An Introduction to Spectroscopic Methods for the Identification of Organic Compounds

VOLUME 2

EDITED BY

F. SCHEINMANN

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Mass Spectrometry, Ultraviolet Spectroscopy, Electron Spin Resonance Spectroscopy, Nuclear Magnetic Resonance Spectroscopy (Recent Developments), Use of Various Spectral Methods Together, and Documentation of Molecular Spectra

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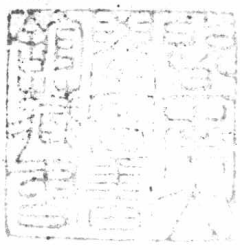

PERGAMON PRESS

Oxford · New York · Toronto
Sydney · Braunschweig

Pergamon Press Ltd., Headington Hill Hall, Oxford
Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, New York 10523
Pergamon of Canada Ltd., 207 Queen's Quay West, Toronto 1
Pergamon Press (Aust.) Pty. Ltd., 19a Boundary Street, Rushcutters Bay, N.S.W. 2011, Australia
Vieweg & Sohn GmbH, Burgplatz 1, Braunschweig

First edition 1974

Library of Congress Cataloging in Publication Data

Scheinmann, F 1933–
An introduction to spectroscopic methods for the identification of organic compounds.

Includes bibliographies.
CONTENTS: v. 1. Nuclear magnetic resonance and infrared spectroscopy. v. 2. Mass spectrometry, ultraviolet spectroscopy, electron spin resonance spectroscopy, nuclear magnetic resonance spectroscopy (recent developments).

1. Spectrum analysis. 2. Chemistry, Organic.
I. Title
QD271.S343 547'.34'085 76-99991

ISBN 0-08-006662-3 (v. 1)

ISBN 0 08 016720 9 (flexicover)
ISBN 0 08 016719 5 (hard cover)

Printed in Great Britain by A. Wheaton & Co., Exeter

Contents of Volume 1

Preface

VOLUME 2 of *An Introduction to Spectroscopic Methods for the Identification of Organic Compounds* follows largely the style adopted for Volume 1. Thus adequate theory, a study of some applications, seminar problems, and worked answers have been provided for:

(a) Mass spectrometry.
(b) Ultraviolet spectroscopy.
(c) Electron spin resonance spectroscopy.
(d) The combined use of data from the various spectral probes for elucidating organic structures.

There are also two additional chapters provided to keep pace with developments in organic spectroscopy and to serve the requirements of graduate students and research workers. These deal with:

(i) Recent developments in nuclear magnetic resonance spectroscopy which includes such techniques as the nuclear Overhauser effect, lanthanide shift reagents, and recent progress involving the use of isotope ^{13}C.
(ii) Documentation of molecular spectra which guides the chemists to the various collections of reference spectra (or data) now available in science libraries.

Many of the problems and answers given in this book have been used at Salford in the seminars given to undergraduates and M.Sc. and Ph.D. students in organic chemistry. The problems are arranged so that they become progressively more difficult with the latter problems in each case being suitable for graduates.

We thank the students and the various referees of the chapters in both Volumes 1 and 2 for their critical and helpful comments.

In finalizing Volume 2 we were very much encouraged by the favourable reviews accorded to Volume 1. It was pleasing to see the book being recommended by universities and colleges, especially The Open University (U.K.) where students receive their lectures and study guide by television, radio and correspondence, and study largely at home. The most serious criticism of Volume 1 was concerned with the absence of the companion chapters and seminar problems which now appear in Volume 2. While it is regretted that both volumes did not appear concurrently, we hope that the inclusion of some recent advances in organic spectroscopy, which have not been previously covered in a textbook at this level, will eventually compensate for the delay and any previous omissions.

It is again a pleasure to thank authors and publishers for permission to reproduce spectra and data where acknowledgements have been given.

