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Fourier Transform Infrared Analyses of Some Particulate Drug Mixtures Using a Diamond Anvil Cell with a Beam Condenser and an Infrared Microscope

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ABSTRACT: Although the diamond anvil cell (DAC) has been used in many forensic science laboratories for the analysis of trace evidence, few applications of this technique for the analysis of controlled substances have been reported. This may be due to both an unfamiliarity on the part of forensic drug chemists with this accessory and the nature and quality of spectra that result from use of a DAC on a dispersive instrument. Along with low energy throughput, which results in relatively high noise levels, strong broad diamond absorptions occur. With the use of a Fourier transform infrared instrument, these do not present a problem and nanogram quantities of materials can be analyzed when the DAC is used with an infrared microscope. Since single crystals can be sampled with the DAC, simple physical separations (involving particle-picking) can be used in certain cases to isolate drugs from particulate mixtures for infrared analysis. This method is especially useful for some "difficult" mixtures and residues, and several examples of such analyses involving samples of forensic science interest are presented.

KEYWORDS: criminalistics, drug identification, spectroscopic analysis, infrared spectroscopy, FTIR, diamond anvil cell, infrared microscope, particle-picking

The high-pressure diamond anvil cell (DAC) with a beam condenser has been used in forensic science laboratories since the early 1960s [*1,2*] for infrared analysis of paint [*2–7*], fibers [*2,8–10*], explosive residues [*11–15*], and other types of trace evidence [*2,7,16–22*]. Most of these analyses were performed using dispersive instruments [*1–5,8–18*] although, more recently, Fourier transform infrared (FTIR) spectrometers have also been used [*6,7,10,15,19–22*]. Few applications of this technique for the analysis of controlled substances have been reported, however, which may be due to an unfamiliarity with the DAC on the part of many forensic drug chemists. Another factor could be the nature of the spectra that result from use of a DAC on a dispersive instrument. Because of low

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energy throughput, spectra having relatively high noise levels result, even when collected under low resolutions. In addition, the presence of strong broad diamond absorptions in these spectra may make interpretation of data difficult, especially when comparing such spectra with those collected by other means. Forensic drug chemists have thus tended to use more conventional methods for infrared microsampling, such as the preparation of KBr micropellets.

With the use of a DAC on an FTIR instrument, the diamond absorptions are not a serious problem since they are compensated for by ratioing the sample scan to that of the empty DAC, and spectra having a "normal" appearance result. This feature and the high signal-to-noise ratio possible with an FTIR instrument have eliminated most of the difficulties previously associated with DAC analyses. One other minor drawback of the DAC has been the lack of spectral data for the 2300 to 1900 cm^{-1} region, where the strongest diamond absorptions occur. Even with an FTIR instrument, the thicknesses of the diamond anvils of the high-pressure DAC preclude an observation of most absorptions in this region. These absorptions can be observed using a low-pressure DAC, which became commercially available in 1984, because its anvils are not as thick as those of the high-pressure cell.

The low-pressure DAC can also be used as a sampling device for an infrared microscope [*23*]. In effect, this combination extends the range of DAC analyses to much smaller samples, the sizes of which are limited only by diffraction. Using a beam condenser, a sample covering the entire anvil face (approximately 0.5 mm or 500 μm in diameter) is desired, and this typically corresponds to a few micrograms of material; with an infrared microscope, samples having dimensions as small as 10 × 10 μm—corresponding to 10 ng or so of material—can be analyzed (10 μm is the wavelength corresponding to 1000 cm^{-1}).

In order to isolate a particular substance from a mixture for infrared analysis, the forensic chemist has traditionally relied upon "wet-chemical" (extraction/partition) methods or preparative chromatography. Using a DAC, single crystals or individual particles of particulate mixtures can be analyzed. A very useful alternative to chemical or chromatographic methods of isolating substances for infrared analysis is thus possible in some cases, involving simple physical separations. For this, a powder mixture is viewed with a stereomicroscope and a particle of interest is removed from this powder and mounted in the DAC. In many cases, the particles of interest will exhibit distinct microscopic features based upon morphology, texture, color, size, and so forth, which allow them to be differentiated from other components in the mixture.

This particle-picking method of sampling has several advantages over conventional time-honored isolation techniques. For some particulate mixtures involving very similar compounds, it may be the *only* practical means of obtaining usable quantities of analyte. For other "difficult" mixtures which require lengthy isolation procedures, particle-picking offers a considerably faster alternative. Unlike some separation methods, an a priori knowledge of the chemical properties of the non-analyte components is not required. For macroscopic samples, the quantity of material sampled is an insignificant fraction of the total material and the analysis is essentially a nondestructive one; for some residues, a significant fraction may be involved, but samples can be recovered from the DAC following an analysis if required.

From an informational standpoint, this method of sampling also has advantages since the analyte is not altered in any manner prior to analysis. With extraction/partition methods or preparative chromatography, for example, the analyte must be dissolved in an appropriate solvent. Following the isolation procedure, the analyte may not necessarily exist in its original form. This may be intentional, as when the salt of a compound is converted to its free acid or base form, but other alterations may also occur in the process of recovering the analyte from solution. These may include a failure of the analyte to recrystallize (that is, the formation of a noncrystalline glass or partial glass), recrystal-

lization to a different crystal form or a mixture of forms due to polymorphism, changes in the hydration state of the crystal, or the formation of a complex between analyte and solvent [*24,25*]. All of these alterations affect the infrared spectrum of an analyte, and information about its original form may be lost. This information may be important for intelligence purposes, in quantitative analyses, in comparing exhibits and, in a few cases, may be required because the statutes governing a particular substance distinguish between different forms.

While not as common, transformations may also occur during spectroscopic sample preparation using conventional methods. With the use of KBr matrices or substrates, ion exchange or other reactions between analyte and KBr (such as oxidation of bromide anion to free bromine) can occur. Since the DAC is a matrix-free sampling method involving an essentially inert substrate, such reactions are not a problem.

The particle-picking method of sampling is an art, but one that is easily mastered with some practice—similar manipulations are performed regularly by forensic trace analysts. While not a panacea for all of the difficulties encountered by forensic chemists faced with complex mixtures, this method does provide a very useful means of obtaining spectra of substances in otherwise intractable matrices in certain cases. In addition, it may occasionally be useful for some "ordinary" samples when knowledge of the original form of a substance is desired or when problems with sample alteration are anticipated. Several examples of such DAC analyses involving samples of forensic science interest are presented. Both a beam condenser and an infrared microscope were used, and a comparison of these two sampling modes is discussed.

Experimental Procedure

Instrumentation

A high-pressure DAC (High Pressure Diamond Optics, Inc.) was used with an Analect 4X beam condenser on an Analect FX-6200 FTIR spectrometer. A broad-band mercury-cadmium-telluride (MCT) detector was used on this spectrometer, which is described in more detail elsewhere [*19*]. A low-pressure (miniature) DAC (High Pressure Diamond Optics, Inc.) was used with a Laser Precision Analytical XAD Plus infrared microscope coupled to a Laser Precision Analytical RFX-40 FTIR spectrometer. The RFX-40 instrument was equipped with a high-temperature water-cooled source and all data were collected at a 4 cm^{-1} resolution using the standard (medium Norton-Beer) apodization function. A narrow-band MCT detector was used on the microscope, and variable rectangular-shaped apertures were formed using four adjustable knife edges. More details of the microscope, which was operated exclusively in the transmittance mode, are given elsewhere [*26*].

Both FTIR systems were purged with dry nitrogen, using a second separate purge stream for the microscope. Unless otherwise indicated, 250 scans were collected for both backgrounds and samples with the beam condenser system and 100 scans for the microscope system. Interferometer gains of 8 to 16 were used for the FX-6200, while gains of 1 or 1R ($R = \sqrt{2}$), depending upon the size of the aperture, were used with the microscope. A few samples were also analyzed with the high-pressure DAC/beam condenser system mounted in the RFX-40 instrument, using a broad-band MCT detector. Interferometer gains of 32R or 64 were used and 500 scans were collected for backgrounds and samples.

Sampling

Powder mixtures to be analyzed were spread onto a clean surface and examined with a stereomicroscope at magnifications of between $\times 15$ and $\times 40$, depending upon the

sizes of the particles involved. Appropriate standards of the compound of interest were examined in a similar manner. Particles were removed and mounted onto the surface of one of the anvils of the DAC using either a probe or a pair of microforceps; the former was usually used for smaller particles. On occasion, both utensils would be used together for dissecting particles or facilitating transfer of small particles to the anvils.

For sampling with the beam condenser system, particles were chosen so that when flattened, the entire anvil surface would be covered. For a single particle, this normally required minimum sample dimensions of approximately one third to one half of the diameter of the anvils (that is, particle sizes of at least 0.2 mm or 200 μm). For sampling with the microscope, particles were flattened so as to cover at most three quarters of an anvil face. The clear portion of the anvil would then be used to obtain a background spectrum. Occasionally, for quite small particles, difficulties were experienced in mounting these particles onto an anvil due to static electricity. It was found useful in such cases to wipe the anvil and the surrounding area with a damp piece of tissue paper.

