J Forensic Sci, Apr. 1975, Vol. 20, No. 2

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A Comparison of Some Mass Spectrometric Ionization Techniques Using Samples of Morphine and Illegal Heroin

The precise identification of drugs in body fluids or in illegal preparations may be accomplished by the relatively sophisticated techniques of mass spectrometry [*1,2*] or gas chromatography-mass spectrometry [*2,3*]. The application of these techniques to drug analysis is well documented [*4-6*]. Recently, more attention has been paid to the type of mass spectra produced by different methods of ionization [*7*]. The most useful mass spectrum for many applications is one in which the molecular ion is large and unambiguous. However, some fragmentation is often a desirable feature because this may help to confirm the identity of a compound, differentiate isomers, or assist in elucidating the structure of an unknown. High pressure ionization methods have been found to be particularly useful for drug identification since they often produce the base peak of the spectrum in the molecular ion region, thus serving to identify the molecular weight of the compound. However, some compounds, notably heroin and morphine, fragment easily when ionized with the high pressure reagent gases used so far.

This paper presents some spectra obtained using a novel reagent gas system, 10% nitric oxide in nitrogen, which we have found to be particularly suitable for heroin and morphine analysis, and compares and evaluates these spectra with those obtained using electron impact ionization and isobutane chemical ionization.

High Pressure Ionization

High pressure ionization mass spectra are produced by ionizing a reagent gas in the mass spectrometer source at the relatively high pressure of about 1 torr and allowing the ions formed [*8*] to interact with sample vapor which may be introduced directly via a probe [*9*] or a gas chromatograph [*10,11*]. The reagent gas ions and sample molecules may react to produce sample ions which are then analyzed by the mass spectrometer. For example, methane (CH_4) reagent gas provides abundant CH_5^+ (*m/e* 17) and $C_2H_5^+$ (*m/e* 29) ions which may undergo proton or hydride transfer reactions with sample molecules [*12*]. That is, where M is a sample molecule:

Received for publication 14 June 1974; revised manuscript received 19 July 1974; accepted for publication 5 Aug. 1974.

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$$CH_5^+ + M \rightarrow MH^+ + CH_4$$

$$C_2H_5^+ + M \rightarrow \begin{cases} MH^+ + C_2H_4 \\ [M - H]^+ + C_2H_6 \end{cases}$$

This type of process is called *chemical ionization.* The sample ions produced may fragment because of the excess energy transferred in these processes, but methane chemical ionization spectra usually provide abundant $(M + 1)^+$ and $(M - 1)^+$ peaks which serve to identify the molecular weight of the sample. Similarly, isobutane (iso-C_4H_{10}) reagent gas upon electron impact at high source pressure produces tert-$C_4H_9^+$ (*m/e* 57) ions as the major species [*13*]. Proton addition to sample with even less excess energy transfer than with methane often produces abundant $(M + 1)^+$ ions with very little fragmentation,

$$C_4H_9^+ + M \rightarrow MH^+ + C_4H_8$$

since $C_4H_9^+$ is a weaker acid than CH_5^+ or $C_2H_5^+$.

This process is useful for the analysis of drugs because they often contain an accessible basic site to which the proton may attach. The simplicity of the chemical ionization spectra often permits drug identification to be made relatively easily [*11,14,15*] and allows analysis of mixtures without prior separation by gas chromatography [*16,17*].

When there is no transferable proton available from the reagent gas, hydride abstraction may still occur or an electron may be extracted from a sample molecule by the reagent gas ion ($G^\ddagger$):

$$G^\ddagger + M \rightarrow M^\ddagger + G$$

This type of process is called *charge exchange ionization* [*18*]. The molecular ion may fragment depending upon the amount of excess energy transferred to the sample from the reagent gas ion as it recombines with an electron. This energy is the total recombination energy of the reactant ion minus the ionization potential of the sample molecule. For example, the recombination energy of helium ions ($He^\ddagger$) is 24.6 eV and, since most organic molecules have ionization potentials in the range from 7 to 13 eV [*19*], a considerable excess is available to cause fragmentation of the molecular ion. Helium charge exchange spectra have been found [*18,20*] to be very similar to electron impact mass spectra which generally employ an electron energy of 70 eV. When the recombination energy is only slightly greater than the ionization potential of the sample, less excess energy is available to provoke fragmentation and a simpler spectrum results as, for example, with $N_2^\ddagger$ (from nitrogen gas), where the recombination energy is 15.3 eV. If the ionization potential of the sample is greater than the recombination energy of the reactant gas ion, no charge exchange should occur.

