BASIC GAS CHROMATOGRAPHY

Second Edition

HAROLD M. MCNAIR
JAMES M. MILLER

WILEY

A JOHN WILEY & SONS, INC., PUBLICATION

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CONTENTS

PREFACE TO THE SECOND EDITION

When the first edition of this book was published in 1998, gas chromatography (GC) was already a mature, popular separation method. Grob's encyclopedic *Modern Practice of Gas Chromatography* was already in its third (1995) edition. But the field has not remained static, and there is much new information that necessitates an update, a second edition of our book. In the meantime, Grob's book (now coedited with Barry) is in its fourth edition (2004) and comprises over 1000 pages. Miller's book on *Chromatography* is also in its second edition (2005).

Our objectives have remained the same, as has our intention to keep the book small, basic, and fundamental. Several topics that were contained in the *Special Topics* chapter of the first edition have been expanded in the second. They are Gas Chromatography–Mass Spectrometry (GC–MS) and Special Sampling Methods, now entitled simply Sampling Methods. In addition, a new chapter on Multidimensional GC has been added. Also, two new topics have been added to the Special Topics chapter, namely, Fast GC and the GC Analysis of Nonvolatile Compounds. The latter includes the original section on Derivatization, supplemented with Inverse GC and Pyrolysis GC. The entire book has been updated with new references, resources, and websites.

The textual material for the two new chapters (11 and 12) has been written by Nicholas Snow and Gregory Slack, both former students of McNair. They are established chromatography authors in their own right, and we welcome them and thank them for their contributions. Further information about them can be found on the Acknowledgments page.

We would be remiss if we did not repeat our expression of gratitude that is included in our original Preface. Many persons have helped us and taught us, including our mentors, students, and many other colleagues. We are also indebted to our wives and families for their support and encouragement. Thank you all.

Harold M. McNair
James M. Miller

PREFACE

A series of books on the *Techniques in Analytical Chemistry* would be incomplete without a volume on gas chromatography (GC), undoubtedly the most widely used analytical technique. Over 40 years in development, GC has become a mature method of analysis and one that is not likely to fade in popularity.

In the early years of development of GC, many books were written to inform analysts of the latest developments. Few of them have been kept up-to-date and few new ones have appeared, so that a satisfactory single introductory text does not exist. This book attempts to meet that need. It is based in part on the earlier work by the same title, *Basic Gas Chromatography*, co-authored by McNair and Bonelli and published by Varian Instruments. Some material is also drawn from the earlier Wiley book by Miller, *Chromatography: Concepts and Contrasts*.

We have attempted to write a brief, basic, introduction to GC following the objectives for titles in this series. It should appeal to readers with varying levels of education and emphasizes a practical, applied approach to the subject. Some background in chemistry is required: mainly general organic chemistry and some physical chemistry. For use in formal class work, the book should be suitable for undergraduate analytical chemistry courses and for intensive short courses of the type offered by the American Chemical Society and others. Analysts entering the field should find it indispensable, and industrial chemists working in GC should find it a useful reference and guide.

Because the IUPAC has recently published its nomenclature recommendations for chromatography, we have tried to use them consistently to promote a unified set of definitions and symbols. Also, we have endeavored to write in

such a way that the book would have the characteristics of a single author, a style especially important for beginners in the field. Otherwise, the content and coverage are appropriately conventional.

While open tubular (OT) columns are the most popular type, both open tubular and packed columns are treated throughout, and their advantages, disadvantages, and applications are contrasted. In addition, special chapters are devoted to each type of column. Chapter 2 introduces the basic instrumentation and Chapter 7 elaborates on detectors. Other chapters cover stationary phases (Chapter 4), qualitative and quantitative analysis (Chapter 8), programmed temperature (Chapter 9), and troubleshooting (Chapter 11). Chapter 10 briefly covers the important special topics of GC–MS, derivatization, chiral analysis, headspace sampling, and solid-phase micro-extraction (SPME) for GC analysis.

