100 Years Weyl, Houben and their Handbook

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Fig. 1 Josef Heinrich Hubert Maria Houben and Theodor Weyl.

"If a useful work is to be created for experimental chemistry in the laboratory, each of the experts involved has to have personally carried out and tested most of the methods described himself."

Theodor Weyl and Josef Houben were two German chemists who made a significant contribution to the field of chemical information at the beginning of the 20th century. They were the first to comprehensively evaluate the organic chemistry literature with regard to its practical usability. In their handbook, *Methods of Organic Chemistry*, experts illustrated various methods for the synthesis of organic compounds and discussed them critically. This meant that the reader did not always have to consult other chemistry handbooks and even the original literature for the planning of syntheses anymore, thus saving valuable time. The editorial concept not only included extensive literature studies and the careful evaluation of preparative methods, but it even incorporated further information relating to the context which helped the reader determine the general applicability of a particular synthetic method. In this way, readers were inspired and their scope for creativity was enhanced. Houben and Weyl were also pioneers in the presentation of organic synthetic information through the introduction of a highly organized hierarchical structure system which enabled the reader to navigate through the content easily.

Even 100 years after its first publication, *Houben–Weyl*, which nowadays is available in an electronic format as part of *Science of Synthesis*, is still appreciated by chemists worldwide as an excellently structured, reliable and comprehensive source of information (**Fig. 2**).

However, the two patrons behind the mark of quality which is *Houben–Weyl* have been largely forgotten and their biographies are largely unknown. The 100-year anniversary of the first *Houben–Weyl* edition published by Thieme in Leipzig in 1909 provides us with an excellent opportunity to have a look at the lives of these two chemists.

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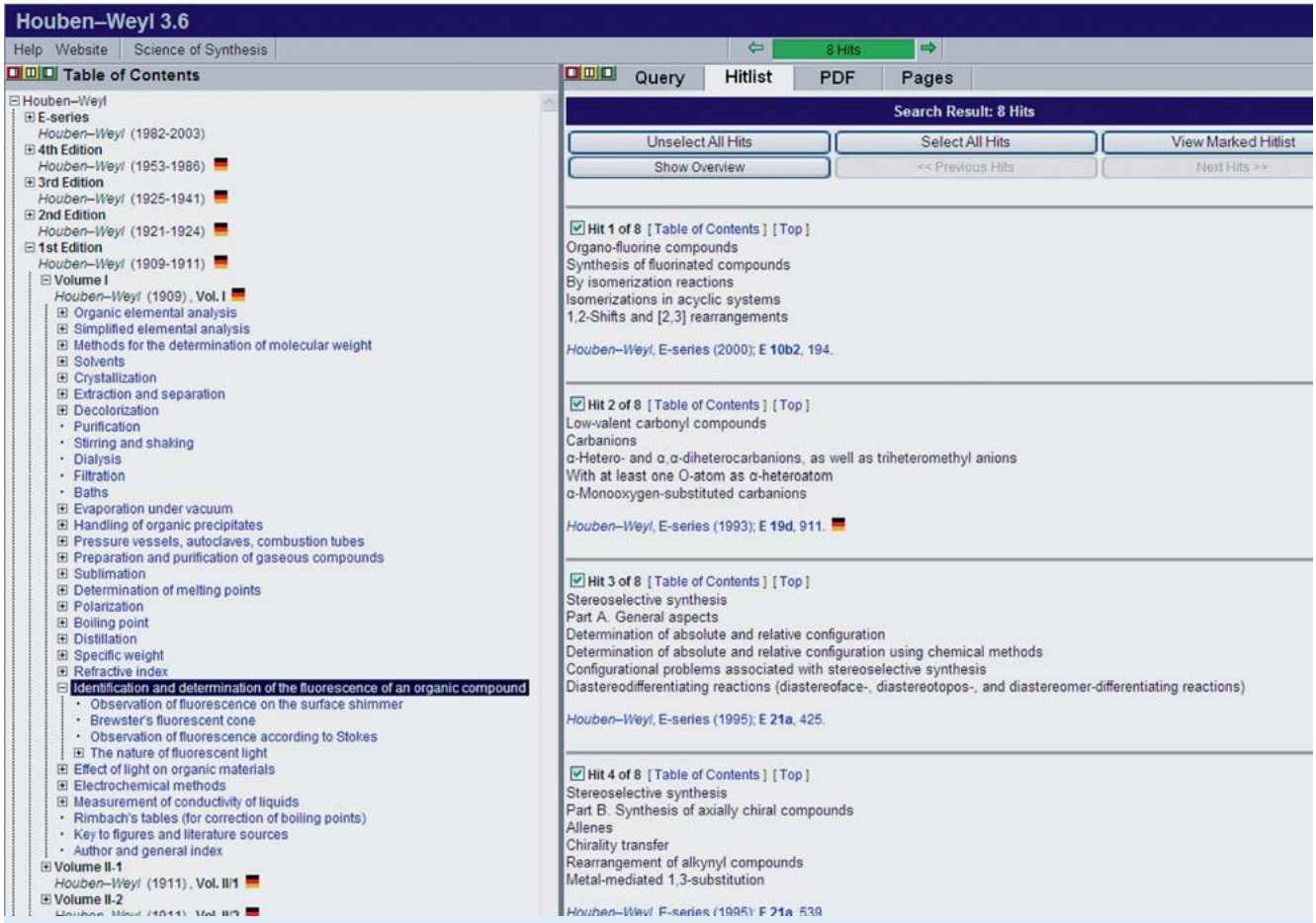