With any reagent gas, addition reactions often occur producing $(M + G)^\ddagger$ ions which may also fragment [*18*].

Recently nitric oxide (NO) has been used [*18,21*] as a high pressure reagent gas. Molecular ions, addition ions $(M + NO)^+$, as well as $(M - 1)$ ions and small amounts of fragmentation have been observed for various compounds. Unfortunately, the NO gas readily oxidizes the mass spectrometer filaments. However, a mixture of 2 to 15 mol% of

NO in N_2 does not appear to have this effect on filament lifetimes. Such mixtures have been found [*22,23*] to produce enhanced molecular ions with retention of useful fragment ions for some compounds. In a 10% mixture of NO in N_2, NO^+ carries approximately 90% of the total ion current and N_2^+ the other 10% at equilibrium. That is, more N_2 may be ionized by the electron beam since there is more present, but the N_2^+ will quickly charge exchange with NO to produce a predominance of NO^+ ions. Therefore, the spectra produced upon introduction of a small amount of sample to this plasma are resulting from interaction of sample with NO^+ with perhaps a small contribution from N_2^+. The recombination energy of NO^+ is approximately 8.3 to 9 eV [*18*].

This paper compares the spectra obtained using a 10% mixture of NO in N_2 to analyze an illegal heroin sample, with the corresponding chemical ionization spectra obtained using isobutane reagent gas and the corresponding 80-eV electron impact spectra. Similar spectra are recorded for a pure morphine sample.

Experimental

All mass spectra were measured on a DuPont 21-491 double-focusing mass spectrometer fitted with a dual electron impact/high pressure ionization source and interfaced to a Varian 2700 gas chromatograph (GC) through a glass jet separator. The source has a separate introduction port for reagent gases. The isobutane and the mixture of 10% nitric oxide in nitrogen were obtained from Union Carbide Corp. and were used at a source pressure of 0.5 to 1 torr. The source temperature was 250°C. The column was 6 ft. by ¼-in. glass packed with 3% OV-101 on 100/120 Chromosorb WHP programmed from 180°C to 280°C and the carrier gas was helium at 40 ml/min.

An illicit heroin preparation was obtained from the Baltimore City Police Department and was extracted with chloroform. The chloroform solution was injected directly onto the column. A portion of the effluent from the column is diverted to a flame ionization detector and the rest to the mass spectrometer. The morphine was obtained as the sulfate and the free base was extracted with chloroform from basic solution. After evaporating the solvent the morphine was inserted directly into the mass spectrometer via the probe.

Results and Discussion

The gas chromatogram of the heroin seizure sample is shown in Fig. 1. In successive runs the four peaks were scanned using electron impact ionization (EI), chemical ionization (CI) using isobutane, and charge exchange (CE) ionization using 10% nitric oxide in nitrogen (10% NO/N_2).

The spectra of Peak 2 were indicative of 6-monoacetylmorphine but were not intense enough to be reproduced here. The EI, CI, and CE spectra of Peaks 1, 3, and 4 are shown in Figs. 2-4, respectively. Ions attributable to the reagent gas in the CI spectra have been omitted.

