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BIOGRAPHICAL MEMOIR

OF

PHOEBUS AARON THEODOR  
LEVENE

1869-1940

BY

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and

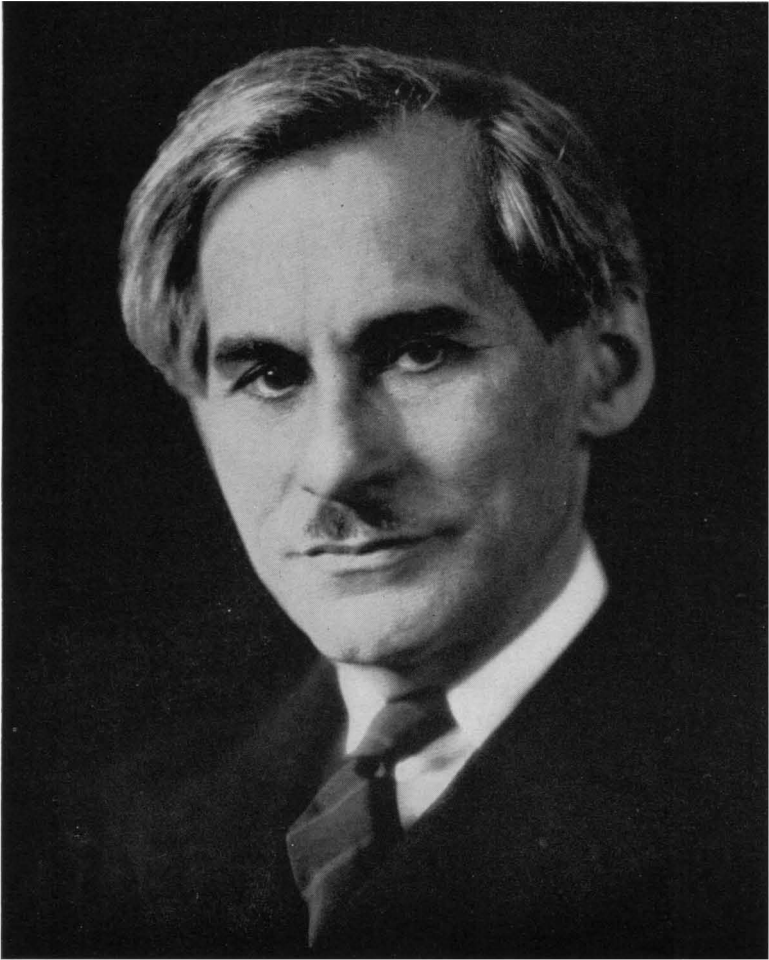
WALTER A. JACOBS

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*P. A. Leneve.*

## PHOEBUS AARON THEODOR LEVENE

1869-1940

BY DONALD D. VAN SLYKE AND WALTER A. JACOBS

Phoebus Aaron Theodor Levene, or Fedya, as he was known to his intimates, was the second of the eight children of Solom and Etta (Brick) Levene. He was born on the twenty-fifth of February, 1869, at Sagor in Russia, and when he was about two years of age his family moved to St. Petersburg, now called Leningrad. He obtained his later schooling at the Classical Gymnasium in St. Petersburg, and finally specialized in medicine at the Imperial Military Medical Academy in that city. He was one of only a few Jewish students who were allowed to enter his class. During his studies there, he was fortunate to have come under the influence of stimulating teachers, and it is of particular interest that among these were Alexander Borodin, the professor of chemistry, but of course now better known as the composer, and Ivan Pavlov, who was at the time a privat dozent in physiology. He studied organic chemistry under Borodin's son-in-law, Professor Alexander Dianin, who was so impressed by the young student that he allowed him the freedom of his laboratory. Here Levene began a first research in organic chemistry on a subject of interest to Dianin, which dealt with the condensation of aldehydes and ketones with phenols. Although he obtained his general training in medicine, it was doubtless during this early period that a strong interest in biochemistry had been awakened. About this time, in 1891, his family, because of growing anti-Semitism in Russia and in order to find broader opportunities and a fuller life, made the decision to migrate to America, and the young Levene accompanied them on the journey. They arrived on July 4, 1891. However, having seen to it that they were safely settled in New York, he returned to St. Petersburg to finish his interrupted studies. But this was temporary for, having once completed his examinations for the medical degree in the autumn of the same year, he decided to try his own fortunes in the New World and thereupon