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Contents

An Introduction to Mass Spectrometry

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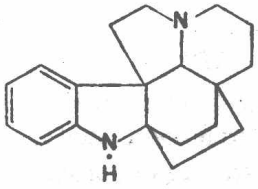
Introduction

Whilst for the elucidation of unknown structures the whole range of available spectroscopic techniques is used whenever possible, one may sometimes be forced to use a limited number in a particular case. For determination of structure of the naturally occurring alkaloid aspidofractinine, the small quantity isolated dictated the methods of analysis, and the molecular formula and structure (I) were elucidated[1,2] by low resolution mass spectrometry in conjunction with i.r. absorption spectroscopy.



(I)

This single example is cited to emphasize the power of mass spectrometry, and illustrates what is possible provided that the processes giving rise to a spectrum are understood and adequate model compounds are available with which to make comparisons. With this sort of precise structural information evident from the mass spectrum, it can perhaps be appreciated that even with a minimum of knowledge of the processes giving rise to the spectrum, quite significant deductions may be made. This is a method of structure elucidation particularly suited to computer manipulation, in the acquisition, presentation, and analysis of data, and with such total equipment very complicated structures can be completely solved with certainty and rapidity,[3] but it is the purpose in this chapter to outline the origin of the spectrum and to introduce and exemplify manual methods of analysis.

In mass spectrometry the compound is induced to ionize in the vapour phase, and the resulting ions are then sorted according to their mass/charge (m/e) ratios. A *mass spectrum* is a record of the masses and relative abundances of the ions produced. These are characteristic of the compound concerned, and the identification of the ions enables deductions to be made about the parent molecule, both about the elements present and the method of their linkage. The great advantage of this spectroscopic technique, which utilizes less than one milligram of sample, is that by using a high resolution mass spectrometer the unique

molecular formula can readily be determined, as can the unique compositions of the fragment ions; low resolution instruments do not yield this information with the same degree of certainty. Since the same atomic groupings in molecules give rise to ions by the same processes, molecules of the same chemical classes give similar spectra, with the differences being largely predictable.

Instrumentation

The generalized block diagram for a mass spectrometer is shown in Fig. 1. Organic mass spectrometry for structural analysis is most usually performed using a high energy electron beam (10–70 eV) to excite molecules from the sample in the vapour state, at elevated tem-

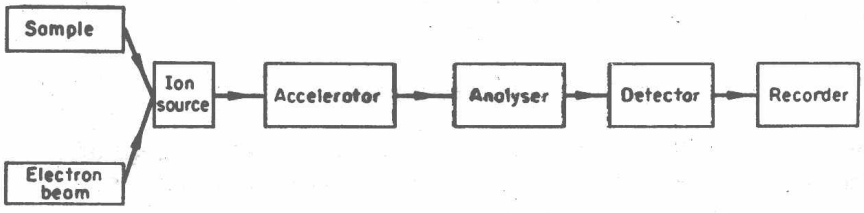


FIG. 1. Block diagram of a mass spectrometer.

peratures if necessary, in a very high vacuum (10^{-5}–10^{-6} torr). The electron beam generates ions from molecules in the *ion source*. There is ejection of an electron to give the *molecular ion* $(M)^+$ (or *parent ion*); this is by far the predominating process, but others also occur, in particular two electrons can be ejected to yield a doubly charged ion $(M)^{2+}$.

[The term molecular ion, symbol $(M)^+$, is preferred to the term parent ion, symbol $(P)^+$. There is now a tendency to apply the latter to all ions, including the molecular ion, which can be shown to give rise by specific processes to other (daughter) ions.]

The energy acquired (from the electron beam) ensures that many molecular ions undergo fragmentation to give ions of smaller mass together with neutral fragments. All the positive ions leaving the ion source are accelerated by means of an electrostatic voltage V and then they enter a magnetic field (in the analyser) H applied at right angles to their line of flight. The deflection they now experience (radius of curvature r) depends upon the m/e ratio and is given by the relationship

$$r^2 = k\ m/e\frac{V}{H^2},$$

where k is a constant. That is, all the ions with the same m/e ratio are deflected by equal amounts; this is the sorting process, and a series of collectors (one for every m/e value) would enable the relative abundances of each sort of ion to be measured by measuring the amount of charge brought to each collector in the same time. It is more convenient, of course, to use one fixed collector–detector and to bring the different sorts of ions successively to it by varying V or H in a known regular manner. The very low pressure employed ensures that each ion can reach the collector without collision with neutral fragments or molecules. For a full treatment of ion optics and modes of action of different mass spectrometers, see ref. 4a.

