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# SOME RESULTS FROM AN INVESTIGATION INTO THE ANALYTICAL POTENTIAL OF MASS SPECTROMETRY–MASS SPECTROMETRY TECHNIQUES, WITH PARTICULAR REFERENCE TO INDUSTRIAL APPLICATIONS*

D. A. CATLOW*
*Imperial Chemical Industries PLC, Pharmaceuticals Division, Hurdsfield Industrial Estate, Macclesfield, Cheshire SK10 2NA (U.K.)*
M. JOHNSON
*Finnigan MAT, San Jose, CA (U.S.A.)*
J. J. MONAGHAN
*Imperial Chemical Industries PLC, Organics Division, Blackley, Manchester (U.K.)*
C. PORTER
*VG Analytical, Manchester (U.K.)*
and
J. H. SCRIVENS
*Imperial Chemical Industries PLC, Petrochemicals and Plastics Division, Wilton, Teeside (U.K.)*
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## SUMMARY

Mass spectrometry–mass spectrometry (MS–MS) techniques have been used in qualitative structural studies and have shown significant advantages over current methods in the areas of impurity identification, background reduction using soft ionisation techniques and extraction of fragmentation information from complex mixtures. Direct MS–MS and gas chromatography–MS–MS have also been employed in the quantitative analysis of known compounds in complex mixtures. The enhanced selectivity and speed of method development are particularly impressive features. The work has been carried out using a Finnigan MAT TSQ triple quadrupole and a VG Analytical 7070EQ hybrid instrument.

## INTRODUCTION

The use of mass spectrometry–mass spectrometry (MS–MS) as a means of deriving structural information about selected ions has been known for some time[1], has been reviewed[2] and applications of the technique to mixture analysis, using a

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triple quadrupole instrument, have more recently been publisheed[3]. With the introduction of more readily available commercial instrumentation, there has been a steady increase in the use of MS–MS over the last couple of years. ICI, in conjunction with two of the major instrument companies, VG Analytical and Finnigan MAT, have investigated the potential of the technique with particular reference to their industrial applications.

## EXPERIMENTAL

MS–MS experiments were performed on two different instruments, a VG Analytical 7070EQ hybrid instrument, and a Finnigan-MAT TSQ triple quadrupole.

Collision energies varied but were typically in the ranges 25–35 eV for the hybrid instrument, with air as the collision gas, and 15–25 eV in the triple quadrupole with argon as the collision gas.

For gas chromatography (GC)–MS (for the trichlorobiphenyl sample) a 30-m SE-54 fused-silica capillary column, held at 60°C for 1 min and then programmed at 20°C min to 275°C, was used.

### *Qualtitative analysis of mixtures*

MS–MS experiments can be very useful in identifying components in complex mixtures. Fig. 1 shows the electron impact (EI) spectrum of an antistatic agent used in conjunction with polymer films. The spectrum is extremely complex and below *m/z* 150 is almost continuous. Three families of compounds are present: an ethoxylated series based on *m/z* 162, polyethylene glycol, and an ethyoxylated series based on *m/z* 530 which also shows losses of 18 daltons. MS–MS techniques can be used to select members of these series for further study. The daughter ion spectra of *m/z* 162 and 206 are shown in Figs. 2 and 3. They enable the series to be characterised. The daughter ion spectrum of *m/z* 100 may also be obtained, even though this information is completely obscured in the original spectrum. In a similar way spectra of the *m/z* 530 + *n* (44) series may be obtained and characterised.

### *Background reduction*

In many soft ionisation techniques such as fast atom bombardment (FAB) and discharge ionisation secondary ion mass spectrometry (DISIMS) intense background peaks often obscure fragmentation information particularly at low *m/z* values. The

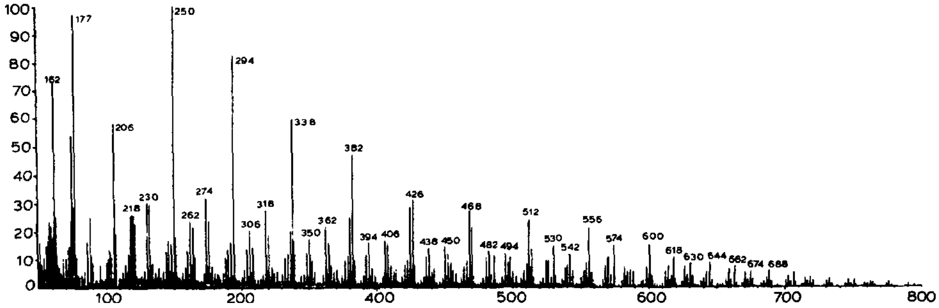


Fig. 1. EI spectrum of an antistatic agent.