rejoined his family in New York, which he reached in March 1892. Not long after, he took his examinations for the practice of medicine in New York, and practiced on the lower East Side until 1896. But he was already convinced of the preëminence of his other leanings, and the fortunate decision was made to turn away from the actual practice of medicine as a permanent career as soon as this became possible. While a practitioner, he continued to take time out for further work in physiological chemistry in the laboratory of Prof. John G. Curtis, in the department of physiology of the College of Physicians and Surgeons of Columbia University, which was at that time located on West 59th Street, New York. He had simultaneously enrolled as a special student in the Columbia School of Mines, and absorbed there whatever he felt essential to round out his chemical training. He continued this arrangement for several years, and in an intervening summer recrossed the ocean to spend a short period in the laboratory of E. Drechsel at Berne. In 1896, he received his first appointment as Associate in Physiological Chemistry in the laboratory of the Pathological Institute of the New York State Hospitals, which was housed at the time in the old Metropolitan Life Building, and which was under the direction of Dr. Ira van Gieson. It was while here that an interest was awakened in the subject of the nucleins and nucleic acids which was to become one of his masterpieces.

This earlier period of his work, however, received an abrupt interruption, for in November of the same year he was stricken with tuberculosis. This necessitated a period of rest for about two years. The first of these was spent at Saranac Lake, during which time he gradually regained his health under the care of Dr. E. R. Baldwin. He was well received by the medical fraternity of Saranac Lake, and Levene's charming friendliness and brilliant mind attracted Dr. Trudeau and his associates. The foundations of enduring friendships were then laid which subsequently took Levene on periodic returns, often on vacations, to Saranac Lake, or brought Trudeau and several of his colleagues on visits to him in his laboratory when they came to New York. And in later years it was on one of these trips to Saranac Lake that he found a very great happiness. For in

the fall of 1919, he met Anna M. Erickson, of Lewistown, Montana, who in the following June became his wife.

After his year of rest at Saranac Lake, a succeeding period of cure at Davos, Switzerland, was needed to assure his return to health. Although he was still far from strong, he wished again to pick up the lost threads of his scientific pursuits, and returned to New York. Levene resumed his place at the New York State Pathological Institute, which Dr. van Gieson had held open for him. But not long after, this was interrupted by the closing of the laboratory, pending its reorganization. He then spent a brief period as a visiting worker at Marburg in the laboratory of Kossel, at that time the authority, among other things, on nucleins and nucleic acids. He also enrolled as a visiting student in the electrochemical laboratory of H. Hofer in Munich. Subsequently, at the invitation of Dr. Trudeau, its director, he was induced to accept an appointment as chemist in the Saranac Laboratory for the Study of Tuberculosis. He remained here for the two years from 1900 to 1902, pursuing active research and cementing friendships already begun. His interests by this time had become sharply attracted to proteins and amino acids, and an intervening summer was very profitably spent at the University of Berlin with Emil Fischer. Following a study there on the hydrolysis of gelatine, he returned to New York to resume work in the chemical laboratory of the Pathological Institute of the New York State Hospitals, which had since reopened on Welfare Island (then called Blackwell's Island), and was now under the direction of Dr. Adolf Meyer. He again took up lost threads, and productive laboratory work was continued, accompanied by many contributions to the journals.

It was at this time that the great turning point in Levene's career occurred, and one which proved so fortunate not only for Levene himself, but for American biochemistry. It had come to be realized that research in the laboratory, at least in certain directions in the medical and biological sciences, might find a broader opportunity if given the proper facilities and environment, unhampered by the distractions which can come from administrative or formal didactic routines, not to mention

