

CONTENTS

Preface	v
Chapter 1. Introduction	1
Chapter 2. Apparatus and Techniques	3
I. High-Pressure Apparatus	3
A. The Reaction Bomb	3
1. Description	3
2. Volume Limitations	5
3. Small Scale Reactors	5
B. Safety Precautions	5
C. Technique	7
II. Low-Pressure Apparatus	8
A. Parr Hydrogenator	8
B. Technique	9
C. Micro-Hydrogenations	10
III. Atmospheric-Pressure Apparatus	11
A. Sloping-Manifold and Similar Hydrogenators	11
1. Description	11
2. Technique	13
B. Brown ² Hydrogenator	15
1. Description	15
2. Technique	17
C. Micro-Hydrogenators	17
1. Brown ² Hydro-Analyzer	17
2. Sloping Manifold Apparatus	18
3. Clauson-Kaas Hydrogenator	18
4. Introduction of the Substrate	18
5. Temperature Control	19
6. Hydrogenations on Chromatography Paper	20
Chapter 3. Catalysts and Conditions	23
I. The Catalyst	23
A. Activity and Selectivity	23
B. Catalyst Systems	24

1. Nickel 24
 - a. Urushibara Catalyst 25
 - b. Supported Catalysts; Nickel on Kieselguhr 25
 - c. Nickel Boride 25
 - d. Raney Nickel 26
 - (1) Different Types 26
 - (2) Deuteration Catalysts 29
 - (3) Storage Limitations 29
 - (4) Acidic Catalysts 29
 - (5) Comparison with Supported Catalysts 30
 - e. Promoters 31
 - f. Inhibitors and Poisons 31
2. Other Raney Catalysts 32
 - a. Raney Cobalt 32
 - b. Raney Copper and **Raney Iron** 32
3. Copper-Chromium Oxide 32
4. Platinum 34
 - a. Platinum Oxide 34
 - b. Platinum Black 34
 - c. Supported Platinum 35
 - d. Promoters 35
 - e. Inhibitors and Poisons 36
5. Palladium 36
 - a. **Supported** Palladium 36
 - b. Asymmetric Catalysts 37
 - c. Promoters 38
 - d. Inhibitors 38
6. Rhodium and Ruthenium 39
 - a. Rhodium 39
 - b. Ruthenium 40
7. Rhenium 40
- II. Reaction Conditions 41
 - A. Temperature 41
 1. Effect on the Rate of Reaction 41
 2. Effect on Reaction Selectivity 41
 3. Side Reactions 42
 - B. Pressure 43
 1. Effect on the Rate of Reaction 43
 2. Effect on Reaction Selectivity 43
 - C. Solvents 44
 1. Neutral Solvents 44
 - a. Limitations 44
 - b. Effect on Reaction Rate and Product Stereochemistry 45
 - c. Use in Dehalogenations 45
 2. Acidic and Basic Solvents 46
 - a. Effect on Reaction Rates 46
 - b. Effect on Product Stereochemistry 46
 - (1) Cyclohexanones and Cyclohexanone **Oximes** 46
 - (2) **Olefins** 47
 - (3) Unsaturated Ketones 47

- D. Quantity of Catalyst 49
 - 1. Effect on the Rate of Reaction 49
 - 2. Effect on Reaction Selectivity 49

Chapter 4. Hydrogenation of Functional Groups I 57

- I. Olefins 57
 - A. Isolated Double Bonds 57
 - 1. Catalysts 57
 - 2. Selectivity 58
 - 3. Stereochemistry 59
 - B. Conjugated Double Bonds 60
 - 1. $C=C-C=C$ Type 60
 - 2. $C=C-C=O$ and $C=C-C\equiv N$ Type 60
 - a. Selectivity 60
 - b. Stereochemistry 61
 - c. α - β , γ - δ Diunsaturated Ketones 62
 - C. Cumulative Double Bonds 62
 - D. Steroidal Double Bonds 63
 - 1. Isolated Olefins 63
 - 2. Ketone Conjugated Olefins 64
 - E. Enol Ethers and Esters 64
 - F. Deuteration and Tritiation of Double Bonds 66
 - 1. Limitations 66
 - 2. Conditions 66
 - G. Asymmetric Hydrogenations 67
 - H. Double Bond Migration 68
 - 1. Effect of Catalyst and Conditions 68
 - 2. Steric Requirements 69
- II. Acetylenes 69
 - A. Catalysts 70
 - B. Selectivity 70
- III. Aromatic Compounds 71
 - A. Substituted Benzenes 71
 - 1. Alkyl Benzenes 72
 - 2. Phenols and Phenyl Ethers 72
 - 3. Anilines 73
 - 4. Aryl Halides 74
 - 5. Benzoic Acids and Esters 74
 - 6. Stereochemistry 74
 - B. Tropones and Tropolones 74
 - C. Polycyclic Aromatics 74
 - 1. Naphthalenes and Biphenyls 74
 - 2. Phenanthrene and Anthracene 75

