Mass detectors in chromatography

This survey of low-cost mass spectrometers for capillary column chromatography was prepared for JAOCS *by Ian Horman of Nestle Research Centre, Nestec Ltd., in Lausanne, Switzerland, at the request of* JAOCS *Associate Editor for News Helmet Traitler, also of Nestec.*

Any mass spectrometrist who takes life seriously spends half the working day hunting vacuum leaks and sealing them up. Hardly surprising then, that the traditional mass spectrometrists of 30 years ago questioned, in the privacy of their thoughts, the sanity of the occasional weirdo who deliberately wanted to bore extra holes in their precious instruments, allowing nasty GC column effluents to diffuse willy-nilly into their sources.

A few blown filaments, high-voltage discharges, tearing of hair among protagonists and antagonists, and years later, the practice of boring extra holes in mass spectrometers was established once and for all. And based on the principle of sample introduction through a controlled leak, GC-MS was born as the first hyphenated MS technique.

Gas Chromatography-Mass Spectrometry

"History is bunk!" said Henry Ford in 1919. But the scientific literature is full of history. So before getting down to the reason for writing this article—namely to survey low-cost mass spectrometers available as mass detectors for capillary column chromatography—a historical preamble:

In 1964, Biemann wrote (1), "The tandem operation of a gas liquid chromatograph with a mass spectrometer for the characterization of the emerging fractions is an intriguing idea of considerable potential, and this principle was demonstrated as early as 1957 (2). It has since been employed in various modes, ranging from simple monitoring of a single mass to the fast scanning of a preselected part of the spectrum, or all of it. . ."

Earlier than this, Ebert remarked that the combination of GC with MS had proved to be an extremely useful tool for the rapid and positive identification of chromatographic cuts (3). He added, "Chromatographic data alone are often ambiguous, and the identification of sample components by this means can be obtained with assurance only by the expenditure of considerable time and effort."

And, obviously thinking of the mass spectrometer as GC detector, Gohlke (4) stated, "It (mass spectrometry) is a rapid, precise method, uses sample sizes of only a few milligrams, and is often capable of identifying single components even if previously obtained standard mass spectra are not available for comparison purposes."

These excerpts from over a quarter of a century ago sum up the basic philosophy and methodology of GC detection via the mass spectrometer as we see it today. Certainly we have improved the technology by using new methods of sample ionization and of ion detection. We have increased convenience and utility by using more vacuum pumps of higher capacity to accept column effluents directly, and by adding powerful data acquisition and processing systems. And we now think in terms of analyzing picogram or even femtogram amounts of samples rather than a few milligrams. But the pioneers quoted above had already graduated—from off-line GC-MS using effluent trapping, to continuous (1,4) of quasi-continuous (3) sampling of the GC effluent, with simultaneous GC and MS detection (4), with multi-column operation (4), and with mass spectral recording at high resolution (1).

FIG. 1. Traditional mass spectrometrists had their doubts. . .

Quadrupole or ion trap?

Strictly speaking, this question is nonsense because the ion trap itself is a quadrupole. However, for the purposes of this article, a "quadrupole" mass analyzer consists of an assembly of four parallel rods through which ions pass in a continuous stream, and "ion trap" mass analyzer consists of a chamber in which ions formed are collected and analyzed in discrete batches.

The first spectrometers used as GC detectors worked either on the principle of time-of-flight or sector field mass analysis, largely because these were all that was available at the time. The first low-cost mass spectrometers for GC, like the MS-30 from AEI (now Kratos) and the 111 from Varian (now Finnigan-MAT), available in the early 1970s were also magnetic sector instruments. But quadrupole mass spectrometer manufacturers slowly conquered problems of low mass range and sensitivity, and in 1976 when Hewlett-Packard introduced their HP-5990A as a fully computerized benchtop GC-MS system, the quadrupole analyzer became the "low-cost" industry standard for mass analyzers.