The spectrum is most conveniently recorded using mirror galvanometers because of

their rapid response. The ion current detected for each *m/e* value activates the galvanometer and a beam of light is deflected by the mirror on to light-sensitive paper. Simultaneous recording at sensitivities of ×1, ×10, and ×100, ensures that for each ion one of the traces will be optimum for measurement purposes. For a complete unknown of molecular weight 350 the spectrum may take 10 min to obtain and will cover a piece of paper 4 m long by 15 cm wide. Part of a spectrum is shown in Fig. 2. The peaks have width at the base because in practice, in the ion source, the generated ions have finite small, different

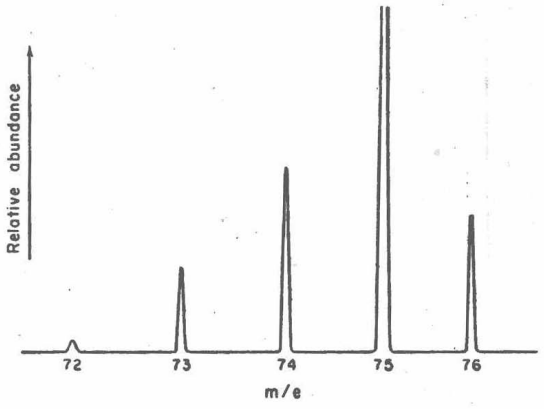


FIG. 2. Part of the mass spectrum of *p*-chloronitrobenzene.

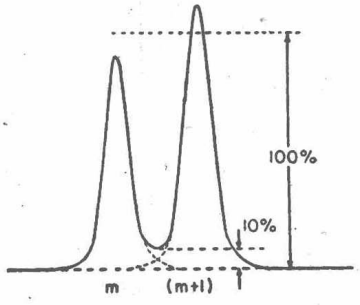


FIG. 3. Peak overlap in a mass spectrum.

velocities even before acceleration. The *m/e* scale is not linear, but decreases exponentially towards the higher *m/e* values, and consequently at high *m/e* values the peaks overlap at the base. This is shown schematically in Fig. 3.

Depending upon the particular mass spectrometer used, at some point in the *m/e* scale it will become impossible to distinguish between two ions one mass unit apart, and to be able to differentiate between such ions is an important function of the instrument. As a useful working figure it is taken that when the height of the valley exceeds 10% of the average height of the two peaks (see Fig. 3), then the two peaks will not be separately resolved. The maximum *m/e* value where this valley contribution does not exceed 10% is termed the *resolution* of the instrument. (Note that some manufacturers give different definitions of resolution.)

Mass spectrometers are classed as high or low resolution instruments. The former class have resolutions exceeding 10,000; the latter have resolutions less than about 3000, and are correspondingly less expensive. A low resolution mass spectrum does not yield all the information obtainable from a high resolution spectrum, but, as will be seen from the following arguments, it is quite adequate for much structural analysis.

PRESENTATION OF SPECTRA

It is evident that it is quite impracticable to reproduce mass spectra such as have been described, in the same way as, for example, n.m.r. or i.r. absorption spectra. The essential information, the masses of the ions together with their relative abundances, may be

presented in two ways. One way is to summarize this information as a simple bar graph, e.g. Fig. 4 shows the mass spectrum of ethyl methyl ketone. The molecular ion peak (*M*) is at *m/e* 72.

