NATIONAL ACADEMY OF SCIENCES

ELMER PETER KOHLER

1865—1938

A Biographical Memoir by

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Elmer Peter Kohler, Sheldon Emory Professor of Organic Chemistry at Harvard, died at the age of 73 on May 24, 1938. Until a few days before his death he had carried the full burden of academic duties with all the vigor of a man twenty years his junior. The friends who were close to him realized how fortunate he was that he could remain an active chemist almost to his dying hour; a career of forty-five years of teaching and research was brought to a close so suddenly that he never knew the pangs that come to those who reluctantly close the laboratory door behind them on the final day.

Kohler was a man who might have said, "For me to live is organic chemistry." Indeed, his words often conveyed this thought; for example, he ushered a visiting European scientist into his private laboratory with the proud declaration, "Here is my own laboratory; here I am the happiest person in the entire world." And this was no chance remark; to understand Kohler one must realize that he continued throughout his life to devote many hours of every week to experimental undertakings carried out with his own hands. Only those who have seen him in his shirt sleeves, crystallizing and recrystallizing his precious materials on his own laboratory bench, have known the man; and only visitors to whom he explained the intricacies of the problem under study with the aid of pen and scratch paper have heard a great teacher at his best. The biography of Elmer Peter Kohler must be primarily the record of a scientist who loved his subject as an art and who delighted most in teaching the art to eager apprentices who themselves aspired to become masters. Indeed, his career is a standing answer to those who proclaim the false dichotomy between research and teaching. One of the keenest observers of the Harvard scene remarked on learning of Kohler's death, "The University has lost its greatest teacher." Yet the list of more than a hundred papers which is appended to this biography is testimony to the unremitting efforts of an investigator who never ceased to be fascinated by the complexities of the chemistry of carbon compounds.

At the beginning of this century it was the custom in many colleges and universities for the professor of organic chemistry to give the freshman course. Before the impact of physical chemistry had transformed even the elements of general theory, the qualitative approach of the organic chemist seemed suitable for the general student,—indeed for many it was far more digestible than the more mathematical introduction which is now the standard diet. The type of freshman course common in colleges fifty years ago, while totally inadequate as a foundation for twentieth-century chemistry, had certain educational values for the student majoring in other fields. The theoretical material was simple and self-contained; the exhaustive treatment of the arguments by which Cannizzaro and his contemporaries established the atomic theory in the mid-nineteenth century provided at least one example of the way science develops. The everyday applications of chemistry and its relation to industry were stressed, and there was ample time available for excursions into pleasant and interesting byways. At all events, many college generations of subsequent lawyers, writers, and businessmen have provided eloquent testimony of how much they enjoyed freshman chemistry presented in this fashion. And none more so than those who took Chemistry A under Professor Kohler.

One of the strange contradictions of Kohler's character was his success as a lecturer and his lifelong diffidence as a public speaker. His delight as an artist was clear when he presented a brilliant lecture, either to freshmen or to advanced students in organic chemistry, or on very rare occasions to a "journal meeting." His anxiety before every such performance was equally real, but known to only a very few. This apprehension which almost deserves the adjective "pathological" was the reason why Kohler made it a firm rule never to speak outside his lecture room. But explanations were seldom given for a policy that appeared so curious and arbitrary to many fellow-chemists. He rarely if ever attended scientific meetings. All of which gained him the entirely undeserved reputation of being an academic snob. He suffered thereby the fate of more than one shy person whose aloofness is attributed to pride.

One episode in Kohler's freshman teaching deserves to be recorded for all who enjoy the hazards of experimental demonstrations before a class. The main subject of a certain lecture in Chemistry A was explosives. The long lecture table was covered with samples of gunpowder: mammoth pieces used in naval ordnance, open vessels of smaller grains used in army guns, samples of sporting powder. About the middle of the hour Professor Kohler introduced the topic of gunpowder with the following words, "There is a common misapprehension that when gunpowder is ignited it explodes, but actually if lighted in the open it burns with a quiet flame." Thereupon he poured a little black powder onto an asbestos sheet, struck a match and applied the flame. The result was a flash along the entire table, a roar and heavy clouds of smoke; an old-fashioned chain reaction had taken place. A spark had jumped from the demonstration to the nearest sample of powder and started off the entire exhibit. The students rushed for the fire escapes. Kohler, who had ducked down behind the table, emerged and held up his hand to quiet the incipient panic. Through the smoke one could just see him from the back of the hall. As the milling throng quieted down, he said, "I have sent for some more gunpowder." After the laughter and cheers had subsided, he performed the experiment without mishap, and then firmly stated, "You see it does burn with a quiet flame; the class is dismissed!"