extramural activities. The Rockefeller Institute for Medical Research was founded at about this time, and Dr. Simon Flexner and his advisers, who planned its organization and scope, realized at the start the importance of biochemistry, and that this discipline would have to share in the activities of the new institution. In seeking for a biological chemist to head its biochemical laboratory, Dr. Flexner had become impressed by the record already made by Levene and by his apparent mastery and appreciation of fundamental biochemical problems, the study of which would fit in with the purposes of such a research institution. He therefore invited the 35-year-old biochemist to join the newly formed organization as an assistant on its scientific staff, an appointment which took effect on January 14th, 1905. This proved to be most fortunate for all concerned. From that time began an association which lasted until his death. From necessarily small beginnings, his opportunities and facilities for work grew with the passing years. When he joined the Institute, its laboratories occupied for a short period temporary quarters consisting of two private dwellings on Lexington Avenue and 50th Street, which had been thrown into one. In the meantime, a new laboratory building was under construction at 66th Street and the East River. In spite of the physical limitations of the temporary laboratory which Levene was given, with only a servant as helper, he threw himself wholeheartedly into the work, and at once initiated the long list of his own share of contributions "From the Laboratories of The Rockefeller Institute for Medical Research," which continued until his death. The success of his activities and the appreciation of his knowledge and experimental genius were so immediate that in the spring of 1907 Levene was made a Member of the Institute, in charge of its Division of Chemistry. Already the recognition which he had achieved was given evidence by the fact that he was among those asked to lecture before the Harvey Society during the very first year of its organization in 1905. The subject of his address was autolysis, and his authoritative treatment of the subject gave immediate evidence of mastery of the historical, as well as factual and theoretical side of biochemistry. During the season of 1905-1906, he was invited also to give the Herter

Lectures in pathological chemistry at the New York University and Bellevue Medical College. He had become a pioneer in biochemical research in its fundamental aspects in this country, as well as a leader of younger men.

On the completion of the new laboratory building in 1906, Levene moved into well-equipped chemical laboratories on its second floor and began work with a few assistants. He continued there until 1918. By this time, the increasing demand of the general Institute activities had made its further physical expansion necessary, and a new laboratory building, the so-called Middle Building of the Institute, was planned which, along with other activities, was to include the Division of Chemistry. In the planning of the new chemical laboratories, Levene was naturally given full opportunity to adapt the benefits of modern improvements in laboratory construction and equipment to the changing requirements of his newer and ever-expanding researches. This was a commission which he undertook with special elation and enthusiasm. Apart from the arrangements in the various laboratories and in the room which was to be his own private workshop, he felt it to be almost as great a responsibility, and found as much personal satisfaction, in the planning of his private office. This became more in the nature of an office library, and no little thought was expended in the selection of its furnishings. This gave opportunity for the expression of the artistic temperament of the man. We remember so well how much experimentation was required for the achievement of the proper shade or tint for the walls and the woodwork. And then in turn these walls and the bookcases were covered, not only with photographs of many of his former assistants, scientific colleagues, and friends, but with reproductions of works of art.

Levene possessed to an unusually great degree this appreciation for art. He took delight in the attempt to analyze not only the technique, but the thought and intent behind the work of the artist. It was undoubtedly from the study of art that he obtained his greatest avocational satisfaction. Because of this, his counsel was frequently sought by those around him in matters

requiring artistic discrimination. In his earlier years, especially when he returned to Europe for so-called vacation periods to work with such leaders as Drechsel, Kossel, and Fischer, he was especially attracted to the work of the Renaissance Schools. He acquired a collection of the works of the older masters in the form of prints or reproductions. In the spring of 1909, following an especially active winter, he sought needed relaxation by a trip to Spain. He came away from there with a new interest in the work of the Spanish schools. He read widely on art and artists, and constantly visited exhibitions of contemporaneous work. His leaning toward the new modes was much in evidence. About 1913, the work of the cubists, which was followed later by the ultramoderns, attracted his attention. The walls of the living room of the Levenes' home and the tops of low bookcases against them were always covered with carefully selected paintings, prints, and other objects of art. The writers recall so well how years ago, when received in an earlier Levene home in West 139th Street, New York, they found themselves in a room where there was but scant wall space between the framed prints of the old masters. In all of this, a great enthusiasm was in evidence, and it was apparent that it was not to be satisfied with half measures, and did not brook restraint. This discriminating taste, along with the gracious kindness of its hosts, has always made the Levene home a scene of cordial social gatherings to which many scientists, artists, and literary people enjoyed to come.

During his very early professional years, Levene began the accumulation of an exceptional personal library. Although this naturally contained much on art and general literature, the largest portion consisted of scientific books and periodicals which steadily increased with the years. The bound volumes numbered so many that they filled his library at home, shelved from floor to ceiling. In fact, the overflow was such that the shelves stretched into the halls and other rooms. This possession was one of his greatest loves and, of course, a tremendous asset in his work. He was a tireless worker and, although long hours were spent in the laboratory, much was accomplished in the way of



reading, study, or writing at home. This was done at a small desk table in his library, under the light of a floor lamp at its side. On this desk there usually rested an open book with a pad and pencil alongside.

