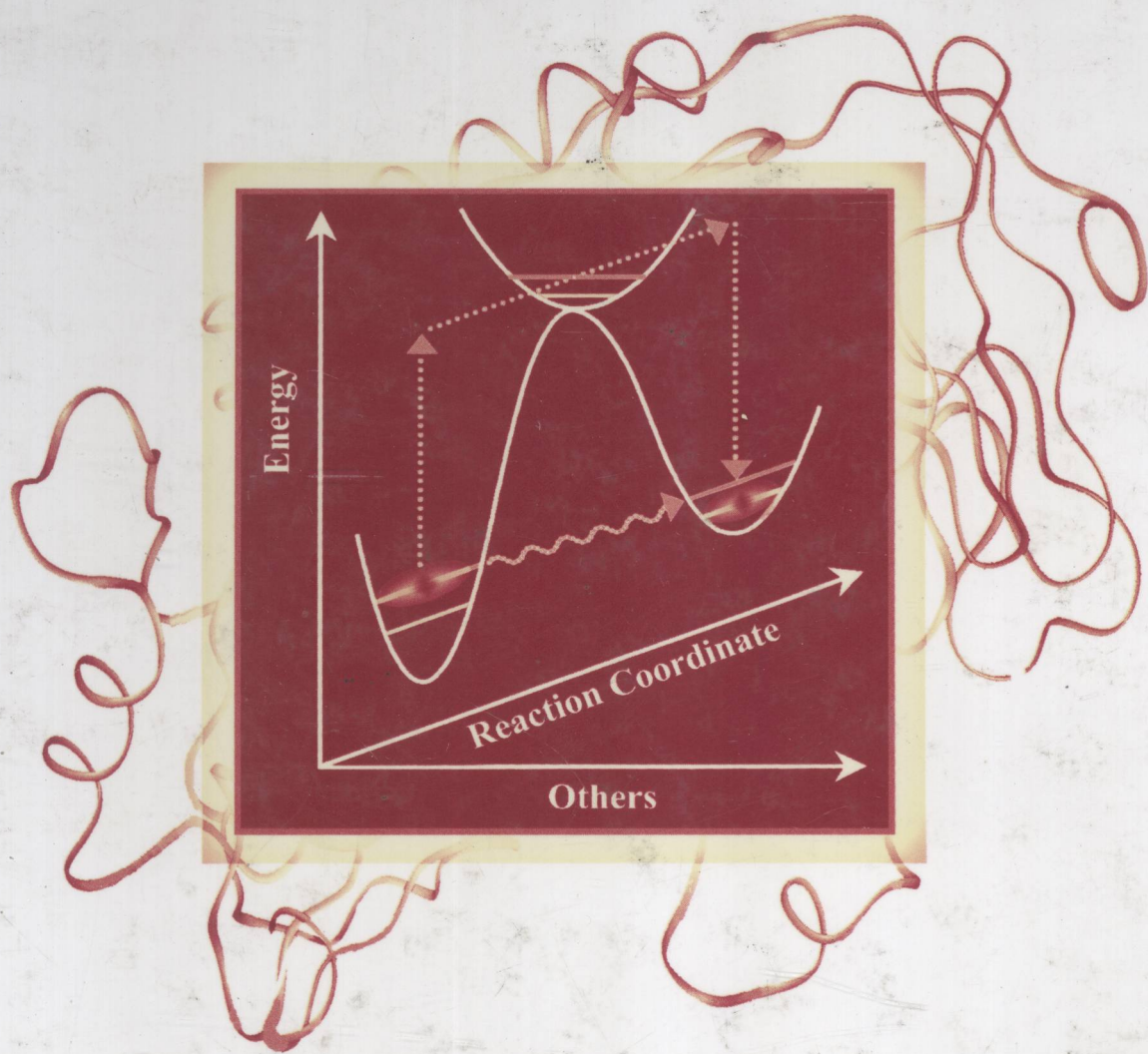


Isotope Effects in Chemistry and Biology



Taylor & Francis
Taylor & Francis Group

Edited by
Amnon Kohen
Hans-Heinrich Limbach

0345
J 85

Isotope Effects ⁱⁿ Chemistry ^{and} Biology

Edited by
Amnon Kohen
Hans-Heinrich Limbach



E200601039



Taylor & Francis

Taylor & Francis Group

Boca Raton London New York

A CRC title, part of the Taylor & Francis imprint, a member of the
Taylor & Francis Group, the academic division of T&F Informa plc.

