

NATIONAL ACADEMY OF SCIENCES

VINCENT DU VIGNEAUD

*1901—1978*

---

*A Biographical Memoir by*  
KLAUS HOFMANN

*Any opinions expressed in this memoir are those of the author(s)  
and do not necessarily reflect the views of the  
National Academy of Sciences.*

*Biographical Memoir*

COPYRIGHT 1987  
NATIONAL ACADEMY OF SCIENCES  
WASHINGTON D.C.



*W. W. Weyland*

## VINCENT DU VIGNEAUD

*May 18, 1901–December 11, 1978*

BY KLAUS HOFMANN

VINCENT DU VIGNEAUD was born in Chicago in 1901. He was of French ancestry, the son of Alfred du Vigneaud, an inventor and machine designer, and Mary Theresa du Vigneaud. He attended Carl Schurz High School in Chicago, from which he graduated in 1918. When he was a freshman in high school, two friends, who had a chemical laboratory at home, invited him to join them in chemical experimentation. They obtained chemicals from a pharmacist and conducted experiments that involved the fabrication of explosives containing sulfur. This was his first contact with science.

World War I was under way, and young people were needed on the farms. Seniors in high school were offered the opportunity of working on the farms in spring and receiving their diplomas in June. Young Vincent worked through spring and summer on a farm near Caledonia, Illinois. He was very proud of the fact that he could milk twenty cows by hand, and he decided to become a farmer. His older sister, Beatrice, changed his mind and suggested that he go to the University of Illinois at Urbana-Champaign to study chemistry. He followed her advice and registered in chemical engineering. He later recalled:

I found during the first year that it was chemistry rather than engineering that appealed to me most. I switched to a major in chemistry since I was deeply impressed by the senior student's work, especially in organic chemistry. I also found that I was most interested in those aspects of organic chemistry that had to do with medical substances and began to develop an interest in biochemistry.

Young du Vigneaud had no money and had to put himself through college and graduate school. Tearing down boilers, picking apples, working in the library, and jerking sodas were some of his occupations. But the job that helped most financially was that of headwaiter. The next most remunerative job turned out to be the teaching of cavalry tactics and equitation as a reserve second lieutenant in the cavalry.

One day, while working as a waiter, Vincent saw a pretty redhead and said to one of his colleagues, "That's the woman I am going to marry"—and he did. The young woman was Zella Zon Ford. She was an English major, but as she and Vincent became better acquainted he saw to it that she took classes in mathematics and chemistry. Although she graduated as an English major, she knew sufficient chemistry so that after their marriage on June 12, 1924, she was able to teach chemistry in high school.

One of the professors at Illinois who exerted a significant influence on young du Vigneaud was Carl Shipp Marvel, known as "Speed." Du Vigneaud was much impressed with Marvel's lectures and research program, and he decided to do his senior thesis with him. Later he selected Speed to become his master's degree adviser. As he progressed with his studies, he became more and more interested in the relations between biochemistry and organic chemistry. He took advanced courses in biochemistry from H. B. Lewis and the nutritionist W. C. Rose, whose studies on nutrition of the white rat later became role models for some of du Vigneaud's metabolic investigations. He was particularly taken with a lec-

ture by Professor Rose in which the work of Banting and Best on insulin was discussed.

Du Vigneaud earned his master's degree in February of 1924 and accepted a position with the Du Pont Company; he later worked for some time with Dr. Walter Karr at the Philadelphia General Hospital. Nevertheless, his mind was set on graduate study and the earning of a Ph.D. degree. Professor Marvel recalls the following episode:

When du Vigneaud received his master's degree he was offered a job with Walter Karr in Philadelphia, but he was too poor and had no money to pay his way to Philadelphia. To help him out I gave him an assignment to make 10 pounds of cupferron for our organic preparations laboratory and told him I would pay him, as a wage, whatever amount he could produce in material for under the price which we would sell it. He did not ask for any hourly work or time, but we generally agreed that way. In producing the 10 pounds, he'd accumulated enough money to get to his Philadelphia job.

In the spring of 1925 du Vigneaud received an invitation from Professor John R. Murlin to join the Department of Vital Economics at the University of Rochester, New York, to undertake graduate work on the chemistry of insulin. Professor Murlin was a physiologist and not a chemist, and du Vigneaud was eager to discuss his chemical problems with other chemists. In this connection, he became acquainted with Hans Clarke, who at the time was working for Eastman Kodak. Later, Clarke became professor and chairman of the Biochemistry Department at the College of Physicians and Surgeons in New York, and the two men struck up a lifelong friendship.

In 1927 du Vigneaud graduated with a Ph.D. degree; the thesis title was "The Sulfur in Insulin." During his last year in Rochester he was awarded a National Research Council Fellowship, which enabled him to pursue postdoctoral studies with John Jacob Abel, professor of pharmacology at the

Johns Hopkins University Medical School. Here, in collaboration with Oscar Wintersteiner and Hans Jensen, the insulin studies were continued. A second fellowship enabled the young du Vigneaud to do some traveling abroad. He became acquainted with the synthesis of peptides in the laboratory of Max Bergmann at the Kaiser Wilhelm Institut in Dresden and spent some time with Professor George Barger in Edinburgh, Scotland. Bergmann, a former student of Emil Fischer, was a pioneer in the peptide field who later became a member of the Rockefeller Institute for Medical Research (now Rockefeller University) in New York.

Broadly equipped to engage in independent scientific pursuits, du Vigneaud accepted a position in the Department of Physiological Chemistry at his alma mater in Illinois. Biochemistry had become his chosen field, and the opportunity presented itself to have graduate students. He spent three happy years in Illinois; at age thirty-one he became professor and chairman of biochemistry at George Washington University Medical School in Washington, D.C. He was saddened to leave the outstanding department at Urbana with such great professors as Adams, Marvel, Shriner, and Fuson in organic chemistry and Professor Rose in biochemistry, but the opportunity for greater independence was decisive.

He stayed at George Washington from 1932 to 1938, when he was invited to head the Department of Biochemistry at Cornell Medical College in New York City, a chair that had been occupied by Stanley R. Benedict. In connection with this move he stated:

When I came to Cornell Medical College, I brought along five members of my research group, Mildred Cohn, George W. Irving, Theodore Loring, Gail Miller, and John Wood. As in the transfer from Illinois to George Washington I thus had continuity, people with whom I had already been working. This I regard as very important when moving from one place to another. Just as in transplanting a tree with some soil around it, if possible it is well to move a man with some of his environment.

The awarding of the 1955 Nobel Prize in Chemistry constituted an unquestionable triumph for du Vigneaud, but he expressed definite opinions pertaining to the awarding of prizes for scientific achievement. He said to a reporter, "I am expecting to stay in the research field, in the academic world, but I want to tell you I will never work for any prize. I refuse to let my rewards rest in the hands of any committee."

In answer to a congratulatory note I sent him on the occasion of his award, he answered: "The real thrill of such an award is sharing the pleasure with one's friends, and particularly with those who have been associated with me on the trail."

The highly productive career at Cornell Medical College came to an end with his assumption of emeritus status in 1967. But a generous invitation from Professor Harold A. Scheraga, then head of the Chemistry Department at Cornell University in Ithaca, made it possible for du Vigneaud to continue his investigations as professor of chemistry. He was very happy and productive in Ithaca and enjoyed his new surroundings. He wrote to his former collaborators and students: "Those of you who know the Ithaca area will appreciate that I have a fantastic view from my office on the sixth floor of the Chemistry Research Building overlooking Cayuga Lake to the northwest and Beebe Lake, waterfalls and the Fall Creek gorge down below."

In addition to his outstanding contributions to science, du Vigneaud was a great teacher and lecturer. His lectures to students were interesting and well prepared. He emphasized the importance of teaching and his advice to the faculty was: "Remember your first obligation is teaching; when you are teaching it takes precedence over research." His presentations at home and abroad were masterpieces of staging. He would go over his slides with the projectionist in the greatest detail so that the presentation would proceed flawlessly. He was a showman, an artist in communicating research find-

ings. It was a genuine pleasure to listen to his presentations, which were as meticulously prepared and rehearsed as were his scientific papers.

Professor du Vigneaud's scientific career was abruptly terminated when he suffered a stroke in 1974. He died on December 11, 1978. His wife, Zella, had passed away one year earlier. Professor du Vigneaud is survived by a son, Vincent, Jr., and a daughter, Marilyn Renée Brown. Both are physicians.

If one views the totality of du Vigneaud's contributions to science, one recognizes a thread of continuity connecting sulfur-containing, biologically important compounds. This thread extends from insulin to cysteine, homocysteine, methionine, cystathionine, biotin, penicillin, oxytocin, and vasopressin. In the Messenger lectures, delivered at Cornell University in Ithaca in 1950, he likened his scientific work to a trail in research; he wrote:

An attempt was made to retrace the research trails originating from a study of insulin that I have had the pleasure of working out in association with various collaborators over a period of twenty-five years. I attempted to present not only the findings encountered, but also in many instances the stepwise evolution of these findings, including the accidents of fate that played a part.

Some of du Vigneaud's earliest researches dealt with the chemical nature of insulin. Abel crystallized insulin in 1926, and Jensen, Wintersteiner, and du Vigneaud investigated the composition of acid hydrolysates of the crystalline hormone. With the rather primitive methods available at the time, the presence in such hydrolysates of cystine and various other amino acids was established. Based on this evidence, it was concluded that insulin was a protein. Du Vigneaud commented later: "It may seem strange to speak of work establishing insulin as a protein because it is now a generally ac-



cepted fact that a hormone can be a protein or that a protein can be a hormone, yet at that time (1928) there was great reluctance in accepting this viewpoint." The thinking at that time was strongly influenced by the concepts of Willstätter regarding the chemical nature of enzymes that were assumed to be composed of a small functional coenzyme and a protein carrier. Insulin was believed to be a small molecule that was attached or absorbed to a high molecular weight carrier.

In 1930 du Vigneaud became acquainted with L. F. Audrieth, a faculty colleague at the University of Illinois, who was an expert in the liquid ammonia field. He was impressed with liquid ammonia as a solvent for insulin and the sparingly soluble cystine. Audrieth's use of metallic sodium as a reducing agent in liquid ammonia prompted du Vigneaud to apply this method to the conversion of cystine to cysteine. He devised the technique of S-benylation of cysteine by adding benzyl chloride to sodium in liquid ammonia-reduced cystine. The observation that the S-benzyl group was removed from S-benzylcysteine by reduction with sodium in liquid ammonia represented a significant contribution to peptide chemistry; it made possible the transient protection of the thiol group of cysteine during peptide syntheses.

In 1932 Bergmann and Zervas introduced the benzyloxy-carbonyl group (carbobenzoxy group) into amino acids and peptides, and with the discovery that this protecting group could be cleaved by catalytic hydrogenolysis they laid the groundwork for the development of modern peptide synthesis. Du Vigneaud became interested in this method and embarked on synthesizing carbobenzoxy derivatives of amino acids. The story has it that in his laboratory the carbobenzoxyamino acids failed to crystallize. One day, Max Bergmann came to visit the laboratory and, lo and behold, from that time on the carbobenzoxyamino acids crystallized beautifully. Did Bergmann carry seed crystals in his pockets? The

discovery that benzyloxycarbonyl groups can be removed from cysteine and cysteine-containing peptides by sodium in liquid ammonia broadened the scope of the carbobenzyoxy method and opened its applicability to peptides containing sulfur.

As we proceed with this discussion, it will become apparent that the techniques du Vigneaud developed early in his career provided answers to problems he encountered at a later time (oxytocin and vasopressin). Much of du Vigneaud's work in intermediary metabolism concerned the formation of cysteine in the animal organism and the metabolic relationships among methionine, cysteine, homocysteine, cystathionine, and choline. He called the underlying reactions "transulfuration" and "transmethylation." It was known that methionine could support growth of laboratory rats on a cysteine-free diet, and Rose had shown that methionine was an essential dietary constituent for the rat. In short, the rat is capable of synthesizing cysteine but not methionine. In 1931 du Vigneaud discovered a new sulfur-containing amino acid while exposing methionine to strong sulfuric acid. This compound was the next higher symmetrical homolog of cystine and he named it "homocystine." Later, he discovered that the reduced form of this amino acid, homocysteine, was a metabolically important compound. Du Vigneaud observed that homocysteine, like methionine, could support the growth of rats on diets deficient in cystine.

These observations pointed to a metabolic relationship between methionine and homocysteine and suggested that demethylation of methionine could be involved in cysteine biosynthesis. Du Vigneaud synthesized L-cystathionine, a thioether in which the carbon chains of cysteine and homocysteine are connected by a single sulfur atom, and found that this compound sustained growth of rats on a cysteine-deficient diet. This observation indicated that the rat was capable of cleaving the thioether linkage with formation of cys-

teine. It was observed further that cystathionine did not give rise to homocysteine, an observation that was supported by *in vitro* studies with liver slices. The addition to liver slices of a mixture of homocysteine and serine resulted in a 60 percent conversion of homocysteine sulfur into cysteine, providing strong evidence for the hypothesis that homocysteine was indeed an intermediate in the formation of cystathionine. The importance of serine as a precursor of cysteine had been demonstrated earlier by Dewitt Stetten.

