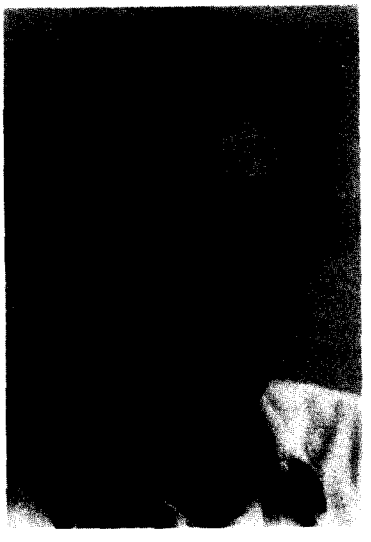
Obituary

Peter Hemmerich, 1929–1981

With the death of Peter Hemmerich at the age of 51 on October 3, 1981, a restless life, full of search for fulfillment, full of ideas and achievement, but also of feuds and skirmishes, has come to an untimely end. With him the initiator and most forceful and vocal exponent of the second era of flavin research – the present day era as opposed to that of the thirties – has passed away. It is probably fair to say that had it not been for his relentless quest into so many aspects of flavin chemistry, his keen interest in seeing the knowledge thus gained related to flavin function in enzymes, and to his uncompromising demand for rigor in doing so our understanding of flavin chemistry and function in catalysis would be lagging behind by one or more decades.

Peter Hemmerich was born in Frankfurt am Main, the elder son of a well-to-do merchant family, on December 30, 1929. With the shortage of places in German universities in the post-war years, he was not able to find a place as a student of chemistry, and so enrolled at the University of Freiburg in 1948 in the mathematics curriculum. With financial aid from an uncle, he transferred the next year to the University of Basel where, a few years later, he entered the prestigious Institute of Inorganic Chemistry as a Ph.D. student of Hans Erlenmeyer. Erlenmeyer was an authority in the chemistry of metal chelates and apparently had some intuition that the function of metals in biological materials might be related to their chelate chemistry. Those happened to be the years (the early fifties) when the idea sprung up, with some apparent experimental support, that riboflavin was a metal chelator and that some of its biological functions could be explained by that property. This became of particular interest, when just then metals were discovered as constituents of a number of flavoproteins such as succinate and NADH dehydrogenases or xanthine oxidase. Erlenmeyer, therefore, suggested to Hemmerich that he look into the chelating ability of riboflavin.

Hemmerich soon became frustrated by the limited solubility of riboflavin and known isoalloxazine derivatives; thus he decided on the bold strategy of replacing the oxygen at the flavin 2 α-position by sulfur and of alkylating this, the N(3)-H and the C(4)-α position with various substituents. The resulting flavins, achieved by new and more efficient synthetic routes, were the product of the first original research of Peter Hemmerich (largely published in *Helvetica Chimica Acta*). In the course of this brilliant research he established the structure of flavin, that we are now so used to seeing, as the 2,4-dicarbonyl tautomer A, rather than the iminohydroxyl tautomer B, which used to be seen frequently (and occasionally still is) in biochemistry texts. The period at Basel also involved studies on the chelation ability of riboflavin. Hemmerich's first paper on this subject (*Helv. Chim. Acta* (1958) 41, 498) with S. Fallab decisively dampened the enthusiasm that had arisen about that subject; he showed that oxidized flavin had only weak chelator properties and that metal chelation was a property only for the flavin radical. This finding, however, had several important consequences. It helped in the recognition that the metals were parts of discrete redox centers and not directly liganded to the flavin. It also led naturally to his decisive studies on the properties of flavin radicals.



