ノート

Rapid Detection of Illicit Drugs by Direct Inlet Chemical Ionization Mass Spectrometry

Yukio OHNO* and Shozo KAWABATA**

*Import Division of Nagasaki Customs
1—36, Dezima-machi, Nagasaki—shi, 850 Japan
**Central Customs Laboratory, Ministry of Finance
531, Iwase, Matsudo—shi, Chiba—ken,271 Japan

Direct inlet electron impact mass spectrometry (DI-EI) and direct inlet chemical ionization mass spectrometry (DI-CI) using isobutane as the reagent gas were comparatively investigated as rapid method of detection for the illicit drugs.

In the DI-CI, the MH^+ions of the CI mass spectra of illicit drugs were mostly recorded as the base peaks and hence they could be easily determined from their mass numbers. DI-CI gave even more reliable results in the analysis of illicit drugs containing component that are greatly different in their boilng points and/or concentrates, or that are equal in numbers.

DI—CI have the feature that permit reliable analysis of drug samples within a few minutes, whether the components are volatile or nonvolatile. It also found that the detection limit was generally tens of nanogram level.

1 Introduction

The abuses of narcotics, hashish, awakening amines, etc. bring people unhealthnss as well as the causes of many types of crimes. And it inflicts injuries on social and economic environment.

Recently, it seems it has become more skillful and malignant day by day in contraband the illicit drugs. Moreover, modern developments in the traffic facilities promote the contraband and extend of its black market world wide. From the standpoint of these facts, the problems on the illicit drugs seem to become more critical as matter of international concern.

As a tool of detection of illicit drugs, many methods such as infrared spectrometry, gas chromatography, thin-layer chromatography, high performance liquid chromatography and mass spectrometry or gas chromatography-mass spectrometry etc. are developed and applied in the field of forensic chemistry hitherto.[1] These methods have their own features and give us excellent results respectively.

Among these methods, gas chromatography-mass spectrometry[2] which may be, in general, characterized by its high resolution, high qualitative and quantitative reliability and high sensitivity to permit trace analysis. But it has drawbacks, that is, run takes 20 to 40 minutes because the GC is of rate determining step. And furthermore, many components must be derived into volatile ones for analysis.

However, in the direct inlet chemical inonization mass spectrometry[3],[4] almost all MH^+ions of illicit drugs were recorded as the base peaks, and hence they could

be easily determined from their mass number of NH^+ions, or in some cases, together with that of their fragment ions.

From the standpoint of the the rapid detection concerning illicit drugs, authors reported a summary of our recent results on the application of direct inlet chemical ionization mass spectrometry.

2　Apparatus and experimental condition

Apparatus : As an apparatus, a Hitachi double-focusing mass spectrometer type M-80B equiped with a data processing unit type M-0101 was used.

The schematic diagram of direct inlet system in this mass spectrometer is shown in Fig. 1. Upper one is an ordinary direct inlet system. That is to say, sample is inserted nearby ionization chamber with a sample tube and then are vaporized at suitable temperature.In this experiment this sample inlet system was generally applied.

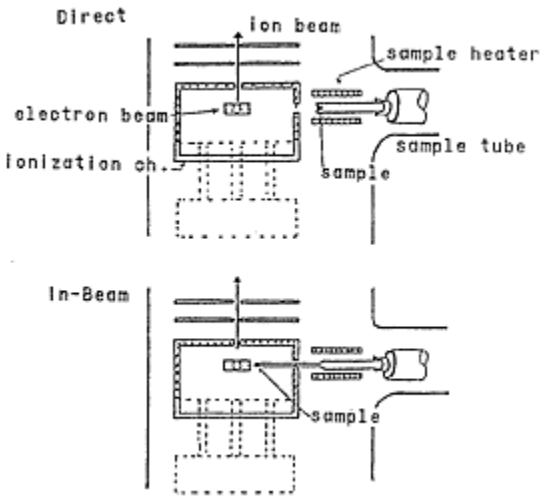

Fig. 1　Schematic diagam of direct inlet system

Lower figure shows a direct inbeam system. As contract with the direct inlet system shown above, sample to be measured is inserted nearer to electron beam in the ionization chamber.

In either case, both modes of the measurements such as electron impact ionization and chemical ionization with reagent gas can be achieved by a transfer device.

Experimental condition：Experimental condition ordinary used are as follows.