Before continuing the discussion of du Vigneaud's work on the intermediary metabolism of sulfur compounds, it seems fitting to have a short synopsis of the status of biochemistry in the 1930s. At that time, the Biochemistry Department of the College of Physicians and Surgeons at Columbia University, under the leadership of Hans Clarke, had developed into one of the outstanding departments in the country and one that made scientific history. It was in this department that Rudolf Schönheimer and his colleagues performed the classical tracer experiments pointing to "the dynamic state of the body constituents." The application of isotopes to the solution of biochemical problems provided the key for these developments, which revolutionized biochemical thinking. Harold C. Urey, also of Columbia University, had developed the methodology for the preparation of deuterium oxide and other elements enriched with respect to stable isotopes, and the availability of these compounds opened far-reaching biochemical frontiers. Because growth experiments had severe limitations, du Vigneaud applied the new tracer techniques to the study of the conversion of methionine to cysteine. He synthesized *DL*-methionine labeled in the  $\beta$  and  $\gamma$  positions with  $^{13}\text{C}$  and containing  $^{34}\text{S}$  and fed this compound to rats. The rats were shaved at the beginning of the experiment and received another haircut after thirty-eight days in the experiment. The cystine isolated from the hair contained  $^{34}\text{S}$ , but no  $^{13}\text{C}$ . From the results of this ex-

periment it was concluded that only the sulfur, not the carbon chain of methionine, was utilized for cysteine biosynthesis. This provided final proof that, in the rat, cysteine synthesis from methionine involves demethylation with formation of homocysteine followed by condensation of the homocysteine with serine to form cystathionine. The latter is cleaved with formation of cysteine and  $\alpha$ -ketobutyric acid. In essence, the conversion of methionine to cysteine involves a transfer of the methionine sulfur to serine. This, according to du Vigneaud, became known as "transulfuration."

An interesting coincidence led to the discovery of the concept of transmethylation or methyl transfer. Here again the crucial evidence was derived from rat feeding experiments. Rose observed good growth of rats fed a methionine-cysteine-free diet that was supplemented with homocysteine. Similar experiments carried out in du Vigneaud's laboratory produced negative results; the rats failed to grow. The animals in both laboratories grew well when the diet was fortified with methionine. The difference in the results was traced to the vitamin supplements used. Du Vigneaud employed crystalline B complex vitamins, but Rose used rice bran extract (Tikitiki) as the vitamin source. Du Vigneaud noted that his rats developed fatty livers while on experiment. It was known from the work of Best that choline inhibited fatty infiltration of the liver, and Du Vigneaud reasoned that this pathology could be the result of a choline deficiency. He decided that the factor missing in his diet could be choline, and this proved to be correct. Accordingly, diets containing both homocysteine and choline were fed, and such a regimen supported growth as well as did methionine.

On the basis of these findings du Vigneaud speculated that choline, a compound rich in methyl groups, could act as a methyl donor for the conversion of homocysteine to methionine. These early findings led to the concept of transmethylation and that of "labile" methyl groups. The obser-

vation that rats grew well and failed to develop fatty livers on a choline-free diet supplemented with methionine suggested to du Vigneaud that the methionine could serve as a methyl source for choline synthesis. These concepts were amply confirmed by tracer experiments. Methionine in which the methyl group was enriched with respect to deuterium was fed to rats, and choline was isolated from the tissues. This choline contained deuterium in its methyl groups, demonstrating transmethylation from methionine. Conversely, choline containing deuterium was given to rats, and deuterium was present in the methyl group of methionine. Thus the hypothesis that methionine was biosynthesized from homocysteine by a methyl transfer from choline was substantiated. It was also observed that the transfer of methyl groups was a continuous process. In addition, du Vigneaud found that the methyl group of creatine was derived from the methyl group of methionine. The transfer of methyl groups from methionine to choline and from choline to methionine is a reversible process, but the methyl group of creatine does not serve as a methyl donor for the conversion of homocysteine to methionine. Based on these studies, du Vigneaud concluded:

From our study, we know only that the methyl group of methionine and choline can be transferred, but we do not know whether methionine or choline react directly or whether they are precursors of derivatives from which the methyl groups are released. Although methionine can be demethylated *in vitro*, the conditions required are drastic. Attention must therefore be directed to any possibility whereby the bond between the methyl group and the sulfur atom may be weakened. The formation of a sulfonium ion would be expected to effect such a labilization.

It remained for Cantoni to identify the methyl donor in biological systems as the sulfonium ion S-adenosylmethionine.

The work on biotin resulted from an invitation to du Vigneaud from Paul György to collaborate in establishing the chemical nature of the anti-egg-white injury factor in liver,

which György had designated as vitamin H. Rats receiving diets containing large proportions of raw egg white as the source of protein develop severe dermatitis and nervous disorders and die if the condition is not relieved. Certain foodstuffs, such as liver and yeast, contain a substance capable of preventing and curing this disorder. The curative factor was named vitamin H by György (H being derived from the German word *Haut*, meaning skin). Biotin, a yeast growth factor, had been isolated from egg yolks by Kögl and Tönnes. Du Vigneaud, György, and collaborators were able to cure egg-white injury with Kögl's pure biotin, demonstrating that vitamin H and biotin were one and the same compound. Biotin was isolated from liver extracts and milk in the Cornell laboratories, and the chemical structure of the compound was established. The structure worked out by du Vigneaud and collaborators was verified by chemical synthesis in the Merck laboratories. Biotin, first discovered as a yeast growth factor, turned out to be a mammalian vitamin.

The Second World War interrupted the operations of the laboratory, and du Vigneaud was invited by the wartime Committee on Medical Research, OSRD, to join the great effort being organized in this country and in England to work on the chemistry of penicillin. Many contributions to penicillin chemistry emanated from the Cornell laboratory. Perhaps the most outstanding were those dealing with the synthesis of minute quantities of the antibiotic and its identification with the natural compound.

One amusing sidelight to the penicillin story comes from Sofia Simmonds. During a discussion with Hans Clarke, she remarked that penicillin must contain sulfur. Hans Clarke, who was in charge of the U.S. part of the super-secret penicillin project, was shocked to hear this and he wanted to know how she'd found out. She said we all could tell; the labs on the second floor, where the work was being done, leaked ben-

zylmercaptan into the hallway—any V du V person knew what that meant.

Du Vigneaud's work on the posterior pituitary principles oxytocin and vasopressin was started in 1932 and continued until 1940, when it was interrupted by the Second World War. During this time, however, the emphasis of the laboratory was on the metabolic aspects, transulfuration and transmethylation, and du Vigneaud referred to his work with the posterior pituitary hormones as his hobby. Some progress had been made in purification of these principles, mainly by the use of precipitation and electrophoretic techniques, but of prime importance were some preliminary observations suggesting that oxytocin and vasopressin were derivatives of cystine. During the war, new techniques became available that had a critical effect on the progress of the posterior pituitary hormone project. Of immediate importance were the Craig countercurrent distribution published in 1944 and the starch column technique of Moore and Stein for the quantitative separation of mixtures of amino acids in acid hydrolysates of proteins on a micro scale.

Du Vigneaud returned to the study of the posterior pituitary principles in 1947. A concentrate he had received from Parke-Davis in 1940 that was stored during the war years was reassayed in 1947 and had retained 50 percent of its original oxytocic potency. Homogeneous oxytocin exhibiting a high level of biological activity was isolated from this material by the Craig countercurrent technique. The amino acid composition of an acid hydrolysate of this material, determined by the Moore-Stein technique, showed the presence of cystine, glutamic acid, aspartic acid, glycine, isoleucine, leucine, proline, and tyrosine in molar ratios of 1:1. In addition to these amino acid residues, the hydrolysate contained three moles of ammonia. The amino acid residues plus ammonia accounted for 97 percent of the hydrolyzed

material. Molecular weight determinations were in agreement with a monomer. Oxytocin was oxidized with performic acid, and the amino acid composition of the oxidized material was determined. The composition was identical to that of the unoxidized material, except that in lieu of cystine two molecules of cysteic acid were present.

It followed from this and other results that oxytocin was a cyclic peptide. Using the dinitrofluorobenzene technique of Sanger, it was shown that oxytocin contained a free amino group that was derived from one of the two cysteine residues; a free carboxyl group was not present. By a combination of the Edman technique and analysis of partial acid hydrolysates, the amino acid sequence of oxytocin was established as H-Cys-Tyr-Ile-Glu-Asp-Cys-Pro-Leu-Gly-OH. The final, as yet unanswered, question related to the sources of the three ammonia molecules. These were shown to be asparagine, glutamine, and glycnamide. Thus the structure of oxytocin was established as H-Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH<sub>2</sub>. In his characteristically cautious approach, du Vigneaud commented as follows: "It is obvious that, in spite of the fact that this was the only structure we could arrive at through the realization of the results from our degradative work, synthetic proof of structure was mandatory."

The crucial steps in du Vigneaud's oxytocin synthesis were based on reactions in liquid ammonia he had investigated many years earlier. When subjected to reduction with sodium in liquid ammonia, oxytocin was converted to the open-chain oxytoceine, and this on air oxidation reconstituted biologically active oxytocin. This behavior of oxytocin was the key for its successful synthesis. Another model study, using the natural hormone, was performed that suggested the strategy for a successful synthesis. Oxytocin was reduced to the open-chain oxytoceine, and benzyl chloride was added to the reaction mixture, affording S,S'-dibenzlyoxytoceine. Deben-



ylation of this material with sodium in liquid ammonia followed by air oxidation regenerated biologically active oxytocin.

The facile ring closure to the 20-membered ring structure of oxytocin from the open-chain peptide oxytoceine indicated that the open-chain structure had a preferred conformation in which the two SH groups are located in close proximity for cyclization to occur. This appears to constitute the first example of the now well-established principle that the amino acid sequence of a protein endows it with the thermodynamic information necessary for folding into a specific conformation. Based on these model reactions, du Vigneaud synthesized N-benzyloxycarbonyl-S,S'-dibenzyloxytoceine and converted the synthetic material into active oxytocin in the manner discussed above. The synthetic oxytocin was identical with the natural hormone. The first oxytocin synthesis was communicated to the *Journal of the American Chemical Society* on July 13, 1953. The paper concluded with the following statement:

If the synthetic product truly represents oxytocin, which it does so far as we are concerned, this would constitute the first synthesis of a polypeptide hormone. What effect slight changes in the structure of a compound of such complexity might have on chemical, physical, and biological properties must be investigated.

While the work on oxytocin was under way, the structure of vasopressin was also determined. With a wealth of data based on degradation studies, paralleling those outlined for oxytocin, a structure for arginine vasopressin was arrived at that was very similar to that of oxytocin. This hormone embodies the same ring structure as oxytocin but contains two amino acid exchanges. Isoleucine is replaced by phenylalanine and leucine is substituted by arginine. Lysine vasopressin contains lysine in lieu of arginine.

A synthesis of lysine vasopressin was completed in 1960. The observation by du Vigneaud that certain combinations of amino acids into peptides can result in compounds exhibiting potent physiological activities opened a vast field of biological and chemical research. He stated, "It is a little startling to think that the amino acids when put together in a certain way, in a particular architecture, can lead to such an array of compounds exhibiting such a variety of physiological and pharmacological properties."

Du Vigneaud's findings with oxytocin and vasopressin were of great fundamental importance: They demonstrated for the first time that replacement of certain amino acid residues in the sequence of a physiologically active peptide can bring about significant changes in biological action. The exchange in oxytocin of isoleucine for phenylalanine and of leucine for arginine (or lysine) alters the physiological activity of the molecule from one of mainly oxytocic to one with mainly vasopressor potency. These discoveries have stimulated much research into the relations between peptide structure and physiological function. Hundreds of analogs of the posterior pituitary hormones have been prepared as a consequence of du Vigneaud's work, and his pioneering studies have spawned the recent explosive activity in the peptide field.

Thus far we have been concerned with the story of du Vigneaud's life and with his many scientific accomplishments. We may now ask: Who was this man and what was the atmosphere in his laboratory that promoted such a wealth of fundamental work? His laboratory was extremely well organized. Since he was a very busy man who was not always available for consultations, he initiated a system of colored slips for communicating with him. There was a pink slip for suggesting new ideas and new research approaches, there

was a green slip for reporting research results, and, finally, a white slip for requesting microanalytical services. The "greens" were du Vigneaud's favorite. He wanted them at least weekly from every researcher in the group, and he read them with extreme care. To those who were reluctant to write up half-finished experiments, he insisted that that was the fun of the research to him. He couldn't remember (he said) the results presented to him in a neat package at the end nearly as well as if he had been in on them as they developed day by day. Many a collaborator was awed by his memory for details in someone else's research reports, from months or years gone by, which he could bring to bear on the problem at hand. The potential aid thus available, once appreciated, did a lot to lighten the task of grinding out the green slips! But, besides all of this red tape, there was ample opportunity to have a private audience with the chief.

The laboratory was a busy place indeed, and hard work was the order of the day. Graduate students were expected to spend several evenings a week in the laboratory, as well as part of Saturday, and papers were frequently written late into the night. Professor du Vigneaud lived in the suburbs of New York, but he maintained a beautifully furnished room in the department where he spent many a night during the week. These were the evenings when he came to visit with his collaborators. Smoking a White Owl cigar, which he gracefully waved poised between his strong fingers, he shared a cold soft drink with us and discussed the latest research results. Speaking quietly and easily, he used such words as "exciting," "surprising," "intriguing"—all suggesting great pleasure in the stepwise evolution of the research. He was always highly interested in the day's results and was truly devoted to his scientific work. He felt very secure and loved his work. To a reporter he said:

I have had the privilege and the thrill of following those researches that I've always wanted to do. I've always had the privilege of working on what I've wanted to work on. I have been accompanied in the various stages of these exploratory researches by a group of fine and loyal associates. I've also been fortunate throughout the years in the generous research support I've received from various sources.

