

ORGANIC PREPARATIONS



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OF LEIPZIG

*Translated and Revised from the
German Text*

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PUBLISHER'S NOTE

This volume is a translation of Part II, "Reaktionen," of Conrad Weygand's *Organisch-chemische Experimentierkunst*, published in Leipzig in 1938. Parts I and III are not included for the following reasons: Part I, on materials and operations necessary for the execution of organic syntheses, deals mainly with German laboratory equipment, so that a literal translation would have limited value for the American reader. An adaptation of the text to American equipment would have necessitated a complete rewriting of this section, a task considered beyond the scope of a translation. Part III of the German book, on the chemical and physical analyses of organic compounds, is covered by a number of excellent American texts. A translation would thus have constituted a duplication we wished to avoid.

There is one major difference between the German original and the English translation. The former contains a number of extensive literal quotations of preparations published in *Organic Syntheses*; these have been replaced in the translation by references to the corresponding volumes of *Organic Syntheses*; and wherever possible references to single volumes of *Organic Syntheses* have been replaced by references to Collective Volume I, 2nd edition, 1941, or to Collective Volume II, 1943.

In the translation of Part II, our collaborators followed the German text as closely as possible, correcting only obvious errors and taking care of a few obvious omissions. Responsibility for the content of the book rests, therefore, with Dr. Weygand. The actual work on the translation was carried out in the following sequence. A rough translation of the German text by A. Schormüller was revised from the linguistic point of view, and corrections in the German text made, by W. A. Gregory, J. E. Jones, C. J. Kibler, J. L. Leiserson, H. D. Porter, I. F. Salminen, and C. V. Wilson, all of Rochester, New York, and H. R. Rosenberg of Wilmington, Delaware. The index was compiled by Mrs. Lucia Dawe, who edited and proofread the text.

During the entire process of the translation and editing of the book we enjoyed the advice and cooperation of H. R. Rosenberg and A. Weissberger, to whom we wish to express our appreciation.

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PREFACE TO THE GERMAN EDITION

(Translated)

Laboratory procedure in organic chemistry can be presented from various viewpoints. In this book it will be treated as an experimental art, which, in view of the wide scope of the material to be included, is the only way to organize all the pertinent facts in a restricted space.

The arrangement follows the natural course of laboratory work in organic chemistry, which usually begins with construction of apparatus and, after a variety of reactions have been investigated, concludes with analysis and physical identification.

The section dealing with chemical reactions is arranged according to one of the customary systems, whose basis is the formation of the various linkages of the carbon atom and their fission. This system is more methodical than the division according to reactive groups alone, and permits of greater elaboration. It also makes more apparent that all the basic reactions can be illustrated by simple, clear examples. Now more than ever the applications to work with complicated natural and synthetic substances must be left to the specialist, who alone is able to cover a particular field with any degree of completeness. The examples were chosen for their usefulness and with the purpose of presenting a representative view of organic chemistry. The simple precepts which are to be found in all elementary laboratory manuals are not repeated in this book.

The most important of the physical methods are included. The difficulty of their general introduction into the organic laboratory is often underrated, particularly by those organic chemists who have little experience with them. There is no lack of special treatises in this field.

The publishers have spared no pains in setting up the book in accordance with the wishes of the author.

The author wishes to thank his assistants, Dr. H. Baumgärtel, Dr. W. Lanzendorf, and Mr. Siebenmark, for their tireless collaboration.