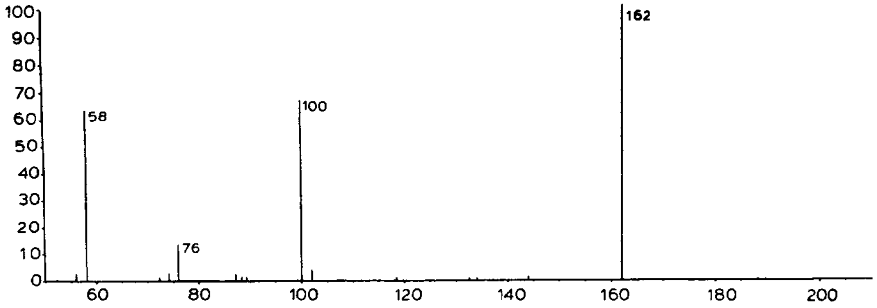


Fig. 2. Daughter ion spectrum of *m/z* 162.

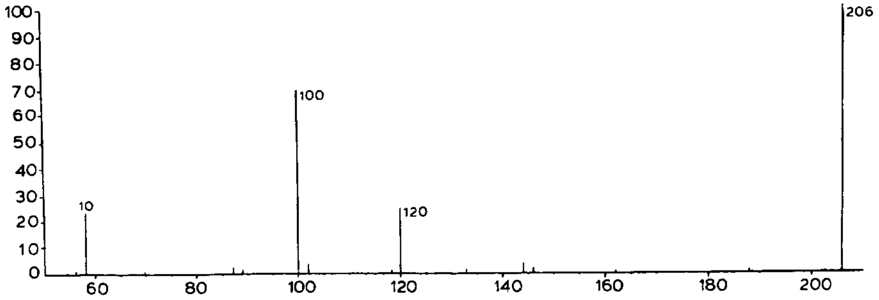


Fig. 3. Daughter ion spectrum of *m/z* 206.

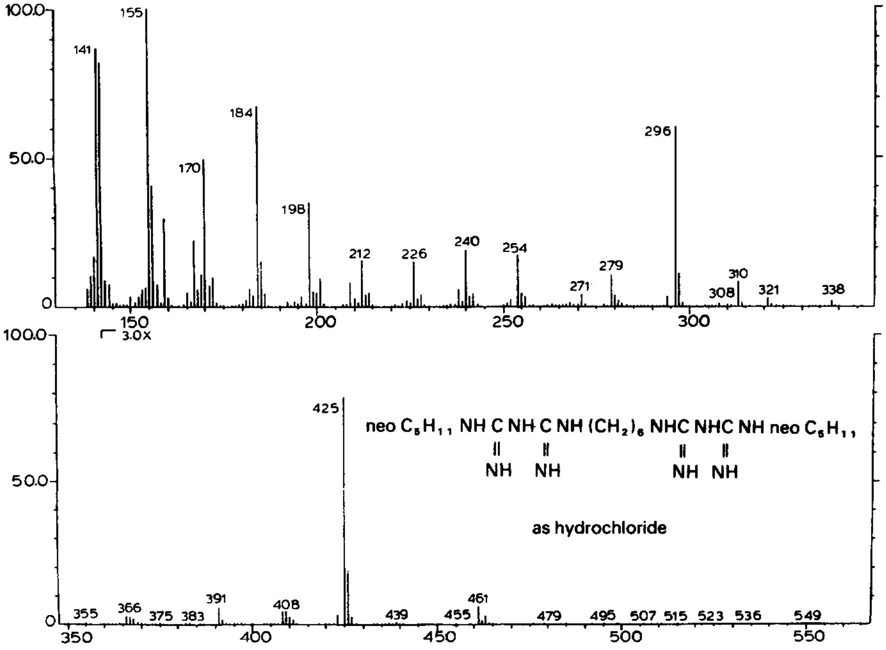


Fig. 4. DISIMS spectrum of an alkyl-ended biguanide.