He had a highly critical attitude toward laboratory results and this permeates his writings. Every possible angle of a project was discussed at great length, and new approaches and ideas that could clarify an issue were explored in depth. Papers were written in collaboration with those who did the work; a secretary was present, and while discussions went on she was typing the latest version of a draft. A great many versions were hammered out before the chief was satisfied.

Unquestionably, du Vigneaud was in command, and he was highly respected by his collaborators. He had a jovial manner with people, and every year he invited his entire crew to his home in Scarsdale for a picnic with softball and other entertainment. "Dee," as he was known by his colleagues over the years, associated with a great number of graduate students, postdoctoral fellows, and visiting professors. All the people who ever worked in Dee's laboratory belonged automatically to the V du V Club. He kept in constant touch with us, and every year during the Federation meetings we all got together for beer and pretzels to share time with former colleagues, the chief, and his charming wife, Zella.

THE AUTHOR IS INDEBTED to Drs. Martha Ferger, Sofia Simmonds, and Marilyn Renée Brown for their help in collecting source materials. A number of the quotations are taken from an interview published in the *Journal of Chemical Education*, 53(1976): 8-12.

## HONORS AND DISTINCTIONS

## DEGREES

B.S., University of Illinois, 1923

M.S., University of Illinois, 1924

Ph.D. (Biochemistry), University of Rochester, 1927

## HONORARY DEGREES

D.Sc., New York University, 1955

D.Sc., Yale University, 1955

D.Sc., University of Illinois, 1960

D.Sc., University of Rochester and St. Louis University, 1965

## UNIVERSITY APPOINTMENTS

National Research Council Fellow, Johns Hopkins University, 1927–28

National Research Council Fellow, Kaiser Wilhelm Institute, Dresden, Germany, and University of Edinburgh Medical School, 1928–29

Associate, University of Illinois, 1927–30

Professor and Head of Department of Biochemistry, School of Medicine, George Washington University, 1932–38

Professor and Head of Department of Biochemistry, Cornell University Medical College, 1938–64

Professor Emeritus of Chemistry, Department of Chemistry, Cornell University, 1964–74.

## MEMBERSHIPS

National Academy of Sciences, 1944

American Philosophical Society, 1944

Royal Society of Sciences of Uppsala, 1950

Honorary Fellow of the Royal Society of Edinburgh, 1954

Honorary Fellow, Royal Institute of London, 1959

## AWARDS AND LECTURESHIPS

Hillebrand Award, Washington Chemical Society, 1936

Foster Lecturer, University of Buffalo, 1939

Harvey Society Lecturer, 1942

- Meade-Johnson Vitamin B Complex Award, American Institute of Nutrition, 1942
- Hitchcock Lecturer, University of California, 1944
- Nichols Medal, New York Section, American Chemical Society, 1945
- Borden Award, Association of American Medical Colleges, 1947
- Visiting Lecturer, American Swiss Foundation for Scientific Exchange, Switzerland, 1947
- Award of Merit for War Research, United States Government, 1948
- Lasker Award, American Public Health Association, 1948
- Stieglitz Memorial Lecturer, University of Chicago, 1948
- Eastman Lecturer, University of Rochester, 1949
- Liversidge Lecturer, University of Cambridge, 1949
- Special Lecturer, University of London, 1949
- Messenger Lecturer, Cornell University, 1950
- Herter Lecturer, New York University, 1952
- Edsel B. Ford Lecture, Henry Ford Hospital, 1954
- Goldforb Lecturer, 1954
- Harvey Society Lecturer, 1954
- Osborne and Mendel Award, 1954
- John Scott Award, Philadelphia, 1954
- Remsen Memorial Lecturer, Johns Hopkins University, 1954
- Scientific Award, American Pharmaceutical Manufacturers' Association, 1954
- Chandler Award, Columbia University, 1955
- Annual Hanna Lecturer, Western Reserve University, 1955
- Nobel Prize in Chemistry, Nobel Foundation, 1955
- Passano Award, Passano Foundation, 1955
- Dakin Memorial Lecturer, Adelphi College, 1956
- Willard Gibbs Medal, Chicago Section, American Chemical Society, 1956
- Nieuwland Lecturer, University of Notre Dame, 1956
- Edgar Fahs Smith Lecturer, University of Pennsylvania, 1958
- Alumni Achievement Award, University of Illinois, 1959
- Martland Memorial Lecturer, 1959
- Nutrition Foundation's 20th Anniversary Award, 1961
- Pirquet Society of Clinical Medicine Medalist, 1964
- American College of Physicians Award, 1965
- The Eli Lilly Lecture Award, Endocrine Society, 1967

## BIBLIOGRAPHY

1924

- With C. S. Marvel. Pressor anesthetics. *J. Am. Chem. Soc.*, 46: 2093-99.
- With C. S. Marvel. A new organic reagent for the detection of nitrates and perchlorates. *J. Am. Chem. Soc.*, 46:2661-63.

1925

- With Walter G. Karr. Carbohydrate utilization. I. Rate of disappearance of *d*-glucose from the blood. *J. Biol. Chem.*, 66:281-300.

1927

- The labile sulfur of insulin. *Proc. Soc. Exp. Biol. Med.*, 24:547-48.
- Some useful modifications of the haldane gas-analysis apparatus. *J. Lab. Clin. Med.*, 13:175-84.
- Is insulin inactivated by glucose? *J. Biol. Chem.*, 73:275.
- The sulfur of insulin. *J. Biol. Chem.*, 75:393-405.

1928

- With H. Jensen and Oskar Wintersteiner. Studies on crystalline insulin. III. Further observations on the crystallization of insulin and on the nature of the sulfur linkage. The isolation of cystine and tyrosine from hydrolyzed crystalline insulin. *J. Pharmacol. Exp. Ther.*, 32:367-85.
- With H. Jensen and Oskar Wintersteiner. Studies on crystalline insulin. IV. The isolation of arginine, histidine and leucine. *J. Pharmacol. Exp. Ther.*, 32:387-95.
- With Oskar Wintersteiner and H. Jensen. Studies on crystalline insulin. V. The distribution of nitrogen in crystalline insulin. *J. Pharmacol. Exp. Ther.*, 32:397-411.
- With E. M. K. Geiling and C. A. Eddy. Studies on crystalline insulin. VI. Further contributions to the question whether or not crystalline insulin is an adsorption product. *J. Pharmacol. Exp. Ther.*, 33:497-509.

1929

- With Max Bergmann and Leonidas Zervas. Synthese arginin-haltiger peptide: *d*-Tyrosyl-*d*-arginin und sein anhydrid. *Ber. Dtsch. Chem. Ges.*, 62:1905-9.

With Max Bergmann and Leonidas Zervas. Acylwanderung und spaltungsvorgänge bei acylierten dioxo-piperazinen. Ber. Dtsch. Chem. Ges., 62:1909-13.

1930

With Leonore Hollander. The resolution of inactive cystine. Proc. Soc. Exp. Biol. Med., 28:46-47.

With L. F. Audrieth and H. S. Loring. The reduction of cystine in liquid ammonia by metallic sodium. J. Am. Chem. Soc., 52:4500-4504.

1931

With Hubert S. Loring. The isolation of two isomeric inactive cystines. Proc. Soc. Exp. Biol. Med., 29:41-42.

With Alice Fitch, E. Pekarek, and W. W. Lockwood. The inactivation of crystalline insulin by cysteine and glutathione. J. Biol. Chem., 94:233-42.

With Leonore Hollander. The resolution of inactive cystine and isolation of pure dextrorotatory cystine. J. Biol. Chem., 94:243-52.

1932

With Curtis E. Meyer. Isolation of methionine by enzymatic hydrolysis. J. Biol. Chem., 94:641-45.

With Robert Ridgely Sealock. The racemization of acetyl-tryptophane. J. Biol. Chem., 96:511-17.

With Curtis E. Meyer. The racemization of amino acids in aqueous solution by acetic anhydride. J. Biol. Chem., 98:295-308.

With Robert Ridgely Sealock and Cecil Van Etten. Availability of d-tryptophane and its acetyl derivative to the animal body. J. Biol. Chem., 98:565-75.

With Ralph Dorfmann and Hubert S. Loring. A comparison of the growth-promoting properties of *d*- and *l*-cystine. J. Biol. Chem., 98:577-89.

With Curtis E. Meyer. The temporary formation of the azlactone ring in the racemization of acyl derivatives of amino acids with acetic anhydride. J. Biol. Chem., 99:143-51.

With Lewis W. Butz. The formation of a homologue of cystine by the decomposition of methionine with sulfuric acid. J. Biol. Chem., 99:135-42.



## 1933

- With Helen M. Dyer and J. Harmon. The growth-promoting properties of homocystine when added to a cystine-deficient diet and proof of structure of homocystine. *J. Biol. Chem.*, 101:719-26.
- With Hubert S. Loring. The isolation and characterization of mesocystine. *J. Biol. Chem.*, 102:287-95.
- With Robert H. Sifferd and Robert R. Sealock. The heat precipitation of insulin. *J. Biol. Chem.*, 102:521-33.
- With Hubert S. Loring and Ralph Dorfmann. The availability of mesocystine for promotion of growth in connection with cystine-deficient diets. *J. Biol. Chem.*, 103:399-403.

## 1934

- With Harold A. Craft and Hubert S. Loring. The oxidation of the stereoisomers of cystine in the animal body. *J. Biol. Chem.*, 104:81-89.
- Insulin and diabetes. *Sci. Mon.*, 38:565-68.
- With Hubert S. Loring and Harold A. Craft. The oxidation of the sulfur of homocystine, methionine and S-methylcysteine in the animal body. *J. Biol. Chem.*, 105:481-88.
- With Helen M. Dyer, Chase B. Jones, and Wilbur I. Patterson. The synthesis of pentocystine and homomethionine. *J. Biol. Chem.*, 106:401-7.
- With Hubert S. Loring. The solubility of the stereoisomers of cystine with a note on the identity of stone and hair cystine. *J. Biol. Chem.*, 107:267-74.
- With Hubert S. Loring and Harold A. Craft. The oxidation of the sulfur of the acetyl and formyl derivatives of *d*- and *l*-cystine in the animal body. *J. Biol. Chem.*, 107:519-25.
- With Robert H. Sifferd. Oxidation of cystine sulfur to sulfate by ferric chloride. *Proc. Soc. Exp. Biol. Med.*, 32:332-33.

## 1935

- With Helen M. Dyer. A study of the physiological availability of pentocystine and homomethionine. *J. Biol. Chem.*, 108:73-78.
- The chemistry of hormones from a structural standpoint. *Sci. Mon.*, 40:138-45.
- With Robert H. Sifferd. A new synthesis of carnosine, with some observations on the splitting of the benzyl group from carbo-

- benzoxy derivatives and from benzylthio ethers. *J. Biol. Chem.*, 108:753-61.
- With Wilbur I. Patterson. The preparation of the optically active isomers of homocystine and the demonstration of their configurational relationship to naturally occurring methionine. *J. Biol. Chem.*, 109:97-103.
- With Helen M. Dyer. A study of the availability of *d*- and *l*-homocystine for growth purposes. *J. Biol. Chem.*, 109:477-80.
- With Robert Ridgely Sealock. Studies on the reduction of pitressin and pitocin with cysteine. *J. Pharmacol. Exp. Ther.*, 54:433-47.
- With Hubert S. Loring. The synthesis of crystalline cystinylglycine and benzylcysteinylglycine and their isolation from glutathione. *J. Biol. Chem.*, 111:385-92.
- With Wilbur I. Patterson. The synthesis of homocystine. *J. Biol. Chem.*, 111:393-98.
- With Byron Riegel. The isolation of homocysteine and its conversion to a thiolactone. *J. Biol. Chem.*, 112:149-54.
- With Robert H. Sifferd and Gail Miller. On the absence of thiohistidine in insulin. *Proc. Soc. Exp. Biol. Med.*, 33:371-73.

## 1936

- With Robert Ridgely Sealock and Cecil Van Etten. The question of the utilization of tryptophane administered subcutaneously. *J. Biol. Chem.*, 112:451-56.
- With Helen M. Dyer. The chemistry and metabolism of compounds of sulfur. *Annu. Rev. Biochem.*, 5:159-80.
- With Wilbur I. Patterson. The synthesis of djenkolic acid. *J. Biol. Chem.*, 114:533-38.
- With Madison Hunt. The synthesis of *d*-carnosine, the enantiomorph of the naturally occurring form, and a study of its depressor effect on the blood pressure. *J. Biol. Chem.*, 115:93-100.
- With Helen M. Dyer. The utilization of glutathione in connection with a cystine-deficient diet. *J. Biol. Chem.*, 115:543-49.
- With Wilbur I. Patterson and Helen M. Dyer. The synthesis of Di-N-methylhomocystine and N-methylmethionine and a study of their growth-promoting ability in connection with a cystine-deficient diet. *J. Biol. Chem.*, 116:277-84.
- With Gail Lorenz Miller. A synthesis of glutathione. *J. Biol. Chem.*, 116:469-76.

1937

With Otto K. Behrens. A method for protecting the imidazole ring of histidine during certain reactions and its application to the preparation of *l*-amino-N-methylhistidine. *J. Biol. Chem.*, 117:27-36.

The cancer symposium of the medical sciences section. *Science*, 84:439-40.

With Robert H. Sifferd and George W. Irving, Jr. The utilization of *l*-carnosine by animals on a histidine-deficient diet. *J. Biol. Chem.*, 117:589-97.

With Gail Lorenz Miller. The cystine content of insulin. *J. Biol. Chem.*, 118:101-10.

