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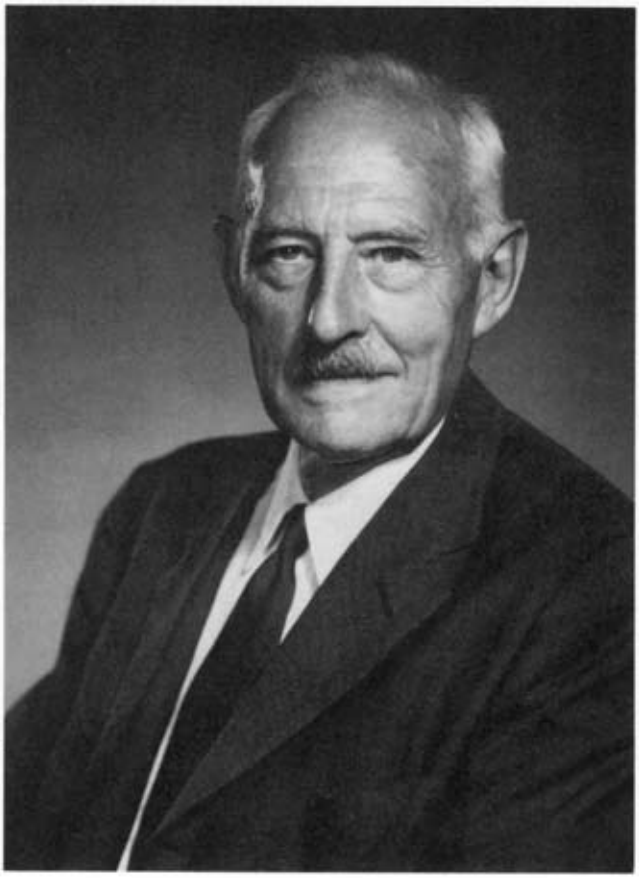
HANS THACHER CLARKE

1887—1972

A Biographical Memoir by
HUBERT BRADFORD VICKERY

Biographical Memoir



Hans T. Clarke

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BY HUBERT BRADFORD VICKERY

DURING THE third and fourth decades of the present century, the discipline long known as physiological chemistry underwent extensive transformation into a discipline more properly referred to as biological chemistry—the chemistry of living tissue. This transformation came about, at least in part, as a result of the recognition by the university authorities concerned with appointments of department heads, of the fact that progress in the science was most likely to occur if persons trained fundamentally as pure chemists—either organic or physical—were to take over the direction of the departments. Outstanding among the many such appointments of the period was that of Hans Thacher Clarke, in 1928, as head of the Department of Biological Chemistry at the College of Physicians and Surgeons of Columbia University. With a background of some fourteen years of industrial research at Eastman Kodak Company on the large-scale production of developers, dyes, and, after the war, of a wide assortment of organic substances previously imported from Germany, he brought to Columbia a vast and detailed knowledge of the organic chemical literature and an unexcelled personal skill and resourcefulness in organic synthesis. Within a few years he had assembled one of the strongest faculties in this country, and his department promptly attracted students and visitors of the highest qualifications.

Today, his graduates are among the leaders of American biochemistry.

Hans Thacher Clarke was born of an American father and a German mother on December 27, 1887, in Harrow, England. His father, Joseph Thacher Clarke (1856–1920), son of a Boston, Massachusetts, physician who died when the son was twelve, was educated in Germany and became an archeologist who, with another young man, excavated Assos, an ancient city near the site of Troy, and subsequently prepared the lavishly illustrated final reports for the Archeological Institute of America.* His interest in photography led him to design and produce a magazine camera, the "Frena," which in turn brought him to the attention of George Eastman. They met in 1886, became close personal friends, and shortly afterwards Clarke was appointed to be the European representative of Eastman affairs, a position in which his knowledge of European languages, of art, and, incidentally, of music, for he was a competent cellist, eminently fitted him. This relationship led quite naturally to the appointment of Hans Clarke, his son, who had become a highly trained organic chemist, when, at the outbreak of the war in 1914, it became necessary for the Eastman Kodak Company to undertake the manufacture of the photographic chemicals that previously had been imported from Germany.