We would like to express our appreciation to our former professors and many colleagues who have in one way or another aided and encouraged us and to those students who, over the years, have provided critical comments that have challenged us to improve both our knowledge and communication skills.

Harold M. McNair
James M. Miller

ACKNOWLEDGMENTS

The authors wish to acknowledge that two chapters, 11 (Multidisciplinary Gas Chromatography) and 12 (Sampling Methods), have been provided for our book by the following colleagues:

1. Professor Nicholas H. Snow, Department of Chemistry and Biochemistry, Center for Academic Industry Partnership, Seton Hall University, South Orange, NJ, 07079 (snownich@shu.edu) and
2. Dr. Gregory C. Slack, Director of Research and Technology Transfer, Clarkson University, Potsdam, NY, 13699 (gslack@clarkson.edu).

Both of these authors wish to acknowledge the support of their respective educational institutions. Snow also gratefully acknowledges Sanofi-Aventis, which established Seton Hall's Center for Academic Industry Partnership and provided financial support. Also, LECO Corporation is acknowledged for providing instrumentation and technical assistance for his GC×GC work.

We also wish to express our appreciation to Mike Shively and the Restek Corporation of Bellefonte, PA for providing the multidimensional gas chromatogram used on the front cover.

Harold M. McNair
James M. Miller

CHAPTER 1

INTRODUCTION

It is hard to imagine an organic analytical laboratory without a gas chromatograph. In a very short time, gas chromatography (GC) has become the premier technique for separation and analysis of volatile compounds. It has been used to analyze gases, liquids, and solids, with the latter usually dissolved in volatile solvents. Both organic and inorganic materials can be analyzed, and molecular weights can range from 2 to over 1000 daltons.

Gas chromatographs continue to be the most widely used analytical instruments in the world. Efficient capillary columns provide high resolution, separating more than 450 components in coffee aroma, for example, or the components in a complex natural product like peppermint oil (see Fig. 1.1). Sensitive detectors like the flame-ionization detector can quantitate 50 ppb of organic compounds with a relative standard deviation of about 5%. Automated systems can handle more than 100 samples per day with minimum downtime, and all of this can be accomplished with an investment of about $20,000.

A BRIEF HISTORY

Chromatography began at the turn of the century when Ramsey [1] separated mixtures of gases and vapors on adsorbents like charcoal and Michael Tswett [2] separated plant pigments by liquid chromatography. Tswett is credited as being the "father of chromatography" principally because he coined the term *chromatography* (literally meaning color writing) and scientifically described

Basic Gas Chromatography, *Second Edition*, by Harold M. McNair and James M. Miller

Peppermint Oil

Column: **DB™-WAX**
60 m x 0.25 mm I.D., 0.25 µm
J&W P/N: **122-7062**
Carrier: Helium at 25 cm/sec (0.73 mL/min)
Oven: 75°C for 8 min
75-200°C at 4°/min
200°C for 5 min
Injector: Split 1:150, 270°C
1µL neat
Detector: FID, 270°C
Nitrogen makeup gas at 30 mL/min

1. α-Pinene
2. β-Pinene
3. Sabinene
4. Myrcene
5. α-Terpinene
6. l-Limonene
7. 1,8-Cineole
8. *cis*-Ocimene
9. γ-Terpinene
10. *para*-Cymene
11. Terpinolene
12. 3-Octanol
13. l-Octen-3-ol
14. *trans*-Sabinene hydrate
15. l-Menthone
16. Menthofuran
17. d-Isomenthone
18. β-Bourbonene
19. Linalool
20. Menthyl acetate
21. Neomenthol
22. Terpinen-4-ol
23. β-Caryophyllene
24. l-Menthol
25. Pulegone
26. α-Terpineol
27. Germacrene-D
28. Piperitone
29. Viridiflorol