With Hubert S. Loring and Gail Lorenz Miller. The synthesis of  $\alpha$ -glutamylcysteinylglycine (isoglutathione). *J. Biol. Chem.*, 118:391-95.

With Helen M. Dyer. The chemistry and metabolism of the compounds of sulfur. *Annu. Rev. Biochem.*, 6:193-210.

With Helen M. Dyer and Chase Breese Jones. Studies of the physiological behavior of the acetyl derivatives of the optical isomers of homocystine; a biological proof of their stereostructure. *J. Biol. Chem.*, 119:47-57.

Some aspects of the study of insulin. *J. Wash. Acad. Sci.*, 27:365.

With Chase Breese Jones. The synthesis of hexocystine and hexomethionine and a study of their physiological availability. *J. Biol. Chem.*, 120:11-20.

With Otto K. Behrens. The synthesis of anserine from *l*-1-methylhistidine. *J. Biol. Chem.*, 120:517-22.

With William T. McClosky, Lloyd C. Miller, and Madison Hunt. On the alleged oxytocic activity of *l*-carnosine. *Proc. Soc. Exp. Biol. Med.*, 37:60-61.

1938

With Oliver J. Irish. The role of the acetyl derivative as an intermediary stage in the biological synthesis of amino acids from keto acids. *J. Biol. Chem.*, 122:349-70.

With George W. Irving, Jr., Helen M. Dyer, and Robert Ridgely Sealock. Electrophoresis of posterior pituitary gland preparations. *J. Biol. Chem.*, 123:45-55.

With Wilbur I. Patterson. The synthesis of tetradeuterohomocystine and dideuteromethionine. *J. Biol. Chem.*, 123:327-34.

- With George W. Irving, Jr. The differential migration of the pressor and oxytocic hormones in electrophoretic studies of the untreated press-juice of the posterior lobe of the pituitary gland. *J. Biol. Chem.*, 123:485-89.
- With Madison Hunt. The preparation of *d*-alanyl-*l*-histidine and *l*-alanyl-*l*-histidine and an investigation of their effect on the blood pressure in comparison with *l*-carnosine. *J. Biol. Chem.*, 124:699-709.
- A brief review of studies on homocystine. *Nucleus*, January.
- With Madison Hunt. A preliminary study of  $\beta$ -*l*-aspartyl-*l*-histidine as a possible precursor of *l*-carnosine. *J. Biol. Chem.*, 125:269-74.
- With Wilbur I. Patterson and Madison Hunt. Opening of the ring of the thiolactone of homocysteine. *J. Biol. Chem.*, 126:217-31.
- The role which insulin has played in our concept of protein hormones, and a consideration of certain phases of the chemistry of insulin. *Cold Spring Harbor Symp. Quant. Biol.*, 6:275-85.
- Earl Baldwin McKinley. *Science*, 88:344-45.

1939

- With Madison Hunt. The synthesis of the next higher and lower homologues of *l*-carnosine:  $\gamma$ -Aminobutyryl-*l*-histidine and glycyl-*l*-histidine. *J. Biol. Chem.*, 127:43-48.
- With Otto K. Behrens. Carnosine and anserine. *Ergebnisse der Physiol. Biol. Chem. Exp. Pharmacol.*, 41:917.
- With Madison Hunt. A further contribution on the relationship of the structure of *l*-carnosine to its depressor activity. *J. Biol. Chem.*, 127:727-35.
- With Marian Wood Kies, Helen M. Dyer, and John L. Wood. A study of the utilization of the optical isomers of N,N'-Dimethylcystine. *J. Biol. Chem.*, 128:207-16.
- With Joseph P. Chandler, A. W. Moyer, and Dorothy M. Keppel. The ability of homocystine plus choline to support growth of the white rat on a methionine-free diet. *J. Biol. Chem.*, 128:cviii.
- With John L. Wood and Oliver J. Irish. The optical inversion of the benzyl derivatives of *d*-cysteine and *d*-homocysteine in vivo. *J. Biol. Chem.*, 129:171-77.
- With John L. Wood. Racemization of benzyl-*l*-cysteine, with a new method of preparing *d*-cystine. *J. Biol. Chem.*, 130:109-14.

- With Helen M. Dyer and Marian Wood Kies. A relationship between the nature of the vitamin B complex supplement and the ability of homocystine to replace methionine in the diet. *J. Biol. Chem.*, 130:325-40.
- With Joseph P. Chandler, A. W. Moyer, and Dorothy M. Keppel. The effect of choline on the ability of homocystine to replace methionine in the diet. *J. Biol. Chem.*, 131:57-76.
- With John L. Wood. A new synthesis of cystine. *J. Biol. Chem.*, 131:267-71.
- With Mildred Cohn, George Bosworth Brown, Oliver J. Irish, Rudolph Schoenheimer, and D. Rittenberg. A study of the inversion of *d*-phenylaminobutyric acid and the acetylation of *l*-phenyl-aminobutyric acid by means of the isotopes of nitrogen and hydrogen. *J. Biol. Chem.*, 131:273-96.
- With Gail Lorenz Miller and Clement J. Rodden. On the question of the presence of methionine in insulin. *J. Biol. Chem.*, 131:631-40.

## 1940

- With Paul György, Donald B. Melville, and Dean Burk. The possible identity of vitamin H with biotin and coenzyme R. *Science*, 91:243-45.
- With John L. Wood. On the synthesis of serine. *J. Biol. Chem.*, 134:413-16.
- With George W. Irving, Jr. A simple laboratory method for obtaining preparations containing pressor and oxytocic activity from the posterior lobe of the pituitary gland. *J. Am. Chem. Soc.*, 62:2080-82.
- With Joseph P. Chandler. The comparative action of choline and betaine in effecting the replacement of methionine by homocystine in the diet. *J. Biol. Chem.*, 135:223-29.
- With Joseph P. Chandler, Mildred Cohn, and George Bosworth Brown. The transfer of the methyl group from methionine to choline and creatine. *J. Biol. Chem.*, 134:787-88.
- With Donald B. Melville, Paul György, and Catherine S. Rose. On the identity of vitamin H with biotin. *Science*, 92:62-63.
- With Paul György, Catherine S. Rose, Klaus Hofmann, and Donald B. Melville. A further note on the identity of vitamin H with biotin. *Science*, 92:609.

1941

- With Mildred Cohn and George W. Irving, Jr. The amphoteric nature of the pressor principle of the posterior lobe of the pituitary gland. *J. Biol. Chem.*, 137:635-42.
- With George Bosworth Brown. The synthesis of S-( $\beta$ -amino- $\beta$ -carboxyethyl)-homocysteine. *J. Biol. Chem.*, 137:611-15.
- With George W. Irving, Jr., and Helen M. Dyer. Purification of the pressor principle of the posterior lobe of the pituitary gland by electrophoresis. *J. Am. Chem. Soc.*, 63:503-6.
- With John L. Wood and Francis Binkley. Acetylation in vivo of *p*-bromophenyl-*d*-cysteine. *J. Biol. Chem.*, 138:369-74.
- With George Bosworth Brown. The synthesis of the new sulfur-containing amino acid (lanthionine) isolated from sodium-carbonate treated wool. *J. Biol. Chem.*, 138:151-54.
- With Joseph P. Chandler and A. W. Moyer. The inability of creatine and creatinine to enter into transmethylation in vivo. *J. Biol. Chem.*, 139:917-23.
- With Dean Burk and Richard J. Winzler. The role of biotin in fermentation and the Pasteur effect. *J. Biol. Chem.*, 140:xxi-xxii.
- With Gail Lorenz Miller and Otto K. Behrens. A synthesis of the aspartic acid analogue of glutathion (asparthione). *J. Biol. Chem.*, 140:411-16.
- With Mildred Cohn, Joseph P. Chandler, Jay R. Schenck, and Sofia Simmonds. The utilization of the methyl group of methionine in the biological synthesis of choline and creatine. *J. Biol. Chem.*, 140:625-41.
- With Klaus Hofmann, Donald B. Melville, and Paul György. Isolation of biotin (vitamin H) from liver. *J. Biol. Chem.*, 140:643-51.
- With George Bosworth Brown. The stereoisomeric forms of lanthionine. *J. Biol. Chem.*, 140:767-71.
- With Klaus Hofmann, Donald B. Melville, and Julian R. Rachele. The preparation of free crystalline biotin. *J. Biol. Chem.*, 140:763-66.
- With George Bosworth Brown. The effect of certain reagents on the activity of biotin. *J. Biol. Chem.*, 141:85-89.
- With Klaus Hofmann and Donald B. Melville. Characterization of the functional groups of biotin. *J. Biol. Chem.*, 141:207-14.

- With Donald B. Melville and Klaus Hofmann. Resynthesis of biotin from a degradation product. *Science*, 94:308-9.
- Interrelationships between choline and other methylated compounds. *Biol. Symp.*, 5:234-47.
- With George Bosworth Brown and Roy W. Bonsnes. The formation of lanthionine on treatment of insulin with dilute alkali. *J. Biol. Chem.*, 141:707-8.
- With Klaus Hofmann and Donald B. Melville. Formation of adipic acid by oxidative degradation of diaminocarboxylic acid derived from biotin. *J. Am. Chem. Soc.*, 63:3237-38.

## 1942

- Biotin. In: *Biological Action of the Vitamins*, p. 44. Chicago: University of Chicago Press.
- With Donald B. Melville, Klaus Hofmann, and Eleanor Hague. The isolation of biotin from milk. *J. Biol. Chem.*, 142:615-18.
- With Klaus Hofmann and Donald B. Melville. On the structure of biotin. *J. Am. Chem. Soc.*, 64:188-89.
- With George Bosworth Brown and Joseph P. Chandler. The synthesis of *l*-S-( $\beta$ -amino- $\beta$ -carboxyethyl)-homocysteine and the replacement by it of cystine in the diet. *J. Biol. Chem.*, 143:59-64.
- With A. W. Moyer. The structural specificity of choline and betaine in transmethylation. *J. Biol. Chem.*, 143:373-82.
- With Juliet Spangler, Dean Burk, Charles Kensler, K. Sugiura, and C. P. Roads. The procarcinogenic effect of biotin in butter yellow tumor formation. *Science*, 95:174-76.
- With Francis Binkley and William P. Anslow, Jr. The formation of cysteine from *l*-S-( $\beta$ -amino- $\beta$ -carboxyethyl)-homocysteine by liver tissue. *J. Biol. Chem.*, 143:559-60.
- With Klaus Hofmann and Donald B. Melville. Adipic acid as an oxidation product of diaminocarboxylic acid derived from biotin. *J. Biol. Chem.*, 144:513-18.
- With Francis Binkley. The formation of cysteine from homocysteine and serine by liver tissue of rats. *J. Biol. Chem.*, 144:507-11.
- The relationship of the chemist to medicine. *J. Am. Med. Assoc.*, 119:207-8.

- With Karl Dittmer, Klaus Hofmann, and Donald B. Melville. Yeast-growth-promoting effect of diaminocarboxylic acid derived from biotin. *Proc. Soc. Exp. Biol. Med.*, 50:374-75.
- With Donald B. Melville and Klaus Hofmann. The hydrolysis of biotin sulfone. *J. Biol. Chem.*, 145:101-5.
- With Karl Dittmer, Eleanor Hague, and Barbara Long. The growth-stimulating effect of biotin for the diphtheria bacillus in the absence of pimelic acid. *Science*, 96:186-87.
- With Glen W. Kilmer, Marvin D. Armstrong, and George Bosworth Brown. Synthesis of a 3,4-diaminotetrahydrothiophene and a comparison of its stability with the diaminocarboxylic acid derived from biotin. *J. Biol. Chem.*, 145:495-501.
- With Klaus Hofmann, Glen W. Kilmer, Donald B. Melville, and Hugh H. Darby. The condensation of phenanthraquinone with the diaminocarboxylic acid derived from biotin. *J. Biol. Chem.*, 145:503-9.
- With Donald B. Melville, Karl Folkers, Donald E. Wolf, Ralph Mzingo, John C. Keresztesy, and Stanton A. Harris. The structure of biotin: A study of desthiobiotin. *J. Biol. Chem.*, 146:475-85.
- With Donald B. Melville, A. W. Moyer, and Klaus Hofmann. The structure of biotin: The formation of thiophenevaleric acid from biotin. *J. Biol. Chem.*, 146:487-92.
- The structure of biotin. *Science*, 96:455-61.
- With Sofia Simmonds. Transmethylation as a metabolic process in man. *J. Biol. Chem.*, 146:685-86.
- The significance of the labile methyl groups in the diet and their relation to transmethylation. *Harvey Lect.*, 38:39-62.

## 1943

- With George W. Irving, Jr. Hormones of the posterior lobe of the pituitary gland. *Ann. N.Y. Acad. Sci.*, 43:273-307.
- With Jay R. Schenck, Sofia Simmonds, Mildred Cohn, and Carl M. Stevens. The relation of transmethylation to anserine. *J. Biol. Chem.*, 149:355-59.
- With Sofia Simmonds, Mildred Cohn, and Joseph P. Chandler. The utilization of the methyl groups of choline in the biological synthesis of methionine. *J. Biol. Chem.*, 149:519-25.
- With Donald B. Melville, Karl Dittmer, and George Bosworth Brown. Desthiobiotin. *Science*, 98:497-99.



With C. J. Kensler, C. Wadsworth, K. Sugiura, C. P. Rhoads, and Karl Dittmer. The influence of egg white and avidin feeding on tumor growth. *Cancer Res.*, 3:823-24.

1944

With Francis Binkley and John L. Wood. A study of the acetylation in vivo of certain *d*-amino acids. *J. Biol. Chem.*, 153:495-500.

