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Impurities and Artifacts of Illicit Cocaine

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ABSTRACT: Mass spectra of impurities and artifacts of illicit cocaine are illustrated and discussed. The methods used in the synthesis of the compounds are described and nuclear magnetic resonance data are presented as proof of structure.

KEY WORDS: toxicology, cocaine, chemical analysis

Cocaine is an alkaloid regulated by the Controlled Substances Act in the United States and the Narcotic Control Act in Canada. In Canada, illicit use of cocaine has been steadily increasing. This has resulted in a greater frequency of requests for analysis, both qualitative and quantitative, by law enforcement officials of seized illicit cocaine samples. Coincidentally, defense attorneys have begun to raise the issue of natural versus synthetic cocaine during the course of cross-examination of analysts. These events have necessitated a complete, definitive analysis of the entire cocaine sample.

Cocaine (benzoylmethylecgonine) is a major alkaloid produced by the plant *Erythroxylon coca* along with a number of minor alkaloids containing the ecgonine nucleus. Because cocaine is a diester, one method of purification of the crude leaf extract is by hydrolysis of the alkaloids to ecgonine with subsequent esterification to yield cocaine. Because of incomplete esterification of the ecgonine base or the decomposition of cocaine, various impurities are commonly encountered in illicit cocaine samples, namely, ecgonine, methylecgonine, and benzoylecgonine. In old cocaine samples or in samples stored under harsh conditions, these decomposition products may form a significant part of the cocaine sample. Herein lies the dilemma, for if the sample is quantified by a method that resolves the components and measures solely the cocaine, as does gas-liquid chromatography, the sample may appear to be "cut." However, if a cumulative method such as ultraviolet spectrophotometry is employed, a true cocaine quantification is not obtained. Identification of the impurities provides information as to the purity of the cocaine and allows the comparison and matching of diverse samples.

Of forensic science interest, identification of the common minor alkaloids of *E. coca* provides solid indirect proof that the cocaine is natural. Two of the minor alkaloids frequently encountered in illicit cocaine samples are *cis-* and *trans*-cinnamoylcocaine [*1*]. These substances can also be used to advantage in comparisons of samples.

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In addition, the presence of artifacts in varying amounts may lead to spurious conclusions regarding the origin or treatment of cocaine if the conditions under which the artifacts are formed are not recognized. The artifact methylecgonidine (methylanhydroecgonine) is frequently encountered when the identification of cocaine is accomplished by gas chromatography/mass spectrometry. Ethylbenzoylecgonine is occasionally encountered when ecgonine is present and the sample is worked up as an ethanol solution.

Experimental Procedure

Mass spectra were obtained with a Finnigan 3100 quadrupole mass spectrometer interfaced to a Finnigan 9500 gas chromatograph by a glass jet separator. The mass spectrometer was equipped with a Finnigan Model 6000 data system. The gas chromatograph contained a 1.8-m (6-ft) by 6-mm (1/4-in.) inside diameter glass column packed with 3% OV-1 on 80–100 mesh Chromosorb W (HP). Helium was used as the carrier gas.

Proton magnetic resonance (PMR) spectra were obtained with a Varian EM 360A, 60 MHz spectrometer as deuterochloroform solutions.

Methylecgonine was prepared by the hydrolysis of 100 mg of cocaine hydrochloride in 5 mL concentrated hydrochloric acid/water (1:29) under conditions of reflux for 24 h and extraction of the hydrolysate with diethyl ether to remove the benzoic acid. The water was then removed with a flash evaporator and the ecgonine residue was dried in a desiccator. The residue was then suspended in methanol and filtered to remove methanol-insoluble salts. One part concentrated sulfuric acid was added for every two parts methanol and the solution was heated on a steam bath for 5 min. The solution was then diluted with water and neutralized with sodium carbonate. The methanol/water solvent was removed with a flash evaporator and the residue was redissolved in water. The solution was extracted with diethyl ether and the ether was evaporated on a steam bath, leaving the oily methylecgonine residue.

Trans-cinnamoylcocaine was prepared from methylecgonine by treatment with cinnamoyl chloride. Cinnamoyl chloride was prepared by heating a mixture of 1 g *trans*-cinnamic acid and 4 mL thionyl chloride under conditions of reflux for 30 min and then removing the condensor until the excess thionyl chloride evaporated. To the cinnamoyl chloride residue was added approximately 100 mg methylecgonine in 5 mL pyridine and the mixture was heated under reflux for 1 h. After the reaction solution cooled, 25 mL of 5% sodium bicarbonate was added and the solvent was removed with a flash evaporator. The residue was redissolved in water and the aqueous solution was extracted with diethyl ether. The ether was evaporated, leaving the cinnamoylcocaine residue.