Chapter 5. Hydrogenation of Functional Groups II 81

- I. Aldehydes and Ketones 81
 - A. Aromatic Carbonyl Groups 81
 - 1. Hydrogenation to the Alcohol 81

- 2. Phenol Ketones 82
- 3. Hydrogenolysis to the Methylene 82
 - a. Phenol Ketones 82
 - b. Palladium Catalyzed 83
 - c. Exceptions 83
- 4. Selectivity 83
- B. Other Activated Ketones 84
- C. Aliphatic Ketones and Aldehydes 85
 - 1. Monocarbonyl Compounds 85
 - 2. α -Hydroxymethylene Ketones 85
 - 3. Polyketones and **Hydroxyketones** 85
 - 4. Stereochemistry 86
 - a. Neutral Media 86
 - b. Basic Media 86
 - c. Acidic Media 87
 - 5. Selective Hydrogenation in the Presence of Double Bonds 87
- D. Ketenes and Ketene Dimers 88
- II. Carboxylic Acids and Derivatives 88
 - A. Carboxylic Acids 88
 - B. Esters and **Lactones** 89
 - C. **Amides** and Imides 90
 - D. Anhydrides 91
- III. Nitro Groups 91
 - A. Aromatic Nitro Compounds 91
 - B. Aliphatic Nitro Groups 93
 - 1. Selectivity 93
 - 2. α -Hydroxy Nitro Compounds 93
 - 3. Stereochemistry 93
 - 4. Vinyl and Styryl Nitro Compounds 94
 - 5. **Hydrogenative** Cyclization 94
- IV. **Nitroso**, Azoxy, and Azo Compounds 95
- V. Azides and Diazo Compounds 95
- VI. **Nitriles** 96
 - A. Hydrogenation to Primary **Amines** 96
 - B. Dinitriles 97
 - C. Cyanohydrins and α -Amino **Nitriles** 98
 - D. Selectivity 99
 - E. Aldehydes From **Nitriles** 99
- VII. Oximes 100
 - A. Unsubstituted Oximes 100
 - B. Oximinoketones 100
 - C. Stereochemistry 101
 - D. Dioximes 101
- VIII. Azines, **Hydrazones**, and Semicarbazones 102
- IX. Imines and Reductive Alkylation 102
- X. Heterocycles 104
 - A. Pyridines 104
 - 1. Catalysts 104
 - 2. Selectivity 104

- 3. Amino- and Hydroxypyridines 105
- 4. Pyridine Acids 106
- B. Quinolines and Isoquinolines 106
- C. Pyrroles 107
- D. **Indoles** 108
- E. Furans 109
- F. Pyrans, Pyrones, Chromones, and **Coumarins** 110
- G. Thiophenes 111
- H. Other Heterocycles 118

Chapter 6. Hydrogenolysis

125

- I. **C—X Bonds** 125
 - A. Aliphatic Halogen Compounds 125
 - 1. Alkyl Halides 125
 - 2. Benzyl, Vinyl, and **Allyl** Halides 126
 - 3. Cyclopropyl Halides 127
 - 4. Deuterolysis 127
 - B. Aryl Halogen Compounds 128
 - C. Heterocyclic Halogen Compounds 129
 - D. Acyl Halides 130
 - 1. Reaction Conditions 130
 - 2. Moderators 131
- II. **C—S Bonds** 131
 - A. Reaction Conditions 131
 - B. Synthetic Applications 132
 - C. Limitations 133
- III. **S—S Bonds** 133
- IV. **C—C Bonds** 133
 - A. Cyclopropanes 133
 - B. **β -Phenylethanols** 134
- V. **C—O Bonds**, 135
 - A. Benzyl Alcohols, Ethers, and Esters 135
 - 1. Benzyl Ethers 135
 - 2. Benzyl Esters 136
 - 3. Carbobenzyloxy Groups 136
 - B. **Allyl Alcohols** 137
 - C. Epoxides 137
 - D. Acetals and Ketals 138
- VI. **O—O Bonds** 139
- VII. **C—N Bonds**; Benzyl Amines 139
- VIII. Other Bonds 142
- IX. Stereochemistry of Hydrogenolysis 142

Appendixes

147

- I. Preparation of Raney Nickel Catalysts 147
 - A. W 2 Raney Nickel 147
 - B. W 4 Raney Nickel 147
 - C. W 6 Raney Nickel 148
 - D. W 7 Raney Nickel 148
 - E. W 8 Raney Nickel: Deuteration Catalyst 148

2. Preparation of Copper-Barium-Chromium Oxide	150
3. Preparation of Platinum Catalysts	151
A. Platinum Oxide	151
B. 5% Platinum on Charcoal	151
4. Preparation of Palladium Catalysts	152
A. 5% Palladium on Charcoal	152
B. 5% Palladium on Barium Sulfate	152
C. Other Supports and Metal Percentages	153
Author Index	157
Subject Index	170