With Karl Dittmer and Donald Melville. The possible synthesis of biotin from desthiobiotin by yeast and the antibiotic effect of desthiobiotin for *L. casei*. *Science*, 99:203-5.

With Jay R. Schenck. A study of the synthesis of  $\beta$ -alanine in the white rat. *J. Biol. Chem.*, 153:501-5.

With Karl Dittmer, Paul György, and Catharine S. Rose. A study of biotin sulfone. *Arch. Biochem.*, 4:229-42.

With Glen W. Kilmer. A synthesis of methionine containing isotopic carbon and sulfur. *J. Biol. Chem.*, 154:247-53.

With Richard J. Winzler and Dean Burk. Biotin in fermentation, respiration, growth and nitrogen assimilation by yeast. *Arch. Biochem.*, 5:25-47.

With Karl Dittmer. Antibiotins. *Science*, 100:129-31.

With Glen W. Kilmer, Julian R. Rachele, and Mildred Cohn. On the mechanism of the conversion in vivo of methionine to cystine. *J. Biol. Chem.*, 155:645-51.

1945

With John L. Wood. The synthesis of optically inactive desthiobiotin. *J. Am. Chem. Soc.*, 67:210-12.

The relationship of structure to biotin and antibiotin activity. (Nichols Medal Lecture). *Chem. Eng. News.*, 23:623-25.

With Herbert McKennis, Jr., Sofia Simmonds, Karl Dittmer, and George Bosworth Brown. The inhibitions of the growth of yeast by thienylalanine. *J. Biol. Chem.*, 159:385-94.

With Sachchidananda Banerjee and Karl Dittmer. A microbiological and fluorometric test for minute amounts of alloxan. *Science*, 101:647-49.

With Sofia Simmonds. A further study of the lability of the methyl group of creatine. *Proc. Soc. Exp. Biol. Med.*, 59:293-94.

With Sofia Simmonds, Joseph P. Chandler, and Mildred Cohn. Synthesis of labile methyl groups in the white rat. *J. Biol. Chem.*, 159:755-56.

Protein chemistry and medicine. *Science*, 102:24–25.  
The role of methionine in the metabolism of the body. In: "The Doctors Talk it Over" Series, November 27, 1945.

1946

- With Mildred Cohn, Sofia Simmonds, and Joseph P. Chandler. The effect of the dietary level of methionine on the rate of transmethylation reactions in vivo. *J. Biol. Chem.*, 162:343–51.
- Scientific contributions of the medalist—Wendell M. Stanley Nichols Medal Award, 1946. *Chem. Eng. News*, 24:752–55.
- With Herbert McKennis, Jr. The synthesis of homodesthiobiotin and related compounds. *J. Am. Chem. Soc.*, 68:832–35.
- With George Bosworth Brown. The thiourea analogue of desthiobiotin. *J. Biol. Chem.*, 163:761–66.
- With Karl Dittmer and Martha F. Ferger. Synthesis of imidazolidone aliphatic acids. *J. Biol. Chem.*, 164:19–28.
- With Joseph P. Chandler, Sofia Simmonds, A. W. Moyer, and Mildred Cohn. The role of dimethyl- and monomethylaminoethanol in transmethylation reactions in vivo. *J. Biol. Chem.*, 164:603–13.
- With Karl Dittmer, Glenn Ellis, and Herbert McKennis, Jr. The effect of amino acids on the microbial growth inhibition produced by thienylalanine. *J. Biol. Chem.*, 164:761–71.
- With John L. Wood. A note on the conversion in vivo of the S-benzyl-N-methyl derivatives of cysteine and homocysteine to the N-acetyl-S-benzyl derivatives of cysteine and homocysteine. *J. Biol. Chem.*, 165:95–96.
- With Sofia Simmonds, Joseph P. Chandler, and Mildred Cohn. A further investigation of the role of betaine in transmethylation reactions in vivo. *J. Biol. Chem.*, 165:639–48.
- With Frederick H. Carpenter, Robert W. Holley, Arthur H. Livermore, and Julian R. Rachele. Synthetic penicillin. *Science*, 104:431–33.
- With Sofia Simmonds and Mildred Cohn. A further investigation of the ability of sarcosine to serve as a labile methyl donor. *J. Biol. Chem.*, 166:47–52.
- With William P. Anslow, Jr., and Sofia Simmonds. The synthesis of the isomers of cystathionine and a study of their availability in sulfur metabolism. *J. Biol. Chem.*, 166:35–45.

1947

- With Marvin D. Armstrong. A new synthesis of djenkolic acid. *J. Biol. Chem.*, 168:373-77.
- With Lyman C. Craig, George H. Hogeboom, and Frederick H. Carpenter. Separation and characterization of some penicillins by the method of counter-current distribution. *J. Biol. Chem.*, 168:665-86.
- With Karl H. Dittmer. Antibiotin activity of imidazolidone aliphatic acids. *J. Biol. Chem.*, 169:63-70.
- With Cosmo G. Mackenzie, Joseph P. Chandler, Elizabeth B. Keller, Julian R. Rachele, Nancy Cross, and Donald B. Melville. The demonstration of the oxidation in vivo of the methyl group of methionine. *J. Biol. Chem.*, 169:757-58.
- With William P. Anslow, Jr. The cleavage of the stereoisomers of cystathionine by liver extract. *J. Biol. Chem.*, 170:245-50.
- With Sofia Simmonds and Mildred Cohn. A study on transmethylation with methionine containing varying amounts of deuterium in the methyl group. *J. Biol. Chem.*, 170:631-33.
- With Carl M. Stevens. Preparation of highly purified mustard gas and its action on yeast. *J. Am. Chem. Soc.*, 69:1808-9.
- With Joseph P. Chandler, Martha W. Gerrard, and W. M. Stanley. The utilization for animal growth of tobacco mosaic virus as a sole source of protein in the diet. *J. Biol. Chem.*, 171:823-28.

1948

- With Cosmo G. Mackenzie. The source of urea carbon. *J. Biol. Chem.*, 172:353-54.
- With Elizabeth B. Keller and John L. Wood. An investigation of transmethylation from N<sup>1</sup>-methylnicotinamide. *Proc. Soc. Exp. Biol. Med.*, 67:182-84.
- With Marvin D. Armstrong. Mercaptals and mercaptoles of cysteine. *J. Biol. Chem.*, 173:749-51.
- With Cosmo G. Mackenzie, Julian R. Rachele, Nancy Cross, and Joseph P. Chandler. Study of the oxidation of the labile methyl group of dietary methionine traced with C<sup>14</sup>. *Fed. Proc. Fed. Am. Soc. Exp. Biol.*, 7(1):170.
- With Martha F. Ferger. The microbial growth inhibition produced by optical isomers of  $\beta$ -2-thienylalanine. *J. Biol. Chem.*, 174:241-46.

- With George A. Maw. Dimethyl- $\beta$ -propiothetin, a new methyl donor. *J. Biol. Chem.*, 174:381-82.
- An illustration of the power of isotopes in a biochemical problem. *U.S. Nav. Med. Bull.*, 48, Suppl. 176.
- With John Eric Wilson. L-penicillamine as a metabolic antagonist. *Science*, 107:653.
- With A. W. Moyer and Joseph P. Chandler. Dimethylthetin as a biological methyl donor. *J. Biol. Chem.*, 174:477-80.
- With Carl M. Stevens, Harold F. McDuffie, Jr., John L. Wood, and Herbert McKennis, Jr. Reactions of mustard-type vesicants with alpha-amino acids. *J. Am. Chem. Soc.*, 70:1620-24.
- With Robert Holley, Frederick H. Carpenter, and Arthur H. Livermore. A synthesis of benzylpenillic acid. *Science*, 108:136-37.
- With Arthur H. Livermore, Frederick H. Carpenter, and Robert W. Holley. Studies on crystalline DL-benzylpenicillenic acid. *J. Biol. Chem.*, 175:721-26.
- Migration of the methyl group on the body. *Proc. Am. Philos. Soc.*, 92:127-35.
- With John L. Wood, Julian R. Rachele, Carl M. Stevens, and Frederick H. Carpenter. The reaction of some radioactive mustard-type vesicants with purified proteins. *J. Am. Chem. Soc.*, 70:2547-50.
- With Frederick H. Carpenter, John L. Wood, and Carl M. Stevens. Chemical studies on vesicant-treated proteins. *J. Am. Chem. Soc.*, 70:2551-53.
- With Carl M. Stevens, John L. Wood, and Julian R. Rachele. Studies on acid hydrolysates of vesicant-treated insulin. *J. Am. Chem. Soc.*, 70:2554-56.
- With Carl M. Stevens and Herbert McKennis, Jr. Studies of the effect of mustard-type vesicants on the phenol color reaction of proteins. *J. Am. Chem. Soc.*, 70:2556-59.
- With Frederick H. Carpenter and Robert A. Turner. Benzylpenicillenic acid as an intermediate in the synthesis of benzylpenicillin (penicillin G). *J. Biol. Chem.*, 176:893-905.
- With Gardner W. Stacy and D. Todd. The synthesis of DL- $\beta$ , $\beta$ -diethylcysteine and DL- $\beta$ -ethyl- $\beta$ -methylcysteine. *J. Biol. Chem.*, 176:907-14.
- With Frederick H. Carpenter, Gardner W. Stacy, Dorothy S. Genghof, and Arthur H. Livermore. The preparation and an-

tibacterial properties of the crude sodium salts of some synthetic penicillins. *J. Biol. Chem.*, 176:915–27.

With George A. Maw. An investigation of the biological behavior of the sulfur analogue of choline. *J. Biol. Chem.*, 176:1029–36.

With George A. Maw. Compounds related to dimethylthetin as sources of labile methyl groups. *J. Biol. Chem.*, 176:1037–45.

## 1949

With Donald B. Melville. The thiocyanate derivative of benzylpenicillin methyl ester. In: *The Chemistry of Penicillin*, ed. Hans T. Clarke, John R. Johnson, and Sir Robert Robinson, pp. 269–309. Princeton: Princeton University Press.

With J. L. Wood and M. E. Wright. The condensation of oxazolones and d-penicillamine and the resultant antibiotic activity. In: *The Chemistry of Penicillin*, ed. Hans T. Clarke, John R. Johnson, and Sir Robert Robinson, pp. 892–908. Princeton: Princeton University Press.

With Frederick H. Carpenter. The  $\gamma$ -lactam of benzylhomopenicilloic acid and related compounds. In: *The Chemistry of Penicillin*, ed. Hans T. Clarke, John R. Johnson, and Sir Robert Robinson, pp. 1004–17. Princeton: Princeton University Press.

With Frederick H. Carpenter, Robert W. Holley, Arthur H. Livermore, and Julian R. Rachele. Synthetic benzylpenicillin. In: *The Chemistry of Penicillin*, ed. Hans T. Clarke, John R. Johnson, and Sir Robert Robinson, pp. 1018–24. Princeton: Princeton University Press.

With Elizabeth B. Keller and Julian R. Rachele. A study of transmethylation with methionine containing deuterium and carbon 14 in the methyl group. *J. Biol. Chem.*, 177:733–38.

With Cosmo G. Mackenzie. Formation of formaldehyde in the biological oxidation of the methyl group of sarcosine. *Fed. Proc. Fed. Am. Soc. Exp. Biol.*, 8:223.

With Martha A. Ferger. The antiphenylalanine effect of  $\beta$ -2-thienylalanine for the rat. *J. Biol. Chem.*, 179:61–65.

With Cosmo G. Mackenzie, Joseph P. Chandler, Elizabeth B. Keller, Julian R. Rachele, and Nancy Cross. The oxidation and distribution of the methyl group administered as methionine. *J. Biol. Chem.*, 180:99–111.

With Arthur H. Livermore. Preparation of high potency oxytocic

- material by the use of counter-current distribution. *J. Biol. Chem.*, 180:365-73.
- With William R. Carroll and Gardner W. Stacy.  $\alpha$ -Ketobutyric acid as a product in the enzymatic cleavage of cystathionine. *J. Biol. Chem.*, 180:375-82.
- With Lester J. Reed and A. R. Kidwai. Preparation of the optically active isomers of S-benzylhomocysteine by enzymatic resolution. *J. Biol. Chem.*, 180:571-74.
- With Lester J. Reed, Dorian Cavallini, Fred Plum, and Julian R. Rachele. The conversion of methionine to cystine in a human cystinuric. *J. Biol. Chem.*, 180:783-90.
- With Roger A. Boissonnas and Robert A. Turner. Metabolic study of the methyl groups of butter yellow. *J. Biol. Chem.*, 180:1053-58.

1950

- With John G. Pierce. Preliminary studies on the amino acid content of a high potency preparation of the oxytocic hormone of the posterior lobe of the pituitary gland. *J. Biol. Chem.*, 182:359-66.
- With Sofia Simmonds, Elizabeth B. Keller, and Joseph P. Chandler. The effect of ethionine on transmethylation from methionine to choline and creatine in vivo. *J. Biol. Chem.*, 183:191-95.
- With Walter G. Verly. Incorporation in vivo of  $C^{14}$  from labeled methanol into the methyl groups of choline. *J. Am. Chem. Soc.*, 72:1049.
- With Cosmo G. Mackenzie, Julian R. Rachele, Nancy Cross, and Joseph P. Chandler. A study of the rate of oxidation of the methyl group of dietary methionine. *J. Biol. Chem.*, 183:617-26.
- With Elizabeth B. Keller and Robert A. Boissonnas. The origin of the methyl group of epinephrine. *J. Biol. Chem.*, 183:627-32.
- With John E. Wilson. Inhibition of the growth of the rat by L-penicillamine and its prevention by aminoethanol and related compounds. *J. Biol. Chem.*, 184:63-70.
- With Martha F. Ferger. Oxidation in vivo of the methyl groups of choline, betaine, dimethylthetin, and dimethyl- $\beta$ -propiothetin. *J. Biol. Chem.*, 185:53-57.
- With Cosmo G. Mackenzie. Biochemical stability of the methyl group of creatine and creatinine. *J. Biol. Chem.*, 185:185-89.

