Lisa M. Brewer,[1] *B.S. and Andrew Allen,*[2] *B.S.*

N-Formyl Cocaine: A Study of Cocaine Comparison Parameters

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ABSTRACT: *N*-formyl cocaine has been found to be a processing impurity (via potassium permanganate oxidation) in clandestine cocaine processing. Chemical isolation and spectroscopic data are presented. Its occurrence in illicit cocaine samples is examined for its value in sample comparisons. A general discussion of clandestine cocaine processing and permanganate oxidation is included.

KEYWORDS: toxicology, criminalistics, cocaine, drug identification

Examination of drug samples continues to take on new depths and legal implications as the technology available to the forensic chemist expands. In addition to the routine identification of controlled substances, many chemists are conducting further analysis using instrumentation and theoretical chemistry in an effort to compare separate exhibits. Chemical investigations by researchers have led to the development of "signatures" for heroin [*1–16*], amphetamine [*17*, *19–23*], methamphetamine [*18*, *24–28*], and cocaine [*29–36*].[3]

The present study of cocaine is an attempt to identify possible "signature" elements—identifying characteristics that result from clandestine cocaine processing. *N*-formyl cocaine was isolated and identified in illicit cocaine samples. The instrumental identification of *N*-formyl cocaine is presented. Also included is a description of illicit cocaine processing and permanganate chemistry.

Clandestine Cocaine Processing

Figure 1 is a flow chart, developed from intelligence sources and practical considerations of alkaloidal chemistry, [*37*] that depicts illicit cocaine processing.

The flow chart describes three different stages of clandestine cocaine processing. These stages have been given the titles *pasta lab*, *base lab*, and *crystal lab* by the clandestine community. Each stage fulfills the purpose of extracting and purifying cocaine. Starting with 100 to 150 kg of dry leaves, the pasta lab produces 1 kg of dry pasta. This is

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[1]Senior criminalist, California Department of Justice, Berkeley, CA; formerly criminalist, California Department of Justice, Salinas, CA.

[2]Ph.D. candidate, The American University, Washington, DC.

[3]Clark, C. C., DEA Southeast Regional Laboratory, Miami, FL, personal communication, Feb. 1983.

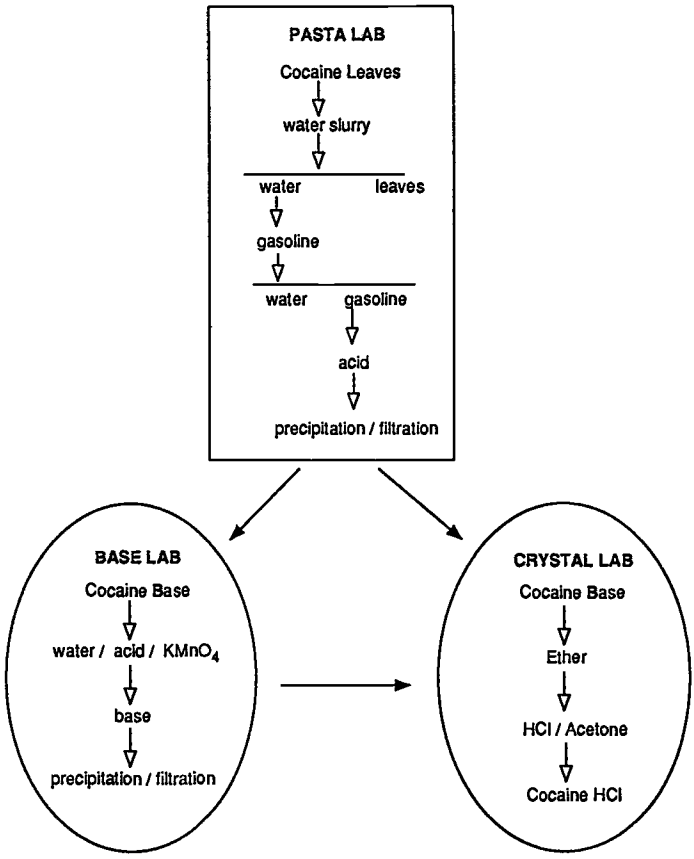

FIG. 1—*Flow chart of illicit cocaine processing.*

accomplished by soaking the dry leaves in water and adding strong base, which will force the nitrogenous alkaloids into an organic phase (gasoline or kerosene). At this point the alkaloidal mixture is composed of cocaine, *cis-* and *trans*-cinnamoylcocaine, tropine, tropacocaine, hygrine, cuscohygrine, ecgonine, benzoylecgonine, methylecgonine, and stereoisomers of truxillines [*38–40*]. This mixture may also contain soluble organic plant waxes, as well as benzoic acid, cinnamic acid, methyl benzoate, and truxinic and truxillinic acids [*29*]. With the addition of a mineral acid (such as sulfuric or hydrochloric acid), the organic solution of alkaloids is precipitated as alkaloid salts. Except for small quantities of entrained impurities, the alkaloids are separated from the nonnitrogenous compounds.