For the high-pressure DAC/beam condenser system, a background spectrum of the empty cell was acquired, stored, and used repeatedly so that a new background did not have to be collected for each sample. After pressing a particle flat to a desired thickness, a minimal pressure—just sufficient to maintain contact between the anvil face and the sample—was applied to the DAC. This minimized scattering while avoiding pressure affects. Excess pressure is not desirable since many crystalline substances lose their crystallinity under pressure. It was observed, for example, that spectral absorption bands would often broaden or coalesce when too much pressure was applied (although not observed in this work, it is also possible that some polymorphic substances may transform to a different crystal structure under pressure).

With samples sandwiched between the two diamond anvils, spectra having baselines above 100% *T* were commonly observed. This results from the greater reflectance losses from the two anvil faces when the cell is empty compared to when a sample is present (the diamond-air interface produces a greater difference in index of refraction than does the diamond-sample junction, which leads to a greater reflectance). For some samples analyzed using the beam condenser system on the FX-6200 instrument, either an adjustable attenuator screen or a decreased instrument gain [*27*] (relative to that used for the background spectrum) was used to adjust the baseline of the sample spectrum to below 100% *T*.

For some powder mixtures, the microscopic appearances of the particles of interest may not differ significantly from those of diluents or excipients and a certain amount of trial-and-error sampling may be necessary before the correct particles are chosen. FTIR instruments equipped with a spectral monitoring mode which perform "on-the-fly" Fourier transforms are particularly useful for such cases, since analysts can view the spectra of their samples within a few seconds after placement of the DAC in the instrument. A number of different particles can thus be screened within a relatively short time period using this feature.

Although a high-pressure DAC/beam condenser system was used in this work, all of the analyses presented can also be performed using a low-pressure system. While hard particles (such as quartz and other hard minerals) cannot be analyzed intact with a low-pressure DAC, the particles comprising the powder mixtures and residues normally encountered by the forensic drug chemist are generally quite soft and do not present a problem.

Materials

The following materials were used: *l*-cocaine base, *d*-methamphetamine hydrochloride, niacinamide (nicotinamide), and potassium bromide (infrared grade), Sigma Chemical

Co.; *l*-cocaine hydrochloride, Merck and Co., Inc.; sodium amobarbital, Ganes Chemicals, Inc.; sodium secobarbital, Eli Lilly and Co.; sodium pentobarbital, Abbott Laboratories; allylisobutylbarbituric acid (butalbital), Applied Science Laboratories, Inc.; *l*-ephedrine hydrochloride and *l*-ephedrine sulfate, Biochemical Industries, Inc.; meperidine (pethidine) hydrochloride, S. B. Penick and Co.; diacetylmorphine (heroin) hydrochloride and diphenoxylate hydrochloride, U.S.P.C., Inc.; chlordiazepoxide hydrochloride, Smith Kline and French Laboratories; and Librax™, Librium™ 5 mg, Amytal™ 65 mg and 200 mg, Seconal™ 50 mg and 100 mg, Nembutal™ 50 mg and 100 mg, Fiorinal™ with Codeine No. 3, Fiorinal, Mepergan™, and Tuinal™ 100 and 200 mg, all purchased locally.

Results and Discussion

DAC/Beam Condenser Analyses

Cocaine figures prominently in the analyses of many forensic drug chemists and the nature of most cocaine-containing exhibits makes them particularly amenable to sampling using particle-picking/DAC methods. In both its common salt and free-base forms, for example, cocaine occurs frequently as discrete particles that are generally easily recognized. In addition, analysts may be asked to examine assorted drug paraphernalia (such as various smoking devices, straws, mirrors, razor blades, and so forth) having only small amounts of residue of this substance associated with them.

The crystals of cocaine hydrochloride occur as flakes composed of multilayered plates. When powders containing this salt are viewed with a stereomicroscope, these crystals can usually be identified readily by practiced analysts since they are distinct from the particles of most common diluents. Users of this technique may also find a microscopic examination to be an excellent method of screening samples, especially in regard to whether diluents are present along with cocaine. As an example, a powder exhibit was observed microscopically to consist of flakes, rods, and clumps of small crystals. The DAC spectrum of a flake from this powder is shown in Fig. 1*a*, and as a comparison, the spectrum of cocaine hydrochloride is depicted in Fig. 1*b*. The noise-like features between 2400 and 1900 cm^{-1} arise from the strong absorptions of the diamond anvils of the high-pressure DAC. Along with cocaine, lidocaine hydrochloride and mannitol were also identified in this exhibit and while "wet-chemical" methods could have been used for isolation, particle-picking provided a much faster alternative.

In most cases, cocaine hydrochloride crystals isolated in this fashion produce spectra free of diluent absorptions. In cases where large amounts of diluent particles are observed clinging to the flakes, this may not be true. For these, a relatively large flake is chosen and the outer layers are scraped off so that only the interior portions are sampled. For finely powdered specimens where this may not be possible, it may help to first wash the powder with acetone, then work with the remaining residue.

In addition to bulk powder samples, the DAC method is ideal for analyzing residues of powder adhering to surfaces of various containers. While our laboratory does not analyze solvent washes of currency [*28–30*] for the presence of cocaine, the surfaces of currency *are* examined to determine whether any visible particulate residue may be present. If observed, such residue is analyzed using the DAC.

The crystals of cocaine base consist of rods or needles, and fans or rosettes of needles may occasionally be observed on the surfaces of some cocaine paraphernalia, such as spoons and glass smoking devices. Scrapings of these crystals can be sampled directly with the DAC. For the more common form of the base ("crack" or "rock"), however, this crystal morphology is often not evident since chunks of polycrystalline material, composed of crystals too small to be observed, are presumably involved. However, in

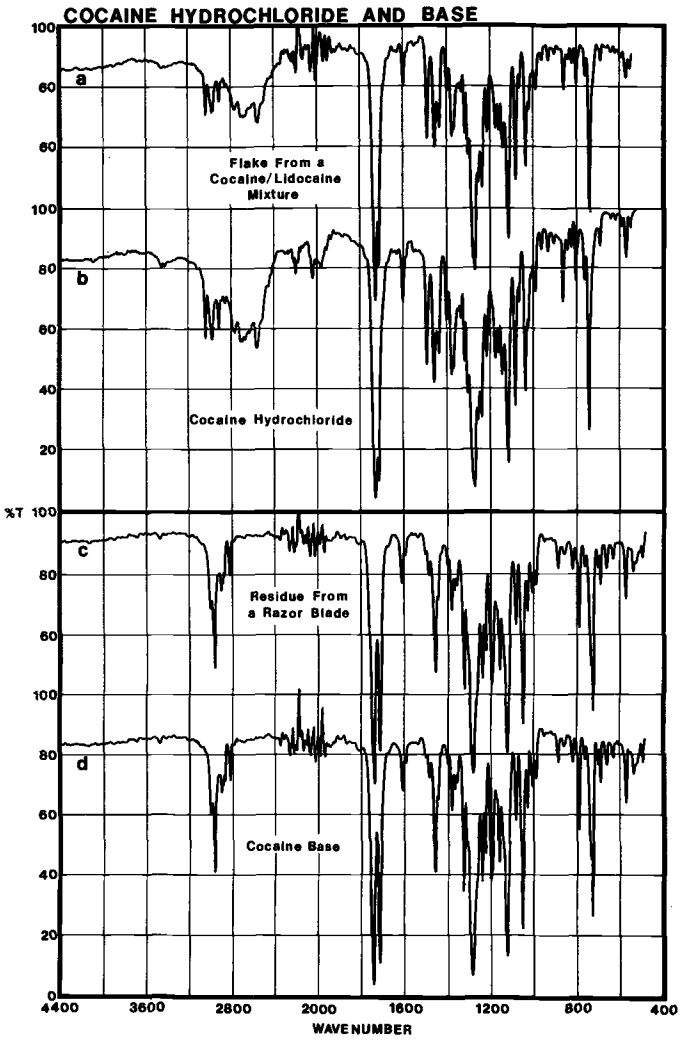

FIG. 1—*DAC/beam condenser spectra of:* (a) *a flake crystal removed from a powder mixture consisting of cocaine hydrochloride, lidocaine hydrochloride, and mannitol;* (b) *cocaine hydrochloride;* (c) *residue removed from a razor blade; and* (d) *cocaine base.*

many cases these chunks consist primarily of cocaine and they, too, may be analyzed intact. As an example, a razor blade having a small amount (probably 10 μg or so) of white residue was received for examination. The DAC spectrum (Fig. 1*c*) of a portion of this residue confirmed the base form of cocaine (Fig. 1*d*).

Because of the large quantities of cocaine hydrochloride powder that may be handled in some laboratories, the possibility of contamination of exhibits may be a concern, particularly for cases involving residues. With the particle-picking/DAC method, the forensic chemist can be assured that the spectrum generated was actually produced by the particle chosen. Thus, if the forensic chemist is certain that the particle chosen for analysis was originally part of an exhibit and not a contaminant, a solid chain of analysis may be established. In describing the feature of observing and delineating sampling fields using an infrared microscope, Reffner et al. [*31*] have noted that "what you see is what

you get"; this statement applies equally well to particle-picking/DAC sampling as far as emphasizing the relationship between evidence in a case and spectral data collected.