- With Walter G. Verly and John Eric Wilson. Incorporation of the carbon of formaldehyde and formate into the methyl groups of choline. *J. Am. Chem. Soc.*, 72:2819–20.
- With Julian R. Rachele, Lester J. Reed, A. R. Kidwai, and Martha F. Ferger. Conversion of cystathionine labeled with  $S^{35}$  to cystine in vivo. *J. Biol. Chem.*, 185:817–26.
- With John G. Pierce. Studies on high potency oxytocic material from beef posterior pituitary lobes. *J. Biol. Chem.*, 186:77–84.
- With Charlotte Ressler and Julian R. Rachele. The biological synthesis of "labile methyl groups." *Science*, 112:267–71.

## 1951

- With Robert A. Turner and John G. Pierce. Purification and amino acid content of pressor principle (vasopressin) of posterior lobe of the pituitary. *Fed. Proc. Fed. Am. Soc. Exp. Biol.*, 10:261.
- With Walter G. L. Verly, John E. Wilson, Julian R. Rachele, Charlotte Ressler, and John M. Kinney. One-carbon compounds in the biosynthesis of the "biologically labile" methyl group. *J. Am. Chem. Soc.*, 73:2782–85.
- With Robert A. Turner and John G. Pierce. The purification and the amino acid content of vasopressin preparation. *J. Biol. Chem.*, 191:21–28.
- With Johannes M. Mueller, John G. Pierce, and Helen Davoll. The oxidation of oxytocin with performic acid. *J. Biol. Chem.*, 191:309–13.
- With Charlotte Ressler, Julian R. Rachele, James A. Reyniers, and Thomas D. Luckey. The synthesis of "biologically labile" methyl groups in the germ-free rat. *J. Nutr.*, 45:361–76.
- With Robert A. Turner and John G. Pierce. The desulfurization of oxytocin. *J. Biol. Chem.*, 193:359–61.
- With Helen Davoll, Robert A. Turner, and John G. Pierce. An investigation of the free amino groups in oxytocin and desulfurized oxytocin preparations. *J. Biol. Chem.*, 193:363–70.

## 1952

- With Cosmo G. Mackenzie. The effect of choline and cystine on the oxidation of the methyl group of methionine. *J. Biol. Chem.*, 195:487–91.
- With Walter G. Verly and John M. Kinney. Effect of folic acid and

- leucovorin on synthesis of the labile methyl group from methanol in the rat. *J. Biol. Chem.*, 196:19–23.
- With Charlotte Ressler and Julian R. Rachele. Studies in vivo on labile methyl synthesis with deuterio-C<sup>14</sup>-formate. *J. Biol. Chem.*, 197:1–5.
- With Edwin A. Popenoe and H. Claire Lawler. Partial purification and amino acid content of vasopressin from hog posterior pituitary glands. *J. Am. Chem. Soc.*, 74:3713.
- With Edwin A. Popenoe, John G. Pierce, and H. B. van Dyke. Oxytocic activity of purified vasopressin. *Proc. Soc. Exp. Biol. Med.*, 81:506–8.
- With John G. Pierce and Samuel Gordon. Further distribution studies on the oxytocic hormone of the posterior lobe of the pituitary gland and the preparation of an active crystalline flavanate. *J. Biol. Chem.*, 199:929–40.
- With Walter G. Verly, Julian R. Rachele, Maxwell L. Eidinoff, and Joseph E. Knoll. A test of tritium as a labeling device in a biological study. *J. Am. Chem. Soc.*, 74:5941–43.

## 1953

- With Henry G. Kunkel and Sterling P. Taylor, Jr. Electrophoretic properties of oxytocin. *J. Biol. Chem.*, 200:559–64.
- With Sterling P. Taylor, Jr., and Henry G. Kunkel. Electrophoretic studies of oxytocin and vasopressin. *Fed. Proc. Fed. Am. Soc. Exp. Biol.*, 12:279–80.
- With John M. Kinney, John E. Wilson, and Julian R. Rachele. Effect of the presence of labile methyl groups in the diet on labile methyl neogenesis. *Biochim. Biophys. Acta*, 12:88–91.
- With Johannes Mueller and John G. Pierce. Treatment of performic acid-oxidized oxytocin with bromine water. *J. Biol. Chem.*, 204:857–60.
- With Charlotte Ressler and Stuart Trippett. Free amino groups of performic acid-oxidized oxytocin and its cleavage products formed by treatment with bromine water. *J. Biol. Chem.*, 204:861–69.
- With Carleton W. Roberts. The synthesis of  $\beta$ -sulfo-L-alanyl-L-tyrosine and L-tyrosyl-L-cysteic acid and their dibromotyrosyl analogues. *J. Biol. Chem.*, 204:871–75.
- With Charlotte Ressler, John M. Swan, Carleton W. Roberts, Pan-



- ayotis G. Katsoyannis, and Samuel Gordon. The synthesis of an octapeptide amide with the hormonal activity of oxytocin. *J. Am. Chem. Soc.*, 75:4879–80.
- With H. Claire Lawler and Edwin A. Popenoe. Enzymatic cleavage of glycinamide from vasopressin and a proposed structure for this pressor-antidiuretic hormone of the posterior pituitary. *J. Am. Chem. Soc.*, 75:4880–81.
- With H. Claire Lawler. Enzymatic evidence for the intrinsic oxytocic activity of the pressor-antidiuretic hormone. *Proc. Soc. Exp. Biol. Med.*, 84:114–16.
- With Sterling P. Taylor, Jr., and Henry G. Kunkel. Electrophoretic studies of oxytocin and vasopressin. *J. Biol. Chem.*, 205:45–53.
- With Edwin A. Popenoe. Degradative studies on vasopressin and performic acid-oxidized vasopressin. *J. Biol. Chem.*, 205:133–43.
- With Charlotte Ressler and Stuart Trippett. The sequence of amino acids in oxytocin, with a proposal for the structure of oxytocin. *J. Biol. Chem.*, 205:949–57.
- With Samuel Gordon. Preparation of S,S'-dibenzyl oxytocin and its reconversion to oxytocin. *Proc. Soc. Exp. Biol. Med.*, 84:723–25.

## 1954

- With Edwin A. Popenoe. A partial sequence of amino acids in performic acid-oxidized vasopressin. *J. Biol. Chem.*, 206:353–60.
- Some studies on the active principles of the posterior pituitary gland. *Harvard Memoirs*, 3:65.
- With Kenneth Nickerson, Roy W. Bonsnes, R. Gordon Douglas, and Peter Condliffe. Oxytocin and milk ejection. *Am. J. Obstet. Gynecol.*, 67:1028–34.
- With Charlotte Ressler. The synthesis of the tetrapeptide amide S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide. *J. Am. Chem. Soc.*, 76:3107–9.
- With John W. Swan. The synthesis of L-glutamyl-L-asparagine, L-glutamine and L-isoglutamine from p-toluenesulfonyl-L-glutamic acid. *J. Am. Chem. Soc.*, 76:3110–13.
- With Panayotis G. Katsoyannis. The synthesis of p-toluenesulfonyl-L-isoleucyl-L-glutamyl-L-asparagine and related peptides. *J. Am. Chem. Soc.*, 76:3113–15.

- With Charlotte Ressler, John M. Swan, Carleton W. Roberts, and Panayotis G. Katsoyannis. The synthesis of oxytocin. *J. Am. Chem. Soc.*, 76:3115-21.
- With Duane T. Gish and Panayotis G. Katsoyannis. A synthetic preparation possessing biological properties associated with arginine-vasopressin. *J. Am. Chem. Soc.*, 76:4751-52.
- With Edwin A. Popenoe. Synthesis of L-phenylalanyl-L-glutamyl-L-asparagine. *J. Am. Chem. Soc.*, 76:6202-3.
- With Charlotte Ressler. Bromination of performic acid-oxidized oxytocin. *J. Biol. Chem.*, 211:809-14.
- With H. Claire Lawler, Sterling P. Taylor, and Ailsa M. Swan. Presence of glutamine and asparagine in enzymatic hydrolysates of oxytocin and vasopressin. *Proc. Soc. Exp. Biol. Med.*, 87:550-52.

## 1955

- With Julian R. Rachele, Edward J. Kuchinskas, and F. Howard Kratzer. Hydrogen isotope effect in the oxidation in vivo of methionine labeled in the methyl group. *J. Biol. Chem.*, 215: 593-601.
- With R. Gordon Douglas and Roy W. Bonsnes. Natural and synthetic oxytocin. *Obstet. Gynecol.*, 6:254-57.
- With D. Wayne Woolley, Robert B. Merrifield, and Charlotte Ressler. Strepogenin activity of synthetic peptides related to oxytocin. *Proc. Soc. Exp. Biol. Med.*, 89:669-73.
- The synthesis of cystine peptides with special reference to the synthesis of oxytocin. *Chem. Soc. Spec. Publ. no. 2.*
- Oxytocin, the principal oxytocin hormone of the posterior pituitary gland: Its isolation, structure, synthesis. *Experientia Suppl.* 2:9.
- Hormones of the posterior pituitary gland: Oxytocin and vasopressin. *Harvey Lect. Ser. L:*1-25.
- The isolation and proof of structure of the vasopressins and the synthesis of octapeptide amides with pressor-antidiuretic activity. *Proc. 3d Int. Congr. Biochem., Brussels*, pp. 49-54.

## 1956

- Trail of sulfur research: From insulin to oxytocin. *Science*, 123: 967-74.

- With M. Frederick Bartlett, Albert Jöhl, Roger Roeske, R. J. Stedman, F. H. C. Stewart, and Darrell N. Ward. Studies on the synthesis of lysine-vasopressin. *J. Am. Chem. Soc.*, 78:2905-6.
- With Panayotis G. Katsoyannis. Synthesis of S-benzyl-N-carbobenzoxo-L-cysteinyl-L-tyrosyl-L-phenylalanyl-L-glutaminyll-asparagine, a pentapeptide derivative related to vasopressin. *J. Am. Chem. Soc.*, 78:4482-83.
- With Darrell N. Ward. Studies on the purification of lysine vasopressin from hog pituitary glands. *J. Biol. Chem.*, 222:951-58.
- With Julian R. Rachele and Alan M. White. A crucial test of transmethylation in vivo by intramolecular isotopic labeling. *J. Am. Chem. Soc.*, 78:5131-32.
- With Roger Roeske, F. H. C. Stewart, and R. J. Stedman. Synthesis of a protected tetrapeptide amide containing the carboxyl terminal sequence of lysine-vasopressin, *J. Am. Chem. Soc.*, 78: 5883-87.
- A trail of sulfur research: From insulin to oxytocin. In: *Les Prix Nobel en 1955*, pp. 446-65. Stockholm: Jungl. Boktr. P. A. Norstedt and Söner.

## 1957

- With Edward J. Kuchinskas. An increased vitamin B<sub>6</sub> requirement in the rat on a diet containing L-penicillamine. *Arch. Biochem. Biophys.*, 66:1-9.
- With Edward J. Kuchinskas and Antonio Horvath. An anti-vitamin B<sub>6</sub> action of L-penicillamine. *Arch. Biochem. Biophys.*, 68:69-75.
- With Duane T. Gish. Synthesis of peptides of arginine related to arginine-vasopressin. *J. Am. Chem. Soc.*, 79:3579.
- With Edward J. Kuchinskas and Antonio Horvath. L-penicillamine and rat liver transaminase activity. *Arch. Biochem. Biophys.*, 69:130-37.
- With Charlotte Ressler. The isoglutamine isomer of oxytocin: Its synthesis and comparison with oxytocin. *J. Am. Chem. Soc.*, 79:4511-15.
- With Panayotis G. Katsoyannis and Duane T. Gish. Synthetic studies on arginine vasopressin condensation of S-benzyl-N-carbobenzoxo-L-cysteinyl-L-tyrosyl-L-phenylalanyl-L-glutaminyll-asparagine and its O-tosyl derivative with S-benzyl-L-

- cysteinyl-L-prolyl-L-arginyl-glycinamide. *J. Am. Chem. Soc.*, 79:4516-20.
- With M. Frederick Bartlett and Albert Jöhl. The synthesis of lysine vasopressin. *J. Am. Chem. Soc.*, 79:5572-75.
- With Albert Light and Roger Acher. Ion exchange chromatography of purified posterior pituitary preparations. *J. Biol. Chem.*, 228:633-41.

## 1958

- With Thomas F. Dillon, B. E. Marbury, Roy W. Bonsnes, and R. Gordon Douglas. Vasopressin as a hemostatic in gynecologic surgery. *Obstet. Gynecol.*, 11:363-71.
- With Panayotis G. Katsoyannis, Duane T. Gish, and George P. Hess. Synthesis of two protected hexapeptides containing the N-terminal and C-terminal sequences of arginine-vasopressin. *J. Am. Chem. Soc.*, 80:2558-62.
- With Roger Acher and Albert Light. Purification of oxytocin and vasopressin by way of a protein complex. *J. Biol. Chem.*, 233:116-20.
- With Duane T. Gish, Panayotis G. Katsoyannis, and George P. Hess. Synthesis of the pressor-antidiuretic hormone, arginine-vasopressin. *J. Am. Chem. Soc.*, 80:3355-58.
- With Albert Light. On the nature of oxytocin and vasopressin from human pituitary. *Proc. Soc. Exp. Biol. Med.*, 98:692-96.
- With Panayotis G. Katsoyannis. Arginine-vasotocin, a synthetic analogue of the posterior pituitary hormones containing the ring of oxytocin and the side chain of vasopressin. *J. Biol. Chem.*, 233:1352-54.
- With Panayotis G. Katsoyannis. The synthesis of the histidine analog of the vasopressins. *Arch. Biochem. Biophys.*, 78:555-62.

