Fast Atom Bombardment of Solids (F.A.B.): A New Ion Source for Mass Spectrometry

By MICHAEL BARBER, ROBERT S. BORDOLI, R. DONALD SEDGWICK,* and ANDREW N. TYLER
(*Chemistry Department, The University of Manchester Institute of Science and Technology, Manchester* M60 1QD)

Summary A new method for obtaining high-quality mass spectra of molecules which previously were difficult or impossible to study by ionisation methods is described.

THE last decade has seen a number of attempts to overcome one of the problems associated with structural mass spectrometry, namely, the requirement that the sample must be presented to the instrument in the gas phase before it is ionised. This has proved especially troublesome in the case of compounds of biological and biomedical importance, where their thermal instability and general polar nature precludes volatilisation, except for a few low molecular weight examples.

Field desorption,[1] secondary ion mass spectrometry using ion beams[2] and ^{252}Cf radiation[3], and laser-induced desorption of ions from surfaces[4] have all been applied to this problem with varying degrees of both success and experimental difficulty. In these laboratories we have developed an ion source which accommodates solid materials and uses the phenomenon of ion sputtering, but employs a beam of fast neutral atoms, typically of Ar of 2—8 keV, as the primary particles. The source of fast atoms in our prototype apparatus consists of a cold cathode discharge ion source and a collision chamber. The discharge ion source produces a beam of Ar^+ of controlled energy in the range 2—10 keV, which is focused into the collision chamber which contains a high pressure, 10^{-3}—10^{-4} Torr, of Ar gas. Resonant charge exchange occurs with little or no loss of forward momentum. This results in a particle beam emanating from the collision chamber which consists of a mixture of Ar atoms and Ar^+, the latter having escaped without being charge exchanged and both components having the kinetic

energy of the original ion beam. The ionic component is cleansed from the beam by a set of electrostatic deflector plates.

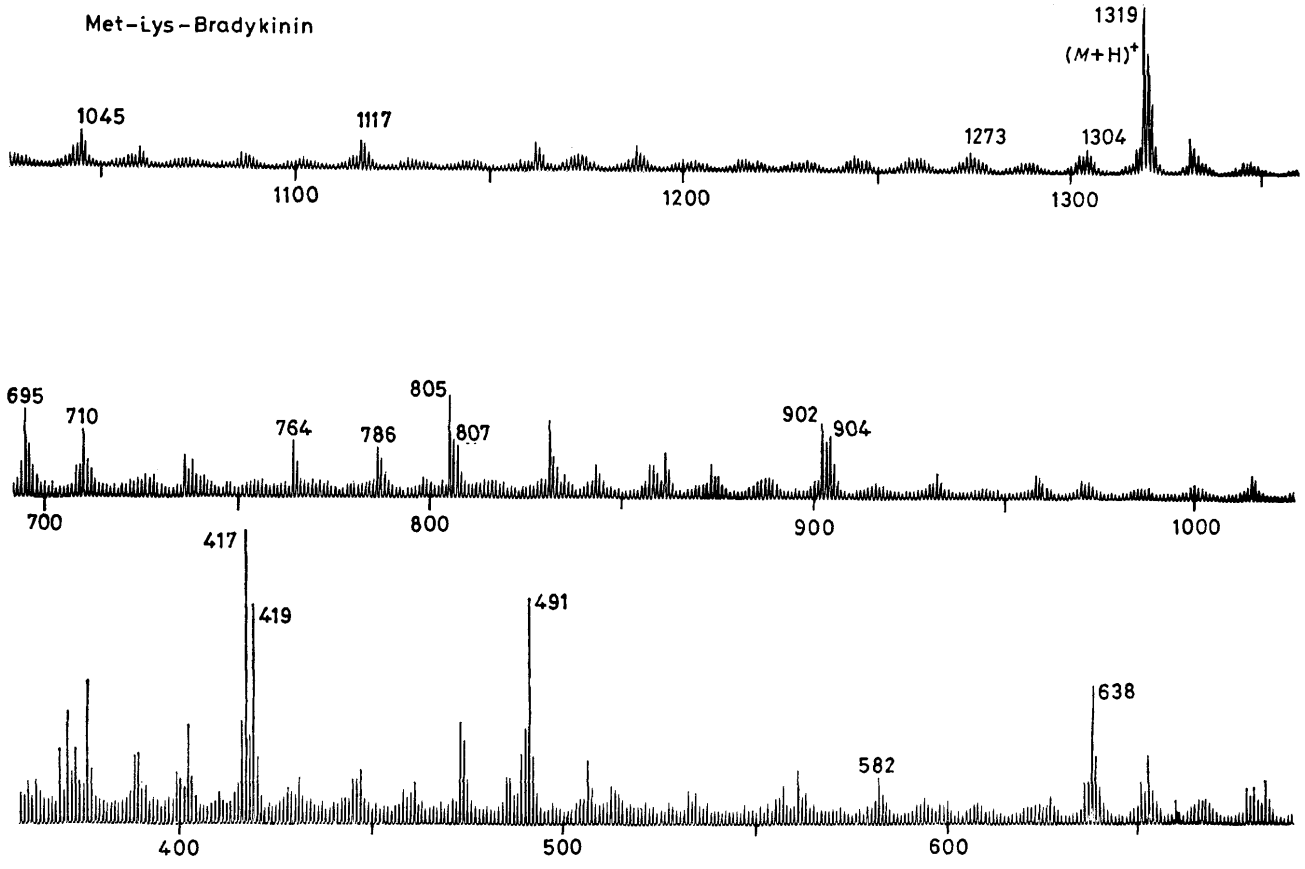
We have modified the ion source region of an A.E.I. MS902 double focusing mass spectrometer to accept our prototype atom gun. Materials can be introduced into the system by first depositing them from solution onto a metal stage which is fixed to the shaft of a solid sample insertion probe. This can then be introduced to the ion source through an axially mounted vacuum lock, in order to intercept the fast atom beam. The ions produced from the sample by the sputtering mechanism are then accelerated to the normal spectrometer potential and pass into the analyser region of the instrument. We have carried out similar modifications to a Vacuum Generators ZAB-1F mass spectrometer which is an instrument of reversed geometry.

