HENRY DRYSDALE DAKIN
1880–1952

H. D. Dakin, a British-born pioneer in biochemistry, long resident in the United States, died peacefully in his sleep on February 10, 1952, at his home in Scarborough-on-Hudson, New York. With his passing, our science has lost a figure whose influence on its development was as benign as it was unobtrusive.

Born in London on March 12, 1880, he spent his youth and early manhood in Leeds, where he studied organic chemistry under Julius B. Cohen. After graduating in 1901 he worked in London at the Lister Institute of Preventive Medicine (then the Jenner Institute) under S. G. Hedin, who inducted him into the field of enzymes. He then embarked on an independent investigation of the mode of action of lipase. This work, briefly interrupted by collaboration with Albrecht Kossel in Heidelberg, where a study of protamines led to the discovery of arginase, enabled Dakin to propound the theory that the primary action of an enzyme consists in its labile attachment to the substrate.

In 1905 he was invited to continue his researches in the private laboratory of Christian A. Herter, founder and benefactor of this *Journal*, in New York. Here he undertook a study of the action of hydrogen peroxide on amino acids and other physiologically important organic compounds. In the course of these experiments, he noted the production of acetone in the oxidative degradation of leucine. This observation led to his well known work on the β-oxidation of fatty acids and to the theoretical interpretation of the results reported a few years previously by Knoop. Coincidentally with these investigations, which profoundly influenced biochemical theory, he carried on extensive studies of the intermediary metabolism of aromatic amino acids and partially elucidated the nature of alcaptonuria.

After Herter's death in 1910, Dakin continued, at Mrs. Herter's request, the operation of the laboratory in New York. In conjunction with A. J. Wakeman, he observed the presence in liver tissue of an enzyme system which effected the dehydrogenation of β-hydroxybutyric acid to acetoacetic acid, and demonstrated the inability of a surviving liver to bring about the hydrolysis of urea to ammonia. He also studied the metabolic fate of amino acids in general, thereby throwing light on the nature of the chemical processes involved in their specific glucogenic and ketogenic functions.

In 1913 he was joined by Harold W. Dudley, also originally from Leeds,

who collaborated with him in the discovery of glyoxalase and its naturally occurring inhibitor antiglyoxalase. A sequel to this work was the remarkable observation that nitrophenylosazones of glyoxals are produced when solutions of α-hydroxy acids and amino acids are incubated with β-nitrophenylhydrazine. The biochemical significance of this reaction is still problematical, although its converse, the metabolic conversion of glyoxals to optically active amino acids, was unequivocally demonstrated.

With Dudley, Dakin extended to proteins his earlier work on the racemization of hydantoins by alkali, which had suggested to him that the nonterminal amino acids in polypeptides might behave similarly. This proved to be the case; when casein was allowed to stand in dilute sodium hydroxide until the optical rotation of the solution had reached a constant level, it was converted into a product which closely resembled casein in solubility but resisted the action of proteolytic enzymes. This was subjected to acid hydrolysis and eleven of the resulting amino acids were isolated; of these all were optically inactive except alanine, valine, leucine, and proline, the first three of which were partially racemic. Gelatin, subjected to the same procedures, yielded active alanine, proline, glutamic acid, and lysine, a finding which suggested a different distribution of the constituent amino acids among the terminal positions of the respective proteins. Some years later, in collaboration with (Sir) Henry H. Dale, this technique was applied by Dakin to the crystalline albumins of the eggs of hens and ducks. These proteins, though practically indistinguishable in amino acid composition, were found to differ both in their immunological specificities and in their stereochemical responses to the action of alkali. As he used to say, Dale and he proved that the hen was not a duck.

In 1914, Dakin returned to Europe in order to take part in the war effort and soon joined Alexis Carrel at a French military hospital where a study of the antiseptic treatment of wounds had been organized. Here he promptly developed the buffered hypochlorite known as Dakin's solution and the use of sodium *p*-toluenesulfochloroamide (chloramine-T). In an investigation of the mode of action of these antiseptics, sponsored by the British Medical Research Committee, he showed that one mole of the oxidant converts amino acids into *N*-monochloro derivatives which decompose into aldehydes, carbon dioxide, and ammonia, whereas two moles yield dichloroamino acids which break down into nitriles.

Dakin further applied the use of chloramine-T to the sterilization of drinking water; he also personally installed in the "Aquitania," in use as a hospital ship during the Gallipoli campaign, a highly effective apparatus for the electrolytic production of hypochlorite.