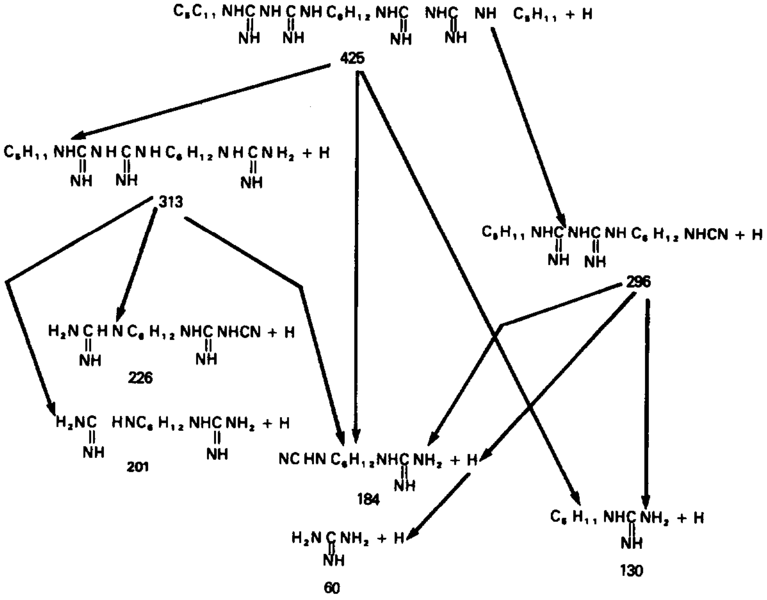


Fig. 5. Biguanide fragmentation scheme derived from MS–MS.

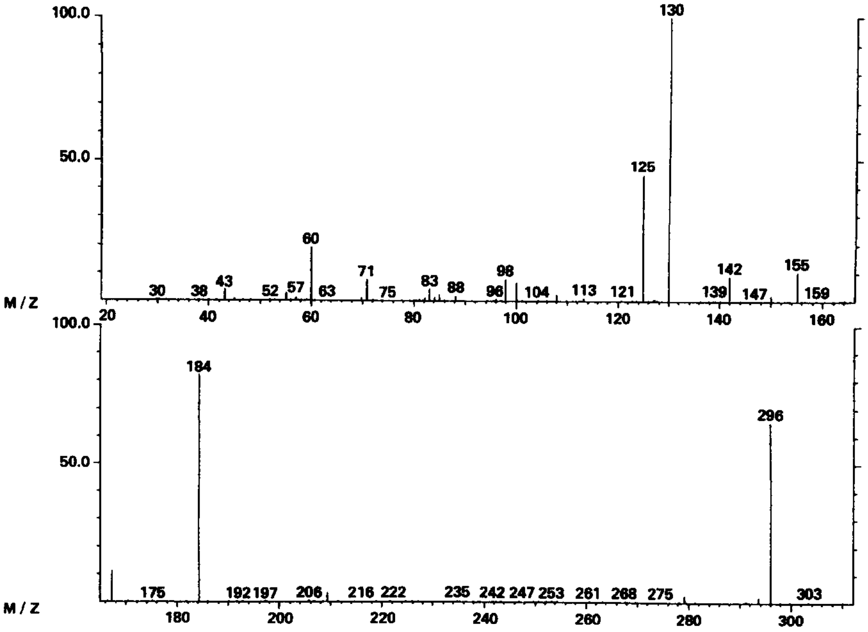


Fig. 6. Daughter ion spectrum of $m/z$ 296 from alkyl-ended biguanide.

