
Nobel Prize Topics in Chemistry

A Series of Historical Monographs on
Fundamentals of Chemistry

Stereochemistry

O. Bertrand Ramsay

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Stereochemistry

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A Series of Historical Monographs on
Fundamentals of Chemistry

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Nobel Prize Topics in Chemistry traces the scientific development of each subject for which a Nobel Prize was awarded in the light of the historical, social and political background surrounding its reception. In every volume one of the Laureate's most significant publications is reproduced and discussed in the context of his life and work, and the history of science in general.

This major series captures the intellectual fascination of a field that is too often considered the domain of specialists, but which nevertheless remains a significant area of study for all those interested in the evolution of chemistry.

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Foreword

By D.H.R. Barton, FRS
(Nobel Laureate in Chemistry, 1969)

In the daily struggle to advance the frontiers of Science, research workers often neglect the history of their speciality. This is regrettable because history, and especially the history of ideas, has much to teach us about the psychology of creative thought.

Every organic chemist recognizes the fundamental importance of structural theory. This is expressed in the concept of constitution, configuration and conformation. It is a fascinating exercise to read how each of these ideas came to be proposed, discussed and finally accepted. In each case the concept was needed to correlate an expanding body of experimental fact. In each case there was surely a large number of chemists who could have proposed the concept but only one or two who did.

The particular case of conformational analysis is now recent history. Here one has to ask why conformational analysis was not recognized much earlier. The work of Hermans and of Boeseken on ring formation from diols or the work of Reeves on carbohydrates is certainly early conformational analysis. But in each case the general chemical public could not appreciate the implications of the papers. Perhaps the time was not ripe. When conformational analysis was finally generally accepted, it was because it was much needed in steroid chemistry where the cortisone problem created hundreds of would-be steroid chemists almost overnight. At the same time the physical methods of electron diffraction, of X-ray crystallography and of calorimetric and computation entropy analysis had reached the point where organic chemists could believe that the conclusions reached were true. In case the reader should think that everything was obvious, it must be pointed out that in the literature for

1935–1950 there are two authoritative papers by well-respected scientists which show that the eclipsed conformation of ethane is *more* stable than the staggered and that the boat conformation of cyclohexane is *more* stable than the chair. Even today the writings of very distinguished chemical physicists continue to confuse configurations with conformations!

This book by Dr Ramsay is a clear, well-written and very interesting account of the history of organic chemical ideas on stereochemistry. It is to be recommended not only to students of the subject but also to active research workers in organic chemistry. Both groups have much to learn about creative thinking from the analysis of the past.

CNRS,
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France

General Editor's Preface

Nobel Prizes in Chemistry have been awarded almost every year since 1901, and the topics covered by these awards have touched upon almost every subject in chemistry. 'Nobel Prize Topics in Chemistry' plans to cover the history of each subject for which a Nobel Prize was awarded and to place particular emphasis on the life and work of the Nobel Prize winner himself. In this way the planned Series will come to describe the whole history of chemistry. The concept is to take one of each Nobel Laureate's most significant publications, to reprint it (as an English translation if appropriate), discuss it, and then to place it within the context of the Laureate's life and works in particular and the history of science in general, if possible going as far back as Egyptian, Babylonian and Greek antiquity. The Series will also look at possible future developments.

Contributions are presented in such a manner that a non-specialist background will suffice for the text to be comprehensible. The intention is to make as many readers as possible aware of and conversant with the problems underlying the development of various areas in the field of chemistry. Each volume attempts to give a smooth outline of the particular topic under consideration, uninterrupted by continual footnotes and references in the text.

The Series is not, in the first instance, aimed at the professional historian, but rather at the chemist, the research worker and the non-specialist who wishes to bring himself up to date on the historical background of one or more areas of chemistry. The student of chemistry and the historian or sociologist who for research wishes to focus broadly on one of the most spectacular disciplines in the natural sciences, can obtain a wide-ranging historical knowledge – knowledge which forms part of the general history of mankind and which can also be used to examine the reciprocal relationship between chemistry and society as a whole. The authors are well-known historians of chemistry or chemists with a solid

knowledge of history. Among the latter group, occasionally a Nobel Prize winner will be our author. Nobel Prize winners are also contributing forewords to many of our volumes.

For certain parts of the texts a reasonable knowledge of chemistry – in some cases, the reading of formulas for example – is required, but the needs of the non-chemist have been anticipated by including in each volume a glossary through which the reader can revise or extend his chemical knowledge. Each volume also contains a chronology of significant events and a detailed bibliography.

It is the aim of the Editor that the readers of this Series should obtain a clear idea of the particular experiences of a chemist in performing his research – research which sometimes led to a discovery of the greatest significance for humanity. It is thus not only the intention to focus exclusively here on the main historical-chemical facts, but also to understand the chemist as a human being and look at the circumstances which led to his discoveries. However, to understand the social and eventually the political background of these historical developments, the reader must inform himself of the facts presented here. This Series thus aims to capture the intellectual fascination of a field that is too often considered to be the domain of specialists, but which nevertheless remains an area of proven intellectual adventure for all those who consider the quest for understanding the highest point to which man can aspire.