Fig. 2 The electronic version of *Houben–Weyl*.

Theodor Weyl (1851–1913)

Theodor Weyl, who was born in Berlin on January 8th, 1851, is a wonderful example of someone who was born with a natural gift which he most probably inherited from his father, Dr. phil. Louis Weyl, whose name was well-known to those interested in literature at that time.

Louis Weyl not only wrote humorous books and essays that he also commonly orated successfully, but he also wrote various handbooks, one of them entitled *A Tourist Guide for Berlin and Potsdam, Guide for Railway Travellers through Berlin, Potsdam, Dessau, Köthen, Halle, Magdeburg, Leipzig, Dresden* or: *How can a traveller get to know all the sights of these cities, their environments and the railways connecting them within eight days*.

When Louis Weyl died in 1852 at the age of only 32, he not only left behind his widowed wife Lina (born Weinberg) and the one-year old Theodor, but also a second son Louis who was born shortly after his father's death. Theodor, who had been a sickly child, first grew up under his mother's custody, then under the guidance of a tutor and only later came to attend a state school. As can be read in a curriculum vitae about Weyl published in *Berichte* in 1913,[1] this lively boy's imagination and thirst for knowledge was particularly focused on botany and music, a love of which accompanied him throughout his life. In his later grammar school years he also developed a significant interest in the ancient classical authors. This knowledge enabled him to recite numerous passages from their writings (in the original language) from memory until his death. Nevertheless, Theodor was not a very good pupil and he only took his A levels at the age of 20. He first studied at the University of Heidelberg (1872 summer semester), then in Berlin and finally in Straßburg (now: Strasbourg). He studied medicine and chemistry, but also led a very merry, often boisterous student life and his distinctive sense of humour was widely known.

During his time as a student at the Institute of Du Bois–Reymond – did he ever hear of his *Ignoramus et ignorabimus*? –, Weyl published some minor studies relating to physiological topics in Berlin and of Hoppe–Seyler in Straßburg. At the latter university, he passed his medical state exam and obtained his doctorate in 1877 (the subject of his doctoral thesis was *Contributions to the knowledge of animal and plant proteins*).

Subsequently, he returned to his hometown and joined the chemical physiological university lab supervised by Baumann, and, as a result of his studies conducted there, he published under the title *On a new Reaction for Creatinine and Creatine*, the color reaction for creatinine that became associated with his name.