DISIMS spectrum of an alkyl-ended biguanide is shown in Fig. 4. As can be seen, no peaks below *m/z* 140 are shown. This was due to the intense background. Also shown (in Fig. 5) is the fragmentation scheme obtained by MS–MS. This shows fragments below that obtained in the conventional DISIMS spectrum. A daughter

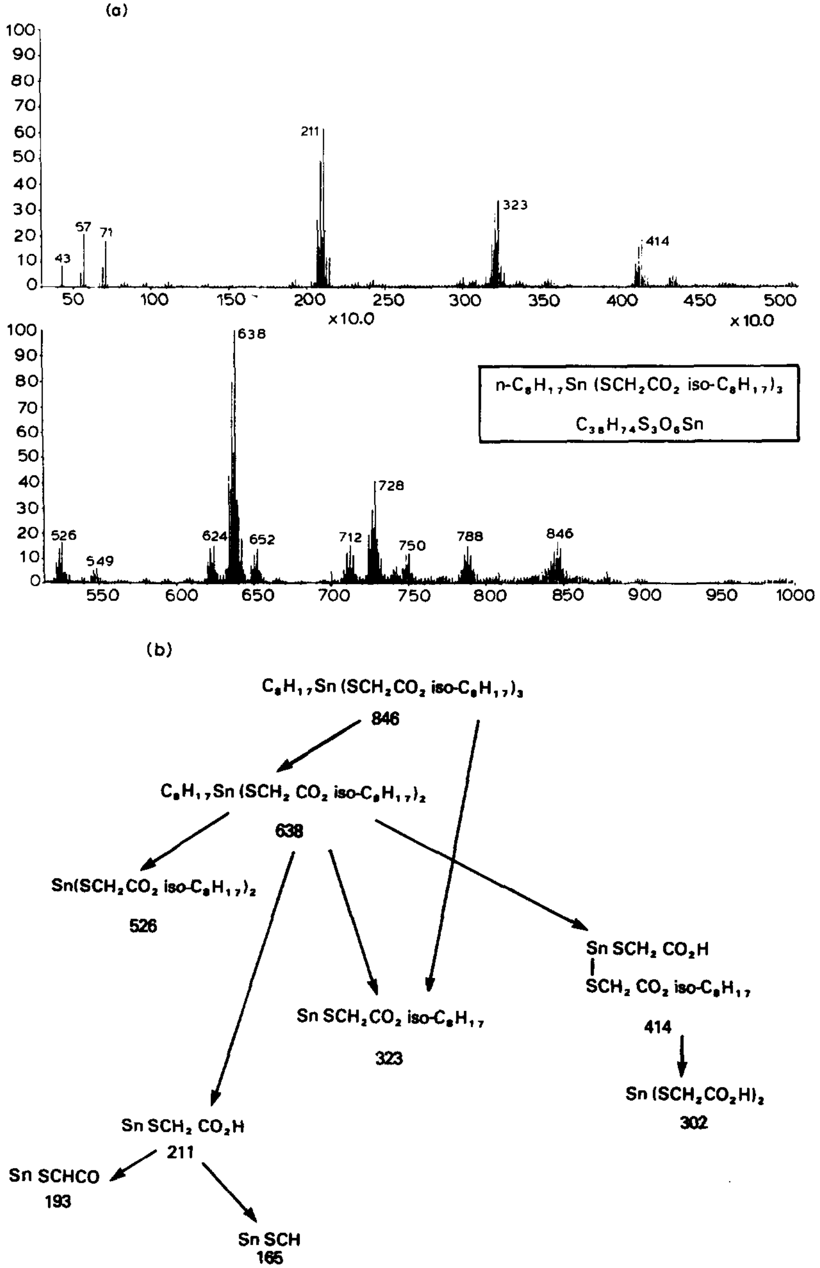
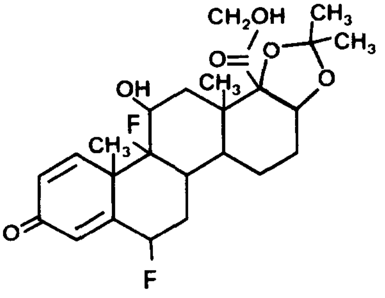


Fig. 7. (a) Positive FAB spectrum of *n*-octyltin triisooctyl thioglycollate. (b) Fragmentation scheme for tin thioglycollate derived from MS–MS.



$C_{24}H_{30}O_6F_2$ 452

Fig. 8. Fluocinolone acetonide structure.

ion spectrum of *m/z* 296 demonstrates this point (Fig. 6). The background due to the soft ionisation technique is eliminated facilitating the identification of fragment ions of lower *m/z*.