The mass spectra obtained by this method are characterised by high pseudo-molecular ion sensitivity, giving $(M + H)^+$ in positive ion spectra and $(M - H)^-$ in the negative ion case. The spectra of either polarity contain structurally sensitive fragment ions and both first and second field-free 'metastables' are observable. The ion source has the facility of producing both positive and negative ion mass spectra with equal ease and similar efficiency and also has a very large potential mass range.

An example of the quality of the mass spectra produced by our ion source is shown in the Figure. This is the positive ion fast atom bombardment (F.A.B.) mass spectrum of the unprotected undecapeptide, methionyl-lysyl-bradykinin, obtained from 1 μg of material. It will be noted that high sensitivity (*ca.* 10^7 ions s^{-1}) is obtained in the molecular ion region and this is maintained for more than 10 min. The spectrum is rich in fragmentation which contains all the information necessary to sequence this peptide. The kinins are by no means the largest peptides which can be studied by this technique. We have to date, successfully ionised the gastrins (*M* 2096) and mellitin (*M* 2845), a peptide amide containing 26 amino-acid units.

As part of our studies of this type of molecule we have carried out detailed work on tracing the fragmentation pathways of the pseudo-molecular ions in peptides using first and second field-free region 'metastable' ion decompositions using the MS902[5] or alternatively the MIKES facility[6] on the ZAB-1F machine. We believe that this is the first time that such phenomena have been demonstrated for a 'sputter' type ion source.

Our prototype apparatus has been operating successfully for 2 years and in this period we have investigated a very large number of molecules of both natural and synthetic origin (*e.g.* see Table) which includes molecules which would be classified as organic, organo-metallic, or metal complexes, or the salts of these. This list gives some idea of the versatility of our ion source, especially since it includes such 'milestones' as vitamin B_{12}, and for the first time by any mass spectrometric method, the co-enzyme of vitamin B_{12}.



FIGURE

TABLE. Classes of compounds which have been successfully investigated by F.A.B. mass spectrometry in their underivatised form.

Oligo-saccharides, up to tri-saccharides
Peptide antibiotics, *e.g.* vancomycin
Glyco-peptides, *e.g.* bleomycin
Penicillins, *e.g.* phenethicillin
Glycoside antibiotics, *e.g.* neomycin sulphate
Oligo-peptides, containing up to 26 amino-acids
Vitamins, *e.g.* B_1, B_2, B_{12}, B_{12b}, B_{12} co-enzyme, C, P
Glycolipids, *e.g.* the gangliosides
Oligo-nucleotides, *e.g.* FAD
Neurotoxins, *e.g.* tetrodotoxin
Polynuclear aromatic sulphonic acids and their salts
Platinum amine complexes
Triphenylphosphine complexes of gold, both covalent and ionic
Manganese Schiff's base complexes.

So far we have been successful in obtaining mass spectra from any molecule to which field desorption has been shown to be applicable. Furthermore, if attention is paid to the solvent and support system in our sample handling, then we can obtain mass spectra which are stable for hours compared with the transience of field desorption spectra. By comparison with the ^{252}Cf system, taking into account our present mass spectrometer's limited resolved mass range, we can show a superiority in spectral quality and molecular weight sensitivity for such materials as vitamin B_{12}. Additionally, in comparison with both these techniques we can show that F.A.B. has superiority in producing non-thermally-induced structurally-related fragmentation and a ready access to metastable information.

In conclusion, it is our opinion that the F.A.B. method of ionisation has the following advantages which will ensure its widespread use in solving problems in structural chemistry and analysis. (i) Ionisation occurs from the solid which may be at room temperature. Sample volatilisation is not necessary and thermal effects are avoided. (ii) Sample preparation is easy in comparison with derivatisation or field desorption techniques. (iii) The method works in either polarity and gives good pseudo-molecular ion sensitivity together with structurally significant fragmentation. (iv) Mass spectra may be obtained from molecules of relatively high molecular weight. These advantages must be tempered by the problems associated with the inadequacy of most mass spectrometers in terms of their energy focusing and ion source extraction efficiencies at the high masses which this new ion source now makes possible.

The authors thank their colleagues and collaborators who provided samples, the S.R.C. and the N.R.D.C. for the funding of the research, and V.G. Analytical Ltd., for the use of their ZAB-1F mass spectrometer.

(*Received*, 19*th January* 1981; *Com.* 063.)

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