This is particularly suitable for making visual comparison with other spectra, but ions of low relative abundance are not readily shown on the same scale and these may be of

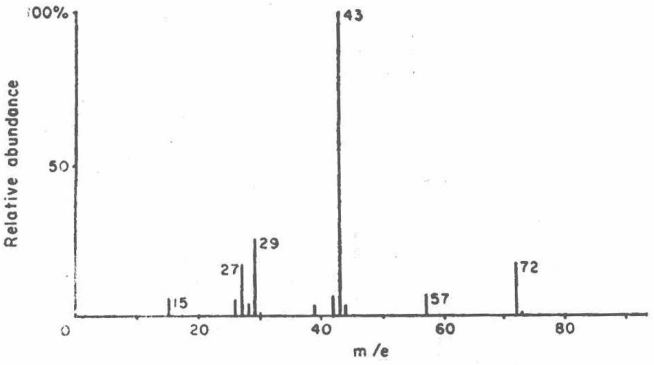


FIG. 4. Mass spectrum of ethyl methyl ketone as a bar graph.

importance in interpretation, e.g. there are such ions from ethyl methyl ketone at *m/e* 73 and 74 [(*M*+1) and (*M*+2) respectively].

In a spectrum one ion is of greatest relative abundance (here with *m/e* 43), and the response from it is said to give the *base peak* (*B*) in the spectrum. The alternative method of presentation is to draw up a table or list of ions (*m/e* values) and to show in parentheses the abundances relative to that of the base peak ion (arbitrarily taken as 100%). Even so, for the important low abundance ions in the vicinity of the molecular ion it may be preferable to report these relative to the molecular ion (taken as 100%). Thus the spectrum could equally be recorded: *m/e* 72 (17·0%) *M*, 57 (6·1), 44 (2·5), 43 (100) *B*, 42 (5·2), 39 (2·2), 29 (24·5), 28 (2·9), 27 (15·7), 26 (5·0), and 15 (5·2), with *m/e* 74 (0·3%) (*M*+2), 73 (4·7) (*M*+1), and 72 (100) (*M*).

(An equivalent method, used on an increasing scale, is to record the abundance of any particular ion as a percentage of the total ion abundance. This has the effect of mitigating the undue weighting otherwise given to the single measurement of the base peak ion.)

Both these presentations have their uses; the former is more like the original spectrum in appearance, but both still omit important information [see below, Metastable ion peaks (pp. 12, 57). It should be realized that manual transfer of the original data to either form is tedious and very time consuming, and, except for limited analysis, undesirable. It is possible to couple the detector in a mass spectrometer to other sorts of recorder,[4b] but the mirror galvanometer is universally used. The most useful development is simultaneous on-line computer recording with a digital computer collecting and processing the data as it is produced,[5, 6] thus eliminating laborious examination of the spectrum. A plotter,

driven by the computer, can subsequently reproduce the spectrum as a bar graph if this is required.[7]

In any analysis of spectra it is essential to know several parameters if the analysis is to be meaningful; e.g. for an n.m.r. spectrum the solvent must be known. Similarly, the appearance of the mass spectrum is dependent on a number of variables, and comparisons can only be meaningfully made when conditions are the same.

Low-boiling liquids are handled by conventional vacuum line techniques. High-boiling liquids and solids are handled by a direct inlet system whereby they are introduced on a probe into the ion source. If the internal pressure is too high, secondary, unwanted reactions may occur. If the temperature is too high, thermally induced reactions may occur. Both pressure and temperature should be the lowest possible consistent with the production of a spectrum suitable for interpretation; it is usual to record the temperature.

Most low resolution spectra in the literature have been determined for an electron beam energy of 70 eV. A beam of lower energy, apart from giving fewer peaks overall, can bring about marked local changes in appearance because fragmentation processes can change. The energy of the ionizing electron beam should be recorded together with the total ion current.

There are other ways of bringing about the ionization of the compound; these are not as yet fully exploited, but developments may be expected. Methods such as field ionization[8] or chemical ionization[9] produce spectra of quite different appearance since the overall processes for ion production are not the same.

Analysis of Spectra

DETERMINATION OF MOLECULAR FORMULAE

For combinations of C, H, N, and O

For ethyl methyl ketone, C_4H_8O, using the whole number atomic weights ^{12}C, ^{1}H, ^{14}N, and ^{16}O, the calculated molecular weight is 72; but there are other combinations of atoms which give the same whole number total [of atomic mass units (a.m.u.)], and some of these are shown in Table 1. If the accurate, fractional values are used for the atomic weights, totals are obtained that differ in the fourth or fifth significant figure.