The crude cocaine salt produced in the pasta lab is passed to the base lab or directly to the crystal lab. The purpose of the base lab is further purification of the alkaloidal mixture. This is accomplished by potassium permanganate oxidation of *cis-* and *trans*-cinnamoylcocaine. Other alkaloids and entrapped plant oils will be attacked more quickly than cocaine. The crucial step in the base lab is deciding when to stop the oxidation process via alkali addition. Overoxidation results in cocaine loss, that is, the conversion of cocaine to *N*-formyl cocaine. This translates into reduced drug profits. Since it is not always profitable, the base lab stage is sometimes omitted.

The final stage occurs in the *crystal lab*, where the crude cocaine base is converted into cocaine hydrochloride. A solvent, such as ether, is used to dissolve the crude cocaine

base. These solvents may be found in cocaine hydrochloride samples and present another comparison parameter.[4] The next step is the addition of aqueous hydrochloric acid dispersed in a bridging solvent such as acetone. The resulting white, often flocculent, cocaine precipitate is collected by filtration.

Experimental Section

Instrumentation

Nuclear magnetic resonance (NMR) hydrogen (^1H) spectra were obtained on a Nicolet (Fremont, California) 200-MHz spectrometer. Tetramethylsilane was used as an internal standard. Mass spectra (MS) were acquired on a Hewlett-Packard (Palo Alto, California) spectrometer. Electron impact (EI) mass spectra were collected at an ionizing potential of 70 eV and a source temperature of 200°C. Sample introduction into the mass spectrometer was accomplished via gas chromatography (GC). The gas chromatograph was fitted with a 25-m by 0.30-mm-inside-diameter fused silica capillary column coated with 5% phenylmethyl silicone. Programed runs were conducted by starting at 100°C, holding for 2 min, ramping at 15°C/min at 300°C, at which point there is no hold. Infrared (IR) spectra were recorded as a neat oil between potassium bromide (KBr) windows on a Perkin-Elmer Fourier transform spectrometer.

Standard

N-formyl cocaine was synthesized by a modified procedure of Banholzer et al. [*41*]. One gram of cocaine hydrochloride was added to an aqueous solution of 1% potassium permanganate ($KMnO_4$) (0.5 g in 50-mL of H_2O). After swirling the mixture and allowing it to stand for 15 min, the solution was extracted with 50 mL of dichloromethane. The organic layer was back extracted with 0.1*N* sulfuric acid (H_2SO_4). Solvent evaporation produced a 20% yield of *N*-formyl cocaine as an oil. Confirmation was made by IR, MS, and NMR.

Sample Analysis

An amount of sample equivalent to 0.5 g of illicit cocaine was placed in a 15-mL glass-stoppered test tube. The sample was dissolved in 2 mL of 0.5*N* sulfuric acid, and then 2 mL of diethyl ether was added. The two-phase solution was shaken vigorously and allowed to separate on standing. The ether layer was removed and placed into a new test tube. A second 2-mL portion of acid was added to the ether, followed by shaking, and then the ether was placed into a new test tube. The ether solution was evaporated to 0.5 mL and approximately 1 to 2 μL was injected into the GC/MS.

Results and Discussion

N-*Formyl Cocaine*

Figure 2 illustrates the reconstructed total ion chromatogram of neutral impurities isolated from clandestinely processed cocaine. The major component is *N*-formyl cocaine, whose spectra via nominal resolution mass spectrometry (Fig. 3), Fourier transform infrared spectrometry (Fig. 4), and Fourier transform proton nuclear magnetic resonance spectrometry (Fig. 5) were identical with those of material synthesized from standard

[4]Kiser, W. O., DEA Southeast Regional Laboratory, Miami, FL, personal communication, July 1986.