Methylecgonidine was prepared by a method identical to the method used in the preparation of methylecgonine except that the cocaine hydrochloride starting material was hydrolyzed under reflux conditions with concentrated hydrochloric acid for 30 h. The cocaine hydrochloride was obtained from the Health Protection Branch, Department of Health and Welfare, Ottawa, Canada.

Discussion

The present study shows that the compound encountered most consistently during gas chromatographic/mass spectral identification of illicit cocaine is methylecgonidine. This compound is formed as the result of elimination of benzoic acid from cocaine in the heated injection port of the gas chromatograph/mass spectrometer (Fig. 1). This reaction has been confirmed by injecting reagent-grade cocaine hydrochloride into a gas chromatograph/mass spectrometer with the injection port temperature set at 250°C. This resulted in the formation and identification of benzoic acid and methylecgonidine. The compound is also formed during the hydrolysis of cocaine with hydrochloric acid and

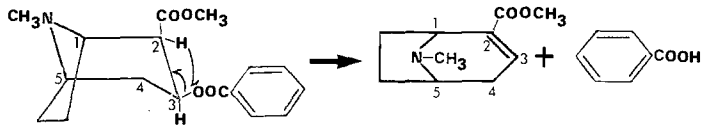


FIG. 1—*Formation of methylecgonidine from cocaine.*

subsequent esterification with methanol. The ratio of methylecgonidine/methylecgonine formed is proportional to the ratio of concentrated hydrochloric acid/water employed during hydrolysis. Use of concentrated hydrochloric acid results almost exclusively in the formation of methylecgonidine. Hydrolysis of cocaine with sodium hydroxide with subsequent esterification with methanol results in the formation of methylpseudoecgonine, not methylecgonine [*2*]. The amount of methylecgonidine encountered during gas chromatographic/mass spectral analysis of cocaine varies appreciably from one sample to the next, even when the same mass spectrometer is operated under identical conditions, and that variation probably indicates the prior presence of methylecgonidine in some cocaine samples as well as its formation in situ.

Although the presence of ecgonidine has been reported in coca extracts [*3*], the formation of methylecgonidine from cocaine as the result of thermal elimination of benzoic acid or by acid hydrolysis leads to the conclusion that this too may have been an artifact of the extraction process. Also, although the compound has been reported as a metabolite of cocaine [*4*], care should be taken in drawing this conclusion, particularly when gas chromatography/mass spectrometry has been used as the method of analysis.

The resolution of the impurities and artifacts encountered in illicit cocaine when an ethanolic solution is injected onto an OV-1 column at 120°C and programmed at 10°C/min to 270°C is illustrated in the reconstructed chromatogram shown in Fig. 2. As with other olefinic compounds [*5*], *cis*-cinnamoylcocaine elutes from the column before *trans*-cinnamoylcocaine [*1*]. The formation of ethylecgonine has been reported as a metabolic artifact when ecgonine is excreted along with ethanol [*6*].

The PMR spectra of cocaine, methylecgonine, and methylecgonidine are illustrated in Figs. 3, 4, and 5, respectively. The assignments of absorption of protons for cocaine and methylecgonine, as illustrated in Figs. 3 and 4, are based on the work of Sinnema et al [*2*]. In cocaine, the protons at C2 and C3 occur at 3.03 and 5.27 ppm, respectively. In methylecgonine, the protons are shifted upfield to 2.75 and 3.85 ppm, respectively, with a hydroxyl proton at 3.60 ppm. In methylecgonidine, the C2 and hydroxyl protons have

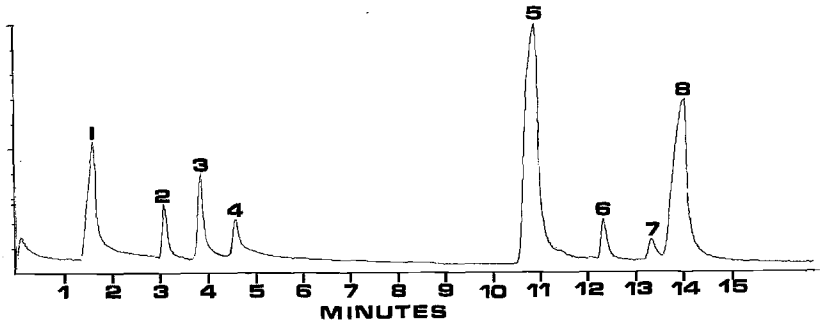


FIG. 2—*Reconstructed chromatogram of an illicit cocaine sample;* (1) *benzoic acid;* (2) *methylecgonidine;* (3) *methylecgonine;* (4) *ethylecgonine;* (5) *cocaine;* (6) cis-*cinnamoylecgonine;* (7) trans-*cinnamoylcocaine; and* (8) *benzoylecgonine.*