Before returning to New York after the war, Dakin began the experimental work on his revolutionary method for the extraction of monoamino

monocarboxylic acids from neutralized protein hydrolysates by wet butanol. This method enabled him to carry out unprecedentedly complete amino acid analyses of two proteins, gelatin and zein. It also resulted in the isolation of a new amino acid, hydroxyglutamic acid, from casein. The chemical constitution of this product, the existence of which has—possibly in consequence of its instability under some conditions—been questioned by some workers, has not yet been cleared up; it was converted by reduction into glutamic acid, but further study of β-hydroxyamino acids failed to confirm the original supposition that it was a compound of that type.

During the early twenties, Dakin devoted much of his time to investigations of the oxidative catabolism of fatty acids, unsaturated acids, hydroxy acids, and amino acids by muscle tissue, liver, and yeast. Present day views on the chemical mechanisms involved in the general metabolism of these compounds owe much to his observations. In 1926, in collaboration with Eleanor B. Newton and Stanley R. Benedict (who from 1920 until his death in 1936 was Managing Editor of this *Journal*) he showed that thiasine, which Benedict had recently isolated from blood, was identical with ergothioneine.

Two years later, he and Randolph West, then a young clinician, discovered an unexpected reaction of amino acids with acetic anhydride in pyridine, whereby methyl α-acetaminoalkyl ketones and carbon dioxide are formed. They then embarked on a laborious and discouraging attempt to isolate the antianemic principle of liver. The chemical fractionation was carried out by Dakin, the potency assays by West. At that time the biological tests could be made only on human cases of pernicious anemia and as liver therapy became more general it became increasingly difficult to find untreated subjects. Nevertheless, the two devotedly persisted in their search, undismayed by false leads and technical obstacles, up to the time of the death of the junior collaborator. Thereafter, Dakin, whose health had weakened under the strain, undertook no major projects.

Dakin was an effective writer. His monograph, "Oxidations and reductions in the animal body," was first published in 1912 and again in 1922, as a second edition which soon went out of print. His "Handbook of chemical antiseptics," written in collaboration with E. K. Dunham, which appeared in 1917, and his article on "Physiological oxidations," published in 1921 in the first volume of *Physiological Reviews*, were highly regarded by specialists.

His work received public recognition in both Europe and America. The University of Leeds conferred upon him the Ph.D. in 1907 and the honorary LL.D. in 1936; he also was given honorary degrees from Yale University and the University of Heidelberg. He was elected to fellowship in the Royal Society at the early age of 37, and twenty-five years later was

awarded the Davy medal by that body. The Chemists' Club of New York bestowed on him the Conné medal. He was a Chevalier of the French Legion of Honor.

He joined the Chemical Society of London in 1901 and the American Society of Biological Chemists in 1906. He was a member of the Editorial Board of this *Journal* from 1911 until 1930, and for a long time had charge of its Herter Fund, which derived great benefit from his wise and careful management. In later years he served on the Board of Scientific Advisers of the Merck Institute for Therapeutic Research and ultimately became a Director of Merck and Company, Inc.

In 1916, Dakin and Mrs. Susan Dows Herter had married. Soon after his return to New York at the close of the war, they moved to a large house, amply surrounded with beautiful grounds, overlooking the Hudson River at Scarborough. There he lived a quiet country life, taking daily walks with his beloved Alsatian police dogs and, even after Prohibition, annually preparing excellent wines. Most of his time, however, was spent in the well equipped laboratory which he had installed in an annex, where he worked alone but for an elderly technician. After 1920, even close collaborations were carried on in separate laboratories. It is regrettable that so few younger colleagues had an opportunity of profiting by daily contact with him, for he was by nature an inspiring mentor.

Though far from a recluse, he shunned the limelight to such a degree that he consistently refused to speak in public. This modesty was one facet of his selflessness, an example of which, as it is a matter of record, may here be cited. In 1926, having investigated the chemical constitution of thyroxine, he submitted to this *Journal* a report of his findings, but, on learning that a former collaborator had independently reached a similar conclusion, he withdrew the manuscript from the hands of the Editors.

Another facet was his devotion to his friends, all of whom called him "Zyme." His keen humor, his kind but critical appraisal of men, even his ripe judgment in scientific matters, were reserved for his intimates. He was one of those fortunate characters whose friendships remain undimmed by time or distance.

Dakin was flawlessly happy in his marriage, though his last years were saddened by the long illness of his wife, throughout which he tended her devotedly. After her death in 1951, he gave the impression of continuing in life only from a sense of propriety; his own end came kindly.

H. T. Clarke