C. WEYGAND

Leipzig, June, 1938

CONTENTS

	PAGE
Publisher's Note.....	v
Author's Preface to the German Edition.....	vi
Introduction.....	1
Chap. 1. Formation of Carbon-Hydrogen Bonds.....	4
I. Formation of C—H Bonds by Addition.....	4
A. Addition of Hydrogen to Unsaturated Carbon Bonds.....	4
1. Addition of Hydrogen to Ethylene Bonds and to Aromatic and Heterocyclic Systems.....	5
2. Catalytic Hydrogenation.....	10
Recovery of Catalysts.....	15
3. Hydrogenation Procedures.....	18
4. Specific Effects of Hydrogenation.....	21
Examples of Catalytic Hydrogenation.....	23
5. Addition of Hydrogen to Acetylene Bonds.....	29
B. Addition of Hydrogen to Radicals and to Alicyclic Systems.....	32
C. Atomic Hydrogen.....	33
D. Addition of Hydrogen to C=O Bonds.....	34
1. Reduction of Aldehydes to Primary Alcohols.....	35
2. Reduction of Ketones to Secondary Alcohols.....	35
3. Catalytic Reduction of the C=O Group.....	36
II. Formation of C—H Bonds by Exchange.....	
A. Replacement of Halogen by Hydrogen.....	40
1. Halogen on a Saturated C—C Bond.....	40
2. Halogen on an Unsaturated C—C Bond.....	44
3. Halogen Bound in Other Ways.....	44
B. Replacement of Oxygen by Hydrogen.....	46
1. Replacement of Hydroxyl Group.....	46
2. Replacement of Carboxyl Oxygen.....	49
3. Replacement of Oxygen in Carboxylic Acids and Esters.....	54
C. Replacement of Trivalent Nitrogen by Hydrogen.....	56
1. Amino Groups.....	56
2. Other Compounds of Trivalent Nitrogen.....	57
D. Replacement of Sulfonic Group in Aromatic Substances by Hydrogen.....	58
Chap. 2. Formation of Carbon-Halogen Bonds.....	59
I. By Addition.....	59
A. Addition of Halogen to Unsaturated Carbon Compounds.....	59
1. Addition to Ethylenic Bonds and to Aromatic Systems.....	59
2. Addition to Acetylenic Bonds.....	64
B. Addition of Hydrogen Halide to Unsaturated Carbon Compounds.....	65
1. Addition to Ethylenic Bonds.....	65
2. Addition to Acetylenic Bonds.....	68

	PAGE
<i>Chap. 2. Formation of Carbon-Halogen Bonds (contd.)</i>	
C. Addition of Halogen to Radicals	69
D. Addition of Hydrogen Hypohalides to Ethylenic Bonds	69
II. <i>By Substitution</i>	71
A. Replacement of Hydrogen by Halogen	71
1. Chlorination and Bromination of Aromatic Hydrocarbons....	78
2. Chlorination and Bromination of Carboxylic Acids.....	79
3. Chlorination and Bromination of Ketones and Aldehydes....	83
4. Chlorination and Bromination of Ethers.....	86
5. Chlorination and Bromination of Phenols and Amines.....	86
6. Chlorination with Hypochlorous Acid and Bromination with Hypobromous Acid	88
7. Iodination	89
8. Fluorination	93
B. Interchange of Halogen Atoms.....	94
1. Action of Elementary Halogen on Halides	94
2. Action of Halogen Ions on Organic Halides	94
C. Replacement of Hydroxyl Group and of Carbonyl Oxygen by Halogen	96
1. Alcoholic Hydroxyl Groups	96
Examples.....	98
2. Phenolic Hydroxyl Group	100
3. Hydroxyl in Carboxyl Group.....	100
D. Replacement of Amino Nitrogen by Halogen	106
E. Replacement by Mercury of Halogen	117
<i>Chap. 3. Formation of Carbon-Oxygen Bonds</i>	119
I. <i>By Addition</i>	119
A. Addition of Oxygen to Ethylene Bond	119
1. Molecular Oxygen	121
2. Ozone.....	122
3. Oxido Compounds, Ethylene Oxides from Ethylene Deriva- tives.....	122
B. Addition of Water to C—C Multiple Bonds	123
1. Addition of Water to Ethylene Bonds.....	123
2. Addition of Water to Acetylene Bond	124
C. Addition of Hydroxyl Groups to Ethylene Bond	126
D. Addition of Oxygen-Containing Compounds to Olefin and Acetyl- ene Bonds.....	127
E. Addition of Organic Compounds to Oxygen Molecule.....	128
II. <i>By Exchange, With Formation of Hydroxyl and Carbonyl Groups</i>	131
A. Replacement of Hydrogen by Oxygen	131
1. Replacement of Hydrogen by Hydroxyl Group	131
2. Replacement of Hydrogen by Carbonyl Oxygen	134
3. Replacement of Hydrogen by Carboxyl Oxygen	137
4. Dehydrogenation of Alcohols to Carbonyl Compounds	142
5. Oxidation of Alcohols and Aldehydes to Carboxylic Acids....	152