Published in 2006 by
CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

© 2006 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group

No claim to original U.S. Government works
Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number-10: 0-8247-2449-6 (Hardcover)
International Standard Book Number-13: 978-0-8247-2449-8 (Hardcover)
Library of Congress Card Number 2005041897

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

No part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC) 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Library of Congress Cataloging-in-Publication Data

Isotope effects in chemistry and biology / edited by Amnon Kohen, Hans-Heinrich Limbach.

p. cm.

Includes bibliographical references and index.

ISBN 0-8247-2449-6

1. Chemical reaction, Conditions and laws of. 2. Isotopes. 3. Chemical kinetics. 4. Isobaric spin. 5. Chemical equilibrium. I. Kohen, Amnon. II. Limbach, Hans-Heinrich. III. Title.

QD501.I8127 2005

541'.394--dc22

2005041897

informa

Taylor & Francis Group
is the Academic Division of Informa plc.

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

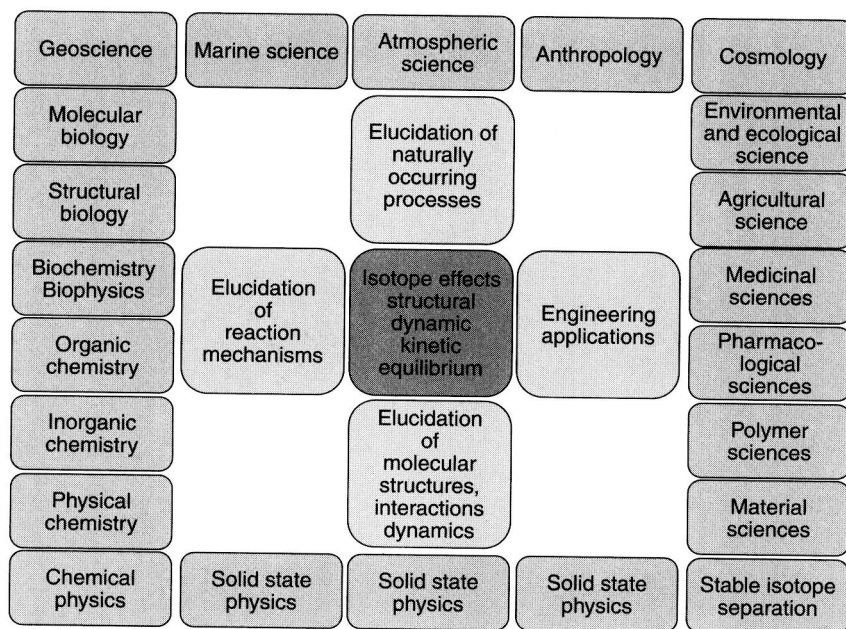
and the CRC Press Web site at
<http://www.crcpress.com>

Isotope Effects in Chemistry and Biology

Preface

The unifying theme of this book is the application of isotopic methods to make significant advances in chemistry and biology. Isotopes are atoms with identical nucleic electrical charges and identical electronic properties. Isotopes contain the same number of protons but a different number of neutrons, hence they exhibit different masses and different nuclear spins. Isotope effects can be classified into three categories, i.e., kinetic isotope effects (KIEs), equilibrium isotope effects (EIEs), and anharmonic isotope effects (AIEs). KIEs are the ratio of reaction rates involving reactants that only differ by their isotopic composition. These are one of the only measures that directly probe the nature of the reaction's transition state, and thus are very useful tools in studies of reactions' mechanisms. EIEs are the ratio of two isotopes that are distributed between stable populations in thermodynamic equilibrium. These are a unique measure of the difference in the chemical potential of these two populations. AIEs lead to geometric changes of molecules and molecular systems via the anharmonicity of zero-point vibrations. Isotope effects are of substantial importance and utility in many fields of science and technology. The use of isotope effects is prevalent in a wide variety of disciplines. Scheme 1 below summarizes many of the areas that utilize isotope effects.