Levene's personal appearance suggested at once the professional man, student, and artist. He was slight of build but wiry, and of dark complexion with deep-set, dark brown, and very frank eyes. In his earlier years his hair was also dark but, as he grew older, it gradually turned to a light grey and he wore it cut rather long. A small mustache and rather heavy eyebrows completed the picture. His clothes, selected with taste and discrimination, conveyed the impression of a well but by no means overdressed man. At his work, he preferred a short, white laboratory coat which reached to his hips.

Because of his brilliant mind, wide reading, and general grasp of problems, many workers, both younger and older, were attracted to him for counsel in professional matters. But also because of his experience, good judgment, and human understanding, they came to him often for advice in regard to their own personal problems. Always of genial and kindly demeanor and with a friendly smile, he listened with an earnest and sympathetic understanding. He was generous, and this generosity reached beyond the demarcations of family ties so that not infrequently there were those who took advantage of an unusually liberal spirit.

Levene was an accomplished linguist. He read voraciously the masters of European literature in their own languages. In addition to his original Russian and the English which he had early mastered, he spoke French and German fluently, and possessed some familiarity with Spanish and Italian. He never lost his Russian accent; although it diminished somewhat with the years, in moments of excitement, such as would come during earnest discussion, it was again more in evidence. His mastery of other tongues served him well in his intercourse with the many foreign visitors who sought him, both in his laboratory and at home. And he was able to guide in their own languages the many foreign students who worked in his laboratory.

Levene was a great teacher, and his mastery of problems as well as of methods for their attack was unusual. He had a very clear way of formulating them. His earnestness, enthusiasm, and courage proved stimulating to his younger co-workers, and he was the obvious master. Although he was very much in his own laboratory or at his desk, a portion of practically every day was devoted to conferences with these younger associates. As a rule, he came to their rooms and engaged in frequent discussions of the problems with them, although in later years such conferences were often held in his office. These discussions were usually long and earnest, and from them new ideas and new points of view emerged which became the starting point of new programs of work. The familiar picture was to see Levene with pencil and paper, poring over problems with the younger man in excited, earnest discussion, and often with a set of molecular models beside them or being manipulated for clearer visualization of some stereochemical question:

When one entered the laboratory where Levene himself was at work, what caught the eye immediately was this small figure of a man surrounded by large pieces of apparatus. There were always a number of operations going on simultaneously and his own and an adjoining room were constantly the scene of active work in which he, the expert manipulator and experimentalist, remained at the controls. Although he naturally had devoted technicians constantly at his side or within call, a great deal was carried on with his own hands, and it was a frequent picture to see this small man shaking a large flask, or pouring from a large precipitation jar into a large Buchner funnel. In the older days when he was preparing the nucleic acids himself from animal tissues, or during his early work in protein chemistry, picric acid was a favorite reagent. Its yellow color was much in evidence throughout the laboratory, and his hands and coat were usually stained with it. He delighted to work himself and felt keenly the desire and responsibility of retaining the "feel" of the operations. Such active laboratory work continued until the very time of his death.

As a rule, especially in later years, Levene spent his lunch period at the desk in his private office where, while mechanically sipping a cup of tea with a light lunch, he read, studied, or wrote. This was followed by a short period of relaxation on a couch, and then he was back in his laboratory, as active as ever. In his work, he was always the enthusiast, and from it he obtained a great personal satisfaction. A restless, untiring energy unconsciously carried him on. A striking quality and one which impressed many who followed him from his earlier days was his unusual capacity to keep pace with, to learn, and to absorb the new as regarded not only the factual side but also the theory and the methodology of his science, and to apply such information to the specific problems which his own fertile imagination formulated. He appeared at home in an ever-changing horizon.