Now if the accurate mass of an unknown molecular ion, *m/e* 72, could be measured, the molecular formula could be uniquely decided. The most difficult case in the table would be to distinguish between 72·057511 and 72·068745. That is, to do this the accuracy would have to be better than 11 parts in 72,000, or 1 part in 7000. This is the same as saying that it would be necessary to count precisely and distinguish between two peaks of *m/e* 7000 and 7001, and this could be done if the mass spectrometer had a resolving power of at least 7000. To determine a unique molecular formula by accurate mass measurement when the molecular weight is much higher requires correspondingly increased resolution, double focusing, or the equivalent, is necessary to achieve this,[4a] and mass spectrometers are

routinely designed in this way. In practice the accurate mass can be measured essentially by comparing the values of the spectrometer controls for the focusing operation with those used for focusing an ion of known mass used as a standard; an ion of mass comparable to that of the unknown is always selected.

To facilitate translation of accurate masses into unique atomic combinations there are published tables, based on either the 1959 standard ($^{16}O = 16{\cdot}000000$)[4c] or on the 1962 standard ($^{12}C = 12{\cdot}000000$)[10] of atomic weights. Each forms a self-consistent set and

TABLE 1
ACCURATE WEIGHTS FOR SOME COMBINATIONS OF C, H, N, AND O ATOMS WHERE THE TOTAL MASS IS NOMINALLY 72 A.M.U., BASED ON THE 1962 ATOMIC WEIGHTS ($^{12}C = 12{\cdot}000000$).

C_4H_8O	72·057511
$C_2H_4N_2O$	72·032360
$C_3H_4O_2$	72·021127
C_3H_6NO	72·045107
$C_3H_8N_2$	72·068745
C_5H_{12}	72·093896

either may be used (the former lists combinations up to 250 and the latter up to 500 a.m.u.). For accurate mass measurement work the reference standard against which the unknown mass is measured must, of course, be appropriate to the set of tables used. Another equivalent compilation[11b] based on the 1962 standard offers an alternative means of using the experimental data. A further alternative is to use a digital computer to process the data; a programme can readily be written to cater for any specific limits which might usefully be made to the possibilities in the light of compound history and/or experience (see ref. 12 for a suitable programme in Fortran).

The measurement of accurate mass may be made whilst the unknown compound is being manipulated in the spectrometer (a process limiting the number of measurements that can be made), or the whole spectrum can be stored on tape[13] or photographic plate[14] in such a way that the measurements can be made subsequently. Although the unique composition of the molecular ion is of greatest interest, the exact compositions of fragment ions are also important, since this greatly aids structure determination [see below, Saturated Aliphatic Hydrocarbons (p.32), and Nitriles (p.48)]. Sometimes a fragment ion so investigated proves to be inhomogeneous. Thus in the actual spectrum of ethyl methyl ketone the ion peak, *m/e* 43, is readily shown to be actually a doublet. The two ions of this nominal mass are $C_2H_3O^+$ and $C_3H_7^+$ (differing by 0·027 a.m.u.), and a resolution of 1600 will separate these. The latter ion is seen to contribute approximately 7% of the peak at *m/e* 43, and obviously a profound rearrangement gives rise to it. For the finer

points of spectrum interpretation it is necessary to have such comprehensive knowledge about the ionic species contributing to each peak.

When the effective resolution is sufficiently high, determination of the ion composition in this way is obviously unambiguous, but as the effective resolution decreases (from one spectrometer to another), so more possibilities must be admitted for consideration. Thus for an unknown compound, if the resolution is 12,000 and the molecular weight is approximately 194, then accurate mass measurement of the molecular ion might indicate a value of 194·227±0·008 based on $^{16}O = 16{\cdot}000000$. The possibilities indicated[4c] are $C_{11}H_{20}N_3$ (194·2278) and $C_{13}H_{22}O$ (194·2292). (With a resolution of 2,000 then the value determined might be 194·25±0·10; this gives seventeen possibilities.) Fortunately there is an aid available by which possibilities for a molecular formula may be limited. This is termed the nitrogen rule.

