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Louis Fieser: An Organic Chemist in Peace and War

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Dedicated to Professor William von Eggers Doering, an early undergraduate student of Louis Fieser, on his 91st birthday

Keywords: Reminiscences / History of organic chemistry / Louis and Mary Fieser / Cancer and smoking / Napalm / Chemical education / Organic synthesis

Louis Frederick Fieser (1899–1977) was an prominent figure among organic chemists of the mid-20th century, identified today for *Reagents for Organic Synthesis*, co-authored with his wife Mary Fieser, and now available electronically. Fieser was first known for his prolific research efforts in quinones, polycyclic aromatics, and steroids, and was also a leading educator and public servant. His activities included not only major achievements in cancer research and cancer prevention through the suppression of smoking, but also participation in war research and the invention of napalm, which are part of his legacy.

Louis Fieser: A Life in Chemistry

Louis Frederick Fieser (1899–1977, pronounced Luee Feezer)[1] was an imposing but ambiguous Figure among organic chemists of the mid-20th century, known especially today for *Reagents for Organic Synthesis*, originally a print series co-authored with his wife Mary Fieser beginning in 1967, and now available electronically. This series, also known as *Fieser's Reagents*, came late in their careers just before their formal retirement. Fieser earlier became known for his prolific research efforts and textbook writing, and was also a leading educator and public servant. His activities included not only extensive achievements in organic synthesis and cancer research and prevention, but also enthusiastic participation in defense research and the invention of napalm, which has darkened his memory. Fieser was a larger than life personality, with an unabashed tendency for self-promotion, and the title of this essay echos that of his own autobiographical memoir, published in 1964.[1a] It was characteristic of his exuberant character that in remembering his undergraduate education he first cited his success as a lineman on an undefeated college football team before his election to the *Phi Beta Kappa* scholastic honorary society, which he jokingly said happened "by accident." Both he and his wife and lifelong research partner Mary (1909–1997) drove sports cars to work (a Nash-Healy, later Corvettes), and welcomed public attention (Figure 1, Figure 2).[2]

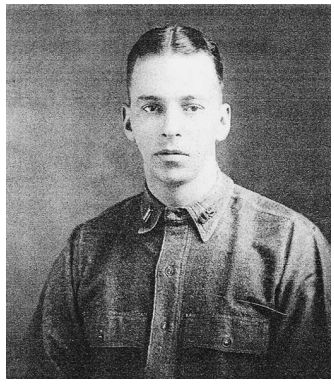

Figure 1. Louis Fieser in military training, 1918–1919.[1f]

His memoir[1a] intersperses descriptions of bomb-making and anti-malarial research with notes on fishing, the raising of Siamese cats, his athletic exploits, and his favorite restaurant in Washington. Now 30 years since his death he is remembered personally by a shrinking number of chemists, but his extroverted character is apparent from his writings.

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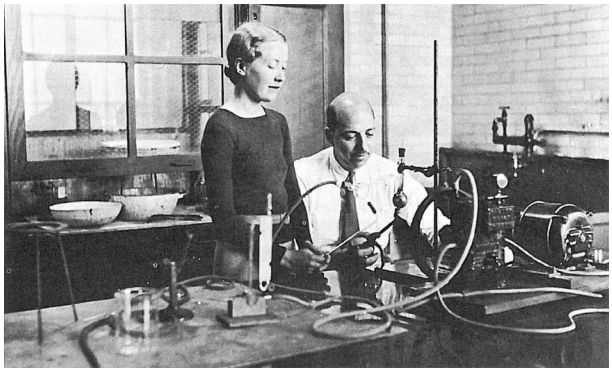


Figure 2. Louis and Mary Fieser in the lab, 1934.[1f]

Figure 3. James Bryant Conant in the laboratory, 1928 [Harvard University Archives, HUP Conant, J. B. (39)].

The Path to Harvard

Frederick Fieser (1815–1891), the grandfather of Louis Fieser was born in Wolfenbüttel (Braunschweig), Germany, was baptized in 1816 in the Evangelical Lutheran church, and married Louise Phillippine Schade in Braunschweig. The couple emigrated to Ohio where Frederick Fieser published German language newspapers, and became Chair of the Board of Education in Columbus, Ohio, where a school and street were named after him. His son and the father of Louis was an engineer, also named Louis Frederick Fieser (1854–1917), and also lived in Columbus, where Fieser was born.

Fieser attended school in Columbus, and graduated from Williams College in Massachusetts in 1920, which was known then and now as an excellent chemistry school. In addition to his chemical studies Fieser was an outstanding college athlete, participating in basketball, track, and American football. He later enjoyed spirited competition with his research students in sports including swimming, football, and baseball.

