical industry, which would be well worth a comprehensive evaluation.

Whilst these close relationships with the chemical industry arose from Fischer's academic research, the outbreak of World War I in 1914 generated very different demands, which were to dominate the years destined to be the closing period of his life. Because of his outstanding reputation, his comprehensive technical knowledge, his organizational skills, and his extensive experience in coordinating science and industry, the German government asked him to mediate between the military and industry.[41,45,46,69] He was appointed to head various government commissions, such as the "Commission on the Supply of Coke Products" that was set up to address the sudden increase in demand for toluene and heavy oils. Notably, he headed the "Saltpetre Commission", set up to boost production of synthetic saltpetre by oxidation of ammonia from the Haber-Bosch process, an urgent necessity due to the interruption of Chile saltpetre imports by the sea blockade. Fischer succeeded in bringing all men together required for the solution of these problems, particularly the industrial leaders in the Rhine and Ruhr districts and moulded a joint effort towards the establishment of various new production sites, and this successfully overcame these shortages.[41] Other war-related projects which he either directed himself or played an active role in, were the utilization of the sulfur in gypsum ($CaSO_4$) and kieserite ($MgSO_4$) in substitution for the diminishing supplies of pyrite ("Gips- und Kieserit-Kommission"), the exploration of alternative sources for glycerol, the substitution of camphor in gunpowder stabilization by dimethyl- and dimethyl-diphenyl-carbamide, the conversion of straw and wood into digestible fodder for cattle ("Nährstoffausschuß"), and the enhancement of nitrogen fertilizer production. In view of these unusually diverse activities, the acute physical pain that tormented him from time to time, the loss of his second and third sons in 1915 and 1917, and the death of scientific workers in his institute due to their military service, it is outright amazing that he found time to continue his scientific research. Or did he rather take refuge to it? It was during this period that his work on depsides received many decisive additions and that the study of fats was started, probably as a result of his involvement in the "War Commission on Oils and Fats". Whatever the case, an abundance of new ideas and observations appeared in the 30 publications written in that time.

5. Fischer's Role in the German Chemical Society

The position Emil Fischer occupied in Berlin meant that his activities went far beyond his institute and his science. He was four times President of the Deutsche Chemische Gesellschaft (1894, 1895, 1902 and 1905) and Vice president no fewer than eight times, though the fairly extensive administrative work was somewhat eased because his predecessor, A. W. von Hofmann, who had founded the Society in 1867, had located both its secretariat and the editorial office for the *Berichte* it issued in the Chemical Institute; this situation lasted until completion of the Society's own building, the *Hofmann-Haus*, in 1901.[38b,42,70] During Fischer's presidencies, some basic changes in the structure and organization of the society were effected, most notably the expansion of its literary tasks by taking over the publication of the third and supplement editions of *Beilstein's Handbuch für Organische Chemie* and the *Chemisches Zentralblatt* in 1895 by means of acquiring the respective publishing rights. These actions were driven through against considerable opposition, and yet proved to be opportune, as the number of subscribers roughly tripled, and the chemical industry honoured the new enterprises by making substantial donations.[38b,42]

A rather odd incident, known as "The Ramsey Case",[6d,71] in which Fischer played a decisive role, is worth mentioning. Ramsay, who had been awarded the Nobel Prize in Chemistry in 1904 "for the discovery of inert gaseous elements in air", had studied in Heidelberg with Bunsen and in Tübingen with Fittig (Dr. phil. in 1872), had been elected an honorary member of the German Chemical Society in 1899 (on the proposition of Fischer). He received its Hofmann Medal in 1903, and furthermore was awarded the Prussian order "Pour le Mérite" in 1911. However, at the beginning of World War I, he violently attacked German science and the entire German race which aroused the rage of his German colleagues to the extent that, in April 1915, at the general assembly of the Society, a strong faction demanded the removal of Ramsay's name from the list of honorary members. In the hot-tempered discussion, Fischer vehemently took the opposite standpoint,[71] saying that "Ramsay discovered the noble gases and is one of the most outstanding chemists of all time, irrespective of the war in which our peoples are engaged",[6d] and, mainly by the impact of his strong personality, he managed to achieve a compromise: Ramsay was to be given the opportunity to justify his actions after the war. This never came about, as Ramsay died in 1917. The Chemical Society (London) in its turn was less restrained on these matters, as Emil Fischer − together with Adolf von Baeyer, Walter Nernst, Wilhelm Ostwald, Otto Wallach, and Richard Willstätter[72] − were removed in 1916 from the list of Honorary and Foreign Members.[71]

Fischer also played a very active role in the Prussian Academy of Sciences in Berlin, to which he had been elected in 1893.[73] Apart from participating in all its meetings, the Academy required from its members the presentation of a comprehensive lecture each year, so it can be safely concluded, that of the 26 lectures Fischer was obliged to deliver, a major portion entered into the well-elaborated lectures that appeared in print.[26h]

6. Emil Fischer's Activities in Establishing the Kaiser Wilhelm Society and Its Institutes

Science is not to be understood as an autonomous development determined by "immanent laws" or "inherent logic" of the respective subject areas. The major contributory parts are specifically cultural, political, industrial and other "exogenic" factors. In this context, we may recall that Fischer's influence far exceeded his scientific work and its material consequences. Indeed, it was largely due to his inspiration and untiring energy that the idea of establishing a research foundation, independent of teaching duties, ultimately took shape and came to be realized in the foundation of the Kaiser-Wilhelm-Gesellschaft in 1911.[74−77] The opening of the first institutes was celebrated in October 1912 (cf. Figure 4): the *Kaiser-Wilhelm-Institute für Chemie* at Berlin-Dahlem, with Ernst Beckmann and Richard Willstätter as its leading figures, and the *KWI für Physikalische and Elektrochemie* with Fritz Haber as its director. Others were to follow, most notably the *KWI für Kohlenforschung* in Mülheim/Ruhr, a joint enterprise of government, chemical industry and the city of Mülheim, and it was Fischer, with his authority, persuasive power, and diplomatic skills, who united these disparate factions into contributing substantial funding towards a common goal. Furthermore, in a 1912 lecture at Solbad Raffelberg near Mülheim entitled "Augmentation of the Intrinsic Values of Coal"[78] Fischer even determined − in a stroke of prophetic foresight − the research programme to be pursued: improvement of the coking process, the generation of synthetic rubber from coking gases, the production of liquid and gaseous fuels by use of catalysts, and the direct generation of electricity from coal. The KWI for Coal Research was opened in July 1914, four days before the outbreak of World War I, and these tasks set by Fischer were all tackled and scientifically solved during the war whilst their large-scale industrial realization started later. In 1925, the production of liquid fuel from coal ("Fischer-Tropsch synthesis") was achieved, the catalytic processes reaching a climax with the work of Karl Ziegler on the metal-catalyst-induced normal-pressure polymerization of ethylene.

Figure 4. Kaiser Wilhelm II at the inauguration of the first two Kaiser-Wilhelm-Institutes (for Chemistry, and for Physical Chemistry and Electrochemistry) in Berlin-Dahlem on 23 October 1912;[24] behind the emperor, the president of the Society, Adolf von Harnack (right), and Emil Fischer (center), its vice-president

7. Fischer's Scientific Progeny

The most advanced discoveries of any age constitute the basis for next. Where Fischer left off, his scientific progeny continued. Thus, Fischer's impact on the subsequent development of organic chemistry and biochemistry derived not only from his monumental research achievements, but also from the experience gained by his doctoral students, postdoctoral associates and research assistants. Some 330[79] scientists from all over the world crowded into his laboratories, first at Erlangen but then in greater numbers at Würzburg (1888−1892) and, over the next 26 years, at the Friedrich-Wilhelms-Universität of Berlin (now Humboldt University).

The Fischer School was formed principally from students who joined his research group to work for their doctorates (223), of whom a sizeable number (46) were from foreign countries, most notably from the U.S. (21) and Great Britain (18). Thus, the greater part of the outstanding work Fischer brought forth during his scientific career of 45 years was, in fact, carried out by doctoral students. Their efficiency in tackling the research topics assigned to them required a superiour research instructor, who knew how to make good use of the advantages of the research programmes required for doctoral candidates at German universities. Of Fischer's 108 remaining postdoctoral associates about one-third (38) had received medical degrees, and − from 1902 onwards, when Abderhalden, himself Dr. med., had joined Fischer's group as *Privatassistent* − the medical men were routinely allocated to Abderhalden for work on the amino acid analysis of proteins.

Most of Fischer's students and associates found employment in the chemical industry or government offices, some attaining high office in such chemical firms as Boehringer-Mannheim or Hoechst. Fischer's greatest contributions to the subsequent later development of the chemical and biochemical sciences derive from the work of his students and associates who remained in academic life or entered scientific research institutions. These workers, 112 in all, comprise some of the most distinguished chemists and biochemists of the 20th century. The genealogical tree of Figure 5 shows twenty *Fischer Schüler* who achieved particular scientific distinction in their later careers, both as leaders of productive research groups and as teachers. Four of those − Otto Diels, Hans Fischer, Fritz Pregl and Adolf Windaus − received the Nobel Prize for Chemistry, two others, Karl Landsteiner and Otto Warburg, for Physiology or Medicine.

The first of the pre-eminent *Fischer Schüler*, whose later work was clearly derived from his mentor's line of research, was **Ludwig Knorr** [1859−1921][80] (Figure 6). His association with Fischer began in Munich and continued in Erlangen, where he obtained his doctoral degree (1882) and his *Habilitation* (1885). Thence, he moved to Würzburg, where he became head of the inorganic section. Knorr's dissertation dealt with piperylhydrazines, work that he was allowed to publish on his own.[81] Shortly afterwards, in 1883, the reaction of phenylhydrazine with ethyl acetoacetate led him to a pyrazole derivative[82] that proved to be a very effective antipyretic and analgesic. Here, too, Fischer's liberality to take the credit for results of research he had himself initiated, was amazing, since he permitted Knorr to obtain a patent on his own account. The product, called "antipyrine", later "phenazone", was manufactured by the Hoechst dyeworks and − this, together with a later and more effective analogue, "pyramidone" − became the then leading antipyretic and analgesic. This also marked the entry of a dyestuff company into the pharmaceutical indus-