## 1959

- With Wilson B. Lutz, Charlotte Ressler, and Donald E. Nettleton, Jr. Isoasparagine-oxytocin: The isoasparagine isomer of oxytocin. *J. Am. Chem. Soc.*, 81:167-74.
- With Miklos Bodanszky. Synthesis of a biologically active analog of oxytocin, with phenylalanine replacing tyrosine. *J. Am. Chem. Soc.*, 81:1258-59.

- With Miklos Bodanszky. An improved synthesis of oxytocin. *J. Am. Chem. Soc.*, 81:2504-7.
- With Miklos Bodanszky. Synthesis of oxytocin by the nitrophenyl ester method. *Nature*, 183:1324-25.
- With Albert Light and Rolf Studer. Isolation of oxytocin and arginine vasopressin by way of a protein complex on a preparative scale. *Arch. Biochem. Biophys.*, 83:84-87.
- With Miklos Bodanszky. A method of synthesis of long peptide chains using a synthesis of oxytocin as an example. *J. Am. Chem. Soc.*, 81:5688-91.
- With Miklos Bodanszky. Synthesis of a biologically active analog of oxytocin, with phenylalanine replacing tyrosine. *J. Am. Chem. Soc.*, 81:6072-75.
- With Panayotis G. Katsoyannis. Arginine vasotocin. *Nature*, 184:1465.
- With Miklos Bodanszky. A new crystalline salt of oxytocin. *Nature*, 184:981-82.

## 1960

- With Rolf Studer. Synthetic work related to arginine-vasopressin. *J. Am. Chem. Soc.*, 82:1499-1501.
- With Johannes Meienhofer. Preparation of lysine-vasopressin through a crystalline protected nonapeptide intermediate and purification of the hormone by chromatography. *J. Am. Chem. Soc.*, 82:2279-82.
- With Thomas F. Dillon, R. Gordon Douglas, and M. L. Barber. Transbuccal administration of pitocin for induction and stimulation of labor. *Obstet. Gynecol.*, 15:587-92.
- With Miklos Bodanszky and Johannes Meienhofer. Synthesis of lysine-vasopressin by the nitrophenyl ester method. *J. Am. Chem. Soc.*, 82:3195-98.
- Experiences in the polypeptide field: Insulin to oxytocin. *Ann. N.Y. Acad. Sci.*, 88:537-48.
- With Harry D. Law. Synthesis of 2-p-methoxyphenylalanine oxytocin (O-methyl-oxytocin) and some observations on its pharmacological behavior. *J. Am. Chem. Soc.*, 82:4579-81.
- With Peter S. Fitt, Miklos Bodanszky, and Maureen O'Connell. Synthesis and some pharmacological properties of a peptide deriv-

- ative of oxytocin: Glycyloxytocin. *Proc. Soc. Exp. Biol. Med.*, 104:653–56.
- With Gershen Winestock, V. V. S. Murti, Derek B. Hope, and Raymond D. Kimbrough, Jr. Synthesis of 1- $\beta$ -mercaptopropionic acid oxytocin (desaminooxytocin), a highly potent analogue of oxytocin. *J. Biol. Chem.*, 235:PC64–66.
- With Johannes Meienhofer. Synthesis of a biologically active analog of lysine-vasopressin, with phenylalanine replacing tyrosine: 2-Phenylalanine lysine-vasopressin. *J. Am. Chem. Soc.*, 82:6336–37.

## 1961

- With Johannes Meienhofer. Synthesis of a lysine-vasopressin derivative with a methyl substituent on the imino nitrogen of the peptide bond between lysine and glycinamide (9-sarcosine lysine-vasopressin). *J. Am. Chem. Soc.*, 83:142–45.
- With Raymond D. Kimbrough, Jr. Lysine-vasotocin, a synthetic analogue of the posterior pituitary hormones containing the ring of oxytocin and the side chain of lysine-vasopressin. *J. Biol. Chem.*, 236:778–80.
- With Derek Jarvis and Miklos Bodanszky. The synthesis of 1-(hemihomocystine)-oxytocin and a study of some of its pharmacological properties. *J. Am. Chem. Soc.*, 83:4780–84.

## 1962

- With Conrad H. Schneider, John E. Stouffer, V. V. S. Murti, Janardan P. Aroskar, and Gershen Winestock. Tritiation of oxytocin by the Wilzbach method and the synthesis of oxytocin from tritium-labelled leucine. *J. Am. Chem. Soc.*, 84:409–13.
- With William D. Cash, Logan McCulloch Mahaffey, Alfred S. Buck, Donald E. Nettleton, Jr., and Christos Romas. Synthesis and biological properties of 9-sarcosine oxytocin. *J. Med. Pharm. Chem.*, 5:413–23.
- With Derek B. Hope and V. V. S. Murti. A highly potent analogue of oxytocin, desamino-oxytocin. *J. Biol. Chem.*, 237:1563–66.
- With Miklos Bodanszky. p-Nitrophenyl carbobenzoxyglycinate. *Biochem. Prep.*, 9:110–12.
- With Conrad H. Schneider. Synthesis of D-leucine-oxytocin, a biologically active diastereoisomer of oxytocin, and demonstration

- of its separability from oxytocin upon countercurrent distribution. *J. Am. Chem. Soc.*, 84:3005-8.
- With Derek B. Hope. Synthesis of desamino-desoxy-oxytocin, a biologically active analogue of oxytocin. *J. Biol. Chem.*, 237: 3146-50.
- With W. Y. Chan. Comparison of the pharmacologic properties of oxytocin and its highly potent analogue, desamino-oxytocin. *Endocrinology*, 71:977-82.
- With John E. Stouffer and Derek B. Hope. Neurophysin, oxytocin and desamino-oxytocin. In: *Perspectives in Biology*, ed. C. F. Cori, V. G. Foglia, L. F. Leloir, and S. Ochoa, pp. 75-80. Amsterdam: Elsevier Publishing Company.
- With Thomas F. Dillon and R. Gordon Douglas. Further observations on transbuccal administration of pitocin for induction and stimulation of labor. *Obstet. Gynecol.*, 20:434-41.

## 1963

- With Julius Golubow. Comparison of susceptibility of oxytocin and desamino-oxytocin to inactivation by leucine aminopeptidase and  $\alpha$ -chymotrypsin. *Proc. Soc. Exp. Biol. Med.*, 112:218-19.
- With Raymond D. Kimbrough, Jr., William D. Cash, Luis A. Branda, and W. Y. Chan. Synthesis and biological properties of 1-desamino-8-lysine-vasopressin. *J. Biol. Chem.*, 238:1411-14.
- With George S. Denning, Jr., Stefania Drabarek, and W. Y. Chan. The effect of replacement of the carboxamide group by hydrogen in the glutamine or asparagine residue of oxytocin on its biological activity. *J. Biol. Chem.*, 238:PC1560-61.
- With Julius Golubow and W. Y. Chan. Effect of human pregnancy serum on avian depressor activities of oxytocin and desamino-oxytocin. *Proc. Soc. Exp. Biol. Med.*, 113:113-15.
- With Derek B. Hope and V. V. S. Murti. Synthesis of 1-hemi-D-cystine-oxytocin. *J. Am. Chem. Soc.*, 85:3686-88.

## 1964

- With J. P. Aroskar, W. Y. Chan, J. E. Stouffer, C. H. Schneider, and V. V. S. Murti. Renal excretion and tissue distribution of radioactivity after administration of tritium-labeled oxytocin to rats. *Endocrinology*, 74:226-32.
- With Derek Jarvis. Crystalline deamino-oxytocin. *Science*, 143: 545-48.

- With George S. Denning, Jr., Stefania Drabarek, and W. Y. Chan. The synthesis and pharmacological study of 4-decarboxamido-oxytocin (4- $\alpha$ -aminobutyric acid-oxytocin) and 5-decarboxamido-oxytocin (5-alanine-oxytocin). *J. Biol. Chem.*, 239:472-77.
- With Julian R. Rachele, John E. Wilson, Fred Plum, and Lester J. Reed. The administration of radioactive L-cystathionine to a human cystinuric. *Adv. Chem.*, 44:82.
- Significance of the chemical functional groups of oxytocin to its pharmacological activity. *Abstr. 6th Int. Congr. Biochem.*, New York City:97-98.
- An organic chemical approach to the study of the significance of the chemical functional groups of oxytocin to its biological activities. *Proc. 8th Robert A. Welch Found. Conf. Chem. Res. Selected Topics in Modern Biochemistry.*

1965

- With Julian R. Rachele. The concept of transmethylation in mammalian metabolism and its establishment by isotopic labeling through in vivo experimentation. In: *Transmethylation and Methionine Biosynthesis*, ed. Shapiro and Schlenk, pp. 1-20. Chicago: University of Chicago Press.
- With Iphigenia Photaki. 4-Deamido-oxytocin, an analog of the hormone containing glutamic acid in place of glutamine. *J. Am. Chem. Soc.*, 87:908-9.
- With Miklos Bodanszky and George S. Denning, Jr. p-Nitrophenyl carbobenzoxy-L-asparaginate. *Biochem. Prep.*, 10:122-25.
- The hormones of the posterior pituitary gland with special reference to their milk-ejecting ability. *Bull. N.Y. Acad. Med.*, 41: 802-3.
- With Donald Yamashiro and H. L. Aaning. Inactivation of oxytocin by acetone. *Proc. Natl. Acad. Sci. USA*, 54:166-71.
- With Derek Jarvis and Barbara M. Ferrier. The effect of increasing the size of the ring present in deamino-oxytocin by one methylene group on its biological properties: The synthesis of 1- $\gamma$ -mercaptobutyric acid-oxytocin. *J. Biol. Chem.*, 240:3553-57.
- With Stefania Drabarek. 2-D-tyrosine-oxytocin and 2-D-tyrosine-deamino-oxytocin, diastereoisomers of oxytocin and deamino-oxytocin. *J. Am. Chem. Soc.*, 87:3974-78.



- With Maurice Manning. 6-Hemi-D-cystine-oxytocin, a diastereoisomer of the posterior pituitary hormone oxytocin. *J. Am. Chem. Soc.*, 87:3978-82.
- With Maurice Manning. 4- $\beta$ -Alanine-oxytocin: An oxytocin analog containing a twenty-one-membered disulfide ring. *Biochemistry*, 4:1884-87.
- With George Flouret. The synthesis of D-oxytocin, the enantiomer of the posterior pituitary hormone, oxytocin. *J. Am. Chem. Soc.*, 87:3775-76.
- With Roderich Walter. 6-Hemi-L-selenocystine-oxytocin and 1-deamino-6-hemi-L-selenocystine-oxytocin, highly potent isologs of oxytocin and 1-deamino-oxytocin. *J. Am. Chem. Soc.*, 87:4192-93.
- With Barbara M. Ferrier and Derek Jarvis. Deamino-oxytocin: Its isolation by partition chromatography on sephadex and crystallization from water, and its biological activities. *J. Biol. Chem.*, 240:4264-66.

1966

- With Barbara M. Ferrier. 9-Deamido-oxytocin, an analog of the hormone containing a glycine residue in place of the glycinamide residue. *J. Med. Chem.*, 9:55-57.
- With Luis A. Branda. Synthesis and pharmacological properties of 9-decarboxamido-oxytocin. *J. Med. Chem.*, 9:169-72.
- With Donald Yamashiro and Dieter Gillissen. Simultaneous synthesis of 1-hemi-D-cystine-oxytocin and oxytocin and separation of the diastereoisomers by partition chromatography on Sephadex by countercurrent distribution. *J. Am. Chem. Soc.*, 88:1310-13.
- With Roderich Walter. 1-Deamino-1,6-L-selenocystine-oxytocin, a highly potent isolog of 1-deamino-oxytocin. *J. Am. Chem. Soc.*, 88:1331-32.
- With George Flouret and Roderich Walter. Synthesis and some biological properties of 4-valine-oxytocin and 1-deamino-4-valine-oxytocin. *J. Biol. Chem.*, 241:2093-96.
- With Luis A. Branda and Stefania Drabarek. The synthesis and pharmacological properties of deamino-4-decarboxamido-oxytocin (1- $\beta$ -mercaptopropionic acid-4- $\alpha$ -aminobutyric acid-oxytocin). *J. Biol. Chem.*, 241:2572-75.

- With John J. Ferraro. 7-D-proline-oxytocin and its deamino analog. Diastereoisomers of oxytocin and deamino-oxytocin. *J. Am. Chem. Soc.*, 88:3847-50.
- With Horst Schulz. Synthesis of 1-L-penicillamine-oxytocin, 1-D-penicillamine-oxytocin, and 1-deaminopenicillamine-oxytocin, potent inhibitors of the oxytocic response of oxytocin. *J. Med. Chem.*, 9:647-50.
- With Luis A. Branda. Deoxy-4-decarboxamido-oxytocin and deamino-deoxy-4-decarboxamidooxytocin. *J. Biol. Chem.*, 241:4051-54.
- With Horst Schulz. The effect of replacing one of the hydrogens of the  $\beta$ -carbon of the  $\beta$ -mercaptopropionic acid residue in deamino-oxytocin by a methyl group on its oxytocic and avian vasodepressor activity. *J. Am. Chem. Soc.*, 88:5015-18.
- With Donald Yamashiro and Dieter Gillessen. Oxytoceine and deamino-oxytoceine. *Biochemistry*, 5:3711-19.
- With Roderich Walter. 8-Alanine-oxytocin, 8-alanine-oxypressin, and their deamino analogs. Their synthesis and some of their pharmacological properties. *Biochemistry*, 5:3720-27.