Peter Hemmerich

His work soon came to the attention of the biochemical community and resulted in close international collaborations with a number of biochemical colleagues, including Anders Ehrenberg in Stockholm, Cees Veeger in Wageningen, Thomas P. Singer in San Francisco and ourselves. Several of these have spanned many years, from his first visits to the U.S.A. in 1964 and 1965,

right up to his death. Indeed in the earlier years he remarked on occasion that he had to travel abroad to find out that there were actually people interested in what he was doing. Hemmerich's collaborations originated from his desire to relate his fundamental chemical studies to the biological roles of flavins, for he was among the first to realize the great chemical versatility of flavins and that not every model chemical reaction necessarily pointed the way to the mechanism of a particular enzymic reaction. He was also quick to seize on correlations of properties of particular flavoproteins and the types of reactions which they catalyzed. Because of his impatience to ferret out the order which he believed must exist in nature, he occasionally made premature judgments and interpretations which proved misleading or confusing. However, even in those cases where it turned out that he was wrong, his catalytic influence on experimentation and discussion in the field was of great importance. His belief that different classes of flavoproteins must have different protein structural elements, but with common structural features within each class, led to the more rational classification scheme for flavoenzymes which he developed in his last years. It was indeed these principles of order that he saw through the thicket of specialized information on some several hundred flavoproteins which occupied his mind most up to his last days. He impressed upon his friends the need to continue his quest into this problem and verify and consolidate his ideas should he fall victim to his disease.

His scientific output was prolific. In the 25 years of his career, he published with students and colleagues 170 research papers and reviews. In addition to those already mentioned, other highlights of his research career include the realization of the ease of formation of covalent adducts of flavins and their possible participation in catalysis, fundamental investigations and practical applications of flavin photochemistry, the determination of properties of flavins in the reduced state, and participation in the elucidation of the structure of flavins covalently linked to proteins. Hemmerich's intense interest and love of flavin research have been passed on to several students and younger colleagues. Notable among these are Franz Müller (Wageningen) and Sandro Ghisla (Konstanz).

Hemmerich was also keenly interested in the structure and function of catalytic groups in enzymes operating in conjunction with flavins such as the iron sulfur clusters or molybdenum, and in copper proteins. Iron-sulfur clusters were first recognized in animal tissues by their unusual EPR signals. The origin of these signals was, of course, not known initially. Hemmerich was among the first to show that iron-complexes, contrary to general opinion, could have EPR resonances with properties similar to the observed unknowns. He also strongly suggested to biochemists to consider sulfur ligands to copper in copper proteins and pointed out the resulting ambiguity in the valency of the copper in such systems. He always kept in his laboratory a research group active in the field of copper and molybdenum model complexes, work which more recently has been pursued and extended by Peter Kroneck (Konstanz), partially in collaboration with Jack Spence (Utah).

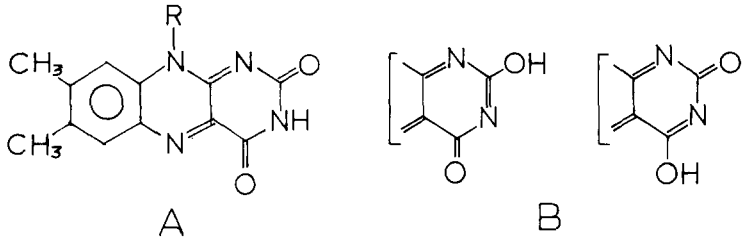


Fig. 1. Possible tautomers of flavin. (A) 2,4-dicarbonyl. (B) iminohydroxyl.

The decisive event in his career occurred in 1967 when the newly founded University of Konstanz tried to assemble a diversified biology faculty. Max Delbrück, who advised the founding rector, drew his attention to Hemmerich's work which was striving toward a synthesis of biological, organic and inorganic chemistry. Thus Hemmerich became one of the first members of that faculty. He stayed at Konstanz for the rest of his life, establishing a flourishing research group devoted to the study of flavins as well as a group working with copper proteins. Konstanz quickly became a world-renowned center for flavin research.

Peter Hemmerich was an enthusiastic hiker, skier, sailor and hunter; however, being the man he was, he would not pursue these activities in conventional ways but at the border of what others may have found exhausting or even dangerous. He was one of those personalities who rarely left people unimpressed – in a positive or in a negative sense – wherever he became involved. He cared strongly about many things; about science, education, his friends, and the environment, particularly about his beloved Bodensee (Lake Constance) and to further these aims he became a member of the Konstanz City Council. He also wrote voluminously and wittily for *Die Zeit*, a prominent German cultural and political weekly.

For those who were close to Hemmerich, life will have become more calm; but it may also have lost some of its more vivid colors.

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The Ludwig Institute for Cancer Research

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