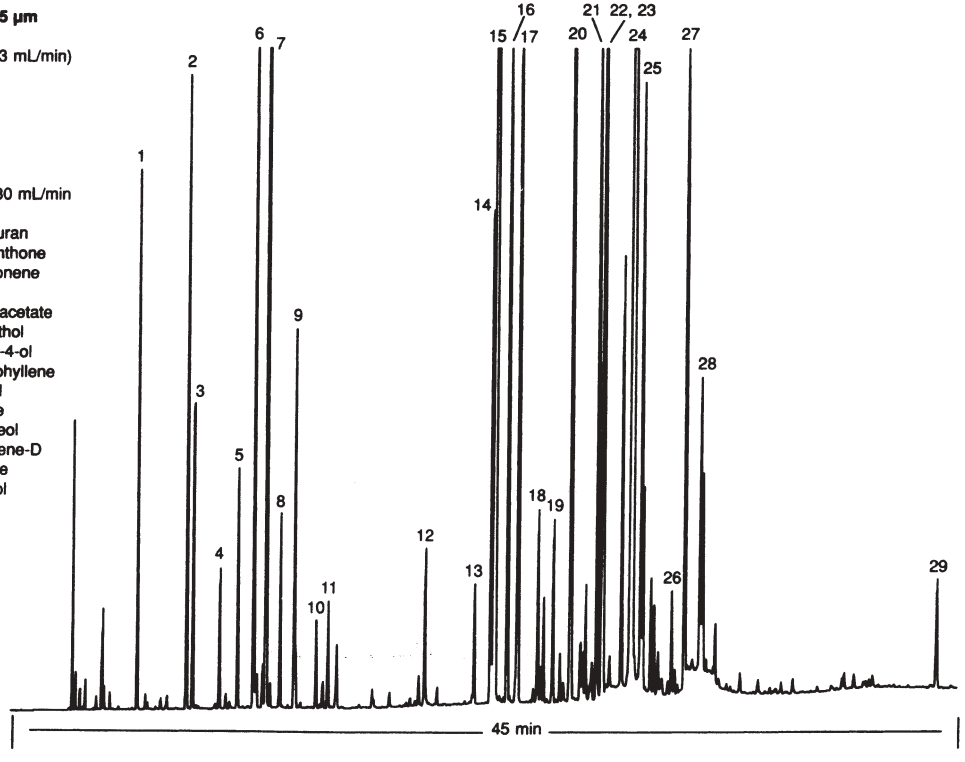

Fig. 1.1. Typical gas chromatographic separation showing the high efficiency of this method. Courtesy of J & W Scientific, Inc.

the process. His paper has been translated into English and republished [3] because of its importance to the field. Today, of course, most chromatographic analyses are performed on materials that are not colored.

Gas chromatography is that form of chromatography in which a gas is the moving phase. The important seminal work was first published in 1952 [4] when Martin and his co-worker James acted on a suggestion made 11 years earlier by Martin himself in a Nobel-prize-winning paper on partition chromatography [5]. It was quickly discovered that GC was simple, fast, and applicable to the separation of many volatile materials—especially petrochemicals, for which distillation was the preferred method of separation at that time. Theories describing the process were readily tested and led to still more advanced theories. Simultaneously the demand for instruments gave rise to a new industry that responded quickly by developing new gas chromatographs with improved capabilities.

The development of chromatography in all of its forms has been thoroughly explored by Ettre, who has authored nearly 50 publications on chromatographic history. Three of the most relevant articles are: one focused on the work of Tswett, Martin, Synge, and James [6]; one emphasizing the development of GC instruments [7]; and the third, which contained over 200 references on the overall development of chromatography [8].

Today GC is a mature technique and a very important one. The worldwide market for GC instruments is estimated to be over $1 billion or more than 30,000 instruments annually.

DEFINITIONS

In order to define chromatography adequately, a few terms and symbols need to be introduced, but the next chapter is the *main* source of information on definitions and symbols.