The EI spectra of methapyrilene (GC Peak 1) and quinine (GC Peak 4) are diagnostically very poor. The base peak in the EI spectrum of quinine at *m/e* 136 results from *a*-cleavage to the nitrogen shown. This facile process produces the same base peak in the CE spectrum. The EI and CE spectra of methapyrilene are also very similar. Again, the peaks at *m/e* 58 represent ions produced by *a*-cleavage, and *β*-cleavage to the thiophene moiety, as shown, leads to ions of *m/e* 97 [*24*]. Although identification of these compounds from these spectra is possible, especially since GC retention information is

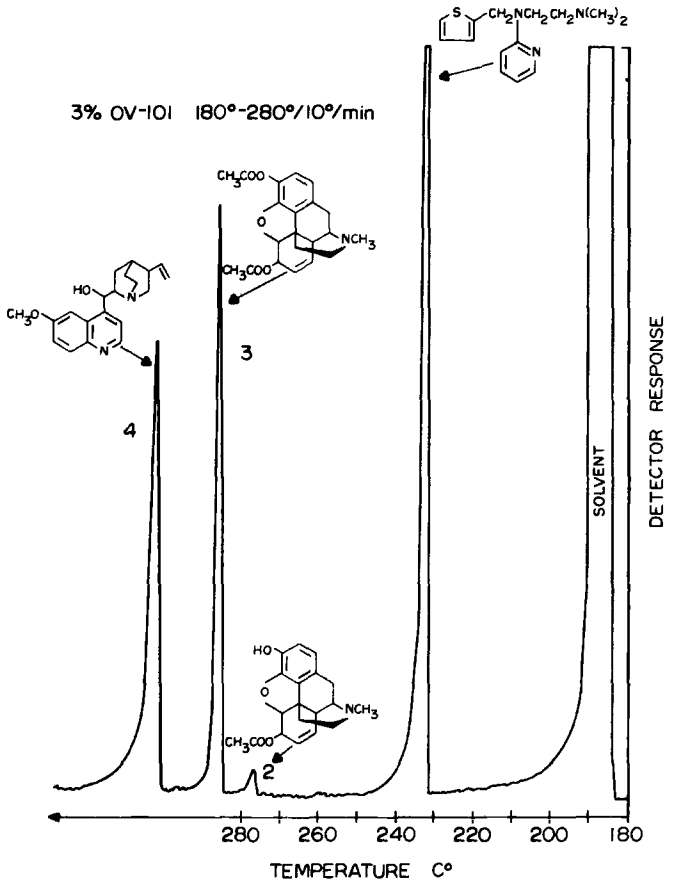

FIG. 1—*Gas chromatogram of heroin seizure sample. Peaks 1, 2, 3, and 4 are methapyrilene, 6-monoacetylmorphine, heroin, and quinine, respectively.*

also available, spectra which more clearly indicate the molecular weights of the compounds are desirable since closely related compounds often yield similar data.

The CI spectra of quinine and methapyrilene display the respective $(M + 1)^+$ ions as the base peaks. There are very few other ions present. The addition of a proton in CI disallows many of the cleavages which result when an electron is abstracted in EI or CE. These CI spectra are diagnostically very useful, although their information content is low.

The base peak in the EI spectrum of heroin occurs at *m/e* 43 ($CH_3C \equiv 0^+$), a mass low enough to be significant in the spectra of many organic compounds. The molecular ion peak is of modest intensity, and structurally significant fragment ions occur at *m/e* 327, 310, and 268.

The CI spectrum of heroin exhibits its base peak at *m/e* 310 which results from loss of the C-6 acetyl group as acetic acid assisted by the allylic double bond. $(M + 1)^+$ ions are of low abundance and no other fragment ions are observed. This has been discussed by other workers [*14,15*].

