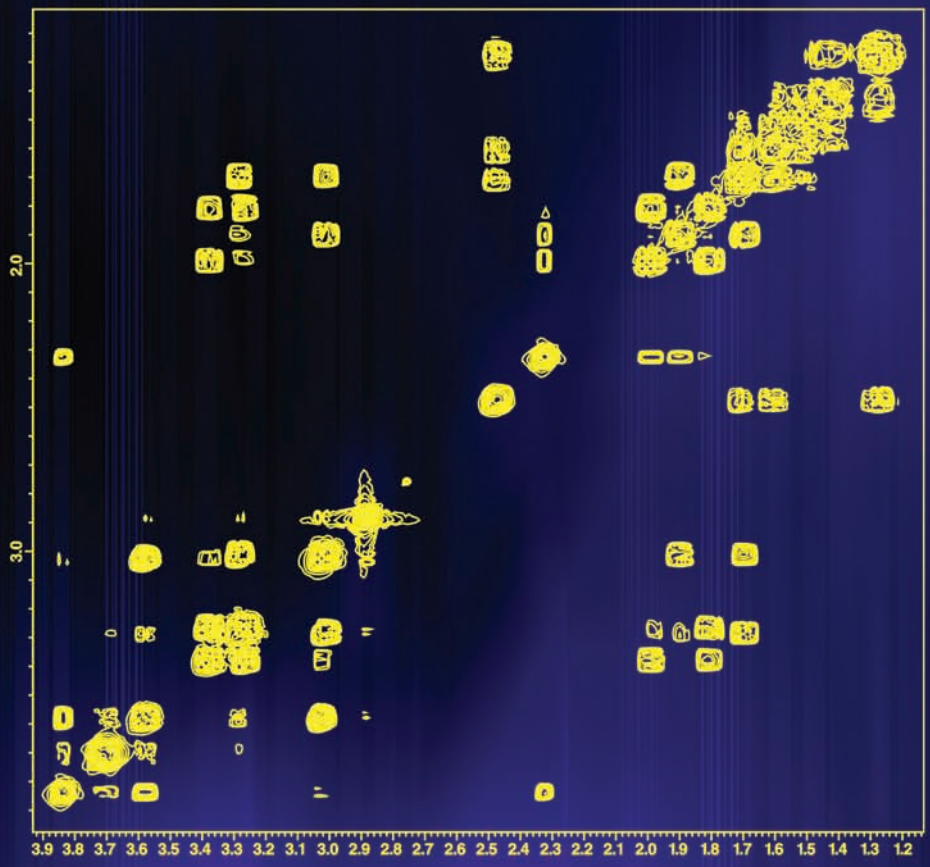


Interpretation of ORGANIC SPECTRA

Yong-Cheng Ning

With a Foreword by Nobel Prize Winner Richard R. Ernst

WILEY

Interpretation of Organic Spectra

Interpretation of Organic Spectra

By

PROFESSOR YONG-CHENG NING

John Wiley & Sons (Asia) Pte Ltd

This edition first published 2011

Registered office
John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop, # 02-01, Singapore 129809

Library of Congress Cataloging-in-Publication Data

Ning, Yong-Cheng.
Interpretation of organic spectra / Yong-Cheng Ning.
p. cm.
Includes index.
ISBN 978-0-470-82516-7 (hardback)
1. Spectrum analysis. 2. Organic compounds–Analysis. I. Title.
QD272.S6N56 2011
543′.5–dc22

2010051188

Print ISBN: 978-0-470-82516-7
ePDF ISBN: 978-0-470-82517-4
oBook ISBN: 978-0-470-82518-1
ePub ISBN: 978-0-470-82531-1

Set in 10/12pt Times Roman by Thomson Digital, Noida, India

Contents

Foreword

Professor Yong-cheng Ning, the well-known author of the two textbooks *Structural Identification of Organic Compounds and Organic Spectroscopy* (in Chinese), published in 2000, and *Structural Identification of Organic Compounds with Spectroscopic Techniques*, published in 2005, has written another remarkable volume *Interpretation of Organic Spectra*. The book is outstanding in its approach which follows what one might call the "Ning gold standard" in the spectroscopic textbook literature: The masterful combination of NMR, mass spectrometry, and infrared spectroscopy that has already been implemented in his first two treatises.

Indeed these three techniques are the most important "weapons" in the spectroscopic arsenal of the organic chemist. With these techniques, virtually any structural analysis problem in organic chemistry can be solved successfully. The author provides a careful exposition of each of the three tools, starting with an in-depth description of the practical aspects of NMR spectroscopy. He concentrates on those aspects that are indispensable for any organic chemist who intends to apply NMR fruitfully. He focuses the description on proton and carbon-13 NMR in their one- and two-dimensional implementations. COSY, NOESY, ROESY, and TOCSY are the well-known acronyms of the most important two-dimensional NMR techniques. Without going into all the theoretical sophistication, he is capable of providing a working knowledge for the practical organic chemist.

The second technique is mass spectroscopy that is also of great value in any structural analysis. Based on the analysis of the molecular and fragment ions, the primary structure of an organic molecule can elegantly be determined. Often, such an analysis precedes the interpretation of NMR spectra that allow one to elucidate also the secondary and tertiary structure of the molecule under consideration. The various methods of generating ions of larger molecules are discussed thoroughly, including the techniques of soft ionization, ESI, CI, FAB, MALDI, and APCI. These abbreviations illustrate the great wealth of available tools in advanced mass spectrometry.

The third tool to be discussed is infrared spectroscopy. It is complementary to the two other techniques. Its main feature is direct access to functional group identification. While NMR focuses on the individual atoms and their nuclei, infrared spectroscopy provides information on entire functional groups. However, what is missing in infrared spectroscopy is the connectivity information of the various functional groups. The connectivity can be deduced from a careful analysis of the NMR spin-coupling pattern and from the larger molecular fragments observed in mass spectrometry.

At the end of this useful book, the three techniques are applied to selected examples for demonstrating an integrated approach of analysis. This is a book that belongs in the hands of

any organic chemist who wants to determine the structure of his molecules and intermediates under actual study. I am convinced that the volume will receive a very positive reception from chemists dealing with the syntheses of molecules or with the study of natural products. It provides the information and the recipes for the successful usage of the indispensable and marvelous tools of spectroscopy.

Zürich, 8 March 2010
Richard R. Ernst
Nobel Laureate Chemistry 1991

Preface

The structural identification of organic compounds, including the confirmation of anticipated structures, is of great significance either for related disciplines or for their applications. This book deals with the structural identification with spectroscopic methods.