There was nothing exhibitionist about Kohler's teaching: he used lecture table demonstrations not for a show but to demonstrate a point. He drove home with relentless logic whatever he undertook to expound; he had no patience with ill-formulated ideas or partial truths. In short, he was a teacher who was at one and the same time both interesting and rigorous. The same basic technique was employed in his course in advanced organic chemistry. For more than twenty-five years he presented the chemistry of the carbon compounds to juniors, seniors and graduate students in Harvard University. His approach was entirely his own. No textbook has ever been written or ever will be that can in any way accomplish what he succeeded in achieving. If ever the lecture system for advanced students had a justification, it was in Kohler's Chemistry 5. For the systematic presentation of the facts of organic chemistry, he had not the slightest use. He assumed that in the more elementary course the students had at least become acquainted with the various common types of substances and knew something about the simple functional groups. He presented the problems of organic chemistry as he saw them at the time. The connection between his lectures and his research interest was never far removed. Not that large sections of the material covered were not essentially orthodox topics treated in advanced books on organic chemistry, but the presentation was Kohler's own; a problem was always in the foreground. Spurning anything approaching the usual mode of classifying organic chemistry with its dreary listing of such topics as "Seven Ways of Preparing Aldehydes," "Five Characteristic Reactions of Aromatic Primary Amines," he rearrranged his material to focus the attention of the class on a series of scientific adventures.

His success was the result of a combination of years of experience and great native skill in the art of speaking to small audiences. His consistent refusal to speak outside his classroom coupled with his annual destruction of his lecture notes kept this native skill from being damaged by those forces which slowly erode the pedagogic talents of so many academic men. Who, however, but a bachelor whose life was centered in his subject could find the time and patience to work over every year a completely new approach to his subject? Kohler kept turning over in his mind for a week or so before it was due the way "this year" he was going to present a certain topic. He would drop a remark or two to a junior colleague that betrayed his preoccupation. And then, if one were bold enough to intrude on the actual preparation of the lecture the day before, one would find Kohler sitting at his small desk in the office making notes on pages torn from the back of old examination blue books. He seemed never to write out even a fraction of the entire lecture. His notes, when one could catch a glimpse of them, seemed to consist of a series of opening sentences of paragraphs—these, and some formulas of the complicated trans-

formations so dear to the heart of the organic chemist.

In retrospect, I think I see that Kohler had unconsciously developed the habit of speaking to those special audiences of his much as some orators have learned to address vast assemblies. By memorizing the opening lines of a paragraph (or, if necessary reading them), I am told, the rest of the argument comes forth with elegance and ease and in a spontaneous fashion. As one of the most finished speakers I have heard once said, "If you have clearly in your mind or available for your eye the key sentences in a speech, the remainder will take care of itself, provided the audience responds." And Kohler's student audience always did respond in an amazing fashion. Formal lectures on such factual material as crams the books of organic chemistry would not seem to offer much opportunity for exciting enthusiasm among college students. But one could summon a host of witnesses to testify to the arresting rhetoric in the small lecture room of a professor too shy to speak in public.

Some men's lives are fascinating to study because of the complexity of their characters; curious patterns of conflicting and inconsistent trains of thought and action are revealed. Over a span of years some men's behavior resembles that of a tornado following an erratic course over a wide area; the creative energy of more than one scientist has boiled out first in one direction and then another. But Kohler's career was of another more consistent type: his mature life was all of a piece. Yet at first sight it appears full of contradictions. A reserved man, almost pathologically shy, yet a brilliant lecturer; a professor who devoted almost all his working hours to his experiments and his students, yet a man whose opinions and judgments were those of no narrow-minded specialist. A man who only a few times in his life undertook administrative responsibility, yet when he did, won the immediate confidence of all concerned by the solidity of his character and the wisdom of his decisions. Those who on first acquaintance were skeptical of the human qualities of the silent man from the laboratory soon were amazed at his insight. As to the independence of his judgment and the firmness of his opinion when once a position was taken, there was never any question. Those who had known him as a luncheon or dinner companion at the Faculty Club (where he took all his meals over many years) were not surprised; the sagacity of his views (never too frequently expressed) had become proverbial among his colleagues. Likewise, advanced students who sought his advice felt they were dealing with one who knew whereof he talked or else refrained from talking; they were dealing with a relatively rare phenomenon among professors, a person whose instinctive responses seemed to spring from an age-old acquaintance with the realities of human nature. Whoever succeeded in drawing him into conversation on general topics was soon in contact with a strong dose of common sense. The reaction of a man of the fields rather than of the library characterized the overtones (but not the content) of Kohler's discussion of matters political, whether national, local or academic.