In some cases involving clandestinely produced substances, it is not unusual for the synthesized products to exhibit microscopic appearances unlike those of the standards. With illicit methamphetamine, for example, the particles of methamphetamine hydrochloride occur frequently as amorphous-appearing brown or orange chunks. This coloration makes them quite conspicuous in powder mixtures and despite their appearance, such particles often yield spectra having little or no extraneous absorptions. Figure 2*a*, for example, was obtained from such a particle and only a weak carbonyl peak (near

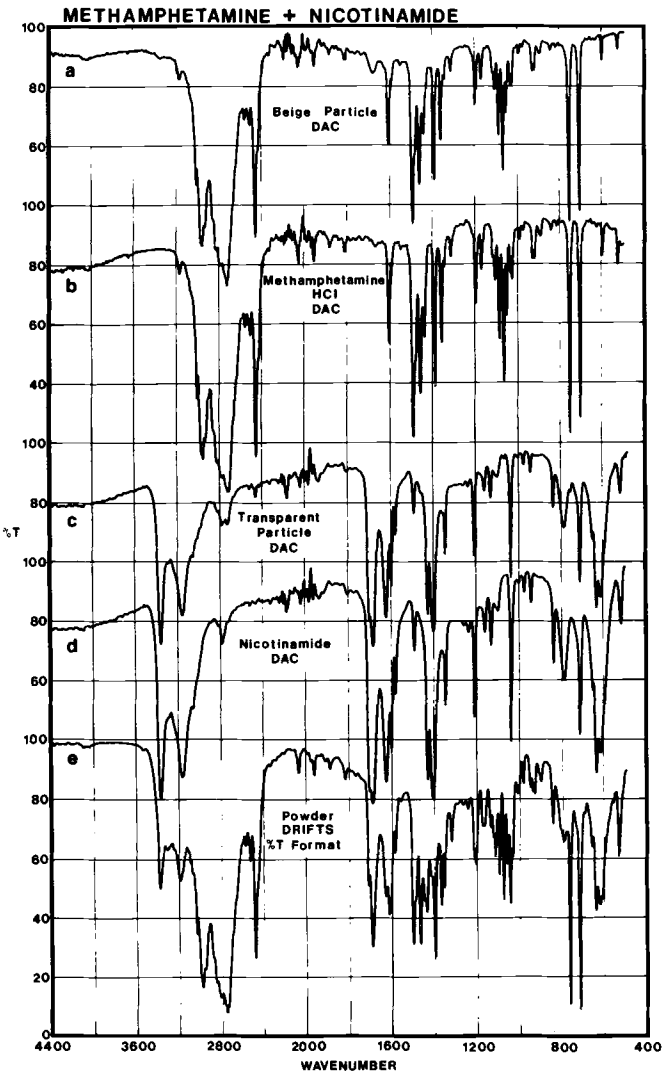

FIG. 2—*DAC/beam condenser spectra of:* (a) *a beige particle removed from a powder mixture containing (among others) methamphetamine hydrochloride and nicotinamide;* (b) dl-*methamphetamine hydrochloride;* (c) *a clear transparent rod-shaped crystal removed from the above powder; and* (d) *nicotinamide.* (e) *Diffuse reflectance (DRIFTS) spectrum of the above powder diluted with excess KBr, presented in a percent transmittance format.*

1700 cm^{-1}) is evident in its spectrum (compare to Fig. 2*b*). A clear rod-shaped crystal picked out from this same powder mixture was identified as nicotinamide (see Figs. 2*c* and 2*d*), and these two components account for most of the absorptions observed in the diffuse reflectance (DRIFTS) spectrum (presented in a transmittance format [*19*]) of this powder exhibit diluted with excess KBr (Fig. 2*e*).

Polymorphism can occur for some controlled substances and variable spectral data may result when such drugs are analyzed as solids. Heroin base, for example, can occur as one of two polymorphs (Forms I and II) having different infrared spectra [*32,33*]. Depending upon the crystallization conditions, one or the other of these polymorphs may be favored [*33*], but often, both forms crystallize together. Conventional infrared methods, which combine numerous individual crystals for sampling, can thus yield different spectra dependent upon the molar ratios of the two forms. As an alternative, individual crystals from recrystallized heroin base can be sampled to give "pure" spectra, as depicted in Figs. 3*a* and 3*b*. For this example, an extract of Mexican "black tar" heroin (the most common type of heroin analyzed in our laboratory) was used. Following isolation[2] and recrystallization, crystals of both polymorphs were observed microscopically. The crystal habits of these polymorphs include [*33*] aggregates of elongated hexagonal plates (Form I) and spherulites (Form II); a plate aggregate and a spherulite were picked out to give the spectra of Figs. 3*a* and 3*b*, respectively. Note in particular the difference in frequency between the lower-frequency members of the carbonyl doublets (Figs. 3*a* and 3*b*). As a comparison, Fig. 3*c* depicts a DRIFTS spectrum of a mixture of the two polymorphs diluted with KBr. Spectra similar to this, along with other intermediate types, often result when conventional sampling is performed.

The analysis of certain salts of some drugs provides an example of the transformations that may occur with conventional KBr pellet sampling. Figure 4*a* depicts the DAC spectrum of *l*-ephedrine sulfate, which may be seen to be quite distinct from the spectrum of *l*-ephedrine hydrochloride [sampled as a KBr pellet (Fig. 4*d*)]. Figures 4*b* and 4*c* depict spectra of *l*-ephedrine sulfate sampled as KBr pellets, and significant differences between these two spectra are evident. For the results shown in Fig. 4*b*, the *l*-ephedrine sulfate was first ground thoroughly to a fine powder neat, then ground together with KBr to a lesser extent. In the second case (Fig. 4*c*), the *l*-ephedrine sulfate and KBr were ground together very thoroughly. From a comparison of the four spectra of Fig. 4, it is clear that for the latter sampling, an ion exchange has taken place and the spectrum (Fig. 4*c*) is primarily that of *l*-ephedrine hydrobromide and potassium sulfate (which has a strong broad absorption at 1120 cm^{-1} and a second absorption at 620 cm^{-1} (compare Figs. 4*c* and 4*d*). A similar transformation occurs when ephedrine nitrate is analyzed. This ion exchange occurs primarily during the grinding process and not when the pellets are pressed (similar results occur using DRIFTS sampling, which does not involve pressing a pellet). For salts where this may be a problem, the DAC provides a matrixless alternative which, additionally, requires little sample preparation.

DAC/Infrared Microscope Analyses

For cases where the particles of interest are too small (after pressing) to cover an entire anvil face, several individual particles may have to be combined for analysis. This may not always be easy to accomplish with some mixtures, however, and an infrared microscope is preferred for the sampling of most small particles. One problem that occurs with

[2]The tar was partitioned between 3*N* hydrochloric acid (HCl) and excess dichloromethane (CH_2Cl_2), and the separated CH_2Cl_2 layer was then partitioned with excess water. The aqueous layer was removed and saturated with sodium bicarbonate ($NaHCO_3$) and heroin base was extracted from this solution using CH_2Cl_2. Excess petroleum ether was added to the latter and this solution was allowed to evaporate on a watchglass. Following evaporation, crystals of the base resulted.

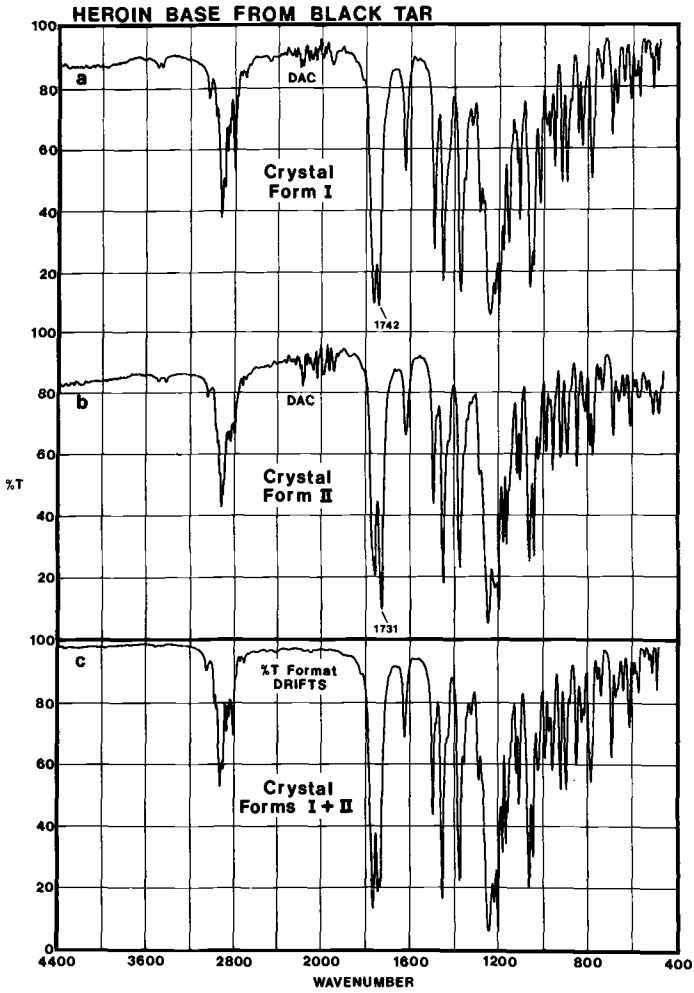

FIG. 3—(a) *DAC/beam condenser spectrum of a crystal (consisting of an aggregation of plates) which was removed from recrystallized heroin base extracted from a "black tar" sample; this spectrum is that of the Form I polymorph;* (b) *DAC/beam condenser spectrum of a second crystal (consisting of a spherulite burr) removed from this same recrystallized product; this spectrum is that of the Form II polymorph (note the difference in frequencies between the lower members of the carbonyl doublets);* (c) *DRIFTS spectrum (percent transmittance format) of a mixture of the two heroin base polymorphs diluted with excess KBr.*

the use of the low-pressure DAC on an infrared microscope is that it invariably produces very strong spectral interference fringes (see Fig. 5*d*). These fringes can be minimized by placement of a KBr particle adjacent to the sample and, after pressing, use of the resulting KBr film as a background. We have found, however, that a more convenient method of minimizing fringes is simply to sample with a single anvil [*34,35*]. The particle is pressed as usual using both anvils (pressing by hand instead of using the screws), then the two anvils are separated. For most particles, sample films will result on both anvil faces; the particular anvil having the more suitable film is used for analysis. With this technique, fringes are either not observed (Fig. 5*c*) or are weak. (In Fig. 6*a*, a portion of one fringe can be seen between 3600 and 4000 cm^{-1}.)