The book's nine parts and 42 chapters provide a comprehensive review of developments in isotope effects studies to date. The chapters were written by internationally recognized leading researchers in their fields. Authors from 13 countries contributed to the book: Canada, Denmark, France, Germany, Israel, Japan, Poland, Russia, Spain, Sweden, Switzerland, UK, and USA (by alphabetical order).



Scheme 1. The many applications and implications of isotope effects and their relationship to many fields of science and technology. This Scheme was drawn by Takano Ishida and modified by Hans Limbach.

Subjects range from the physical and theoretical origin of isotope effects to modern uses of these effects in chemical, biological, geological, and other applications. The following Table of Contents clearly emphasizes the multidisciplinary nature of this book. The book starts with the problem of isotope effects on molecular geometries arising from anharmonic vibrations and the consequences for isotope-dependent non-covalent interactions. Chemical bond breaking and formation dynamics are then addressed using the examples of simple molecules in the gas phase, also including the motif of hydrogen transfer. Novel mass independent isotope effects are discussed. The problem of hydrogen transfer, tunneling, and exchange is picked up for condensed matter, ranging from polyatomic molecules to enzymes. When the barrier for hydrogen or proton transfer becomes small, the area of low-barrier hydrogen bonds is reached and explored experimentally and theoretically. A unique application is provided in a chapter devoted to water isotope effects under pressure. Isotope effect studies in organic and organometallic reactions are needed for the understanding of the sessions that follow on isotope effects in more complex enzyme reactions.

The book brings together a wide scope of different points of view and practical applications based on our current knowledge at the beginning of the new millennium. Some chapters summarize the perspective of a well-established subject while others review recent findings and ongoing research. It may appear that some of these later items are not consistent with each other. This reflects contemporary conclusions and controversies in the field. We chose to present such studies only in cases where clear scientific arguments and discussion are presented by all relevant authors. This approach demonstrates the way research progresses, and we hope it will enhance the reader's curiosity and interest.

Editors

Amnon Kohen was born in a kibbutz in northern Israel. He received his B.Sc. degree in chemistry in 1989 from the Hebrew University in Jerusalem and his D.Sc. in 1994 from the Technion-Israel Institute of Technology. After that he was a postdoctoral scholar with Judith Klinman at the University of California at Berkeley. In 1999, he moved to the University of Iowa and is currently (2005) an associate professor in the Department of Chemistry. His main interest is bioorganic chemistry, and he enjoys studying the mechanisms by which enzymes activate C–H bonds and N₂ triple bonds. His research focuses on the relationship between enzyme structure, dynamics, and catalytic activity. Isotope effects were one of the main tools used by his group in recent years.

Hans-Heinrich Limbach was born in Bruehl near Cologne, Germany. He studied chemistry at the Universities of Bonn and Freiburg. He did his doctoral research (Dr. rer. nat.) under the direction of Herbert W. Zimmermann at the University of Freiburg. After his Habilitation he was a visiting scientist with C.S. Yannoni at the IBM Research Laboratory, San Jose and with C.B. Moore at U.C. Berkeley. He is currently a professor of physical chemistry at the Freie Universität Berlin. His research interests include the chemistry of hydrogen and its isotopes in liquids, organic solids, and mesoporous systems up to enzymes, which he is studying by liquid and solid state nuclear magnetic resonance.