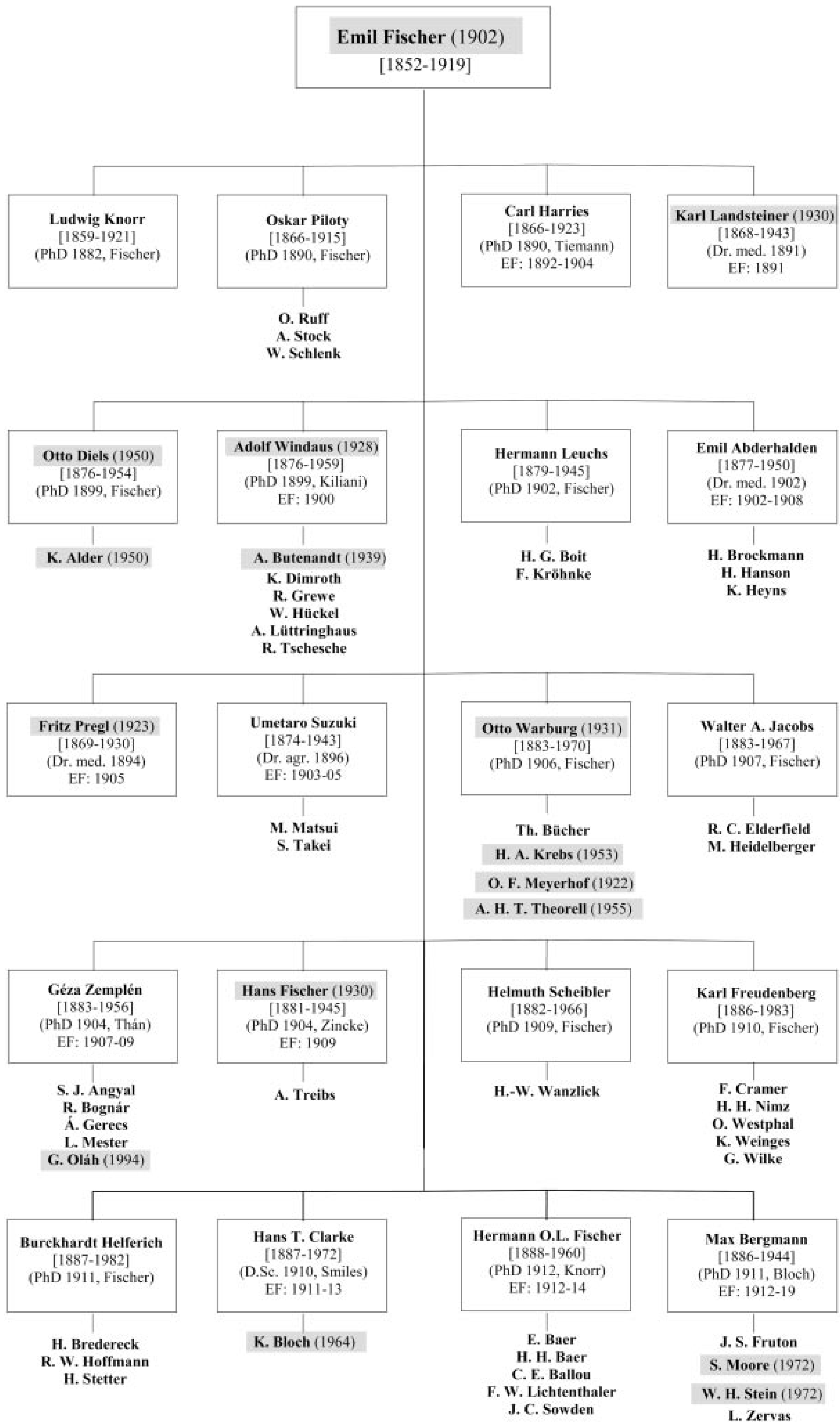

Figure 5. Emil Fischer as the founder of a great scientific tradition; his example and importance shows organic chemistry to be at the basis of biological, medicinal, and clinical chemistry through his scientific progeny; six of these developed fields which subsequently generated Nobel Prizes (names and year of award indicated by shading); amongst the following generation, i.e. Fischer's "grandchildren", were some of the most distinguished chemists and biochemists of the 20th century, of whom nine received Nobel Prizes for their scientific achievements

Figure 6. Ludwig Knorr

try.[83] In 1889, Knorr became professor of chemistry at Jena, where over the years he directed a large research group. His major achievements were his outstanding studies on pyrazoles and pyrroles ("Knorr pyrrole synthesis"), on alkaloids related to morphine and on the keto-enol tautomerism in 1,3-dicarbonyl compounds, in which H. O. L. Fischer (Dr. phil. 1911) participated,[84] as his father did not want to do his doctoral work under his supervision.[85]

Oskar Piloty [1866−1915][86] (Figure 7) was long associated with Fischer (1888−1900), first in Würzburg where he participated in the experimentally difficult studies on sugars by preparing higher homologues of rhamnose [87] and reduction products of saccharic acid[88] − work which gained him the Dr. phil. degree in 1890. He continued as Fischer's research assistant, and moved with him to Berlin in 1892 to head the inorganic section and there became heavily involved in the work for constructing a new chemical institute. As Harries later noted:[86] "He was one of the paladins of Emil Fischer who helped him to accomplish his great achievements." Piloty's independent career started promisingly with studies on aliphatic nitroso compounds, which in 1898 led to his habilitation. In 1900, he accepted an associate professorship of inorganic chemistry in Baeyer's institute in Munich, where he engaged in studies on the constitution of the blood pigment, leading to many valuable contributions to pyrrole chemistry, from which the later investigations of Hans Fischer profited immensely. At the outbreak of World War I, Piloty volunteered for the army, despite of being over the age of compulsory military service. He was made a company commander, and died in action in 1915.

Figure 7. Oskar Piloty

From among the 17 research students who had worked with Piloty during his abruptly terminated scientific career, three attained particular importance as professors at universities and as outstanding researchers, curiously enough in the field of inorganic chemistry: **Otto Ruff** [1871−1939],[89] **Alfred Stock** [1876−1946],[90] and **Wilhelm Schlenk** [1879−1943].[91] All three were, in one way or another, closely connected with Emil Fischer, Schlenck even succeeding Fischer in 1921.

Otto Ruff, having obtained his Dr. phil. degree with Piloty in Berlin (1897) for work on aliphatic nitroso compounds,[92] then joined Fischer in his work on sugars.[93] When starting out independently, Ruff chose to work on carbohydrates. Immediately, he discovered the still most useful method for shortening the carbon chain of a sugar, simply requiring oxidation of an aldonic acid salt with hydrogen peroxide in the presence of ferric acetate − a procedure that entered the literature as the "Ruff degradation".[94] It is much simpler than the one by Wohl,[95] also developed in Fischer's institute, which involves the removal of cyanide from acetylated aldononitriles in a retro-cyanohydrin synthesis fashion. The decisive turning point in Ruff's career occurred in 1902, when Fischer offered him the position of head of the inorganic section of the new institute on condition that he devotes himself solely to inorganic chemisty both in teaching and research. Ruff adjusted easily to this self-denying ordinance and started his successful 40-year encounter with inorganic chemistry.[89]

The career of Alfred Stock was also predetermined by Emil Fischer because following his Ph. D. with Piloty on bromination products of acrolein (1899),[96] Fischer gave him an assistant position, and, a few months later, sent him for a year (with a Prussian fellowship, yet retaining his Berlin salary) to the leading inorganic chemist of the time, Henri Moissan,[97] in Paris. There, Stock was assigned the task of preparing boron and silicon, both unknown at the time, yet nonetheless he succeeded in making two silicon borides.[98] Later, outstanding studies on these two elements established Stock's scientific fame.[90] Even Fischer acknowledged this work in his biographical memoirs as "most beautiful achievements in this field".[38c] There, he also remarked laconically "that doing his doctoral thesis in organic chemistry was not detrimental to his experimental education".

Carl Harries [1866–1923][99] (Figure 8) obtained his Dr. phil. degree when working with Tiemann at Berlin in 1890, and then became an assistant in the experimental lectures given by A. W. von Hofmann. In that year, Fischer gave a lecture in Berlin on his work on sugars,[100] which must have deeply impressed Harries, as he later wrote: "I never have heard a better lecture in form and content, full of passion and noble restraint; the really great researcher emerged. For us, Emil Fischer became the criterion for all other personalities."[39] When two years later, in 1892, Fischer succeeded von Hofmann in the chair of chemistry at Berlin, he retained Harries as assistant for his own experimental lecture courses, and, soon realizing his talent, advised him to do independent research and strive for his *Habilitation*. This he achieved in 1897 with his stereochemical investigations in the piperidine series,[101], to be followed by his appointment as section head of the Institute in 1900. Their twelve-year association led even to a joint paper dealing with an improved apparatus for vacuum distillation applicable even to methyl glucoside and rubber.[102] Their relationship was not without tension though as Harries remarked: "In later years there developed an ever-stronger estrangement between Fischer and me, which I sincerely regretted. However, I could not change our relationship without giving up some of my rights."[39] Nevertheless, he could always count on Fischer's encouragement and advise, such that Fischer wrote in his memoirs:[38d] "Through the continuous personal and scientific relationship we had over the years, he has surely learned so much from me, that he may be counted as one of my pupils." In 1904, Harries accepted the chair of chemistry at the University of Kiel where his extensive studies on the ozonization of olefins and rubber in particular won him wide acclaim.

Figure 8. Carl Harries

By contrast, **Karl Landsteiner**'s [1868–1943][103] (Figure 9) association with Emil Fischer was relatively brief. After receiving a Dr. med. degree in his native Vienna in 1891 he spent the next five years in organic-chemical laboratories, in Fischer's Würzburg Institute doing research on glycolaldehyde, the key intermediate in the generation of monosaccharides in the formose reaction.[104] He also worked with Bamberger in Munich and with Scholl in Zürich on organic topics[105] before embarking, after his return to Vienna in 1896, on his memorable research in immunology. This work led to the discovery of the human-blood groups (1901) and their classification into the well-known subgroups (1909). In 1922 he moved to the Rockefeller Institute of Medical Research, were other former Emil Fischer associates, such as P. A. Levene and W. A. Jacobs, were already working and Landsteiner continued to investigate blood groups and the chemistry of antigens, antibodies, and other immunological phenomena, such as the Rh-factor in blood. These monumental achievements were recognized by the Nobel Prize in Physiology or Medicine in 1930. It was one of his great merits to have introduced chemistry into the service of serology, only possible for a man thoroughly trained in preparative organic chemistry.

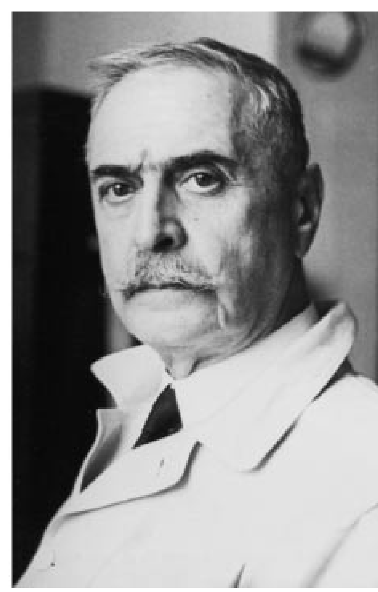

Figure 9. Karl Landsteiner

Otto Diels [1876–1954][106] (Figure 10) was associated with Fischer for the unusually long period of 20 years (1896–1916) which indelibly marked his later most successful career. After studying chemistry at Berlin University, he joined Fischer's group as a research student and gained his Dr. phil. degree in 1899 for work on cyanur compounds. He published his dissertation under his sole name,[107] yet it bore the unmissable words "at the instigation of Professor Emil Fischer" in the introduction. Promoted to assistant, he began independent work, leading to his *Habilitation* in 1904 and to his appointment as section head in 1913. Dur-

Figure 10. Otto Diels

Figure 11. Adolf Windaus

ing this time Diels discovered carbon suboxide and worked on a variety of other topics including the chemistry of cholesterol (with Abderhalden) − studies he continued at the University of Kiel on moving there in 1916 as successor to Harries. There, he made decisive contributions to the elucidation of the structure of the steroid nucleus by introducing the selenium dehydrogenation as an extremely useful tool (1927) and, in 1928, in collaboration with his doctoral student Kurt Alder [1902−1958] discovered the reaction which bears their joint names and for which they were awarded the Nobel Prize in Chemistry in 1950.