Just as such qualities governed his scientific activities, they similarly determined his avocational pursuits. His moments of relaxation away from his science were occupied with interests which gave him a satisfaction approaching that obtained in his chemical work. Of art we have already spoken. In his later years, he became very much interested in the history of chemistry and read widely on chemists of the past and their influence on the development of the science. Since he was a born student, he always sought to perfect the machinery of his mind by studying other disciplines, such as physics and mathematics. One of his regrets, perhaps, was that he was not a real mathematician, for he began to experience the increasing need for the mathematical analysis and development of certain aspects of the problems in stereochemistry and the Walden rearrangement, which occupied much of the later years of his researches.

Any attempt to present in brief form an adequate picture of Levene's scientific work is made difficult by the fact that his interests grew to include in succession topics of such variety and were so extensive in scope that to cover them would require a long and detailed account. In the span of his scientific activity, which stretched from the work reported in his first paper of 1894 to that to be found in the group of posthumous

papers of 1941, over 700 papers were published. The great majority were original reports of experimental work. Only a minor fraction of the long list consisted of reviews, general articles, and lectures. These he did extremely well, but he seldom took time for them unless pressed to do so. The array of titles, which fall into a number of categories, bears witness at once to the versatility of mind and interests and the tireless energy which made such work in the laboratory possible. The authorship was shared with a long list of younger collaborators who, in the course of years, came to his laboratory for training and stimulation under his guidance. Many of these subsequently gained individual distinction, which they attribute in no small measure to the inspiration they received from him.

Levene appeared on the scene when certain basic problems in biochemistry had come to the fore and were inviting attack. Already the classical researches of Fischer had established the fundamentals of carbohydrate and purine chemistry and had reached the earlier stages of his amino acid and peptide studies. The essential ground work had been laid which could be extended to the investigation of many biochemical problems. Levene was quick to take full advantage of such an opportunity and in succession mastered each of these fields. As we have already related, his original training was in the medical sciences; but he then became a biochemist and, in later years, an accomplished organic chemist who made profitable use also of physical chemistry.

The subjects of Levene's many contributions, while exhibiting, as we have said, an unusually wide range of topics and interests, can nevertheless be grouped according to definitely coherent trends, purposes, and fields. The subjects cover phases of the chemistry of vital mechanisms, and especially the chemical structure and nature of tissue constituents. A list of the fields might be as follows, with no real attempt at a chronological arrangement, since much was simultaneously carried on: autolysis and enzymes; proteins and amino acids; conjugated proteins, such as nucleoproteins and glycoproteins in which, in turn, their prosthetic groups, the nucleic acids and amino sugars or hexo-

samines, became central points of interest. Both the nucleic acids and the hexosamines or conjugated hexosamines required in turn the solution of many problems in sugar chemistry, such as the determination of the ring structures and places of substitution of the sugars and carbohydrate derivatives. The problem of the structure and stereochemistry of the hexosamines especially caused him to undertake extensive investigations into the nature and circumstances of the Walden rearrangement and of the stereochemical configurations of a large number of interrelated synthetic substances. Interspersed in this work was the study of phospho sugars, of phospho hydroxyamino acids, of the sole validity of the peptide chain theory of protein structure as against the possibility of the occurrence of diacipiperazines in the protein make-up. His isolation in 1906 of prolyglycine anhydride among the products of the prolonged tryptic digestion of gelatine was a challenge to the peptide chain theory, which was finally explained only by later work. Systematic and very productive studies in the difficult and laborious field of the lipoids were also carried on under his guidance, or with his own hands. An investigation on the concentration and isolation of the vitamin B complex was also given attention in his laboratory and finally, during the last few years of his life, the chemistry of the gums and pectins attracted his interest.

Levene was a member of many scientific societies, in a number of which election to membership signifies scientific eminence. Other honors came to him, among which was the award of the Willard Gibbs Medal of the Chicago Section of the American Chemical Society in 1931, and of the William H. Nichols Medal of its New York Section in 1938.