Contributors

Vernon E. Anderson

Department of Biochemistry
Case Western Reserve University
Cleveland, Ohio

Katsutoshi Aoki

Synchrotron Radiation Research Center
Kansai Research Establishment
Japan Atomic Energy Research Institute
Kansai, Japan

Jaswir Basran

Department of Biochemistry
University of Leicester
Leicester, United Kingdom

Jacob Bigeleisen

Department of Chemistry
State University of New York
Stony Brook, New York

Adam G. Cassano

Center for RNA Molecular Biology
Case Western Reserve University
Cleveland, Ohio

W. Wallace Cleland

Institute for Enzyme Research and
Department of Biochemistry
University of Wisconsin
Madison, Wisconsin

Paul F. Cook

Department of Chemistry and Biochemistry
University of Oklahoma
Norman, Oklahoma

Janet E. Del Bene

Department of Chemistry
Youngstown State University
Youngstown, Ohio

Gleb S. Denisov

V.A. Fock Institute of Physics
St. Petersburg State University
St. Petersburg, Russian Federation

Ileana Elder

Department of Pharmacology
University of Florida
Gainesville, Florida

Antonio Fernández-Ramos

Department of Physical Chemistry
Faculty of Chemistry
University of Santiago de Compostela
Santiago de Compostela, Spain

Paul F. Fitzpatrick

Department of Biochemistry & Biophysics
Texas A&M University
College Station, Texas

Perry A. Frey

Department of Biochemistry
University of Wisconsin-Madison
Madison, Wisconsin

Yasuhiko Fujii

Tokyo Institute of Technology
Research Institute for Nuclear Reactors
O-okayama, Meguro-ku, Tokyo, Japan

Nikolai S. Golubev

V.A. Fock Institute of Physics
St. Petersburg State University
St. Petersburg, Russian Federation

Sharon Hammes-Schiffer

Department of Chemistry
Davey Laboratory
Pennsylvania State University
University Park, Pennsylvania

Poul Erik Hansen

Department of Life Sciences and Chemistry
Roskilde University
Roskilde, Denmark

Michael E. Harris

Center for RNA Molecular Biology
Case Western Reserve University
Cleveland, Ohio

Alvan C. Hengge

Department of Chemistry and Biochemistry
Utah State University
Logan, Utah

Michael Hippler

Department of Chemistry
University of Sheffield
Sheffield, United Kingdom

James T. Hynes

Department of Chemistry and Biochemistry
University of Colorado
Boulder, Colorado

Takanobu Ishida

Department of Chemistry
State University of New York
Stony Brook, New York

William E. Karsten

Department of Chemistry and Biochemistry
University of Oklahoma
Norman, Oklahoma

Philip M. Kiefer

Department of Chemistry and Biochemistry
University of Colorado
Boulder, Colorado

Judith P. Klinman

Department of Chemistry and
Department of Molecular and Cell Biology
University of California
Berkeley, California

Heinz F. Koch

Department of Chemistry
Ithaca College
Ithaca, New York

Amnon Kohen

Department of Chemistry
University of Iowa
Iowa City, Iowa

Alexander M. Kuznetsov

Department of Chemistry
Technical University of Denmark
Lyngby, Denmark

Jonathan S. Lau

Department of Chemistry
University of California
San Diego, California

René Létolle

l'Universite Pierre et Marie Curie
Paris, France

Brett E. Lewis

The Albert Einstein College of Medicine
Bronx, New York

Hans-Heinrich Limbach

Institut für Chemie
Freie Universität
Berlin, Germany

John D. Lipscomb

Department of Biochemistry, Molecular
Biology and Biophysics
University of Minnesota
Minneapolis, Minnesota

Laura Masgrau

Department of Biochemistry
University of Leicester
Leicester, United Kingdom

Olle Matsson

Department of Chemistry
Uppsala University
Uppsala, Sweden

Zofia Mielke

Faculty of Chemistry
University of Wrocław
Wrocław, Poland

Dexter B. Northrop

Division of Pharmaceutical Sciences
School of Pharmacy
University of Wisconsin-Madison
Madison, Wisconsin