The combination of qualities which together made Kohler such a consistent character can be compared perhaps to those of a mountain guide. The comparison first came to my mind when in preparing this memoir I recalled how gladly Kohler always sought the mountains of Canada, Switzerland and the United States and how fondly he described his long walks through mountain country. But the analogy, I believe, rests on something far less superficial. In the first place, a teacher of advanced students in a discipline where mastery of techniques is essential before one can work alone, is in the same position as a guide on ice or rock with the novices strung out behind him on the rope. He leads the climb both in order to get to the summit (and he enjoys it!) and to show how the art of mountaineering can be mastered. In the second place, a mountain guide has his life anchored to his village; a rural economy and a small group of neighbors provide the fixed reference points to which he instinctively refers both in his adventures on the high peaks and in judging the behavior of his clients from distant lands and cities. He knows human nature in a special way because he combines with the shrewdness of a countryman a wide observation of the foibles of those who can and do gladly come to him from afar for instruction in a hazardous sport. Replace the mountains by the laboratory, the climbing party by the candidates for the Ph.D., and the mountain village by Egypt, Pennsylvania and the analogy is complete.

Kohler never turned his back on the Pennsylvania "Dutch" community in which he was born and bred. In a sense one may say he never left Lehigh County except for lengthy expeditions to the laboratories in Bryn Mawr and later, Harvard. Not that his homeland intruded into the conversation; quite the contrary. It was hardly ever mentioned. But anyone who talked with Kohler long was in contact with a frame of reference only distantly related to either the laboratory or academic Cambridge.

One might almost say Kohler camped out, bivouacked perhaps, in the spot handiest to his laboratory—a few rooms to provide rest and shelter; breakfast, lunch and dinner at the Faculty Club according to an unvarying schedule; billiards for an hour or so with a few cronies, and then back to the climb; that is, the laboratory. The permanent base was evidently not in Cambridge; it was in fact his family home in Egypt. To this he returned almost always unattended at Christmas, Easter, and for a part at least of every summer. His father and mother were long-lived and clearly the journey home continued to be a central feature of Kohler's plans well past middle age. In the congenial surroundings of his home Kohler found the deepest satisfaction in taking an active part in the workings of a very small community based on the land.

The house in which Kohler was born on November 6, 1865 and from which his body was taken to be buried in the near-by cemetery, had been in the family for generations. He was the son of Lewis A. and Elizabeth (Newhardt) Kohler; the lands which were cultivated by his family were acquired before the American Revolution. Jacob Kohler settled in the vicinity of what was later to be known as Egypt in 1728. His descendants were farmers, millers, storekeepers, in the villages and towns which were dotted over the prosperous farming lands of the so-called Pennsylvania Dutch. The people were bilingual. Muhlenberg College in Allentown (a short distance from Egypt), from which Kohler was graduated in 1886, was in the nineteenth century a "Pennsylvania Dutch" college. The adaptation of the old-world German culture to the highly successful farming life of

Pennsylvania had produced by the end of the nineteenth century a very stable amalgam; only the mechanization of the twentieth century could destroy it. It represented no alien streak in the American pattern. Those who accepted it as a matter of course found no difficulty in moving in and out of communities with more diverse sets of mores. But for one who never married and whose center of daily interest was in the world of the adventures of the mind, the pull of this homogeneous community was irresistible. It would seem that Kohler's ultimate values were those derived from the homestead which stood in the hamlet overlooking the fruitful lands the ancestors had so wisely tended.

Lehigh Valley today is not primarily agricultural. Industry, steel and cement long ago moved in. This process which was taking place in Kohler's youth was everywhere bringing to the younger generation in small communities the realization that the United States was a land of vast distances and great possibilities. Those who were looking for adventure would hardly be content to settle down to the life of their forefathers. So Kohler, like many another of his contemporaries, went West. By accident he seems to have landed a job with the Santa Fe railroad and soon became a traveling passenger agent. Concerned with the welfare of those traveling over the rails seeking a new home and fortune, he came to know the vicissitudes of the prospectors. Perhaps he might have become one himself. But instead, he decided to become a practitioner of the science they most required—the assaying of minerals. For the need for an honest assessment of the samples brought in by lone explorers impressed him greatly; examples of chicanery based on spurious analyses must have come dramatically to his attention. For the purpose of learning to analyze ores, he returned East to begin the study of chemistry at the Johns Hopkins University.