Hans Clarke's mother was Agnes von Helferich (1858–1935), the daughter of Hans von Helferich, Professor of Political Economy at the University of Munich. A cousin, B. Helferich, was Emil Fischer's private assistant during the period in 1912 and 1913 when Clarke worked in Fischer's Laboratory.

There seems to be little information in family records about Clarke's grandfather, Luther Whipple Clarke (1825–1868), save that he was born in Marietta, Ohio, and practiced medicine in

* Joseph T. Clarke, Francis H. Bacon, and Robert Koldewey, *Expedition of the Archaeological Institute of America: Investigations at Assos* (London: Barnard Quaritich, Henry Sotheran and Co., 1902).

Boston from about 1850. His wife was Mary Gray Thacher (1823–1875), the daughter of a well-known Boston merchant who could trace her ancestry back through a long line of New Englanders to John Howland and others who came over in the *Mayflower*. Her direct ancester was Antony Thacher, a clergyman. He and his wife were the only survivors of a ship that was wrecked in 1635 on what became known as Thacher Island near Gloucester. They were traveling from Newbury to Marblehead, Massachusetts, to take up Thacher's duties as minister of the church there.

Hans Clarke was the second child in a family of two boys and two girls. He has recorded that he "was exposed from early childhood to intellectual and musical stimuli. Independent reading in an extensive and catholic parental library was encouraged, and [I] took part in family string quartets from the age of eight." He attended the University College School in London from 1896 to 1905, where he "preferred subjects (such as algebra) which had a scientific flavor and, in the last two years definitely recognized chemistry as a major interest." He especially disliked Latin grammar, but enjoyed modern languages that were imaginatively taught. His home occupations, "apart from music and general reading, were mainly manual (carpentry and metal work). Practical chemistry and glassblowing were encouraged, and facilities for them were provided in the home."

In 1905 Clarke entered University College, London, where he concentrated on the study of chemistry under Sir William Ramsey, J. N. Collie, and Samuel Smiles. A minor field of study was physiology, under E. H. Starling. It was in this period that he was first exposed to physiological chemistry, for he took a course given by R. H. Aders Plimmer that involved the isolation of a few crystalline proteins, carbohydrates, and amino acids as well as lecithin and kephalin, and also some exercises in urine analysis. He has recorded that "these exer-

cises did not greatly appeal to me; I found them intellectually far less rewarding than the rich fare offered by Collie and Smiles in their courses on organic chemistry."

This is an interesting comment from a man who later became one of the leaders of modern biochemistry in this country. It suggests the reason why he always insisted that his students acquire a fundamental training in organic chemistry before tackling biochemistry itself. It was also in this period that he was active in athletics, playing rugby football and tennis. He was twice heavyweight boxing champion of the school.

After graduation as B.Sc. in 1908, he continued in research with Smiles and A. W. Stewart, while holding a minor teaching position.

In 1911 he was awarded an 1851 Exhibition scholarship and spent three semesters in the laboratory of Emil Fischer in Berlin and one with A. W. Stewart at Queen's College, Belfast. He found that although Fischer visited him almost daily to discuss his work, discussion between the students of their problems was sharply discouraged. He has reported, "This was so contrary to British tradition that I was interested to find out the reason; it appeared that most of the chemists who were working on topics of their own were retained as consultants by one or another of the German manufacturing firms, which had priority on any patentable discoveries made by the individuals concerned. This system appeared to me, as it still does, as being at variance with the prime function of an academic laboratory." On his return from the studies in Germany and in Belfast, he was awarded the D.Sc. degree by the University of London.

Clarke had been occasionally consulted on organic chemical matters by his father's friend George Eastman, and early in the summer of 1914 he was asked by Eastman to come to Rochester to evaluate a newly invented process for the chemical modification of cellulose. Here he found that he was the only organic chemist employed by the company. However, with the out-

break of the war in August and the subsequent impossibility of obtaining chemicals from Germany, he soon became involved in devising methods for the large-scale synthesis of developers and sensitizing dyes. The research laboratory itself was enlarged and in 1918 began the preparation of many substances in short supply in this country. The organic chemicals division of Kodak was thus started. He was also active in contributing methods to *Organic Syntheses* and in checking many methods contributed by others to this publication.