Adolf Windaus [1876−1959][108] (Figure 11) originally studied medicine at his native city of Berlin, passing the *Physikum* in 1897, but Emil Fischer's lectures on chemistry aroused his enthusiasm for the subject, convincing him that this was the science "for which I am best suited."[109] Continuing his studies in Freiburg, he switched to chemistry, joined the group of Kiliani, and received his Dr. phil. degree in 1899 for studies on the cardiac poisons of digitalis. Windaus spent the following two years in Fischer's laboratory working on quaternary aniline homologues.[110] He then returned to Freiburg to begin work on sterols, at Kiliani's suggestion. This was particularly appropriate, as Kiliani's Institute for Medical Chemistry was affiliated with the medical faculty. "On Cholesterol" was the short title of the thesis that gained him his habilitation in medicine (1903). The most remarkable achievements of his 45-year active career (from 1915 on as director of the Wöhler-Institut in Göttingen) was his intercorrelation of steroids with bile acids by transforming cholesterol into cholanic acid (1919) and by demonstrating (together with the New York physiologist Alfred F. Hess) that vitamin D can be produced from yeast ergosterol through irradiation with ultraviolet light (1927). Another productive investigation was that of imidazole, involving the elaboration of the structure of histidine and the discovery of histamine. In 1928, these notable achievements were recognized by the award of the Nobel Prize in Chemistry. Another major contribution to the advancement of chemistry was his establishment of an outstanding research school, from which an unusually high proportion of graduates chose academic careers (cf. Figure 5), thereby providing some of the most distinguished teachers and researchers of the next generation.

Of very a different nature was **Hermann Leuchs** [1879−1945][111] (Figure 12). In his memoirs, Fischer described him as having[38e] "a quiet scholarly personality, characterized by discretion, calm and seriousness. He carried out the work for his doctoral thesis under my direction on the synthesis of oxyamino acids, the most beautiful result being the synthesis of serine and glucosamine. The skill and conscientiousness which he showed, induced me to select him as private assistant in the difficult investigations on polypeptides. ... He is a very intelligent chemist and exceedingly skilful in experimentation. After two years of excellent work, he became a teaching assistant, and section head after Diels' move to Kiel. I hope he will obtain an independent position in the not too distant future." This highly appreciative opinion of Fischer was a most adequate portrait of Leuchs at the time, and, indeed, his academic career began promisingly. He received his Dr. phil. degree in 1902,[112] his independent status from 1904 onwards, *Privatdozent* (1910) and associate professor (1914). He discovered the *N*-carboxyanhydrides of amino acids, made basic contributions to the chemistry of spiranes, and, in 1908, started his extensive investigations on strychnos alkaloids described in over 120 publications.[111] For reasons not apparent even to his closest associates he turned down offers of full professorships at the Universities of Graz and Braunschweig, which would have considerably improved his position, in favour of a personal full professorship at the Berlin Institute. He ended his life during the fall of Berlin in the final days of World War II.

Figure 12. Hermann Leuchs

Among those who worked with Fischer, **Emil Abderhalden** [1877−1950][113] (Figure 13) occupies a special position. Having obtained a Dr.med. degree from the University of Basel in 1902, he joined Fischer's research group at a time when it was principally engaged in work on amino acids and peptides, first as assistant in his private laboratory, then increasingly as supervisor to the succession of postdoctoral medical men who flocked Fischer's laboratory from all over the world. To them, invariably, was assigned the determination of the amino acids contained in various proteins by the "ester method", that is conversion of amino acid mixtures from protein hydrolysates into esters followed by distillatory separation. Although long-winded and not very original, a large number of publications resulted therefrom (ca. 100) providing a first, albeit qualitative, overview of the amino acid composition of a large variety of proteins. Together with work on proteolytic enzymes, this led to his *Habilitation* in 1904 and a professorship at the Berlin veterinary school (1908). In Berlin, and from 1911−1945 as professor of physiological chemistry at the University of Halle, Abderhalden continued with the research topics to which he had been introduced by Fischer, particularly in the application of the halogenoacyl halide method for the assembly of polypeptides − a nonadecapeptide of questionable purity, by today's standards, was synthesized in 1912. By contrast, Fischer had ceased to use this procedure after 1910, realizing that it would not lead to the synthesis of the natural proteins he was heading for. Extensive work was also invested into proving the likelihood of the occurance of diketopiperazines (cyclic dimers of amino acids) in proteins, one of Fischer's suggestions which he had not explored further. The formation of diketopiperazines on hydrolysis of silk fibrin, which was taken as evidence that they are structural elements of the protein,[114] was shown later to be an artefact arising from the method of preparation. In addition to extensive studies on the chemistry of proteins, Abderhalden worked on a variety of biochemical subjects, such as enzymes, protein metabolism, hormones, and vitamins. His claim, in 1907, to have discovered the so-called *Abwehrfermente* eventually aroused much controversy. These were protective enzymes formed upon administering parenteral protein into the blood plasma and were said to be capable of degrading the injected protein only.[115] Although Michaelis in 1914 and van Slyke in 1916 were unable to reproduce the experiments, for the next 35 years Abderhalden carried out extensive studies to prove their validity.[116] A brief renaissance of the *Abwehrferment-Reaktion* ensued in the 1950s with the introduction of the Niehans cellular therapy, though it was soon clinically refuted[117] and finally "buried" in 1998.[118] Abderhalden was endowed with seemingly inexhaustible energy, and not only produced over 1200 scientific papers,[119] but also numerous books which he either edited or wrote himself. To give three examples, his *Lehrbuch der physiologischen Chemie* (1906) was translated into English and Russian and went through 26 editions in 42 years, and he edited the *Biochemisches Handlexikon* (14 vols.) and the *Handbuch der biologischen Arbeitsmethoden* (107 vols.). In addition, from 1931 to 1950 Abderhalden served as President of the German Academy of Natural Scientists Leopoldina in Halle.[113b]

Figure 13. Emil Abderhalden

When **Fritz Pregl** [1869−1939][120] (Figure 14) joined Fischer's laboratory in 1905, he held a Dr. med. degree from the University of Graz, and had already habilitated in physiology with studies on the C/N ratio in human urine. Accordingly, as a matter of routine, he was turned over to

Figure 14. Fritz Pregl

Abderhalden for work on the amino acid composition of egg albumin and the characterization of certain amino acid derivatives in urine. Whilst his stay in Berlin lasted less than a year, his work generated two publications,[121] and he always emphasized that his chemical research with Fischer and the stimulus of working in Fischer's laboratory were the most valuable influences on his life.[120a] Upon returning to his native Graz, Pregl began investigating the components of albumins and the analysis of bile acids. However, shortages of starting materials compelled him to develop methods that used smaller amounts for quantitative elemental analysis. In 1917 he had devised a series of new instruments, including a sensitive microbalance, and proper techniques for the analysis of 2−3 mg samples. Recognition for this most significant technical advance in micro-analytical methodology − not a discovery, but the ingenious perfection of existing methods − led to the award of the Nobel Prize in Chemistry in 1923.

Among Fischer's foreign research fellows in Berlin were five Japanese who all pursued academic careers after returning to Japan.[122] The most prominent was **Umetaro Suzuki** [1874−1943].[123] Having studied agricultural chemistry at Tokyo University, where he obtained a Dr.agr. degree in 1901, he spent the next five years in Europe, first with Bamberger at Zürich working on plant alkaloids, and, from 1903 to 1905, with Fischer in his Berlin Institute. There he took part in the work on amino acids and polypeptides, which led to four joint papers.[124] When Suzuki left Berlin at the end of 1905, Fischer advised him, that back in Japan "he should work on research topics that are genuinely Japanese". Taking this advice, Suzuki began studies on the nutritional values of polished and unpolished rice and found that consumption of the former led to nutritional deficiencies (beri-beri) in chickens. Having been appointed to a full professorship at Tokyo University in 1907, in 1911 he succeeded in isolating a crude substance from rice bran, which proved to be an effective anti-beri-beri factor.[125] This was marketed by Sankyo Co. in 1912 for therapeutic treatment of beri-beri disease. The active principle, vitamin B_1 or thiamine, was also isolated in 1911 by Casimir Funk at the Lister Institute in London,[126] yet despite substantial research efforts in many laboratories, it was another 25 years before Williams succeeded in elucidating its structure.[127] Suzuki continued his research on rice constituents, isolating for example, phytin from rice bran as well as phytase, which was the first phosphorylating enzyme to be reported. Valuable further contributions resulted from his extensive studies on vitamin B_6 and other natural products. The hitherto unknown amino acids L-citrulline, L-canavanine, and food constituents such as tea catechines, were all isolated by people connected with Suzuki. In 1924 he founded the Agricultural Chemical Society of Japan,[128] served as its first president, and became chief researcher of the National Physical and Chemical Institute (RIKEN). He received many honours, among them the Imperial Award of Japan (1924) and the Order of Cultural Merit (1943). When he had the privilege of presenting a lecture to Emperor Hirohito, he, signally, chose to talk about Emil Fischer and biochemistry. In 1993, fifty years after his death, a conmemorative postage stamp (cf. Figure 15) was issued by the Japanese Government depicting aside Suzuki the (partially hidden) formula of vitamin B_1.

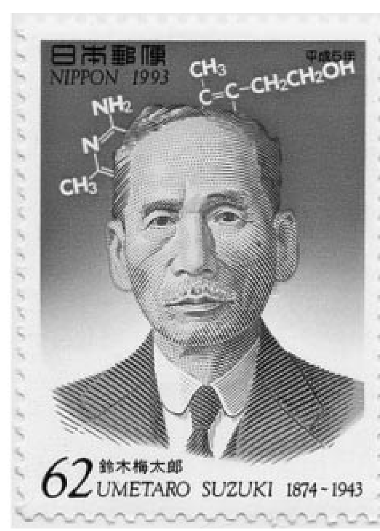

Figure 15. Umetaro Suzuki

Among the distinguished biochemists emerging from Fischer's school, **Otto Warburg** [1883−1979] (Figure 16) is especially outstanding[129] as his work during the 1930s represents a peak of biochemical achievements in the 20th century. He studied chemistry at the University of Berlin and gained his Dr. phil. degree in 1906 for work with Emil

Fischer on the synthesis of a series of peptides.[130] He then gave up preparative organic chemistry entirely as his interest in medical problems led him to study medicine at the University of Heidelberg, where he obtained a Dr. med. degree in 1909 for work with Ludolf von Krehl on the respiration of sea urchin eggs. Throughout his life he acknowledged the importance of his association with Fischer which had given him the foundation for his later successes. Indeed, Fischer, as vice-president of the Kaiser Wilhelm Society, was responsible for Warburg's appointment as head of the laboratory of the Kaiser-Wilhelm-Institut at Berlin-Dahlem in 1914, where he was to conduct his important researches for the next 55 years, interrupted only by four years military service during World War I. Around 1920, he resumed his studies on cellular respiration, particularly concerning the oxidative metabolism and glycolysis of tumour cells. He also initiated investigations on the assimilation of carbon dioxide in plants, and on the nature of the oxygen transferring respiratory enzyme (the *Atmungsferment*, i.e. cytochrome-c oxidase). Indeed, brilliant studies earned him the Nobel Prize in Physiology or Medicine in 1931. His later researches, since 1931 as Director of the *Kaiser-Wilhelm-Institut für Zell-Physiologie* in Berlin, led to the discovery of the first flavoproteins and the proof that flavin and nicotinamide are the active groups of the hydrogen-transferring enzymes, thereby providing, together with the "iron oxygenase" discovered earlier, a remarkable account of the oxidation and reduction processes in the living world.