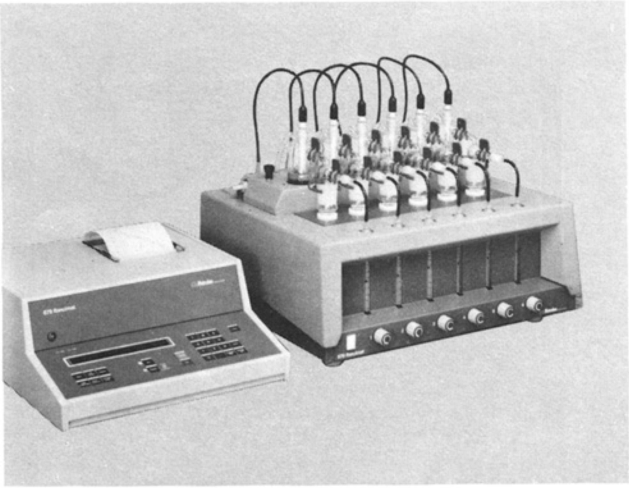
At the same time, the HP-5990A established once and for all the principle of GC-MS as a technique in its own right, consciously exploiting the synergy between the gas chromagraph and the mass spectrometer. Up to then, GC had been looked upon by most mass spectrometrists as just another means of sample introduction to the MS, while chromotographers had seen the MS as an alternative mode of detection. This synergy is still one of the most important elements in the concept of mass detection in capillary chromatography.

The reasons why quadrupole mass analysis replaced sector field and time-of-flight are summarized in Figure 2, which compares the characterization of different classes of mass analyzers. For most routine applications of the mass detector in chromatography, a limited mass range with unit mass resolution is acceptable, so long as this is accompanied by good sensitivity, rapid mass scanning, a good dynamic range, and quantitation possibilities: all in an instrument simple to use and maintain, and which costs only half an arm rather than an arm and a leg.

It is clear from Figure 2 that quadrupole mass analyzers differ markedly from their sector or time-of-flight (TOF) cousins, and globally fit the above requirements. But ion trap analyzers are seen to share many of the characteristics of quadrupoles, including the important attributes of simplicity of operation and relatively low cost. Thus in 1984, Finnigan-MAT introduced its novel ITD-700 Ion Trap Detector instrument on the market as the first commercial mass analyzer based on the ion trap principle.

Table 1 summarizes the low-cost mass detectors for capillary chromatography currently on the market. They are all constructed around either the ion trap or the quadrupole. But before going into further detail, a comparison of these two principles of operation is warranted. In short, the terms "continuous" and "batchwise" qualify the operation of quadrupole and ion trap mass detectors respectively. By analogy, we can imagine water streaming from a tap: we can drink directly from the stream or we can use a cup.

All mass spectrometers consist of a sample introduction system, an ion source, a mass analyzer and an ion detector. The main difference with the ion trap compared to most other mass spectrometers is that the ion source and the mass analyzer are combined in a single unit. This permits storage of ions as they are formed. Ions can thus be accumulated in the trap to a predetermined level—typically one million ions or so—prior to analysis. Thus, over a wide dynamic