Mats H. M. Olsson

Department of Chemistry
University of Southern California
Los Angeles, California

Piotr Paneth

Institute of Applied Radiation Chemistry
Technical University of Lodz
Lodz, Poland

Charles L. Perrin

Department of Chemistry
University of California
San Diego, California

Ehud Pines

Department of Chemistry
Ben-Gurion University of the Negev
Be'er Sheva, Israel

Bryce V. Plapp

Department of Biochemistry
The University of Iowa
Iowa City, Iowa

Martin Quack

Physical Chemistry
ETH Zürich
Zürich, Switzerland

Daniel M. Quinn

The University of Iowa
Department of Chemistry
Iowa City, Iowa

François Robert

Laboratoire de Minéralogie
Centre National de Recherche Scientifique
Paris, France

Emil Roduner

Institut für Physikalische Chemie
Universität Stuttgart
Stuttgart, Germany

Etienne Roth

National des Arts et Métiers
Paris, France

Justine P. Roth

Department of Chemistry
Johns Hopkins University
Baltimore, Maryland

Richard L. Schowen

Simons Laboratories
Higuchi Biosciences Center
University of Kansas
Lawrence, Kansas

Vern L. Schramm

The Albert Einstein College of Medicine
Bronx, New York

Steven D. Schwartz

Departments of Biophysics and Biochemistry
The Albert Einstein College of Medicine
Bronx, New York

Nigel S. Scrutton

Department of Biochemistry
University of Leicester
Leicester, United Kingdom

Willem Siebrand

Steacie Institute for Molecular Sciences
National Research Council of Canada
Ottawa, Canada

David N. Silverman

Department of Pharmacology
University of Florida
Gainesville, Florida

Zorka Smedarchina

Steacie Institute for Molecular Sciences
National Research Council of Canada
Ottawa, Canada

Lucjan Sobczyk

Faculty of Chemistry
University of Wrocław
Wrocław, Poland

C. M. Stevens

Naperville, Illinois

Michael J. Sutcliffe

Department of Biochemistry
University of Leicester
Leicester, United Kingdom

Donald G. Truhlar

Department of Chemistry and
Supercomputing Institute
Minneapolis, Minnesota

Jens Ulstrup

Department of Chemistry
Technical University of Denmark
Lyngby, Denmark

W. Alexander Van Hook

Chemistry Department
University of Tennessee
Knoxville, Tennessee

Jordi Villà-Freixa

Grup de Recerca en Informàtica
Biomedica, IMIM/UPF
Barcelona, Spain

Arieh Warshel

Department of Chemistry
University of Southern California
Los Angeles, California

Ralph E. Weston Jr.

Chemistry Department
Brookhaven National Laboratory
Upton, New York

Max Wolfsberg

Chemistry Department
University of California
Irvine, California

Table of Contents

Chapter 1 Theoretical Basis of Isotope Effects from an Autobiographical Perspective	1
<i>Jacob Bigeleisen</i>	
Chapter 2 Enrichment of Isotopes	41
<i>Takanobu Ishida and Yasuhiko Fujii</i>	
Chapter 3 Comments on Selected Topics in Isotope Theoretical Chemistry	89
<i>Max Wolfsberg</i>	
Chapter 4 Condensed Matter Isotope Effects	119
<i>W. Alexander Van Hook</i>	
Chapter 5 Anharmonicities, Isotopes, and IR and NMR Properties of Hydrogen-Bonded Complexes	153
<i>Janet E. Del Bene</i>	
Chapter 6 Isotope Effects on Hydrogen-Bond Symmetrization in Ice and Strong Acids at High Pressure	175
<i>Katsutoshi Aoki</i>	
Chapter 7 Hydrogen Bond Isotope Effects Studied by NMR	193
<i>Hans-Heinrich Limbach, Gleb S. Denisov, and Nikolai S. Golubev</i>	
Chapter 8 Isotope Effects and Symmetry of Hydrogen Bonds in Solution: Single- and Double-Well Potential	231
<i>Jonathan S. Lau and Charles L. Perrin</i>	
Chapter 9 NMR Studies of Isotope Effects of Compounds with Intramolecular Hydrogen Bonds	253
<i>Poul Erik Hansen</i>	
Chapter 10 Vibrational Isotope Effects in Hydrogen Bonds	281
<i>Zofia Mielke and Lucjan Sobczyk</i>	