Another book by the same author, *Structural Identification of Organic Compounds with Spectroscopic Techniques*, was published by Wiley-VCH in 2005. The principles of NMR, MS, IR, and Raman spectroscopy were discussed in depth. However, the book did not present enough examples about the interpretation because of the limited space.

This book contains six chapters. Chapters 1–5 present the ^{1}H spectrum, the ^{13}C spectrum, the two-dimensional NMR spectrum, the mass spectrum, and the infrared spectrum, respectively. Chapter 6, which occupies about two thirds of this book, discusses 20 examples connected with comprehensive interpretation.

This book discusses the structures of a wide range of organic compounds, containing several carbon atoms to 47 carbon atoms. Therefore, this book can be used for both beginners and researchers.

Although the interpretation for NMR spectra has become a perfect method, this book illustrates some important rules, for example, the symmetrical plane rule, which determines the complexity of the ^{1}H spectrum and the ^{13}C spectrum, by use of examples. The author has also emphasized good coordination while using the different kinds of NMR spectra for the comprehensive interpretation of several kinds of NMR spectra.

The interpretation of MS and IR spectra seems to be neglected in some existing books dealing with the structures of organic compounds. However, the application of MS and IR spectra (especially the former) can solve some structural problems, which are difficult to solve by the use of NMR spectra. Some interesting examples, which have been accumulated by the author himself in practice, show their important applications. The interpretation of the mass spectrum includes that of the mass spectra produced by the soft ionization and by the tandem mass spectrometry.

The author wishes to express his deepest gratitude to Prof. Dr. Richard R. Ernst, the single Nobel Prize winner in chemistry in 1991, who wrote the foreword to this book. The success of the Chinese version of my former book, of which more than 25 000 copies have been sold so far in China, is greatly credited to his foreword. It is certain that his current foreword to this book will continue to play an important role.

The author likes to record his appreciation to Prof. Di-hui Qin of the Department of Foreign Languages, Xidian University. He has proofread and refined the manuscript. This is the second cooperation with him, which is effective and pleasant.

Gratitude is also extended to the following professors and experts, who provide spectra for this book so that the book can cover a wide range of applications. They are Hai-jun Yang

of Tsinghua University, Wen-yi He of the Beijing Pharmaceutical Institute, Ya-fei Zhu of Zhongshan University, Hao Gao of Jinan University, Xiu-yan Sun of Yantai University, Xuan Tian of Lanzhou University, and Xiu-qing Song of the Beijing Chemical Engineering University.

Finally, the author expresses his thanks to his wife, Mrs. Chong-wei Liu, for her understanding and unswerving support in his writing books for years.

1

Interpretation of ^{1}H NMR Spectra

As described in the preface to this book, the NMR is the most important method to identify the structure of an unknown organic compound, because the information obtained from (one dimensional and two dimensional) NMR spectra is more abundant and interpretable than that obtained by other spectroscopic methods. Since ^{1}H NMR spectra have higher sensibility than other NMR spectra, ^{1}H NMR spectra can be acquired more easily in some ways, and we present ^{1}H NMR spectra in the first chapter of this book.

Because the ^{1}H NMR spectrum can be interpreted in detail, it is possible to deduce the structure of an unknown compound, whose structure is not complex, only by using its ^{1}H NMR spectrum, ^{13}C NMR spectrum and the information about its molecular weight (without two dimensional NMR spectra). When we need to select the most reasonable structure from several possible structures, the ^{1}H NMR spectrum of that compound can play a very important role.

Even when two dimensional NMR spectra were applied, the information, especially that from the analysis of coupled splittings in the ^{1}H NMR spectrum, would still be useful to deduce an unknown structure.

The main parameters of ^{1}H NMR spectra are chemical shifts, coupled constants (and splitting patterns) and peak areas. If we consider a ^{1}H NMR spectrum from the viewpoint of physics, there is a fourth parameter, that is, relaxation times. However, relaxation times are short for ^{1}H NMR spectroscopy. Therefore, the variation of relaxation times does not produce variations of peak areas of ^{1}H NMR spectra. And relaxation times do not affect the interpretation of ^{1}H NMR spectra.

The abscissa of the ^{1}H NMR spectrum is the chemical shift δ, which characterizes the position in a ^{1}H NMR spectrum of the peak of a functional group.

Because of coupling interactions between magnetic nuclei, peaks in the ^{1}H NMR spectrum will show splittings. The splitting distance between two related split peaks is characterized by the coupling constant, measured in hertz. The magnitude of coupling constants reflects the strength of coupling interaction.

The related knowledge about the chemical shift and the coupling constant will be presented later.

The ordinate of the ^{1}H NMR spectrum is the intensity of peaks. Because peaks in the ^{1}H NMR spectrum have some widths, integral values of peak areas are applied as the

Interpretation of Organic Spectra, First Edition. Yong-Cheng Ning.

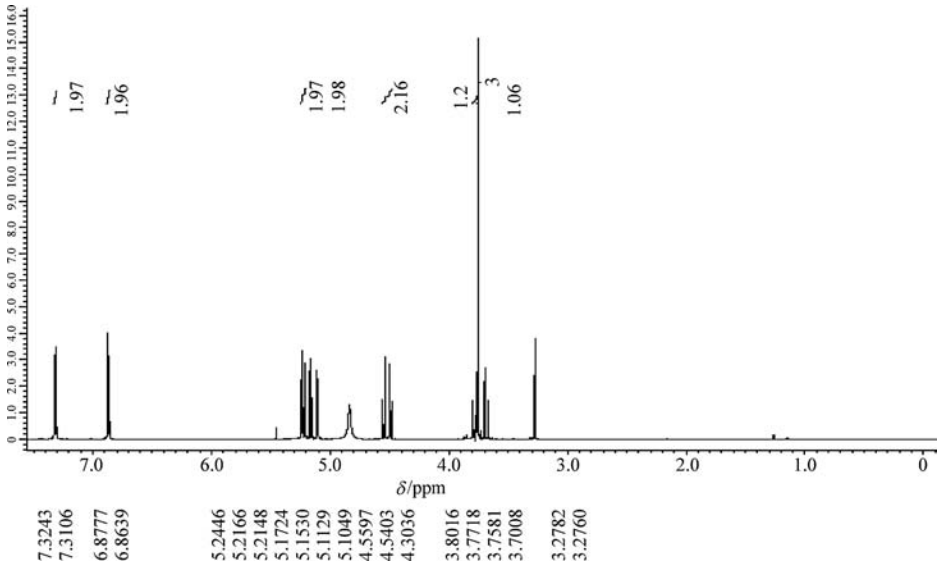


Figure 1.1 The ^{1}H spectrum of compound **C1-1**

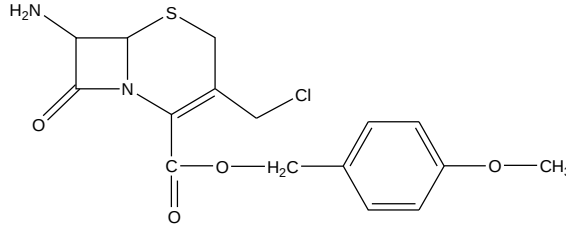
measurements of intensities of peaks. Integral values, denoted under or beside the corresponding peaks, are proportional to the numbers of hydrogen atoms of related functional groups. The quantitative relationship of the ^{1}H NMR spectrum is good with errors less than 5%.