Ion Source：EI/CI modes
Ionization Voltage：70 eV (EI), 10 O eV (CI)
Ion Acceleration Voltage：3.0 KV
Ionic Chamber Temperature：180℃
Scanning Intervals：4 sec—8 sec
Reagent Gas：Isobutene

3　Direct inlet EI and CI mass spectra of standard illicit drugs

Mass spectra of typical standard illicit drugs measured by direct inlet EI and CI mode were summarized as follows. All samples used in these experiments were salt-types.

Morphine : Parent ion of morphine was appeared predominantly at M/Z 285 both in EI and CI mass spectra, but in CI spectrum of morphine quasi molecular ion of $(M+H)^+$and a fragment ion at M/Z 268 which being attributed to the elimination of OH radical from OH group at the 6th position of morphine structure are observed intensely. However, CI mass spectra does not show a M-57 (C_3H_7N) ion, which is considered to be characteristic fragment ion of the compounds having morphinan skeltons and,which is being detected by EI mode, was not appeared (Fig. 2).

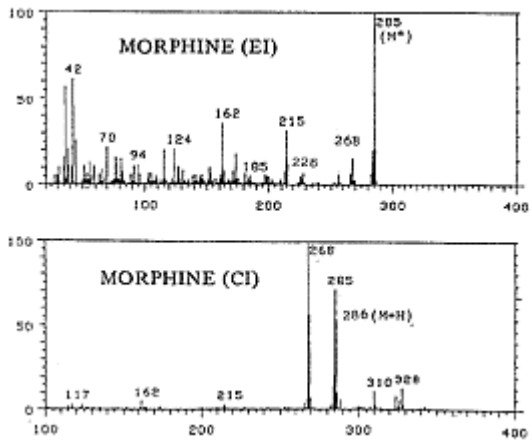

Fig. 2　EI and DI mass spectra of morphine

Codeine and other opium alkaloids : In the mass spectra of codeine, similar ions are observed by the measurement of EI and CI mode (Fig. 3). Other principal opium alkaloids such as papaverine, thebaine showed also strongly their parent ions or quasi molecular ions. But in the case of narcotine (M.W : 419), fragment ion of M/Z 220 was only observed both in the measurement by EI and CI mode. This seems to be attributed to the thermal or ionic stabilitty of narcotine.

Pulverized opium : the example is a case of pulverized opium which is a complex mixture of opium alkaloids and others.

Fig. 4 is a total ion chromatogram of pulverized opium measured by EI mode. Two peaks were observed and mass spectrum measured at the maximum point peak is showed in Fig, 5.

A characteristic fragment ion of narcotine was observed in the mass spectrum of first maximum point.

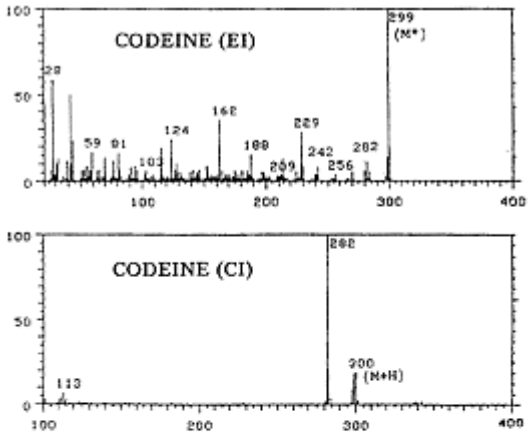

Fig. 3 EI and CI mass spectra of codeine

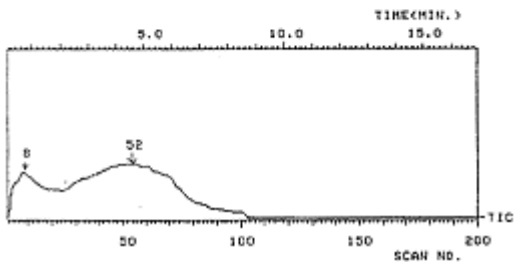

Fig. 4 Total ion chromatogram of pulverized opium(EI)