Chromatography

Chromatography is a separation method in which the components of a sample partition between two phases: One of these phases is a stationary bed with a large surface area, and the other is a gas that percolates through the stationary bed. The sample is vaporized and carried by the mobile gas phase (the *carrier gas*) through the column. Samples partition (equilibrate) into the stationary liquid phase, based on their solubilities at the given temperature. The components of the sample (called solutes or analytes) separate from one another based on their *relative* vapor pressures and affinities for the stationary bed. This type of chromatographic process is called *elution.*

The "official" definitions of the International Union of Pure and Applied Chemistry (IUPAC) are: "Chromatography is a physical method of separation in which the components to be separated are distributed between two phases, one of which is stationary (stationary phase) while the other (the mobile

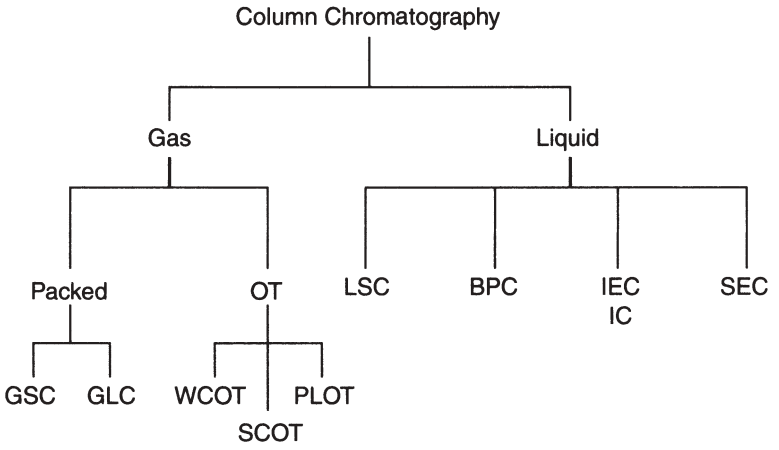

Fig. 1.2. Classification of chromatographic methods. (Acronyms and abbreviations are given in Appendix I.)

phase) moves in a definite direction. Elution chromatography is a procedure in which the mobile phase is continuously passed through or along the chromatographic bed and the sample is fed into the system as a finite slug" [9].

The various chromatographic processes are named according to the physical state of the mobile phase. Thus, in gas chromatography (GC) the mobile phase is a *gas,* and in liquid chromatography (LC) the mobile phase is a *liquid.* A subclassification is made according to the state of the stationary phase. If the stationary phase is a solid, the GC technique is called gas–solid chromatography (GSC); and if it is a liquid, the technique is called gas–liquid chromatography (GLC).

Obviously, the use of a gas for the mobile phase requires that the system be contained and leak-free, and this is accomplished with a glass or metal tube referred to as the column. Since the column contains the stationary phase, it is common to name the column by specifying the stationary phase, and to use these two terms interchangeably. For example, one can speak about an OV-101* column, which means that the stationary liquid phase is OV-101 (see Chapter 4).

A complete classification scheme is shown in Fig. 1.2. Note especially the names used to describe the open tubular (OT) GC columns and the LC columns; they do not conform to the guidelines just presented. However, all forms of GC can be included in two subdivisions, GLC and GSC; some of the capillary columns represent GLC while others represent GSC. Of the two major types, GLC is by far the more widely used; consequently, it receives the greater attention in this work.

*OV designates the trademarked stationary liquid phases of the Ohio Valley Specialty Chemical Company of Marietta, Ohio.

The Chromatographic Process

Figure 1.3 is a schematic representation of the chromatographic process. The horizontal lines represent the column; each line is like a snapshot of the process at a different time (increasing in time from top to bottom). In the first snapshot, the sample, composed of components A and B, is introduced onto the column in a narrow zone. It is then carried through the column (from left to right) by the mobile phase.