The quantitative relationship between the integral values of peak areas and the numbers of hydrogen atoms of corresponding functional groups is important for deducing an unknown structure.

If a measured sample is a mixture, the quantitative ratio of components can be obtained from the quantitative relationship.

By using the quantitative relationship in ^{1}H NMR spectroscopy, some important results can be obtained. For example, the averaged additional number of ethylene oxides, n, in a non-ionic surfactant, $RO(CH_2)_nH$, can be measured easily by using ^{1}H NMR spectroscopy when we analyze this kind of surfactant. And the averaged value of n is more important than individual numbers which participate in average calculation for evaluating the character of this kind of surfactant. Otherwise, if we apply thin layer chromatography to analyze the surfactant, after its development by thin layer chromatography, we will get a series of spots on the thin plate. Each spot corresponds to a particular additional number and all numbers form a normal distribution shape. In this case, an average number is more important than these individual numbers which participate in average calculation.

The ^{1}H spectrum of Compound **C1-1** is shown in Figure 1.1.



C1-1

From Figure 1.1 we know that the abscissa of the ^1H spectrum is the chemical shift whose accurate values are denoted under (or above) corresponding peak sets. The ordinate of the ^1H spectrum is the peak intensity. The integral values which show the areas of peak sets are denoted above (or under) corresponding peak sets.

There are split peak sets in the ^1H spectrum. Because split distances are measured in Hz, the higher the frequency of the NMR spectrometer, the shorter the split distance in peak sets. Since Figure 1.1 was obtained through measurement by an NMR spectrometer with 600 MHz, the split distances are very short.

1.1 Chemical Shift

1.1.1 Conception of Chemical Shift

From the name of "chemical shift" one can know that in a ^1H spectrum peak positions of functional groups will be shifted compared with the peak position of a reference according to the chemical characters of different functional groups, that is, chemical shifts (values) characterize peak positions of functional groups in a ^1H spectrum. The symbol of the chemical shift is δ.

The reference of the chemical shift, which is applied most frequently, is TMS (tetramethylsilane). The position of its peak, which is a singlet, is set as the origin of the abscissa of the ^1H spectrum. Its sign is negative when a signal is positioned on the right side of the standard and positive when on the left side. Common functional groups have positive chemical shift values, that is, their peaks are situated on the left side of the signal of TMS.

The unit of chemical shift (value) is ppm (parts per million), which is dimensionless.

From the physical consideration, the chemical shift value reflects the magnitude of the extranuclear electron density of hydrogen atoms which is measured by ^1H NMR spectroscopy. Because the hydrogen atom has only s electron, the electron density is the s electron density. The greater the density of s electron around the nucleus, the smaller the chemical shift value and vice versa. If any factor makes the peak move towards the right (to decrease its chemical shift value), the function of the factors is called the shielding effect. Conversely, if any factor makes the peak move towards the left (to increase its chemical shift value), the function of the factor is called the deshielding effect.

The chemical shift values (varying ranges) of common functional groups containing hydrogen atoms are shown in Table 1.1.

From Table 1.1 we can know that δ values of functional groups are quite different. And the chemical shift value of a functional group can vary within a range.

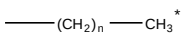
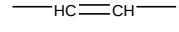
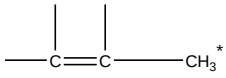
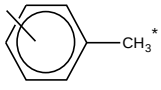
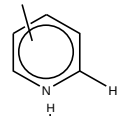
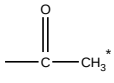
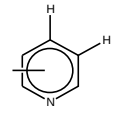
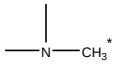
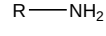
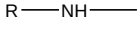
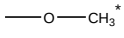
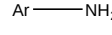
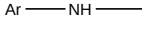
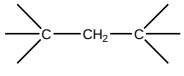
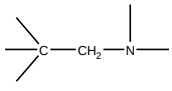
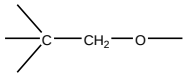
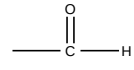
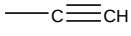
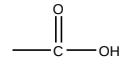
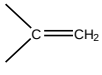
1.1.2 Factors Affecting Chemical Shifts

Factors affecting the chemical shift can be discussed from the following aspects: kind of functional groups, effects of substituents, effects of the medium, and so on.

1.1.2.1 Chemical Shift Values are Determined Mainly by the Kind of Functional Group

Functional groups have obvious differences in chemical shift value. Generally speaking, saturated groups have smaller chemical shift values than unsaturated groups.

Table 1.1 Chemical shift values (varying ranges) of common functional groups containing hydrogen atoms

Functional group	δ_H (ppm)	Functional group	δ_H (ppm)
	0.87		4.5–8.0
	1.7–2.0		6.5–8.0
	2.1–2.4		8.0–8.8
	2.1–2.6		6.5–7.3
	2.2–3.1		0.5–3.0
	0.5–3.0		
	3.5–4.0		3.0–4.8
	3.0–4.8		
	1.2–1.4		0.5–5.0
	2.3–3.5		4.0–10.0
	3.5–4.5		9.5–10.0
	2.2–3.0		9.0–12.0
	4.5–6.0		

And unsaturated groups have smaller chemical shift values than aromatic groups. The above-mentioned phenomenon can be explained by the following influence factors.

s-p Hybridization of the Connected Carbon Atom The δ value of hydrogen atoms connected with an unsaturated carbon atom is greater than that of hydrogen atoms connected with a saturated carbon atom, which can be explained by the percentages of s electrons in the

carbon atom. The increment of the percentage from 25 to 33% leads to the bond electron approaching the carbon atom, which produces a deshielding effect on the hydrogen atoms connected with the unsaturated carbon atom.