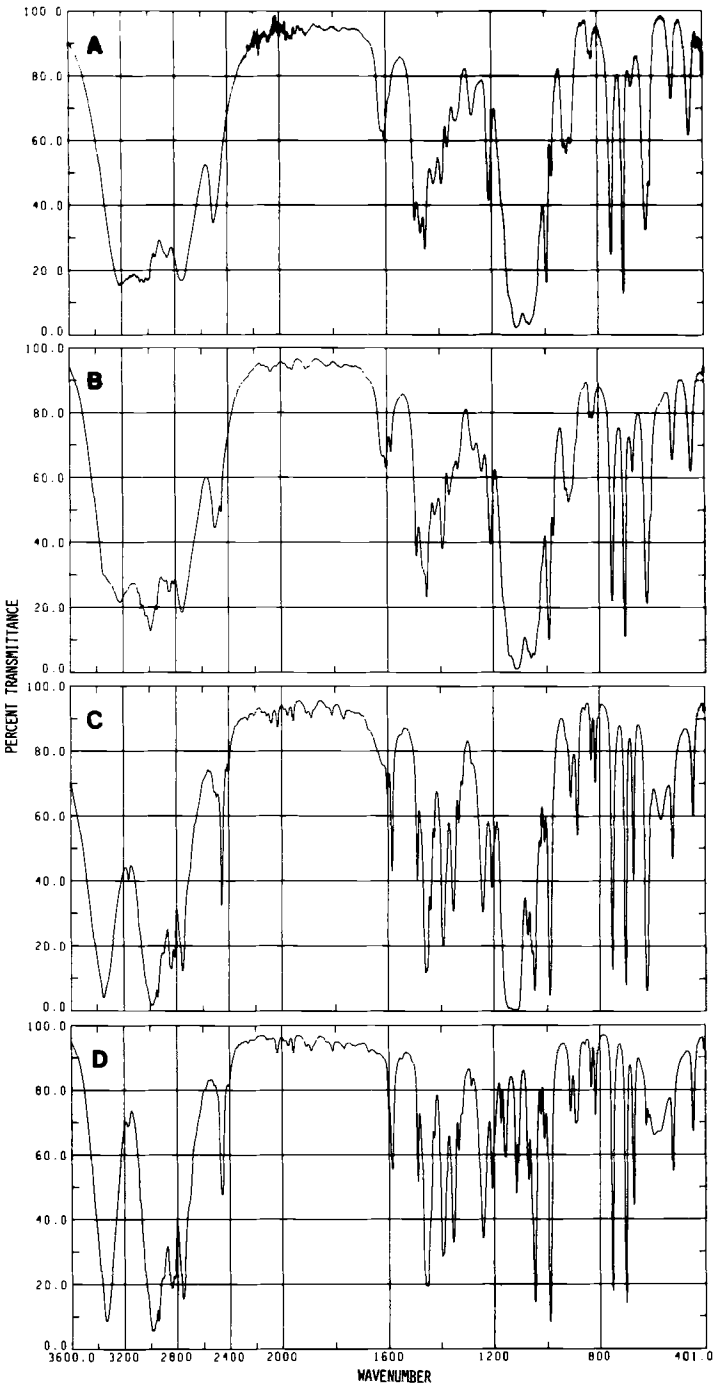

FIG. 4—(a) *DAC/beam condenser spectrum of* l-*ephedrine sulfate obtained using the DAC/beam condenser system on the RFX-40 instrument;* (b) *KBr pellet spectrum of* l-*ephedrine sulfate; the sample was ground neat to a fine powder, then ground slightly with excess KBr;* (c) *KBr pellet spectrum of* l-*ephedrine sulfate; the sample was ground thoroughly together with excess KBr;* (d) *KBr pellet spectrum of* l-*ephedrine hydrochloride.*

The single-anvil method also provides a better "window" for the 2300 to 1900 cm^{-1} spectral region, as can be seen from comparison of the spectrum (obtained using the infrared microscope) of a single anvil (Fig. 5*a*) versus that of both anvils (Fig. 5*b*). The drug chosen for Fig. 5, diphenoxylate hydrochloride, was used because it has a weak nitrile absorption at 2237 cm^{-1}, and this peak can be seen clearly (on the side of the strong amine hydrochloride stretching absorption) in Fig. 5*c*. One other practical benefit of sampling with a single anvil is that this minimizes contact between the two anvil faces, which decreases the chance of scratching the anvils.

While alternative substrates to a single anvil can be used for sampling with the infrared microscope, we have found most of these to be unsuitable for long-term use. KBr substrates are too soft and become easily dented or scratched when particles are pressed onto them; harder salt windows, such as barium fluoride (BaF_2), are brittle and may crack when too much pressure is used. Regardless of the substrate material, however, the particle chosen for sampling should be pressed to a thin film for analysis. When sampled intact, most particles give poor or less-than-optimal spectra since the particles are too thick, produce non-Beers-Law-type sampling (since variable sample path lengths are involved), or produce considerable scattering, manifested as low or sloping spectral baselines. For quite small particles, pressing has the added benefit that larger apertures can usually be used.

An analysis where the microscope was very useful involved the examination of a white powder exhibit which was sold as "China White." A DRIFTS spectrum of this powder indicated that nicotinamide was the primary constituent. A weak carbonyl doublet was also present in this spectrum, and color tests indicated the possible presence of heroin. While crystals similar to those of heroin hydrochloride were not evident from the stereomicroscopic examination, amorphous-appearing white chunks, dissimilar to most of the other crystalline particles observed, were seen. The spectrum of one of these chunks, which was approximately 150 μm in size, is shown in Fig. 6*a*. As a comparison, the spectrum of heroin hydrochloride is depicted in Fig. 6*b*. Several other chunks were also sampled and they all produced similar spectra. While useful for this particular exhibit (and at least one other powder received the year before), the applicability of this method to powder heroin samples in general is not known, since our laboratory receives heroin in this form infrequently.

Pharmaceutical Capsule Powders

In principle, particle-picking should be applicable to all capsule powders (including illicitly produced capsules) where discrete particles of drugs are involved. In practice, this method is mostly limited to those preparations where the drug particles are distinct enough or numerous enough that the analyst can isolate them without resorting to an undue amount of trial-and-error sampling.

The level of difficulty in isolating the correct particles from capsule powders varies considerably. Probably the easiest analysis of this type involves the identification of chlordiazepoxide hydrochloride as present in Librium and Librax. For these two preparations, the largest particles of chlordiazepoxide hydrochloride have dimensions up to 0.3 mm (300 μm) in size and, equally important, have a slight beige tint. These particles occur as distorted hexagonal crystals with beveled edges, having an appearance somewhat like coffins. Only the larger crystals have a coloration and this, together with their size and morphology, makes them quite easy to spot. The DAC/beam condenser spectrum of one such crystal removed from a Librax capsule powder is shown in Fig. 7*a*, together with that of the chlordiazepoxide hydrochloride standard (Fig. 7*b*).