It was those early successes that probably helped him gain an assistantship at the Physiological University Institute in Erlangen as well as an assistant professorship at the medical faculty in the same year. His postdoctoral thesis (1879) was entitled *On Protein Digestion and on the Cleavage of Tyrosine by Decay*. He fulfilled his obligatory military service in two stages in 1874 and 1878.

Fig. 3 Theodor Weyl (1851–1913)
(Source: E. Börnstein: Theodor Weyl. *Ber. Dtsch. Chem. Ges.* **1914**, *47*, 2395–2404. Copyright Wiley-VCH Verlag GmbH & Co.)

Shortly after he had obtained his postdoctoral lecturing qualification ("Habilitation"), he married his cousin Elise, born Weinberg, the daughter of a Danzig (now: Gdańsk)-based merchant. They never had any children.

Several years of active scientific research followed in which Weyl, partly together with his students, published studies on hippuric acid and benzoic acid excretion during fever, on carbon oxide hemoglobin, on oxygen absorption of pyrogallol in alkaline solution, on the ammonia content of basic air, on the impact of chemical agents on the assimilation capacity of green plants and many more.

In the winter of 1880/1881 Weyl spent several months in Naples. Due to his connections to Du Bois–Reymond and in a contract with the Berlin Academy of Sciences, he got a position at Dohrn's Zoological Station founded in 1870 to study the electric organ of the electric ray. Not only did his research residency prove very productive but those months in Naples provided Weyl with some of the happiest memories of his life so that he later returned to that city many more times.

Despite of all of these successes, Weyl resigned from his position in Erlangen after three years and returned to Berlin. There he set up a laboratory of his own, in which he worked on numerous scientific topics from biochemistry and natural products chemistry, but he focused primarily on the field of terpenes.

However, as he had never wanted to work on chemistry projects exclusively he then diversified into other fields that were unresolved at that time and that increasingly captured the interest of the authorities, e.g. public health.

It was the time when Robert Koch celebrated his first big successes and he was leading the way with his bacteriological methods. One could now detect some fatal infectious diseases in victims with an early diagnosis, trace the spreading of the disease by studying pathogens, and finally fight the disease effectively by using appropriate preventive measures. Weyl had by this time decided to close down his own laboratory and retrain as a university lecturer. He joined the Hygienic Institute managed by Koch at the Berlin-Charlottenburg Technical University. His first studies referring to hygienic questions covered the field of (toxic) food coloring. Weyl's campaign against dinitrocresol, then a common saffron surrogate, and Martius yellow deserve to be mentioned.

Weyl was ideally suited to this field because of his qualifications both in chemistry and medicine. The enthusiasm he held for this type of research can be seen from the titles of some of his works which were published in rapid succession: *Spontaneous Tuberculosis in Dogs; Poisoning due to Cotton Dyed with Lead Chromate; Tar Dyes Taking into Account Hazards and Legislation in Particular; Obtaining Preserved Milk; Knowledge of the Lymph; The Chemistry and Toxicology of the Tubercle Bacillus* and many others.

However, his interest in questions related to everyday chemistry and environmental chemistry, as we would nowadays call it, went far beyond the aforementioned subjects, so that one could without doubt describe him as one of the founders of ecological chemistry.

Related to this, his work on eliminating (and sorting/recycling!) domestic waste is particularly worth mentioning. He wanted to introduce the combustion of domestic waste, most notably common in London, also to Berlin. This, however, could not be realized due to the totally different composition of the waste from Berlin (brown coal was used for heating in Berlin, whereas black coal was used in London). Weyl suggested disposing of fecal waste through combustion and specified an appropriate combustion apparatus primarily designated for barracks, hospitals etc. Weyl also revived an idea suggested originally by Werner Siemens concerning the construction of an ozone apparatus which could free the drinking water within municipal pipes from harmful germs using ozone. He designed an appropriate apparatus together with Siemens & Halske. The practical implementation of that method, however, was reserved for a (much) later period in time. Another one of Weyl's proposals also experienced delayed implementation. In 1891 he put forward a proposal to throw the winter snow from Berlin's streets into the city's waterways instead of transporting it for many kilometres and disposing of it outside the city. This was a proposal that he frequently referred to, but unfortunately during his lifetime he did not manage to overcome the resistance of the municipal authorities. Six months after Weyl's death, the magistrate began to have the piles of snow removed from the streets and thrown into the rivers and channels.