Figure 16. Otto Warburg

The scientific stature of **Hans Fischer** [1881−1945][131] (Figure 17) was rather different, as his independent career started at a Medical Clinic and his research moved straightforwardly into the core of synthetic organic chemistry. After studying chemistry at Marburg (Dr. phil. in 1904 with Zincke) and medicine at Munich (Dr. med. 1908), he became a research assistant of Emil Fischer in Berlin, working on glycosides of lactose and maltose.[132] As early as 1910, however, he terminated his association with Emil Fischer, returned to Munich and, on the advice of the distinguished clinician Friedrich von Müller who had reasoned that bile pigments are formed from hemoglobin, Hans Fischer began investigating the constitution of the blood pigments in a laboratory of the second medical clinic. He obtained his *Habilitation* in 1911 in medicine and succeeded Windaus at Innsbruck (1916), Ludwig at Vienna (1918), and finally Heinrich Wieland in the chair of chemistry at the Technical University of Munich (1921). His outstanding achievements there over a 20-year period reached their zenith in the total syntheses of hemin (1929), for which he was awarded the Nobel Prize in Chemistry in 1930, and of bilirubin (1934) as well as extensive studies on chlorophyll, which eventually led to the solving of its structure. Fischer took his own life at the end of the World War II after his laboratories had been destroyed in the bombing of Munich.

Figure 17. Hans Fischer

Among Emil Fischer's students who made important contributions in fields unrelated to his main research interests was **Helmuth Scheibler** [1882−1966][133] (Figure 18). After studying in Geneva, Munich and Berlin, he obtained his Dr. phil. degree in 1909 for work with Fischer on valine dipeptides and on the Walden inversion,[134] and, as a research assistant, he first continued with the investigations of amino acids. He then turned to the study of thiophene components of ichthyol oil with which he habilitated in 1915 at the Technical University of Berlin (Charlottenburg), which was to become his place of work for both, teaching and research for the next 40 years, first as associate and then as full professor. His main line of research, beginning in about 1925,[135] centered on compounds with divalent carbon, leading to many fundamental contributions which laid the basis for carbene chemistry.

Figure 18. Helmuth Scheibler

Among those who worked with Fischer in the years before World War I were four men who continued research on problems to which they had been introduced by Fischer: G. Zemplén, K. Freudenberg, B. Helferich, and H. O. L. Fischer, the eldest of his three sons.

Géza Zemplén [1883−1956][136] (Figure 19), is justly considered to be the founder of organic chemistry in Hungary.[136c] He had studied chemistry at the University of Budapest, received his Dr. phil. degree in 1904 for work with Károly Thán on the surface tension of aqueous solutions and, in 1905 he joined the Mining and Forestry School at Selmeczbánya (Schemnitz, today Slovakia) as an assistant. With a fellowship from the Hungarian Ministry of Agriculture he spent nearly three years (1907−1910) in Fischer's laboratory in Berlin, successfully working on topics of amino acid chemistry (synthesis of D- and L-proline, ornithine, and piperidones[137]) and sugars (derivatization and enzymatic behavior of cellobiose[138]), as evidenced by eight joint publications, and by several comprehensive accounts for Abderhalden's *Handbuch der biologischen Arbeitsmethoden*. After his return to Selmeczbánya, he continued research on carbohydrates, with which he habilitated in 1912 at the University of Budapest. When, in 1913, the first Chair of Organic Chemistry in Hungary was established at the Technical University of Budapest, Emil Fischer played a decisive part in Zemplén's appointment. He was only 29 at the time and there were several applicants for the post; but the then rector, G. Rados, sought Fischer's advise, and, on a most favorable assessment,[139,140] Zemplén was appointed. In the selection of his research topics and particularly in the way he carried them out, Zemplén was greatly influenced by Emil Fischer, as he continued research in the field of carbohydrates and, over the years − interrupted by the destruction of his institute during World War II − turned out an impressive series of important papers on the synthesis of oligosaccharides and of numerous naturally occuring glycosides. His legacy lives on in his many pupils, some of whom achieved particular eminence in Hungary as well as abroad (see Figure 5).

Figure 19. Géza Zemplén

Karl Freudenberg [1886−1983][141,142] (Figure 20) worked with Fischer between 1908 and 1914, first as a doctoral student, receiving his Dr. phil. degree in 1910 for studies on phenolcarboxylic acid derivatives,[143] then as a research assistant carrying out the first investigations on depsides and tannins.[144] Strength of purpose and self-confidence were shown early by the young Freudenberg in that he managed to start work independently while still with Fischer, and, perhaps even more characteristically, it was he who effected the disengagement from his illustrious teacher. As a first independent research topic he had chosen to study the configurational relationships between tartaric, malic, lactic, and glyceric acids[145] by converting levorotatory malic acid in a series of reactions into the equally levorotatory glyceric and lactic acids. When, before publication, he presented the results with apparent success at an institute colloquium, the renowned physicist Madelung overwhelmed him with unstinted praise saying: "Das war eine echte Fischer-Arbeit". Freudenberg's reaction was that of a painful awakening: "If somebody had hit me on the head with a truncheon, the effect would have been the same; what Madelung said was true, alarmingly true, and in a flash I realized to what extent I was caught in the world of ideas of my teacher." [141a] His immediate response was to distance himself from Emil Fischer, accepting an assistantship with Harries at the University of Kiel only a few days later. There, he was able to complete his *Habilitation* in the autumn of 1914, just before military service in World War I interrupted all scientific activities for four years. In 1919 he resumed his position at Kiel, and this was followed in rapid succession by professorships at Munich (1920), Freiburg (1921), Karlsruhe (1922), and finally at Heidelberg (1926) as the successor to Curtius.

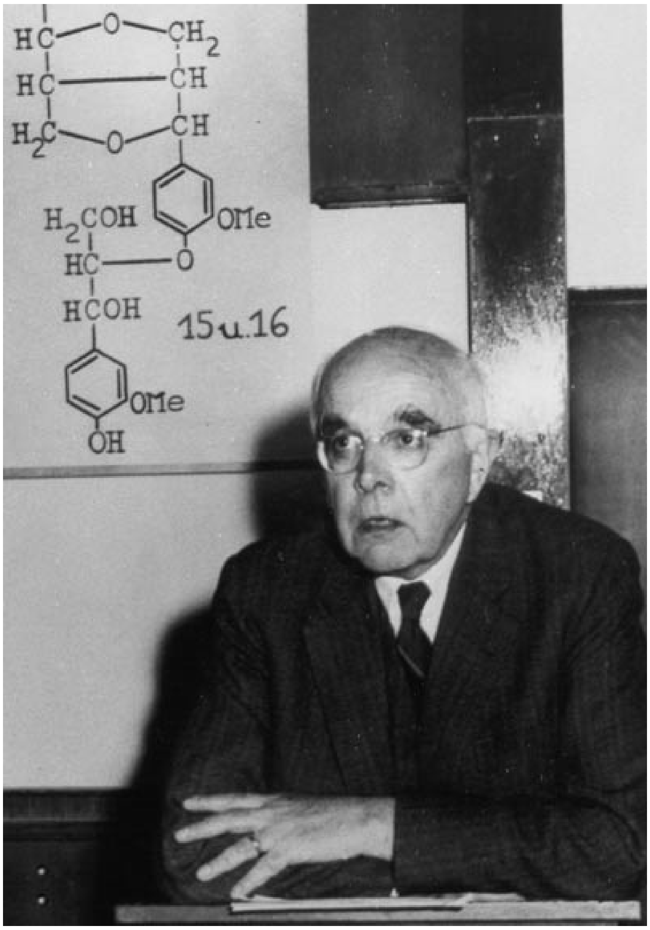

Figure 20. Karl Freudenberg

Three major lines of research, clearly emanating from Freudenberg's time with Emil Fischer, were taken up in the early 1920s and, growing in scope and intensity, carried on through his scientific career which lasted almost 50 years. These investigations were on the absolute configuration of sterically related compounds culminating in the basic textbook *Stereochemie* in 1933,[146] further exploration of the chemistry of tannins, and studies on mono- and polysaccharides, particular highlights being the proposition in 1921 that "cellulose is composed of cellobiose units to the extent of 60%, and, most probably, totally",[147] the proof being provided in March 1928,[148] a month before it was also submitted by Haworth.[149] The first proposal of a helical structure for starch was to follow in 1939[150] in the context of clarifying the constitution of the cyclodextrins. Freudenberg's main occupation in the last four decades of his unusually long scientific life was concerned with unravelling of the complex framework of lignin − tenacious and, for that time, truly pioneering studies. It bears to his unusual vigour and productive capacity that, at the age of 80, he not only conceived a constitutional scheme for the lignin of spruce but also provided the basis for its biochemical formation in the plant.[151]

After studying at Lausanne and Munich, **Burckhardt Helferich** [1887−1982][142,152] (Figure 21), was accepted by Emil Fischer as doctoral student in 1909, received his Dr. phil. degree in 1911 for work on the synthesis of glucosides,[153] and continued that research as *Privatassistent* which led to the preparation of the first nucleosides[154] by a method that became known as the "Fischer-Helferich procedure".[155] After serving for four years as an artillery officer in World War I, he resumed his position at the Chemical Institute in Berlin, started independent research which led to his *Habilitation* in 1920 and professorships in Frankfurt (1922), Greifswald (1925), and Leipzig (1930). In 1945, he was relocated by the American occupying forces, and was at the University of Bonn from 1947 to 1960. The main lines of research he pursued through all these moves had originated in Berlin, i.e. extensive studies on the specifity of enzymes, especially of sweet-almond emulsin, and systematic investigations into the stereoselective synthesis of di- and oligo-saccharides − the latter a term proposed by Helferich in 1930.[156] This work also led to the introduction of the highly useful trityl group for blocking primary hydroxyls in sugars.[157] Notably, his first [153] and last publication on this subject[158] are 63 years apart. A good many other topics were pursued, extending into non-carbohydrate and even inorganic themes. Altogether 328 publications emanated from Helferich's laboratory[152b] giving ample evidence of the prolific flow of his ideas and his powerful dynamism that enabled him to realize them. Throughout his long life, Helferich was nonetheless aware of to whom he owed his success. As he remarked in 1951 upon receiving the German Chemical Society's Emil Fischer Medal:[159] "I had the privilege to work for years − first as doctoral student, then as assistant − with Emil Fischer, by whom I was led to whatever I have accomplished".