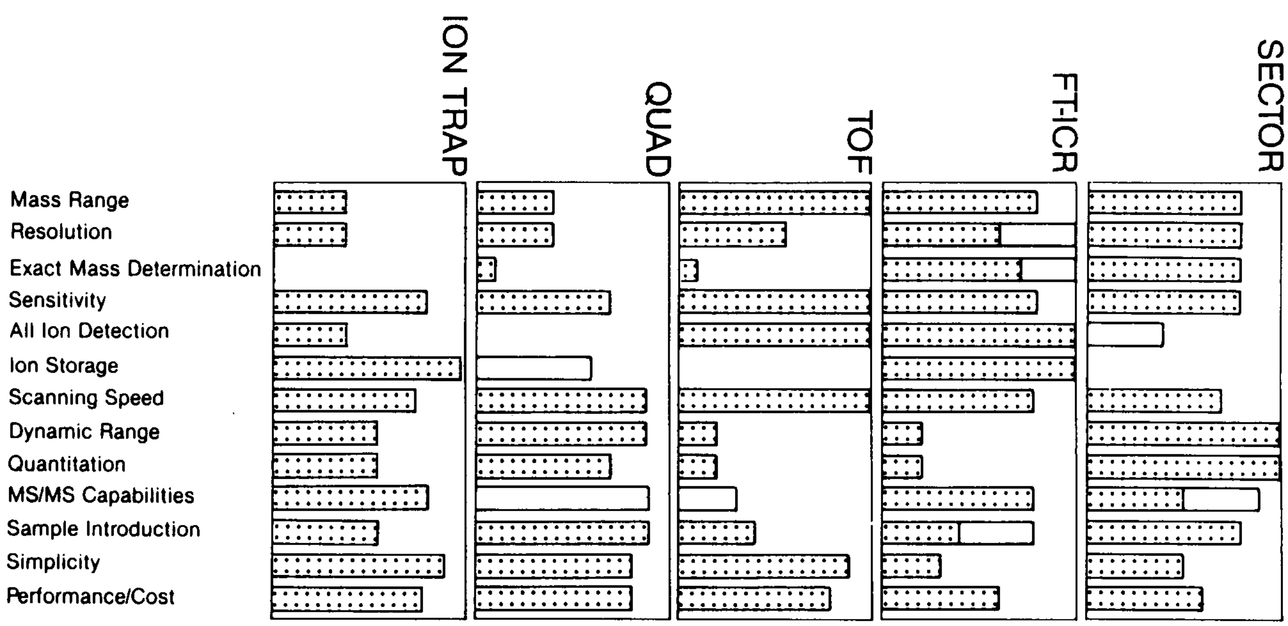


FIG. 2. Comparative characteristics of different classes of mass analyzers (Furnished by C. Brunnee, Finnigan-MAT, Bremen, FRG).

range of sample, the intensity of full scan mass spectra from modern commercial ion trap detectors is essentially independent of sample size. In comparison, today's quadrupole mass detectors are fitted with conventional ion sources, where ions are instantaneously evacuated from the source and transmitted through the analyzer as they are formed. Spectral intensity is then approximately proportional to sample size over the whole sample dynamic range.

Data systems

When we talk about mass spectrometers today, we also talk about computer control. Indeed, even the low-cost mass detectors all come complete with extensive data systems. These permit monitoring and adjustment of instrument parameters, and choice of ionization mode, such that almost all contact with the instrument with the exception of physical maintenance is now done via the keyboard. They also govern operations like automatic tuning, calibration of the mass scale and data acquisition, and provide a wide variety of data processing possibilities for exploiting and visualizing results, including spectral library comparisons. With some of the mass detectors, they not only acquire and treat MS data but also chromatographic data.

Qualitative or quantitative analysis

Routine qualitative analysis usually involves target compound identification or the recognition of unknowns by comparison of full scan electron impact (EI) mass spectra recorded from the sample with a collection of EI reference spectra in a mass spectral library. All of the modern mass detectors cited in this article include as an option the National Institute of Science and Technology (NIST, formerly NBS) library now containing almost 50,000 mass spectra, and all offer the user the possibility of creating libraries. However, not all library search algorithms operate at the same speed (and not all manufacturers give details of this in their standard specifications). But this is a point to bear in mind in comparing the different mass detectors and data systems, because it is evident that whether a library search takes 5 or 50 sec can make a big difference to productivity in a day of routine analysis.

In practical terms, the ion storing capacity of ion trap detectors generally gives them lower detection limits than quadrupoles for full scan spectra. This probably argues in favor of ion trap instruments for applications involving the routine qualitative analysis of components present in mixtures at trace levels.

In our own laboratories, working with a Finnigan-MAT ITD-800 Ion Trap Detector, we have recorded interpretable full scan (EI) mass spectra of methyl stearate on as little as 2 pg entering the source (5). With quantities >10 ng, we observe enhanced pseudomolecular ions at $(M+1)^+$, but spectra still retain a predominantly EI character and are readily recognized by library comparison routines (6). This possible disadvantage of increased $(M+1)^+$ intensity at higher sample levels characteristic of the ITD-800 is not seen in quadrupole detectors which retain a consistent spectral purity as sample levels increase. But even with ion trap detection, the problem appears to have been largely solved in the newly introduced Finnigan-MAT ITS-40 by a modified control of the motion of ions stored in the trap, known as axial modulation.