Weyl passionately campaigned for all these ideas in public both through written documentation and oral presentations. Due to his long-term position as the secretary of the Berlin "Association for Public Health Care" he personally met with numerous representatives from the field of scientific and practical hygiene both in Germany and abroad. As a result of this and his research he was granted several memberships and honorary member-

ships in foreign scientific associations. He was also frequently consulted regarding matters of hygiene by private individuals and different authorities. For example, he went as an expert to Moscow in 1896, then travelled to South Russia and finally ended up in Constantinople where he received several significant Turkish awards for his scientific advice on solving some of the city's hygiene problems. Other travels took him to the United Kingdom and Hungary.

His practical and travel experiences were reflected in his extensive literary activities that, in addition to several monographs, resulted in numerous handbooks, amongst others, the large *Handbook of Hygiene* that comprised ten volumes in its first edition (from 1896), *Progress in Street Hygiene* (1901), *The Handbook of Workers' Diseases* (1908), *The Sanitization (improvement of house building for hygienic, social, technical reasons) of Cities in Single Representations* (from 1906, among those examples is a volume written by himself on his beloved Naples) and many others. For all these collections, he prepared a plan, recruited the authors for individual contributions, acted as the editor and wrote significant portions himself.

This would be a good point at which to turn our attention to the work *Methods of Organic Chemistry*. However, before we deal with it in detail, we shall describe the further course of Weyl's life and the life of his significantly younger "coauthor" Josef Houben.

In 1911 Weyl was awarded the title of (senior) lecturer, however, for some reason his position was to remain that of a private lecturer. It was said several times that he was considered for an academic chair of hygiene, but none of those hopes were ever realized. Whether his Jewish origin contributed to that cannot be ascertained anymore. However, it was clearly anti-Semitic to completely conceal his name in the necrology for Houben published in *Angewandte Chemie*[2] in 1941 and in which the work *Methods of Organic Chemistry* was honored explicitly.

At this point we would like to name some of the works that Weyl published in the field of chemistry during the last period of his life: *The Impact of Ozone on Sulfur-Containing Substances and Sulfur; A Simple Apparatus to Help Determine the Melting Point; The Behavior of Protein Bodies with Respect to Acetone; Reductions Using Amorphous Phosphorus* – again, this illustrates how enormous his range of interests was.

In late March 1913 he returned ill to Berlin after having made a trip in order to compile an expert evaluation (*The Impact of Methyl Alcohol on the Health of Workers Dealing Therewith*). Weyl suffered a serious liver disease which restricted him to his sick bed and after several difficult weeks he passed away on June 6th. The life of this highly talented and incredibly diligent person had finally come to an end.

Fig. 4 Josef Heinrich Hubert Maria Houben (1875–1940) (Source: http://www.ub.hu-berlin.de/bibliothek/sammlungen/portraet/)

Josef Heinrich Hubert Maria Houben (1875–1940)

Josef Houben was born in Waldfeucht (near Jülich) in the Rhineland on October 27th 1875, nearly a generation after Theodor Weyl, as the son of the retired royal lieutenant and master of the bursary Heinrich Houben and of his wife Anna (born Virnich). After a pretty typical school education, finishing at the Beethoven Gymnasium in Bonn, and after he had passed his A levels (in 1894), he began to study mathematics and astronomy at the University of Bonn only to later turn to chemistry under the influence of Kekulé whom he had highly admired throughout his life. It can be assumed that Houben did know Kekulé personally given that Kekulé died in 1896. In 1898 Houben earned his doctorate as a student of Bredt with a work on the derivatives of camphoric acid (the subject of his dissertation was: *Chlorocamphoric Acid Ester and Dehydrocamphoric Acid*). After a short period of time working in industry he returned to the university, namely to the Chemical Institute of the University of Berlin that ranked among the "elite institutions" in Germany at the beginning of the 20th century. It was run under the directorship of Emil Fischer and attracted numerous talented young people. In 1908 Houben obtained a postdoctoral lecturing qualification there. Houben's documents recording how he achieved his postdoctoral lecturing qualification ("Habilitation") survived the chaos and catastrophes of the times so they are worth taking a closer look at.