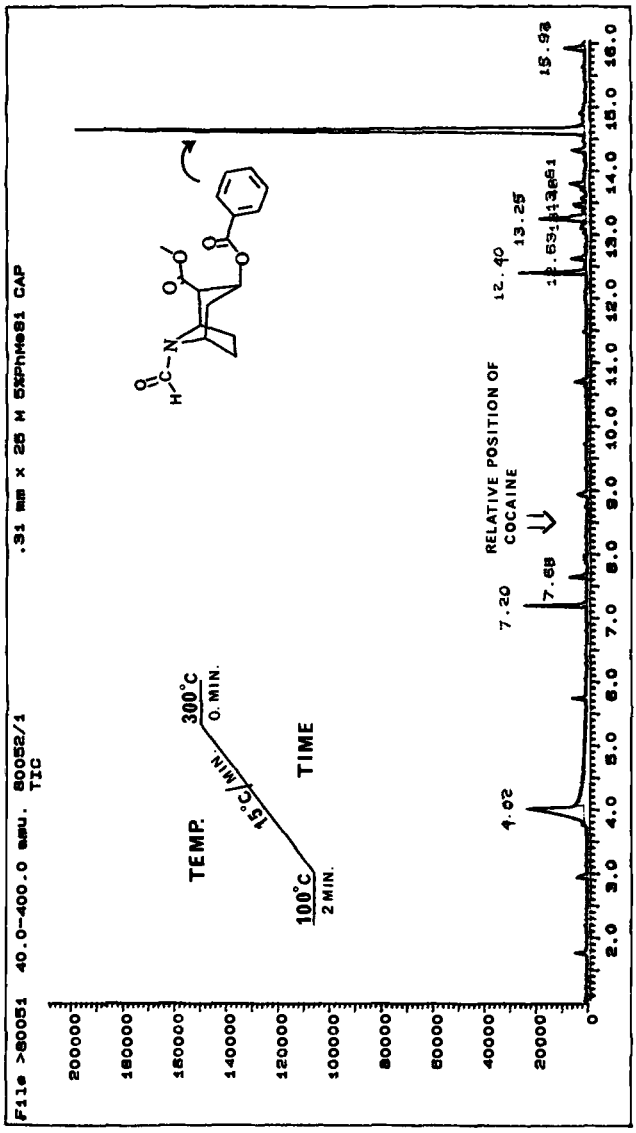

FIG. 2—*Reconstructed total ion chromatogram via GC/MS, programed from 100°C at 15°C/min to 300°C, representing neutral impurities isolated from acid extraction of clandestinely processed cocaine. The major neutral impurity is* N*-formyl cocaine (VII); the retention time is 14.66 min.*

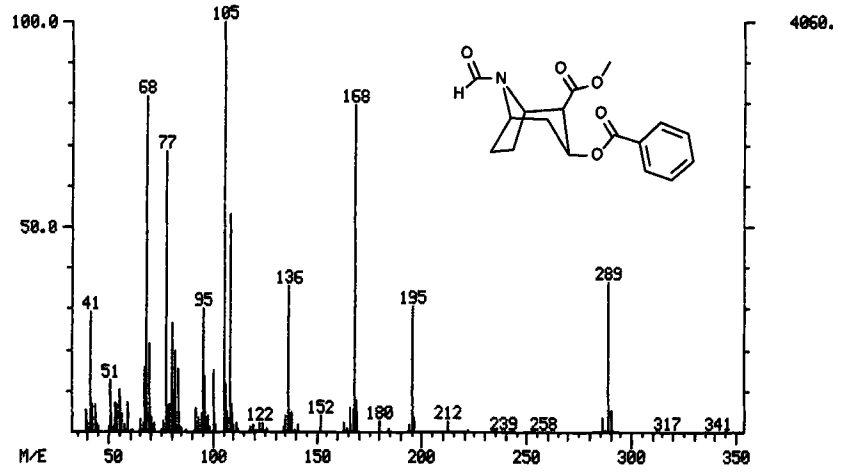

FIG. 3—*Nominal resolution mass spectrograph of* N-*formyl cocaine (VII),* $C_{17}H_{19}NO_5$ = *317* m/z, *showing an initial loss of carbon monoxide with hydrogen migration (317 − 28 = 289* m/z). *The sample was introduced via GC.*

cocaine. Spectral data interpretation is also consistent with this assignment. The ^{1}H NMR (Fig. 5) shows time-dependent states, that is, a doubling of all resonance lines, typical of amide-hindered rotation through equilibrium. The IR spectrum (Fig. 4) has three distinct carbonyl absorptions: two ester carbonyls (1742 and 1719 cm^{-1}) and one amide carbonyl (1668 cm^{-1}). The EI-MS data (Fig. 3) have a molecular ion of 289 *m/z* and subsequent fragmentation consistent with *N*-formyl cocaine.