Quantitative analysis using mass detection generally involves Selected Ion Monitoring (SIM): that is, obtaining mass fragmentograms by monitoring mass signals characteristic of the compound or compounds to be analyzed. If ion trap detectors generally show much lower detection limits than quadrupoles for full scan spectra, the quadrupoles catch up when it comes to recording in the SIM mode. Here, ion traps only gain a factor of two or three in sensitivity relative to their performance in the full scan mode, whereas quadrupoles gain about two orders of magnitude. This is principally because the ion storage capacity of the ion trap ceases to play a predominant role, and because the dwell time on each mass monitored in the quadrupole is much longer than in the scanning mode. For both categories of instrument, sensitivity in the SIM mode largely depends on the intrinsic rate of ion production.

Whereas qualitative analysis commonly uses posi-

TABLE 1

Low-Cost Mass Detectors Currently on the Market[a]

Instrument	"System" or[b] "Stand alone"	Quad or Ion Trap	Negative Ion option	CI option	Mass range (amu)	Remarks
Finnigan-MAT, 355 River Oaks Parkway, San Jose, CA 95134, USA; Postfach 14 40 62, D-2800 Bremen 14, Federal Republic of Germany						
ITD-800A	Stand alone	Ion trap	no	yes	10-650	Can be installed on any capillary GC
ITD-806A	System	Ion trap	no	yes	10-650	Varian 3400 GC with ITD-800A ion trap
ITS-40	System	Ion trap	no	yes	10-650	Varian 3400 GC with "axially modulated" ion trap
Incos-50	System	Quadrupole	yes	yes	4-1000	Varian 3400 GC; can also be used for solids probe work and in LC-MS mode
Perkin-Elmer, 761 Main Ave., Norwalk, CT 06859, USA; Post Office Lane, Beaconsfield, Bucks HP9 1QA, England						
GC/ITD	System	Ion trap	no	yes	10-650	Perkin-Elmer 8500 or 8700 GC with Finnigan-MAT ITD 800 ion trap
Carlo Erba, Strada Rivoltana, 20090 Rodano (Milan), Italy						
QMD 1000	System	Quadrupole	yes	yes	2-1000	Carlo Erba MEGA GC with VG Trio-1 mass analyzer
Nermag, 49 Quai du Halage, 92500 Rueil-Malmaison, France **Delsi Inc., 15701 West Hardy Rd., Houston, 77060 Texas, USA**						
Automass	Stand alone	Quadrupole	yes	yes	4-1000	Can be connected to any type of GC; can also be used with solids probe
Shimadzu, Albert-Hahn-Strasse 6-10, D-4100 Duisburg, Federal Republic of Germany **Shinjuku Mitsui Bldg., 1-1 Nishi-Shinjuku 2-chome, Shinjuku-ku, Tokyo 163, Japan**						
QP-2000	System	Quadrupole	?	yes	10-900	Includes Shimadzu GC-14A chromatograph
VG, Floats Rd., Withenshaw, Manchester M23 9LE, England; 300 Broad St., Stamford, CT 06901, USA						
Trio-1	Stand alone	Quadrupole	yes	yes	2-1000	
Hewlett-Packard, 2 Choke Cherry Rd., Rockville, MO 20850, USA; 7 Rue du Bois-de-Lan, C.P. 365, 1217 Meyrin 1, Switzerland						
HP 5970 B MSD HP 5971 A	System					
Interion, Unit 5, Britannia Road, Sale, Manchester M33 2AA, England Vestec, (no address available)						
?	System	Quadrupole	yes	yes[c]	10-800[d] or 10-1200	Principally LC-MS, but SFC-MS. Interfaces can be adapted to all popular quadrupole instruments and ITD

[a] Information given as completely as possible. All instruments permit positive ion EI operation in full scan or selected ion mode.

[b] "System" implies a GC/MS installation complete with data system and software.
"Stand alone" implies mass detector only with associated software for instrument control, data acquisition and processing.

[c] Pseudo-CI.