Levene presents the picture of an investigator who found a great happiness in the solution of biochemistry's riddles. His constant success was the reason for an innate optimism and a never-diminishing driving force during his lifetime, which developed into a scientific philosophy. This philosophy can be well discerned in the closing paragraphs of his address on "The Revolt of the Biochemists," delivered on the occasion of the

Willard Gibbs Award, in which he refers to the biochemistry of the future:

“Granting that the problem of the directive force (of living matter) will be solved, it may also be granted that the entire mystery of life will not be solved by this achievement. Chemistry, however, is already preparing a new attack. A more essential characteristic of living matter than the directive force of individual chemical reactions is the power to coordinate all chemical reactions in such a way that the organism may function as a whole for the purpose of maintaining its normal equilibrium and for the purpose of growth and reproduction. This may be regarded as the integrating force of the living organism. The discoveries of the last decade alone furnish proof of the simplicity of the agents acting towards this end. Think of all the hormones and vitamins! Only those which as yet have not been isolated may be thought of as complex and mysterious. Those obtained in pure state are most generally found to be much simpler in chemical structure than many of the ordinary tissue components and definitely simpler than certain common drugs. In fact, many of them are nothing more than degradation products of common tissue constituents. Thus, it seems that in the living organism the very wear and tear of the living matter makes for its restitution and for its preservation. A decade is only an infinitesimal interval in the life of mankind and without hesitation or doubt, one may predict that the nature of all hormones and vitamins and other biologically important integrating substances will eventually be discovered.

“Thus, step by step, one mystery of life after another is being revealed. Whether the human mind will ever attain complete and absolute knowledge of and complete mastery of life is not essential. It is certain, however, that the revolt of the biochemist against the idea of a restriction to human curiosity will continue. Biochemistry will continue to function as if all knowledge, even that of life, were accessible to human understanding. The past has taught that the solution of one problem always opens up a new one. New discoveries in physics, in mathematics, in theoretical chemistry furnish new tools to biochemistry, new tools for the solution of old problems and for the creation of new ones. So long as Life continues, the human mind will create mysteries and biochemistry will play a part in their solution.”

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KEY TO ABBREVIATIONS

- Am. J. Physiol. = American Journal of Physiology.  
Am. Med. = American Medicine.  
Ann. Inst. Pasteur = Annales de l'Institut Pasteur.  
Arch. Neurol. and Psychopath. = Archives of Neurology and Psychopathology.  
Ber. chem. Ges. = Berichte der Deutschen chemischen Gesellschaft.  
Biochem. Z. = Biochemische Zeitschrift.  
Bull. U. S. Fish Com. = Bulletin, United States Fish Commission.  
Centr. Physiol. = Zentralblatt für Physiologie.  
Chem. and Ind. = Chemistry and Industry.  
Chem. Rev. = Chemical Review.  
Chem. Weekbl. = Chemisch Weekblad.  
Contrib. Biol. Lab. U. S. Fish Com. = Contributions, Biological Laboratory, United States Fish Commission.  
Ergebn. Physiol. = Ergebnisse der Physiologie biologischen Chemie und experimentellen Pharmakologie.  
J. Am. Chem. Soc. = Journal, American Chemical Society.  
J. Am. Med. Assn. = Journal, American Medical Association.  
J. Biol. Chem. = Journal of Biological Chemistry.  
J. Chem. Physics = Journal of Chemical Physics.  
J. Exp. Med. = Journal of Experimental Medicine.  
J. Gen. Physiol. = Journal of General Physiology.  
J. Immunol. = Journal of Immunology.  
J. Ind. and Eng. Chem. = Journal of Industrial and Engineering Chemistry.  
J. Med. Res. = Journal of Medical Research.  
J. Mt. Sinai Hosp. = Journal, Mt. Sinai Hospital.  
J. Org. Chem. = Journal of Organic Chemistry.  
J. Pharmacol. and Exp. Therap. = Journal of Pharmacology and Experimental Therapeutics.  
J. Physic. Chem. = Journal of Physical Chemistry.  
J. Physiol. = Journal of Physiology.  
Med. Klin. = Medizinische Klinik.  
Med. News = Medical News.  
Med. Rec. = Medical Record.  
N. Y. State Hosp. Bull. = New York State Hospital Bulletin.  
Proc. Nat. Acad. Sci. = Proceedings, National Academy of Sciences.  
Proc. N. Y. Path. Soc. = Proceedings, New York Pathological Society.

Proc. Soc. Exp. Biol. and Med. = Proceedings, Society for Experimental Biology and Medicine.

Z. physiol. Chem. = Zeitschrift für physiologische Chemie.

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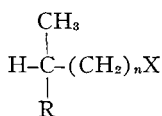
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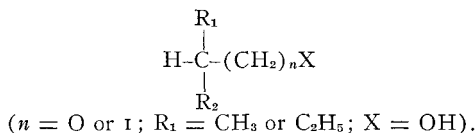
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