In 1928, at the suggestion of his friend H. D. Dakin, Clarke was invited to become Professor of Biological Chemistry and head of the department in the College of Physicians and Surgeons of Columbia University. The medical school had recently moved to its then new location on West 168th Street, New York, and the department was ill-equipped. Under Clarke's vigorous direction and with the aid of grants from the Chemical Foundation, this situation was soon corrected; the library was greatly enlarged, and a large open laboratory was provided for the graduate students. Clarke always maintained that students who worked in close proximity learned more from each other than from their teachers.

The small but extremely able faculty was promptly enlarged, and the department soon became the home of a long and distinguished list of postgraduate students and visitors, many of whom were German refugees who remained for years, ultimately becoming members of the faculty. Of the ninety-four graduate students who were trained under Clarke's direction, forty-three later attained sufficient eminence to be elected members of one or another of the six societies that form the Federation of American Societies for Experimental Biology; and several are today heads of biochemistry departments or leaders of productive research groups in various institutions throughout the country.

Clarke's first publication, a paper with Smiles on diethoxy-

thioxan, initiated an interest in organic compounds of sulfur that remained throughout his life. Of approximately thirty journal papers in which he described the synthesis of new compounds, no less than eighteen deal with such substances. The year and a half he spent in Fischer's laboratory was devoted to the synthesis of thiazans, which he prepared for the first time, and to the study of the reactivity of analogous compounds that contained nitrogen, oxygen, or sulfur in all of the possible pairs.

The fourteen years at the Kodak research laboratory resulted in few publications in the journal literature, but in this period there were twenty-six descriptions of the preparation of a wide variety of substances published in *Organic Syntheses.* He also acted as one of the checkers of no less than sixty-five preparations submitted by others. A number of other preparations were contributed after the removal to Columbia in 1928. He also served as the editor of two of the annual volumes of this series.

Clarke retained a connection with the Kodak research laboratory for the rest of his life. On leaving Rochester, he was invited to serve as a consultant who would spend two days a month with the organic research group. He resigned from this responsibility only in 1969 when the deterioration of his health made it necessary.

The years at Columbia were happy ones. Clarke has recorded that "my chief activities, listed in the order in which they absorbed my time were: 1) training of graduate students, 2) experimental research, 3) instruction of medical students, 4) administration . . . with the passage of the years, the amount of time available for research with my own hands (I could never work at ease with a technical assistant) continually decreased, finally dwindling to about ten percent." The parenthesis in this statement is especially interesting. Clarke was a master glassblower, and his bench and shelves were littered

with devices for special uses that he had made himself—liquid-liquid extractors, distillation columns, filtering apparatus, and so forth. These items were fragile, and their use was sometimes by no means obvious. Aside from the difficulty of explaining to an assistant what he wanted done, was the danger that the use of this equipment in inexperienced hands might lead to the necessity of a repair job at the blast lamp: thus, his unease.

The problem of the graduate student who applied for admission to Clarke's laboratory was a serious one. The professor refused to pay much attention to college grades, but required a long personal interview in which the applicant's course work, his laboratory experience, and especially his capacity to coordinate such background as he had acquired in college were thoroughly discussed. If the impression made was favorable, the student was admitted, but then was frequently told to go back to college and broaden his acquaintance with organic and physical chemistry at both theoretical and practical levels. He was also directed to take courses in biology, if deficient in this discipline. To many, this was a devastating blow, but there was no alternative. A year later they were welcomed into the courses in biochemistry where they soon found that the additional training had been necessary. When the time arrived for the selection of a research problem, Clarke gave the student a wide choice, especially if he had developed some special interest. There was no attempt to direct him into some field allied to the professor's personal research. Thus, the list of titles of papers with graduate students in his bibliography ranges from studies of fatty acids, of amino acids, and of analytical methods, to a problem having to do with rickets in children and another concerning plasma volume. Nevertheless, a considerable number of students chose to work on amino acids and especially on cystine, the most puzzling amino acid of all. With deliberate pedagogic intent, Clarke took advantage

of the large laboratory, where all of the graduate students worked, to ensure a wide degree of diversification in the themes of departmental research.