[d] Depends on data system used.

tive ion EI mass spectra, quantitative analysis calls upon both positive and negative ion mass spectrometry, and on both EI and Chemical Ionization (CI) modes. In the same way that Electron Capture Detection (ECD) gives lower detection limits for certain chemical classes, negative ion mass spectra of electrophylic compounds or derivatives are often much more intense than their positive ion analogues. A good example here is the pentafluorobenzyl derivatives used for the routine quantitative estimation of prostaglandins (7). Further, CI spectra generated using an appropriate ionizing gas frequently show characteristic ions at the high mass end of the spectrum often making them more appropriate for reliable quantitation. Of the various mass detectors in Table 1, all offer both EI and CI modes of ionization. But not all offer negative ion operation as an alternative to the classical positive ion mode, although this may well change in the near future as manufacturers innovate and new developments become available.

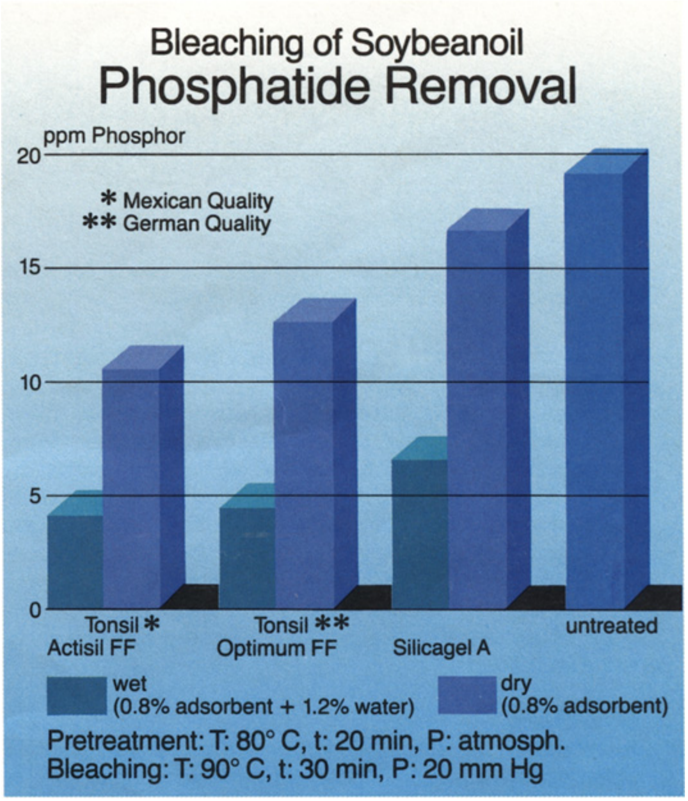
And what about mass range? Some instruments in Table 1 have an upper mass limit of 650 amu, others as much as 1000 amu. How significant is this? The simple answer is—only if the samples analyzed have significant mass peaks between m/z 650 and 1000. Realistically, for most GC-MS applications on a routine low-cost mass detector, would this be the case? Figure 3 suggests it would not. In fact, among all of the compounds in the NBS library of over 42,000 EI mass spectra, less than 2% have molecular weights greater than 650.

So what is the ideal mass detector? This question has been addressed by Brunnee (8) in an excellent general review of mass spectrometry entitled "The Ideal Mass Analyzer—Fact or Fiction?" He concludes that today, the applications of mass spectrometry are so many and varied that no single analyzer can be optimum for all applications at the same time. Indeed, the ideal analyzer depends on the nature of samples to be run and problems to be solved.

A questionnaire for the potential buyer

When contemplating purchase of a mass detector, there are several points to be clarified. In the hope of presenting here a complete analysis of possibilities and constraints associated with the instruments listed in Table 1, I sent a questionnaire to each of the manufacturers asking for details. The response was low, and only Finnigan-MAT and Perkin-Elmer (whose GC-MS system is also based on a Finnigan-MAT ion trap) have replied completely, so the information available to me and summarized in Table 1 is fragmentary.