It is our sincere wish that the individual volumes in this Series shall realize these aims and intentions.

J. W. van SPRONSEN
The Hague

Author's Preface

The award of Nobel Prizes in Chemistry in 1969 made jointly to Odd Hassel and Derek H. R. Barton, and in 1975 to John W. Cornforth and Vladimir Prelog, mark the recognition of major turning-points in the history of stereochemistry. In order to understand the importance of the research that led to these awards, a major portion of this book will be concerned with the development of stereochemistry from the middle of the 19th century until the 1950s when stereochemical research underwent a significant change in emphasis. Later chapters examine the nature of this change and attempt a look into the future of stereochemical research. The first chapter contains biographical and other information about the Nobel Laureates in order that the reader can more fully appreciate the significance of the four key papers that follow. The reader with only a marginal background in stereochemistry may wish to defer the reading of these papers until the completion of the remaining chapters.

The early chapters discuss some of the theoretical and experimental studies undertaken in the early part of the 19th century which finally led to the simultaneous proposals of J. H. van't Hoff and J. A. Le Bel in 1874, a date that might be considered to mark the birth of stereochemistry. The designation of birthdates is perhaps historically irrelevant, but it would seem that 1874 does mark the beginning of a paradigmatic shift in chemistry equal in significance to the introduction of the theory of valency by August Kekulé and A. S. Couper in 1858. The changes brought about by the publications of Hassel, Prelog and Barton in the early 1950s, while dramatic, cannot be considered paradigmatic. The contrast can be seen in the reception of the ideas. The proposals of Barton, in particular, were almost immediately adopted and exploited by a large number of chemists; the proposals of Van't Hoff and Le Bel, on the other hand, were initially greeted with indifference and sometimes with hostility. It would seem that in this case there were not a sufficient number of prominent chemists actively interested in the problems to which the proposals of

Van't Hoff and Le Bel were directed. Throughout the book I have concentrated on the internal development of stereochemistry, and only considered in a superficial way the impact of stereochemistry on research in other areas such as biochemistry and inorganic chemistry, an exception being made as regards the inclusion of a discussion of studies concerned with the stereochemistry of biosynthetic reactions.

The organization of the topics in this book might strike the historian of science as somewhat unconventional. The reason for this is that a secondary aim of the book is to introduce the reader to some of the basic concepts and terminology of stereochemistry. Although it is assumed that the reader will not have an extensive background in either chemistry or the history of chemistry, it is to be hoped that the specialists in these areas will not find the book without interest.

The first draft of this book was written while on Sabbatical leave from Eastern Michigan University in 1973-74. The support of the University during this leave is gratefully acknowledged. Library and study facilities were generously provided during my stay at the University of Reading, England. I should like to thank Professors Andrew Gilbert, Neil Isaacs, Ernest Halberstadt, Derek Bryce-Smith, George Esselmont and Jim Irwin for their encouragement and for making my first trip to England such a pleasant one.

I am particularly grateful for the encouragement given to me by Professor Ernest L. Eliel, who devoted considerable time to a critical reading of the first draft. I should also like to express my appreciation to my wife, Patricia, for her continued support and encouragement.

June 1981

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To

Patricia and Sean

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Key papers by Odd Hassel, Derek H. R. Barton, Vladimir Prelog and John W. Cornforth

BIOGRAPHICAL NOTES AND COMMENTARY ON THE SIGNIFICANCE OF THE ARTICLES

In 1969 the Nobel Prize in Chemistry was awarded jointly to Odd Hassel, of the University of Oslo, and Derek H. R. Barton, of the Imperial College of Science and Technology (London), 'for developing and applying the principles of conformation in chemistry'. The term conformation might be defined as the three-dimensional arrangements of a molecule that are possible by virtue of rotation about single bonds.

Conformation ideas form such an integral part of present-day discussions of organic chemistry that it is perhaps difficult to appreciate the importance and impact of the introduction of such ideas in the middle of the 20th century. A dramatic shift in the direction of stereochemical research took place as a result of the publication of Barton's paper in the journal *Experientia* in 1950. Barton was able to apply the results of earlier physical chemical studies concerning the conformation of molecules to show how the conformation of a molecule determined some of its physical and chemical properties. The introduction of conformational analysis, which is the study of this interrelationship, into chemical research has been considered by many chemists as representing the first real advance in stereochemistry since the introduction of the theory of Van't Hoff and Le Bel in 1874. Prior to 1950 stereochemical research was largely concerned with the investigation of the phenomena of stereoisomerism. The change that took place in stereochemical research may be illustrated with reference to the history of the structure of one particular compound, cyclohexane. The historical details of the development of the studies concerned with the structure and conformation of cyclic compounds are provided in Chapters 13 and 14.