Capsules from three different lots of Librax and Librium were tested, along with three generic brands (Barr Labs, Cord Labs Inc., and Geneva Generics) of chlordiazepoxide

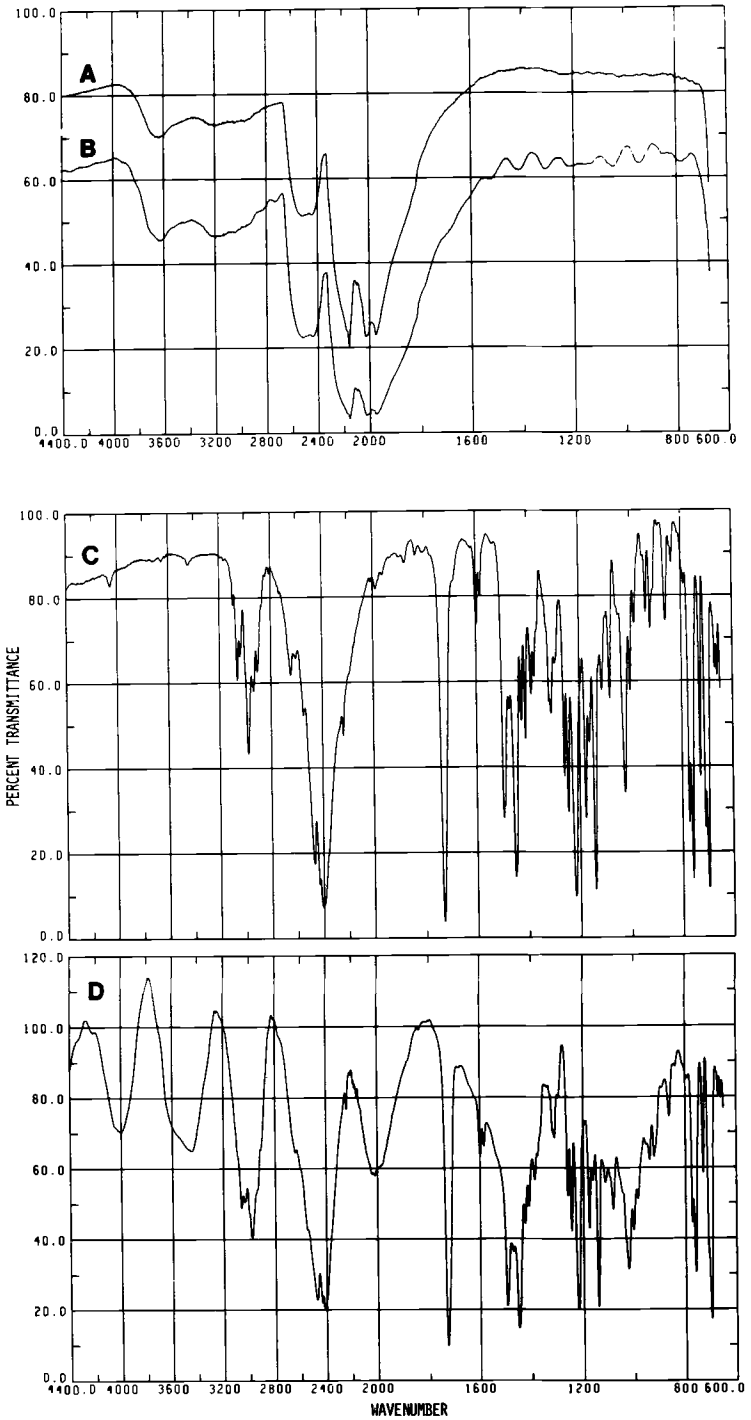

FIG. 5—*Infrared microscope spectra of:* (a) *a single anvil of the low-pressure DAC;* (b) *both anvils of the low-pressure DAC;* (c) *diphenoxylate hydrochloride pressed onto a single anvil of the low-pressure DAC; and* (d) *diphenoxylate hydrochloride between both anvils of the low-pressure DAC. Because of the significantly greater reflectance losses of the empty cell in this case, a lower gain was used for the sample relative to that used for the background (1 versus 1R); note the very prominent interference fringes in this spectrum.*

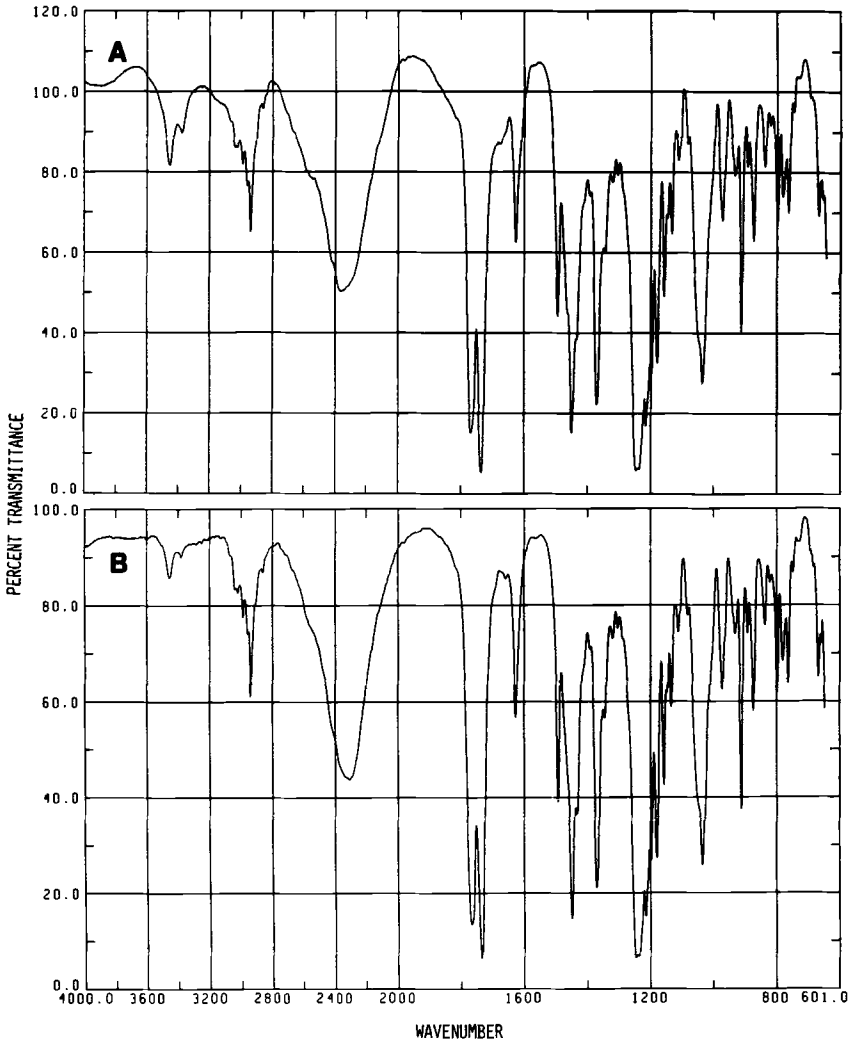

FIG. 6—*Infrared microscope spectra of:* (a) *a particle removed from a powder mixture containing (among others) heroin hydrochloride and nicotinamide; and* (b) *heroin hydrochloride.*

hydrochloride capsules. For the generic capsule powders, the chlordiazepoxide crystals were smaller than those of Librax and Librium and tinted crystals were not observed. While not as conspicuous, the chlordiazepoxide crystals could still be isolated from these capsules based upon their morphologies. Because of their smaller sizes, the infrared microscope was used for these analyses.

A preparation which may contain even larger drug crystals is Mepergan, which contains a mixture of pethidine hydrochloride and promethazine hydrochloride. The pethidine hydrochloride crystals in these capsules consist of (among others) transparent elongated hexagonal striated plates, the largest of which may be nearly 1 mm in length. The spectra of one of these plates and pethidine hydrochloride standard are shown in Figs. 8*a* and 8*b*, respectively.

The barbiturates provide a good example of the difficulties encountered when con-

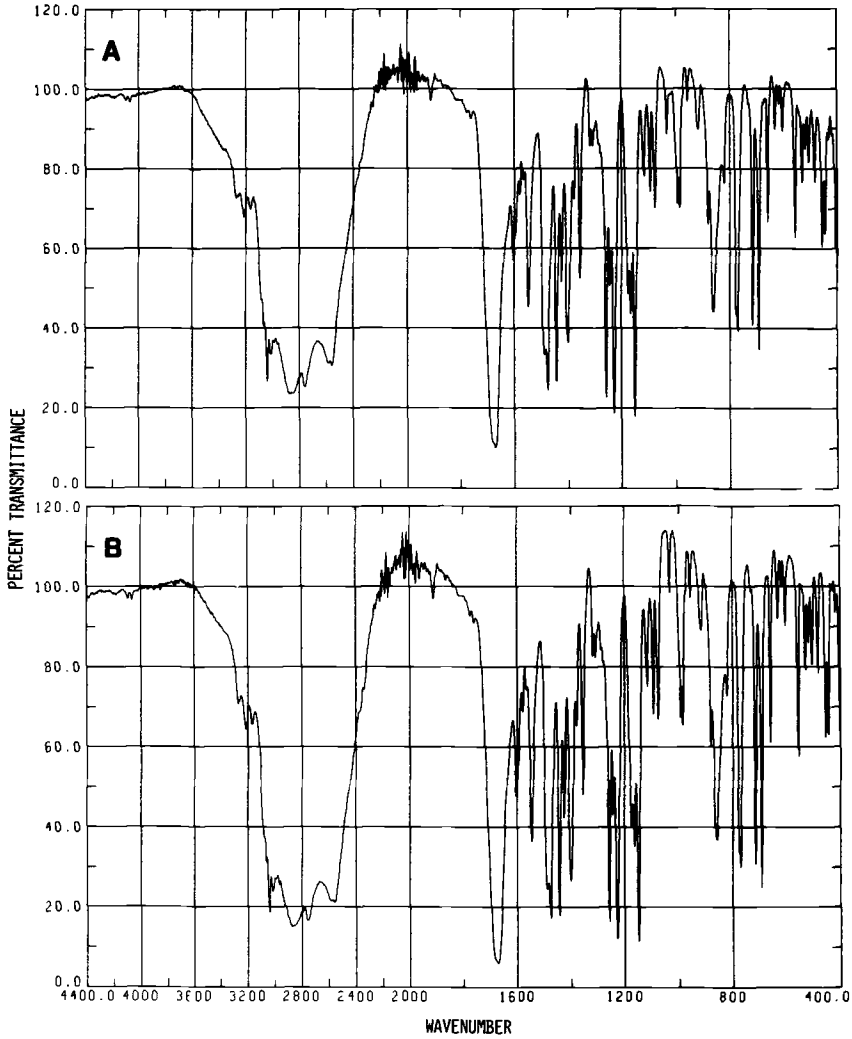

FIG. 7—*DAC/beam condenser spectra of:* (a) *a beige hexagonal crystal (approximately 300 μm in size) removed from a Librax capsule powder; and* (b) *chlordiazepoxide hydrochloride. The RFX-40 instrument was used for these.*

ventional isolation techniques are used, since many of these drugs are polymorphic and produce variable infrared spectra [*36–38*] when extracted from pharmaceutical preparations. One method to avoid this is recrystallization of extracted product and sampling of individual barbiturate crystals [*31*], as described earlier for heroin base. For capsules, particle-picking offers a more direct approach and although the crystals of most barbiturates (or their salts) are not as distinct as those of chlordiazepoxide in Librium and Librax, the dosages (50 mg or more) are relatively high so that a fair proportion of a typical capsule powder is that of the barbiturate.