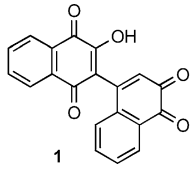
Fieser began graduate research at Harvard University in 1920 where he was an early doctoral student of James Bryant Conant (Figure 3),[3a,3b] who had an abbreviated but brilliant career as a scientist, which was diverted when he became President of Harvard in 1933. Conant was from Massachusetts and learned the German language in a public high school, which was later a great advantage when he became U. S. High Commissioner in Germany (1953–1955) and Ambassador to the Federal Republic (1955–1957). He then had a further career promoting educational reform in the U. S. Conant was a pioneer in the nascent fields of physical-organic and biorganic chemistry, including studies of "superacids", isotope labeling to detemine metabolic pathways, reaction kinetics, and the chemistry of chlorophyll. Among his other Ph. D. students were Paul D. Bartlett and Frank Westheimer, both of whom later also served on the Harvard chemistry faculty. Fieser's graduate research was a groundbreaking study of quantitatve measurements of oxidation potentials for quinone oxidation,[3c–3f] which had a lasting impact.

Fieser continued work in quinone chemistry throughout his career, and become friends with Samuel C. Hooker (1864–1935),[3h] a pioneering investigator of oxidation reactions in America in the 19th century who then devoted most of efforts to the sugar industry. Fieser's last research paper dealt with bis(napthoquinone) (**1**),[3g] and was a reinvestigation using NMR structure proof of his earlier work with Hooker. Fieser inherited Hooker's collection of quinone samples, which were later utilized in his work on anti-malarials.

Following his quinone work Fieser stayed on for some months with Conant for research in hemoglobin chemistry.[3i,3j] However, as will be seen, he did not follow a career path into mechanistic chemistry. Even at this time he showed his later talent for practical applications as he developed a method of gas analysis based on course work for G. P. Baxter which he reported as an appendix to his thesis. From this work was developed Fieser's solution (an aqueous solution of potassium hydroxide, sodium hydrogen sulfite, and sodium anthraquinone β-sulfonate) for gas purification, which was published and became the most cited of his research papers.[3k] After he received his Ph. D. in 1924 Fieser did postdoctoral work in 1924–1925 at Oxford with W. H. Perkin Jr., and then in Frankfurt with Julius von Braun (1875–1939)[3l] on catalytic hydrogenation of anthraquinone (Figure 4).[3m] J. von Braun was born in Warsaw, Poland, and was a very prolific investigator, with more than 400 publications. He had a Jewish mother and while found not formally in violation of the Nuremberg racial laws he was dismissed from his position in 1935 at the peak of his career but without explanation by Bernhard Rust, the Minister of Science, Education, and National Culture. J. von Braun argued against his dismissal, but this was upheld although his students were allowed to complete their degrees.[3l,n,o] Wilhelm Jander, a personal friend of Rust and a strong National Socialist, was appointed to the position in Frankfurt.[3l,3o]

Figure 4. Julius von Braun (1875–1939) (by courtesy of the GDCh).

Figure 5. Mary Fieser (Courtesy of Bryn Mawr College Library).



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Fieser's first independent academic position was at Bryn Mawr College near Philadelphia, beginning in 1925. Bryn Mawr is another of the uniquely American institutions primarily for undergraduate education (but with a Chemistry Ph. D. program at Bryn Mawr) which nevertheless have long records of distinguished teaching and research in Chemistry. Elmer P. Kohler (1865–1938)[4a] was Professor at Harvard while Fieser was a student, and had earlier taught at Bryn Mawr (1892–1912), and Fieser followed his career path. Arthur C. Cope,[4b] who later became Head of the Chemistry Department at MIT, also began his teaching career at Bryn Mawr (1934–1940).

Fieser commented[4c] on the good research atmosphere and the talented female students at Bryn Mawr, whom he noted also had other attractions for unmarried male faculty, and when he returned to Harvard in 1930 as Kohler's successor one of his students from Bryn Mawr, Mary Peters, enrolled in graduate school at Radcliffe College in Cambridge (Figure 5). Radcliffe was a women's college associated with Harvard, and over the years this connection has become much closer and Radcliffe is now The Radcliffe Institute for Advanced Study of Harvard University. Louis and Mary were married in 1932, and for the rest of his life she was his constant companion and collaborator both in experimental research and in textbook writing. Subsequent references to Fieser in this essay usually imply Fieser and Fieser. She was a full participant in their writing, with greater literary skills than Louis, and this was often contentious, as they were said to argue for an hour over the placement of a comma, and Fieser vs. Fieser was suggested as an appropriate name for the pair.[4c]

Even as a graduate student Mary Fieser[5] had to work in a laboratory separate from Harvard students, and never received a salary from Harvard. She completed a Master's degree at Harvard (an A. M., as is the Harvard custom in chemistry) but did not attempt a doctorate, as she said "I could see I was not going to get along well on my own, [but as Mrs. Fieser] I could do as much chemistry as I wanted."[5a] She was only honored with the title of Research Fellow of Chemistry at Harvard after 20 years of service, but ranks as one of the leading female organic chemist of the 20th century, and was responsible for much of the prodigious output from their collaboration. For her contributions to chemistry and chemical education, Mary Fieser was awarded the Garvan Medal of the American Chemical Society in 1971, and in 1996 she dedicated the Louis and Mary Fieser Laboratory for Undergraduate Organic Chemistry at Harvard University.[5c] Her bequest of the major part of her estate to the Harvard Chemistry Department provides a number of research fellowships.