GC/MS analysis of 100 random cocaine cases revealed that 60% of the samples contained detectable levels of *N*-formyl cocaine. The fact that 40% lacked *N*-formyl cocaine implies that not all clandestine cocaine processing includes the base lab stage with its oxidation step.

Chemistry of Permanganate Oxidation

Cis- and *trans*-cinnamoylcocaine often constitute major impurities in illicit cocaine. During the base lab purification process, potassium permanganate oxidizes cinnamoylcocaine (I) to ecgonine (II), as illustrated in Fig. 6. Ecgonine is extremely water soluble, allowing the clandestine chemist to isolate cocaine from ecgonine by precipitating cocaine from a basic solution or by organic extraction.

However, not only the cinnamoyl portion of these molecules is under attack by the permanganate. Cocaine (III) is subject to cleavage of the 2-carbomethoxy or the benzoyloxy groups (Fig. 7) to yield benzoylecgonine (IV), ecgonine methyl ester (V), or ecgonine (II). These compounds are also products of acid or base hydrolysis and have been used for comparative signature purposes.[5]

In addition, permanganate may oxidize the *N*-methyl group of cocaine to an *N*-formyl moiety producing *N*-formyl cocaine (Fig. 8). Although some confusion has appeared in the literature regarding the resultant product of permanganate oxidation of tropane alkaloids [*42,43*], our spectroscopic data indicate that *N*-formyl cocaine (VII) is the resultant compound. Subsequent hydrolysis of *N*-formyl cocaine may lead to norcocaine (VIII). However, mechanistic studies indicate that the nor- series results from hydrolysis of the Schiffs base (VI) [*44*]. The nor- series of processing impurities has been exploited

[5]See Footnote 3.