Particles of the sodium salts of pentobarbital, secobarbital, and amobarbital have been isolated from the various dosages of Nembutal, Seconal, and Amytal capsules, respectively. The crystal habits of the salts as present in these capsules may vary and include

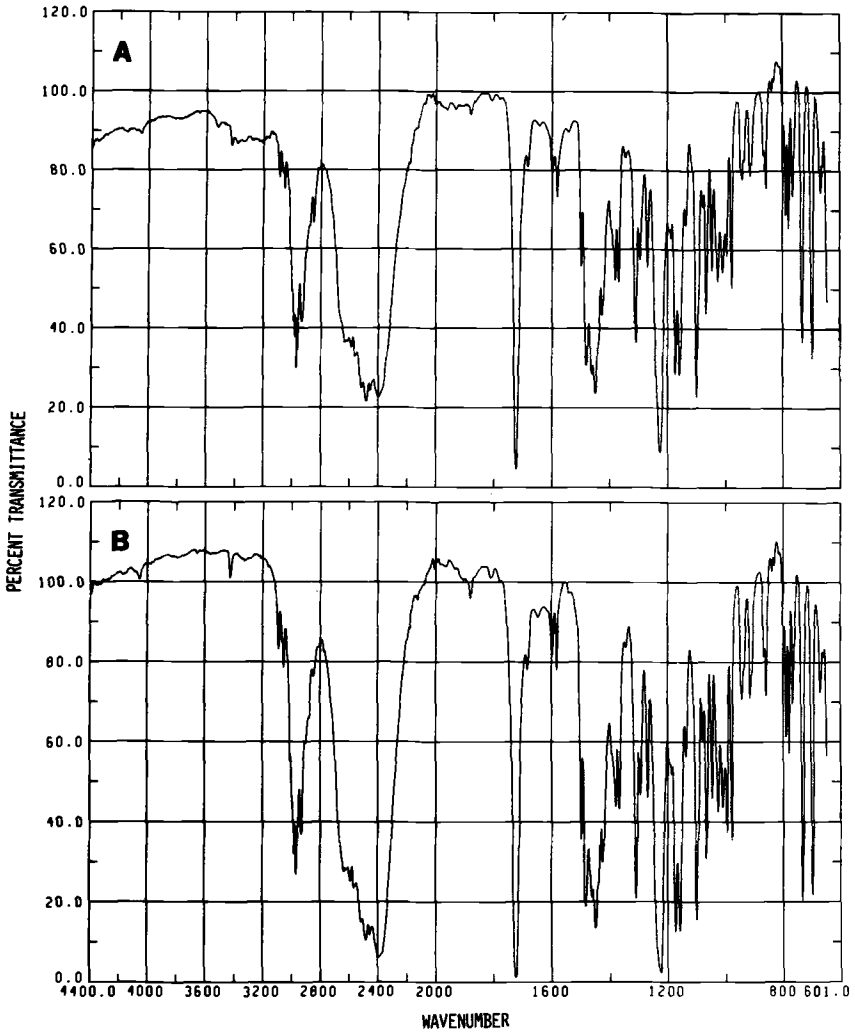

FIG. 8—*Infrared microscope spectra of:* (a) *a plate crystal removed from a Mepergan capsule powder; and* (b) *pethidine hydrochloride.*

clear glasslike particles, semiopaque chunks having a firm consistency, or fairly soft clumps of very small crystals. Excipient particles of lactose or starch may have somewhat similar appearances, but can usually be differentiated from those salts with some practice. The sizes of the barbiturate crystals vary, and both the microscope (see Fig. 9) and the beam condenser have been used for sampling. In general, the larger soft clumps are not used since it is more likely that they may consist of a mixture of barbiturate and excipient particles.

This method is particularly appropriate for the analysis of Tuinal capsules since two barbiturates (which would be difficult to isolate using normal techniques) are present. Although it may be difficult to distinguish microscopically between the particles of sodium amobarbital and sodium secobarbital present in these capsules, the barbiturate crystals can more easily be distinguished from excipient particles. The spectra of two semiopaque

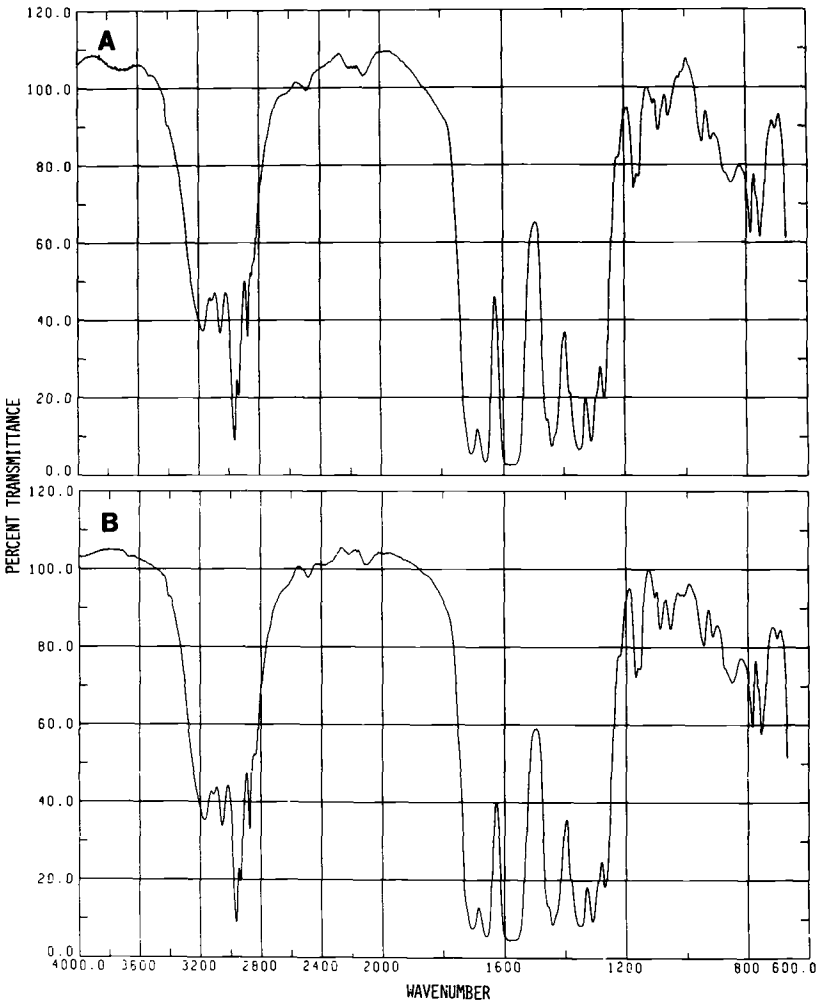

FIG. 9—*Infrared microscope spectra of:* (a) *a particle removed from a Nembutal 100 mg capsule powder; and* (b) *sodium pentobarbital.*

chunks removed from a Tuinal 100 mg capsule powder are shown in Figs. 10*a* and 10*c*. The particles were approximately 200 μm in size and the beam condenser was used for sampling. Spectra of sodium amobarbital, sodium secobarbital, and sodium pentobarbital are depicted in Figs. 10*b*, 10*d*, and 10*e*, respectively. The spectrum of sodium pentobarbital provides a useful comparison since this barbiturate is an isomer of sodium amobarbital and, like sodium secobarbital, it has a 1-methylbutyl sidechain (Fig. 10).

Another barbiturate capsule product which contains a mixture of drugs is Fiorinal and Fiorinal with Codeine. Along with 50 mg of butalbital (allylisobutylbarbituric acid), 325 mg of acetyl salicylic acid (aspirin) and 40 mg of caffeine are present in these preparations; Fiorinal with Codeine also contains 7.5 to 30 mg of codeine phosphate. The analyses of these capsule powders are among the most difficult, and a fair amount of patience, luck, and a good "eye" may all be required to achieve isolations on a consistent basis.