The chemical shift value of alkyne hydrogen atoms, which corresponds to sp hybridization, is between that of saturated hydrogen atoms and that of alkene hydrogen atoms, which will be otherwise explained later.

The Ring Current Effect of the Cyclic Conjugation System We discuss this effect with a benzene ring as an example. Under the effect of an applied magnet field $\boldsymbol{B_0}$, a ring current produced from the delocalized electrons of the benzene is induced. It produces an induced magnetic field, which opposes $\boldsymbol{B_0}$ in the middle of the molecule but reinforces $\boldsymbol{B_0}$ at the periphery. Although the benzene molecule tumbles in its solution, its NMR signal has the value averaged from all its directions, so the hydrogen atoms of a benzene molecule still have a larger δ value than alkene hydrogen atoms.

Anisotropic Shielding Effects of Chemical Bonds All single bonds, double bonds and triple bonds show anisotropic shielding effects, which means they have different shielding or deshielding effects in different directions.

If a six-membered ring can not reverse rapidly, two geminal hydrogen atoms (an axial hydrogen atom and an equatorial hydrogen atom) connected with the same carbon atom are not exchangeable. Their chemical shift values are different. The chemical shift value of the axial hydrogen atom is about 0.5 ppm less than that of the equatorial one, which results from the anisotropic shielding effect.

Because the π electrons of a carbon-carbon triple bond rotate around the bond axis, there is a strong shielding effect along the axial direction where the alkyne hydrogen atom lies. That is why alkyne hydrogen atoms have a smaller chemical shift value than alkene hydrogen atoms.

Stereo Effect If a hydrogen atom is close to another atom with a distance shorter than the sum of the Van der Waals radii of the two atoms, the extranuclear electron of the hydrogen atom is repelled so that the electron density will be decreased and the chemical shift value of the hydrogen atom will be increased.

1.1.2.2 Effects of Substituents

Because of effects of substituents, the chemical shift value of a functional group can be changed within a certain range. It should be noticed that a substituent can show different effects for different functional groups.

Effects of Substituents for Aliphatic Hydrogen Atoms The substitution of an electronegative functional group will increase the chemical shift value of the hydrogen atoms connected to the substituted carbon atom, that is, the δ value of the α-hydrogen atoms will be increased. The value of the β- hydrogen atoms will be increased also but by a smaller quantity. This phenomenon can be understood easily from the induction effect. The electronegative substituent attracts electrons from the substituted functional group, with the electron density of the latter to be decreased so that its δ value will be increased.

Effects of Substituents for Aromatic Hydrogen Atoms The effects of substituents for aromatic hydrogen atoms are different from those for aliphatic hydrogen atoms. In this case, the induction effect and the conjugation effect have to be considered together.

We divide substituents into three types [1].

The first type of substituents includes alkyl groups and halogen atoms. They are saturated groups and they are not, or not strongly, electronegative. Therefore, these substituents do not change obviously the electron density of the substituted benzene ring.

Groups of $-CH_3$, $-CH_2-$, –CH<, –CH=CHR, $-C\equiv CR$, –Cl, –Br, and so on, belong to this type.

The second type of substituents is the functional groups that contain saturated heteroatoms. Because of the p-π conjugation between the non-bonding electrons of the heteroatom and the delocalized electrons of the substituted phenyl ring, the electron density of the substituted phenyl ring is increased, especially at the ortho- and para- positions. From the point of view of NMR, the ortho- and para-hydrogen atoms have an upfield shift after the substitution. The ortho-hydrogen atoms have an upfield larger shift than the para-hydrogen atoms. The meta-hydrogen atoms also have an upfield shift but the shifted magnitude is less than that of the ortho- and para-hydrogen atoms.

Groups of –OH, –OR, $-NH_2$, –NHR, $-NR'R'$, and so on, belong to this type.

The third type of substituents is the groups which contain unsaturated heteroatoms. Because of the electronegativity of the heteroatom, the electron density of the substituted phenyl ring is decreased, especially at the ortho-position. From the point of view of NMR, all the remaining hydrogen atoms in the substituted phenyl ring, especially the two ortho-hydrogen atoms, have a downfield shift after the substation.

Groups of –CHO, –COR, –COOR, –COOH, –CONHR, $-NO_2$, –N=NR, and so on, belong to this type.

1.1.2.3 Effects of the Medium and Hydrogen Bond

The effects of the medium are that of the solvent which is applied in the NMR experiment.

Because the same sample molecules experience different magnetic field strengths in different solvents and because different functional groups in the same molecule are affected with different strengths by solvent molecules, NMR spectra (including the ^1H spectrum), measured in different solvents can be changed. The ^1H spectrum of a sample can change obviously with different solvents. The change relates to chemical shift values and peak shapes. Therefore, the solvent applied in the measurement of ^1H spectra should be identical in order to make a comparison between the ^1H spectrum of a sample and that of a standard substance.

Both intermolecular and intramolecular hydrogen bonds can affect chemical shift values of functional groups. The carboxyl group is an outstanding example of the effect of hydrogen bonds, whose chemical shift value can exceed 10 ppm. The chemical shift value of enol is the largest one, which can reach 16 ppm because of the effect of hydrogen bonds.

Because the chemical shift values of a functional group are related to the functional groups and with its substituents, it is possible to deduce the probable functional group and its substituent from its chemical shift value.

It is sufficient just to known factors affecting chemical shift values without related calculation equations and parameters, because chemical shift values can be estimated by the software ChemDraw (refer to section 1.5.8).

Since the range of chemical shift values of common function groups is less than 10 ppm, peak sets of a sample can overlap or partially overlap in a ^{1}H spectrum. In this case, heteronuclear shift correlation spectra, for example, the HMQC spectrum, are very important for analyzing the overlapped peak sets. We will deal with it in Section 3.2.

1.2 Coupling Constant *J*

Although the title of this section is the coupling constant *J*, our discussion in this section includes peak splittings because the coupling phenomenon and peak splittings are connected together.

1.2.1 Coupling Effect and Coupling Constant *J*

First of all, we should know which kind of nuclei has coupling effects? Simply speaking, coupling effects exist between magnetic nuclei whose magnetic quantum numbers are not zero. Non-magnetic nuclei have no coupling effect and they can not be measured by NMR.

Magnetic nuclei, which produce coupling effects, include hydrogen nuclei and other magnetic nuclei, such as ^{19}F, ^{31}P, and so on. Within some numbers of chemical bonds, hydrogen nuclei couple each other. Since 99% of carbon atoms are ^{12}C, which are non-magnetic nuclei, there are no coupling splittings between hydrogen and carbon atoms except so-called "satellite-peaks" which are situated besides the two sides of strong peaks in a ^{1}H NMR spectrum. They are produced by ^{13}C which possesses only 1% of the carbon atoms.