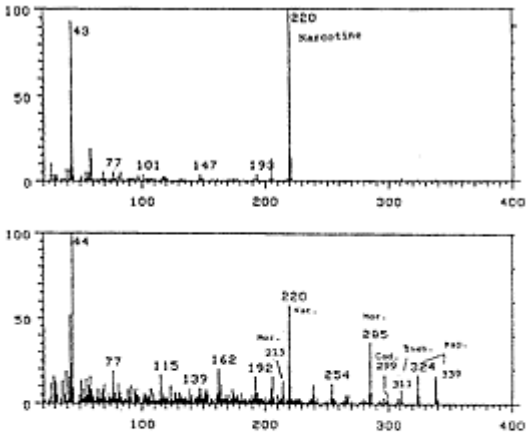

Fig. 5 EI mass spectra of purverized opium

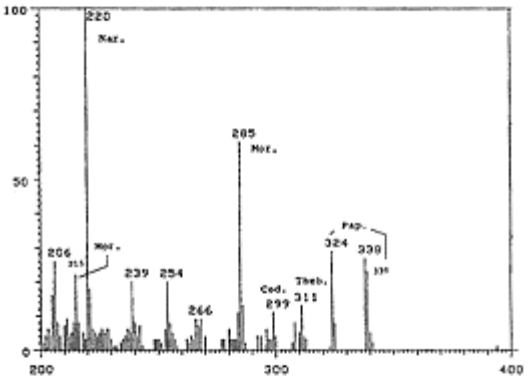

Fig. 6 EI mass spectrum of purverized opium

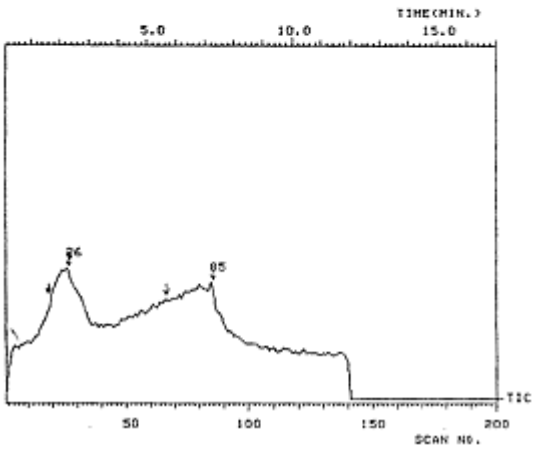

Fig. 7 Total ion chroimatogram of pulverized opium(CI)

From the second one, the existences of morphine, codeine, thebaine, papaverine and narcotine could be identified by the presence of their parent ions together with each characteristic fragment ions. A part of enlarged spectrum in the higher mass region was shown in Fig. 6.

From these results it was considered that direct inlet method permitted to apply to these complex mixture.

In the measurement by CI mode, total ion chromatogram similar to that obtained by EI mode was shown in Fig.7. Mass spectra measured at 4 points marked on the total ion chromatogram were summarized in Fig. 8. A part of enlarged spectrum in the higher mass region was shown in Fig. 9. These spectra obtained by CI mode were in somewhat simplified figures compared to EI measurements.

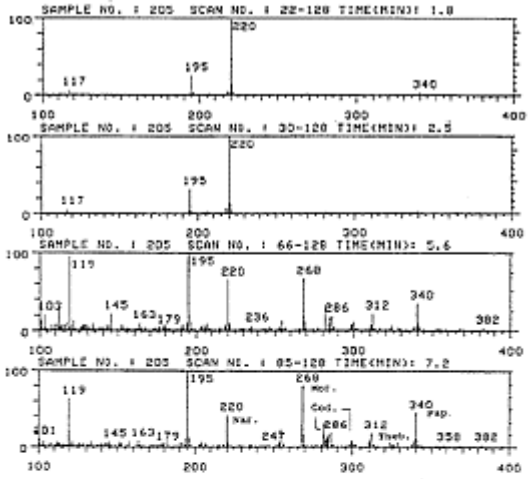

Fig. 8　CI mass spectra of purverized opium

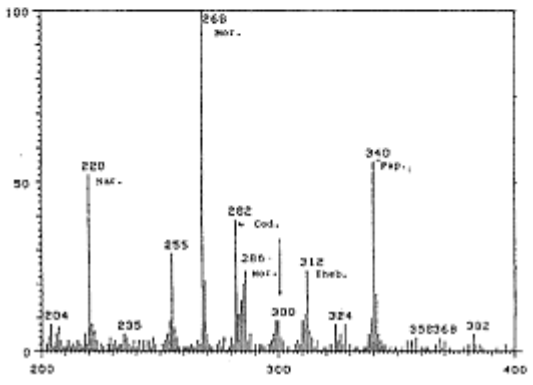

Fig. 9　CI mass spectrum of purverized opium

Quasi molecular ions of morphine (M/Z : 286), codeine (M/Z : 300), thebaine (M/Z : 312), papaverine (M/Z : 340) and their characteristic fragment ions such as M/Z 268 (morphine), M/Z 282 (codeine), and M/Z 220 (narcotine) were clearly appeared. So, the measurement by CI mode was better for the application to complex illicit mixtures.