From Quinones to Polycyclic Aromatics and Steroids

After his return to Harvard Fieser rapidly extended his research interests into studies of steroids and polycyclic aromatic compounds, and later into naphthoquinone-based antimalarials. As noted before due to his graduate work with J. B. Conant it might have been expected that he would pursue mechanistic studies and physical organic chemistry, but his career instead was primarily involved with synthesis and structural elucidation. He played an active role in the series *Organic Syntheses*, serving as an editor and as a frequent contributor.[1c]

Early in his career Fieser's interest in benzoquinones had extended to polycyclic derivatives, and he pursued research on these, and also the analogous polycyclic hydrocarbons, which led to cancer and steroid research.[6] In 1934 it was reported[6a] from the Royal Cancer Hospital in London that 20-methylcholanthrene (**2**) was a potent cancer causing agent, which initiated studies by Fieser in the synthesis and properties of this and other polycyclic aromatic compounds. The first preparation of **2** was by degradation of the steroid desoxycholic acid,[6b] and Fieser found the transformation could be done more efficiently using cholic acid as a source, and this provided Fieser an entree into steroid research.[6c] Melvin Newman, the postdoc involved in this study, became one of the best known of Fieser's many students. Fieser also developed a chemical synthesis of **2**.[6d] Ste-

roid chemistry became a major theme of Fieser's research, and in 1936 his pioneering book *Natural Products Related to Phenanthrene* appeared, with the 4th edition (1959), with Mary Fieser, entitled simply *Steroids*. This text appeared at a propitious time to be widely used during the great expansion of steroid and alkaloid investigations in the following decades. Carl Djerassi, who led the effort to prepare birth control pills at Syntex in the 1950s, named this as the "bible" of steroid chemistry (Figure 6).[6j]

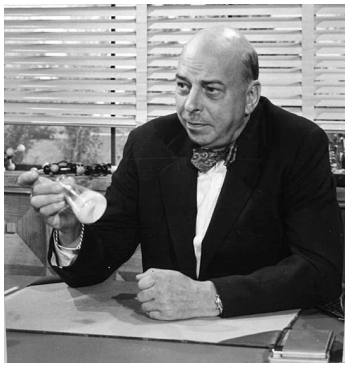
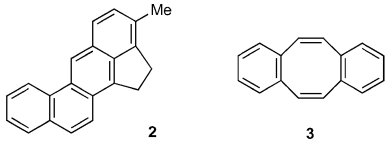
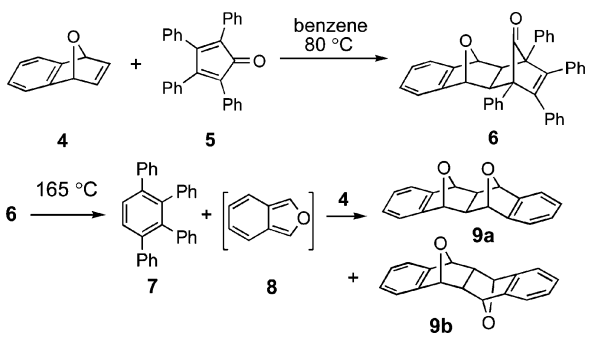


Figure 6. Louis Fieser in his office (by courtesy of *Organic Syntheses*[1c]).



Fieser's studies of steroids involved many compounds with strong UV chromophores, and the extensive data he collected were used in the correlation of UV spectra with structure known as the Woodward–Fieser rules. Proposed by R. B. Woodward in 1941[7a] and expanded by Fieser[7b] these are found in many basic organic chemistry textbooks,[7c] and caused disputes between Fieser and Woodward for the credit for the rules.[7d]

The interest in aromatic compounds led to a study by 1940 of the properties of cyclooctatetraene, whose existence and possible aromaticity were in dispute at the time, and in 1946 Fieser reported a preparation of 1,5-dibenzocyclooctatetraene (**3**). On the basis of the UV absorption and ease of hydrogenation he concluded that the molecule lacked aromatic conjugation in the eight-membered ring.[7e]



One of his last papers dealt with another unusual potentially aromatic compound, the transient intermediate isobenzofuran (**8**).[7f] Reaction of tetraphenylcyclopentadienone (**5**) with **4** at 80 °C gave **6**, and on heating **6** with **4** at 165 °C 1,2,3,4-tetraphenylbenzene (**7**) and the adducts **9a** and **9b** of isobenzofuran (**8**) were obtained. Numerous applications of **8** in synthesis have been reported.

Smoking and Cancer

Fieser's studies of **2** and other carcinogenic polycyclic aromatics[6e] were supported by the National Cancer Institute in the United States when it first began grants in 1937,[6f] and were recognized by the Katherine Berkham Judd Prize for Cancer Research in 1941. As a leading expert on cancer Fieser was chosen in 1962 as the only chemist on the U. S. Surgeon General's Advisory Committee to study the health effects of smoking, and was mainly responsible for the chapter on the chemical composition of cigarette smoke.[6g] The report of the Committee in 1964[6h] generated major interest in the U. S., and gave strong impetus to the effort to reduce smoking. This has resulted in a significant decrease in smoking in North America, a trend gaining momentum in many countries around the world. There were earlier efforts to discourage smoking, notably in Germany in the 1930s, but with limited success.