Each component partitions between the two phases, as shown by the distributions or peaks above and below the line. Peaks above the line represent the amount of a particular component in the mobile phase, and peaks below the line represent the amount in the stationary phase. Component A has a greater distribution in the mobile phase and as a consequence it is carried down the column faster than component B, which spends more of its time in the stationary phase. Thus, separation of A from B occurs as they travel through the column. Eventually the components leave the column and pass through the detector as shown. The output signal of the detector gives rise to a *chromatogram* shown at the right side of Fig. 1.3.

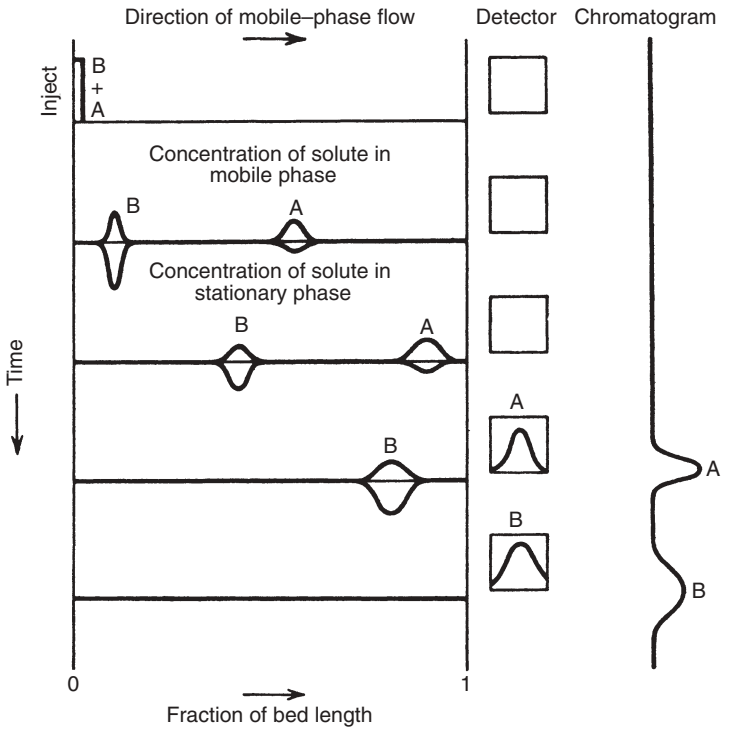

Fig. 1.3. Schematic representation of the chromatographic process. From Miller, J. M., *Chromatography: Concepts and Contrasts*, 2nd ed., John Wiley & Sons, Hoboken, NJ, 2005, p. 44. Reproduced courtesy of John Wiley & Sons, Inc.

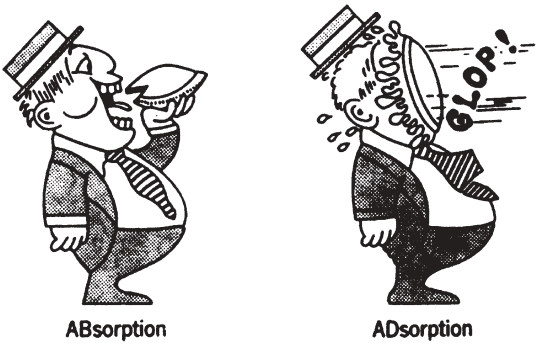

Fig. 1.4. Comical illustration of the difference between absorption (partition) and adsorption. From Miller, J. M., *Chromatography: Concepts and Contrasts*, 2nd ed., John Wiley & Sons, Hoboken, NJ, 2005, p. 45. Reproduced courtesy of John Wiley & Sons, Inc.

Note that the figure shows how an individual chromatographic peak widens or broadens as it goes through the chromatographic process. The exact extent of this broadening, which results from the kinetic processes at work during chromatography, will be discussed in Chapter 3.

The tendency of a given component to be attracted to the stationary phase is expressed in chemical terms as an equilibrium constant called the *distribution constant*, K_c, sometimes also called the partition coefficient. The distribution constant is similar in principle to the partition coefficient that controls a liquid–liquid extraction. In chromatography, the greater the value of the constant, the greater the attraction to the stationary phase.