	PAGE
6. Preparation of Alcohols and Carboxylic Acids by Cannizzaro Reaction	153
B. Replacement of Halogen by Oxygen	154
1. Replacement of Halogen by Hydroxyl Group	154
2. Replacement of Halogen by Carbonyl Oxygen	156
3. Replacement of Halogen by Carboxyl Oxygen	157
C. Replacement of Nitrogen by Oxygen	157
1. Replacement of Primary Amino Group by Hydroxyl Group	157
2. Replacement of Nitrogen by Carbonyl Oxygen	159
3. Replacement of Nitrogen by Carboxyl Oxygen; Hydrolysis of Nitriles to Carboxylic Acids	161
D. Replacement of Sulfonic Acid Group by Hydroxyl Group	162
III. <i>By Replacement of Halogen with Formation of Additional C—O Bonds: Ethers, Esters, and Acetals</i>	163
A. Ether Linkage	163
1. Open Chain Ethers	163
2. Cyclic Ethers	168
B. Ester Linkage	170
1. Esterification of Carboxylic Acids	171
2. Esterification of Alcohols and Phenols (Acylation)	180
3. Formation of Esters from Aldehydes by Dimerization	185
C. Preparation of Acid Anhydrides	190
1. Preparation of Anhydrides by Dehydration of Acids	191
2. Preparation of Anhydrides by Double Decomposition Reactions	192
Chap. 4. Cleavage of Carbon-Oxygen Bonds	194
A. Cleavage of Ether Linkage	195
B. Cleavage of Ester Linkage	197
1. Saponification of Esters	198
2. Interchange of Components of Esters	199
C. Saponification of Acetals and Ortho Esters	200
Chap. 5. Formation of Organic Derivatives of Trivalent Nitrogen	204
I. <i>Amines</i>	204
A. Primary Amines	204
1. By Addition of Ammonia to Ethylene Bond	204
2. By Exchange	205
3. By Reduction of Nitrogen-Containing Compounds	217
4. Other Methods	230
B. Secondary Amines	232
1. By Addition to Ethylene Bond	232
2. By Exchange	232
C. Tertiary Amines	235
D. Purely Aromatic Secondary and Tertiary Amines	237
E. Quaternary Ammonium Compounds	238
II. <i>Hydrazines</i>	238
A. Hydrazines with Free Amino Group	238
1. Formation of Substituted Hydrazines by Addition	238