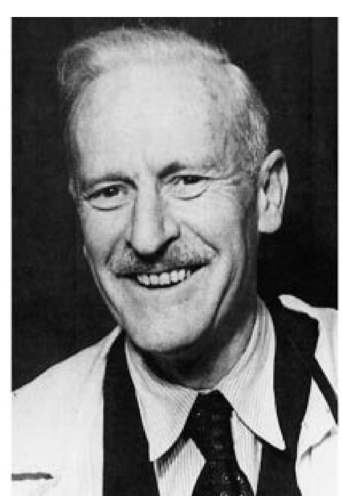

Figure 21. Burckhardt Helferich

The scientific career of **Hermann O. L. Fischer** [1888−1960],[85,142,160] the eldest of Emil Fischer's three sons, was to follow an unusually cosmopolitan course. After studying chemistry at the Universities of Berlin and Cambridge, England, at the behest of his father, he did his doctoral work with Ludwig Knorr at the University of Jena, because in another university which the young Fischer would have preferred, "the habits in the chemical institute were considered to be somewhat too alcoholic".[85] After being granted the Dr. phil. degree in 1912 for studies on the enol form of β-diketones,[84] Hermann Fischer joined his father's laboratory to continue research under his guidance for a two-year period, which generated four joint publications on the synthesis of naturally occurring depsides.[161] This work was ruthlessly interrupted by the outbreak of World War I in which Hermann served in a military warfare unit. On his return in 1918, he started to redevelop his career in chemistry, a task that aside the disturbed political conditions was made all the more difficult by the devastating loss of his father in July 1919. However, he succeeded in gathering together a small research group with which he gradually developed two main lines of research, one comprising the difficult chemistry of phosphorylated lower-carbon sugars, the other dealing with cyclic plant acids, such as quinic and shikimic acid. With these studies he habilitated in 1922 and held the position of assistant professor for the next ten years, the Berlin Institute only returning to its normal functioning in about 1924 under the leadership of Wilhelm Schlenk, Emil Fischer's successor.

Seeking to escape the tragic events that were to occur in the later 1930s and which were already taking shape at the beginning of that decade, Hermann Fischer first moved to Switzerland where for five years he was associate professor of chemistry at the Pharmaceutical Institute of the University of Basle, and in 1937 emigrated to Canada, accepting a research professorship at the Banting Institute of the University of Toronto. The major reasons for this at the time unusual move were not only the very favorable research conditions he was offered there, but, in his words,[85] "it was too clear that war was coming and I did not want my sons to serve in the army where ideals did not conform with those of the family"; another reason may have been that his wife was Jewish. He became a Canadian citizen in 1938 by a special act of Parliament. However, in 1953, he adopted the American citizenship having joined the newly established Biochemistry Department of the University of California at Berkeley in 1948.

Hermann Fischer's contributions to carbohydrate chemistry and biochemistry are characterized by their elegance, precision, and biological significance. In 1932 he synthesized D,L-glyceraldehyde 3-phosphate[162] of which Warburg, Embden, and Meyerhof showed that only the D-enantiomer is fermentable. In a remarkably stereoselective aldol addition that today would be labeled "biomimetic", dihydroxyacetone and D-glyceraldehyde were shown under very mild basic conditions to give D-fructose and D-sorbose in high yields.[163] Work on quinic and shikimic acid eventually led to the establishment of their structures and absolute configurations during 1932−1937,[164] yet the real reward for this meticulous work was to come some 15 years later when a sample prepared by Fischer enabled B. D. Davis[165] to identify shikimic acid as a major biosynthetic intermediate in the formation of aromatic amino acids. Simple procedures for ascending and descending the sugar series were developed, as well as a novel synthesis of 3-amino sugars by cyclization of sugar dialdehydes with nitromethane.[166] His synthesis of D-erythrose 4-phosphate[167] proved to be of biochemical significance as it soon was shown by D. B. Sprinson to be converted by *E. coli*, in the presence of phosphoenolpyruvate, to 5-dehydroshikimic acid.[168] It is a tribute to the intelligence, imagination, and assiduousness of Hermann Fischer that despite the delayed start of his academic career, the emotional shock of a war in which he lost all his immediate family, his frequent moves with their attendant adjustments, and the handicap − or was it a challenge? − of having to live up to the reputation of his illustrious father, he produced so many significant and highly original works.

The centenary of Emil Fischer's birth − 9 October 1952 − was celebrated at UC Berkeley by the official opening of the Biochemistry and Virus Laboratory and the donation by Hermann Fischer of a unique and valuable library of approximately 4000 volumes to the University − a collection which was started by the father and kept intact by the son throughout his three moves from country to country. Wendell M. Stanley, the eminent virologist,[169] in his capacity as Chairman of the Department, officially accepted the library and the bronze bust of Emil Fischer (Figure 22), which bears an inscription on the pedestal "Emil Fischer, Father of Biochemistry". The library, which still cherishes this bust, today is named "Emil and Hermann Fischer Library". Another memorable occasion was at the 1952 fall meeting of the American Chemical Society in Atlantic City, when Hermann Fischer presented Claude S. Hudson[170]

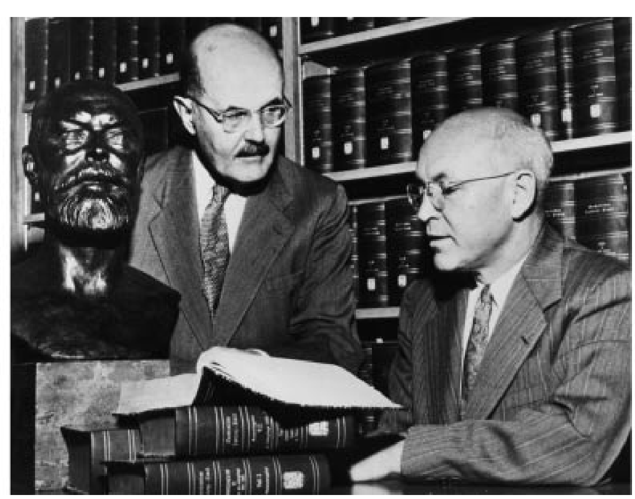

Figure 22. Hermann O. L. Fischer and Wendell M. Stanley[169] (right) on 9 October 1952, the 100th birthday of Emil Fischer, at the dedicatory ceremony donating his father's personal library to the Biochemistry and Virus Laboratory of the University of California, Berkeley

Figure 23. Claude S. Hudson (left) at the 1952 fall meeting of the American Chemical Society in Atlantic City, after being presented Emil Fischer's golden watch and chain by Hermann O. L. Fischer

with his father's gold pocket watch and chain (see Figure 23 and Figure 2, top right) recognizing him as a true successor to Emil Fischer. Hudson used to wear it only on "state occasions".

The profound influence of Fischer's scientific successors was particularly evident in the 20th century development of biochemistry in the United States. The first of the notable Americans to work in Fischer's Berlin Institute − albeit only briefly in the summer of 1902 analyzing gelatine for its amino acid composition[171] − was **Phoebus A. T. Levene** [1869−1940][172] (Figure 24), a physician who had emigrated from Russia to New York. In 1905, he joined the newly formed Rockefeller Institute for Medical Research, New York, where he remained for the rest of his career working on an extraordinary variety of biochemical problems. His major achievements were the identification of the carbohydrate components of nucleic acids such as ribose (1909) and deoxyribose (1929).

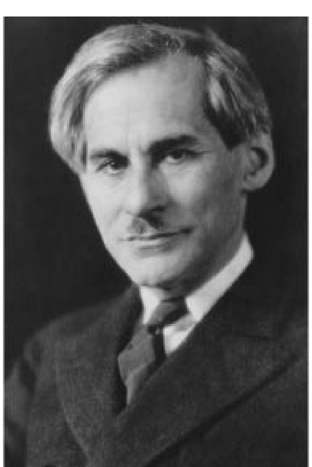

Figure 24. Phoebus A. T. Levene

Similarly brief in his association with Fischer was **Donald D. van Slyke** [1883−1971][173] (Figure 25). He had received his Ph. D. for work with Gomberg at the University of Michigan in 1907, joined the research group of Levene at the Rockefeller Institute in 1908, working on peptides from partial hydrolysates of proteins, and, most notably, developing his classic nitrous acid method for the quantitative determination of aliphatic amino nitrogen.[174] In 1911, Levene arranged for him a stay with Fischer in Berlin, where van Slyke had the privilege of working in Fischer's private laboratory on reactions of pyrrole carboxylic acid.[175] After returning to the Rockefeller Institute, he spent there the next 36 years of his distinguished scientific career continuing research on proteins, showing that they are completely hydrolyzed in the mammalian digestive tract and that amino acids disappear from the blood on passing through the tissues. He also made decisive contributions to clinical chemistry, e.g. acid-base equilibra and CO_2 transport in blood; even in his seventies, he succeeded in isolating a new amino acid from gelatine and showed it to be ε-hydroxy-lysine.

Figure 25. Donald D. van Slyke

A genuine *Fischer Schüler*, who joined the Rockefeller Institute, first as assistant to Levene (1908), then as research associate with independent status (1912) and a full member leading the pharmacology laboratory (1923), was **Walter A. Jacobs** [1883−1967][176] (Figure 26). A native of New York City, he attended Columbia University to receive an A. B. degree in 1904 and an A. M. in 1905, after which he enrolled at the University of Berlin for study with Fischer to earn his Dr. phil. in 1907 for work on the resolution of racemic amino acids.[177] During his subsequent affiliation with the Rockefeller Institute, which lasted nearly 50 years, he made many decisive contributions in various fields of organic chemistry and biochemistry, e.g. demonstrated that yeast nucleic acid is composed of ribonucleotides (1910 with Levene), discovered Tryparsamide, an arsenical effective in treating African sleeping sickness (1918), established the structure of the cardiac aglycones (1923−1934), and later, on extensive studies of alkaloids, first obtained lysergic acid as a characteristic aglyconic building block and elucidated the intricately complex structures of ergot and veratrum alkaloids.

Figure 26. Walter A. Jacobs

This illustrious group of former Emil Fischer associates at New York's Rockefeller Institute for Medical Research was joined in 1922 by Landsteiner and, in 1933, by **Max Bergmann** [1886−1944][178] (Figure 27) who as a Jew had been dismissed from his scientific position in Dresden and sought refuge in the United States. Bergmann had studied chemistry at the Universities of Munich and Berlin, and received his Dr. phil. degree with I. Bloch for work on acyl polysulfides in 1911. He then entered Fischer's group, soon becoming his chief research assistant, during World War I de facto running the institute via extensive correspondence with his teacher, who was frequently absent for long periods to recuperate from various illnesses. His research activities with Fischer were highly varied, comprising work on amino acids,[179] carbohydrates,[180] depsides,[181] and glycerides.[182] After Fischer's death in 1919, Bergmann automatically became his scientific executor, assuming responsibility for the completion and publication of unfinished researches, and the editing of his autobiographical memoir[38] and collected papers.[26c−26f] In 1920, he habilitated at the University of Berlin, yet only a year later already was appointed to head the newly established *Kaiser-Wilhelm-Institut für Lederforschung* in Dresden. There he continued his investigations on carbohydrates and peptides, strongly emphasizing that the latter should conform with the demands of the Institute, which was concerned with chemical studies of leather and tanning processes. A series of important contributions emanated from the research during this decade: the preparation of diketopiperazines from serine and cystine, the elaboration of a general method for the acquisition of dehydro amino acids, the exploitation of azlactones for peptide synthesis, and the useful process for racemization of amino acids with acetic anhydride. In 1932, Bergmann with his student Zervas developed what was perhaps his greatest contribution to peptide synthesis, the "carbobenzoxy" method. This was immediately adopted as a standard practice by other workers as, unlike Fischer's halogenoacyl halide procedure, it allowed the facile synthesis of polypeptides containing all amino acids. From 1933, when he left Germany and continued his work at the Rockefeller Institute, Bergmann's efforts were largely directed towards the study of enzyme specificity, first of a dipeptidase, then of papain and various other plant and animal enzymes, as well as towards the development of new methods for the amino acid analysis of proteins. This work, at first, was interrupted by Bergmann's untimely death in 1944, but was then continued by his associates William H. Stein and Stanford Moore, who shared the 1972 Nobel Prize in Chemistry for their achievements in this field.