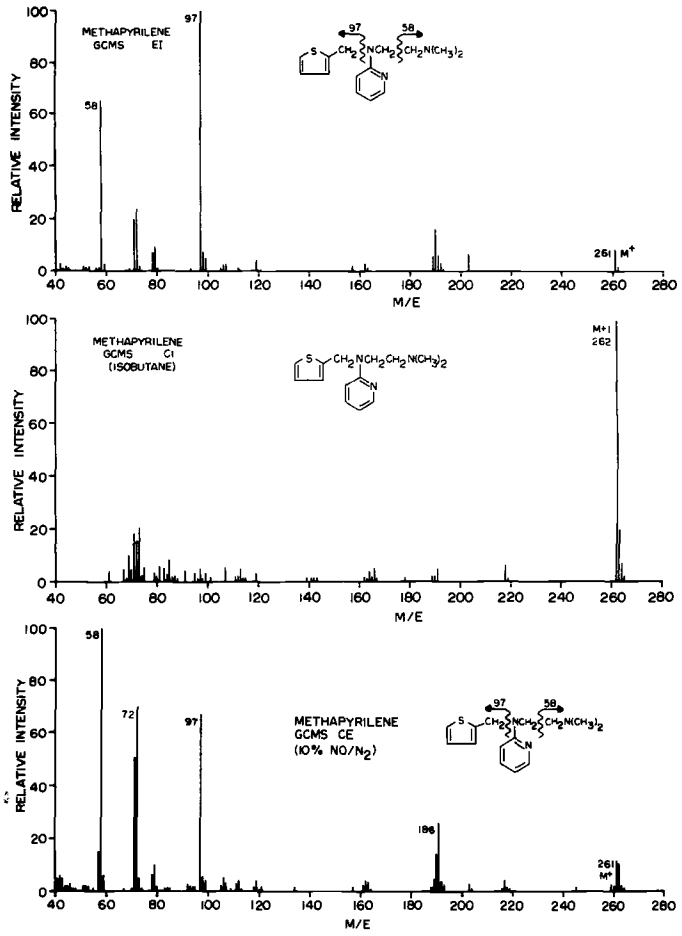

FIG. 2—*Mass spectra of methapyrilene.*

The CE spectrum of heroin displays the desired features discussed above. That is, the base peak is the molecular ion and there is also useful confirmatory structural information in the peaks at *m/e* 327, 310, and 268. Since the ionization potential of the tertiary nitrogen in heroin is less than 8 eV [*19*], charge exchange from NO^+ is presumably taking place here. However, unlike methapyrilene and quinine, *a*-cleavage does not immediately expel a charged nitrogen containing species and fragment the molecular ion since the nitrogen is fixed in a ring.

By way of comparison the EI, CI, and CE spectra of morphine were obtained using a probe sample. The spectra are shown in Fig. 5. The EI spectrum in this case contains more information than the corresponding CE spectrum. The CE spectrum contains essentially only the molecular ion peak group and thus would be more useful for analyzing probe mixture samples. The CI spectrum has similar diagnostic disadvantages