Alternatively, the attraction can be classified relative to the *type* of *sorption* by the solute. Sorption on the surface of the stationary phase is called *ad*sorption and sorption into the bulk of a stationary liquid phase is called *ab*sorption. These terms are depicted in comical fashion in Fig. 1.4. However, most chromatographers use the term *partition* to describe the absorption process. Thus they speak about adsorption on the surface of the stationary phase and partitioning as passing into the bulk of the stationary phase. Usually one of these processes is dominant for a given column, but both can be present.

The distribution constant provides a numerical value for the total sorption by a solute *on* or *in* the stationary phase. As such, it expresses the extent of interaction and regulates the movement of solutes through the chromatographic bed. In summary, differences in distribution constants (parameters controlled by thermodynamics) effect a chromatographic separation.

Some Chromatographic Terms and Symbols

The IUPAC has attempted to codify chromatographic terms, symbols, and definitions for all forms of chromatography [9], and their recommendations will be used in this book. However, until the IUPAC publication in 1993, uniformity did not exist and some confusion may result from reading older pub-

TABLE 1.1 Chromatographic Terms and Symbols

Symbol and Name Recommended by the IUPAC	Other Symbols and Names in Use
K_c Distribution constant (for GLC)	K_p Partition coefficient K_D Distribution coefficient
k Retention factor	k' Capacity factor; capacity ratio; partition ratio
N Plate number	n Theoretical plate number; no. of theoretical plates
H Plate height	HETP Height equivalent to one theoretical plate
R Retardation factor (in columns)	R_R Retention ratio
R_s Peak resolution	R
α Separation factor	Selectivity; solvent efficiency
t_R Retention time	
V_R Retention volume	
V_M Hold-up volume	Volume of the mobile phase; V_G volume of the gas phase; V_O void volume; dead volume

Source: Data taken from reference 9.

lications. Table 1.1 compares some older conventions with the new IUPAC recommendations.

The distribution constant, K_c, has just been discussed as the controlling factor in the partitioning equilibrium between a solute and the stationary phase. It is defined as the concentration of the solute A in the stationary phase divided by its concentration in the mobile phase.

$$K_c = \frac{[A]_S}{[A]_M} \tag{1}$$

This constant is a true thermodynamic value that is temperature-dependent; it expresses the relative tendency of a solute to distribute itself between the two phases. Differences in distribution constants result in differential migration rates of solutes through a column.

Figure 1.5 shows a typical chromatogram for a single solute, A, with an additional small peak early in the chromatogram. Solutes like A are retained by the column and are characterized by their *retention volumes*, V_R; the retention volume for solute A is depicted in the figure as the distance from the point of injection to the peak maximum. It is the volume of carrier gas necessary to elute solute A. This characteristic of a solute could also be specified by the retention time, t_R, if the column flow rate, F_c, were constant.*

$$V_R = t_R \times F_c \tag{2}$$

*Because the chromatographic column is under pressure, the carrier gas volume is small at the high-pressure inlet, but expands during passage through the column as the pressure decreases. This topic is discussed in Chapter 2.

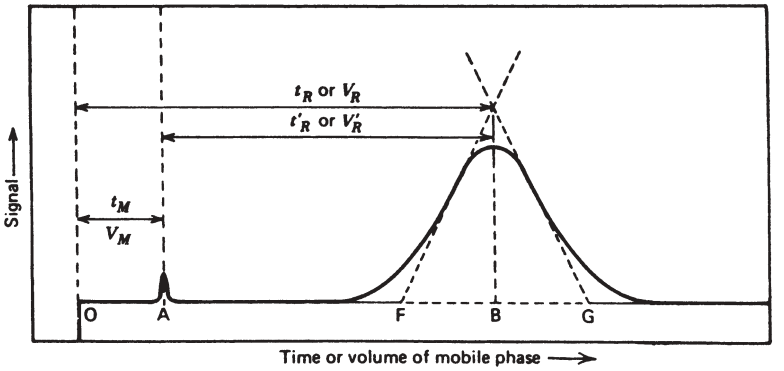

Fig. 1.5. Typical chromatogram. From Miller, J. M., *Chromatography: Concepts and Contrasts*, 2nd ed., John Wiley & Sons, Hoboken, NJ, 2005, p. 46. Reproduced courtesy of John Wiley & Sons, Inc.