Figure 27. Max Bergmann

To these distinguished scientists of the Rockefeller Institute, who have all left their mark on the development of the biochemical sciences in the United States, must be added another former Fischer associate, the Englishman **Hans Thacher Clarke** [1887−1872][183] (Figure 28), a cousin, in fact, of B. Helferich. In 1905, Clarke entered University College London, obtained a B. Sc. in 1908, and was awarded a scholarship in 1911 which enabled him to work in Fischer's laboratory in Berlin as a research guest for three semesters. Although working on problems of his own (the synthesis of alkylthiazines[184]) he had the privilege of being visited by Fischer almost daily for extensive discussions.[183a] In 1914, Clarke joined the research staff of the Eastman Kodak Co. in Rochester, N. Y., and, in 1928, accepted the challenge to head the Department of Biological Chemistry at the College of Physicians and Surgeons of Columbia University where, within a few years, he had assembled one of the strongest faculties in biochemical research and education in the U.S. This success was the result of his liberal policy in encouraging his associates to undertake independent research and seeking out talented research workers. This attitude opened up the laboratory to students who had left Germany due to the prevailing racial policy, such as Konrad Bloch,[185] who worked for his Ph. D. under Clarke's guidance. He also attracted a distinguished array of scientists, such as Erwin Chargaff, Zacharias Dische, Karl Meyer, David Nachmansohn, Rudolf Schoenheimer, and Heinrich Waelsch, who ultimately became members of the faculty. Due to Clarke's long association with industry, his output of scientific papers was modest. However, he did contribute over 30 entries to *Organic Synthesis*, edited two volumes, and made some important advances in cystine chemistry which were of considerable use in his laboratory by Williams for elaborating the structural formula of vitamin B_1.[127]

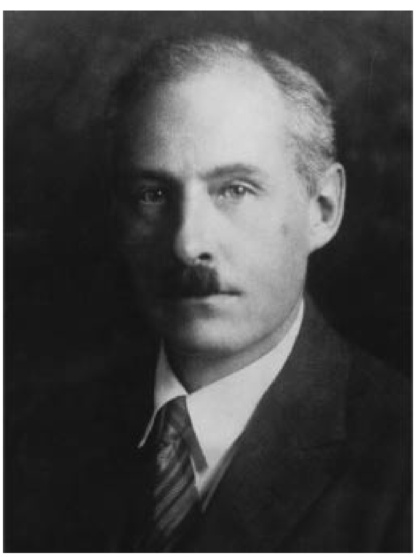

Figure 28. Hans T. Clarke

As altogether 112 of Fischer's doctoral students and postdoctoral associates decided for research careers in universities and research institutions, not only the twenty mentioned in the geneological tree of Figure 5 gained later distinction, but many others as well. **Ernest Fourneaux** [1872−1949],[186] for example, who divided his postdoctoral education in Germany between Curtius (Heidelberg), Fischer (Berlin, 1901[187]), and Willstätter (Munich), later was head of the Poulenc research laboratories (1902−1910) and then, for 33 years, of the Pasteur Institute, became the founder of French therapeutical chemistry.[186a] **Martin O. Forster** [1872−1945] was one of the first of the 18 Englishmen who did his doctoral work with Fischer (Würzburg 1892), continued research at the London Royal College of Science, and later advanced to director of the Salters' Institute of Industrial Chemistry (1918−1922) and the Indian Institute of Science, Bangalore (1922−1933). In 1920, he presented a most authoritative "Emil Fischer Memorial Lecture" before the Royal Society of Chemistry.[5] **Edward F. Armstrong** [1878−1945] may also be mentioned here, as his two years (1901−1902) with Fischer − after having obtained a Dr. phil. degree in Berlin for work with van't Hoff − were unusually productive, leading to novel disaccharides and various sugar osones.[188] Later associated with several British industrial firms, he continued work on sugars, notably writing a successful textbook on carbohydrates[189] that went through five editions and was even translated into German.

These biographical notes about the more notable *Fischer Schüler* leave the crucial question of assessing the role that direct association with a famous leader has played in their later work. In the case of those who followed in Fischer's scientific footsteps after an extended stay in his laboratory, a positive influence is unambiguous. It is more difficult, however, to trace the extent to which membership in his research group, especially when relatively brief, was reflected in the choice of problems for independent research of the others and in their subsequent scientific output. There can be little doubt, though, that any member of the Fischer school was profoundly influenced by Fischer's unswerving singleness of purpose as a researcher, by his immense capacity for sustained work, his well-premediated selection of the research fields that focussed on the organic matter on which life is built, and his style of leadership in successfully establishing and running a huge teaching and research laboratory. Inevitably, all profited from their association with one of the really great scientists of the last century in later tackling their challenges in organic and biochemistry.

8. Epilogue

In concluding this tribute to one of the towering figures of our science, whose prodigious focus on the chemistry of purines, carbohydrates, polypeptides, and, finally, fats − the four families of organic matter on which the living world is built − laid the foundations of organic chemistry and biochemistry as we know them today, we must marvel at his foresight in choosing the research fields in which he decided to spend his life. But we also admire his perseverance in pursuing his scientific work in the face of devastating events: he was tormented from time to time by severe pain mainly resulting from his excessive exposure to phenylhydrazine,[43] bowed down by the tragic death of his wife Agnes (neé Gerlach) from meningitis after only seven years of marriage, and also the loss of his sons Walter (1891−1915), who committed suicide, and Alfred (1894−1917), a physician, who died of typhoid fever while on military service in Romania. These blows of fate left their mark on Emil Fischer, as a photograph from October

1917 (Figure 29) clearly shows. Yet his undaunted spirit seemed to find refuge in the calm pursuit of scientific inquiry, his calvinistic sense of duty and his uncompromising singleness of purpose as a research chemist being the dominant factor. In 1917/18 he was stricken with pneumonia and increasingly by intestinal disorders[190] which necessitated his taking cures in Locarno and Karlsbad, during which time he started writing his autobiography.[38] The cures were apparently successful, as he continued his autobiography which carries the subtitle "Written in the year of misfortune 1918". He wrote up papers, publishing 17 in 1918/19. He further devoted much of his time to matters of the Kaiser Wilhelm Society, for instance conducted extensive negotiations with Konrad Adenauer (then Lord Mayor of the City of Cologne and member of the "Herrenhaus" in Berlin) about the establishment of a Kaiser-Wilhelm-Institute for Nutritional Physiology in Cologne, for which one of its citizens was willing to donate 1.2 million marks.[50]

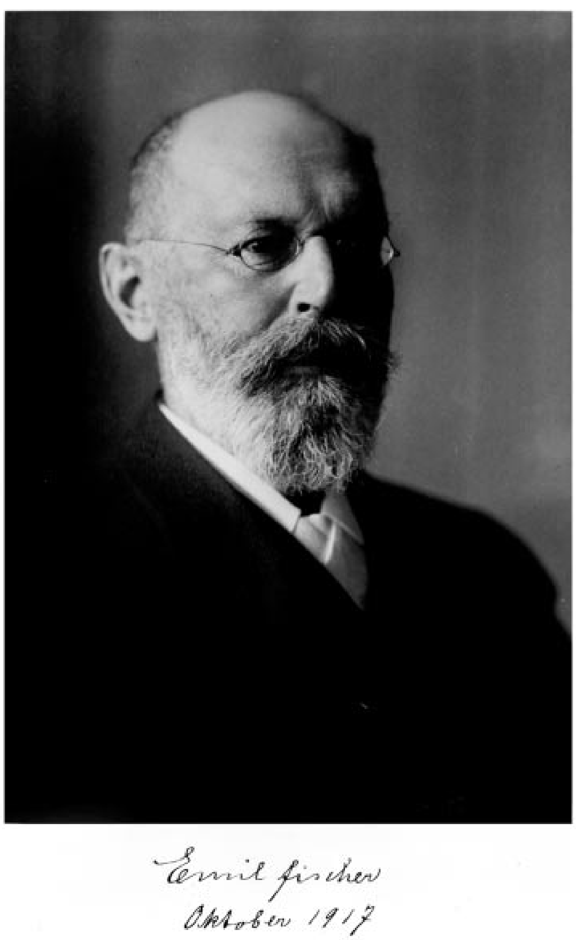

Figure 29. Emil Fischer

On 11 July 1919 he was striken by a severe disorder accompanied by great pain and high fever, which was diagnosed as resulting from an intestinal carcinoma[191] from which even an immediate operation would leave little if any chance of recovery.[192] Even then, he still retained the deep-rooted attitudes which had underpinned his scientific achievements, and which were most lucidly put into words 50 years ago by Karl Freudenberg:[193]

"Fischer clearly saw the problems in front of him, he tackled them and solved them. He never let his ship drift in the wind, on the stream or on the ocean of research. He deliberately steered his ship and reached his destination."[194]

His personal philosophy enabled him to undertake the final act of his life, which he ended by his own reasoned choice in the night of 14 July 1919. All there is left to us is to bow to the lastly unexplainable.

It is typical of Fischer's character and personality that this last step was well premeditated as was all that he did during his lifetime. Characteristic, too, how he prepared everything before his death; he sent off his last two papers, most notably dealing with sugars,[195] and he spent the better part of the morning of 14 July with a lawyer to finalize his testament, which contains the following passage:[196]

"I, Emil Fischer, hereby determine in the case of my death what follows, thereby invalidating any other previous dispositions. I establish a foundation which is to bear the name "Emil-Fischer-Stiftung". It is to be provided with a capital of 750000 marks. This sum is to be realized by my heir from among the better performing stocks of my estate ... and dedicated (to the Foundation). The profit from this capital is to be used to support young German chemists who work in organic, inorganic or physical chemistry; from the applicants, if equally well qualified, members of the Chemical Institute in Berlin of which I was in charge are to be preferred. ... The Foundation is to be affiliated with and administered by the Physikalisch-Mathematische Klasse of the Prussian Academy of Sciences.[197]

The "Emil Fischer Foundation" was truthfully established under the patronage of the Prussian Academy of Sciences with Ernst Beckmann presiding over the "Kuratorium". The Foundation suffered a deplorable fate, although three research grants were conferred in 1921 (to M. Bergmann, B. Helferich, and H. Scheibler), and another four in 1922.[196] A year later inflation had deprived the Foundation of its resources.