	PAGE
<i>Chap. 5. Formation of Organic Derivatives of Trivalent Nitrogen (contd.)</i>	
2. By Exchange	239
3. By Reduction	240
B. Secondary Hydrazines, without Free Amino Group	242
1. By Exchange	242
2. By Reduction	243
III. Diazotates, Azo and Azoxy Compounds	245
A. Diazotates	245
B. Azo Compounds	247
1. Dehydrogenation of Hydrazines	247
2. By Direct Reduction of Nitrogen Compounds	249
IV. Imines and Schiff Bases	251
V. Hydrazones, Semicarbazones, Phenylhydrazones	253
VI. Nitriles	255
VII. Nitroso Compounds	256
A. Nitroso Groups Attached to Carbon	256
B. Nitroso Group Attached to Nitrogen	261
VIII. Hydroxylamines	262
1. By Addition to Ethylene Bond	262
2. By Reduction and Oxidation	262
IX. Oximes	264
X. Nitrogen Derivatives of Carboxylic Acids	270
Acid Amides	270
1. By Removal of Water from Ammonium Salts	270
2. Addition of Water to Nitriles	271
3. From Carboxylic Acid Halides, Anhydrides, and Esters	272
<i>Chap. 6. Cleavage of Carbon-Nitrogen Bonds</i>	275
<i>Chap. 7. Formation of Carbon-Pentavalent Nitrogen Linkages</i>	279
<i>Nitro Compounds</i>	279
A. Nitro Groups by Addition	279
B. Nitro Compounds by Replacement	280
1. By Substitution of Nitro Group for Hydrogen	280
2. Replacement of Halogen in Aliphatic Compounds by Nitro Group	292
3. Replacement of Alkyl Group by Nitro Group	294
4. Replacement of Sulfonic Acid Group by Nitro Group	294
5. Replacement of Carboxyl Group by Nitro Group	294
6. Replacement of Diazonium Group by Nitro Group	295
7. Replacement of Hydroxyl by Nitro Group	296
<i>Chap. 8. Carbon-Divalent Sulfur Bonds</i>	297
1. Sulfhydryl Compounds, Mercaptans	297
(a) By Reduction of Sulfonyl Chlorides and of Disulfides	297
(b) By Replacement of Hydroxyl Group	298
(c) By Replacement of Halogen	298
2. Thio Ethers	299
3. Disulfides	300

	PAGE
4. Thio Aldehydes and Thio Ketones.....	301
5. Thiocarboxylic Acids and Dithiocarboxylic Acids.....	302
6. Sulfur-Containing Heterocyclic Compounds.....	304
Chap. 9. Carbon-Hexavalent Sulfur Bonds.....	306
I. <i>Aliphatic Sulfonic Acids</i>	306
II. <i>Aromatic Sulfonic Acids</i>	307
Direct Introduction of Sulfonic Acid Group.....	307
Chap. 10. Unsaturated Carbon Bonds.....	314
I. <i>Ethylene Linkages</i>	314
A. Isolated Ethylene Bonds.....	314
1. Removal of Halogen.....	314
2. Removal of Hydrogen Halide.....	316
3. Dehydration of Alcohols.....	318
4. Removal of Ammonia from Amines.....	322
B. Conjugated Double Bonds.....	323
II. <i>Formation of the Acetylene Linkage</i>	325
III. <i>Formation of the Allene Bond</i>	329
Chap. 11. Formation of Carbon-Carbon Bonds.....	331
Part One: By Addition.....	331
<i>Single Bonds</i>	331
A. Only Hydrogen at New Bond.....	331
1. Addition to Ethylene Bond.....	331
2. Polymerization of Ethylene Derivatives.....	332
3. Polymerization of Butadiene and of Butadiene Derivatives...	333
4. Diene Syntheses.....	334
5. Polymerization of Acetylene and Its Derivatives.....	340
B. Oxygen at New Bond.....	341
1. Aldol Type.....	341
2. Benzoin Type.....	342
3. Pinacol Type.....	343
4. Addition of Carbon Dioxide.....	344
C. Halogen at the Bond.....	344
D. Nitrogen at the Bond.....	345
1. Addition of Hydrogen Cyanide to Carbonyl Group.....	345
2. Addition of Formaldehyde and Amines.....	347
Part Two: By Replacement.....	347
I. <i>Formation of Single Bonds without Condensing Agents</i>	347
A. Removal of Hydrogen.....	347
1. Pyrogenic Reactions (Autocondensations).....	347
2. Catalytic Removal of Hydrogen.....	349
3. Oxidation, Removal of Hydrogen.....	351
B. Removal of Halogen.....	353
1. Spontaneous Removal of Halogen and Halogen Halide.....	353
2. Catalytic Removal of Halogen.....	354
3. Spontaneous Removal of Halogen as Halide.....	355
II. <i>Formation of Single Bonds with Condensation Agents</i>	379
A. Removal of Halogen as Halide.....	379