Ironically Fieser was a chain smoker and the only member of the Committee who did not stop smoking at the time, and even endorsed the Lark brand of filter cigarettes. Earlier he had dismissed as spurious the association of smoking with cancer, but then in 1965 he was diagnosed with lung cancer, and had an operation that year. He finally changed his position with his usual zeal, and in 1966 he wrote in the popular magazine *Reader's Digest*,[6i] claimed to have a circulation in many languages of 26 million copies per issue at the time: "Why did I not stop smoking?...I think that my main reason for not trying was the feeling that, after almost constant smoking for 40 years, I would not be able to break the habit." "On August 27 (1965) I stopped smoking, ...Actually I found it surprisingly easy." He was proud of his physical prowess (Figure 7), and that he was able, albeit belatedly, to overcome his smoking habit. His efforts to promote the conclusions of the Committee were a significant factor in the slow but building realization of the dangers of smoking.

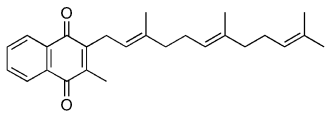
Figure 7. Fieser at bat at a group picnic.[1f]

Vitamin K and the Race for the Nobel Prize

Henrik Dam[8a] (Figure 8) in Copenhagen reported in 1929 of a dietary deficiency in chicks ascribed to the lack of a particular antihemorrhagic factor in the diet.[8b] In 1935 Dam reported further on the isolation and identification of this factor[8c,d] and proposed the name "vitamin K" (**K**oagulations-Vitamin in German and the Scandinavian languages)fortheactiveprinciple.IndependentlyHermanAlmquist[8e–g] (Figure 9) at the College of Agriculture of the University of California, Berkeley, had made similar discoveries, but as reported by Thomas Jukes[8g] he was delayed in submitting his results by bureaucratic reviews at the University of California regarding intervening studies of this substance, and then when finally submitted his paper was rejected by the journal *Science*. The paper was then submitted to *Nature*, but published 10 weeks after that of Dam.[8f] Vitamin K became the center of attention in 1938 when it was used successfully in the treatment of a human with a life-threatening hemorrhage.[8h]

Figure 8. Henrik Dam (1895–1976) (by courtesy of the The Danish Society for Biochemistry and Molecular Biology)[8i].

Figure 9. Herman Almquist (1903–1994) (by courtesy of *The Journal of Nutrition*).



Vitamin K

The flag had been dropped and the race was on, and in 1939 in *Journal of the American Chemical Society* there was an intense competition in the characterization and synthesis of vitamin K_1.[9–13] The papers were often submitted by telegram, and published very quickly, with for example a manuscript received in August 25, 1939 being published in the September, 1939, issue of the *Journal* (at that time published monthly). Almquist was first off the mark, with papers in the February and March issues of the *Journal*,[10] and was joined in May by Edward A. Doisy of the Medical School at St. Louis University (Figure 10),[9,11] and later in July by Fieser.[12] There were four papers on the subject in this journal in 1939 by Doisy and six by Almquist, while Fieser produced eight despite a later start, and there were also reports by others in 1939[13a,b] and later. Thomas Jukes suggested[8g] that Almquist was victimized in that publication of his papers was sometimes delayed for joint publication with those of others, but the reported dates of receipt do not substantiate this suggestion. Fieser had the advantage of being located at Harvard where Arthur Lamb[13c] was Editor of the journal, and so Fieser enjoyed ready submission of his work, without the need to use the telegraph, and may well have seen the work of his competitors before publication. Fieser summarized the saga in a lecture on October 24, 1939, that was published in January 1940,[12i] and noted his group began work on May 18, 1939, inspired by the work already published by others and his long experience in quinone chemistry. His first paper on the subject was submitted on June 12, 1939.[12a] Fieser begins his report "I have a story to tell tonight about the naming of a cat" and describes how their latest Siamese cat was born that year, and named in honor of vitamin K.[12j]

Figure 10. Edward A. Doisy (1881–1965) (by courtesy of St. Louis University).

In 1941 J. P. Strömbeck, Professor of Surgery in Lund, Sweden, nominated Almquist, Doisy, and Fieser for the Nobel prize in Physiology or Medicine for studies of vitamin K, and made a separate nomination of Henrik Dam for the discovery of Vitamin K. However, there were no awards in 1941 or 1942, and in 1943 the award was given to Dam "for his discovery of vitamin K" and to Doisy, "for his discovery of the chemical nature of vitamin K".[13d] Fieser and Almquist were not nominated in 1943 for the prize, and so were not then eligible for the award. While the records of the deliberations of the Nobel Committee for this period are now available for scholarly study we have so far been unable to travel to Stockholm to do so, and can only speculate on the motives of the Committee in this instance, and whether Fieser's belated entry into the field entered into the discussion and affected his chances.