*Impurity identification*

In Fig. 7 is shown the positive-ion FAB spectrum of *n*-octyltin tri-isooctyl thioglycollate together with a fragmentation scheme, obtained from MS–MS experiments. Of interest is the absence in the scheme of the cluster at *m/z* 728. This was

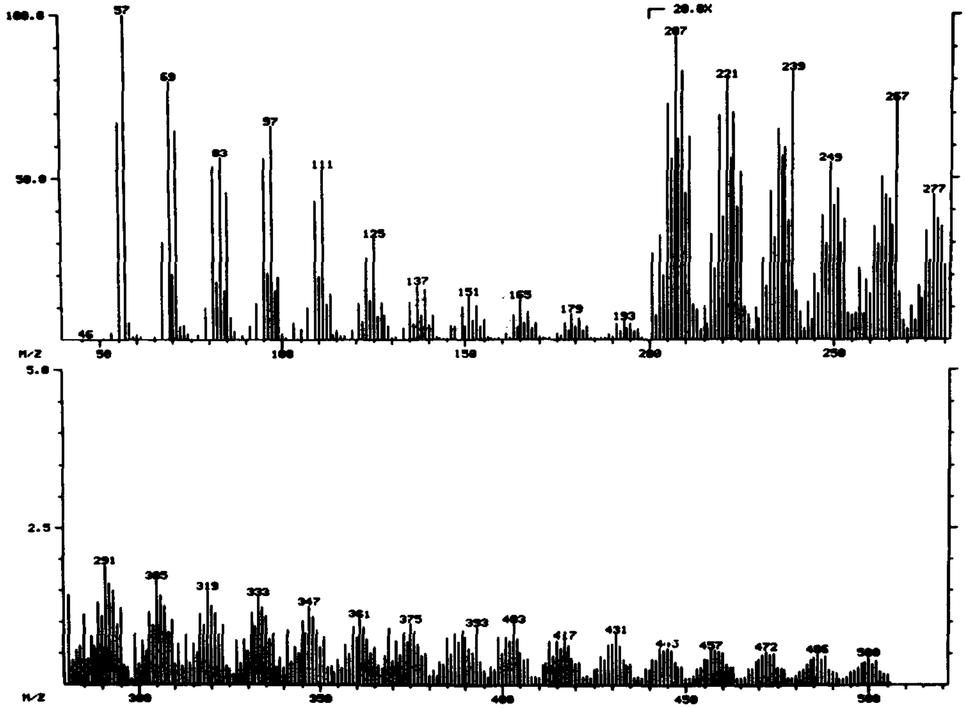


Fig. 9. EI spectrum of cream containing steroid.

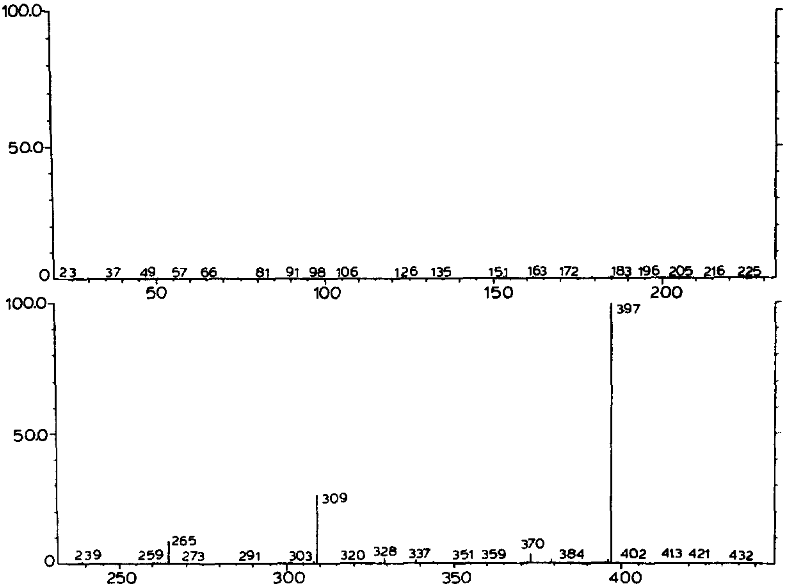


Fig. 10. Daughter ion spectrum of *m*/*z* 432 (standard).

later shown to be a fragment of an impurity, namely tin tetraisooctyl thioglycollate. This demonstrates quite clearly the utility of MS–MS in differentiating between impurities and fragment ions of the major component.