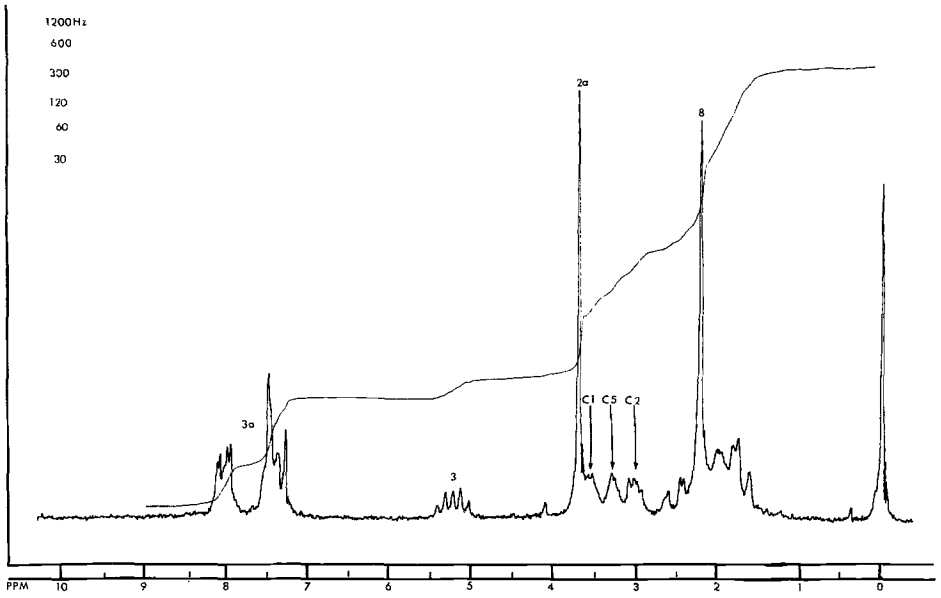


FIG. 3—*The PMR spectrum of cocaine.*

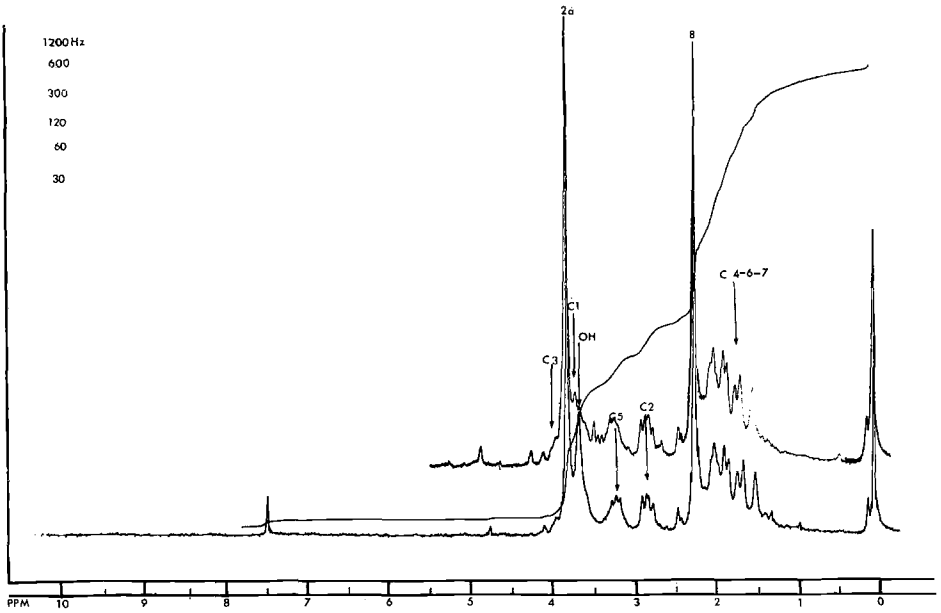


FIG. 4—*The PMR spectrum of methylecgonine.*

both disappeared and the C3 proton has shifted downfield to 7.75 ppm, consistent with a methylene proton. This downfield shift of the C3 proton with the concomitant loss of the hydroxyl and C2 protons confirms the position of the double bond at the C2 position.