Clarke's personal research led to a number of important and useful advances. With the cooperation of a number of graduate students, he established the details of the reduction of cystine by sulfite, studied the form of labile sulfur in proteins, and found conditions under which the whole of the cystine sulfur could be converted into the so-called lead-blackening sulfur, previously a most confusing problem. Perhaps his best-known contribution was his development in 1935 of the structure of the sulfur-containing moiety of R. R. Williams' recently isolated specimen of pure vitamin B. Williams had found that the crystalline vitamin could be decomposed by treatment with sulfite into two substances, one of which he recognized to be a pyrimidine derivative. The other substance was a strong nitrogenous base containing sulfur. He submitted this material to Clarke, who promptly recognized that its stability to alkaline plumbite before treatment with nitric acid and its lability afterwards indicated that it contained a thiazole nucleus. This enabled Williams to write a tentative structure for the vitamin, the details of which were later corrected. Clarke and Gurin next synthesized a thiazole derivative that was identical to Williams' basic substance obtained from the vitamin. In this brilliant accomplishment Clarke made shrewd use of the results of his studies with other students of the properties of cystine.

A further example of his extraordinary resourcefulness in developing the formula of an organic substance containing sulfur was related to the writer by Professor duVigneaud, whose extended studies of biotin had led in 1942 to the accumulation of data that suggested a possible structure. One evening, he laid the data before Clarke and asked what he thought the structure might be. Clarke pondered for a short

while and then wrote a formula that to his mind conformed with the evidence. DuVigneaud then took from his pocket a sheet of paper on which he had written the structure that he had derived. The two formulas were identical in every detail.

In addition to his duties at Columbia and Kodak, Clarke found time for other and extensive professional relationships. In Rochester, he had been chairman of the local section of the American Chemical Society (1921) and was a member of the Editorial Board of *Organic Syntheses* (1921–1932). In 1924–1925 he was chairman of the Division of Organic Chemistry of the American Chemical Society. He was an associate editor of the *Journal of the American Chemical Society* from 1928 to 1938 and on the Editorial Board of the *Journal of Biological Chemistry* from 1937 to 1951. In 1942 he was president of the Harvey Society and was chairman of the New York Section of the American Chemical Society in 1946. He was president of the American Society of Biological Chemists in 1947 and a member of the Biochemical and Nutrition Study Section of the United States Public Health Service from 1948 to 1957. He was also a member of the Committee on Research of the American Philosophical Society during the same period. An important honor was to be appointed Science Attaché at the American Embassy in London in 1951–1952.

A great responsibility was placed upon him in 1944 when he was asked to be Assistant to the Director of OSRD to coordinate the many reports of the then highly confidential research on penicillin. Later he served, together with Sir Robert Robinson and Professor J. R. Johnson as editor of the huge book in which these researches were published by the Princeton University Press in 1949.

Clarke retired from Columbia in 1956 at the mandatory age of 68 and accepted a long-standing invitation from a former student, Professor Joseph Fruton, to come to New Haven to the biochemical laboratory in the Graduate School as a guest

of Yale. Here for nearly eight years, Clarke enjoyed the luxury of full-time research. He was an active participant in seminars, attended occasional lectures, gave a short course of lectures on antibiotics a few times, and was always available to students who were puzzled over some problem in organic chemistry. His glassblowing skill was frequently in demand for the repair or development of apparatus. In 1968 the University required the laboratory space he was occupying for newly appointed members of the department, and Clarke then accepted an invitation from Dr. Sidney Farber to continue his work at the Children's Cancer Research Foundation in Boston. Here he spent the years from 1963 to 1970, when increasing ill health compelled him to discontinue active research. He had been engaged since the Yale days in a study of the action of hypochlorite on sulfanilate with the object of preparing azobenzene-4,4′-disulfochloride, a reagent he had suggested to Professor F. M. Richards as possibly useful for interaction with proteins. This turned out to be by no means a simple problem, and he spent years in isolating and identifying the numerous unexpected by-products that were formed. The outcome was the publication in 1971 of his last paper, which contains registry numbers of more than twenty new compounds isolated or prepared in the course of the investigation.