If the studied compound contains other magnetic nuclei, such as ^{19}F and ^{31}P, hydrogen atoms will be coupling-split by these nuclei. We will discuss it in Section 1.4.5. Because two isotopes of chlorine (^{35}Cl, ^{37}Cl) and two isotopes of bromine (^{79}Br, ^{81}Br) have a spin quantum number of 3/2, these nuclei will change their orientations rapidly, so that they have no coupling effects on hydrogen atoms. Therefore, they do not produce coupling splittings for peak sets of functional groups containing hydrogen atoms. We can interpret their ^{1}H NMR spectrum as they are non-magnetic nuclei.

Because magnetic nuclei have different orientations in an applied magnetic field, the peak set of the functional groups connected with the magnetic nuclei will be split. The peak set will be shown as multiplets.

By induction, a $2nI + 1$ rule can be introduced, where n is the number of magnetic nuclei that participate in coupling and *I* is the spin quantum number of the magnetic nuclei.

If $I = 1/2$, the $2nI + 1$ rule is simplified as the $n + 1$ rule.

In the interpretation of ^{1}H spectra, the $n + 1$ rule can be applied when the magnetic nuclei with which we deal have the spin quantum number of 1/2. This is the most frequent situation.

The $n + 1$ rule can be described as follows. The peak set of a functional group, which is connected with another functional group containing n hydrogen atoms, will be shown as a multiplet with the peak number of $n + 1$. It must be noted that n is the number of the hydrogen atoms which participate in coupling but is not the hydrogen atom number of the functional group studied.

It can be proved by the related theory or it can be known from the experience by the interpretation of ^{1}H spectra that if coupled functional groups have different chemical shift

values, their coupling splits are shown in their ^{1}H spectrum. Otherwise, if they have the same chemical shift value, their coupled splits can not be shown in their ^{1}H spectra, although their coupling effect still exists. The same chemical shift value mentioned above involves two cases. In the first case, the two functional groups have the same chemical shift value because they are symmetrical in a molecule. In the second case, the two functional groups incidentally have the same chemical shift value. The above-mentioned conclusion is very important for interpretation of ^{1}H spectra.

The magnitude of coupling effects is measured by coupling constants. The coupling effects transfer through chemical bonds. The smaller the number of the chemical bonds through which the coupling effects transfer is, the stronger the coupling effects. Therefore, an Arabic number, which means the number of the chemical bonds through which the related coupling effects transfer, is marked at the upper-left corner of the coupling constant J. For example, ^{3}J means the coupling constant across three chemical bonds.

We will discuss the coupling constant according to the number.

Coupling constants are algebra values. They have a positive or a negative sign. Since coupling constants are shown generally as an absolute value, we will not differentiate their signs in this book. Only in some special situations can the sign of a coupling constant change a ^{1}H spectrum. Readers who are interested in this topic can read the reference [1].

We use s, d, t, q and m to express the split patterns of singlet, doublet, triplet, quartet and multiplet, respectively, for the related simplification.

1.2.2 Discussion of Coupling Constants According to their Kinds

1.2.2.1 ^{1}J

^{1}J is the coupling constant across one chemical bond.

From what we have described above, we can know that $^{1}J_{C-H}$ is not shown in the ^{1}H spectrum in general. However, $^{1}J_{C-H}$ will be shown in ^{13}C NMR spectra if decoupling to hydrogen atoms is not applied.

The coupled splits, from magnetic nuclei with the chemical valence as 1, such as ^{19}F, are not shown in the ^{1}H spectrum, since its structural formula can not be continued.

The coupled splits from magnetic nuclei with multiple chemical valences, such as ^{31}P, will be shown in the ^{1}H spectrum. The ^{1}J value of ^{31}P is about 700 Hz.

1.2.2.2 ^{2}J

^{2}J is the coupling constant across two chemical bonds.

We mainly discuss ^{2}J between H–H, and the coupling is named geminal coupling.

It is important to differentiate two kinds of ^{2}J. The value of ^{2}J in a saturated structural unit is different greatly from that in an unsaturated structural unit.

The typical value of ^{2}J in a terminal alkene group is about 2.3 Hz.

The typical value of ^{2}J in a saturated chain is about 12 Hz, which is much larger than that of ^{3}J, which is encountered most frequently for interpreting the ^{1}H spectrum.

^{2}J in a saturated group is always shown in the following cases.

The two hydrogen atoms of a CH_2 group in a saturated ring have different chemical shift values because they experience different anisotropic shielding effects from their adjacent functional groups. Therefore, the coupling splits will be shown in their ^{1}H spectrum.

If the two hydrogen atoms of a CH_2 group in a saturated chain have different chemical shift values, their coupling splits will be shown in their ^1H spectrum. Since the value of ^2J in a saturated group is rather large, the coupled splits from it are prominent. We will discuss it in Section 1.4 in detail. The coupled splits by ^2J can be shown frequently for a compound whose structure is not simple.

The factors affecting the value of ^2J are as follows:

1. The absolute value of ^2J will decrease with the increase of the electronegativity of the substituent. For example,

Compounds	CH_4	CH_3Cl	CH_2Cl_2
^2J(Hz)	−12.4	−10.8	−7.5

   A vicinal π bond makes the saturated ^2J shift in the negative direction, which means the absolute value of ^2J will increase.
2. The value of ^2J is affected by the tension of a saturated ring, which is determined by the size of the ring. The special feature of the three-membered ring makes the absolute value of ^2J smaller than that of other sizes of saturated rings.

1.2.2.3 ^3J

We focus our attention on the ^3J coupling between two hydrogen atoms. Their coupling is named vicinal coupling.

Since the splits by ^2J are always absent due to two geminal hydrogen atoms frequently having approximately the same chemical shift value and the splits by long-range couplings being not obvious, the coupled splits from ^3J dominate the split shapes in general.

If a compound has several conformations, its ^3J value is the average value of those conformations.

The factors affecting the value of ^3J are as follows:

Dihedral Angle Φ Two vicinal hydrogen atoms and the two carbon atoms between these two hydrogen atoms form a dihedral angle Φ. The value of ^3J depends on the dihedral angle that is formed by the related H–C–C–H, as shown in Figure 1.2.

We can know that the value of ^3J has a minimum value when $\Phi = 90°$, and that the value of ^3J has a maximum value when $\Phi = 0°$ or 180°, while the value of ^3J when $\Phi = 180°$ is greater than that of ^3J when $\Phi = 0°$.