The crystals of aspirin, the primary constituent, consist of relatively large thick rods or slabs and these are easy to recognize microscopically. The particles of butalbital,

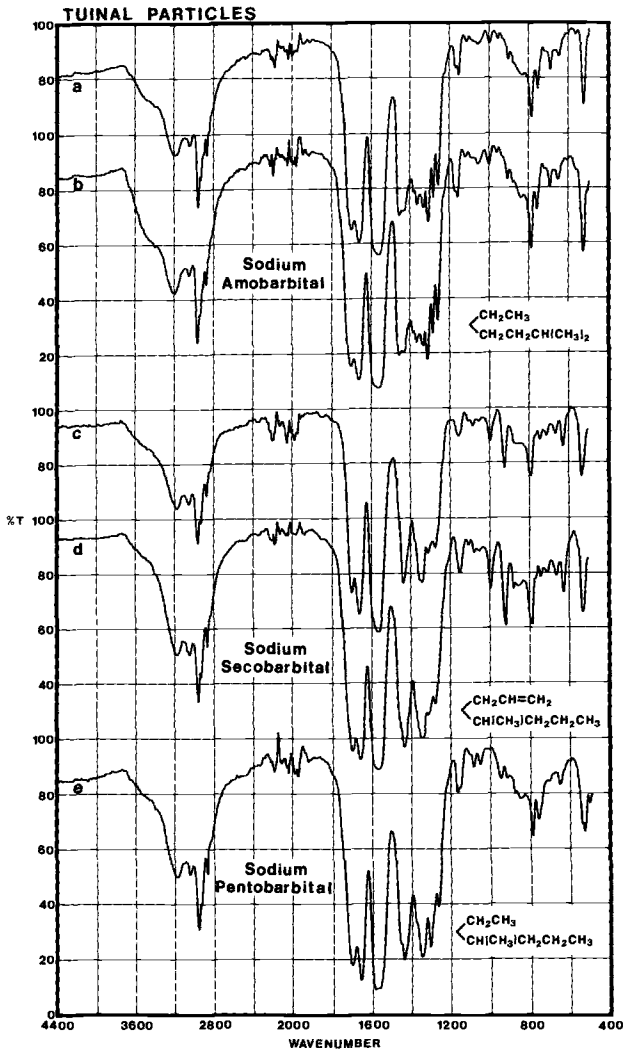

FIG. 10—*DAC/beam condenser spectra of:* (a) *a particle removed from a Tuinal 100 mg capsule powder;* (b) *sodium amobarbital;* (c) *a second particle from the above Tuinal capsule;* (d) *sodium secobarbital; and* (e) *sodium pentobarbital. The two alkyl groups of the three mentioned barbiturates are shown along with their spectra.*

however, are not easily distinguished from those of caffeine, as both consist of soft clumps of very small crystals. For butalbital, these tend to consist of small plates whereas for caffeine, they are generally more rod-like. In some cases, this difference is evident and butalbital particles can be identified and removed. In others, this may not be true and a certain amount of trial-and-error sampling may be required. Figures 11*a* and 11*b* depict spectra (obtained using the infrared microscope) of a Fiorinal with Codeine particle and butalbital, respectively. Occasionally, the butalbital particles may have small amounts of talc excipient adhering, as evidenced by a spectral absorption near 1010 cm^{-1} (and also near 3680 cm^{-1} if enough talc is present). If possible, the interior portions of butalbital particles (or individual plates) should be sampled to avoid this.

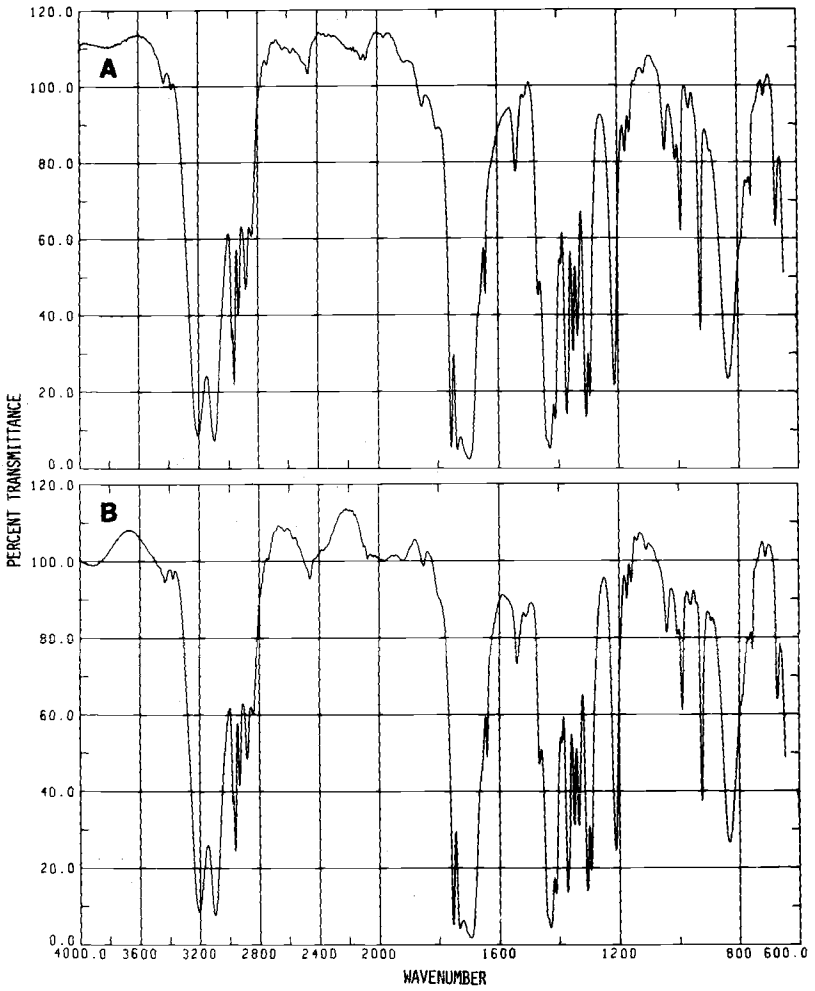

FIG. 11—*Infrared microscope spectra of:* (a) *a particle removed from a Fiorinal with Codeine No. 3 capsule powder; and* (b) *butalbital (allylisobutylbarbituric acid).*

For some Fiorinal or Fiorinal with Codeine capsule powders, ultraviolet fluorescence may provide a better visual discrimination between butalbital and caffeine. The powder is viewed microscopically while being illuminated with ultraviolet light using little or no conventional illumination; a hand-held lamp set to long-wavelength ultraviolet light works well for this. Although none of the original capsule ingredients are known to fluoresce, all of the tested capsule powders contained numerous particles that produced a blue fluorescence. This undoubtedly is due to small amounts of salicylic acid that are produced from the slow hydrolysis of aspirin. Interestingly, the aspirin particles themselves exhibit little or no fluorescence and the salicylic acid seems to adhere mostly to caffeine particles (which may not be too surprising considering the acid-base properties involved). Sampling of the nonfluorescent clumps generally produced better results than random sampling.

Although butalbital has been successfully isolated from every Fiorinal with Codeine capsule tested, the same cannot be said for codeine phosphate, which probably occurs as smaller particles. Although this isolation has been achieved, it appears to be an even

more difficult task than isolating butalbital. Particles of phenacetin, which is no longer used in Fiorinal preparations, have also been isolated from some older Fiorinal and Fiorinal with Codeine capsules, and this may complicate the analysis of older capsules.

Comparison of the Two Sampling Methods

Since all of the applications described above can be performed with an infrared microscope, it might be assumed that there is no need to use a beam condenser system. For those mixtures involving quite small particles where it is difficult enough to isolate one particle of interest—much less several particles—one should certainly use the microscope. For cases where either system can be used, assuming this option exists, there are advantages to using the beam condenser. The primary advantage arises from the low-frequency limitations of the narrow-band MCT detector, which is normally used with an infrared microscope. The cutoff point for this detector occurs between 600 and 700 cm^{-1}, depending upon the individual detector used. The cutoff points of the broad-band MCT detector and the deuterated triglycine sulfate (DTGS) detector occur near 450 cm^{-1}, and below 200 cm^{-1}, respectively. Assuming that the beam condenser is used with one of these detectors, more spectral information can be obtained than with the infrared microscope.

While this lower-frequency spectral region is generally more useful for distinguishing between inorganic compounds, it is also of use for some drugs. The sodium salts of some barbiturates (Fig. 10) provide an example of this: few significant differences exist above 1400 cm^{-1} and while there are some differences from 1400 to 700 cm^{-1}, this region is not particularly rich in absorptions and an extended range would be desirable. In fact, the region below 700 cm^{-1} is especially useful for distinguishing between barbiturates [*39*].

A second advantage of the beam condenser system is that it may provide a faster analysis since it involves fewer manipulations than a microscope analysis. Assuming that a prestored background scan is used, one need obtain only a sample scan using a beam condenser. With the microscope, an aperture must usually be selected for each sample, and both background and sample scans must be collected.

An ideal combination would consist of a low-pressure DAC that could be used with both a beam condenser and an infrared microscope. With such a dual system, the analyst could decide which accessory to use *after* a particle has been selected and pressed. To be able to collect data to 225 cm^{-1}, the FTIR instrument for the beam condenser should be equipped with CsI optics and a DTGS detector. Such a combined system would provide both flexibility and the means to collect the maximum amount of spectral data for the larger samples.

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References

[*1*] Corrigan, A. R., 5th International Criminology Congress, Montreal, Canada, 1965.