To help the potential buyer complete the picture, my questionnaire is listed in Table 2. It may not be complete, but it establishes a good profile of any product for comparison purposes. One point to watch in particular is detection limits and sensitivity. The main reason for manufacturers quoting these values is to establish a specification for their instrument at the time of installation. However, there is no industry standard unit permitting direct comparison be-



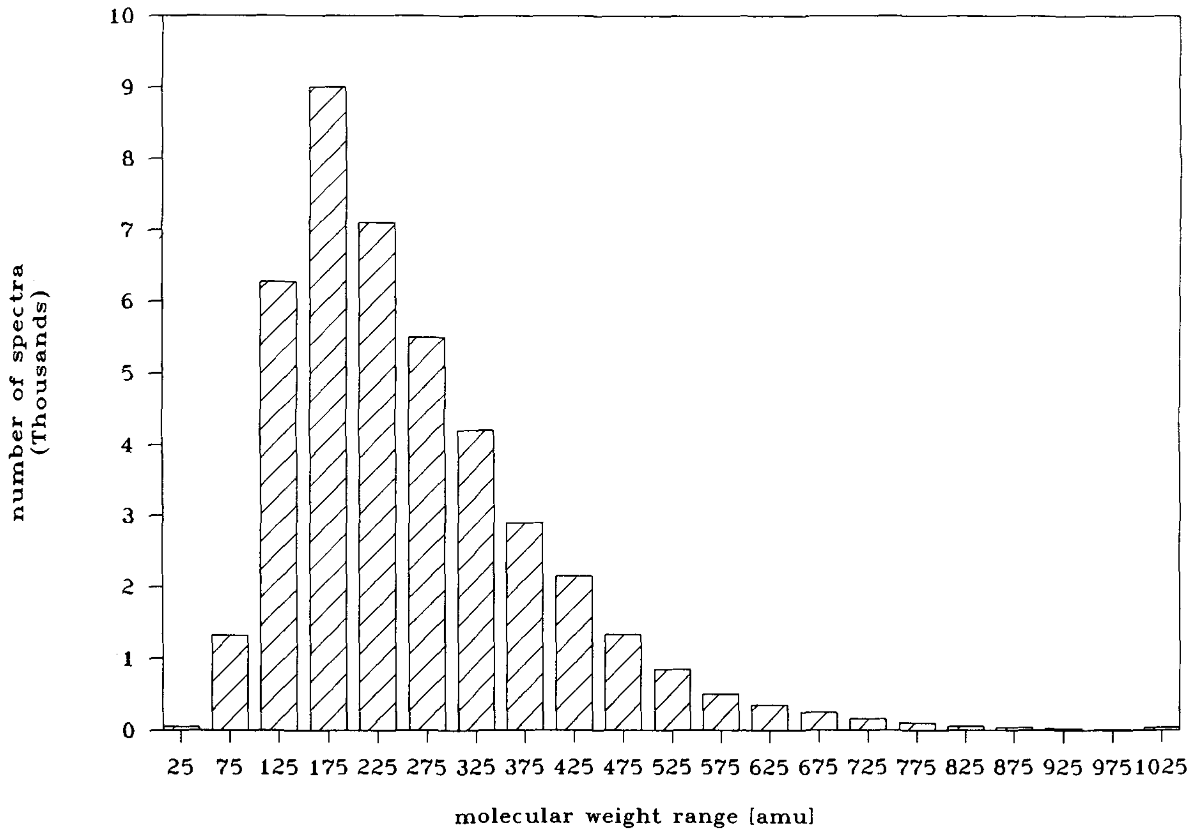


FIG. 3. Molecular weight distribution of compounds in the NBS library of over 42,000 mass spectra (Furnished by H. Traitler, Nestlé Research Centre, Nestec Ltd., Verschezles-Blanc, Switzerland).

tween instruments, and a wide variety of test substances—methyl stearate, naphthalene, hexachlorbenzene, benzophenone, etc.—are alternatively used. For obvious reasons these specifications are generally on the safe side, and although values quoted by different manufacturers give an idea of the sensitivity and detection limits attainable, the real question for any buyer is, "How will it perform with my samples?" So, in addition to the questionnaire, tests with the set of well-chosen samples characteristic of the type of analysis to be performed complete the comparative picture.