The last word of this homage to one of the greatest figures of our science may be accorded to Adolf von Harnack, theologian and President of the Kaiser Wilhelm Society, with whom Fischer worked closely for nearly 20 years in founding and further developing this Society and who paid his tribute in his funeral oration:[198]

"What he wanted, because he considered it both necessary and beneficial, he carried through without force or enmity, for his objectivity and openhearted amiability disarmed any opposition. Everyone had to feel: this man did not strive for influence or power as such, but for his work. His work was his science in all the relationships of his life. It was his work that he carried in his heart and for which he lived."[199]

Acknowledgments

I am grateful to Professor James A. Barnett, University of East Anglia, Norwich, for most constructive suggestions on the first draft of this article, to Professor Lothar Jaenicke, Universität Köln, for valuable comments, and to Dr. Siegfried Peters, of this institute, for invaluable assistance in securing the pictures, various rare literature and data gathered in the genealogical tree (Figure 5). I am also grateful to Joseph S. Fruton, whose exemplary, thought-provoking essays on the history of organic chemistry and biochemistry, most notably on Emil Fischer,[49] gave essential impulses for this account.

[1] http://www.nobel.se/chemistry/laureates/1902/fischer-bio.html

[2] L. Knorr, "Über die wissenschaftlichen Arbeiten und die Persönlichkeit Emil Fischers", *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 132−149.

[3] C. Harries "Emil Fischers wissenschaftliche Arbeiten", *Naturwissenschaften* **1919**, *7*, 843−860.

[4] E. Abderhalden, "Die Bedeutung von Emil Fischers Lebenswerk für die Physiologie und die gesamte Medizin", *Naturwissenschaften* **1919**, *7*, 860−868.

[5] M. O. Forster, "Emil Fischer Memorial Lecture", *J. Chem. Soc.* **1920**, *117*, 1157−1202.

[6] [6a] K. Hoesch, "Emil Fischer, sein Leben und sein Werk", *Ber. Dtsch. Chem. Ges.* **1921**, *54* (special issue); also issued as a book with the same title, Verlag Chemie, Berlin/Leipzig, **1922**. This biography, written in an overly pathetic, pompous style appears to have been well perceived by many of Fischer's contemporaries, as evidenced by enthusiastic letters of approval, e.g. from C. Duisberg, A. Gabriel, C. Neuberg and H. Pringsheim.[6b] However, it also met strong criticism; e.g. by C. Harries, who over years had been the assistant in the experimental lecture courses given by A. W. von Hofmann and E. Fischer (from 1892 on), and in the years 1920−22 happened to be President of the German Chemical Society, which had commissioned the biography; he strongly disapproved of the fact that he was deprived of seeing the manuscript before publication, and added:[6c] "It is a poetic achievement, a well-accomplished dithyramb on the adored teacher. Unfortunately, however, the author was carried away by his temperament and made statements that transgress the poetically allowed, which for historical reasons cannot remain uncontradicted. What primarily has to be objected is the comparison of August Wilhelm von Hofmann, Adolf von Baeyer, and Viktor Meyer with Emil Fischer. It is certainly permitted to make comparative evaluations of illustrious personalities, however, a protest must be made about the form, in which this was done here. Quite bluntly, the intended portrayal of Emil Fischer as the greatest is obvious. A. W. von Hofmann and Viktor Meyer come off quite badly. Instead, we should be delighted that we had such a series of great men, and, hence, should not attempt to exalt one to be the most important, since each of them more or less stood on the shoulders of the others." Richard Willstätter also criticizes Hoesch's presentation "for lack of depth, insufficient inside knowledge, and its pathetic style, that is in sharp contrast with Fischer's refreshing informality".[53a] H. O. L. Fischer, Emil Fischer's son, initially (1922) approved of the biography: "I am delighted that you have solved your task in a literarily splendid, comprehensive, and sympathetic, warmhearted form."[6b] In later years (1959) he had arrived at a different opinion: "The Hoesch biography of my father is essentially unreadable, even by an educated German" (personal communication to C. E. Ballou and the author). [6b] Letters to K. Hoesch, dating from 1922 and 1923, preserved in the *Emil Fischer Papers*, Bancroft Library, University of California, Berkeley. [6c] Presentation at a board meeting of the German Chemical Society in Berlin on 3 July 1923; the manuscript is in possession of the Bancroft Library. [6d] pp. 184−186; quote from p. 186.

[7] M. Bergmann, "Emil Fischer", in *Das Buch der Großen Chemiker* (Ed.: G. Bugge), Verlag Chemie, **1930**, vol. 2, pp. 408−420.

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[9] K. Freudenberg, "Emil Fischer, ein Wegbereiter der Biochemie", Festrede 7. Juni 1953, *Sitzungsber. Heidelberger Akad. Wiss.*, Jahresheft **1953−55**.

[10] B. Helferich, in *Great Chemists* (Ed.: E. Farber), Interscience, New York, **1961**, pp. 981−995.

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[18] L. Jaenicke, "Ein Jahrhundertdatum: 1902. Das Geburtsjahr der Peptid-Chemie", *Chemie Unserer Zeit* **2002**, *36*, 338−341.

[19] H. Kunz, *Angew. Chem.* **2002**, *114*, 4619−4632; *Angew. Chem. Int. Ed.* **2002**, *41*, 4439−4451.

[20] Otto Philipp Fischer (1852−1932), chemistry studies in Bonn and Straßburg, Dr. phil. 1874 with A. Baeyer, Straßburg, Habilitation 1875, Univ. of Munich, from 1885 on, in succession of Emil Fischer, his cousin, professor of chemistry at the University of Erlangen.

[21] Emil Fischer, "Über Fluorescein und Phthalein-Orcin", *Inaugural-Dissertation*, Universität Straßburg, **1874**; printed in ref.[26h], pp. 1−28.

[22] Jacob Volhard (1834−1910), chemistry studies with Liebig at Gießen (Dr. phil. 1855), work with A. W. von Hofmann in London, and H. Kolbe (Marburg), Habilitation 1863 (Munich), 1869 Associate Professor (Munich), 1879 Professor at Erlangen, 1882 Professor at Halle; Editor of *Justus Liebigs Ann. Chem.* since 1871 for 39 years. For a detailed biography, see: D. Vorländer, *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 1854−1902.

[23] J. Volhard, E. Fischer, "Lebensbild A. W. von Hofmanns", *Ber. Dtsch. Chem. Ges.* **1902**, *35*, special issue.

[24] Documentary evidence of the photographs for which permission of reproduction was duly obtained in each case: Archiv zur Geschichte der Max-Planck-Gesellschaft, Berlin-Dahlem (Figures 3, 4, 16), Archiv Deutsche Akademie Naturforscher Leopoldina, Halle (Figure 13), The Bancroft Library, University of California, Berkeley (Figures 1, 2, bottom right, 23, 24, 29), Edgar Fahs Smith Collection, University of Pennsylvania Library, Philadelphia (Figures 2, bottom left and right, 6, 17, 24, 25, 28), Gesellschaft Deutscher Chemiker, Frankfurt (Figures 7, 8, 10−12, 14, 18), and the Rockefeller University Archives, New York (Figures 9, 26, 27). The image Figure 2, top left, is from the congratulatory album of photographs presented to August von Kekulé on the occasion of his 60th birthday (September 6, 1889), preserved in the collection of Kekulé papers, in the Institut für Organische Chemie, Technische Universität Darmstadt.

[25] [25a] W. Koenigs, E. Knorr, *Sitzungsber. Bayr. Akad. Wiss.* **1900**, *30*, 108; *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 957−981. [25b] T. Curtius, W. Bredt, "Wilhelm Koenigs", *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 3787−3830.

[26] [26a] E. Fischer, *Untersuchungen über Triphenylmethanfarbstoffe, Hydrazine und Indole* (Ed.: M. Bergmann), Springer, Berlin, **1924** (860 pp., 115 papers). [26b] E. Fischer,

Untersuchungen in der Puringruppe (1882−1906), Springer, Berlin, **1907** (608 pp., 47 papers). [26c] E. Fischer, *Untersuchungen über Kohlenhydrate und Fermente (1884−1908)*, Springer, Berlin, **1909** (912 pp., 109 publications). [26d] E. Fischer, *Untersuchungen über Kohlenhydrate und Fermente II (1908−1919)* (Ed.: M. Bergmann), Springer, Berlin, **1922** (534 pp., 46 papers). [26e] E. Fischer, *Untersuchungen über Aminosäuren, Polypeptide und Proteine (1899−1906)*, Springer, Berlin, **1906** (770 pp.). Of the 74 publications in this collection, the last 18 are brief summaries of papers from E. Abderhalden and his group, published in *Hoppe-Seyler's Z. Physiol. Chem.* comprising little more than analytical data on the amino acid composition of various proteins. [26f] E. Fischer, *Untersuchungen über Aminosäuren, Polypeptide und Proteine II (1907−1919)* (Ed.: M. Bergmann), Springer, Berlin, **1923** (922 pp., 86 papers). [26g] E. Fischer, *Untersuchungen über Depside und Gerbstoffe (1908−1919)*, Springer, Berlin, **1919** (541 pp.); a collection of 32 papers, the last one being on hamameli-tannin by K. Freudenberg, *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 177−186. [26h] E. Fischer, *Untersuchungen aus verschiedenen Gebieten. Vorträge und Arbeiten allgemeinen Inhalts* (Ed.: M. Bergmann), Springer, Berlin, **1924** (914 pp., 120 papers).

[27] C. S. Hudson, "Emil Fischer's Discovery of the Configuration of Glucose", *J. Chem. Educ.* **1941**, *18*, 353−357.

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[29] E. Fischer, O. Fischer, *Ber. Dtsch. Chem. Ges.* **1876**, *9*, 891−900. For the 13 joint papers following, see ref.[26a], Nr. 3−14 and 17.

[30] [30a] E. Fischer, "Ueber aromatische Hydrazinverbindungen", *Ber. Dtsch. Chem. Ges.* **1875**, *8*, 589−599. [30b] G. B. Kauffmann, R. P. Ciula, "Emil Fischer's Discovery of Phenylhydrazine", *J. Chem. Educ.* **1977**, *54*, 295.

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[35] E. Fischer, "Synthese von Polypeptiden, XVII", *Ber. Dtsch. Chem. Ges.* **1907**, *40*, 1754−1767.

[36] Letter E. Fischer to A. von Baeyer, 5 December 1905, Bancroft Library, UC Berkeley.

[37] [37a] E. Fischer, M. Bergmann, H. Bärwind, "Neue Synthese von α-Monoglyceriden", *Ber. Dtsch. Chem. Ges.* **1920**, *53*, 1589−1605. [37b] E. Fischer, E. Pfähler, "Über Glycerin-aceton, seine Verwendbarkeit zur Reindarstellung von α-Glyceriden, und eine Phosphorsäure-Verbindung des Glykols", *Ber. Dtsch. Chem. Ges.* **1920**, *53*, 1606−1620. [37c] E. Fischer, "Wanderung von Acyl bei den Glyceriden, *Ber. Dtsch. Chem. Ges.* **1920**, *53*, 1621−1634.