The following two cases will be encountered frequently.

Because the dihedral angle formed by two trans-hydrogen atoms is 180° and that by two cis- hydrogen atoms is 0°, the coupling constant value from two trans-hydrogen atoms is greater than that from two cis-hydrogen atoms. Their typical values are 15–17 Hz and 10–11 Hz, respectively.

In a saturated six-membered ring, if two vicinal hydrogen atoms are situated at axial bonds (in this case their coupling constant is denoted as J_{aa}), the coupling constant from these two hydrogen atoms is greater than that from two vicinal hydrogen atoms, which are situated at equatorial bonds (in this case their coupling constant is denoted as J_{ee}), or that from these two hydrogen atoms, with one hydrogen atoms situated at an axial bond and its vicinal hydrogen atom situated at an equatorial bond (in this case their coupling constant is

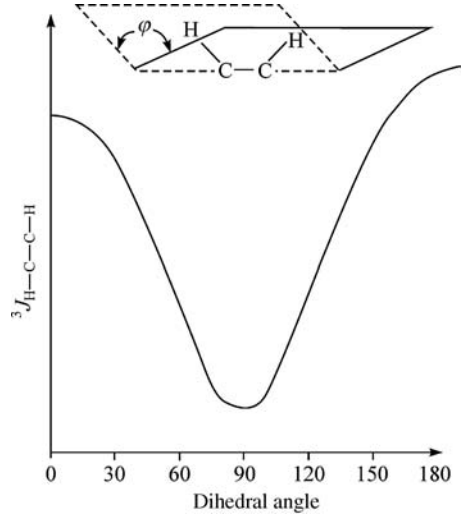


Figure 1.2 $^3J_{H\text{-}C\text{-}C\text{-}H}$ is the function of the related dihedral angle

denoted as J_{ae}). These phenomena can be explained by the following facts: Φaa ≅ 180, and Φae ≅ Φee = 60. Therefore, $J_{aa} > J_{ae} \geq J_{ee}$.

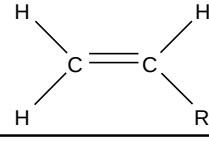
In addition, erythro- and threo- forms can be differentiated by using the relationship between coupling constants and dihedral angles. Readers who are interesting in this topic can read the reference [1].

Electronegativity of Substituents The substitution of an electronegative group will decrease the value of ^3J. This phenomenon can be encountered frequently.

The value of ^3J in a saturated alkyl group is about 7 Hz. If a saturated alkyl group is substituted by a hydroxyl group, the ^3J value will decrease by less than 5 Hz. Therefore, the decrease of ^3J value will be shown obviously in its ^{1}H spectrum.

We will discuss the split patterns in the ^{1}H spectrum later. The changes of the values of coupling constants will obviously affect split patterns.

The substitution of an alkene group by an electronegative group will decrease the values of coupling constants of trans-two hydrogen atoms and that of cis-two hydrogen atoms. For example,

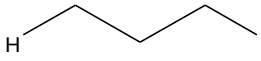
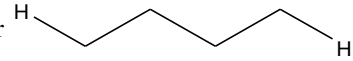


R	$^3J_{cis}$	$^3J_{trans}$
-Li	19.3	23.9
-SiR_3	14.6	20.4
-CH_3	10.0	16.8
-Cl	7.3	14.6
-F	4.7	12.8

There are other factors affecting ^3J values. However, their effects are smaller than the above-mentioned two factors. Therefore, we omit them [1].

1.2.2.4 Coupling Constants of Long-Range Couplings

In the ^1H spectrum, the couplings across four or more bonds are called long-range couplings.

The coupling constants in a saturated system decrease rapidly with an increase in the number of chemical bonds between two coupled nuclei. Only particular structural units, such as  or  have a small long-range coupling constant (generally less than 2 Hz).

In an unsaturated system, through the action of π electrons, long-range couplings can be transferred to other chemical bonds. Therefore, ^4J and even ^5J between two hydrogen atoms in an unsaturated chain can exist. There are long-range couplings in the following structural units:

① Allylic system: H–C=C–C–H.
② Homoallylic system: H–C–C=C–C–H.
③ Conjugated systems.
④ Systems containing accumulated unsaturated bonds.
⑤ Coupling between the hydrogen atom in the ortho-position of the substituted phenyl ring and those in the side chain.

An example of long-range couplings will be presented in Example 11 of Section 6.2.

1.2.2.5 Couplings in a Phenyl Ring or in a Heteroaromatic Ring

The ^3J value in a phenyl ring is larger than that in a saturated chain, because coupling effects are transferred better there than in a saturated chain. The typical ^3J value in a phenyl ring is about 8 Hz.

Because of the existence of a nitrogen atom in a pyridine ring, the electronegativity of the nitrogen atom affects ^3J values just as was mentioned above: the substitution of an electronegative group will decrease the value of ^3J. When the two vicinal hydrogen atoms are close to the nitrogen atom (for example, when they are situated in 2- and 3- positions), their ^3J typical value is about 5 Hz. When the two vicinal hydrogen atoms are far from the nitrogen atom (for example, when they are situated in 3- and 4- positions), their ^3J typical value is about 8 Hz.

The ^3J value in a five-membered heteroaromatic ring (furan, etc.) is similar to that in the pyridine ring. However, the ^3J value in a five-membered heteroaromatic ring is smaller than that in the pyridine ring, respectively.

The typical coupling constants of common functional groups are listed in Table 1.2.

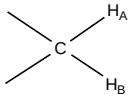
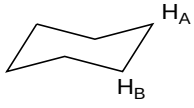
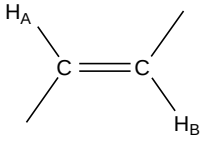
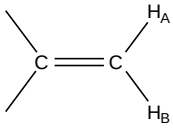
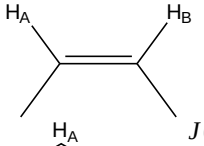
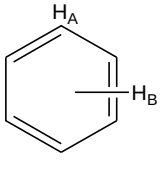
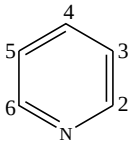
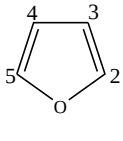
1.3 Chemical Equivalence and Magnetic Equivalence

Because of the importance of the ^1H spectrum, it is certain to measure first the ^1H spectrum of a sample for determining its structure or confirming its structure.

When we interpret a ^1H spectrum, the following question constantly arise. Why is a ^1H spectrum complicated when the structure of the sample seems uncomplicated? (Or one can even wonder if it is **really** its ^1H spectrum.)