Houben had to choose one topic from three different proposals for his trial lecture and he chose a theme which is also a popular one today: *Carbon and Carbon Dioxide within Nature's Cycle*. Also the subject of his first lecture, "The Future Synthesis of Naturally Occurring Products", would still be very relevant even 100 years later. His postdoctoral thesis was a collection of topics and was rather lukewarmly assessed by his mentor Emil Fischer: "Although Dr. Houben's studies lack depth and do not provide a solution to any specific problem, they nevertheless reveal the talent of their author to observe new phenomena correctly and identify their relation to things known. Furthermore, these studies significantly enrich synthetic methodology. Having

taken everything into consideration I feel that some good things may be expected from him as a scientific researcher and that his performance has been satisfactory enough to serve as the basis for a fruitful lecturing career. I request that we admit him for a trial lecture." The second thesis reader/supervisor Nernst agreed with Fischer's opinion with two comments – he was no expert in this field, and, he was in no position to evaluate the content of the work.

World War I initially disrupted the work that followed. This work included an examination of the reactivity of recently made organomagnesium compounds (Grignard compounds) that, amongst others, resulted in the first productive synthesis of dithiocarbonic acids; a new synthesis of arylamine carbonic acids from halogen magnesium anilides and carbonic acid; the transfer of Kolbe's salicylic acid synthesis of phenols to arylamines, and, extensive studies on the Fischer–Hepp rearrangement of arylnitrosamines. At the beginning of the war, Houben was a battalion adjutant, whereas later, having gained many injuries, he headed the war laboratories and held administrative positions.

It was only in 1921, the year in which the 46-year-old Houben married Elsbet Wagenhäuser, that he could actually begin to carry out independent research. He was appointed to a senior lectureship and to the post of the head of the chemical laboratory at the Biological Reich Institute in Berlin–Dahlem ("Biologische Reichsanstalt") where he was later appointed as an *Oberregierungsrat* (senior government official) in 1925. In 1931 he was awarded the degree of a Dr.-Ing. e. h. from the Dresden Technical University for his scientific achievements. In October 1933 he was forced to retire for political reasons. Unfortunately, we did not succeed in finding out the actual reason for that forced retirement. According to the "proof of Aryan ancestry" papers handed down, (the Roman-Catholic) Houben did not have any Jewish ancestors, and, by his own account, he had always belonged to "organizations at the political right or to the center, respectively". Therefore the two most common reasons for a dismissal from a university career during the Third Reich were unlikely in his case.[3]

Josef Houben died in Tübingen in the summer of 1940 (28th June). His marriage was also childless.

As far as his research was concerned, Houben essentially dealt with three large areas: Firstly, he worked on magnesium-containing organic compounds and their reactive behavior. After World War I he then developed the famous ketone synthesis as well as the synthesis of aromatic ketones and ketone imines from phenols, nitriles and hydrochloric acid. The synthesis originated from extensive preliminary studies on imido ester, ketimines, and others based on Gattermann's aldehyde synthesis. Houben always claimed this reaction as his own although it had been published by Hoesch prior to Houben. The Houben–Hoesch method, as we call it to this day, could be extended over a very broad range when the appropriate condensing agents were selected and also resulted in the synthesis of many natural products. The third area he explored was terpene chemistry, an area which he was already familiar with from his times as a doctoral student with Bredt. This area essentially covered the study and determination of the structure of addition and rearrangement products, with the aim of converting enantiomers into each other in order to confirm van't Hoff's predictions on the "asymmetric C atom".

