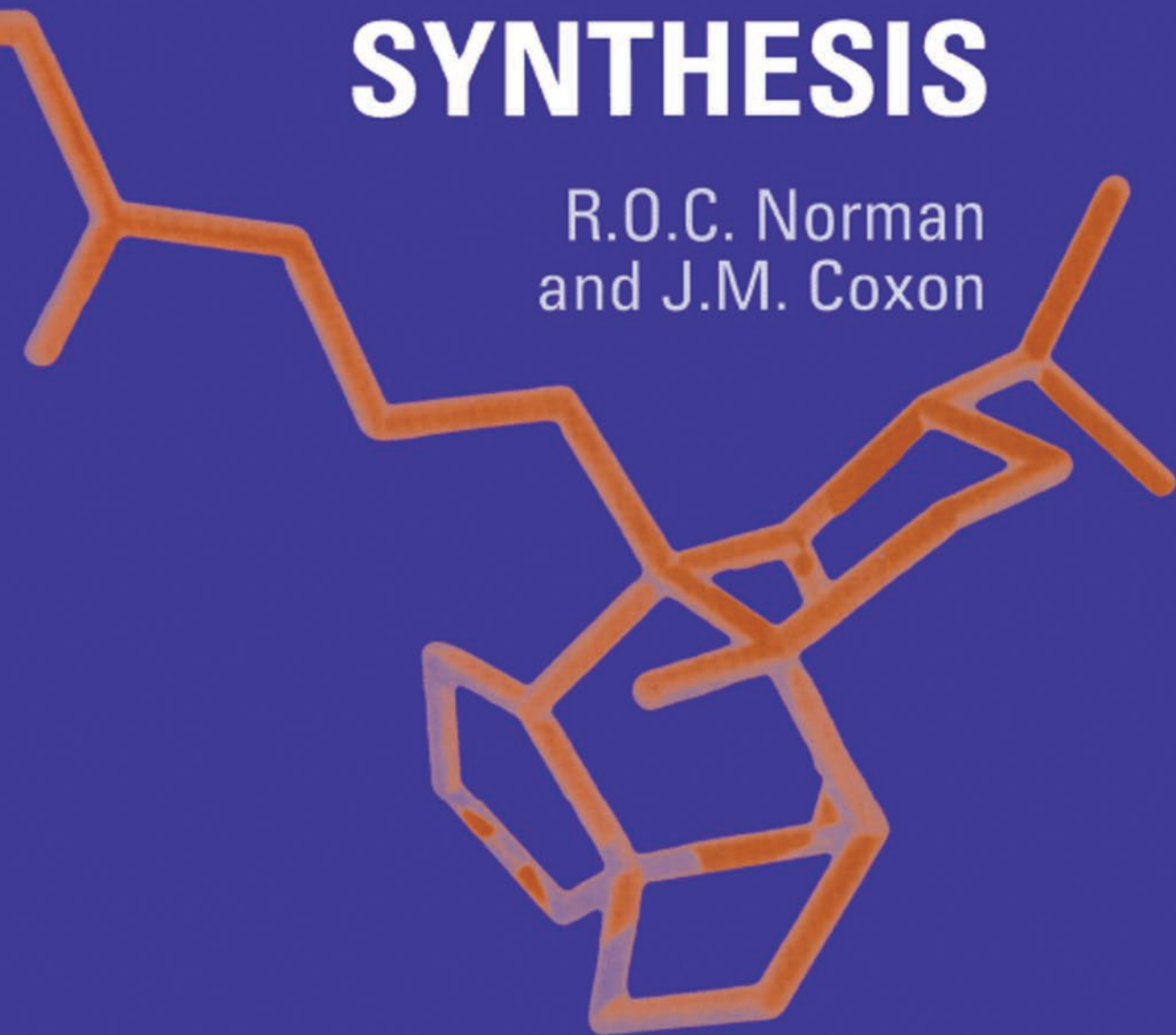


Third Edition

PRINCIPLES OF ORGANIC SYNTHESIS

R.O.C. Norman
and J.M. Coxon



CRC Press
Taylor & Francis Group

Third Edition

PRINCIPLES OF ORGANIC SYNTHESIS

To J. and F.

Third Edition

PRINCIPLES OF ORGANIC SYNTHESIS

Sir Richard Norman, **KBE, FRS**
*Rector, Exeter College
University of Oxford, U.K.*

J.M. Coxon
*Professor of Chemistry
University of Canterbury, New Zealand*



CRC Press

Taylor & Francis Group

Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

Library of Congress Cataloging-in-Publication Data

Catalog record is available from the Library of Congress

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 authors and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

Neither this book nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming, and recording, or by any information storage or retrieval system, without prior permission in writing from the publisher.

The consent of CRC Press LLC does not extend to copying for general distribution, for promotion, for creating new works, or for resale. Specific permission must be obtained in writing from CRC Press LLC for such copying.

Direct all inquiries to CRC Press LLC, 2000 N.W. Corporate Blvd., Boca Raton, Florida 33431.

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

Visit the CRC Press Web site at www.crcpress.com

© 1968, 1978, 1993 by R. O. C. Norman and J. M. Coxon

No claim to original U.S. Government works
International Standard Book Number 0-7487-6162-4

Preface

Organic chemistry is one of the most rapidly developing of the sciences. Each year, there are new applications of organic compounds, for example, in medicine, in agriculture, and in the new technologies such as optoelectronics and superconductors; tens of thousands of new compounds are synthesized or isolated from natural sources; and new synthetic methods and reagents are introduced. It might seem to the student that ever more needs to be learned.

Fortunately that is not so. The profound increase in our understanding of the pathways by which organic compounds react – their mechanisms of reaction – has provided a relatively simple superstructure on which the vast array of the facts of the subject can be hung. The mechanistic principles are relatively few, and yet they account for the enormous range of reactions of organic compounds.

The purpose of this book is to show how these principles can be applied both to acquiring a knowledge of organic synthetic processes and to planning the construction of organic compounds. It is designed for those who have had no more than a brief introduction to organic chemistry. Nor is it intended to be comprehensive; for example, the vast body of evidence on which reaction mechanisms are based is not included, nor are experimental details given. The object has been to convey a broad understanding rather than to produce a reference text.

The book is in two parts. In Part I, reaction mechanism is set in its wider context of the basic principles and concepts that underlie chemical reactions: chemical thermodynamics, structural theory, theories of reaction kinetics, mechanism itself, and stereochemistry. In Part II, these principles and concepts are applied to the formation of particular types of bonds, groupings, and compounds: for example, how small molecules can be built on to give larger ones by the construction of new carbon–carbon bonds, or how one functional group can be transformed into another. The final chapter in Part II describes the planning and detailed execution of the multi-step syntheses of several complex naturally occurring compounds.

There have been numerous important developments since the second edition of this book was published, and every chapter has been brought up to date to include them. Among the more notable are: the stereochemical control of reactions, reflecting the need to synthesize efficiently compounds with several asymmetric centres; the use of organotransition-metal reagents, leading to a new chapter; the exploitation of lithium diisopropylamide (LDA) as a base in the formation of new C—C bonds; free-radical reactions for the synthesis of C—C bonds; uses of

organosilicon compounds; and subtle new protective and condensing reagents in polypeptide synthesis.

The text is extensively cross-referenced and there is a detailed index.