[*2*] Tweed, F. T., Cameron, R., Deak, J. S., and Rogers, P. G., "The Forensic Microanalysis of Paints, Plastics, and Other Materials by an Infrared Diamond Cell Technique," *Forensic Science*, Vol. 4, 1974, pp. 211–218.

[3] Rodgers, P. G., Cameron, R., Cartwright, N. S., Clark, W. H., Deak, J. S., and Norman, W. W., "The Classification of Automotive Paint by Diamond Window Infrared Spectrophotometry—Parts I, II, and III," *Canadian Society of Forensic Science Journal*, Vol. 9, Nos. 1, 2, and 3, 1976, pp. 1–14, 49–68, 103–111.

[4] Ryland, S. G. and Kopec, R. J., "The Evidential Value of Automobile Paint Chips," *Journal of Forensic Sciences*, Vol. 24, No. 1, Jan. 1979, pp. 140–147.

[5] Norman, E. W. W., Cameron, R., Cartwright, L. J., Cartwright, N. S., Clark, W. H., and MacDougall, D. A., "The Classification of Automotive Paint Primers Using Infrared Spectroscopy—A Collaborative Study," *Canadian Society of Forensic Science Journal*, Vol. 16, No. 4, 1983, pp. 163–173.

[6] Suzuki, E. M., "Forensic Science Applications of Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS): IV. Direct Analysis of Metallic Paints—Sampling Considerations," *Journal of Forensic Sciences*, Vol. 34, No. 1, Jan. 1989, pp. 164–179.

[7] Suzuki, E. M. and Brown, J. A., "Forensic Science Applications of Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS): V. Direct Analysis of Metallic Paints—Screening of Panels," *Journal of Forensic Sciences*, Vol. 34, No. 1, Jan. 1989, pp. 180–196.

[8] Read, L. K. and Kopec, R. J., "Analysis of Synthetic Fibers by Diamond Cell and Sapphire Cell Infrared Spectrophotometry," *Journal of the Association of Official Analytical Chemists*, Vol. 61, No. 3, May 1978, pp. 526–532.

[9] Hartshorne, A. W. and Laing, D. K., "The Identification of Polyolefin Fibres by Infrared Spectroscopy and Melting Point Determination," *Forensic Science International*, Vol. 26, 1984, pp. 45–52.

[10] Gaudette, B. D., "The Forensic Aspects of Textile Fiber Examination," *Forensic Science Handbook*, Vol. 2, Prentice-Hall, Englewood Cliffs, NJ, 1988, pp. 209–272.

[11] Beveridge, A. D., Payton, S. F., Audette, R. S., Lambertus, A. J., and Shaddick, R. C., "Systematic Analysis of Explosive Residues," *Journal of Forensic Sciences*, Vol. 20, No. 3, July 1975, pp. 431–454.

[12] Midkiff, C. R. and Washington, W. D., "Systematic Approach to the Detection of Explosive Residues: IV. Military Explosives," *Journal of the Association of Official Analytical Chemists*, Vol. 59, No. 6, 1976, pp. 1357–1374.

[13] Washington, W. D., Kopec, R. J., and Midkiff, C. R., "Systematic Approach to the Detection of Explosive Residues: V. Black Powders," *Journal of the Association of Official Analytical Chemists*, Vol. 60, No. 6, 1977, pp. 1331–1340.

[14] Midkiff, C. R., "Arson and Explosive Investigation," *Forensic Science Handbook*, Vol. 1, Prentice-Hall, Englewood Cliffs, NJ, 1982, pp. 222–266.

[15] Kinard, W. D. and Midkiff, C. R., Jr., "Developments in Firearms Residue Detection," *Forensic Science*, 2nd ed., American Chemical Society, Washington, DC, 1986, pp. 241–257.

[16] Washington, W. D. and Midkiff, C. R., "Forensic Applications of Diamond Cell—Infrared Spectroscopy: I. Identification of Blasting Cap Leg Wire Manufacturers," *Journal of Forensic Sciences*, Vol. 21, No. 3, July 1976, pp. 862–867.

[17] Washington, W. D., Midkiff, C. R., and Snow, K. B., "Dynamite Contamination of Blasting Cap Leg Wire Identification," *Journal of Forensic Sciences*, Vol. 22, No. 2, April 1977, pp. 329–331.

[18] Kopec, R. J., Washington, W. D., and Midkiff, C. R., "Forensic Applications of Sapphire Cell—Infrared Spectroscopy: Companion to the Diamond Cell in Explosive and Leg Wire Identification," *Journal of Forensic Sciences*, Vol. 23, No. 1, Jan. 1978, pp. 57–65.

[19] Suzuki, E. M. and Gresham, W. R., "Forensic Science Applications of Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS): I. Principles, Sampling Methods, and Advantages," *Journal of Forensic Sciences*, Vol. 31, No. 3, July 1986, pp. 931–952.

[20] Suzuki, E. M. and Gresham, W. R., "Forensic Science Applications of Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS): III. Direct Analysis of Polymeric Foams," *Journal of Forensic Sciences*, Vol. 32, No. 2, March 1987, pp. 377–395.

[21] Kirkwood, I. and Isaacs, M. D. J., "The Analysis of Vehicle Sidelight Plastics," *Forensic Science International*, Vol. 43, 1989, pp. 51–62.

[22] Harris, J. and MacDougall, D., "Characterization and Dating of Correction Fluids on Questioned Documents Using FTIR," *Canadian Society of Forensic Science Journal*, Vol. 22, No. 4, 1989, pp. 349–376.

[23] Katon, J. E., Lang, P. L., Schiering, D. W., and O'Keefe, J. F., "Instrumental and Sampling Factors in Infrared Microspectroscopy," *The Design, Sample Handling, and Applications of Infrared Microscopes*, American Society for Testing and Materials, Philadelphia, PA, 1987, pp. 49–63.

[24] Sy, W. W., By, A. W., Neville, G. A., and Wilson, W. L., "A Direct Synthesis of O^6-Monoacetylmorphine from Morphine," *Canadian Society of Forensic Science Journal*, Vol. 18, No. 2, 1985, pp. 86–91.

[25] Beckstead, H. D. and Neville, G. A., "Fourier Transform Infrared (FT-IR) Characterization of the Ethyl Acetate Complex of O^6-Acetylmorphine," *Journal of Forensic Sciences*, Vol. 33, No. 1, Jan. 1988, pp. 223–229.

[26] Shearer, J. C. and Peters, D. C., "Fourier Transform Infrared Microspectrophotometry as a Failure Analysis Tool," *The Design, Sample Handling, and Applications of Infrared Microscopes*, American Society for Testing and Materials, Philadelphia, 1987, pp. 27–38.

[27] Suzuki, E. M. and Gresham, W. R., "Forensic Science Applications of Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS): II. Direct Analysis of Some Tablets, Capsule Powders, and Powders," *Journal of Forensic Sciences*, Vol. 31, No. 4, Oct. 1986, pp. 1292–1313.

[28] Sorgen, G. J. and Heagy, J. A., "Extraction of Cocaine from Currency," *Microgram*, Vol. 16, No. 8, Aug. 1983, pp. 132–133.

[29] Aaron, R. and Lewis, P., "Cocaine Residues on Money," *Crime Laboratory Digest*, Vol. 14, No. 1, Jan. 1987, p. 18.

[30] Hudson, J. C., "Analysis of Currency for Cocaine Contamination," *Canadian Society of Forensic Science Journal*, Vol. 22, No. 2, 1989, pp. 203–218.

[31] Reffner, J. A., Coates, J. P., and Messerschmidt, R. G., "Chemical Microscopy with FTIR Microspectrometry," *American Laboratory*, Vol. 19, April 1987, pp. 86–97.

[32] Borka, L., "The Polymorphism of Heroin and its Forensic Aspects," *Acta Pharmaceutica Suecica*, Vol. 14, 1977, pp. 210–212.

[33] Ravreby, M. and Gorski, A., "Variations in the Infrared Spectra of Heroin Base," *Journal of Forensic Sciences*, Vol. 34, No. 4, July 1989, pp. 918–927.

[34] Suzuki, E. M., "Fourier Transform Infrared (FTIR) Analysis of Particulate Drug Mixtures Using Diamond Anvil Cell and Infrared Microscope Accessories," presented at the Annual Meeting of the American Academy of Forensic Sciences, Las Vegas, NV, Feb. 1989.

[35] Lin-Vien, D., Bland, B. J., and Spence, V. J., "An Improved Method of Using the Diamond Anvil Cell for Infrared Microprobe Analysis," *Applied Spectroscopy*, Vol. 44, No. 7, 1990, pp. 1227–1228.

[36] Cleverley, B. and Williams, P. P., "Polymorphism in Substituted Barbituric Acids," *Tetrahedron*, Vol. 7, 1959, pp. 277–288.

[37] Mesley, R. J. and Clements, R. L., "Infrared Identification of Barbiturates With Particular Reference to the Occurrence of Polymorphism," *Journal of Pharmacy and Pharmacology*, Vol. 20, 1968, pp. 341–347.

[38] Mesley, R. J., "Spectra-Structure Correlations in Polymorphic Solids—II. 5,5-Disubstituted Barbituric Acids," *Spectrochimica Acta*, Vol. 26A, 1970, pp. 1427–1448.

[39] Berens, L. J., "Barbiturate Identification by Far Infrared Spectroscopy," *Microgram*, Vol. 4, No. 5, June 1971, pp. 100–120.

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