The mass spectrum of cocaine (Fig. 6) has peaks at *m/e* 303, 182, and 82 resulting from the fragmentation of the ecgonine nucleus (Fig. 7). The peak at *m/e* 82 is characteristic of most tropanes [*7*]. The peak at *m/e* 182 results from the molecular ion [*8*].

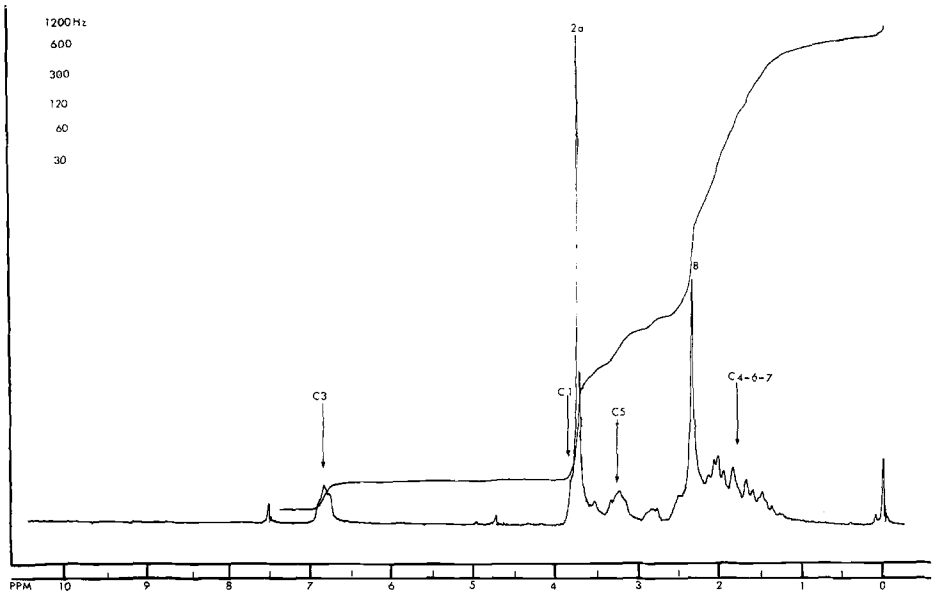


FIG. 5—*The PMR spectrum of methylecgonidine.*

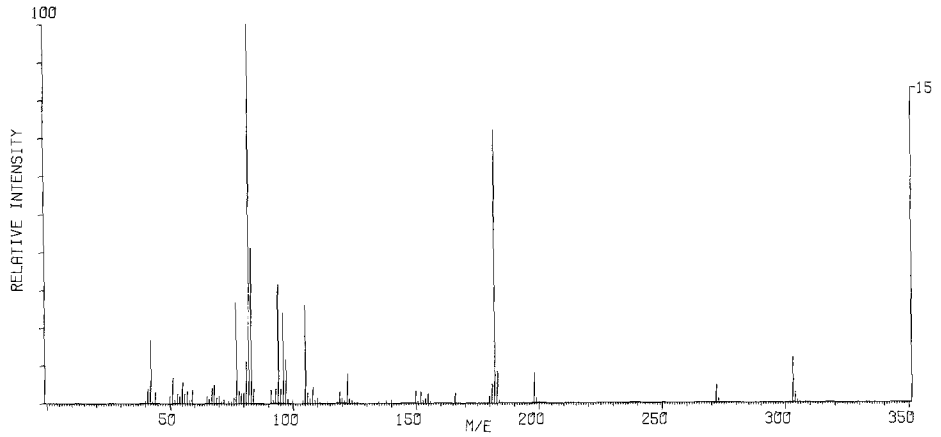
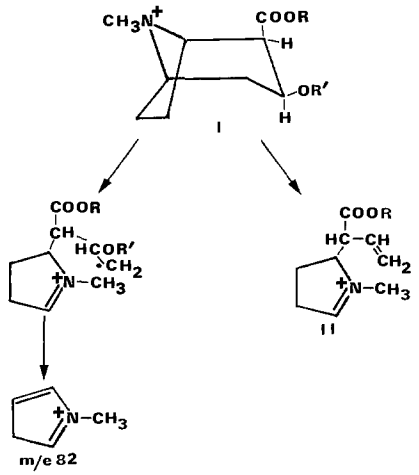