Chapter 11	Isotope Selective Infrared Spectroscopy and Intramolecular Dynamics	305
	<i>Michael Hippler and Martin Quack</i>	
Chapter 12	Nonmass-Dependent Isotope Effects	361
	<i>Ralph E. Weston, Jr.</i>	
Chapter 13	Isotope Effects in the Atmosphere	387
	<i>Etienne Roth, René Létolle, C. M. Stevens, and François Robert</i>	
Chapter 14	Isotope Effects for Exotic Nuclei	417
	<i>Olle Matsson</i>	
Chapter 15	Muonium — An Ultra-Light Isotope of Hydrogen	433
	<i>Emil Roduner</i>	
Chapter 16	The Kinetic Isotope Effect in the Photo-Dissociation Reaction of Excited-State Acids in Aqueous Solutions	451
	<i>Ehud Pines</i>	
Chapter 17	The Role of an Internal-Return Mechanism on Measured Isotope Effects	465
	<i>Heinz F. Koch</i>	
Chapter 18	Vibrationally Enhanced Tunneling and Kinetic Isotope Effects in Enzymatic Reactions	475
	<i>Steven D. Schwartz</i>	
Chapter 19	Kinetic Isotope Effects for Proton-Coupled Electron Transfer Reactions	499
	<i>Sharon Hammes-Schiffer</i>	
Chapter 20	Kinetic Isotope Effects in Multiple Proton Transfer	521
	<i>Zorka Smedarchina, Willem Siebrand, and Antonio Fernández-Ramos</i>	
Chapter 21	Interpretation of Primary Kinetic Isotope Effects for Adiabatic and Nonadiabatic Proton-Transfer Reactions in a Polar Environment	549
	<i>Philip M. Kiefer and James T. Hynes</i>	
Chapter 22	Variational Transition-State Theory and Multidimensional Tunneling for Simple and Complex Reactions in the Gas Phase, Solids, Liquids, and Enzymes	579
	<i>Donald G. Truhlar</i>	

Chapter 23	Computer Simulations of Isotope Effects in Enzyme Catalysis	621
<i>Arieh Warshel, Mats H. M. Olsson, and Jordi Villà-Freixa</i>		
Chapter 24	Oxygen-18 Isotope Effects as a Probe of Enzymatic Activation of Molecular Oxygen	645
<i>Justine P. Roth and Judith P. Klinman</i>		
Chapter 25	Solution and Computational Studies of Kinetic Isotope Effects in Flavoprotein and Quinoprotein Catalyzed Substrate Oxidations as Probes of Enzymic Hydrogen Tunneling and Mechanism	671
<i>Jaswir Basran, Laura Masgrau, Michael J. Sutcliffe, and Nigel S. Scrutton</i>		
Chapter 26	Proton Transfer and Proton Conductivity in Condensed Matter Environment	691
<i>Alexander M. Kuznetsov and Jens Ulstrup</i>		
Chapter 27	Mechanisms of CH-Bond Cleavage Catalyzed by Enzymes	725
<i>Willem Siebrand and Zorka Smedarchina</i>		
Chapter 28	Kinetic Isotope Effects as Probes for Hydrogen Tunneling in Enzyme Catalysis	743
<i>Amnon Kohen</i>		
Chapter 29	Hydrogen Bonds, Transition-State Stabilization, and Enzyme Catalysis	765
<i>Richard L. Schowen</i>		
Chapter 30	Substrate and pH Dependence of Isotope Effects in Enzyme Catalyzed Reactions	793
<i>William E. Karsten and Paul F. Cook</i>		
Chapter 31	Catalysis by Alcohol Dehydrogenases	811
<i>Bryce V. Plapp</i>		
Chapter 32	Effects of High Hydrostatic Pressure on Isotope Effects	837
<i>Dexter B. Northrop</i>		
Chapter 33	Solvent Hydrogen Isotope Effects in Catalysis by Carbonic Anhydrase: Proton Transfer through Intervening Water Molecules	847
<i>David N. Silverman and Ileana Elder</i>		