This question just concerns the subject which we will discuss in this section: chemical equivalence and magnetic equivalence.

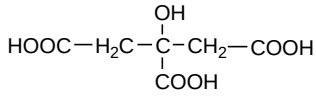
Table 1.2 Typical coupling constants of common functional groups

Structural unit	Typical coupling constant J_{AB} (Hz)
	–10– –15
CH_ACH_B	7
 *ax-ax* *ax-eq* *eq-eq*	8–11 2–3 2–3
	15–17
	0–2
	10–11
 J(ortho) J(meta) J(para)	8 2 0.3
 *J*(2–3) *J*(3–4) *J*(2–4) *J*(3–5) *J*(2–5) *J*(2–6)	5 8 1.5 1 0.8 0
 *J*(2-3) *J*(3-4) *J*(2-4) *J*(2-5)	1.8 3.6 0.8 1.5

1.3.1 Chemical Equivalence

Chemical equivalence is an important concept in stereochemistry. If two atoms (or two identical functional groups) have the same chemical environment, they are chemically equivalent. If the two functional groups are measured by NMR, they have the same chemical shift value. If two identical groups are not chemically equivalent, they may have different rates of reaction and they may have different results in their spectroscopic measurements.

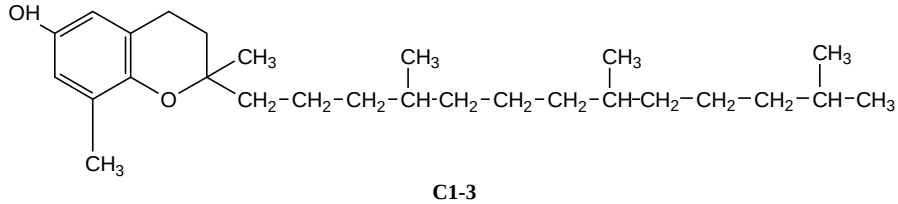
The citrate acid, **C1-2**, has the following structure:



C1-2

From the structural formula it looks as if the two carboxyl groups were chemically equivalent. However, in zymolytic reactions they have different rates, which means that the two carboxyl groups are chemically non-equivalent.

The δ-vitamin E, **C1-3**, is another example:



C1-3

The two methyl groups connected to the same carbon atom show obviously two peaks in their ^{13}C spectrum even if measured by an NMR instrument with 400 MHz, that is, its ^{13}C spectrum illustrates that the two methyl groups are chemically non-equivalent.

There are many other examples similar to those mentioned above. The problem which we encounter frequently is that since two identical functional groups in a chain are connected to the same carbon atom, so it seems reasonable that the two functional groups are chemically equivalent because their positions are exchangeable through the rotation of the carbon chain and that they should have the same chemical shift value.

The above-mentioned discussion also involves two hydrogen atoms connected to the same carbon atom, because they are a special case of two identical functional groups. It seems that these two hydrogen atoms have the same chemical shift value.

A very important rule for interpreting ^1H spectra is that there are no coupled splits of two hydrogen atoms in their ^1H spectrum if they have the same chemical shift value. Otherwise, if two hydrogen atoms have different chemical shift values, their coupled splits will be shown in their ^1H spectrum. If two geminal hydrogen atoms have different chemical shift values, their coupled splits will be prominent since the value of ^2J is much greater than that of ^3J. As a consequence, their ^1H spectrum will be complicated.

To sum up, whether for two hydrogen atoms attached to a carbon atom or for two identical functional groups attached to a carbon atom, it is not possible to determine in a simple way whether they are chemically equivalent or not.

It is necessary for us to apply the symmetrical plane rule to determine whether two identical functional groups (including two hydrogen atoms) attached to a common carbon

atom are chemically equivalent or not. If two identical functional groups are determined to be chemically equivalent, they have the same chemical shift value and as a consequence, their coupled splits will not be shown in their ^1H spectrum. Otherwise, if two identical functional groups do not satisfy the requirement of the symmetric plane rule, they will have different chemical shift values and they will produce a complex ^1H spectrum.

The symmetrical plane rule can be presented as follows.

If the molecule to be discussed has a symmetrical plane and the symmetrical plane bisects the angle of XCX, where two X groups are the two identical functional groups attached to a common carbon atom, these two X groups are enantiotopic (if rapid intramolecular motions exist, this symmetrical plane should bisect the angle for every conformer). If the solvent applied for NMR measurement is an achiral solvent, these two X groups are chemically equivalent and they have the same chemical shift value. If the solvent applied is chiral, these two X groups may have different chemical shift values.

If this condition is not totally satisfied, these two X groups are not chemically equivalent.

The symmetrical plane rule can be presented further as follows.

If the molecule to be discussed has no symmetrical plane, two identical functional groups (including two hydrogen atoms) attached to a common carbon atom are not chemically equivalent. This means that they should have different chemical shift values from the theoretical consideration. However, it is not certain that this difference in chemical shift values can be measured. The measurement of this difference can also be determined depending on experimental conditions, such as the frequency of the NMR spectrometer applied, solvent applied, temperature in measurement, and so on.

Because the compound **C1-3** has no symmetrical plane, the two methyl groups attached to a common CH are not chemically equivalent. They have two signals in their ^{13}C spectrum.

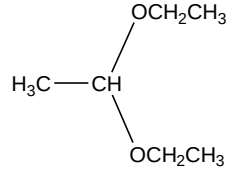
If the molecule has a symmetrical plane but rapid intramolecular motions exist, the condition that two identical functional groups be chemically equivalent is that the symmetrical plane bisects the XCX angle for every conformer and the measurement is carried out in an achiral solvent.

It is a pity that this important rule is seldom dealt with in detail in the existing books on nuclear magnetic resonance. Some books only describe a few examples concerning this rule without a theoretical discussion of the rule itself; some books describe the rule briefly without a discussion of related examples.

According to many years of research and teaching of the author himself, the above question about the rule may be the one most frequently encountered in interpreting ^1H spectra for students.

We now explain the rule further with a simple example.