Cocaine : CI mass spectrum of cocaine was very simple one (Fig. 10). It provides intense quasi molecular ion at M/Z 304 as a base peak. Moreover, a characteristic fragment ion at M/Z 182 occured by the lost of benzoic acid (C_6H_5 COOH, M. W.122) from quasi molecular ion appeared intensely even in the CI spectrum.

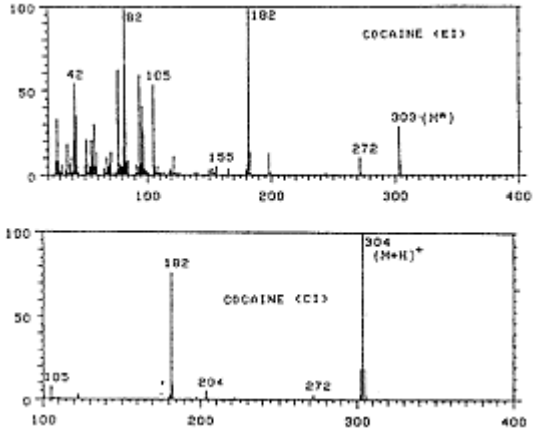

Fig. 10　EI and CI mass spectra of cocaine

These suggested to be very effective identification of the compound.

LSD (Lysergic acid diethylamide, tartrate) : The EI and CI mass spectra of LSD tartrate closely resembles that of the base showing that salt dissociates readily. Fragment ions from tartaric acid appear only at low mass values and therefore do not interfere with the analytically significant portion of the spectrum.

In both spectrum, the base peak is the molecular ion at M/Z 323 and quasi molecular ion at M/Z324 respectively. The most prominent cluster of fragment ions under electron impact is in the region M/Z 221 to

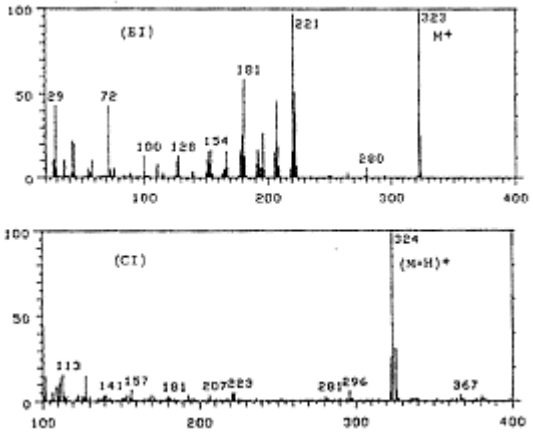

Fig. 11 EI and CI mass spectra of LSD

223 ; these ions are formed via the loss of the side chain, that is α-and β-cleavages of the amide carbonyl group. M/Z 223 yield M/Z 222 and M/Z 221 by losing H-atom (Fig. 11, Fig. 12)

However, in the CI mass spectrum, small peaks are only observed at this region.

Methamphetamine and Phentermine : The mass spectrum of methamphetamine has its base peak at M/Z 58 ($CH_3CH{=}NHCH_2$) and does not show the molecular ion under electron impact. Moreover, this fragmentation pattern is closely similar to that of phentermine, which is an isomer of methamphetamine. This is an important feature since it is often requested