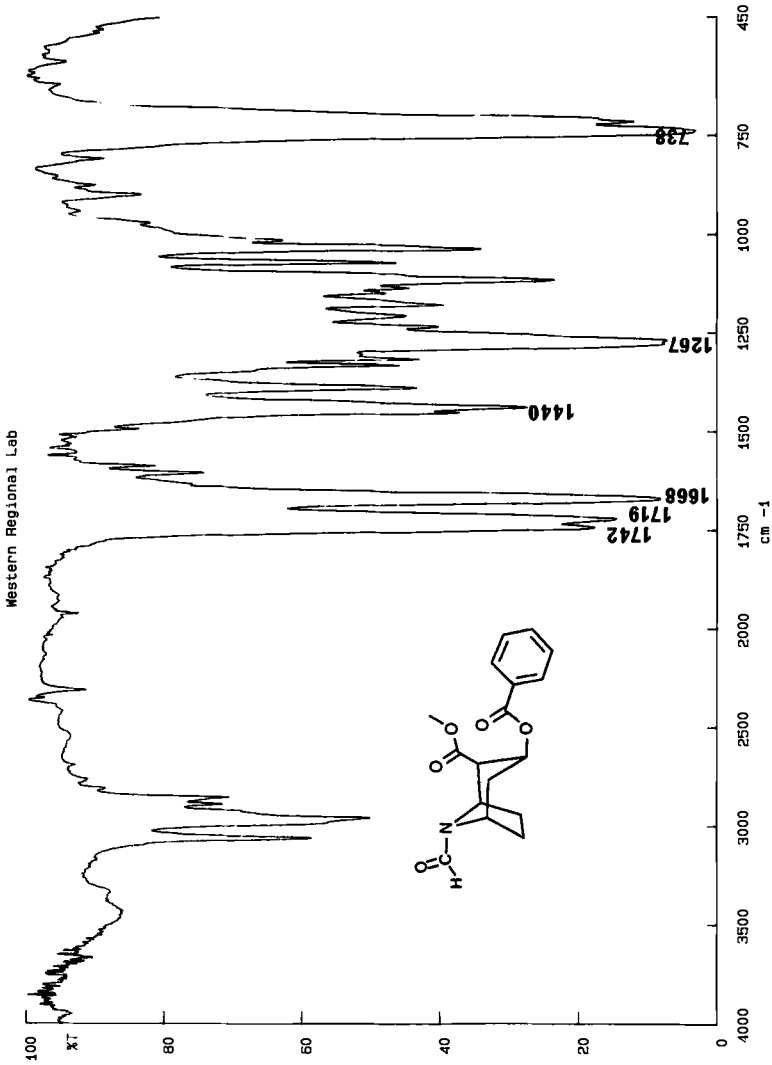

FIG. 4—*Infrared spectrograph of* N*-formyl cocaine (VII), obtained as a neat oil on potassium bromide windows, showing ester carbonyls of 2-carbomethoxy and 3-benzoyloxy at 1742 and 1719 cm*$^{-1}$*. The amide carbonyl of the* N*-formyl absorbed at 1668 cm*$^{-1}$.

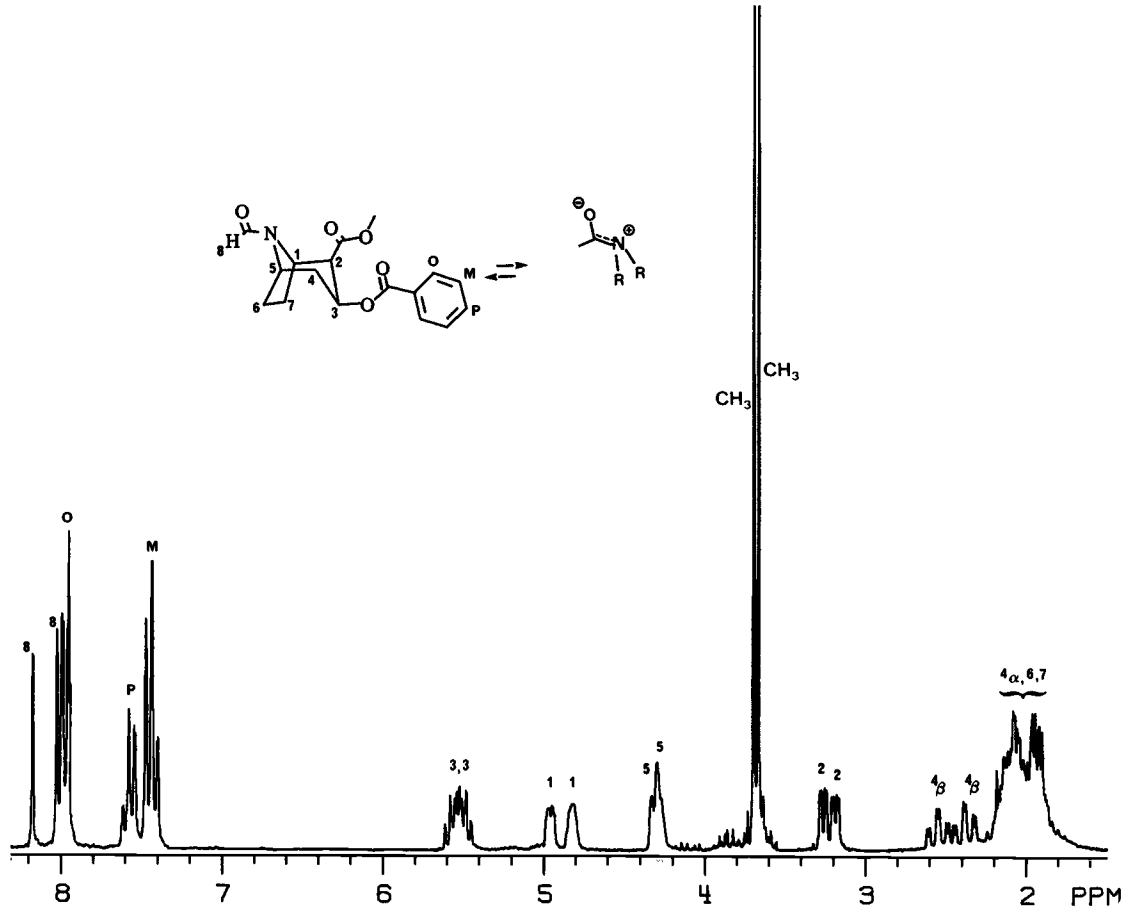

FIG. 5—*Nuclear magnetic resonance spectrograph of* N-*formyl cocaine (VII), obtained at 200 MHz in deuterated chloroform ($CDCl_3$) with tetramethylsilane (TMS) as zero reference. The double resonances are due to hindered rotation of the amide bond; that is, the* N-*formyl hydrogen No. 8 resonates at 8.01 and 8.18 ppm.*