R. O. C. NORMAN

J. M. COXON

Contents

Preface	v
PART I	
Introduction to Part I	3
1 Chemical thermodynamics	5
1.1 Equilibrium	5
1.2 Free energy	5
1.3 Bond energies	6
1.4 Entropies	9
1.5 Further applications of thermodynamic principles	12
2 Molecular structure	20
2.1 Bonding	20
2.2 The covalent bond	20
2.3 Delocalization	24
2.4 Applications of structural theory	27
3 Chemical kinetics	52
3.1 Rates of reaction	52
3.2 The orders of reaction	52
3.3 The effect of temperature on reaction rates	55
3.4 Collision theory	55
3.5 Transition-state theory	58
3.6 Applications of kinetic principles	59
4 Mechanism	71
4.1 Unit processes in organic reactions	71
4.2 Types of reaction	80
4.3 Addition	82
4.4 Elimination	93
4.5 Substitution	102
4.6 Condensation	120
4.7 Rearrangement	121
4.8 Pericyclic reactions	123
4.9 Oxidation–reduction	127

5 Stereochemistry	134
5.1 Optical isomerism	134
5.2 The stereochemistry of cyclic compounds	152
5.3 Stereochemistry and reactivity	159
 PART II	
Introduction to Part II	179
 6 Formation of carbon–carbon bonds: organometallic reagents	184
6.1 Principles	184
6.2 Organomagnesium compounds (Grignard reagents)	186
6.3 Organosodium compounds	196
6.4 Organolithium compounds	197
6.5 Organocopper compounds	200
6.6 Organocadmium compounds	203
6.7 Organomercury compounds	203
6.8 Organozinc compounds	204
 7 Formation of aliphatic carbon–carbon bonds: base-catalyzed reactions	206
7.1 Principles	206
7.2 Reactions of enolates with aldehydes and ketones	209
7.3 Reactions of enolates with esters	226
7.4 The alkylation of enolates	233
7.5 Addition of enolates to activated alkenes	240
7.6 Reactions involving alkynes	241
7.7 Reactions involving cyanide	244
 8 Formation of aliphatic carbon–carbon bonds: acid-catalyzed reactions	251
8.1 Principles	251
8.2 The self-condensation of alkenes	252
8.3 Friedel–Crafts reactions	253
8.4 Prins reaction	255
8.5 Reactions of aldehydes and ketones	256
8.6 Mannich reaction	261
 9 Pericyclic reactions	270
9.1 Cycloadditions	270
9.2 Electrocyclic reactions	284
9.3 Cheletropic reactions	287
9.4 Sigmatropic rearrangements	290
9.5 The ene-reaction and related reactions	295
 10 Formation of aliphatic carbon–nitrogen bonds	299
10.1 Principles	299

10.2	Substitution by nucleophilic nitrogen at saturated carbon	301
10.3	Addition of nucleophilic nitrogen to unsaturated carbon	306
10.4	Substitution by nucleophilic nitrogen at unsaturated carbon	316
10.5	Reactions of electrophilic nitrogen	319
10.6	α -Amino acids, peptides, and proteins	324
11	Electrophilic aromatic substitution	344
11.1	The mechanism of substitution	344
11.2	Directive and rate-controlling factors	347
11.3	Formation of carbon-carbon bonds	360
11.4	Formation of carbon-nitrogen bonds	376
11.5	Formation of carbon-sulfur bonds	381
11.6	Formation of carbon-halogen bonds	383
11.7	Other reactions	387
11.8	The preparation of derivatives with specific orientations	392
12	Nucleophilic aromatic substitution	396
12.1	Principles	396
12.2	Displacement of hydride ion	398
12.3	Displacement of other anions	399
12.4	Substitution <i>via</i> benzyne	404
12.5	The $S_{RN}1$ reaction	406
12.6	Bucherer reaction	407
13	Aromatic diazonium salts	409
13.1	The formation of diazonium ions	409
13.2	The reactions of diazonium ions	410
13.3	Reactions in which nitrogen is eliminated	411
13.4	Reactions in which nitrogen is retained	419
13.5	The synthetic value of diazo-coupling	424
14	Molecular rearrangements	429
14.1	Types of rearrangement	429
14.2	Rearrangement to electron-deficient carbon	429
14.3	Rearrangement to electron-deficient nitrogen	441
14.4	Rearrangement to electron-deficient oxygen	445
14.5	Rearrangement to electron-rich carbon	447
14.6	Aromatic rearrangements	450
15	Reagents containing phosphorus, sulfur, silicon or boron	458
15.1	Introduction	458
15.2	Phosphorus-containing reagents	459
15.3	Sulfur-containing reagents	468
15.4	Silicon-containing reagents	476
15.5	Boron-containing reagents	483

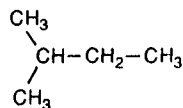
16 Photochemical reactions	496
16.1 Principles	496
16.2 Photoreduction	499
16.3 Photoaddition	500
16.4 Photorearrangement	505
16.5 Photooxidation	511
16.6 Photochemical aromatic substitution	513
16.7 Photochemical fragmentation	515
17 Free-radical reactions	523
17.1 Principles	523
17.2 Formation of carbon–halogen bonds	530
17.3 Formation of carbon–carbon bonds	537
17.4 Formation of carbon–nitrogen bonds	551
17.5 Formation of carbon–oxygen bonds	555
17.6 Formation of bonds to other elements	558
18 Organotransition metal reagents	561
18.1 Principles	561
18.2 Titanium	565
18.3 Chromium	568
18.4 Iron	571
18.5 Cobalt	573
18.6 Rhodium	575
18.7 Nickel	575
18.8 Palladium	577
19 Oxidation	587
19.1 Introduction	587
19.2 Hydrocarbons	588
19.3 Systems containing oxygen	608
19.4 Systems containing nitrogen	621
19.5 Systems containing sulfur	625
19.6 Systems containing phosphorus	626
19.7 Systems containing iodine	626
20 Reduction	629
20.1 Introduction	629
20.2 Hydrocarbons	630
20.3 Hydrogenolysis	643
20.4 Aldehydes and ketones	649
20.5 Epoxides	656
20.6 Acids and their derivatives	657
20.7 Systems containing nitrogen	666
20.8 Systems containing sulfur	672

21 The synthesis of five- and six-membered heterocyclic compounds	676
21.1 Introduction	676
21.2 Five-membered rings containing one heteroatom	684
21.3 Five-membered rings containing two heteroatoms	694
21.4 Six-membered rings containing one heteroatom	699
21.5 Six-membered rings containing two heteroatoms	715
21.6 Six-membered rings containing three heteroatoms	723
22 The syntheses of some naturally occurring compounds	728
22.1 Reserpine	728
22.2 Adenosine triphosphate	735
22.3 Penicillin and cephalosporins	739
22.4 Chlorophyll	745
22.5 Prostaglandins E ₂ and F _{2α}	754
22.6 Ibogamine	762
22.7 11-Oxygenated progesterones	763
22.8 Fredericamycin A	772
22.9 Daphnilactone A and methyl homodaphniphyllate	778
Index	791

Nomenclature and conventions

Some readers of this book will have taken introductory courses in organic chemistry in which the systematic nomenclature of the International Union of Pure and Applied Chemistry (IUPAC) was used; others will be used to the more common names of organic compounds. We have continued the practice of the previous editions of using common names for most simple compounds because this is still the language used by professional chemists – for example, in papers in the literature describing their research results – so that early familiarity with it is important. We have largely followed the conventions of the *Journal of Organic Chemistry*.