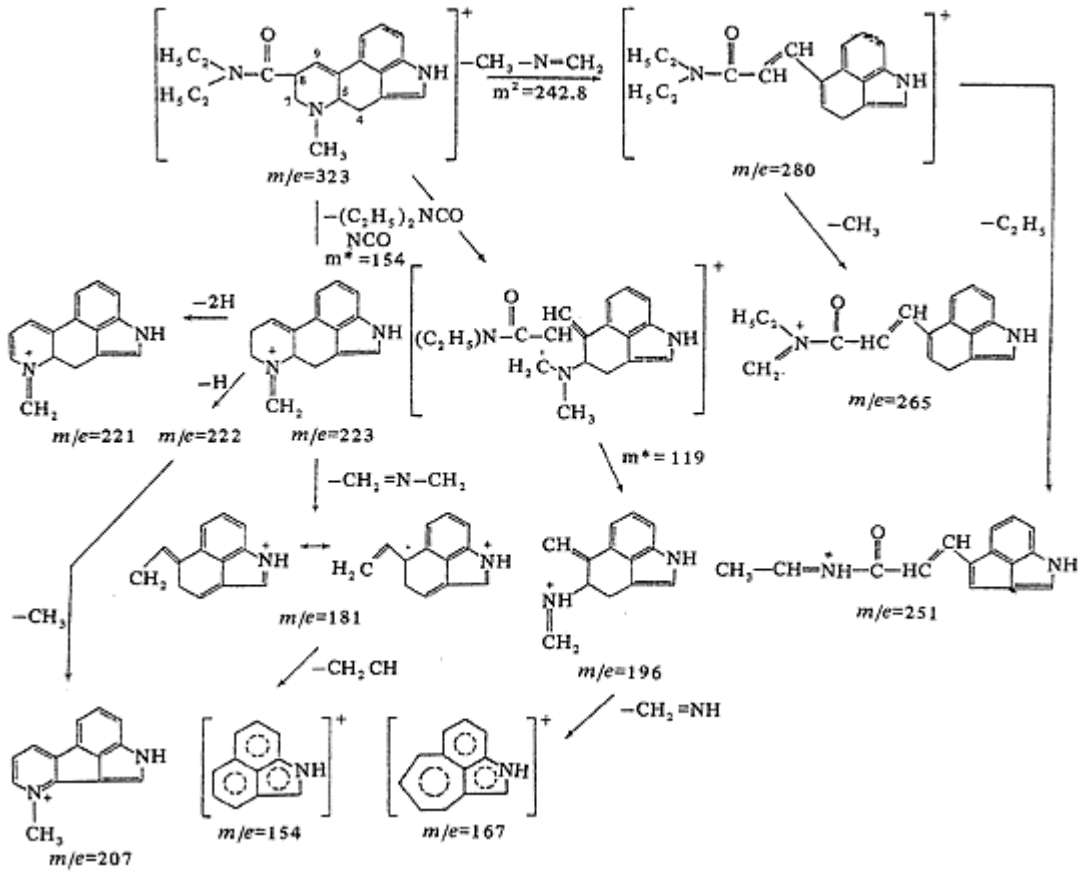

Fig. 12 Fragmentation of LSD under electron[5)]

to quantify the methamphetamine or phentermine in a sample seizured.

As against this, in the chemical ionization mass spectrum of these compounds quasi molecular ions are appeared at M/Z150 as the base peak respectively. But, important fragment ions, resulting from the loss of

an amino function from their molecules were also noted for each compound in low relative intensity. Such a

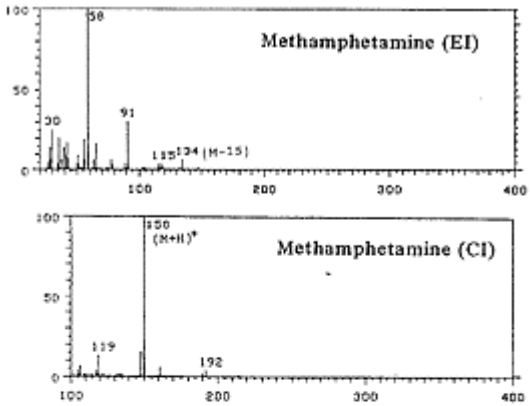

Fig. 13　EI and CI mass spectra of methamphetamine

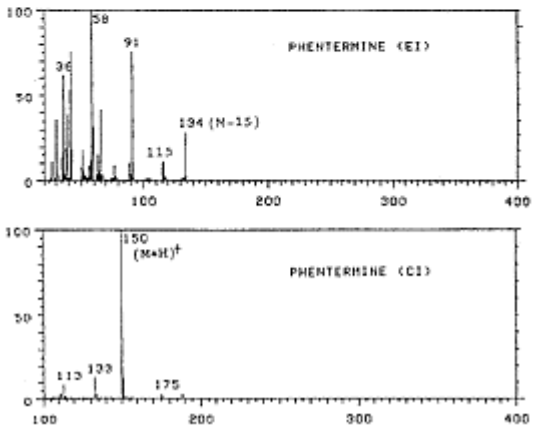

Fig. 14　EI and CI mass spectra of phentermine

fragment ions at M/Z 119 ($MH^+-CH_3NH_2$) in the case of methamphetamine and at M/Z 133(MH^+-NH_3) in that of phentermine are mentioned respectively (Fig. 13, Fig. 14).