Chapter 34	Isotope Effects from Partitioning of Intermediates in Enzyme-Catalyzed Hydroxylation Reactions	861
<i>Paul F. Fitzpatrick</i>		
Chapter 35	Chlorine Kinetic Isotope Effects on Biological Systems	875
<i>Piotr Paneth</i>		
Chapter 36	Nucleophile Isotope Effects	893
<i>Vernon E. Anderson, Adam G. Cassano, and Michael E. Harris</i>		
Chapter 37	Enzyme Mechanisms from Isotope Effects	915
<i>W. Wallace Cleland</i>		
Chapter 38	Catalysis and Regulation in the Soluble Methane Monooxygenase System: Applications of Isotopes and Isotope Effects	931
<i>John D. Lipscomb</i>		
Chapter 39	Secondary Isotope Effects	955
<i>Alvan C. Hengge</i>		
Chapter 40	Isotope Effects in the Characterization of Low Barrier Hydrogen Bonds	975
<i>Perry A. Frey</i>		
Chapter 41	Theory and Practice of Solvent Isotope Effects	995
<i>Daniel M. Quinn</i>		
Chapter 42	Enzymatic Binding Isotope Effects and the Interaction of Glucose with Hexokinase	1019
<i>Brett E. Lewis and Vern L. Schramm</i>		
Index	1055

1 Theoretical Basis of Isotope Effects from an Autobiographical Perspective

Jacob Bigeleisen

CONTENTS

I.	From Soddy–Fajans through Urey–Greiff	1
II.	Equilibrium Systems — General	3
III.	Equilibrium in Ideal Gases	4
	A. Classical and Quantum Mechanical Systems	4
	B. The Reduced Partition Function Ratio of an Ideal Gas	5
	1. Numerical Calculation of the Reduced Partition Function Ratio	7
	C. Corrections to the Bigeleisen–Mayer Equation	8
IV.	Isotope Chemistry and Molecular Structure	12
	A. The First Order Rules of Isotope Chemistry	12
	B. Statistical Mechanical Perturbation Theory	13
	C. Polynomial Expansions of the Reduced Partition Function Ratio	14
V.	Kinetic Isotope Effects	18
VI.	Condensed Matter Isotope Effects	25
	Acknowledgments	32
	References	33

I. FROM SODDY–FAJANS THROUGH UREY–GREIFF

Isotopes were discovered in radiochemical investigations of the decay of the heavy elements. Products were found with different nuclear properties, which could not be separated chemically, but stood in the same place in the Periodic Table; e.g. Radium, ^{226}Ra , an α emitter with a half life of 1600 years, Mesothorium 1, ^{228}Ra , a β emitter with a half life of 5.7 years and Actinium X, ^{223}Ra , an α emitter with a half life 11.7 days. They were named isotopes by Soddy¹ from the Greek words ισοσ τοπος , the same place. Isotopes had the same nuclear charge, but different atomic masses. This was firmly established by the determination of the atomic weights of the lead isotopes which were the end products of the three radioactive series. Lead from the thorium series was found to have an atomic weight of 207.77; lead from the uranium–radium series had an atomic weight of 206.08. Fajans,² a major figure in radiochemistry, concluded that isotopes had similar, but not identical, chemical properties. Since isotopes have different atomic masses, molecules substituted with sister isotopes (isotopomers) would have different vibrational frequencies. Consequently they would have different heat capacities, entropies, and free energies. After WWI, Lindemann^{3,4} subsequently known as Lord Cherwell, derived the equations for the differences in vapor pressures