In a similar way to Weyl, Houben could also refer to an extensive list of his own literary works ranging from original publications in a monograph format (e.g., *Anthracene and Anthraquinones*) to also the editing of handbooks (e.g., *Progress in Curative Chemistry*), one of them of course being the internationally successful *Houben–Weyl*.

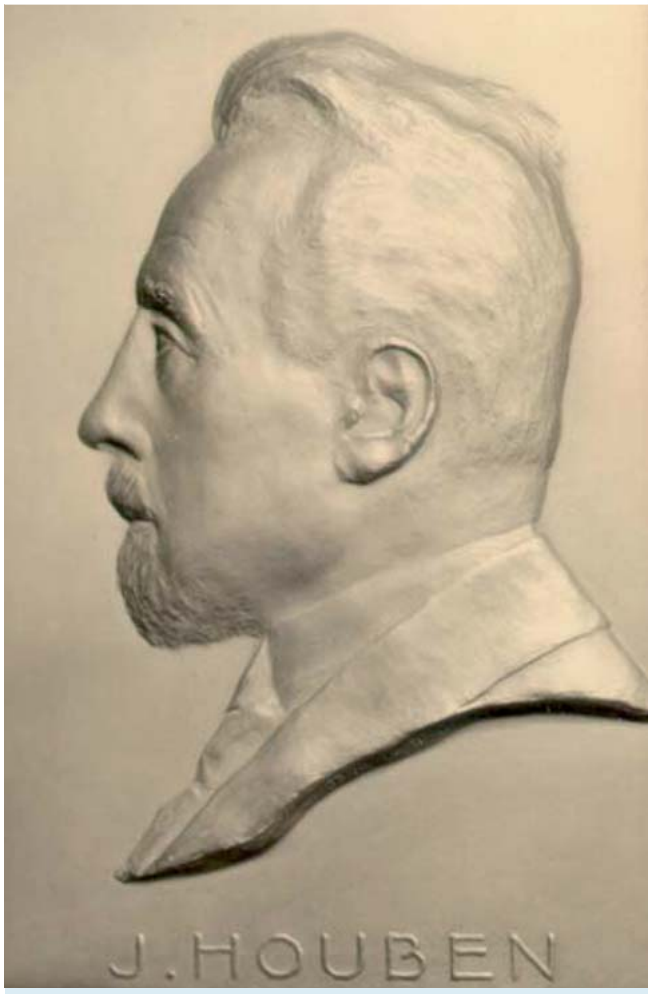

Fig. 5 Source: http://www.ub.hu-berlin.de/bibliothek/sammlungen/portraet/

The *Houben–Weyl* handbook that actually should have read the *Weyl–Houben* handbook

As can easily be derived from what has been discussed so far, both Weyl and Houben were certainly highly enough qualified to edit a chemistry reference work, the more senior of them not least because he, in addition to all his other numerous activities, had given the prestigious "physician's lecture" in chemistry for many years and had also written the textbook *Organic Chemistry for Physicians* (in 1891).

Weyl was the sole and first editor of *Methods of Organic Chemistry, First Volume, General Part*, published by Thieme, Leipzig in 1909 (**Fig. 6**).

In the preface he describes in detail the reasons that prompted him to edit the work comprising four volumes: "[After the analytic segment of chemistry had been thoroughly researched in the works of such classic scholars as Lavoisier, Berzelius, Dumas, Liebig etc.] the synthetic era began. The first real advocate of synthetic chemistry was Marcellin Berthelot whose work *Chimie or-*

Fig. 6 Together *Houben–Weyl* and *Science of Synthesis* span 100 years – From the first edition of *Die Methoden der organischen Chemie* in 1909 (top) to *Science of Synthesis* series completed in 2009.

Fig. 7 The print edition of *Science of Synthesis* (Category 1).