It is considered that this facts permit to predict the chemical structure of the compound which shows the similarity in the CI mass spectrum profiles.

Ephedrine and ethylephedrine : The fragmentation patterns of ephedrine and methylephdrine under electron impact are similar to that of methamphetamine. But, CI mass spectra of the compounds both gave significant quasi molecular ion and a fragment ion caused by the loss of H_2O from MH^+, quasi molecular ion at

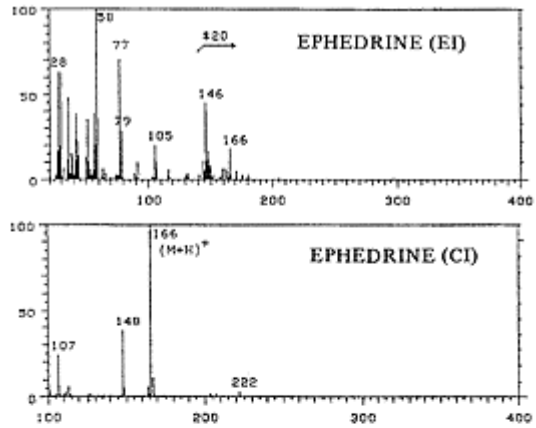

Fig. 15　EI and CI mass spectra of ephedrine

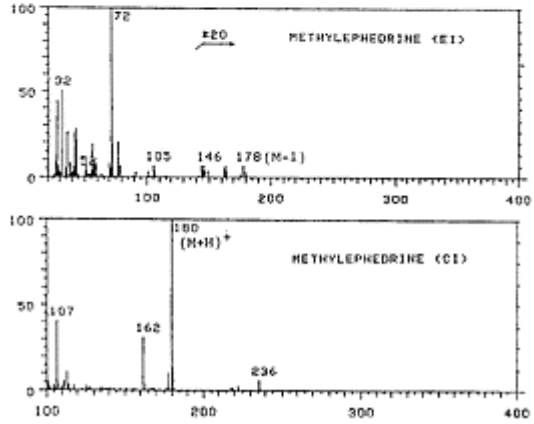

Fig. 16　EI and CI mass spectra of methylephedrine

corresponding mass numbers.

This fragment ion also contributes to identify the ephedrine and its derivatives (Fig. 15, Fig. 16).

4　Application to practical problems

This direct inlet ionization mass spectrometry was applied to some drugs seizured at air port.

4. 1　Example

As the result, this drug tablets were proved to be containing cocaine, lidocaine and inositol. Among them, lidocaine is a local anesthetic and inositol is a diluent. In this case, direct inlet inbeam method was applied to the measurement of its mass spectra under

EI andCI.

Fig. 17 was a total ion chromatogram of the seizured drug by EI mode. The chromatogram was appeared sharply on the measurement by direct inbeam method. Mass spectra measured at 4 points marked on this chromatogram were summarized in Fig. 18. From these mass spectra, the existence of cocaine and lidocaine can be identified by the presence of their parent ions together with each characteristic fragment ions ;

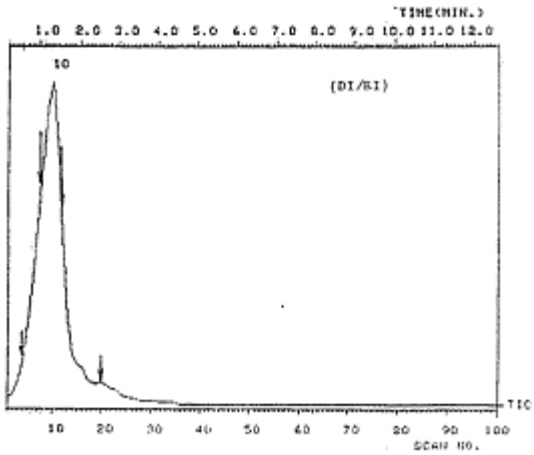

Fig. 17 Total ion chromatogram of seizured illicit drug

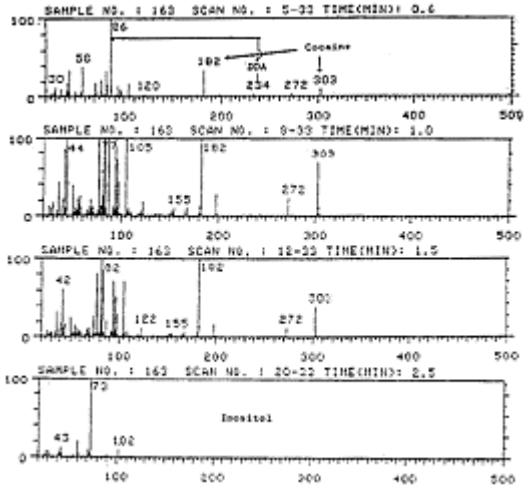

Fig. 18 EI mass spectra of seizured illicit drug

Cocaine : M/Z 303(M^+), 272, 182

Lidocaine : M/Z 234(M^+), 86.