	PAGE
Chap. 11. <i>Formation of Carbon-Carbon Bonds (contd.)</i>	
1. Wurtz and Fittig Syntheses.....	379
2. Removal of Halogen with Copper, Silver, Zinc, and Alkali Alcoholates.....	382
B. Removal of Halogen as Hydrogen Halide.....	389
1. Friedel-Crafts Synthesis.....	389
2. Gattermann-Koch Synthesis.....	401
3. Tiemann-Reimer Synthesis.....	403
C. Removal of Metal as Halide.....	403
D. Removal of Water.....	404
1. Formation of a Single New Bond.....	404
2. Removal of Water and Formation of Several New Carbon Bonds.....	408
E. Removal of Alcohol, Carbonic Acids, etc.....	408
1. Ester Condensations.....	408
2. Removal of Carboxylic Acids.....	414
F. Removal of Nitrogen.....	414
III. <i>Formation of Ethylene Bonds and Aromatic Systems</i>	416
A. Removal of Water with Formation of New Ethylene Bond.....	416
B. Removal of Halogen with Formation of New Ethylene Bond...	416
1. Spontaneous Removal of Halogen as Hydrogen Halide.....	416
2. Removal with Metals.....	417
3. Removal with Alkalies.....	417
C. Formation of New Ethylene Bonds by Removal of Metal with Halogen.....	418
D. Formation of Double Bond by Removal of Water.....	418
General Remarks on Perkin-Claisen-Knoevenagel Synthesis.....	419
Examples.....	422
E. Removal of Carbon Dioxide and Water from Carboxylic Acids..	438
Chap. 12. <i>Fission of Carbon-Carbon Bonds</i>	444
I. <i>Thermal Decomposition</i>	445
A. Removal of Carbon Dioxide.....	445
B. Removal of Other Fragments.....	451
II. <i>Oxidative Degradation</i>	452
1. Degradation of Aliphatic Chains Starting from the End.....	452
2. Degradation of Aliphatic Chains from Within.....	454
3. Degradation of Alicyclic Ring Systems.....	458
4. Degradation of Aromatic and Heterocyclic Ring Systems....	463
III. <i>Reductive Degradation</i>	464
IV. <i>Hydrolytic Degradation</i>	464
Chap. 13. <i>Rearrangements of Carbon Compounds with the Exception of Steric Rearrangements</i>	470
I. <i>Shifting of Multiple Bonds</i>	471
A. Shifting of Ethylene Bond.....	472
B. Shifting of Acetylene Bond.....	474
II. <i>Shifting of Halogen</i>	475

	PAGE
III. <i>Rearrangements of Oxygen Compounds</i>	477
1. Keto-Enol Tautomerism and Related Phenomena.....	477
2. Cannizzaro Rearrangement of Keto Aldehydes and Related Reactions.....	482
3. Fries Rearrangement.....	484
IV. <i>Tautomerism of Nitrogen Compounds</i>	489
V. <i>Rearrangement of Carbon Skeletons</i>	490
1. Rearrangement of Hydrocarbons	490
2. Rearrangement of Oxygen-Containing Compounds.....	492
3. Nitrogen-Containing Compounds	495
VI. <i>Rearrangement Accompanied by Degradation of Carbon Skeleton</i>	496
1. Oximes.....	496
2. Acid Amides	497
Index	499

INTRODUCTION

Preparative organic chemistry has as its purpose the preparation from specific starting materials of compounds with carefully defined properties. In the classification of the multitude of reactions useful for the preparation of substances, the problem of starting material must be disregarded, because whatever raw material can be procured cheaply, or procured at all, depends on many conditions which are highly variable, such as the economic and geographic situation.

All organic substances have one property in common; that is, their carbon structure. In preparative organic chemistry classification can rest on the distinctions which are exemplified by the following conditions.

1. The carbon structure in the starting material is already formed. This is illustrated by the formation of benzoic acid from toluene or of acetaldehyde from ethanol.