*Quantitative analysis*

***Steroid in cream formulation.*** In addition to the use of MS–MS techniques an

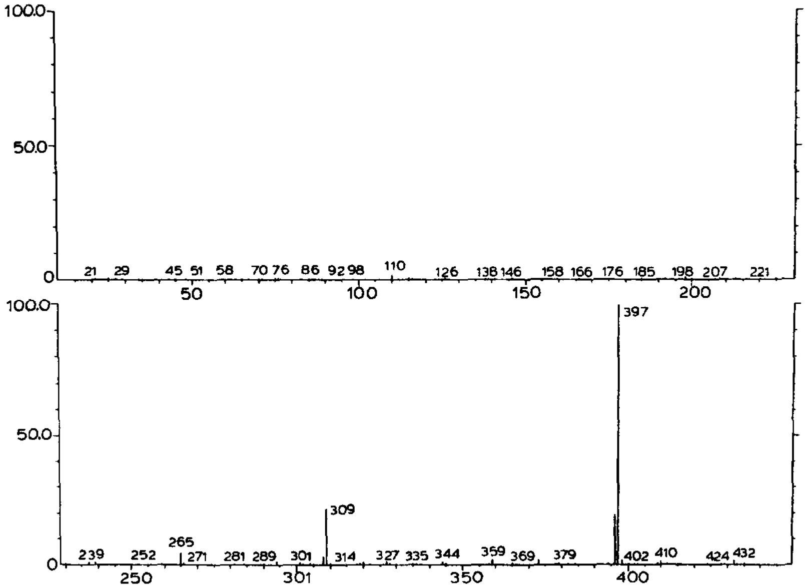


Fig. 11. Daughter ion spectrum of *m*/*z* 432 (cream).

extra degree of selectivity may be obtained by the choice of ionisation technique. Fig. 8 shows the structure of a steroid, fluocinolone acetonide, which is used in a cream formulation for the treatment of skin disorders. Electron impact and positive chemical ionisation (CI) did not give the required selectivity due to interferences from cream components (see Fig. 9 for EI spectrum of the cream). Negative CI, however, gave the degree of selectivity required. The daughter ion spectra of $m/z$ 432 obtained from a standard and the cream formulation were identical and are shown in Figs. 10 and 11, respectively. The steroid was present at 0.025% in the cream. It is clear that, using selected reaction monitoring, a far lower detection level could be obtained.

*Trichlorobiphenyl analysis.* It was required to obtain the total trichlorobiphenyl (TCB) concentration in a number of complex reaction mixtures. Single-ion monitoring GC–MS gave unreliable results due to interferences from other components of the complex mixtures. Fig. 12 shows a typical total ion current trace from one such reaction mixture, using EI ionisation. Multiple reaction monitoring GC–MS–MS was used to improve the selectivity of the method, monitoring the 258→186 and 256→186 transitions. This gave an extra check since the ratio of these transitions was known. Three standards (2,4,6; 2,3,6; 2,4,5) were available and traces for these are shown in Fig. 13. Results for two reaction mixtures (A and B) are also shown, in Figs. 14 and 15, with total estimated trichlorobiphenyl concentrations of 5000 and 300 ppb*, re-