Organic compounds are frequently expressed on paper by a formula such as



for 2-methylbutane. This can be cumbersome for all but small molecules, and we have generally used a convention in which a C—C bond is represented by a line; when more than one is present in an aliphatic chain, a zigzag line is used except for alkynes, which are linear; and hydrogen atoms attached to carbon are not shown. Examples are:



butane



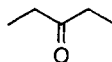
2-methylbutane



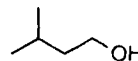
trans-2-butene



propyne



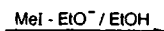
3-pentanone



3-methyl-1-butanol

In Part II especially, we have also used abbreviations for groups such as Et (ethyl) and Bu^t (tertiary butyl, or 2-methyl-2-propyl).

In reaction schemes, when two or more reagents are present they are connected by hyphens, and when a compound is present which acts only as a solvent it follows an oblique; for example



indicates that the reactant is treated with methyl iodide and ethoxide ion in ethanol solvent. Notice the difference between



where ammonia is involved only as solvent in the former but as both solvent and reagent (the source of protons in reduction by sodium) in the latter.

The following are the more frequently used common names with their usual representation.

Aliphatic hydrocarbons

ethylene	$\text{CH}_2=\text{CH}_2$
propylene	
acetylene	$\text{H}-\text{C}\equiv\text{C}-\text{H}$

Alcohols

isopropanol	
t-butanol	
ethylene glycol	$\text{HO}-\text{CH}_2-\text{CH}_2-\text{OH}$
pinacol	

Aldehydes

formaldehyde	$\text{CH}_2=\text{O}$
acetaldehyde	
propionaldehyde	

Ketones

acetone	
pinacolone	

Acids

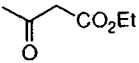
formic acid	HCO_2H
acetic acid	AcOH
propionic acid	
butyric acid	
acrylic acid	
oxalic acid	$\text{HO}_2\text{C}-\text{CO}_2\text{H}$
malonic acid	$\text{HO}_2\text{C}-\text{CH}_2-\text{CO}_2\text{H}$
succinic acid	$\text{HO}_2\text{C}-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H}$
glutaric acid	$\text{HO}_2\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H}$
adipic acid	$\text{HO}_2\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H}$
maleic acid	
fumaric acid	
glycolic acid	$\text{HO}-\text{CH}_2-\text{CO}_2\text{H}$
lactic acid	
tartaric acid	

Amines

methylamine	MeNH_2
dimethylamine	Me_2NH
trimethylamine	Me_3N
triethylamine	Et_3N

Other aliphatic compounds

diethyl ether	Et_2O
chloroform	CHCl_3
carbon tetrachloride	CCl_4
ethyl orthoformate	$\text{HC}(\text{OEt})_3$
acetonitrile	MeCN
acrylonitrile	$\text{CH}_2=\text{CHCN}$
diglyme	$(\text{MeOCH}_2\text{CH}_2)_2\text{O}$

acetoacetic ester	
malonic ester	$\text{EtO}_2\text{C}-\text{CH}_2-\text{CO}_2\text{Et}$

Aromatic compounds

acetophenone	
--------------	---

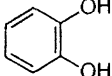
aniline	PhNH_2
---------	-----------------

anisole	PhOMe
---------	----------------

benzaldehyde	PhCHO
--------------	----------------

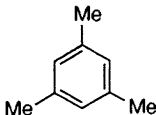
benzoic acid	PhCO_2H
--------------	-------------------------

benzophenone	
--------------	---

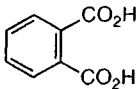
catechol	
----------	---

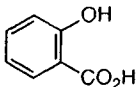
cinnamic acid	$\text{Ph}-\text{CH}=\text{CH}-\text{CO}_2\text{H}$
---------------	---

cumene	PhCHMe_2
--------	-------------------

mesitylene	
------------	---

phenol	PhOH
--------	---------------

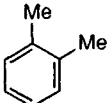
phthalic acid	
---------------	--

salicylic acid	
----------------	---

stilbene	$\text{Ph}-\text{CH}=\text{CH}-\text{Ph}$
----------	---

styrene	$\text{Ph}-\text{CH}=\text{CH}_2$
---------	-----------------------------------

toluene	PhMe
---------	---------------

xylene	 + <i>m</i> - and <i>p</i> -isomers
--------	---

Common names for groups

methyl, Me	CH_3
------------	---------------

ethyl, Et CH_3CH_2
 isopropyl, Prⁱ $(\text{CH}_3)_2\text{CH}$
 butyl, Bu $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$
 isobutyl $(\text{CH}_3)_2\text{CHCH}_2$
 t-butyl, Bu^t $(\text{CH}_3)_3\text{C}$
 neopentyl $(\text{CH}_3)_3\text{CCH}_2$

vinyl $\text{CH}_2=\text{CH}$
 acetyl, Ac CH_3CO
 phenyl, Ph C_6H_5
 tolyl $\text{CH}_3-\text{C}_6\text{H}_4$
 tosyl $4\text{-CH}_3-\text{C}_6\text{H}_4-\text{SO}_2\text{O}$



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

Part I



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

Introduction to Part I

The five chapters which comprise Part I are concerned with the principles that govern organic reactions.

In chapters 1–3, the principles of chemical thermodynamics, the theory of molecular structure, and the principles of reaction kinetics are briefly summarized (textbooks on physical chemistry should be consulted for detailed treatments); the emphasis in these chapters is on the application of the principles and theories to the structures and reactions of organic compounds.

Thermodynamic principles show that a reaction will ‘go’ – that is have an equilibrium constant greater than unity – only if the products have a lower free-energy content than the reactants. The free energy of a species is related to its enthalpy, which is determined essentially by the strengths of the bonds it contains, and to its entropy, which is a measure of its degree of disorder: a low free energy corresponds to strong bonding forces and a high degree of disorder. From thermodynamic considerations there follows, for example, an understanding of why it is possible to reduce acetylene to ethylene at room temperature and to carry out the reverse reaction at high temperatures, why small changes in structure can have a very large effect on the position of dynamic equilibrium between isomers, and why some ring-closure reactions occur so much more efficiently than equivalent bimolecular reactions.

In the second chapter, the strengths of bonds and the shapes of organic compounds are related to the theories of molecular structure. Delocalized bonds are emphasized; for example, the different chemical behaviour of benzene and ethylene is related to the very large stabilization energy in benzene which arises from delocalization. Other properties of organic compounds that are of importance in synthesis, such as the acidities of C—H bonds in various environments, also follow from structural theory.

That there should be a negative free-energy change is in practice a necessary but not a sufficient condition for a reaction to occur, for the *rate* at which it takes place may be negligible. Thermodynamic considerations alone indicate that hydrocarbons should not coexist with air, for the free-energy change involved in their oxidation to carbon dioxide and water is significantly negative; in practice, however, their rates of combustion at ordinary temperatures are negligible. The third chapter sets out the theories of reaction kinetics and the effects of temperature on rate, and then introduces correlations of the rates of specific types of reaction with structure.

4 PRINCIPLES OF ORGANIC SYNTHESIS

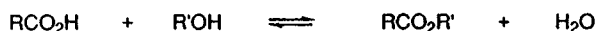
The planning of syntheses is helped considerably by an understanding of the mechanisms by which reactions occur. It must be emphasized that mechanisms are *theories* and not *facts* of the subject: they have been deduced from experimental observations and in some instances they transpire to be incorrect or at least in need of refinement. One should say, 'the mechanism is thought to be', rather than 'the mechanism is'. Nonetheless, the current mechanistic theories, which are surveyed in the fourth chapter, not only provide an intellectually satisfying and unifying picture of the complexity of reactions, but also enable predictions to be made, with increasing assurance as the degree of rationalization of the subject increases, of the effects which structural modifications will have on the course of a reaction.