Today a young man of twenty-three who had never studied more than one course in chemistry would be bold indeed who decided so late in life to undertake the training required of a professional chemist. But things were simple in the '80's. Kohler entered the Johns Hopkins University and at once enrolled under one of the leading chemists of the United States, Ira Remsen. (In later years he seemed to think his intimate knowledge of German was chief among the factors which persuaded Remsen to accept a candidate with so little previous exposure to science.) He completed the necessary formal work in short order and soon began work on a research problem under the immediate direction of Remsen. His interest in minerals and analytical chemistry was short-lived; he had found what he wanted in the joy of investigations of organic chemistry.

Kohler received his Ph.D. degree in 1892 and at once started his academic career. The President of Bryn Mawr, Miss M. Carey Thomas, so famous for her skill in spotting promising young instructors, offered him a position as an instructor. For twenty years he taught general and organic chemistry in this famous women's college. In due course he advanced through the academic hierarchy and was made a professor in 1900. Not long after, when the head of the department, Professor Keiser, left to take a position in another educational institution, Kohler became Chairman of the Chemistry Department. In 1912 he was called to Harvard as a professor with the understanding that he would give both the freshman course in general chemistry and the advanced course in organic chemistry.

There are many stories of Kohler's academic independence. One which I had from his own lips about his call to Harvard can now be put on record without embarrassment. Although Kohler in 1912 was forty-seven years of age, had twenty years of academic service and was the author of some thirty papers, it was proposed that he come to Harvard as an assistant professor. (The rate of promotion in many American universities, it must be remembered, was of a different order of magnitude forty years ago from what it is today.) The offer came from the chairman of the department, an eminent chemist, and I am sure was politely tendered. It was equally politely but quite firmly declined. Mutual friends attempted to negotiate as they still sometimes do in academic circles. Kohler refused to budge. Finally, the President of the University, learning of these discussions and having his own independent assessment of Kohler, wrote a few lines asking if the Bryn Mawr professor would come to Harvard as a professor of chemistry. Kohler replied in not more than three lines in the affirmative. The appointment was made and, as Kohler more than once said privately, he had a "presidential appointment," and was in a sense, he felt, "independent" of the department.

This story must be balanced by a clear statement that though Kohler was certainly a very independent member of the department, he was also cooperative to a high degree and never independent for the sake of asserting any petty rights. He cheerfully carried more than his share of the teaching load, and later in his life was an effective chairman for a long period of time. As a wise and understanding older man he assisted not only his students but more than one junior member of the department in solving human problems. As a shrewd judge of character as well as of scientific ability he helped shape the department policy so that, as far as possible, only the most likely candidates received appointments. In guiding his students and his junior colleagues into academic and industrial positions, he was utterly candid to the prospective employer, yet sympathetic and helpful to the younger man.

Kohler's contribution to science is difficult to summarize in any brief biography. The qualities which made him so excellent an instructor of the novice in research to some degree impaired his own effectiveness. To use an overworked analogy, he was a tactician and not a strategist. With good fortune he might have made an experimental discovery which would have assured his work a place on the permanent roll of the outstanding contributors to organic chemistry. He had no such luck, however. Many of his papers are important, none of them is trivial, but none quite hits the bull's eye.

His mode of work was determined largely by his keen interest in the art of organic chemistry. To return to the analogy of a Swiss guide, he was fascinated by the technique and loved to do what he could with stubborn material with his own hands. By the time he had come to Harvard he was aware of the fact that many complicated transformations of carbon compounds could be followed if one could isolate pure compounds in each step. As the techniques of experimentation then stood, this was possible only if one could obtain crystalline products. By fractional crystallization, particularly in Kohler's skillful hands, many complicated mixtures could be separated. If one were dealing with liquids, distillation as then practiced would have been a hopeless method of separating pure substances. And I must remind the readers of this biography who lack chemical training that the purity of a substance is to the chemist what the accurate control of a physical variable is to a physicist.