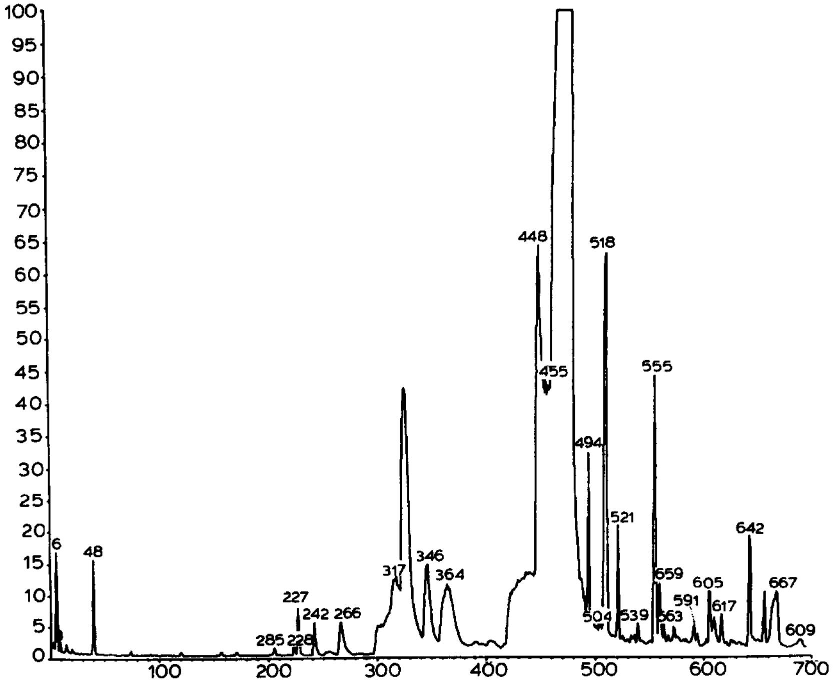


Fig. 12. Total current trace from a reaction mixture.

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* Throughout this article, the American billion ($10^9$) is meant.

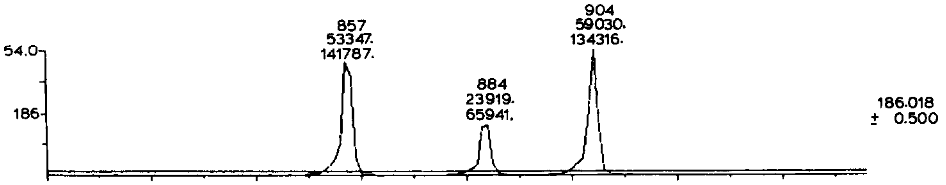

Fig. 13. Trichlorobiphenyl standards, GC–MS–MS. 2,4,6-Isomer: 500 ppb; 2,36-isomer: 200 ppb; 2,4,5-isomer: 400 ppb. *m*/*z* 258→186 transition.

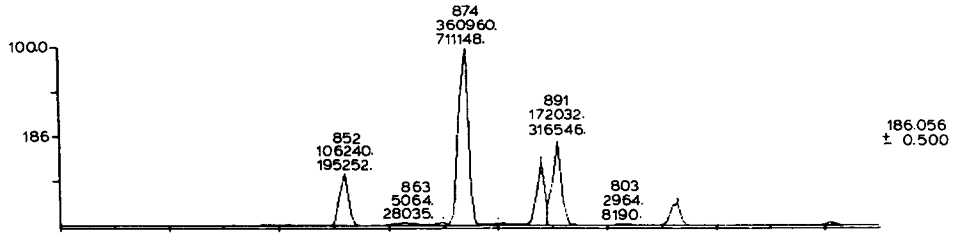

Fig. 14. Reaction mixture A, GC–MS–MS. *m*/*z* 256→186 transition. Total calculated trichlorobiphenyl concentration 5.7 ppm.

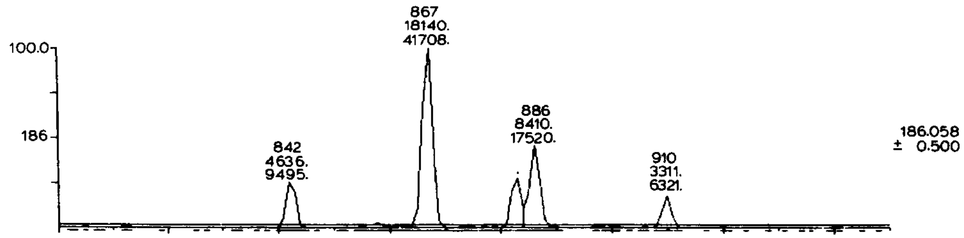

Fig. 15. Reaction mixture B, GC–MS–MS. *m*/*z* 256→186 transition. Total calculated trichlorobiphenyl concentration 300 ppb.

spectively. The ratio of transitions was in good agreement with the expected values. Results obtained with triple quadrupole and hybrid instruments were in excellent agreement.