FIG. 6—*Mass spectrum of cocaine.*

In addition, the spectrum contains peaks at *m/e* 105 from the benzoyl ion and *m/e* 77 from the phenyl ion. The mass spectrum of cinnamoylcocaine (Fig. 8) contains ions at *m/e* 82 and 182, as does cocaine. Differences arise because the presence of the ethylene group in cinnamic acid results in an increase of 26 mass units. Thus the molecular ion shifts to *m/e* 329 from 303, the benzoyl ion at *m/e* 105 becomes the cinnamoyl ion at 131, and the phenyl ion at *m/e* 77 becomes the styryl ion at *m/e* 103.

No outstanding differences could be discerned in the spectra of *cis*- and *trans*-cinnamoylcocaine. In the mass spectrum of benzoylecgonine (Fig. 9), the peak at *m/e* 182 in cocaine shifts to *m/e* 168 because of the unesterified carboxylic acid group at C2. In addition, the spectrum has a base peak at *m/e* 124 because of the loss of carbon dioxide from the *m/e* 168 ion. Methylecgonine and ethylecgonine, which have an unesterified hydroxy



	R	R'	m/e ION I	m/e ION II
Cocaine	OCH_3	CO⟨⟩	303	182
Cinnamoylcocaine	OCH_3	COCH=CH⟨⟩	329	182
Benzoylecgonine	H	CO⟨⟩	289	168
Methylecgonine	OCH_3	H	199	–
Ethylecgonine	OCH_2CH_3	H	213	–

FIG. 7—*Mass fragmentation pattern of substituted ecgonines.*

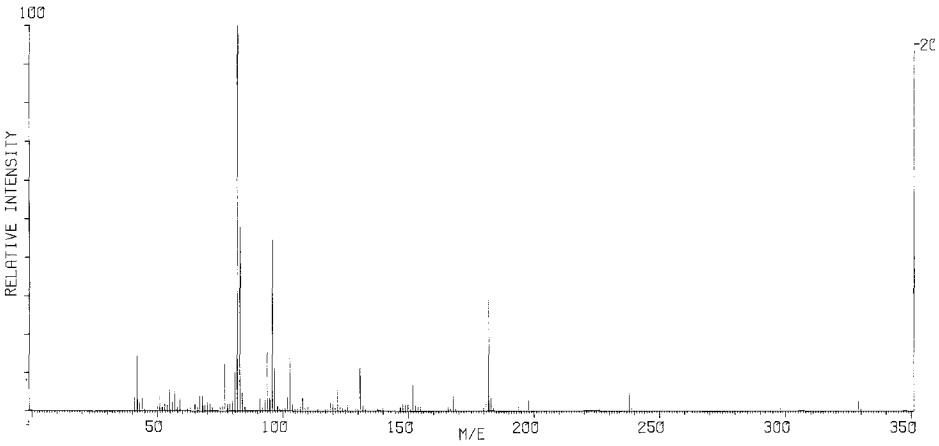


FIG. 8—*Mass spectrum of cinnamoylcocaine.*

group at C3, lack the ion formed as a result of the loss of the acid group through a McLafferty rearrangement (Ion II in Fig. 7) but possess the prominent ion at *m/e* 82. The mass spectra of methylecgonine and ethylecgonine are illustrated in Figs. 10 and 11, respectively. The mass spectrum of methylecgonidine (Fig. 12) differs somewhat from the spectra of the substituted ecgonines because of the olefinic bond at C2. Thus the driving