Stereochemistry – the study of the spatial relationships of atoms and bonds – would in the past have been a natural adjunct of the study of molecular structure. It is now as important to considerations of chemical dynamics as to those of chemical statics, and follows naturally, in the last chapter, the study of kinetics and mechanism. Indeed, it is closely intertwined with mechanism: many naturally occurring compounds have a complex and highly specific stereochemistry and it has only been through an understanding of the stereoelectronic principles of reactions that their syntheses have been successfully planned and executed.

Chemical thermodynamics 1

1.1 Equilibrium

All chemical reactions are in principle reversible: reactants and products eventually reach *equilibrium*. In some cases, such as the esterification of an acid by an alcohol,



the position of the equilibrium is quite closely balanced between reactants and products, whereas in other cases the equilibrium constant is either very high or very low, so that the reaction goes essentially to completion in one direction or the other (given the appropriate conditions). From the point of view of devising an organic synthesis it is necessary to know whether the position of equilibrium will favour the desired product. The factors which determine the equilibrium constant of a reaction and its variation with changes in conditions follow from the principles of thermodynamics.

1.2 Free energy

Chemical systems are subject to opposing influences: the tendency to minimize their enthalpy (heat content), H , is opposed by the tendency to maximize their entropy (degree of disorder), S . Chemical reactions are usually carried out at constant pressure and under these conditions the compromise between the two trends is determined by the value of the function ($H - TS$): this function tends to decrease, and the compromise situation – equilibrium – corresponds to its minimum value. It is convenient to define a new function, G , the Gibbs free energy, as $G = H - TS$. A process will occur spontaneously if, as a result, G decreases and it will continue until G reaches a minimum.

The principles of thermodynamics lead to an equation that relates the equilibrium constant, K , to the change in free energy accompanying a reaction. If the sums of the free energies of reactants and products in their standard states (i.e. for 1 mole at a pressure of 1 bar) at temperature T are G_1^0 and G_2^0 respectively, then the change in free energy on reaction, ΔG^0 , is $G_2^0 - G_1^0$ and is given by

$$RT \ln K = -\Delta G^0$$

where R is the gas constant ($8.314 \text{ J K}^{-1} \text{ mol}^{-1}$).

6 PRINCIPLES OF ORGANIC SYNTHESIS

A knowledge of the standard free energies of reactants and products thus enables us to predict whether a given set of reactants is likely to yield a desired set of products. If ΔG^0 is negative, the equilibrium constant (greater than 1) is favourable to the formation of the products, whereas if ΔG^0 is positive it is correspondingly unfavourable.

Standard free energies have been measured for a number of organic and inorganic compounds. For example, those of ethylene, ethane, and hydrogen in the gaseous state at 25°C are 68, -33, and 0 kJ mol⁻¹ respectively. (By convention, the most stable allotrope of an *element* in its standard state at 25°C is assigned a free-energy value of zero. The scale of free energies is therefore an arbitrary one, but this is immaterial since we are always concerned with *differences* in free energies.) Therefore the reaction



has $\Delta G^0 = +101 \text{ kJ mol}^{-1}$, so that we cannot obtain ethylene from ethane in significant amount under these conditions although we may expect to obtain ethane from ethylene. Notice, however, that even though a free-energy change may be favourable, the *rate* of formation of the product may be too slow for the reaction to be practicable, or the reaction may take a different course (e.g. ethylene might react with two molecules of hydrogen to give two molecules of methane, which is also a thermodynamically favourable process). Fulfilment of the thermodynamic criterion is therefore a *necessary* but not a *sufficient* condition for a reaction to occur. The factors which control rates of reaction and the pathways which reactions take are discussed in subsequent chapters.

Thermodynamic data also give no information about the *reasons* why the free energies of compounds have particular values. Ethylene, for example, has a positive standard free energy of formation, whereas that for ethane is negative; that is, ethylene is unstable with respect to carbon and hydrogen and ethane is stable. These are empirical *facts*; the reasons underlying them lie in the realm of *theory*, namely, the theory of chemical structure and bonding, which is discussed in the next chapter.

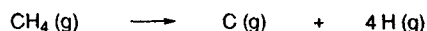
1.3 Bond energies Since $G^0 = H^0 - TS^0$ and $RT \ln K = -\Delta G^0$, it follows that

$$RT \ln K = -\Delta H^0 + T\Delta S^0$$

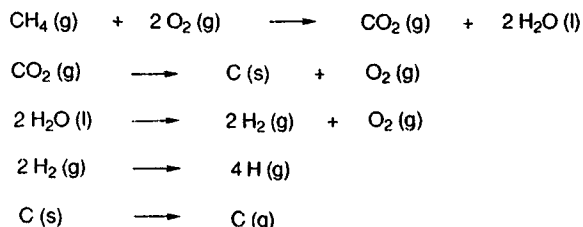
Therefore a knowledge of the differences between the enthalpies and entropies of reactants and products gives information about whether a reaction will 'go'. This is generally a more useful approach than considering free-energy differences, for three reasons: free energies are not known in most cases; enthalpy differences – the heats of reactions – can be calculated with reasonable precision from those of reactions which have been measured; and entropy differences can usually be inferred to the accuracy required (section 1.4) (in the conditions of most organic

reactions the $T\Delta S^0$ term is in any case much smaller than the ΔH^0 term).

The calculation of enthalpy differences is based on the first law of thermodynamics: if the heats of the reactions $A \rightarrow B$ and $B \rightarrow C$ are respectively x and y , then that of the reaction $A \rightarrow C$ is $(x + y)$, since otherwise it would be possible to construct a cycle of reactions that generated energy, in contravention of the first law. The calculations are facilitated by constructing a table of *bond energies*, taking as the reference point the heat of formation of molecules from their constituent atoms. For example, the bond energy of the C—H bond is defined as one-quarter of the heat of the reaction



since four C—H bonds are broken in this process. It is not possible to determine this experimentally, but it can be calculated since it is the sum of the heats of the following reactions which have been measured*:



The importance of bond energies is that, to a close approximation, they are constant for a particular bond in different structural environments, so that, given the bond energies 414, 357, and 462 kJ mol⁻¹ for C—H, C—O, and O—H bonds respectively, the total bond energy of methanol that contains three C—H, one C—O, and one O—H bond, is calculated to be 2061 kJ mol⁻¹, in fair agreement with the experimental value (1985 kJ mol⁻¹) derived from the heat of combustion of methanol.

Bond energies for a number of commonly occurring structural units are given in Table 1.1.

Bond energies quoted above are *average* bond energies and it is often more useful to know the energy required to break a particular bond in a compound, i.e. the *bond dissociation energy*. Although the O—H bond energy is, by definition, one-half the heat of formation of water, in fact a greater quantity of energy is required to break the first O—H bond in water ($\text{H}_2\text{O} \rightarrow \text{HO} + \text{H}$; $\Delta H = 491 \text{ kJ mol}^{-1}$) than the second ($\text{HO} \rightarrow \text{O} + \text{H}$; $\Delta H = 433 \text{ kJ mol}^{-1}$). The bond dissociation energy is therefore greater than the bond energy and this is commonly the case, except for diatomic molecules for which the values are necessarily identical. Some typical bond dissociation energies are set out in Table 1.2.