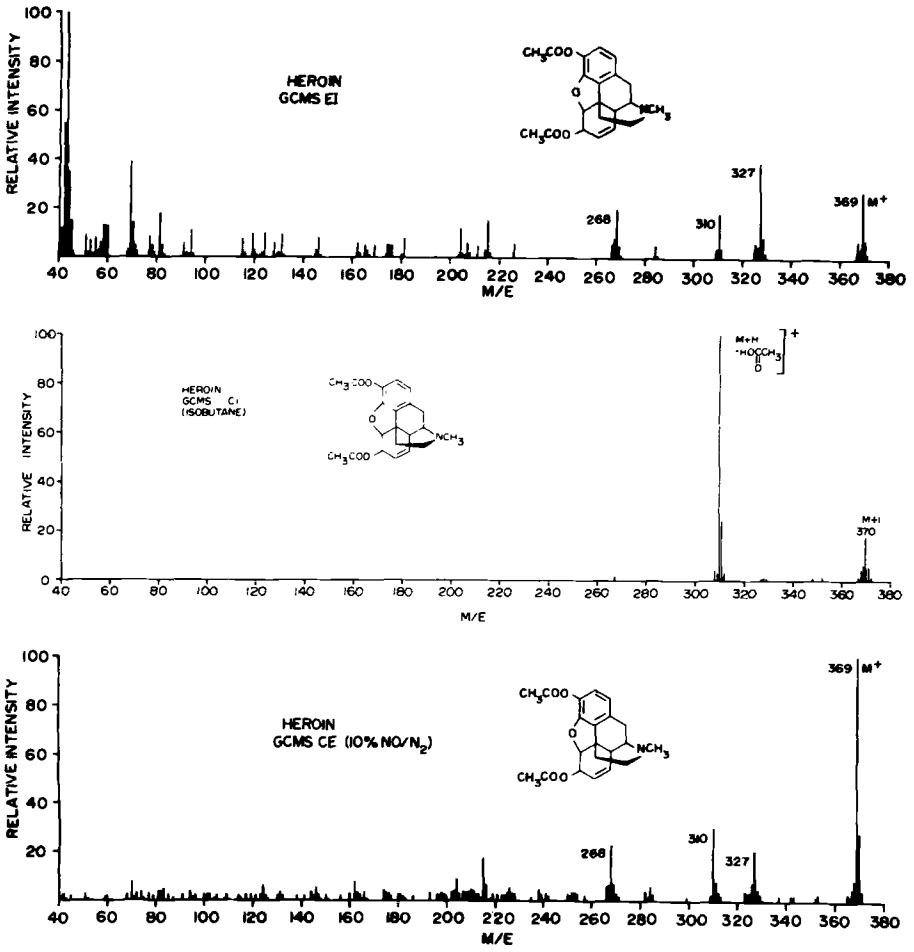

FIG. 3—*Mass spectra of heroin.*

to the CI spectrum of heroin, that is, a facile loss of H_2O assisted by the allylic double bond [*14*] which greatly reduces the intensity of the $(M + 1)^+$ ion.

Conclusions

None of the three ionization modes used produces optimal spectra for all the major constituents of the illicit heroin sample, that is, spectra in which the molecular ion peak is the largest peak and in which a few significant fragment ion peaks occur. However, the appropriate choice of ionization mode can produce a spectrum which unambiguously identifies the molecular weight of a given component of the mixture. Thus, charge exchange ionization with diluted nitric oxide produces the spectrum of heroin which most easily permits the compound to be identified and characterized.