Unless specified otherwise, a constant flow rate is assumed and retention time is proportional to retention volume and both can be used to represent the same concept.

The small early peak represents a solute that does not sorb in the stationary phase—it passes straight through the column without stopping. The IUPAC [9] has selected the name *hold-up volume* for V_M and defined it as "the volume of the mobile phase (MP) required to elute the unretained compound from the chromatographic column and reported at column temperature and ambient pressure." The analogous time parameter is hold-up time, t_M, "the time required for the MP to pass through the chromatographic column." Because the original terms were found to be misleading or superfluous, the IUPAC has reexamined the concept of hold-up volume and has published more precise, new definitions [10] and now recommends that the term *dead volume* not be used. In GC, air or methane is often used as the unretained component, and the peak labeled A in Fig. 1.5 is sometimes referred to as the *air peak*.

Equation (3), one of the fundamental chromatographic equations,* relates the chromatographic *retention volume* to the theoretical distribution constant.

$$V_R = V_M + K_C V_S \tag{3}$$

V represents a volume and the subscripts R, M, and S stand for retention, mobile, and stationary, respectively. V_M and Vs represent the volumes of mobile phase and stationary phase in the column respectively. The retention volume, V_R, can be described by reference to Fig. 1.5.

*For a derivation of this equation. see: B. L. Karger, L. R. Snyder, and C. Horvath, *An Introduction to Separation Science*, Wiley, NY, 1973, pp. 131 and 166.

An understanding of the chromatographic process can be deduced by reexamining equation (3). The total volume of carrier gas that flows during the elution of a solute can be seen to be composed of two parts: the gas that fills the column or, alternatively, the volume through which the solute must pass in its journey through the column as represented by V_M, and, second, the volume of gas that flows while the solute is not moving but is stationary on or in the column bed. The latter is determined by the distribution constant (the solute's tendency to sorb) and the amount of stationary phase in the column, V_S. There are only two things a solute can do: move with the flow of mobile phase when it is in the mobile phase, or sorb into the stationary phase and remain immobile. The sum of these two effects is the total retention volume, V_R.

OVERVIEW: ADVANTAGES AND DISADVANTAGES

GC has several important advantages as summarized in the list below.

Advantages of Gas Chromatography

- Fast analysis, typically minutes
- Efficient, providing high resolution
- Sensitive, easily detecting ppm and often ppb
- Nondestructive, making possible on-line coupling; e.g., to mass spectrometer
- Highly accurate quantitative analysis, typical RSDs of 1–5%
- Requires small samples, typically μL
- Reliable and relatively simple
- Inexpensive

Chromatographers have always been interested in fast analyses, and GC has been the fastest of them all, with current commercial instrumentation permitting analyses in seconds. Figure 1.6 shows a traditional orange oil separation taking 40 mins, a typical analysis time, and a comparable one completed in only 80 sec using instrumentation specially designed for fast analysis.

The high efficiency of GC was evident in Fig. 1.1. Efficiency can be expressed in plate numbers, and capillary columns typically have plate numbers of several hundred thousand. As one might expect, an informal competition seems to exist to see who can make the column with the greatest plate count—the "best" column in the world—and since column efficiency increases with column length, this has led to a competition to make the longest column. Currently, the record for the longest continuous column is held by Chrompack International [11] who made a 1300-m fused silica column (the largest size that would fit inside a commercial GC oven). It had a plate number of 1.2 million, which was smaller than predicted, due in part to limits in the operational conditions.