The compound **C1-4** has a simple structure:



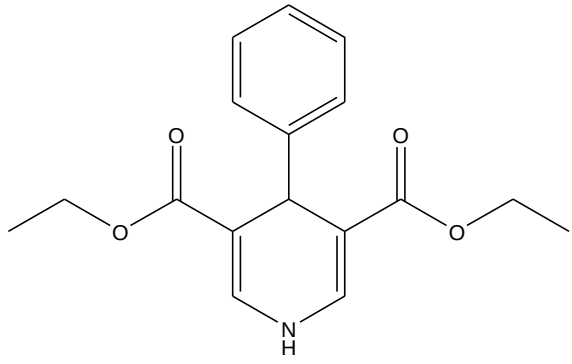
C1-4

Since the compound has a symmetrical plane, two ethoxyl groups are chemically equivalent. Therefore, the two CH_3 groups have the same chemical shift value and so do

the two CH_2 groups. However, the symmetrical plane does not bisect the H–C–H angle, and the two hydrogen atoms in a CH_2 group are not chemically equivalent. Therefore, the two hydrogen atoms produce geminal coupling, that is, the two hydrogen atoms form two sets of doublets. By splitting from its adjacent methyl groups, the CH_2 group produces 16 peaks. However, because the two CH_2 groups are symmetrical in the molecule, their lines are strictly overlapped in the same positions.

Next we shall discuss a more complicated example.

The compound **C1-5** has the following structure:



C1-5

The ^{1}H spectrum of the compound **C1-5** is shown in Figure 1.3.

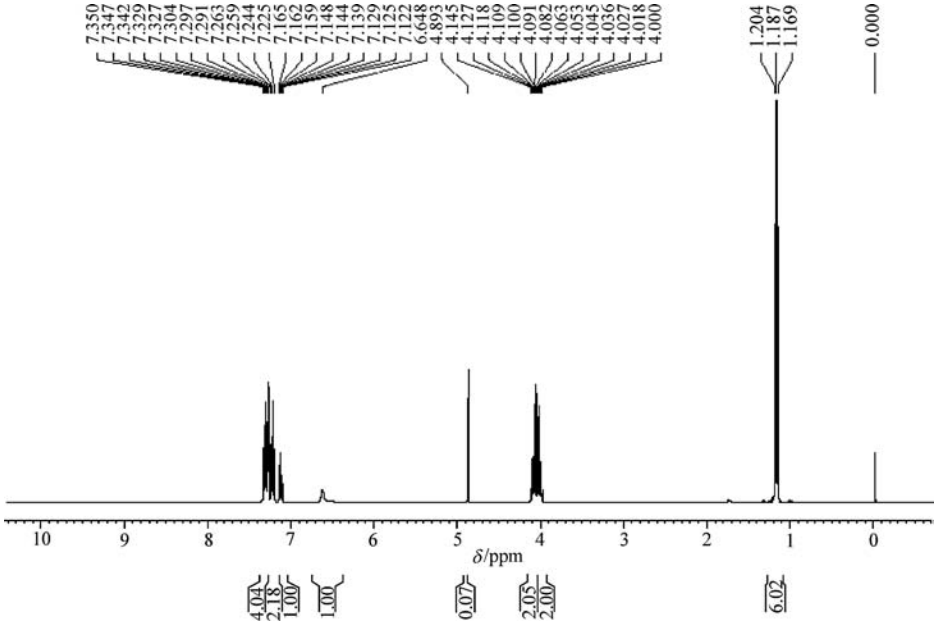


Figure 1.3 The ^{1}H spectrum of the compound **C1-5**

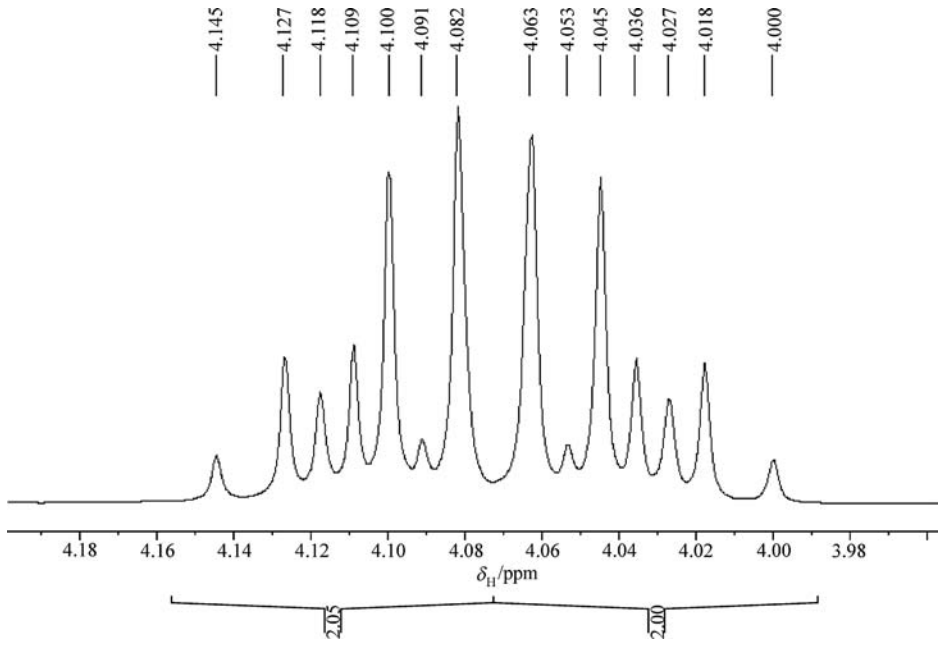


Figure 1.4 The locally enlarged ^{1}H spectrum in the region near 4.1 ppm in Figure 1.3

The locally enlarged ^{1}H spectrum in the region near 4.1 ppm in Figure 1.3 is shown in Figure 1.4.

We will present a detailed interpretation of the ^{1}H spectrum later. We just assign Figures 1.3 and 1.4 now. The integral value of the peak sets at about 7.3 ppm is 7 which corresponds to aromatic hydrogen atoms. The triplet at 1.19 ppm, whose peak area is 6, corresponds to two methyl groups. The peak sets, whose area at about 4.07 ppm is 4, correspond to two CH_2 groups. Readers will ask the question: Why do two CH_2 groups produce so many peaks?

First of all, let us analyze the split pattern of the peak sets.

Fourteen peaks are shown in Figure 1.4. In fact, the 14 peaks result from the partially overlapped 16 peaks. Since the 14 peaks show a symmetrical distribution, we can mark them with 1 to 14, respectively, either from the left side or from the right side. After a careful interpretation, we can find four quartets. They are:

1,	2,	4,	6;
3,	5,	7,	8;
7,	8,	10,	12;
9,	11,	13,	14

The distance between two adjacent peaks in a quartet corresponds to the ^3J coupling constant between CH_3 and CH_2. Since Figure 1.4 was measured by an NMR spectrometer with 400 MHz, the coupling constant can be calculated as 7.2 Hz by using related data.