But, inositol showed only their fragment ions, so it was very difficult to deduce the structure of this compound.

As against this, in the measurement of CI mode, total ion chromatogram was appeared as the peaks. This fact is attributed to the ionic strength increased by the measurement under CI mode.

From the CI spectra showed in Fig. 20, each mass spectrum became more simple and identification of the compound was easily achieved. Moreover, inositol which contained as diluent also identified from their quasi molecular ion at M/Z 181 and together with their fragment ions.

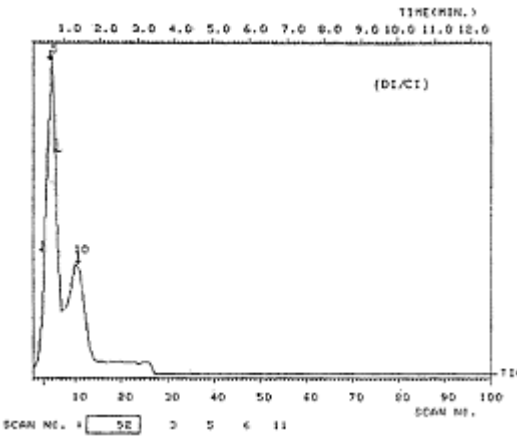

Fig. 19 Total ion chromatogram of seizured illicit drug

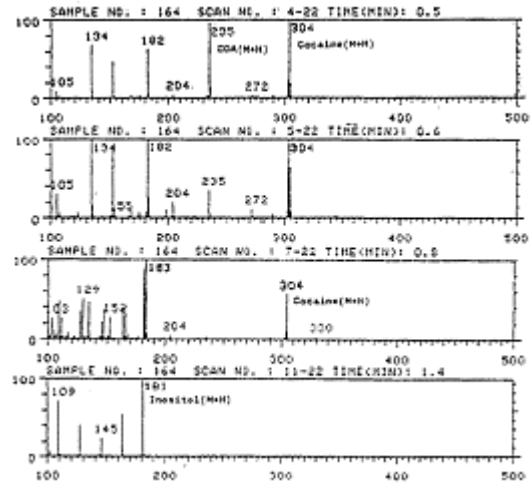

Fig. 20 CI mass spectra of seizured illicit drug

Total ion chromatogram measured under electron impact, after etherfication by trimethylsilyl reagent, was shown in Fig. 21 as reference (GC/MS). It showed that lidocaine and cocaine was clearly separated. But it took ten times or more to obtain this chromatogram compared with above mentioned method.