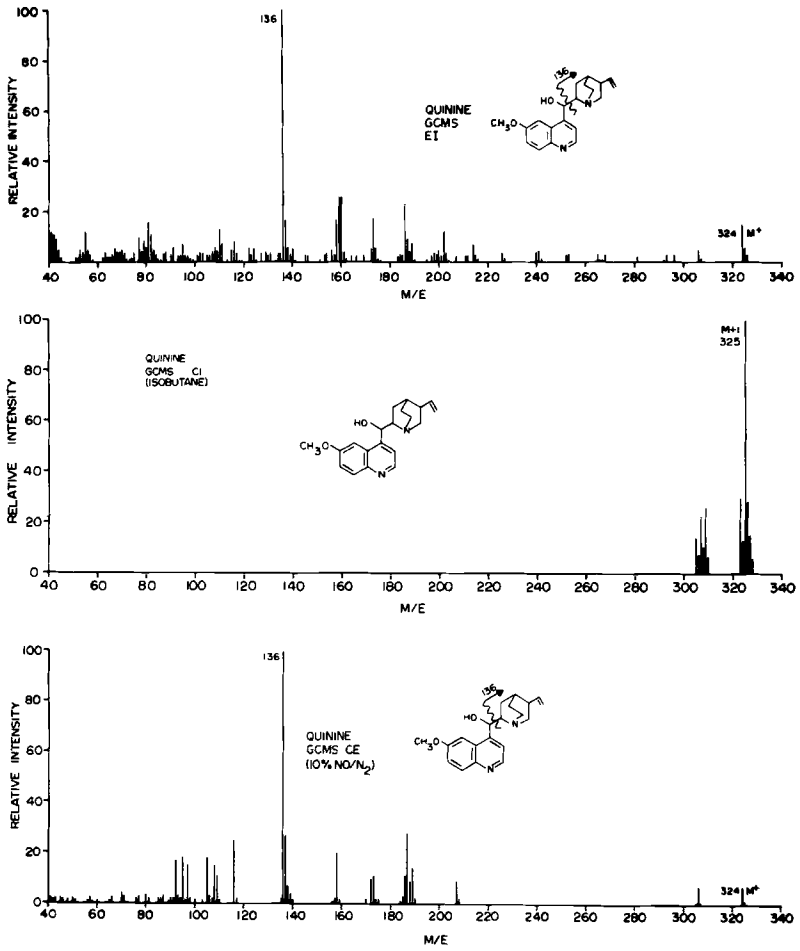

FIG. 4—*Mass spectra of quinine.*

Because the analytical potential of the three techniques varies from compound to compound, the chemist faced with a completely unknown drug or diluent may wish to employ charge exchange ionization as well as electron impact and chemical ionization in order to obtain the most easily interpretable and unambiguous spectrum.

Acknowledgments

We would like to thank Dr. A. Kemppainen of the Baltimore City Police Department for the heroin seizure sample and Dr. Solomon H. Snyder of our Department for the morphine sulfate sample. This research was supported by Public Health Service Grants GM-16492 and KO-4-6M-70417, and by the Andrew W. Mellon Foundation.

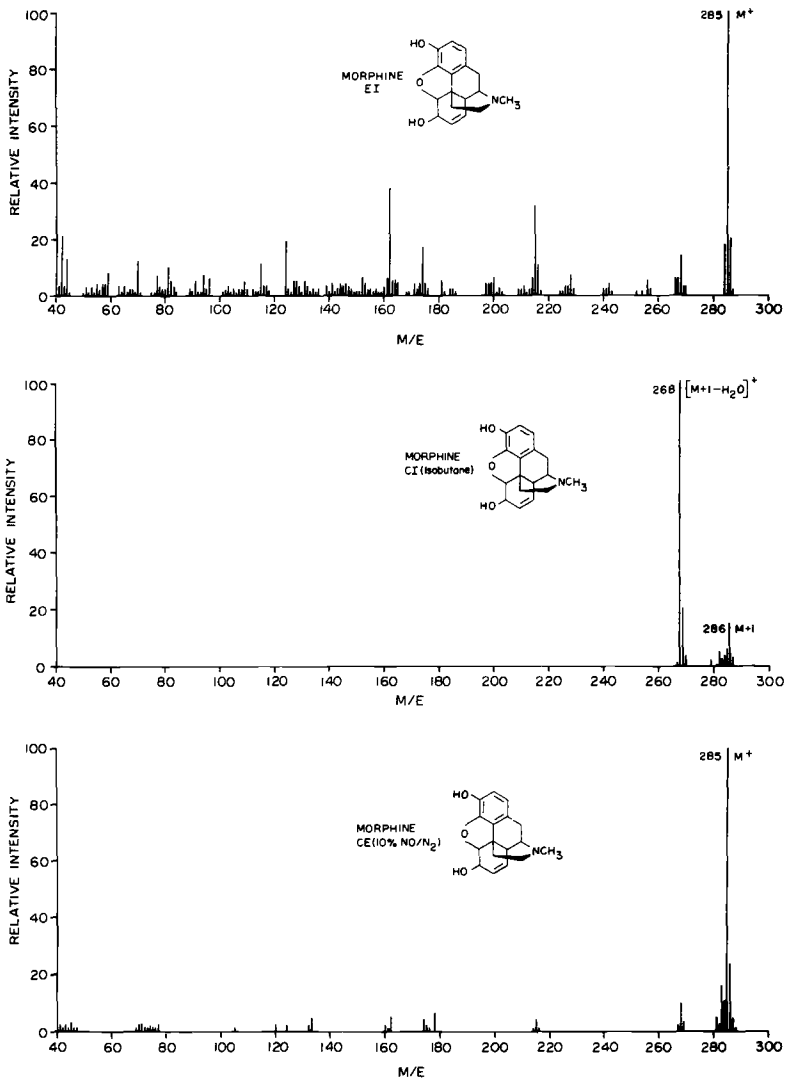

FIG. 5—*Mass spectra of morphine.*

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