of isotopes. For a monatomic solid with a Debye frequency distribution, Lindemann found

$$\ell n(P'/P) = 9/8(\Theta' - \Theta)_D/T \quad [\Theta_D = h\nu_D/k > 2\pi] \quad (1.1)$$

$$\ell n(P'/P) = 3/40(\Theta'^2 - \Theta^2)_D/T^2 \quad [\Theta_D = h\nu_D/k < 2\pi] \quad (1.2)$$

where Θ' and Θ are the Debye temperatures for the light and heavy isotopomers, respectively. Equation 1.1 and Equation 1.2 were derived for the case that there was a zero point energy associated with a vibration. He calculated the difference in vapor pressures of ^{206}Pb and ^{208}Pb and predicted the ratio of the vapor pressures of $^{206}\text{Pb}/^{208}\text{Pb}$ to be 1.0002 at 600 K. A much larger effect of the opposite sign was predicted for the case of no zero point energy. Since no such difference was found, Lindemann correctly concluded that there was a zero point energy. In actual fact, Lindemann's calculation for the zero point energy case is a factor of ten too large; the correct calculation from Equation 1.2 leads to a result of 0.002%; the light isotope, ^{206}Pb , has the higher vapor pressure. Equation 1.2, which had been derived independently by Otto Stern, provided the incentive for Keesom and Van Dijk⁵ to achieve a partial separation of the neon isotopes by low temperature fractional distillation.

In planning a search for an isotope of mass 2, Urey⁶ decided to carry out an enrichment of hydrogen of natural abundance by a Raleigh distillation. He used Equation 1.1 to estimate the difference in vapor pressures of H_2 and HD . Urey then turned his attention to the question of isotope effects in chemical reactions. He had his student, David Rittenberg, calculate, using quantum statistical mechanics, the equilibrium constant for the exchange reaction



as a function of temperature.⁷ Their calculations were confirmed by experiment.⁸ The method of Urey and Rittenberg was extended to the case of polyatomic molecules by Urey and Greiff.⁹ For the isotopic exchange reaction



they expressed the equilibrium constant in terms of partition function ratios.

$$K = (\text{AY}/\text{A}'\text{Y})/(\text{AX}/\text{A}'\text{X}) = (Q/Q')_{\text{AY}}/(Q/Q')_{\text{AX}} \quad (1.5)$$

$$Q = \sum_i \exp(-\varepsilon_i/kT) \quad (1.6)$$

For the partition function ratio of molecules of like symmetry, (Q/Q') , and for which the translation and rotation obeyed classical statistical mechanics, they obtained

$$(Q_1/Q_2) = (M_1/M_2)^{3/2}[(ABC)_1/(ABC)_2]^{1/2} \prod_i [(e^{(u_{2i}-u_{1i})/2})(1 - e^{-u_{2i}})/(1 - e^{-u_{1i}})] \quad (1.7)$$

In Equation 1.7 subscripts 1 and 2 refer to the heavy and light isotopes, respectively; M is the molecular weight, A , B , and C are the principal moments of inertia and $u_i = hu_i = h\nu_i/kT$. The terms $e^{(u_{2i}-u_{1i})/2}$ and $(1 - e^{-u_{2i}})/(1 - e^{-u_{1i}})$ are, respectively, the contributions from the zero point energy differences between the light molecule, u_2 , and the heavy molecule, u_1 , and the Boltzmann excitation factors. Urey and Greiff⁹ tabulated values of (Q_1/Q_2) for compounds of the light elements as a function of temperature between 273 and 600 K. The values of (Q_1/Q_2) varied from an order of magnitude for the isotopes of hydrogen to a few percent for isotopes of the elements in the first two rows of the periodic table. The ratios decreased with temperature. The equilibrium constant for an isotopic exchange reaction, which is the quotient of two partition function ratios, is of the order of a few percent excepting those reactions which involve the isotopes of hydrogen. Urey was able to utilize small differences in the chemical properties of the light