In order to work with crystalline material, Kohler studied the transformation of what are often called "side chain compounds." He was interested in the behavior of compounds whose characteristic structure contained the double carbon link of ethylene (C=C) and the carbonyl group of aldehydes and ketones (CO). But a study of his papers or the excellent résumé of this phase of Kohler's work in Chapter VI, Volume I of Gilman's ORGANIC CHEMISTRY (1942) demonstrates that in almost every case the structure included one or more aromatic residues (e.g. phenyl groups C_6H_5). The presence of such groups conferred on the compounds the physical properties Kohler desired, namely solubility in organic solvents, crystalline form and melting points between 50° and 200° C. Alas, more often than not, however, a mixture of such substances presented to the unwary investigator only a brittle resin or a gummy material. Kohler and his students spent endless hours coaxing crystals from such unattractive tars. The patience and skill needed for success in this enterprise cannot be portrayed to the uninitiated by any words.

The bulk of Kohler's work dealt with the reaction of various types of compounds of the general nature just described. In the parlance of the craft he was concerned with the behavior of unsaturated and conjugated systems. He had only a very slight interest, however, in the problems that were then arising in industry which were connected with such behavior. This fact is both characteristic of the man and symptomatic of the times. A quick glance at the history of physics and chemistry from, say 1880 to 1930, will show that in this period the academic men for the most part made a virtue of being uninterested in any application of their science. Maxwell's famous and rather snobbish account to a British audience in the 70's of Graham Bell's invention is indicative of the trend. Rowland, addressing his fellow physicists of America in 1899 said, "He who makes two blades of grass grow where one grew before is the benefactor of mankind; but he who obscurely worked to find the laws of such growth is the intellectual superior as well as the greater benefactor of the two." Some of the academic men on both sides of the Atlantic were in touch with industrial developments occasionally to their financial benefit. But, on the whole, scientists rallied around one banner; inventors, engineers and practical men, around another. Kohler was a strict member of the scientific fraternity. As a consequence, though some of the revolutions in applied chemistry during his lifetime were very close to his own sphere of scientific work (synthetic rubber and plastics, to name but two), Kohler pursued his study of unsaturated compounds without reference to those industries founded on the unique behavior of such substances.

Early in his career as an investigator, Kohler encountered a completely unexpected reaction of a class of compounds known as alpha beta unsaturated ketones. The exploration of the peculiarities thus uncovered, almost by accident, led him into a careful study of the phenomenon known as 1,4 addition. Both the origin of the problem and Kohler's method of completing the research are so characteristic as to warrant the intrusion of some details of organic chemistry into this general account of a chemist's life.

Shortly after the turn of the century, the attention of organic chemists was attracted by two discoveries in widely separate fields. Grignard, a French chemist, showed his fellow workers a new powerful synthetic tool in the form of an ethereal solution of organic magnesium halides, shortly to become known as the Grignard reagent; by means of such compounds as phenyl magnesium bromide C_6H_5MgBr, carbonyl compounds (ketones and aldehydes) could be transformed into carbinols. Moses Gomberg at the University of Michigan had reported some very strange reactions of triphenylmethyl halides when treated with metals and had interpreted his results by assuming the existence of the free radical triphenylmethyl. Kohler as was his practice throughout his life had kept in close touch with the recent publications and realized the full significance of both Grignard's and

Gomberg's work. He thought he saw the possibility of using the Grignard reagent to prepare a chloride similar to triphenylmethyl chloride but differing from it by the presence of an ethylenic linkage in its structure. He envisioned the following reaction:

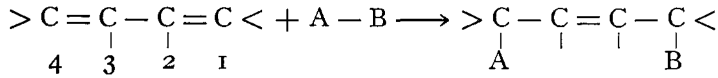
$$\underset{\text{(Grignard reagent)}}{C_6H_5MgBr} + \underset{\text{I}}{C_6H_5CH{=}CH\overset{}{\underset{\underset{O}{\|}}{C}}C_6H_5} \longrightarrow$$

$$\underset{\text{II}}{C_6H_5CH{=}CH\underset{\underset{OH}{|}}{C}(C_6H_5)_2} \rightarrow \underset{\text{III}}{C_6H_5CH{=}CH\underset{\underset{Cl}{|}}{C}(C_6H_5)_2}$$