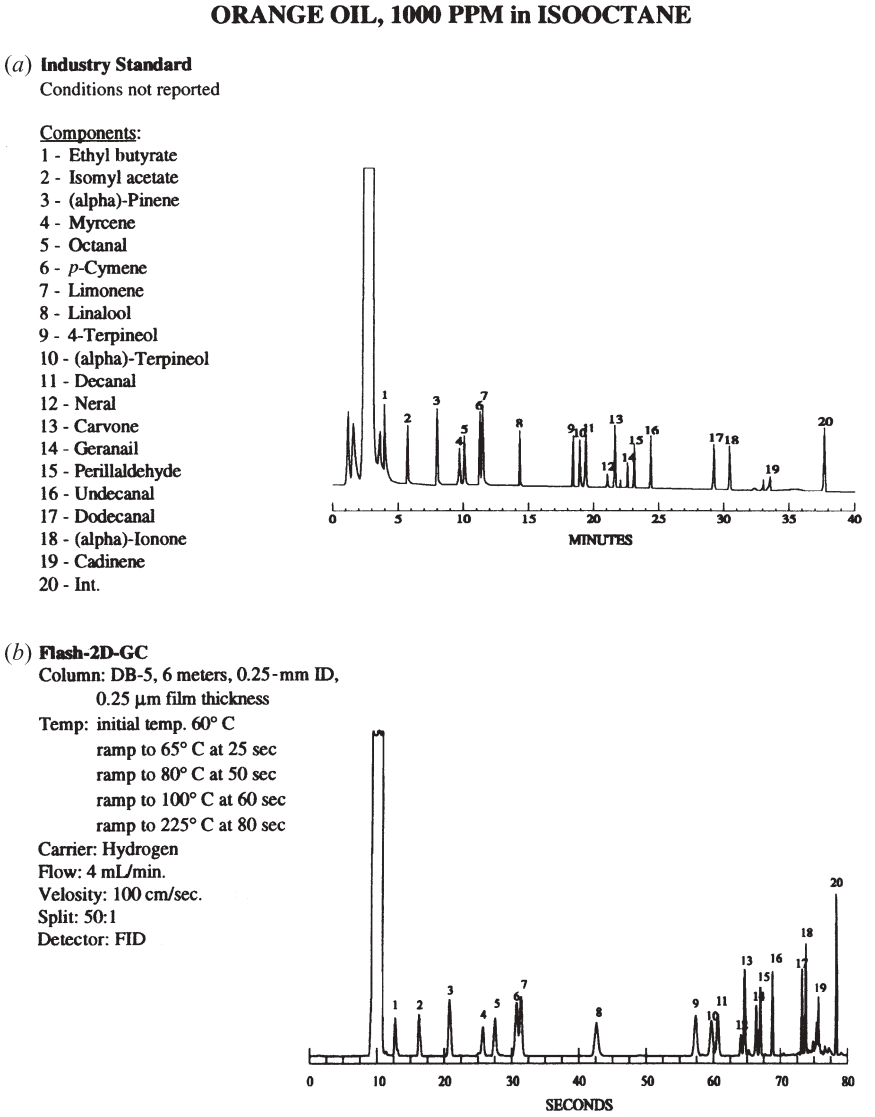

Fig. 1.6. Comparison of orange oil separations: (*a*) A conventional separation. (*b*) A fast separation on a Flash-GC instrument. Reprinted with permission of Thermedics Detection.

Later, a more efficient column was made by connecting nine 50-m columns into a single one of 450 m total length [12]. While much shorter than the Chrompack column, its efficiency was nearly 100% of theoretical, and it was calculated to have a plate number of 1.3 million and found capable of separating 970 components in a gasoline sample.

Because GC is excellent for quantitative analysis, it has found wide use for many different applications. Sensitive, quantitative detectors provide fast,