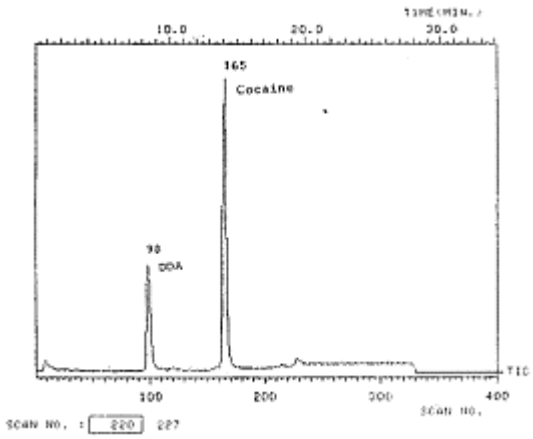

Fig. 21　Total ion chromatogram of seizured illicit drug by GC／MS

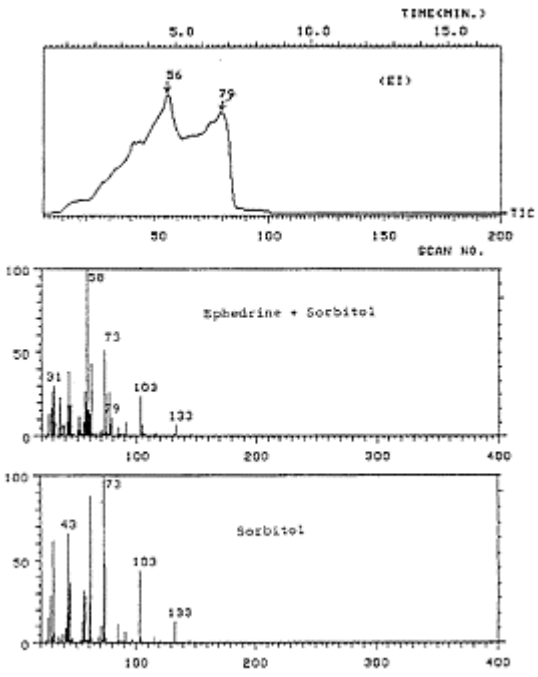

Fig. 22　Total ion chromatogram and EI mass sectra of seizured illicit drug

4．2　Example 2

Example 2 is a case of illicit drug containing ephedrine and sorbitol. The total ion chromatogrm obtained under electron impact was shown in upper figure (Fig. 22). Mass spectra measured at 2 points marked on this chromatogram are middle and lower figure. It is evident that the existence of ephedrine was uncertain by the interference with intense fragment ions from sorbitol.

As compared with this EI mode, total ion chromatogram under CI mode showed that mutual separation of these components during ionization process proceeds in the case of this mixture. This fact was proved from

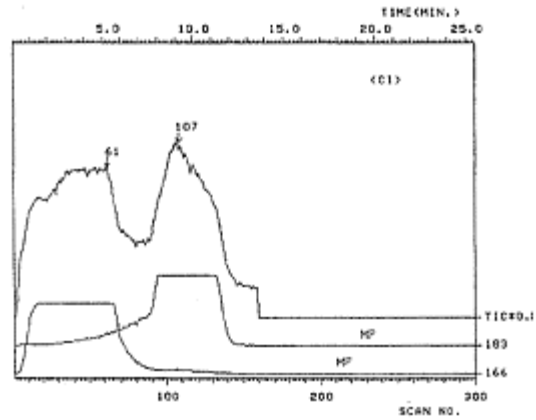

Fig.23　Total ion Chromatogram of seizured illicit drug(DI/CI)

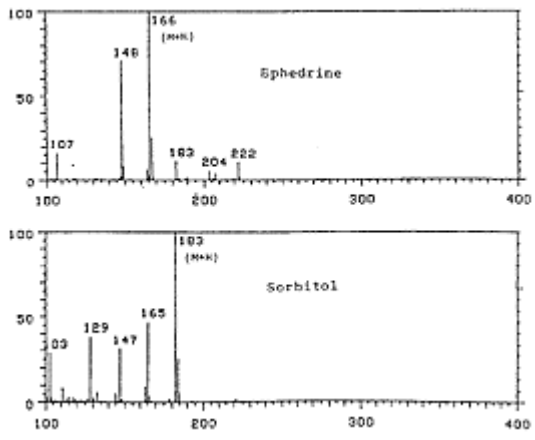

Fig.24　CI mass spectra of seizured illicit drud

the results of mass fragmentgraphy using their prominent quasi molecular ions such as M/Z 166 (for ephedrine) and M/Z 183 (for sorbitol) (Fig. 23).

Mass spectra obtained at 2 points marked on the chromatogram were shown in Fig. 24. From these mass spectra, ephedrine and sorbitol could be easily identified within 5 minutes.

5 Conclusion

Chemical ionization mass spectrometry showed following benefit：

(1) The analysis could be carried out in a minute amount of 0.1 to 1mg scale. Detection limit is generally tens of nanogram level.

(2) It can be operated within a very short period of 5 min.

(3) Pretreatment for the separation is unnecessary, and no influence by diluents in the preparation is observed.

(4) We can use the benefit that it gives mass spectrum of free base in spite of any kind of salt.

References

1）T.A. Gough, P.B. Baker, J. Chromatog. Sci., 20 **289** (1982)

2）T.A. Erettell, J. Chromatogr., 257, **45**(1983)

3）J. M. Chao, R. Saferstein, J. Manura, Anal. Chem., 46, **296** (1974)

4）T. Murata, J.Nakamura, T. Shimoda, T. Sawabe, Bunseki Kagaku, 34, **329** (1985)

5）I.C. Nigam, J.L. Holmes, J. Pharm. Sci., 58 **506**(1969)

(Presented in part at the Meeting on Technical Aids for the Detection of Illicit Drugs, Ottawa, October, 1985)