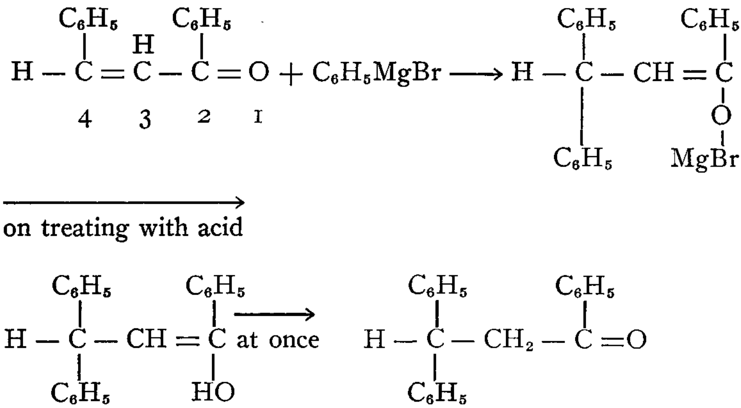
A comparison of the last formula written (III) with that of triphenylmethyl chloride, $(C_6H_5)_3CCl$, makes evident the analogy Kohler had in mind. Would the group $C_6H_5CH{=}CH{-}$ in combination with only *two* phenyl groups confer the peculiar properties on the halide which Gomberg had reported? Kohler thought the unsaturated linkage $CH{=}CH{-}$ would be roughly the equivalent of the phenyl group, and subsequent work several decades later proved his intuition to have been correct. But Kohler was not to explore these possibilities; for it soon developed that the reaction he had envisaged proceeded quite differently from what had been confidently predicted. The interaction of phenyl magnesium bromide and benzalacetophenone (I) yielded a compound whose structure was that of a saturated ketone (IV below) not the unsaturated carbonyl (II).

$$\underset{\text{IV}}{(C_6H_5)_2CH{-}CH_2COC_6H_5}$$

Why had things taken this unpredicted course? This was the type of question Kohler loved and illustrates the kind of chemical research to which he devoted almost all his labors. There were really two questions: (1) By what steps had the transformation taken place, *i.e.*, what was the mechanism of the reaction? (2) What were the peculiarities of the structure of benzalacetophenone (I) that resulted in the Grignard reagent apparently uniting with the ethylenic linkage ($C{=}C$) rather than the carbonyl group (C=O)? After Kohler had become convinced of the true structure of his product, he saw that the reaction he had been studying was similar to those made famous by the German chemist Thiele at just about this time. Thiele had directed attention to the anomalous behavior of certain compounds containing ethylenic linkages in alternation (christened by him "conjugated linkages") and elaborated a theory of "partial valence" to account for the fact that addition reactions of such systems could proceed as follows:

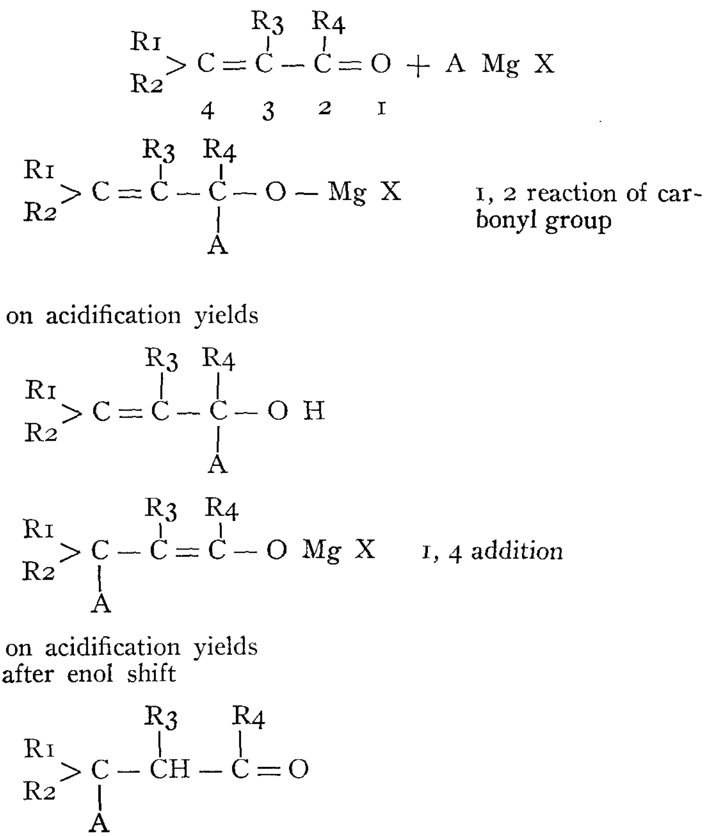


As to the theory, Kohler was indifferent; but to the significance of the fact of 1,4 addition, he was very much alive. He proceeded to demonstrate to the satisfaction of most critics that the first step in the reaction between phenyl magnesium bromide and benzalacetophenone was an example of 1,4 addition to a conjugated system followed by the shift of an enolic hydrogen atom after the reaction mixture was acidified. The mechanism was thus:



Unstable enol Final Product

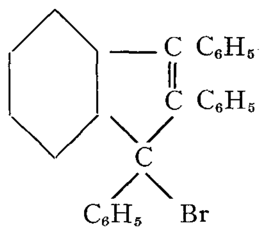
The nature of his evidence for the structure of the first product was not all that might be desired and he later returned to the subject reinforcing his earlier argument. But what was more significant at the time (1907) was his study of the interaction of two Grignard reagents with a variety of unsaturated ketones and aldehydes. This investigation which has remained a classic in the field showed that while a conjugated system *may* combine with an addendum by 1,4 addition, the single carbonyl group may also react in the more usual fashion. There were clearly two competitive reactions involved which in general terms may be indicated as follows:



If $R_1=C_6H_5$, R_2, R_3, $R_4=H$ and A is either C_6H_5 or C_2H_5, no 1,4 addition takes place; if $R_1=C_6H_5$ and R_4 is either C_6H_5,

$CH(CH_3)_2$ or $C(CH_3)_3$, 1,4 addition predominates if A is either C_6H_5 or C_2H_5 and is appreciably less in the first case than the second. In short, Kohler demonstrated that the way a conjugated system may react depends both on the substituents and the character of the addendum. All the work in this field which has been done since 1907, it is fair to say, has added relatively little to these principles.

Kohler returned from time to time to a study of conjugated systems always employing the same technique of using phenyl groups or substituted phenyl groups to insure the desired physical characteristics of the compounds. In a series of papers in the 1930's he amplified the data on the effect of substituents on the mode of addition of unsaturated ketones. It is interesting and significant that he did not pursue his original intention of studying the interaction of unsaturated halides and metals except for one observation. In a paper published in 1908 he showed that a combination of phenyl groups and unsaturation in a ring system conferred upon an adjacent carbon-halogen bond some of the properties characteristic of triphenylmethyl chloride. For on treating 1,2,3, triphenylindyl bromide (V) with metals he obtained a solution



V

which showed all the properties characteristic of that of a free radical. The point he set out to test when he started on the abortive synthesis of the unsaturated carbinol (II) might be considered to have been settled. Yet clearly there was a great deal more work to do if one were to determine what other group could be substituted for the phenyl groups of triphenylmethyl. Indeed in 1908 it was far from clear that triphenylmethyl was the dissociation product of an "orthodox" crystalline material hexaphenylethane. Other chemists took up the lead given them by Gomberg's highly significant publication. But Kohler often said when discussing the history of this subject that he had no desire to rush into another man's territory and exploit someone else's discovery.

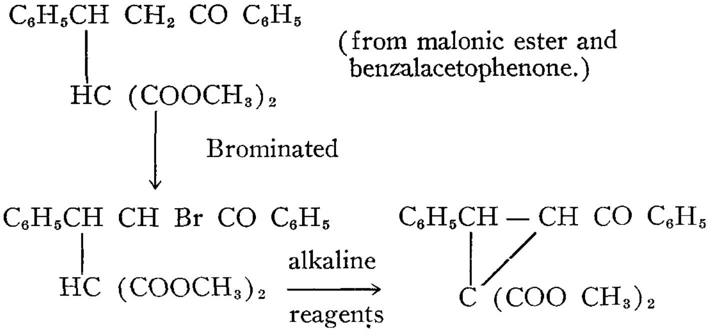
At all events, in the second decade of the nineteenth century Kohler turned his attention to the three carbon system characteristic of glutaconic acid of which the formula is:

$$H\ O\ O\ C\ CH_2\ CH = CH\ C\ O\ O\ H$$

The unsymmetrical derivatives of this acid can exist in several isomeric forms depending on the structural and stereochemical relations of the substituents to the double bond. In the last forty years all the phenomena have been adequately accounted for without postulating any special type of linkage. But in the period 1910-1920, there was discussion of the possibility that the system—$CH_2 - CH = CH$—should be formulated—$CH -$
[H]
$CH - CH$ to indicate the lability of the hydrogen atom, as some investigators were then inclined when discussing the behavior of acetoacetic ester. Kohler felt that labile isomers could be studied only if crystalline solids were at hand. Therefore, he undertook to prepare compounds of the following type:

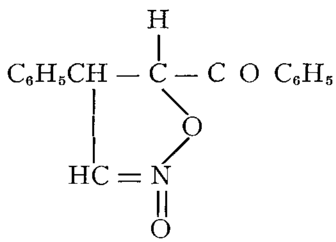
$$\begin{array}{l} C_6H_5\ C = CH\ CO\ C_6H_5 \\ \quad\quad\ \ | \\ \quad\quad\ CH_2\ C\ O\ O\ H \end{array}$$

He started with malonic ester and his old friend benzalacetophenone. But once again the vagaries of organic reactions led him into an unsuspected field. The desired unsaturated keto acid was not obtained; instead a convenient method of preparing keto-cyclopropanes was discovered. The steps in the transformation were shown to be as follows:



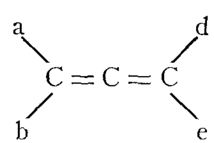
Having been thus brought to the study of the simplest of alicyclic systems, Kohler and his graduate students at Harvard devoted considerable attention to the reactions of substituted cyclopropanes. They showed that the labile ring in keto cyclopropane acids could open in several ways, and the reactions were to some degree reminiscent of alpha beta unsaturated ketones.

Nitro compounds had long been a matter of interest to Kohler; therefore, it was not surprising that he should seek to discover the behavior of nitrocyclopropanes which he showed could be readily prepared by a series of reactions similar to those indicated above if nitromethane were substituted for malonic ester. But there was also formed in the course of these reactions a type of compound known as isoxazoline oxides of which the following formula may serve as an example:



Here was a convenient road into a new and fascinating type of unsaturated compound. By the use of appropriate aryl groups crystalline products could be obtained (at least by Kohler though the technical difficulties were often great). A study of the behavior of compounds containing the $-C=\overset{|}{N}=O$ system led into a consideration of other unsaturated nitrogen compounds. Then followed papers on pseudo bases, cyclic nitrones as well as further studies on isoxazoline oxides.

From first to last Kohler was interested in theoretical organic chemistry. With all the developments in this wide field he was in close touch and as the preceding paragraphs attempt to show, he made significant contributions to the study of the mechanism of a wide variety of reactions. He had little interest in the classic examples of the elucidation of the structure of complex plant and animal compounds. In his course he devoted little or no time to those investigations of the alkaloids, the terpenes, the natural dyes and the polypeptides which were generally accounted among the triumphs of nineteenth century organic chemistry. Sugar chemistry was another story: this he expounded with elegance and enthusiasm, probably both because it illustrates so well the principles of stereochemistry and also because of the obvious connection with medicine and biology. In the last years of his work he made one of his most striking contributions by his resolution of an allenic compound into the optical isomers (with J. T. Walker and M. Tishler 1935). By so doing he brought further experimental evidence to show that the phenomenon of optical activity is connected with an asymetric *molecule*. Stereochemical models of allenic compounds of the following type show that two mirror images are possible; this had been well known as a theoretical possibility but it remained for Kohler and his students to prepare a compound with such groups as permitted resolution by the usual methods of stereochemistry.



Allenic Compound having two optically active isomers

One may conclude this memoir by a word as to Kohler's role in World War I. He was brought to Washington as one of the two top civilian advisers to those in charge of the research work of the Chemical Warfare Service. The area assigned to him was offense, while his opposite number, Professor W. K. Lewis of the Massachusetts Institute of Technology, was responsible for the defensive work. In this one and only excursion into administrative work away from the academic scene, Kohler showed his wisdom about human problems as well as his insight into scientific matters. Though the term of service was short, all who came in contact with him were deeply impressed by the effectiveness of his labors. In the subsequent years there were many occasions when his assistance would have been gladly welcomed by those concerned with what might be called the public aspects of science. But Kohler was not interested. He would leave his laboratory though reluctantly, to perform a patriotic duty in a World War. But no less an emergency could justify his parting from his beloved compounds and their vagaries.

Kohler was elected to the National Academy of Sciences (Section of Chemistry) in 1920. His place in the history of American chemistry is assured by his publications and above all by his influence on his students. To all who had the rare privilege of working closely with him, his unique personality will remain one of the compelling forces in their lives.

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