2. The formation of the carbon structure is from 2 or more molecules with a lesser number of carbon atoms. Examples are acetophenone from benzene and acetic anhydride (2 molecules), Michler's ketone from dimethylaniline and phosgene (3 molecules), and rubber from isoprene (many molecules).

3. The carbon structure is obtained by degradation of a compound containing a greater number of carbon atoms. The formation of heptaldehyde and undecylenic acid from castor oil and of phthalic acid from naphthalene serves as examples.

4. The carbon structure is obtained by rearrangement of an existing one. This is illustrated by the pinacol-pinacolone rearrangement. These four basic types of reaction will frequently occur successively or even simultaneously and are called, respectively: (1) molecular change without a change in the carbon structure, (2) formation of a carbon structure, (3) degradation of the carbon structure, (4) molecular rearrangement of the carbon structure.

The reactions that lead to ring closure occupy a somewhat different position, but they are not different in principle from those in which bonds

are formed or broken. They can be classified into one or more of the four basic groups shown by the following illustrations.

1. The formation of phthalic anhydride from phthalic acid or the formation of pyrrole from ammonium mucate does not involve a change in carbon structure.

2. The formation of mesitylene from acetone and the formation of mesityl oxide are similar in nature.

3. Cyclopentanone is obtained from calcium adipate in exactly the same manner as acetone is obtained from calcium acetate.

4. The rearrangement of camphene hydrochloride to isobornyl chloride corresponds to the formation of pinacolone from pinacol.

The typical chemical processes fall very nicely into this system of classification. In Group 1 belong all reactions such as hydrogenation, chlorination, nitration, oxidation, reduction, etc. Group 2 includes those addition and condensation reactions that increase the number of carbon atoms in the molecule as well as polymerization. The separation of degradation reactions (Group 3) from the rearrangement reactions (Group 4) is novel.

The preparation of benzaldehyde (a) from toluene through benzene or benzyl chloride, (b) from benzene and hydrocyanic acid (Gatterman-Koch reaction), from bromobenzene by the Grignard reaction with formic ester, (c) from stilbene by treatment with ozone, or from diphenyl glycol treated with lead tetraacetate is not treated under one reference, "aldehydes," as is usual in the textbooks and handbooks of organic chemistry. Instead, the important reactions are discussed essentially under a single heading.

A difference of opinion about the principle of classification within the four main groups might arise. However, the characteristic common to all organic reactions is that they all consist of the breaking of existing bonds and the formation of new ones. It is advantageous, especially for the purpose of avoiding repetition, to use as the basis of classification, not the preparation of certain groups, but the formation of bonds. This book progresses from the simpler linkages to the more complex.

Most bonds can be formed by addition as well as by replacement. This creates a natural subdivision of the main chapters. The existence of few types of linkage that are of practical importance in organic chemistry simplifies the examination of the material in this manner. It is sufficient to consider the elements, hydrogen, oxygen, nitrogen, sulfur, phosphorus, and the halogens, in their different kinds of linkage and their valences.

The preparation of an organic compound may be achieved in different ways, depending upon the starting material and upon the chemical nature of the desired product. Two special cases can be distinguished:

1. The reacting compounds in one case exhibit such preference to react with each other in only one way that the process proceeds in one direction only. Even under very different conditions, and therefore with varying velocity, the same reaction products are obtained. In this case, the success of the synthesis depends primarily on the preparation of the starting materials.

2. In the second case, several different reactions compete with each other, thus inevitably forming a mixture of reaction products. The success of the preparative work depends on directing the reaction by the choice of suitable conditions (temperature, pressure, radiation) and reagents (solvents, catalysts) so that the desired product is formed in optimum yield and is accompanied only by by-products from which it can be conveniently separated.

The reactions of the first type are marked by the presence of so called key elements which easily break their bond with carbon in favor of another, especially an ionic bond.