In 1955 Fieser was also nominated by Maurice Auméras and Jean Doeuvre of the University of Lyon, for studies of cholesterol and of carcinogenisis for the Chemistry Nobel prize. This nomination was also unsucceesful, and it was noted that others who were not nominated also contributed in this area.[13e] The nominators had no obvious connection to Fieser, and their published research does not seem related to his.

Chemical Education[14]

Fieser was responsible for teaching the basic organic chemistry course at Harvard for more than 30 years, and thousands of students received their introduction to the subject from him. Many of these were strongly influenced by Fieser and went on to success elsewhere, including William S. Knowles, who shared the Chemistry Nobel prize in 2001 with Ryoji Noyori and K. Barry Sharpless. Knowles credited Fieser with sparking his interest in organic chemistry, leading to a doctorate at Columbia University.[14d] A much larger number of individuals used one of his many organic textbooks, and this includes the current authors. Fieser recounted[1a] how his textbook *Organic Chemistry* originated during WW II when he was primarily involved in war work (vide infra) and separated from teaching, but often had time available while traveling or with delays in tests of munitions, and he used the opportunity for writing this text, with strong participation by Mary. The book of 1091 pages was published in July, 1944, and remained in print for 11 years. Its availability as the newest book on the market coincided with the surge in university education after the war. The text went through many editions and various titles, and was available in several languages. Fieser's student Koji Nakanishi made a translation into Japanese, published in 1952, and recounted how the royalties he received were very welcome when he began his academic career in postwar Japan on a very limited income.[14a] Fieser is perhaps most remembered now for his writings, which include *Reagents for Organic Synthesis*, volume 1 of which appeared in 1967, *Natural Products Related to Phenanthrene*, *Steroids*, *Organic Chemistry*, *Textbook of Organic Chemistry*, *Introduction to Organic Chemistry*, *Basic Organic Chemistry*, *Advanced Organic Chemistry*, *Topics in Organic Chemistry*, and *Current Topics in Organic Chemistry*, *Experiments in Organic Chemistry* (three editions, 1935–1955), followed by *Organic Experiments* (eight editions, 1964–1998, with K. L. Williams as coauthor from 1975), and *Style Guide for Chemists*. Already in 1935 his lab manual contained a section on reagents, the precursor to his later volumes on the subject. A feature of his books were brief historical vignettes of the chemists responsible for specific chemical discoveries. This essay would not have been written by the current authors without the fascination fostered by Fieser's books not only for chemical discovery but for the individual creators.

The Fiesers were dedicated experimentalists who were constantly in the lab themselves, and an experiment designed by Fieser has been vividly remembered by many students who used his laboratory manual. A sequence of reactions starting with 1-naphthol led through a succession of brightly colored crystalline products culminating in Martius yellow (2,4-dinitro-1-naphthol), and a competition was held to see who could complete the sequence most rapidly with the best yields. Fieser himself took part, and held the record until bested by his student Nakanishi.[14a] Part of the sequence is shown on the blackboard in Figure 11. He also devoted great energy to the design of simple laboratory apparatus, developed an inexpensive set of molecular models which is still widely used and available from Sigma–Aldrich (see Supporting Information), and even provided a useful template for drawing chemical structures (the Fieser triangle) which was very helpful in the days when chemical structures were drawn by hand (see Supporting Information). His success in teaching was recognized by the award of the James Flack Norris Award in the Teaching of Chemistry (1959), the Manufacturing Chemists Association Award in Teaching (1959), and the Nichols award of the ACS New York Section in 1963 as a "Superlative Lecturer, Teacher and Writer on Organic Chemistry. Pioneering Investigator of Polynuclear Compounds", and the ACS Award in Chemical Education (1967).[14b]

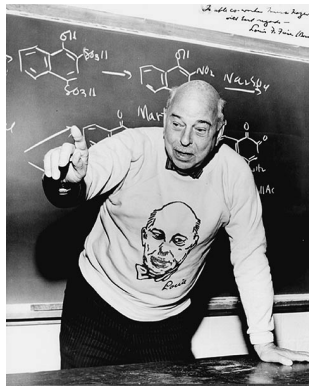


Figure 11. Fieser at a classroom celebration. The structure of Martius yellow is visible behind Fieser's head (by courtesy of Mukhlaf Haddadin).

