# **Chemical Creativity**

Ideas from the Work of Woodward, Hückel, Meerwein, and Others



Weinheim · New York · Chichester · Brisbane · Singapore · Toronto

# Table of Contents

Preface vii

## Chapter 1 Introduction 1

- 1.1 Objectives 1
- 1.2 What is Special About This Book? 2
- 1.3 The Nature of Science and the History of Science 5
- 1.4 This Book: An Experiment 7
- 1.5 Acknowledgments 8
- 1.6 References 8

# Chapter 2 Discoveries Missed, Discoveries Made: Two Case Studies of Creativity in Chemistry 9

- 2.1 Science and the Individual 9
- 2.2 Diels, Alder, Their Competitors, and the Discovery of the "Diene Synthesis" (Diels-Alder Reaction) 9
- 2.3 Predecessors and Near-Discoverers 14
- 2.3.1 Early Workers 14
- 2.3.2 von Euler and a Near Miss 14
- 2.3.3 The Mystery of Albrecht 17
- 2.4 Thiele and Albrecht 18
- 2.5 Thiele's Nature 20
- 2.6 The Alternation Effect and the Discovery of Orbital Symmetry Conservation 24
- 2.7 Experimental Stimulus for the Orbital Symmetry Rules 25
- 2.8 Theory 26
- 2.9 Predecessors: Havinga, Schlatmann, Oosterhoff 26
- 2.10 Oosterhoff's Scientific Style 28
- 2.11 Conclusions 30
- 2.12 Acknowledgments 31
- 2.13 References 31

# Chapter 3 Erich Hückel and the Theory of Aromaticity: Reflections on Theory and Experiment 33

- 3.1 Hückel's Contributions 33
- 3.2 Biographical Introduction 34
- 3.3 The Debye-Hückel Theory of Electrolytic Solutions 35
- 3.4 The Nature of the Double Bond 36
- 3.5 Hybridization in Double Bonds 42

- 3.6 The Benzene Problem 43
- 3.6.1 Hückel's "First Method" 44
- 3.6.2 Hückel's "Second Method" 47
- 3.7 A Chilly Reception from the Experimentalists 50
- 3.8 Experimental Tests of the MO Description of Conjugated Cyclic Compounds 52
- 3.9 Orbital Symmetry, the Extension of Cyclic  $\pi$ -Electron MO Theory to Transition States of Pericyclic Reactions 53
- 3.10 Connectivity as a Strong Determinant of Spin in Non-Kekulé Molecules. Violations of Hund's Rule in Biradicals 55
- 3.11 Reflections on Hückel's Career 58
- 3.12 Hückel's Uncomfortable Location and Professional Flaws 59
- 3.13 Hückel's Personality 59
- 3.14 Illness, Politics, and War. Hückel and the Nazis 60
- 3.15 The Ambiguities of Morality 64
- 3.16 The Response of Academic Institutions to Assaults on Academic Freedom 66
- 3.17 Summary and Outlook 69
- 3.18 Acknowledgments 70
- 3.19 References 70

#### Chapter 4 The Dienone-Phenol Mysteries 77

- 4.1 Introduction 77
- 4.2 Isolation of the Estrogens 77
- 4.3 Approaches to Synthetic Estrogens by Aromatization of Ring A Alicyclic Steroids 78
- 4.3.1 By Pyrolysis 79
- 4.3.2 By Dienone-Phenol Rearrangement 80
- 4.3.3 Woodward's Challenge 82
- 4.3.4 Misgivings about the Structures 83
- 4.3.5 Why Did Woodward Undertake the Correction of the Phenolic Structures? 83
- 4.4. Woodward and the Total Synthesis of Steroids. Targets, Approaches, and Achievements 84
- 4.4.1 Stage I. Rings A-B Aromatic Steroids 86
- 4.4.2 Stage II. Hydroaromatic Steroids 86
- 4.5 A Mechanistic Motivation 88
- 4.5.1 Woodward's First Experiment. The Model Dienone 89
- 4.5.2 Subtleties and Complications. The Effect of Reaction Conditions 93
- 4.5.3 Further Complications. Alternative Rearrangement Routes. The Bridgehead → Bridgehead Methyl Shift 95
- 4.5.4 Woodward's Second Experiment. The Methylene Migrations: Successive 1,2-Rearrangements or 1,3-Rearrangement via a Π-Complex? 97

- 4.5.5 The Direct 1,3-Rearrangement Mechanism in the Phenol-Phenol Rearrangement 101
- 4.6 Conclusions 102
- 4.7 Acknowledgments 103
- 4.8 References 104

# Chapter 5 Meditations on the Special Convictive Power of Symmetrization Experiments 109

- 5.1 Introduction 109
- 5.2 Enolization as a Mechanism of Symmetrization. The Menthone Problem 110
- 5.3 Tricyclene and the Wagner-Meerwein Rearrangement 116
- 5.4 The Pinacol Controversy 119
- 5.5 Meerwein's First Hypothesis: Rearrangement via Divalent Carbon Intermediates 121
- 5.6 Ruzicka's Experiment and Support for the Tricyclene Hypothesis. Optical Activity Despite Achirality? 124
- 5.7 Meerwein's Response 127
- 5.8 Carbonium Ions (Carbocations) as Intermediates in the Wagner Rearrangements 130
- 5.9 Racemization of Camphene and Related Symmetrization Phenomena 132
- 5.10 The Favorskii Rearrangement. Symmetrization yes, but via Which Intermediate? 136
- 5.11 Symmetrization yes, but is There a Symmetrical Intermediate? Racemization Machines with no Achiral Parts Reaction Symmetrization Without Molecular Symmetry 139
- 5.11.1 Case d. Symmetrization via a Multi-step Mechanism Without Symmetrical Intermediates 143
- 5.12 The Direct Nucleophilic Displacement Reaction, and how we came to know its Stereochemistry 149
- 5.12.1 Phillips and Kenyon 150
- 5.12.2 The Walden Inversion 151
- 5.12.3 The Significance of Kinetic Form 157
- 5.12.4  $S_N l$  and  $S_N 2$  157
- 5.12.5 The Peculiar Attraction of Symmetrization Experiments 159
- 5.13 The Human Response to the Symmetrical 161
- 5.14 Symmetry in Cosmology and Aesthetics 162
- 5.15 Kepler, Symmetry, and Perfection 164
- 5.16 Kepler and the Secret of the Universe 165
- 5.17 The Attraction of Symmetry: Biological and Evolutionary Necessity or Illusory Concept? 169
- 5.18 Gestalt Psychology and Aesthetics 169

## Table of Contents

- 5.19 Symmetry in Ethology and Psychobiology. Is There a Biological Preference for Symmetry? 171
- 5.20 Visual Detection of Bilateral Symmetry 172
- 5.21 Conclusions 174
- 5.22 Acknowledgments 175
- 5.23 References 175

Chapter 6 Epilogue 181

Author Index 183

Subject Index 189