* The heat of the last reaction, the atomization of carbon, is necessary because the heat of formation of carbon dioxide is measured for solid carbon whereas bond energies refer to atoms, i.e. 'gaseous' carbon.

Table 1.1 Bond energies (kJ mol^{-1}) at 25°C

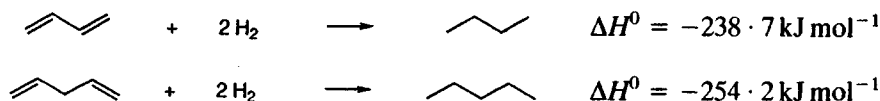
H—H	435	C—C	347	C—O	357
H—F	560	C=C	610	C=O ^a	694
H—Cl	428	C≡C	836	C=O ^b	736
H—Br	364	N—N	163	C=O ^c	748
H—I	297	N=N	418	H—C	414
F—F	150	N≡N	940	H—N	389
Cl—Cl	238	C—N	305	H—O	462
Br—Br	188	C=N	614	O—O	155
I—I	150	C≡N	890	S—S	251

^a In formaldehyde.^b In other aldehydes.^c In ketones.**Table 1.2** Bond dissociation energies (kJ mol^{-1})

H—CH ₃	426	H—OH	491	CH ₃ —F	447
H—CH ₂ CH ₃	401	H—NH ₂	426	CH ₃ —Cl	339
H—CH(CH ₃) ₂	385	CH ₃ —OH	376	CH ₃ —Br	280
H—C(CH ₃) ₃	372	CH ₃ —NH ₂	334	CH ₃ —I	226
H—CH ₂ Ph	322	CH ₃ —CH ₃	347	CH ₃ —NO ₂	238

The premise on which the use of Table 1.1 is based, that bond energies are constant for a particular bond in different environments, requires closer examination. If it were strictly true, the heats of combustion of the three isomeric pentanes, for example, each of which contains four C—C and 12 C—H bonds, would be the same. In fact, they are different: $\text{CH}_3(\text{CH}_2)_3\text{CH}_3$, 3533; $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_3$, 3525; $(\text{CH}_3)_3\text{CCH}_3$, 3513 kJ mol^{-1} . Nevertheless, the percentage differences are so small in this and many similar cases that bond-energy data are of considerable use. However, there are certain structural environments in which appreciable differences between observed and predicted bond energies occur. One example, in Table 1.1, concerns the carbonyl group, whose bond energy is nearly 10% greater in ketones than in formaldehyde, and is greater still (804 kJ mol^{-1}) in carbon dioxide.

A more general deviation occurs with *conjugated* compounds, that is, compounds possessing alternating single and double bonds. For example, consider the following hydrogenations:



If bond energies were strictly additive, the heats of hydrogenation in the above reactions should be the same since, in each, two C=C double bonds are converted into single bonds, two H—H bonds are broken, and four C—H bonds are formed. The lower value for 1,3-butadiene shows that this is a more stable

compound than predicted by examination of 1,4-pentadiene, and this proves to be so for other conjugated systems. We shall refer to the difference between predicted and observed values of heats of hydrogenation as the *stabilization energy*.

The attachment of alkyl groups to an alkene also leads to the introduction of stabilization energy. For example, whereas the heat of hydrogenation of ethylene is 137 kJ mol^{-1} , that of propylene ($\text{CH}_3\text{CH}=\text{CH}_2$; one alkyl group) is 126 kJ mol^{-1} and that of *trans*-2-butene ($\text{CH}_3\text{CH}=\text{CHCH}_3$; two alkyl groups) is 115 kJ mol^{-1} , i.e. the stabilization energies are 11 and 22 kJ mol^{-1} , respectively.

For those cyclic, conjugated compounds which are aromatic (section 2.4b) heats of hydrogenation are in many cases very considerably less than the predicted values. The stabilization energies of benzene, naphthalene, and anthracene are respectively 150, 255, and 349 kJ mol^{-1} .

An understanding of the origin of stabilization energies follows from current theories of molecular structure (chapter 2). It is necessary here to emphasize that bond-energy data must be used with care but that, nevertheless, conjugated and aromatic systems excepted, they provide a useful working basis for predictive purposes.

1.4 Entropies

Molecules undergo three types of motion: translation, rotation, and vibration. For each, in accord with quantum theory, only certain *energy states* occur. The entropy of a compound is related to the number of ways in which the molecules can be distributed amongst these energy states; the greater the number, the larger is the degree of disorder, i.e. the larger is the entropy. The total entropy is the sum of the individual contributions:

$$S_{\text{tr}} + S_{\text{rot}} + S_{\text{vib}}$$

The distribution of molecules amongst the energy states is governed by the *Boltzmann distribution function*: the number of molecules in an excited state, n_e , as a fraction of the number in the lowest, or ground, state, n_l , is given by $n_e/n_l = \exp(-\varepsilon/kT)$ where ε is the energy difference and k is the Boltzmann constant. It follows that the larger the energy difference is, the smaller is the population of an excited state and so the smaller is the contribution to the entropy. In the extreme case, the first excited state could be so much higher in energy than the ground state that all the molecules would be in the latter: this would correspond to complete order and therefore to $S = 0$. Conversely, the more closely spaced the energies of the states, the more heavily populated the excited states will be: the number of permutations possible for the arrangement of the molecules increases and the entropy rises*.

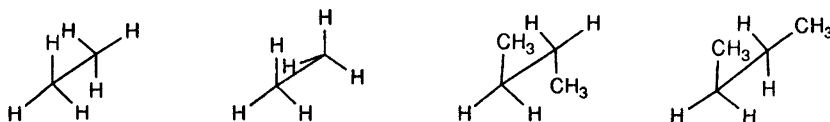
The translational energy levels of a molecule are very closely spaced, so that the higher levels are well populated and S_{tr} is relatively large; for example, for

* If, for example, the spacing of the levels is such that, of six particles, one is likely to be in the excited state, then, since any one of the six may be that particle, there are six ways in which the system can be arranged; if two are likely to be in the excited state, the number of possibilities is 30; and so on.

methane $S_{\text{tr}}^0 = 144 \text{ J K}^{-1} \text{ mol}^{-1}$ at 25°C . Rotational energy levels are less closely spaced and S_{rot} is correspondingly smaller; for example, $S_{\text{rot}}^0 = 32 \text{ J K}^{-1} \text{ mol}^{-1}$ for methane at 25°C .

There are two forms of vibrational motion: stretching and bending vibrations*. The energy levels for stretching vibrations are usually widely spaced, so that the vibrational contribution to the entropy is negligible. The energy levels for bending vibrations are closer together and the contribution to the entropy, particularly for a molecule which has a large number of bending modes, is significant.

Many polyatomic molecules possess entropy by virtue of their undergoing *internal rotations* which correspond to bending vibrations. For example, the methyl groups in ethane, $\text{CH}_3\text{—CH}_3$, rotate with respect to each other, so that the molecule can adopt any of a number of possible *conformations*. In one of the two shown in the projection diagram below, the hydrogen atoms on adjacent carbons eclipse each other, and in the other they are fully staggered (p. 27). Two conformations of butane, showing possible arrangements of the four carbon atoms, are also drawn. The conformations are not necessarily equally energetic: in butane, for example, the first of the below two structures is of lower energy content than the second, largely because of the repulsive forces between the two methyl groups in the latter (p. 28). Nevertheless, the energy differences are normally small, so that there is a contribution to the entropy of the molecule. The magnitude of conformational entropy increases with the number of available conformations and hence with the length of the chain of atoms.