[38] E. Fischer, *Aus meinem Leben*, Springer, Berlin, **1987** (reprint of the original 1922 version with an English commentary by B. Witkop); [38a] quote from p. 98; [38b] pp. 177−188; [38c] quote from p. 193; [38d] quote from p. 188; [38e] quote from p. 200.

[39] C. Harries, "Emil Fischer", *Die Umschau* **1919**, *23*, 609−613.

[40] C. Duisberg, "Emil Fischer und die Industrie", *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 149−164; quote from p. 154.

[41] A. von Weinberg, "Emil Fischers Tätigkeit während des Krieges", *Naturwissenschaften* **1919**, *7*, 868−873.

[42] H. Wichelhaus, "Emil Fischer's Verdienste um die Deutsche Chemische Gesellschaft", *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 129−132.

[43] L. Lewin, "Eine toxikologische Erinnerung an Emil Fischer", *Naturwissenschaften* **1919**, *7*, 878−884.

[44] F. Herneck, "Emil Fischer als Mensch und Forscher", *Z. Chem.* **1970**, *10*, 41−48.

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[58] F. R. Lillie, "The Mechanism of Fertilization in Arabica", *J. Exp. Zool.* **1914**, *16*, 523−590.

[59] S. F. Gilbert, J. P. Greenberg, "Intellectual Traditions in the Life Sciences: Stereocomplementary", *Pers. Biol. Med.* **1984**, *28*, 18−34.

[60] T. Curtius, "Über das Diamid (Hydrazin)", *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 1632−1634.

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[62] Letter E. Fischer to C. Duisberg, 22 February 1919; copy in the *Emil Fischer Papers*, Bancroft Library, UC at Berkeley.

[63] Joseph Freiherr von Mering [1849−1908], Dr. med., from 1890 on Professor of Pharmacology in Halle, introduced paracetamol into the clinic (1893), and did extensive work on the interrelationship of pancreas and diabetes that led to the discovery of insulin.

[64] [64a] E. Fischer, J. v. Mering, "Über eine neue Klasse von Schlafmitteln", *Therapie der Gegenwart* **1903**, March issue; *Therap. Monatsh.* **1903**, *17*, 208. [64b] Letter E. Fischer to J. v. Mering, 13 May 1903, *Emil Fischer Papers*, Bancroft Library, UC at Berkeley.

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[66] G. Klemperer [1865−1946], Dr. med. (Berlin) 1886, Habilitation 1889, Professor 1905, from 1906 on chief physician of the

Berlin Moabit Hospital, personal physician and friend of Emil Fischer, published extensively on clinical topics. Being a Jew, he was obliged to leave Germany in 1936 and went to the U.S. at the age of 71.
[67] E. Fischer, G. Klemperer, "Über eine neue Klasse von lipoiden Arsenverbindungen", *Ther. Ggw.*, **1913**, January issue.
[68] The Collection of *Emil Fischer Papers*, housed in the Bancroft Library at the University of California, Berkeley, consists of 34 boxes of material: lab notes, manuscripts, drafts of his autobiography "Aus meinem Leben", which differ from the published version[38], and about 20000 catalogued letters, that reached Fischer during his scientific career as well as copies of those he wrote. The papers eventually reached Berkeley through Fischer's son, Hermann O. L. Fischer, who carried this collection along with him through all the stations of his unusually cosmopolitan career: Privatdozent in Berlin, Professor of Pharmaceutical Chemistry in Basel, Director of the Banting Institute, Toronto, and Professor of Biochemistry at the University of California, Berkeley. The papers were donated to the Bancroft Library by Mrs. H. O. L. Fischer in November 1970.
[69] G. D. Feldman, "Industrie und Wissenschaft in Deutschland" in *Forschung im Spannungsfeld von Politik und Gesellschaft. Geschichte und Struktur der Kaiser-Wilhelm-/Max-Planck-Gesellschaft* (Eds.: R. Vierhaus, B. vom Brocke), Deutsche Verlags-Anstalt, Stuttgart, **1990**, pp. 657−672.
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[75] J. A. Johnson, "Vom Plan einer chemischen Reichsanstalt zum ersten Kaiser-Wilhelm-Institut: Emil Fischer", in *Forschung im Spannungsfeld von Politik und Gesellschaft. Geschichte und Struktur der Kaiser-Wilhelm-/Max-Planck-Gesellschaft* (Eds.: R. Vierhaus, B. vom Brocke), Deutsche Verlags-Anstalt Stuttgart, **1990**, pp. 486−515.
[76] E. Fischer, E. Beckmann, *Das Kaiser-Wilhelm-Institut für Chemie Berlin-Dahlem*, F. Vieweg, Braunschweig, **1913**.
[77] R. Vierhaus, B. vom Brocke (Eds.), *Geschichte und Struktur der Kaiser-Wilhelm-/Max-Planck-Gesellschaft*, Deutsche Verlagsanstalt, **1990**, 1010 pp.
[78] Emil Fischer, "Vermehrung des inneren Wertes der Kohle", Lecture given on 29 July 1912 before about 150 representatives of Government, the Kaiser-Wilhelm-Gesellschaft, the Rhenish-Westphalean Industry and the City of Mülheim. The title of the printed version (ref.[26h], pp. 810−822) was changed to "Die Aufgaben des Kaiser-Wilhelm-Instituts für Kohlenforschung zu Mülheim-Ruhr".
[79] Based on "The Fischer Research Group", a list of doctoral students, postdoctoral co-workers and other associates, painstakingly compiled by J. S. Fruton (ref.[49], Appendix 6, pp. 375−403), slightly corrected by some newer information, and not counting those as Fischer pupils, who came into his institute as section heads and pursued independent research, e.g. *Siegmund Gabriel* [1851−1924], Dr. phil. 1874 (Bunsen), a. o. Professor 1874−1921 Berlin; *Alfred Wohl* [1863−1939], Dr. phil. 1886 (von Hofmann), Priv.-Doz. 1891−1904 Berlin, Professor 1904−1933 Danzig; *Robert Pschorr* [1868−1930], Dr. phil. 1894 (Knorr, Jena), Priv.-Doz. 1895−1913 Berlin, Prof. TH Charlottenburg 1914−1930; *Franz Fischer* [1877−1947], Dr. phil. 1899 (Elbs, Gießen), Priv.-Doz. 1903 Univ. Berlin, head inorganic section 1904−1911, Professor TH Charlottenburg 1911, Director KWI Mülheim/Ruhr 1913−1943.
[80] [80a] P. Duden, H. P. Kaufmann, "Ludwig Knorr zum Gedächtnis", *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 1−34. [80b] H. W. Flemming, "Ludwig Knorr, Begründer Hoechster wissenschaftlicher Tradition", *Dokumente aus Hoechster Archiven*, Frankfurt/Main, **1968**, Nr. 31.
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[97] H. Moissan [1852−1907], Professor of Chemistry at the Sorbonne, Paris; prepared fluorine for the first time; Nobel Prize in Chemistry 1906; see http://www.nobel.se/chemistry/laureates/1906/moissan-bio.html
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[122] Aside Suzuki, these were: *Koichi Matsubara* [1872–1956], Dr. phil. 1906 Tokyo, research fellow with Perkin, Jr. 1905 and Fischer 1906/7, Professor of Chemistry, Tokyo University 1909–1933; *Yukata Teruuchi* [1873–1936] Dr. med. 1900 Tokyo, research fellow 1905–1908 with Fischer in Berlin, Professor at Keio University, Tokyo and director of the Department of Medical Chemistry at the Kitasato Institute for Infectious Diseases, Tokyo (1915–1936); *Takaoki Sasaki* [1878–1966], Dr. med. 1903 Tokyo, research fellow with Hofmeister in Straßburg and Fischer in Berlin 1905–1910, Professor of Internal Medicine, Kyoto, founder of Sasaki Institute, chief of the Cancer and Tuberculosis Research Institute, published extensively on topics in bacteriology and biochemistry; *Tokuhei Kametaka* [1872–1935], Dr. phil. Tokyo, research fellow 1909 Berlin, Professor of Pharmaceutical Chemistry, Tokyo.
[123] [123a] S. Takano, *Umetaro Suzuki*, Poplar Co., Tokyo, **1958** (350 pp., in Japanese). [123b] Admirers of U. Suzuki, *Biography of U. Suzuki*, Asakura Publ. Co., Tokyo, **1967** (354 pp., in Japanese).
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[192] In this context, it appears more than a simple coincidence, that his son Hermann, at the time professor emeritus at the University of California, Berkeley, died during an intestine operation in 1960 at the age of 71.

[193] K. Freudenberg, "Acceptance Speech on being awarded the Emil-Fischer-Medal of the German Chemical Society in 1952", *Angew. Chem.* **1952**, *64*, 352.

[194] Original version: "Fischer hat die Probleme vor sich gesehen und er hat sie angegriffen und gelöst. Er hat sein Schifflein nicht vor dem Wind treiben lassen, auf dem Strom oder auf dem Ozean der Forschung. Er hat das Schifflein bewusst gesteuert und ist zum Ziel gekommen."

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[196] The testament addition, the statutes of the "Emil Fischer Foundation", and the records of the commission deciding on the research grants, are preserved in the stock-list of the Prussian Academy of Sciences, *Archiv, Berlin-Brandenburgische Akademie der Wissenschaften*, II–XI-26.

[197] Original version: "Ich, Emil Fischer, bestimme hiermit für meinen Todesfall was folgt, indem ich alle etwaigen bisherigen Verfügungen von Todeswegen aufhebe. Ich errichte eine Stiftung, welche den Namen "Emil-Fischer-Stiftung" führen soll. Sie soll mit einem Kapital von 750000 Mark ausgestattet werden. Diese Summe soll von meinem Erben in guten Wertpapieren aus meinem Nachlaß nach deren Kurswert berechnet und gewidmet werden. Die Erträge dieses Kapitals sollen verwendet werden zur Unterstützung von jungen deutschen Chemikern, die auf dem Gebiete der organischen-anorganischen oder physikalischen Chemie arbeiten; unter den Bewerbern sind im Zweifelsfalle bei gleicher Würdigkeit Angehörige des früher von mir geleiteten Chemischen Instituts in Berlin zu bevorzugen. Diese Stiftung soll der Physikalisch-Mathematischen Klasse der Preußischen Akademie der Wissenschaften angegliedert und unterstellt werden."

[198] A. v. Harnack, "Grabrede für Emil Fischer" on 18 July 1919, in the Neue Kirche zu Wannsee, Archiv zur Geschichte der Max-Planck-Gesellschaft, Berlin-Dahlem.

[199] Originalversion: "Was er wollte, weil er es für notwendig und gut hielt, das setzte er auch durch ohne Zwang und ohne Feindschaften; denn durch seine Sachlichkeit und seine aufgeschlossene Liebenswürdigkeit entwaffnete er jeden Widerstand. Mußte doch jeder fühlen: dieser Mann trachtete nicht nach Einfluß oder Macht als solcher, sondern nach seinem Werk; sein Werk aber war seine Wissenschaft in allen Beziehungen des Lebens. Sie trug er auf dem Herzen und für sie lebte er."

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