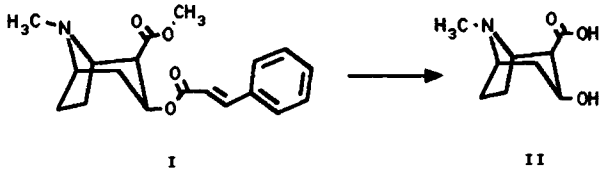

FIG. 6—*Potassium permanganate oxidation of clandestine cocaine paste used to remove cinnamoylcocaine (I). The product is ecgonine (II), an alkaloid easily removed from cocaine because of their differing solubilities.*

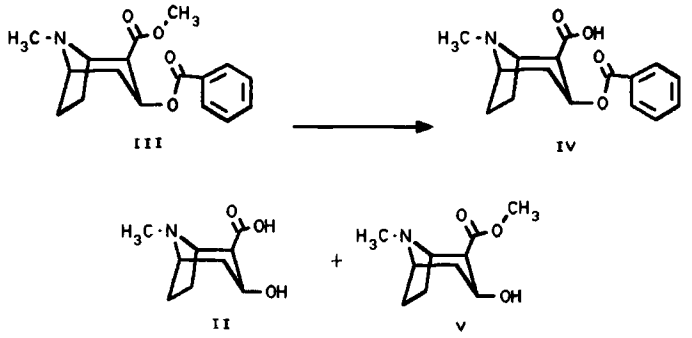

FIG. 7—*Persistent oxidation of clandestine cocaine paste with permanganate, oxidation of cocaine (III) to benzoylecgonine (IV), ecgonine (II), and methylecgonine (V).*

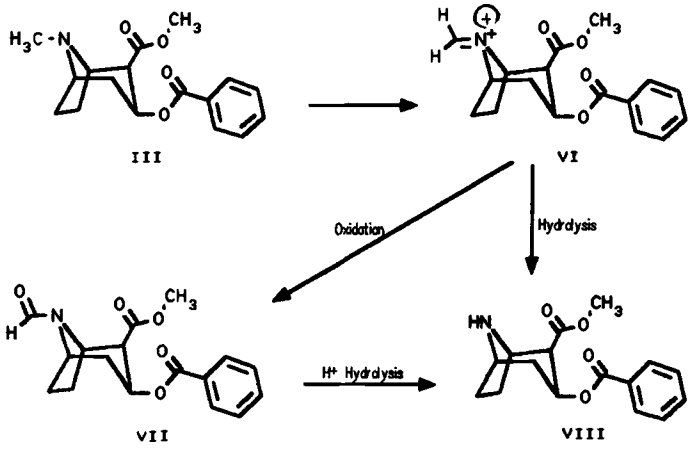

FIG. 8—*Oxidation of cocaine (III) affected at the* N*-methyl to yield the Schiff base intermediate (VI). Oxidation of (VI) produces* N*-formyl cocaine (VII), while hydrolysis of (VI) and (VII) yields norcocaine (VIII).*

by J. Moore et al. in connection with heroin signatures [*2*]. In the case of norheroin, however, other chemical influences such as peroxides in ether facilitate *N*-demethylation [*2,6*].

Conclusions

The study presented shows the value of *N*-formyl cocaine as a means to characterize illicit cocaine samples. Its origin is through an illicit cocaine processing procedure using potassium permanganate to oxidize impurities. Its absence indicates that the permanganate oxidation step was not employed. Our analytical data demonstrate that this omission frequently occurs, since only 60% of the samples contained *N*-formyl cocaine.

It may be concluded that samples originated from dissimilar clandestine cocaine processing when one sample contains *N*-formyl cocaine and another does not. Further sample comparison is not necessary in this case. The presence of *N*-formyl cocaine in compared samples indicates which ones were processed with potassium permanganate. However, their commonality or batch origin is not conclusive. Further investigation of solvent processing impurities,[6] trace alkaloid impurities [*31–36*],[7] nor- series impurities [*2*], and truxinic/truxillinic acid impurities [*29,30*] should be conducted in order to determine if the samples are from a common batch origin.

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Address requests for reprints or additional information to
Lisa M. Brewer, Criminalist
California Department of Justice
DNA Laboratory
c/o Lawrence Berkeley Laboratories, MS 934-47A
Berkeley, CA 94720