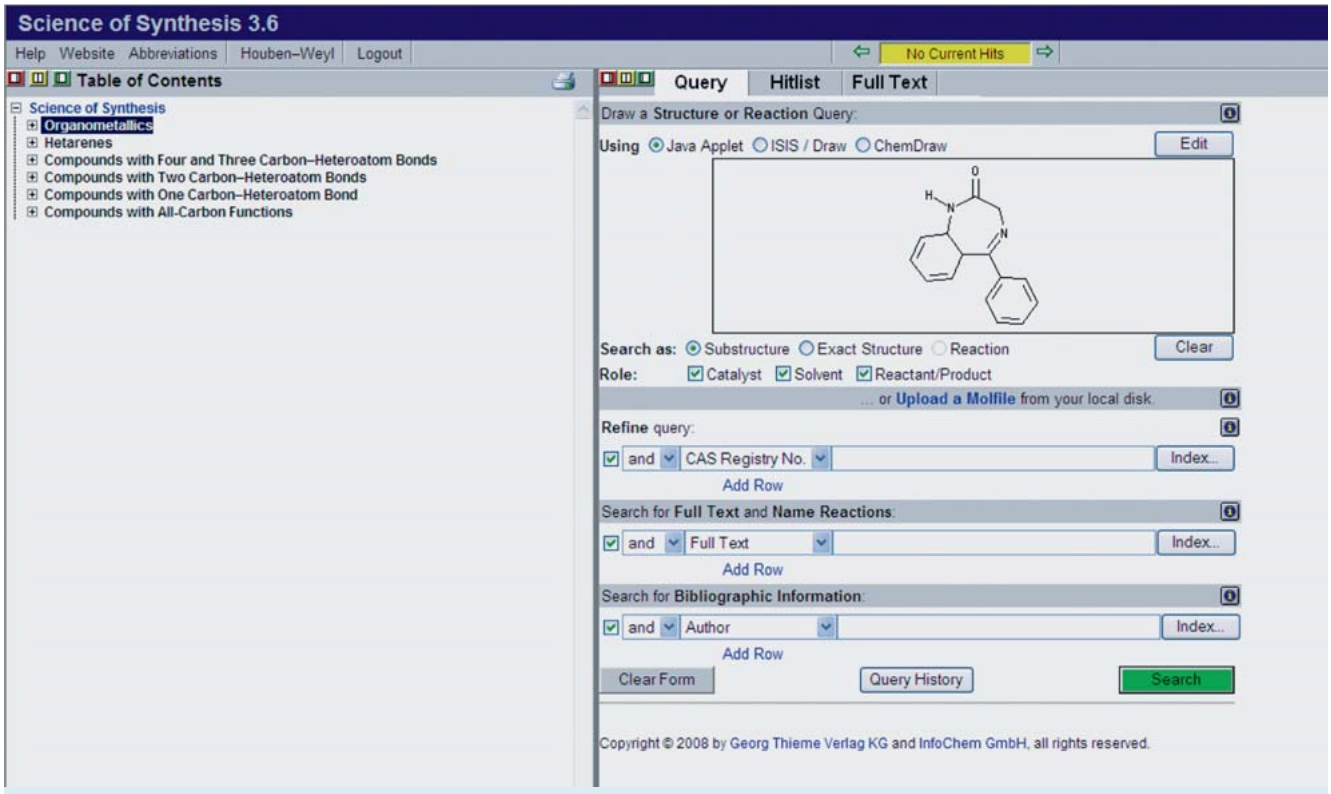

Fig. 8 The electronic version of *Science of Synthesis* – structure searching.