The most significant aspects of the above discussion are, first, the importance of the translational entropy and, second, the significance of the conformational entropy.

(i) In a reaction which results in an increase in the number of species, such as the fragmentation $\text{A} \rightarrow \text{B} + \text{C}$, there is a considerable increase in entropy because of the gain of three degrees of translational freedom. (There are also changes in the rotational and vibrational contributions to the entropy but these are normally much smaller and can be neglected for the present argument.) On the other hand, such reactions may result in a decrease in the number of bonds and, associated with this, an increase in the enthalpy of the system. The simplest example of such a reaction is the dissociation of the hydrogen molecule, $\text{H}_2 \rightarrow 2\text{H}\cdot$ ($\Delta H^0 = +435 \text{ kJ mol}^{-1}$). Even when there is no overall change in the number of bonds, there may still be an increase in the enthalpy of the system; an example

* A non-linear molecule containing n atoms ($n > 2$) has $3n - 6$ vibrational modes of which $n - 1$ are stretching modes and $2n - 5$ are bending modes, together with three translational and three rotational degrees of freedom.

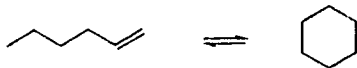
is the dehydrogenation of ethylene, $\text{CH}_2=\text{CH}_2 \rightarrow \text{CH}\equiv\text{CH} + \text{H}_2$ ($\Delta H^0 = +167 \text{ kJ mol}^{-1}$). In these cases, the enthalpy and entropy terms are opposed and whether ΔG^0 is negative or positive (and hence whether K is greater or less than unity) depends on whether the gain in translational entropy is larger or smaller than the increase in enthalpy.

For the dissociation of the hydrogen molecule at 25°C , $\Delta S_{\text{tr}} \sim 100 \text{ J K}^{-1} \text{ mol}^{-1}$, and for the dehydrogenation of ethylene, $\Delta S_{\text{tr}} \sim 117 \text{ J K}^{-1} \text{ mol}^{-1}$. The contributions from the increase in translational freedom to the decrease in free energy during the forward reaction ($=T\Delta S^0$) at 25°C are therefore ~ 30 and 35 kJ mol^{-1} , respectively. In each case, these values are far smaller than the values for the increase in enthalpy, so that ΔG^0 is large and positive and equilibrium lies essentially completely to the left. In general, this is true of such fragmentations unless ΔH^0 is less than about 40 kJ mol^{-1} .

At much higher temperatures, however, this situation may be reversed. For example, for the dehydrogenation of ethylene at 1000°C , $\Delta S_{\text{tr}} \sim 150 \text{ J K}^{-1} \text{ mol}^{-1}$, so that $T\Delta S^0 \sim 190 \text{ kJ mol}^{-1}$. The free-energy change is now significantly negative and equilibrium lies almost completely to the right so, whereas it is possible to reduce acetylene at or near room temperature to obtain ethylene, it is also possible to dehydrogenate ethylene at very high temperatures in order to produce acetylene and this process has been used industrially.

In contrast to fragmentations, the entropy changes which accompany reactions in which there is no change in the number of species, such as $\text{A} + \text{B} \rightarrow \text{C} + \text{D}$, are usually small: for a typical case, the esterification of acetic acid by methanol, ΔS_{tr}^0 is $-4.6 \text{ J K}^{-1} \text{ mol}^{-1}$ at 25°C , equivalent to a contribution of only 1.4 kJ mol^{-1} to the free-energy change at this temperature. The equilibrium constant in such reactions tends, therefore, to be governed over a wide temperature range by the enthalpy change. However, exceptions to this generalization occur when, particularly in equilibria involving ions, one or more of the species is *solvated*; entropy changes associated with the 'freezing' of solvent molecules become important.

(ii) Consider the equilibrium between 1-hexene and cyclohexane,



for which $K = 6 \times 10^9$ at 25°C . The enthalpy change is favourable: ΔH^0 from bond-energy data is -84 kJ mol^{-1} , in close agreement with the experimental value of -82 kJ mol^{-1} . If this factor alone were involved, K would be $\sim 10^{14}$. The entropy change is, however, unfavourable because the number of conformations of 1-hexene (which arise from rotations about C—C bonds) is much greater than that for cyclohexane, where rotations are restricted by the ring structure. It is this factor which accounts for almost the entire entropy change of $-86.5 \text{ J K}^{-1} \text{ mol}^{-1}$.

For the formation of the six-membered ring above, the entropy change, though markedly negative, does not offset the favourable enthalpy change: ΔG^0 is -52 kJ mol^{-1} . Smaller rings, however, are *strained* because the bond angles are distorted from their natural values (section 2.4a) so that the ΔH term is less

favourable. Although less internal freedom is lost on ring closure (for the smaller open chain compounds have fewer possible conformations), the free-energy change is less favourable. This is also true of the formation of larger rings, for although the ring strain is very small (for 7- to 11-membered rings) or zero (for larger rings) (section 2.4a), the loss of internal freedom increases with increase in ring size.

1.5
Further
applications of
thermodynamic
principles

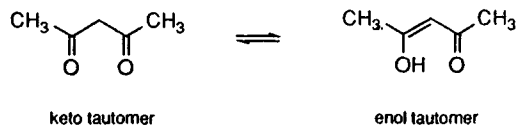
(a) *Tautomerism*

In principle, it might be possible to establish equilibrium between any two isomers, e.g.



In practice, it is common to find that conditions are not available for attainment of the equilibrium: each isomer may be isolated and is stable with respect to the other indefinitely. However, there are many systems in which isomers exist in dynamic equilibrium; their interconversion involves the detachment of a group from one position and its re-attachment at another. The isomers are then known as *tautomers* and the phenomenon as *tautomerism*.

The most frequently encountered tautomeric systems are those in which the tautomers differ in the position of a hydrogen atom. For example, 2,4-pentanedione consists of a mixture of keto and enol forms:



Its solution in hexane consists of 8% of the keto tautomer and 92% of the enol tautomer and it exhibits the reactions typical of both the carbonyl group, $\text{C}=\text{O}$, and the enol group, $\text{C}=\text{C}-\text{OH}$. On the other hand, acetone, whose tautomeric equilibrium is also between keto and enol forms,

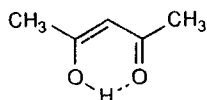


contains only about $10^{-5}\%$ of the enol.

The entropy changes in these reactions are negligible and the reason for the

difference between them lies in the enthalpy terms. The equilibrium constant for the enolization of acetone, *c.* 10^{-7} , corresponds to an enthalpy change in favour of the keto form* of *c.* 39 kJ mol^{-1} , and this is consistent with the bond-energy data in Table 1.1 which show that replacement of $\text{C}=\text{O}$, $\text{C}-\text{C}$, and $\text{C}-\text{H}$ bonds in the keto form by $\text{C}-\text{O}$, $\text{C}=\text{C}$, and $\text{O}-\text{H}$ bonds in the enol is strongly endothermic. The enthalpy change for enolization of the dione, for which *K* is *c.* 11, is *c.* 6.6 kJ mol^{-1} in favour of the enol form: relatively, therefore, the enol form of the dione is about 45 kJ mol^{-1} more stable than the enol of acetone.