### *Type analysis*

***Phthalates.*** CI spectra of dialkyl phthalates show a characteristic peak at *m*/*z* 149. A wide range of phthalates can be easily characterised by using a parent ion scan of *m*/*z* 149. A typical spectrum is shown in Fig. 16. This shows a wide range of phthalates ranging from diethyl to above ditridecyl. This experiment can be repeated very rapidly and typical results using a short GC column are shown in Fig. 17. This gives a total experiment time of less than 1 min.

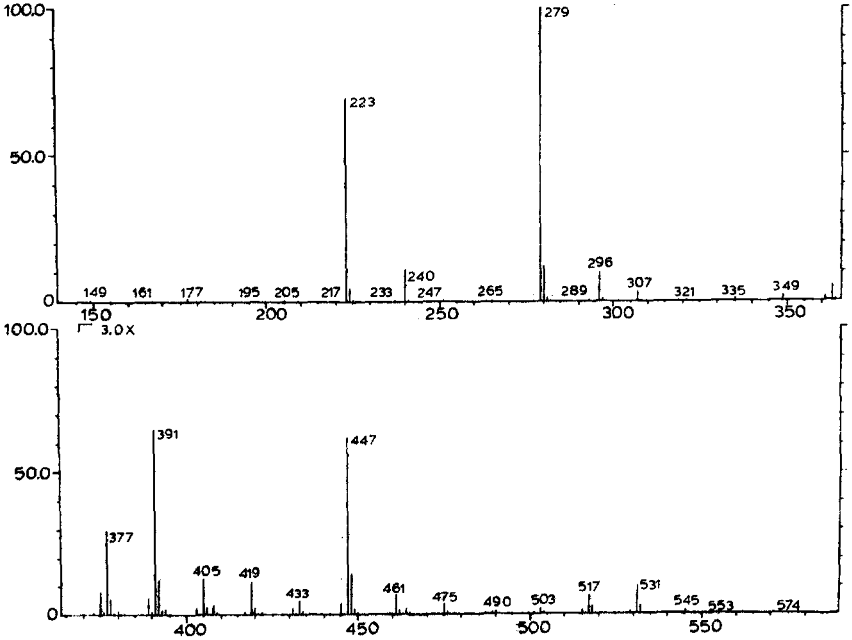

Fig. 16. Phthalate mixture: parents of $m/z$ 149.

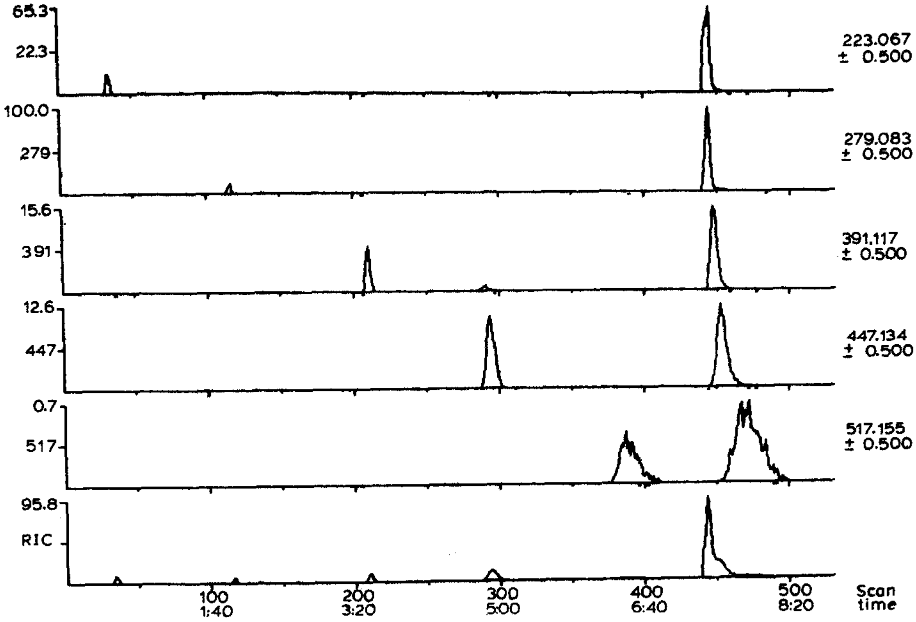

Fig. 17. Phthalate analysis. GC–MS–MS: parent ions of $m/z$ 149. Column: 1 ft. OV-1.

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