Formation of Carbon-Hydrogen Bonds

The reactions establishing C—H bonds are divided into two groups. The first is characterized by the fact that only hydrogen is taken up by the reacting molecule. In the second hydrogen replaces other atoms or atom groups, forming new compounds such as water, hydrochloric acid, etc. Substitution, the usual designation for reactions of the second group, proceeds primarily by way of addition compounds; but these intermediates are usually not isolated, as the purpose is to isolate the end-products. In accordance with the general plan, the only reactions that belong in this section are those in which there is no degradation of the type characterized by a breaking of C—C bonds.

In this chapter, therefore, the opening of the smaller carbon ring, which is important only from the standpoint of classification, will be described. The cleavage, by hydrogenation proper, will be dealt with in the chapter on degradation (see page 444). The only exception made here is in the treatment of the relatively unimportant transformation of acid amides into primary, secondary, or tertiary amines (see page 226).

I. FORMATION OF C—H BONDS BY ADDITION

A. Addition of Hydrogen to Unsaturated Carbon Bonds

General Aspects

The addition of hydrogen to unsaturated carbon bonds is effected by means of a great number of reactions which can be divided into two groups. In the first group belong the reactions in which hydrogen functions in the so called nascent state; that is, in the atomic state. In the same group belong the reductions with hydrogen iodide, phosphonium iodide, and sodium hyposulfite. The second group consists of the catalytic reactions in which molecular hydrogen either adds to the substances to be reduced, or is transferred from a molecule richer in hydrogen to one poorer in hydrogen.

To date, direct hydrogenation with free, atomic hydrogen is still of no practical importance, although it may become important at some future date. Only scanty observations on this topic have been reported.

In a separate chapter, some of the most important papers on the organic chemistry of heavy hydrogen, deuterium, will be discussed.

1. Addition of Hydrogen to Ethylene Bonds and to Aromatic and Heterocyclic Systems

The reduction of aliphatic double bonds to form more saturated systems depends upon whether reducible groups other than those with one or more ethylene bonds are present in the molecule.

No generally applicable rule can be established for the reduction methods which are suitable for individual cases. The hydroxyl group, for instance, is quite resistant to many reducing agents; *e.g.*, to most catalytic ones. But this is true only for the existing hydroxyl group. Hydroxyl groups might be expected to be formed in the course of reduction of aldehydes or ketones. In many cases the carbonyl oxygen is completely replaced by hydrogen. In this chapter the methods in question are considered primarily with respect to their ability to saturate double bonds, either aliphatic, or alicyclic, or aromatic and heterocyclic, respectively. First, the methods which are generally applicable are discussed.

Preparation of Nascent Hydrogen

1. Sodium plus alcohol (ethyl, butyl, amyl, and occasionally capryl alcohols) in general is a mild reducing agent. Isolated double bonds remain intact, conjugated double bonds are reduced, but the isolated double bond thus formed remains. Ethylene bonds next to the phenyl nucleus (as in styrene and cinnamic acid derivatives) undergo reduction, although a number of exceptions exist. β,γ -Unsaturated carboxylic acids can also be reduced. The most important use is for the reduction of esters to alcohols, the method of Bouveault and Blanc.

It is comparatively easy partially to reduce condensed aromatic ring systems with sodium and alcohol. Amyl alcohol is used in most cases; naphthalene yields tetralin; phenanthrene and acenaphthene give tetrahydro compounds. When ethanol is used, naphthalene yields only dihydronaphthalene. Heterocyclic systems such as pyridine and other pyridine bases easily yield piperidine derivatives; pyrazoles change to pyrazolines. The naphthylamines are attacked very easily by sodium and amyl alcohol. In the case of α -naphthylamine only the unsubstituted nucleus is hydrogenated, while with β -naphthylamine the substituted nucleus is preferentially reduced. α - and β -naphthol act in a very similar manner. In no case does the hydrogenation proceed beyond the tetrahydro stage.

The method consists simply in adding pieces of metallic sodium to the boiling alcoholic solution. Sometimes a large excess is used, for