The nitrogen rule

It happens that, with one exception, for all the common elements encountered in compounds of which mass spectra are obtainable, the common isotopes of even mass number have even valencies and common isotopes of odd mass number have odd valencies. For example, ^{12}C, ^{16}O, and ^{32}S have even valencies, ^{1}H, ^{35}Cl, and ^{31}P have odd valencies. The one exception is ^{14}N which has even mass but odd valency. This has an important consequence which may be stated as the *nitrogen rule*: molecules of odd molecular weight must contain an odd number of nitrogen atoms; molecules of even molecular weight must contain either an even number of nitrogen atoms or no nitrogen atoms.

An examination of genuine molecular formulae will convince the reader that this is so, and this rule can be most useful in molecular formula assignment.

The tables of combinations of C, H, N, and O atoms (e.g. refs. 4c, 10) contain under any particular a.m.u. total all the combinations (with certain exceptions noted)† of atoms giving this gross mass and not just combinations that are capable of being translated into complete molecules (e.g. C_3H_6NO for 72, and $C_{11}H_{20}N_3$ for 194 a.m.u.).

Thus, for instance, in the case of the compound above, of molecular weight 194, the nitrogen rule enables rejection of $C_{11}H_{20}N_3$ as a possible molecular formula, and the experimental value for the accurate molecular weight, when the resolution is 12,000, then gives $C_{13}H_{22}O$ as the unique molecular formula. (In this case, when the resolution is 2000, the nitrogen rule enables six of the seventeen possibilities to be rejected.)

Obviously it is advantageous to use the highest resolution possible; if only a low resolution instrument is available, then it may be possible to determine the molecular weight to the nearest whole number only. In this event another technique must be adopted to obtain the unique molecular formula from the available data. This involves the principle of isotope abundance analysis.

† For example, under 262 a.m.u. will not be found $C_{10}H_{14}O_8$, it being reasoned that this is a molecular formula that the user will encounter most infrequently, if at all. There are similar omissions throughout, and the user is referred to the introductory explanations to the individual tables.

For combinations of C, H, N, and O

Using the whole number atomic weights ^{12}C, ^{1}H, ^{14}N, and ^{16}O, the calculated molecular weight of ethyl methyl ketone is 72. This is the figure obtained from the spectrum (see Fig. 4) by recognition of the molecular ion peak. But natural carbon atoms consist not only of ^{12}C but of ^{13}C, and the relative abundances are 98·89 : 1·11. Thus one in every hundred carbon atoms is not ^{12}C but ^{13}C, so that in a bulk sample of ethyl methyl ketone, for every twenty-four molecules containing ^{12}C only there is one molecule containing three ^{12}C atoms and one ^{13}C atom. The molecular weight of this molecule is 73.

Similarly, natural hydrogen, nitrogen, and oxygen contain the heavier isotopes ^{2}H, ^{15}N, ^{17}O, and ^{18}O, and other molecules will have a molecular weight of 73 if they contain one ^{15}N atom in place of ^{14}N, etc., and a molecule that contains one ^{18}O atom in place of ^{16}O, or one ^{13}C and one ^{2}H atom in place of ^{12}C and ^{1}H, etc., will have a molecular weight of 74. These give the ions producing what are termed the *first* and *second isotope peaks* $(M+1)$ and $(M+2)$ respectively.

Now from known natural relative abundances of these heavier isotopes it is possible to calculate[4d, 10] relative to the molecular ion the expected abundances of the ions giving the first and second isotope peaks. That is, the expected relative heights of the (M), $(M+1)$ and $(M+2)$ peaks in the spectrum can be calculated. For some combinations of atoms of 72 a.m.u. these figures appear in Table 2 together with the ratio of heights $(M+1)/(M+2)$.

TABLE 2
CALCULATED RELATIVE HEIGHTS OF THE FIRST AND SECOND ISOTOPE PEAKS FOR COMBINATIONS OF C, H, N AND O ATOMS OF 72 A.M.U.