## 1967

- With Donald Yamashiro, Robert T. Havran, and H. L. Aanning. Inactivation of lysine-vasopressin by acetone. *Proc. Natl. Acad. Sci. USA*, 57:1058-59.
- With Derek Jarvis. The effect of decreasing the size of the ring present in deamino-oxytocin by one methylene group on its biological properties: The synthesis of 1-mercaptoacetic acid-oxytocin. *J. Biol. Chem.*, 242:1768-71.
- With Luis A. Branda and Victor J. Hruby. 2-Isoleucine-oxytocin and deamino-2-isoleucine-oxytocin: Their synthesis and some of their pharmacological activities. *Mol. Pharmacol.*, 3:248-53.
- With Derek Jarvis and Maurice Manning. 1-Mercaptoacetic acid-4- $\beta$ -alanine-oxytocin. *Biochemistry*, 6:1223-30.
- With W. Y. Chan and Robert Fear. Some pharmacologic studies on 1-L-penicillamine-oxytocin and 1-deaminopenicillamine-oxytocin: Two potent oxytocin inhibitors. *Endocrinology*, 81:1267-77.
- With Dieter Gillessen. The synthesis and pharmacological properties of 4-decarboxamido-8-lysine-vasopressin, 5-decarbox-

amido-8-lysine-vasopressin, and their l-deamino analogues. *J. Biol. Chem.*, 242:4806-12.

With Horst Schulz. Synthesis and some pharmacological properties of 6-L-penicillamine-oxytocin. *J. Med. Chem.*, 10:1037-39.

1968

With Donald Yamashiro. Synthesis of "acetone-oxytocin" from an isopropylidene derivative of S-benzyl-L-cysteinyl-L-tyrosine. *J. Am. Chem. Soc.*, 90:487-90.

With Herbert Takashima and R. B. Merrifield. The synthesis of deamino-oxytocin by the solid phase method. *J. Am. Chem. Soc.*, 90:1323-25.

With Donald Yamashiro and Derek B. Hope. Isomeric dimers of oxytocin. *J. Am. Chem. Soc.*, 90:3857-60.

With Donald Yamashiro, H. L. Aanning, Luis A. Branda, William D. Cash, and V. V. S. Murti. A synthesis of [1-(N-methyl-hemi-L-cystine)]-oxytocin and a study of its reaction with acetone. *J. Am. Chem. Soc.*, 90:4141-44.

With W. Y. Chan, Victor J. Hruby, and George Flouret. 4-Leucine-oxytocin: A natriuretic, diuretic and anti-ADH polypeptide. *Science*, 161:280-81.

With Alfred T. Blomquist, Daniel H. Rich, Victor J. Hruby, Louis L. Nangeroni, and Paula Glose. Deuterated oxytocins. The synthesis and biological properties of three crystalline analogs of deamino-oxytocin deuterated in the 1- $\beta$ -mercaptopropionic acid position. *Proc. Natl. Acad. Sci. USA*, 61:688-92.

With Victor J. Hruby and Donald Yamashiro. The structure of acetone-oxytocin with studies on the reaction of acetone with various peptides. *J. Am. Chem. Soc.*, 90:7106-10.

Hormones of the mammalian posterior pituitary gland and their naturally occurring analogues. *Johns Hopkins Med. J.*, 124:53-65.

With Robert T. Havran. The structure of acetone-lysine-vasopressin as established through its synthesis from the acetone derivative of S-benzyl-L-cysteinyl-L-tyrosine. *J. Am. Chem. Soc.*, 91:2696-98.

With Victor J. Hruby. The detection of a Schiff base intermediate in the formation of acetone-oxytocin. *J. Am. Chem. Soc.*, 91:3624-26.

- With Robert T. Havran. The synthesis and pharmacological properties of [2-isoleucine]-8-lysine-vasopressin and its 1-deamino analog. *J. Am. Chem. Soc.*, 91:3626–28.
- With Victor J. Hruby and George Flouret. The synthesis and some of the pharmacological properties of [4-L-isoleucine]-oxytocin and [4-L-leucine]-oxytocin. *J. Biol. Chem.*, 244:3890–94.
- With Victor J. Hruby. Synthesis and some pharmacological activities of [2-L-valine]-oxytocin and [2-L-leucine]-oxytocin. *J. Med. Chem.*, 12:731–33.
- With Alfred T. Blomquist, Daniel H. Rich, Bruce A. Carlson, G. Ashley Allen, Victor J. Hruby, Herbert Takashima, Louis L. Nangeroni, and Paula Glose. Deuterated oxytocins: The synthesis and biological properties of a crystalline analog of deamino-oxytocin deuterated in the 5-asparagine position. *Proc. Natl. Acad. Sci. USA*, 64:263–66.
- With George Flouret. The synthesis and some pharmacological activities of [4-L-norvaline]-oxytocin and [4-L-norleucine]-oxytocin and their deamino analogs. *J. Med. Chem.*, 12:1035–38.
- With Herbert Takashima and Wolfgang Fraefel. The synthesis and certain pharmacological properties of deamino-oxytocinoic acid methylamide and deamino-oxytocinoic acid dimethylamide. *J. Am. Chem. Soc.*, 91:6182–85.

1970

- With Herbert Takashima and Victor J. Hruby. The synthesis of [1-deamino,4-L-leucine]-oxytocin and [1-deamino,4-L-isoleucine]-oxytocin and some of their pharmacological properties. *J. Am. Chem. Soc.*, 92:677–80.
- With Wolfgang Fraefel. The synthesis and pharmacological properties of [1-( $\delta$ -mercaptovaleric acid)]-oxytocin, a homolog of deamino-oxytocin containing a twenty-two-membered ring. *J. Am. Chem. Soc.*, 92:1030–32.
- With Victor J. Hruby and W. Y. Chan. [2,4-Diisoleucine]-oxytocin. An analog of oxytocin with natriuretic and diuretic activities. *J. Med. Chem.*, 13:185–87.
- With Herbert Takashima. The synthesis of deamino-oxytocinoic acid and acetone-oxytocinoic acid and their use in the preparation of deamino-oxytocinoxyloxytocin and oxytocinoxyloxytocin. *J. Am. Chem. Soc.*, 92:2501–4.

- With Dieter Gillissen. Synthesis and pharmacological properties of 4-decarboxamido-8-arginine-vasopressin and its 1-deamino analog. *J. Med. Chem.*, 13:346–49.
- With Wolfgang Fraefel. [1-( $\delta$ -Mercaptoundecanoic acid)]-oxytocin, a 28-membered ring homolog of deamino-oxytocin. *J. Am. Chem. Soc.*, 92:4426–27.
- With W. Y. Chan. Natriuretic, diuretic and anti-arginine-vasopressin (ADH) effects of two analogs of oxytocin: [4-Leucine]-oxytocin and [2,4-diisoleucine]-oxytocin. *J. Pharmacol. Exp. Ther.*, 174:541–49.

## 1971

- With George Flouret. Deamino-D-oxytocin. *J. Med. Chem.*, 14: 556–57.
- With P. H. Von Dreele, A. I. Brewster, H. A. Scheraga, and M. F. Ferger. Nuclear magnetic resonance spectrum of lysine-vasopressin and its structural implications. *Proc. Natl. Acad. Sci. USA*, 68:1028–31.
- With Victor J. Hruby and Martha F. Ferger. Synthesis and pharmacological properties of deaminotocinamide and a new synthesis of tocinamide. *J. Am. Chem. Soc.*, 93:5539–42.
- With Jim D. Meador, Martha F. Ferger, G. Ashley Allen, and Alfred T. Blomquist. The synthesis and biological properties of [1-deaminopenicillamine]-oxytocin deuterated in the 1-position. *Bioorg. Chem.*, 1:123–28.

## 1972

- With Myles A. Wille and W. Y. Chan. Solid phase synthesis of [3,4-dileucine]-oxytocin and a study of some of its pharmacological properties. *J. Med. Chem.*, 15:11–12.
- With Raymond J. Vavrek, Martha F. Ferger, G. Ashley Allen, Daniel H. Rich, and Alfred T. Blomquist. Synthesis of three oxytocin analogs related to [1-deaminopenicillamine]-oxytocin possessing antioxytocic activity. *J. Med. Chem.*, 15:123–26.
- With Martha F. Ferger, Warren C. Jones, Jr., and Douglas F. Dyckes. Four cyclic disulfide pentapeptides possessing the ring of vasopressin. *J. Am. Chem. Soc.*, 94:982–84.
- With P. H. Von Dreele, A. I. Brewster, F. A. Bovey, H. A. Scheraga, and M. F. Ferger. Nuclear magnetic resonance studies of lysine-vasopressin: Structural constraints. *Proc. Natl. Acad. Sci. USA*, 68:3088–91.

- With John D. Glass. Synthesis and certain pharmacological properties of lysine-vasopressinoic acid methylamide and lysine-vasopressinoic acid dimethylamide. *J. Med. Chem.*, 15:486-88.
- With Victor J. Hruby, Clark W. Smith, David K. Linn, and Martha F. Ferger. Synthesis and some pharmacological properties of tocinoic acid and deaminotocinoic acid. *J. Am. Chem. Soc.*, 94:5478-80.
- With P. H. Von Dreele, A. I. Brewster, J. Dadok, H. S. Scheraga, F. A. Bovey, and M. F. Ferger. Nuclear magnetic resonance spectrum of lysine-vasopressin in aqueous solution and its structural implications. *Proc. Natl. Acad. Sci. USA*, 69:2169-73.
- With P. H. Von Dreele, H. A. Scheraga, D. F. Dyckes, and M. F. Ferger. Nuclear magnetic resonance spectrum of deaminolysine-vasopressin in aqueous solution and its structural implications. *Proc. Natl. Acad. Sci. USA*, 69:3322-26.

## 1973

- With John D. Glass. Solid-phase synthesis and pressor potency of [1-deamino-9-ethylenediamine]-lysine-vasopressin. *J. Med. Chem.*, 16:160-61.
- With Douglas F. Dyckes, Martha F. Ferger, and W. Y. Chan. Synthesis and some of the pharmacological properties of [4-leucine]-8-lysine-vasopressin and [1-deamino,4-leucine]-8-lysine vasopressin. *J. Med. Chem.*, 16:843-47.
- With Warren C. Jones, Jr., and John J. Nestor, Jr. Synthesis and some pharmacological properties of [1-deamino,9-thioglycine]oxytocin. *J. Am. Chem. Soc.*, 95:5677-79.

## 1974

- With Douglas F. Dyckes, John J. Nestor, Jr., and Martha F. Ferger. [1- $\beta$ -Mercapto- $\beta$ , $\beta$ -diethylpropionic acid]-8-lysine-vasopressin, a potent inhibitor of 8-lysine-vasopressin and of oxytocin. *J. Med. Chem.*, 17:250-52.
- With W. Y. Chan and Victor J. Hruby. Effects of magnesium ion and oxytocin inhibitors on the uterine activity of oxytocin and prostaglandins  $E_2$  and  $F_{2\alpha}$ . *J. Pharmacol. Exp. Ther.*, 190:77-87.
- With W. Y. Chan, John J. Nestor, Jr., and Martha F. Ferger. Inhibition of oxytocic responses to oxytocin in pregnant rats by

[1-L-penicillamine]oxytocin and [1- $\beta$ -mercapto- $\beta,\beta$ -diethylpropionic acid]oxytocin. *Proc. Soc. Exp. Biol. Med.*, 146:364-66.

With Douglas F. Dyckes, John J. Nestor, Jr., Martha F. Ferger, and W. Y. Chan. [1- $\beta$ -Mercapto- $\beta,\beta$ -diethylpropionic acid, 4-leucine]-8-lysine-vasopressin and [1- $\beta$ -mercapto- $\beta,\beta$ -diethylpropionic acid, 4-leucine]oxytocin, compounds possessing antihormonal properties. *J. Med. Chem.*, 17:969-71.

With Douglas F. Dyckes, Clark W. Smith, and Martha F. Ferger. Synthesis and some pharmacological properties of [1- $\alpha$ -Maa]LVP and [1- $1\gamma$ -Mba]LVP. *J. Am. Chem. Soc.*, 96:7549-51.

## 1975

With John J. Nestor, Jr., and Martha F. Ferger. [1- $\beta$ -Mercapto- $\beta,\beta$ -pentamethylenepropionic acid]oxytocin, a potent inhibitor of oxytocin. *J. Med. Chem.*, 18:284-87.

With J. J. Nestor, Jr., and M. F. Ferger. The retention of anti-oxytocic activity by the ring moieties of [1- $\beta$ -mercapto- $\beta,\beta$ -diethylpropionic acid]-oxytocin and [1- $\beta$ -mercapto- $\beta,\beta$ -pentamethylenepropionic acid]oxytocin. *Proc. 4th Am. Peptide Symp.*, pp. 755-59. Ann Arbor, Mich.: Ann Arbor Science Publishers.

## 1976

With R. A. Plane. Reminiscences of a biochemist. *J. Chem. Ed.*, 53:8-12.