Fieser contributed a chapter "Theory of the Structure and Reactions of Aromatic Compounds" for the authoritative text *Organic Chemistry, An Advanced Treatise*, Editor Henry Gilman, published by Wiley in 1938.[14c] This text contains some appreciation of the aromatic character of benzene, and of the mechanism of electrophilic aromatic substitution, but a chapter by Linus Pauling in the same work seems to presage the path followed by the modern organic textbooks that appeared therafter. In the 2nd edition of the book (1943) there was an addition to Fieser's chapter by Paul D. Bartlett entitled "The Electronic Theory of Aromatic Substitution" (p. 205–213). Fieser published studies in 1935 and 1936[14e-h] arguing that naphthalene and phenanthrene had fixed double and single bonds, and disagreeing with the analysis by Pauling and Wheland[14i] for a delocalized system. Chemical theory was not Fieser's strong point, and his books were slow in their assimilation of the

great progress in this area from the 1920s. As reported by Nakanishi in 1950 back to his teachers in Japan: "He (Fieser) is regarded as belonging to the classical school, and he himself admits that he is not good at the electronic theory prevailing at Harvard."[14a]

War Work

Fieser had some brief military training while a student in 1918–1919 (Figure 1), but was able to complete his studies and enroll in graduate school in 1920. However as the United States drew closer to involvement in WW II Fieser together with many other American scientists became involved in war work. Fieser entered this effort with his characteristic enthusiasm, as evidenced by his memoir,[1a] and engaged in an extensive effort for the synthesis of potential new antimalarial compounds, and many papers on the subject were published after the war. Another major effort involved research into munitions (see Figures 12, 13, and 14), including a project for preparation of mixed aliphatic and aromatic nitro compounds as explosives that was published in 1946.[15] Mary Fieser also participated in this work, as did many of Fieser's students. They worked on many types of weapons, most notably his invention of napalm, which was employed against Germany and particularly Japan with devastating effect.[16a] The name napalm arose from a misunderstanding, in that gasoline was gelled using aluminum salts of fatty acids, and a sample labeled to contain aluminum palmitate was later found to be primarily the salt of lauric acid.[1a]

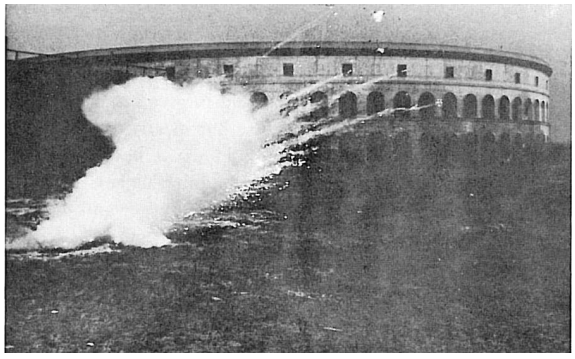


Figure 12. Bomb test in front of the Harvard University stadium.[1f]

In his book Fieser shows genuine dedication for this effort, which was the normal feeling of those who were inspired to do their patriotic duty. It involved new types of invention and problem solving, and he was exhilarated by the challenge. As a practical man he also recounts times when field work at remote weapons testing sites permitted him to satisfy his love of fishing. Indeed almost all of his fellow chemists in the U. S. who were called upon willingly joined the defense effort, including later spokesmen for peace such as Linus Pauling and J. Robert Oppenheimer. The same was true in other countries, including chemists in Germany such as Wilhelm Schlenk and Heinrich Wieland.

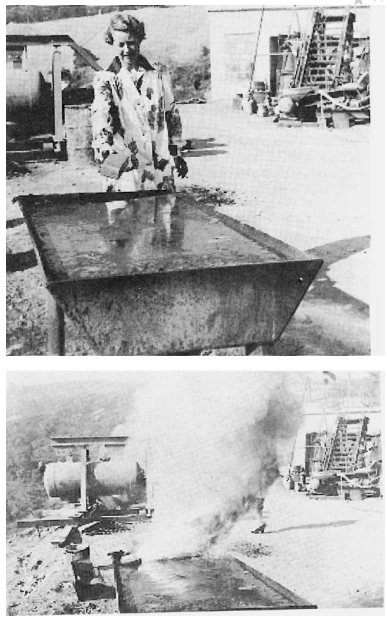


Figure 13. Mary Fieser testing an explosive device.[1a]

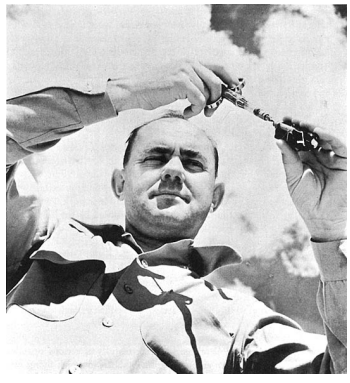


Figure 14. William G. Young inserting the fuse attached to a bat bomb.[1a]

One of the less conventional approaches by Fieser was the use of "bat bombs", which occupies an entire chapter of his memoir.[1a] These had been suggested by a civilian dental surgeon, and involved small incendiary bombs to be attached to bats which would be released near target cities, and when the bats sought shelter in wooden buildings and the bombs detonated large fires could result. Fieser was skeptical but nevertheless the idea was pursued and based in California, where those involved included John D. Roberts (later Professor and Provost at California Institute of Technology) and William G. Young (Professor at the University of California, Los Angeles). The project was moved to Carlsbad Air Force Base near Carlsbad Caverns in New Mexico to ensure a ready supply of bats, and one test there resulted in inadvertently setting fire to the administrative office of an auxiliary air field. After several years the project was cancelled before it could be put into practice.[16b]