ganique fondée sur la synthèse was published in 1860 (following 10 years of initial studies) and was the first milestone on what was to be an endless path of discovery […] The new challenges of research required new methodology. Because if chemists had been limited to the tools that they had worked with up until then, i.e. 'age old equipment and materials', they would have had to have given up altogether. In a similar way to newly qualified professional builders who would aspire to build tall commercial and residential buildings, large railway premises, deeply entrenched bridge piers and kilometre long tunnels through mountains but without the tools they really needed, e.g. iron, glass, cement, explosives, and drilling machines." Preparative methods provided new tools for chemistry, without them the preparation of new substance classes would not have been possible. But it would not be enough to just summarize the continuously increasing number of new methods; or in Weyl's words: "Literature studies don't determine everything! If a useful work is to be created for experimental chemistry in the laboratory, each of the experts involved has to have *personally carried out and tested* most of the methods described *himself* in order to be able to make a noteworthy assessment on their practical usability and limits. … The second part of the reference work poses the greatest difficulty. It describes the recognition, determination, introduction and elimination of individual atom groups and describes them in such a way

that it is less the theory but more the practical execution of the reactions which provides guidance in their preparation."

The "Weyl" edition kept this fundamental philosophy, when in 1921 Josef Houben was entrusted with editing the new edition of the work and later, despite all of his recognized achievements in the field of experimental chemistry, it was this work that was to be considered his major lifetime achievement. It is not entirely clear as to what extent Houben and Weyl knew each other. Houben, however, was ranked among the contributing authors of the *Specific Part of the Second Volume* published two years prior to Weyl's death in 1911 and he was a private lecturer in Berlin at this point. Later, in the preface to the second edition (from 1921), Houben states that he decided to edit the "*Weyl*" edition anew, since it was a work "written by me to a significant extent anyway".

The third edition, which again was edited by Houben, was only completed in 1941, one year after Houben's death. The foreword was written by his wife Elsbet who particularly thanked Edgar Pfankuch, one of her husband's former employees at the Reich Biological Research Centre, for his considerable assistance. Pfankuch significantly contributed to the first electron microscope recording of the tobacco mosaic virus and went missing in Silesia in the final phase of World War II – yet another example of a *Houben–Weyl* contributor who later did not leave any traces behind him.

Despite mass devastation in Germany, the meanwhile worldwide established *Houben–Weyl* survived the war and postwar periods and the 4th edition was published from 1958 onwards with Eugen Müller as the Editor-in-Chief. When the *Houben–Weyl* print edition was finally complete in 2003 it had reached a scope of 162 volumes (it also included many supplementary volumes on topics such as stereoselective synthesis, organofluorine compounds and peptides).

By the time *Houben–Weyl* had been completed it had become clear that organic chemistry was a field that was truly international and that a wealth of new information relating to organic methodology was being published on a continuous basis. In order to properly facilitate the users of such chemical information an electronic version of a reference work such as *Houben–Weyl* would be needed in addition to the print product.

Therefore an entirely new edition of *Houben–Weyl* was launched in 2000 and was called *Science of Synthesis* (**Figs. 6** and **7**).

This new edition was designed to provide a new and critical treatment of synthetic organic chemistry and so an Editorial Board comprising nine leading international experts was appointed. Today there are more than 50 volume editors and over 800 authors involved with the *Science of Synthesis* project. A highly qualified team of Ph.D. chemists provides support from the Editorial Office in Stuttgart. Both the print edition and online version are used extensively worldwide at many of the leading universities and top research institutions. The high quality editorial standards and invaluable insights to organic synthetic methodology have been retained in keeping with the tradition of *Houben* and *Weyl*.

Literature

1 E. Börnstein, *Ber. Dtsch. Chem. Ges.* **1914**, *47*, 2395–2404.
2 Anon., *Angew. Chem.* **1941**, *54*, 139.
3 Houben's personnel file available in the archive of the Federal Biological Research Centre in Braunschweig, the legal successor of the Reich Biological Research Centre, states that he was dismissed based on Section 6 of the law on reconstructing the civil service. This paragraph had been introduced to "simplify administration". Whether its application to Houben had anything to do with a dispute on scientific questions that in form of a disciplinary complaint even reached the Reich Minister for Nutrition and Agriculture cannot be established anymore. Section 3 of the law explicitly refers to the removal of Jewish employees from the civil service status. We thank Dr. Gerlinde Nachtigall (Federal Biological Research Centre) for this information.