	(M)	$(M+1)$	$(M+2)$	$(M+1)/(M+2)$
C_4H_8O	100	4·49	0·28	16
$C_2H_4N_2O$	100	3·03	0·23	13·2
$C_3H_4O_2$	100	3·38	0·44	7·7
C_3H_6NO	100	3·76	0·25	15
$C_3H_8N_2$	100	4·13	0·07	59
C_5H_{12}	100	5·59	0·13	43

In practice one determines these quantities from the spectrum (obviously not from the bar graph presentation), and searches for a "best fit" with the calculated values. If ethyl methyl ketone were used as an unknown compound, typical experimental figures might be respectively 100, 4·7, 0·3, and 15·7, and these would indicate clearly a molecular formula of C_4H_8O. Suitable tables of calculated isotope abundance ratios exist for up to 250 a.m.u.[4c, 15] and up to 500 a.m.u.[10]

Unfortunately there are circumstances encountered, resulting from the nature of the particular compound and the operating conditions, when the method fails. The most common effect is when the first and second isotope peaks are inflated by unknown, variable amounts, and the only indication that an incorrect molecular formula has been selected may be inconsistencies in the subsequent interpretation of the fragmentation pattern. Compounds which are readily protonated are particularly prone to give misleading experimental figures. [Experimental measurements are also affected by any unduly high background to the spectrum; see below, under The molecular ion peak (p. 14).] In any event, relative peak heights should be averaged from several spectra to eliminate fortuitous errors in a single spectrum.

[Even without recourse to tables it is possible to make simply a useful deduction about the molecular formula. For compounds not unduly rich in nitrogen, by far the largest contribution to the first isotope peak comes from the ions with ^{13}C in place of ^{12}C. Thus if the height of this peak (relative to that of the molecular ion peak as 100%) is divided by 1·1 and the result rounded off to the next lowest whole number, then this integer almost always gives the number of carbon atoms in the molecule.]

For combinations other than C, H, N, and O only

It is clear that whatever elements comprise the compound, the isotope distribution pattern will be manifest in the spectrum in the vicinity of the molecular ion peak. Fortunately in many cases these patterns are readily recognized and distinguished one from another, and this enables easy identification of such elements.

For example, Fig. 5 shows the low resolution spectrum of an unknown compound (II) of molecular weight 157. Whilst there is nothing untoward about the relative height of the first isotope peak (*m/e* 158), simple inspection shows that the height of the second isotope peak (*m/e* 159) is approximately one-third of the height of the molecular ion peak [measured relative abundances are *m/e* 157 (100), 158 (7·2), 159 (33·2), 160 (2·4), and 161 (0·2)]. This

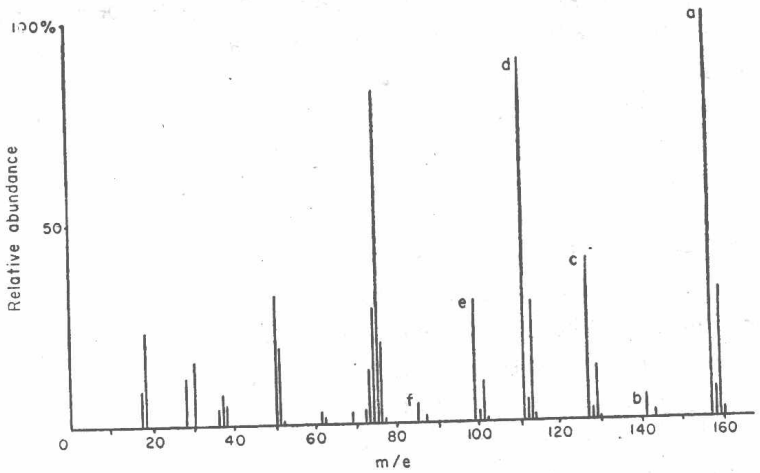


FIG. 5. Mass spectrum of compound (II), mol. wt. 157. Peaks at a, b, c, d, e and f are each accompanied by peaks at 2 atomic mass units higher having approximately one-third relative intensity.