Clarke was elected to the National Academy of Sciences in 1942 and received the King's Medal for service in 1948. The University of Rochester awarded him an honorary degree in 1953 and Columbia in 1957. He was a skilled editor, who invariably improved the many manuscripts that passed through his hands while serving on the boards of the *Journal of the American Chemical Society* and the *Journal of Biological Chemistry*. His own writing was characterized by clearness, brevity, and grace of statement, qualities that he passed on to many of his students, and by his vast scholarship. He was rarely at a loss, in discussing some organic reaction, to point out significant analogies and other examples.

An important phase of Clarke's life resulted from his purchase in 1929 of about fifty acres of property in Scotland, Connecticut, mostly woodland, but with a charming old house and huge barn and several acres of open fields. Here he brought up his young family of two sons and two daughters to share in the frequently heavy labor involved in damming a brook to form a swimming pool, building a dormitory to accommodate the children when the frequent guests arrived, developing the lawn, mowing the fields, maintaining the buildings, and planting and caring for several acres of conifers on what had been low-grade pasture land. Not only his children, but guests were also soon drawn into these activities, so that a weekend with the Clarkes could sometimes develop into an exhausting experience. Clarke was a large and very strong man skilled with axe, saw, and scythe, and had little patience with the weaknesses of his less well-endowed friends.

No account of Hans Clarke would be complete without mention of his interest in music. That he played in family groups from childhood has been mentioned. His favorite instrument was the clarinet, which he played at almost a professional level. He was competent on the viola and the double bass, and when occasionally called upon by the Rochester orchestra, could play the bass clarinet. He married Frieda Planck, daughter of Professor Adelbert Planck and niece of Max Planck, as well as an accomplished violinist, in 1914. Together in Rochester, they played frequently with an amateur orchestra and in smaller groups. Later in New York they played with a small group of friends for twenty-five years, usually in private, but occasionally in concert.

In these groups Clarke was a demanding performer. Every marking of the music for tempo and phrasing was noted, and a mistake by some unlucky member would bring a shout of protest. His knowledge of chamber music was extensive. He had inherited his father's large library and had added to it. He could produce on demand the parts for almost any chamber

music, including those of many of the more modern composers, all of which he played with taste and fine discrimination. An accident to his right hand with a scythe in 1960 brought an end to his clarinet playing, but did not interfere with the playing of string instruments.

There were four children, two boys and two girls, all of whom were brought up to use tools skillfully and to play an instrument in the frequently assembled chamber music groups. Their mother died in 1960, and in 1963 Clarke married Flora de Peyer, who survives him.

Clarke was widely recognized as one of the finest organic chemists of the period in this country. He had friends and colleagues both here and in Britain and Germany with whom he frequently corresponded on technical matters. His students were devoted to him, and a memorial meeting in New York shortly after his death brought together a large group in spite of inclement weather. At this meeting, a number of his musical friends played several of his favorite works, and brief addresses were made by former associates. He leaves a gap in American biochemistry that will be difficult, if not impossible, to fill.

IN PREPARING THIS MEMOIR, I have had the use of a document Clarke deposited with the Academy in the 1950s and supplemented in 1968. Also of his "Impressions of an Organic Chemist in Biochemistry," published by *Annual Reviews of Biochemistry* in 1958, of a bibliography and other documents kindly sent to me by Dr. J. Meienhofer of the Jimmy Fund in Boston, and of much genealogical and other information from his son, Dr. Eric Clarke, and from Mrs. Clarke. For all of this help, I am most grateful.

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KEY TO ABBREVIATIONS:

Arch. Intern. Med. = Archives of Internal Medicine
Ind. Eng. Chem. = Industrial and Engineering Chemistry
J. Am. Chem. Soc. = Journal of the American Chemical Society
J. Biol. Chem. = Journal of Biological Chemistry
J. Chem. Soc. = Journal of the Chemical Society (London)
J. Org. Chem. = Journal of Organic Chemistry

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