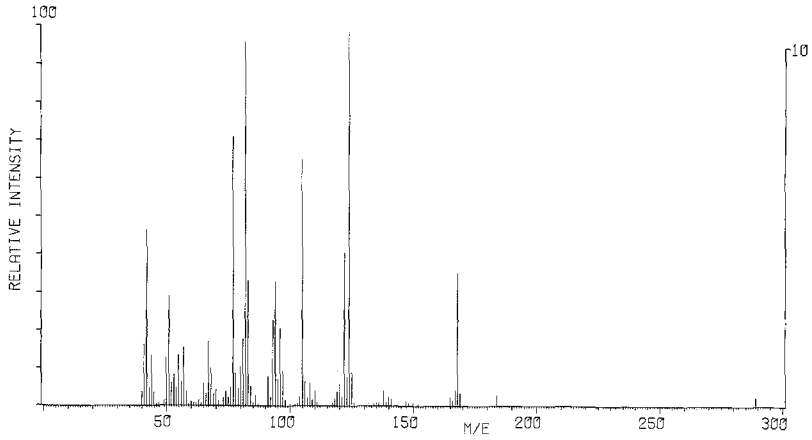


FIG. 9—*Mass spectrum of benzoylecgonine.*

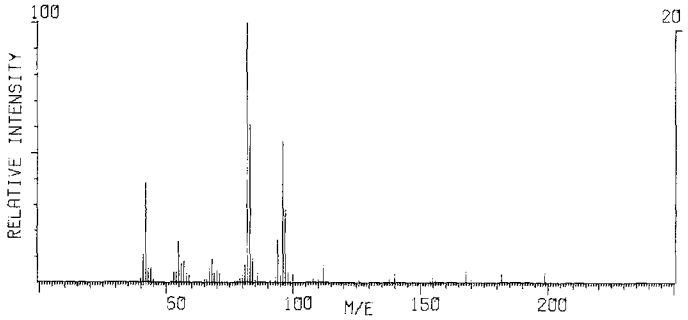


FIG. 10—*Mass spectrum of methylecgonine.*

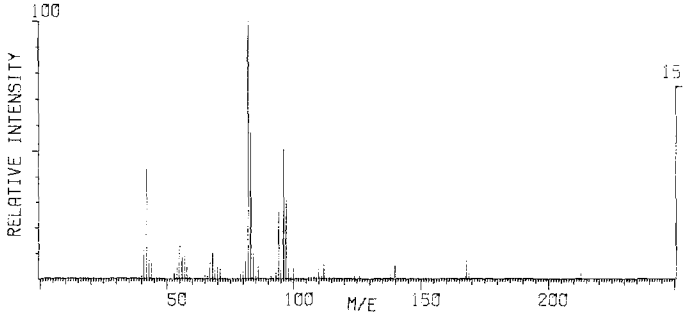


FIG. 11—*Mass spectrum of ethylecgonine.*

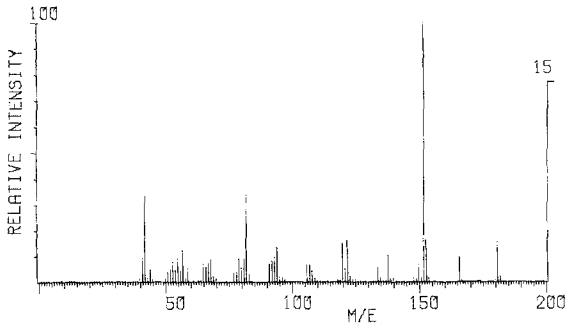


FIG. 12—*Mass spectrum of methylecgonidine.*

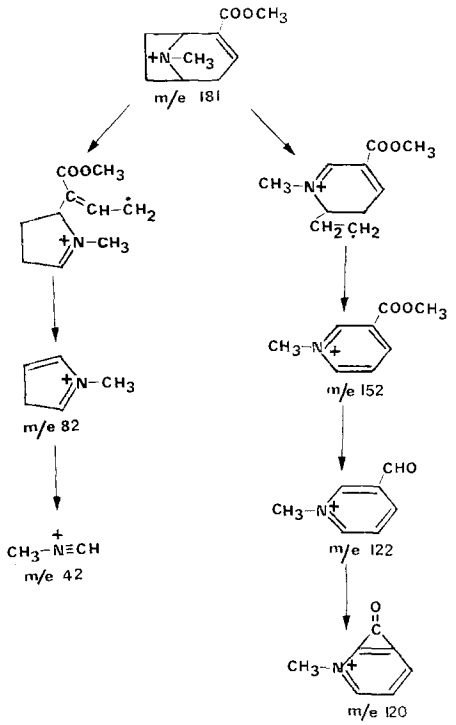


FIG. 13—*Proposed fragmentation pattern of methylecgonidine.*

force of the fragmentation process leading to the formation of the base peak is aromatization resulting in a substituted pyridine and a base peak at *m/e* 152 (Fig. 13). The spectrum does contain the characteristic ions at *m/e* 82 and 42.

Summary

A gas chromatographic/mass spectral analysis of illicit cocaine is described. The mass spectra of a number of impurities and artifacts of illicit cocaine are illustrated and the formation of the impurities and artifacts are discussed. The PMR spectra are presented

as confirmation of the structure of the artifact formed, and the mass spectral fragmentation patterns are discussed.

Acknowledgments

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