This difference can be accounted for by two factors which increase the bonding of the enol form of the dione compared with that in the enol form of acetone. First, the $\text{C}=\text{C}$ bond in the former is conjugated to $\text{C}=\text{O}$, corresponding to a stabilizing interaction of about 17 kJ mol^{-1} . Second, its hydroxylic hydrogen is *hydrogen-bonded* to the carbonyl group (p. 34),



and the strength of this bond is about 25 kJ mol^{-1} . These two effects provide extra bonding of 42 kJ mol^{-1} , in close agreement with the experimental value.[†]

In contrast, phenol exists essentially entirely in the enol form:



This is because the enol possesses the stabilization energy of the aromatic ring (*c.* 150 kJ mol^{-1}) whereas the keto tautomer, which is conjugated but not aromatic, has a very much smaller stabilization energy (*c.* 20 kJ mol^{-1}): the enthalpy change is therefore strongly in favour of the enol.

The situation is different when a second phenolic group is introduced, *meta* to the first,

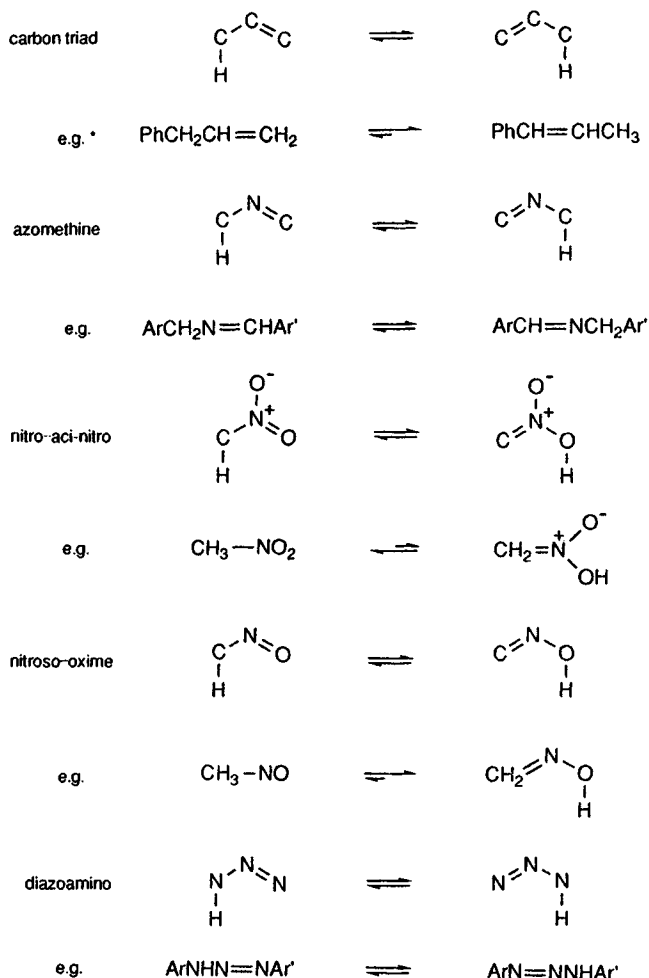


* If $\Delta S^0 = 0$, $RT \ln K = -\Delta H^0$; $RT = \text{c. } 2.4 \text{ kJ mol}^{-1}$ at room temperature, whence $\Delta H^0 = \text{c. } 39 \text{ kJ mol}^{-1}$.

[†] In water, 2,4-pentanedione consists of 84% of keto and 16% of enol tautomer. The keto tautomer is now stabilized by hydrogen-bonding of its two carbonyl-oxygen atoms with the solvent, effectively nullifying one of the stabilizing influences in the enol tautomer.

Simple calculation leads to a ΔH^0 value close to zero, essentially because two strongly bonded carbonyl groups are present in the keto structure to offset the aromatic stabilization energy of the enol. Consistent with this, *m*-dihydroxybenzene has properties characteristic of both a phenol and a ketone: for example, it undergoes the rapid electrophilic substitutions such as bromination which are characteristic of phenols (p. 386) and it is reduced by sodium amalgam to 1,3-cyclohexanedione in the manner characteristic of $\alpha\beta$ -unsaturated carbonyl compounds (p. 638). An extension of the argument rationalizes the behaviour of 1,3,5-trihydroxybenzene, which is more fully ketonized.

Many other systems of general structure $X=Y-Z-H$ are tautomeric: $X=Y-Z-H \rightleftharpoons H-X-Y=Z$. Those most frequently met are the following:

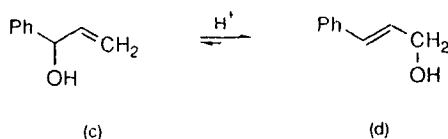


* Equilibrium, attained by heating with a strong base, lies to the right because the product possesses stabilization energy owing to the conjugation between the $\text{C}=\text{C}$ bond and the aromatic ring.

Tautomerism in which the tautomers differ in the position of a hydrogen atom is referred to as *prototropy*, for the mechanisms of interconversion involve the removal of a proton from one position and the gain of a proton at the other (pp. 145, 146). There are also systems in which the migrating group is of anionic type, such as hydroxyl, and this form of tautomerism is referred to as *anionotropy*. For example, alcohols (a) and (b) form an equilibrium mixture when either is treated with dilute sulfuric acid at about 100°C:*



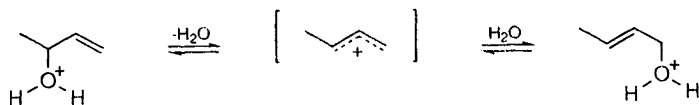
As with prototropic systems, the equilibrium constant in anionotropic systems is strongly dependent upon the structures of the tautomers. For example, although in the anionotropic system above the equilibrium is relatively balanced between the tautomers, in the equilibrium between (c) and (d),



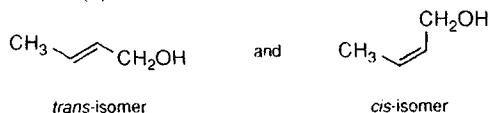
equilibrium is so strongly in favour of the latter tautomer that the former is not detectable in the equilibrated mixture.

The position of equilibrium is dictated mainly by the enthalpy term, for the entropy change in a reaction $A \rightleftharpoons B$ is small. The more highly conjugated of two tautomers is therefore the predominant one at equilibrium, for it possesses the larger stabilization energy: the conjugated alcohol (d) has a lower enthalpy than

* The acid acts by protonating the hydroxyl group in small degree; water leaves the molecule to form a *delocalized cation* (p. 110) which it can re-attack at either of two carbon atoms. Repeated reactions of this type lead to the equilibrium mixture:



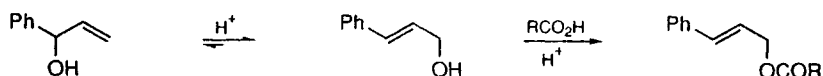
1,2-Disubstituted alkenes such as (b) exist in isomeric forms,



Both are formed in these equilibria, but the *trans*-isomer is generally the more stable and predominates. For simplicity, only the *trans*-isomer is shown in this and later examples.

the non-conjugated alcohol (c). Neither (a) nor (b) is conjugated, but in the latter the C=C bond is attached to two alkyl substituents whereas in the former it is attached to one. This leads to a *small* enthalpy difference (p. 34). (The difference in free energies corresponding to an equilibrium of 70% (b) and 30% (a) is only 2 kJ mol^{-1} at 25°C .)