This type of work was expected and unquestioned at the time, but the use of the atomic bomb at the end of the war caused doubts, even among many who helped develop nuclear weapons. Similarly the work of Fieser as the inventor of napalm has made him less than universally admired, espcially when this became notorious during the involvement of the United States in the war in Vietnam in 1963–1974. This marked a turning point in attitudes which continues to this day.[17]

Fieser publicized his invention of napalm and was awarded a patent for this discovery,[18a,b] which may have earned substanial financial rewards. The formula was reported to be based on a recipe devised to rid his lawn of crabgrass. He relished the publicity and acclaim for his efforts, and broadcast his efforts in defense work in his memoir in 1964,[1a] but seemed unaware of the change in public attitudes. As substantial opposition to the Vietnam war developed in the late 1960s the manufacture of napalm by Dow Chemical Co. became a frequent target of antiwar protesters in the U. S., and often Dow recruiters on campus were harassed by hostile demonstrations (Figure 15), and Fieser was also a conspicuous target. Fieser reported he was an interested spectator at such an occasion in 1968, but given the rebellious temperament of the times Fieser emerged relatively unscathed, but unapologetic. He was taken aback by the criticism, and was quoted[18c–e] as saying he did not feel "any guilt" for his role in the invention, and "I would do it again, if called upon, in defense of the country." It was however reported "he protested to the White House when the latter (napalm) was used in Vietnam."[5c]

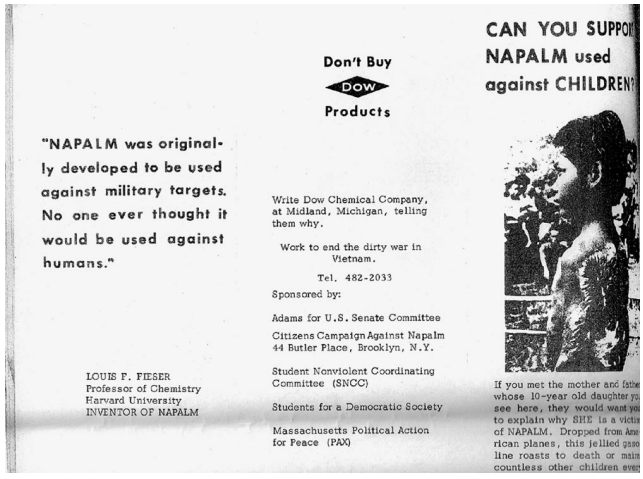


Figure 15. Anti-napalm brochure 1968, collected by Louis Fieser.[1f]

Today the work of scientists is frequently subjected to public scrutiny and criticism in areas such as research involving animals, genetic modification, or the use of stem cells, and the actions of other scientists in the 20th century are frequently examined. A prominent example is Fritz Haber,[19] who in WW I developed the use of poison gas, an activity that incited widespread horror, and a worldwide ban meant it has not been used since in major wars. Another chemist who was inspired by patriotism was Eduard Buchner,[20] Nobel laureate in 1907, who long served in an army reserve unit, and was on duty at the front with his unit in 1917 when he was mortally wounded. Fieser, Haber, and Buchner all clearly relished their participation in the military, and were frequently photographed in uniform (see Figures 16, 17, and 18), although Fieser was technically not in military service, except for some training in 1918–1919.

Figure 16. Fritz Haber (2nd from left) explaining the advantages of poison gas (photo from http://www.greatwar.nl/).

Figure 17. Eduard Buchner (center) with his army unit (by courtesy of the GDCh).

Figure 18. Fieser in Braunschweig, Germany, April 1945.[1f]

Fieser deserves to be remembered, not only for his career in chemistry and his outsized personality, but also for his other accomplishments, which have much relevance to the present day, with both very positive and less attractive connotations. Fieser's own personal memoir[1a] emphasizes that his legacy includes his war-related research during WW II, just as he desired. The fierce energy he directed to this task and the pride he felt for his efforts is somewhat unnerving in today's climate, even if this was in a just cause.

Travels in Germany

Near the end of WW II Fieser went to Germany on March 6, 1945, as part of the Alsos mission, whose goal was to assess German war research, and especially the German effort to build an atomic bomb. The name Alsos is Greek for "grove", and hints at the name of Major General Leslie M. Groves, the military director of the U. S. atomic bomb project. Fieser visited Braunschweig from where his grandparents had immigrated to America a century before, and entered the IG Farbenindustrie plant in Ludwigshafen immediately after it was captured to interview the Directors and chemists. Fieser was personally acquainted with many German chemists such as Heinrich Wieland, Karl Freudenberg, Richard Kuhn, Friedrich Weygand, and Adolf Butenandt, among others, from his travels there in 1937, but as he admitted was not an expert on nuclear physics. Fieser recorded that when it became clear that German efforts to make an atomic bomb posed no threat he "decided to concentrate on diversionary activities and in particular to sound out the temper of my German colleagues. It soon became apparent that these men had not been sacrificing their scientific activities for the war effort, as I had, and I decided it was time for American chemists to get back to research and scholarship."[1a] However, Fieser is somewhat disingenuous in his comments, for while he published a total of only 3 papers (one per year) from 1943–1945, as compared to 31 in 1940 alone, he had a group of 11 professional chemists and 4 technicians working on naphthoquinone antimalarials on a government contract during WW II, and many papers based on this work appeared afterward.[1a] The participation of German chemists in war-related research is also well documented. He flew home from Paris the day the war ended and notes he was back in Washington two days later for dinner at his favorite restaurant there (Harvey's[21]).