LC-MS and SFC-MS

A recent symposium on combined chromatographic-mass spectrometric techniques concluded that "while neither LC-MS nor SFC-MS seems destined to replace GC-MS, they will become increasingly important tools in the laboratory" (9). No doubt aware of this trend, the manufacturers of mass detectors are also moving in this direction, and Table 1 shows that a few low-cost systems are already available. Here, it is worth noting that in addition to offering the complete systems indicated, Vestec Corporation also makes both LC-MS and SFC-MS interfaces to use with mass detectors from other manufacturers.

Conclusions

To put things in perspective, "low cost" GC-MS still means a minimum investment in the USA of $40,000 for a stand-alone mass detector and associated software to add on to an existing GC, to $130,000 or more for a complete GC-MS installation including data system, EI and CI, and both positive and negative ion operation. However, these costs are only a fraction of the investment buying a GC-MS installation only 20 years ago, and today's compact instruments can be installed on a laboratory bench instead of taking up a whole laboratory. In the same 20 years, the performance/price ratio has increased at least 1000-fold.

Aston once said (10), "The mass spectrometer behaves at times in the most capricious and unaccountable manner. When all is well the instrument is capable of good performance. On the other hand, after dismantling became imperative and it had to be cleaned and rebuilt, exactly as before as far as one could tell, no results of any value were obtained during the weeks of work." This was 60 years ago, but even today, instruments are sometimes capricious and unaccountable.

This brings in a further factor not mentioned in either Table 1 or 2, namely the quality of after-sale service. Not that any manufacturer intentionally provides a bad service, but the increased popularity of GC-MS and other hyphenated techniques since the

(Continued)

TABLE 2

Questions to Ask When Comparing Mass Detectors

1. Cost of instrument including data handling, either as a GC-MS or LC-MS combined system, or as an "add-on" mass detector.
2. Mass range.
3. Sensitivity/detection limit, both for a full scan spectrum and in selected ion mode.
4. Dynamic range of mass spectrometer.
5. Practical dynamic range of sample size which can be injected and analyzed, including examples of comparative spectral quality over the whole range.
6. If a complete system including chromatograph, types of injectors offered.
7. Description of GC-MS or LC-MS interface.
8. Type of mass analyzer (quadrupole, ion trap, other).
9. MS ionization and analytical facilities (i.e., +ve ion, −ve ion, EI, CI, qualitative, quantitative).
10. MS libraries offered.
11. Can software be used on a range of makes of computers, or is it limited to a given model or make?
12. Can the MS part of the system be added on to any make or model of GC, or is it limited to a given make or model?
13. Can the MS be run with LC or SFC?
14. Dimensions of instrument.
15. An idea of "user friendliness" of instrument for the non-specialist in MS. Here, a list of current users who can be contacted is helpful.
16. Any specification sheets, applications, notes or other general information.

introduction of low-cost dedicated mass detectors has often resulted in service capacities being overloaded. So with all technical deliberations aside, having a service engineer who lives in the next street has become a strong argument in directing the choice of one instrument relative to another.

Finally, when you write to one or the other of the manufacturers listed in Table 1 to express your interest in their product, be sure to tell them you are interested in buying one. Maybe then, unlike me, you will not have to wait two months for a reply!

REFERENCES

1. Watson, J. T., and K. Biemann, *Anal. Chem.* 36:1135 (1964).
2. Holmes, J. C., and F. A. Morrell, *Appl. Spectry.* 11:86 (1957).
3. Ebert, A. A. Jr., *Anal. Chem.* 33:1865 (1961).
4. Gohlke, R. S., *Anal. Chem.* 31:535 (1959).
5. Horman, I., H. Traitler and J. Aeschlimann, *J. High Res. Chromatogr.* 12:308 (1989).
6. Horman, I., and H. Traitler, *Anal. Chem.* In press.
7. Waddell, K. A., J. Wellby and I. A. Blair, *Biomed. Mass Spectrom.* 10:83 (1983).
8. Brunnee, C., *Int. J. Mass Spectrom., Ion. Proc.* 76:121 (1987).
9. Warner, M., *Anal. Chem.* 59:855A (1987).
10. Aston, F. W., *Proc. R. Soc. London* A115:487 (1927).