The rates of interconversion in anionotropic systems vary widely, tending to be greater under given conditions when more highly conjugated systems are involved. This can be important in synthesis, e.g. an attempt to convert alcohol (c) into an ester in acid-catalyzed conditions would give the ester of (d):



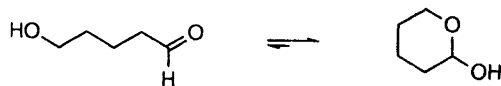
(b) Ring closure

Organic reactions frequently lead to the formation of cyclic compounds from open-chain (acyclic) compounds. We shall consider two general classes of ring-closure reactions: (i) $\text{A} \rightarrow \text{B}$ and (ii) $\text{A} \rightarrow \text{B} + \text{C}$.

The comparison of a ring closure of type $\text{A} \rightarrow \text{B}$ with an analogous intermolecular reaction is instructive. For example, acetaldehyde exists in aqueous solution in equilibrium with its hydrate:



The equilibrium lies to the left, despite a favourable decrease in enthalpy, because of the unfavourable entropy change ($-68.5 \text{ J K}^{-1} \text{ mol}^{-1}$, equivalent to a contribution of 20.4 kJ mol^{-1} to ΔG^0 at 25°C) which results mainly from the loss of translational freedom. For the analogous equilibrium between the acyclic and cyclic forms of 5-hydroxypentanal, however, the equilibrium lies well to the right ($K \sim 16$):



This is because ΔS_{tr}^0 is zero and the principal source of the entropy change is the loss of internal freedom which, for six-membered cyclization, is less than the loss of translational freedom for the corresponding intermolecular reaction.

The equilibrium between 4-hydroxybutanal $\text{HO}-(\text{CH}_2)_3-\text{CHO}$, and its cyclic form is slightly less favourable ($K = 8$) because, although the entropy factor is more favourable than for formation of the six-membered ring, the five-membered ring is slightly strained (p. 28) so that the enthalpy factor is less favourable. The equilibrium constants for the corresponding three- and four-membered rings are

negligible because ring strain is considerable* and those for rings with more than six atoms decrease rapidly because the entropy factor becomes increasingly unfavourable (for rings containing 7–11 members, there is also some internal strain). For example, $K = 0.2$ and 0.1 , respectively, for the seven- and eight-membered rings.

(c) *Unstable compounds*

The use of the words *stability* and *instability* often gives rise to confusion. The thermodynamic definitions are clear: the stability of a compound refers to the standard free energy of its formation; a compound may be stable or unstable with respect to its elements. This use of stability must be distinguished from that relating to other reactions, for example a compound may be unstable to heat (e.g. a peroxide), to water (e.g. an acetal in the presence of acid) or to air (e.g. a drying-oil). We shall always refer to the conditions in which a compound is unstable and here draw attention to the thermal stability of organic compounds.

Most organic compounds are stable to heat to temperatures of over 200°C , and since reactions are usually carried out below this temperature the decomposition of one of the reactants does not usually present a problem. Thermal instability within this temperature range is, however, associated with certain structural groups. The extent of decomposition at a particular temperature and within a given time does not depend directly on the thermodynamic properties of the material, but is determined by the *rate* of decomposition. Nevertheless, the rate is usually related to the thermodynamic properties (see section 3.6) and in general weaker bonds undergo faster bond-cleavage than stronger bonds. For example, the extent of decomposition of methane ($D_{\text{C-H}} = 426 \text{ kJ mol}^{-1}$) is negligible at 100°C , whereas that of dibenzoyl peroxide ($\text{C}_6\text{H}_5\text{COO}-\text{OCOC}_6\text{H}_5 \rightarrow 2\text{C}_6\text{H}_5\text{CO}_2\cdot$; $D_{\text{O-O}} = 130 \text{ kJ mol}^{-1}$) is about 50% after 30 minutes.

Such instability may be usefully applied. For example, certain organic reactions may be initiated by the introduction of a reactive species such as the benzoyloxy radical (section 17.1) and these reactions can be brought about by adding dibenzoyl peroxide and heating to a temperature at which the rate of generation of benzoyloxy radicals brings about the initiated reaction at a practicable rate.

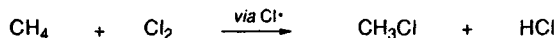
Other commonly occurring weak bonds are those of the halogens. Many compounds containing C—H bonds may be chlorinated or brominated[†] by being

* α -Hydroxyaldehydes form *dimers* (six-membered ring) which revert to the monomers in aqueous solution:



[†] Fluorine is not normally introduced in this way since the reactions are so strongly exothermic (because of the very weak bond energy of F—F as compared with H—F and C—F) as to be violent.

heated with the halogen, reaction occurring through the mediation of halogen atoms, e.g.



Again, however the thermodynamic criterion for a reaction to occur ultimately dictates the issue. In the chlorination of methane, ΔS^0 is very small and ΔH^0 (-100 kJ mol^{-1} ; cf. Tables 1.1 and 1.2) is dominant in the free-energy change. For the iodination of methane, however, $\Delta H^0 = +53 \text{ kJ mol}^{-1}$ and the free-energy change is unfavourable so that despite the ease with which suitable conditions for iodination can be established (i.e. the generation of iodine atoms), reaction does not occur.

Finally, certain compounds are unstable to heat not because they contain any intrinsically weak bonds but because decomposition can lead to the formation of a strongly bonded molecule. For example, azobisisobutyronitrile decomposes fairly rapidly below 100°C because of the favourable enthalpy change in the process owing mainly to the formation of the strongly bonded molecular nitrogen:



Such compounds are also useful as initiators of free-radical reactions (section 17.1).

- Problems** 1. The bond energies (25°C) of $\text{C}-\text{C}$, $\text{C}=\text{C}$, $\text{C}-\text{H}$, and $\text{H}-\text{H}$ are, respectively, 347, 610, 414, and 435 kJ mol^{-1} . Calculate the enthalpy of the reaction,



In practice, the reduction of ethylene to ethane can be carried out readily at room temperature. Under what conditions might it be possible to carry out the reverse reaction?

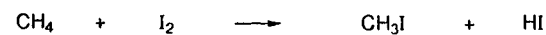
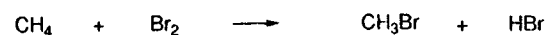
2. Estimate ΔH^0 (from the data in Tables 1.1 and 1.2) for the following reactions:



In which cases would you expect ΔS to contribute significantly to ΔG ? Which are likely to have favourable equilibrium constants for the forward reaction at

room temperature? What would be the effect on the equilibrium constants of increasing the temperature?

- The entropy changes for the formation of ethyl chloride by (a) the chlorination of ethane ($\text{C}_2\text{H}_6 + \text{Cl}_2 \rightarrow \text{C}_2\text{H}_5\text{Cl} + \text{HCl}$), and (b) the addition of hydrogen chloride to ethylene ($\text{CH}_2=\text{CH}_2 + \text{HCl} \rightarrow \text{C}_2\text{H}_5\text{Cl}$), are (a) +2 and (b) $-130 \text{ J K}^{-1} \text{ mol}^{-1}$. Comment.
- For which of the following reactions would you expect K to be <1 at room temperature? (Assume that the entropy changes in the reactions of ethylene are all $-130 \text{ J K}^{-1} \text{ mol}^{-1}$ and state any other assumptions you make.)



What effect would raising the temperature have?