Fieser in Retrospect

Fieser came to Harvard as a replacement for Elmer P. Kohler upon his retirement, and while Kohler was a respected teacher and many of his students achieved great prominance he was a retiring individual who did not travel and lecture on his research, and so did not have great impact elsewhere. Chemists such as Roger Adams at Illinois and Henry Gilman at Iowa State, who had been students at Harvard before 1920, were among the leading young people in the field, and Adams had a strong supporting cast at Illinois that made this the leading synthetic organic group in the U. S. in the 1930s. Other schools in the midwest were likewise gaining stature, and Harvard was unsuccessful in an attempt to hire Adams in the 1930s. Reginald P. Linstead came to Harvard as Professor in 1939 but took leave in 1942 for defense work in the UK, before resigning from Harvard 1945 and later becoming Professor at Imperial College, London. Thus Fieser was the primary synthetic organic chemist at Harvard until the 1940s, and was joined by many excellent students who went on to enhance the reputations of other Departments in the U. S., including James Cason (California, Berkeley), William S. Johnson (Wisconsin and Stanford), Melvin Newman (Ohio State), Wyman Vaughn (Michigan and Connecticut), Alex Nickon (Johns Hopkins), Donald J. Cram (UCLA),[22], William G. Dauben (California, Berkeley), Ernst Berliner (Bryn Mawr), Richard B. Turner (Rice), Koji Nakanishi (Columbia), Charles C. Price (Pennsylvania), and Marshall Gates (Rochester). Others served abroad, including Guy Ourisson (Strasbourg), Mukhlaf Haddadin (American University of Beruit), Musa Nazer (Jordan), Huang-Minlon (Shanghai), Toshio Goto (Nagoya), and Wei-Yuan Huang (Shanghai Institute of Organic Chemistry), and many made important contributions in industry, of whom Alfred Bader (Sigma–Aldrich) is perhaps the best known.

Louis Fieser lived a full life, as did his wife Mary. Both of them were among those cited in 1998 by *Chemical and Engineering News* as voted by the readers as the "Top 75 Distinguished Contributors to the Chemical Enterprise" during the 75 years of C&EN's existence. This poll however reflected more Fieser's well-publicized persona than his scientific achievements. Mary's life appears unambiguously successful: she was a well known chemist and author, and a pioneer woman in science. Louis was honored by Membership in the U. S. National Academy of Sciences and was Sheldon Emery Professor[23] at Harvard from 1939 until 1967. However, he was in a Department in which the other full Professors of organic and bio-organic chemistry, and his rivals for prestige, were Nobel laureates Robert B. Woodward, Elias J. Corey, and Konrad Bloch, together with Paul D. Bartlett, and Frank Westheimer, each of whom accumulated significantly more research honors than did Fieser, who received no major primarily research award from the American Chemical Society. However, while he did not rank scientifically with some of his colleagues he never lacked for drive and determination, and gave his best effort. His service in fighting cancer deserves lasting respect, although this is obscured by the cost of his enthusiastic participation in war work. His books are another lasting legacy, especially the pioneering *Reagents for Organic Synthesis*, and he will be long remembered for this. His spirit is well captured by the words upon his retirement by R. B. Woodward, who noted "the immense zest, verve and energy with which he attacked any problem. He stormed bastions, he adored the big push, he delighted in rallying his collaborators to superhuman exertions, inspiring them by example to make efforts of which they could not have believed them-

selves capable".[1d] Absent are compliments for his imagination and scientific brilliance, but many might aspire to match his achievements.

Supporting Information (see also the footnote on the first page of this article): Additional text and photographs.

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[2] Mary Fieser was even reported by Rolf Huisgen to have green hair on his visit to Harvard in 1950, and a co-worker at the time reports she did use green nail polish. A contemporary photograph (see Supporting Information) shows her dashing appearance, which may have given this impression. There was a popular film "The Boy with Green Hair" in 1948, which had antiwar overtones.

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[21] Harvey's was a well-known restaurant in Washington for more than 80 years, but is no longer in existence.

[22] Cram is not mentioned in Fieser's memoir,[1a] and his Ph. D. thesis "Syntheses and reactions of 2-(ketoalkyl)-3-hydroxy-1,4-naphthoquinones" (1947) was not published. In his own recounting of his career (D. J. Cram, *From Design to Discovery*, American Chemical Society, Washington, **1990**) he does not comment on his research with Fieser.

[23] Other holders of the Sheldon Emery Professorship include Arthur Lamb (1926–1929), James Bryant Conant (1930–1938), E. J. Corey (1968–2000), and Eric Jacobson (2001–now).

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