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Microcrystalline Identification of Drugs of Abuse: The "White Cross Suite"

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ABSTRACT: The microcrystallographic properties of the dilituric (5-nitrobarbituric acid) derivatives of the amine drugs found in the illicit street drug preparations known as "white crosses" have been determined. The crystallographic properties, such as the crystal morphology, the extinction angles, the sign of elongation, and front face refractive indices serve to identify the drugs found in the illicit preparations. These data can be used with ultraviolet and infrared spectroscopic and chromatographic evaluations as a major method for the identification of drugs of abuse.

KEYWORDS: toxicology, crystallography, amines, chemical microscopy, drugs of abuse, "white cross suite," amine dilituric acid derivatives, polarizing microscope, crystal morphology, refractive index, extinction angle, photomicrography

The forensic analyst is often challenged to identify drug constituents of an unknown powder, tablet, capsule, or liquid. In most cases, rapid microcrystal [*1*] and color tests [*2*] can be made to delimit the number of drugs present, and thus these tests serve a valuable role in the identification of abused drugs. Other analytical methods used to identify drug samples include thin-layer chromatography (TLC) [*3,4*], gas-liquid chromatography (GLC) [*5,6*], and infrared and ultraviolet spectroscopy [*7,8*] techniques. However, chemical microscopy is a rapid, specific, visible technique [*9-11*] that can be used to identify closely similar chemical compounds [*12,13*]. In many instances, it may be the only feasible method available for the identification of microgram amounts of the drug sample.

"White cross" tablets, known to the street drug abuser as "mini-bennies," are small, white, cartwheel-shaped tablets alleged to contain 2 to 8 mg of *d*-methamphetamine [*14*]. Before the Controlled Substances Act of 1970 was enforced [*15*], these tablets were analyzed at values close to the labeled concentration. However, after more restrictive control measures were imposed on clandestine laboratories and illicit suppliers, amphetamine drugs became scarce on the street drug market. Since 1970, street drug preparations have appeared that contain less than the declared concentration of *d*-methamphetamine, and they also have been substituted freely with other drugs. During the late 1970s, white cross tablets appeared in the marketplace with a substitution rate of at least 70% [*16*] of the alleged labeling. It is the purpose of this communication to present chemical microscopy data and methods that

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will assist forensic scientists in the identification of the more common drug substances of the "white cross tablet suite."

Experimental Procedure

Materials

The drugs commonly found in the white cross suite were obtained from chemical supply houses or from drug manufacturers[3] in the form of their acid salts. Dilituric acid (5-nitrobarbituric acid) used to make the crystalline derivatives was purchased from Eastman Kodak Co., Rochester, N.Y. (EK-2502). The index of refraction reference standards were purchased from R. P. Cargille Co., Cedar Grove, N.J.

Instrumentation

A polarizing (petrographic) microscope was used in the research; however, a standard, bright-field microscope may be used for the evaluation of crystal morphology. Photomicrographic equipment included a Zeiss-RA model microscope fitted with Zeiss 35-mm photomicrographic equipment, including a Zeiss photomicrographic Model-CS camera, a Zeiss "Planapochromat" 10×/0.32 objective, and a Zeiss green contrast filter VG-9. Specifications for photomicrography included the following: Kodak 135 black and white Plus-X film (ASA 125/DIN 22); an Osram 12-V/100-W halogen lamp operated at 5 to 8 V; 100 × magnification; and 0.5- to 2.0-s stop times.

Preparation of Crystalline Derivatives

The crystals for observation were prepared on microscope slides as follows [*17*]. A very small amount of the drug, about 50 to 100 μg, was placed on the microscope slide, and a drop of concentrated (10 mg/mL) dilituric acid in water solution was added. Crystals appeared in seconds to minutes on the slide, which was then covered with a cover slip. When tablets or capsules were the source of the drug chemical under investigation, the unit dosage forms were extracted with a small amount of dilute (70%) methanol. The extract was then reacted with the reagent dilituric acid solution as above to produce the crystalline derivatives. The resultant crystal morphologies are described in the crystal drawings (Fig. 1), the photomicrographs (Fig. 2), and the outlines in Tables 1 and 2.

When the diliturates were prepared for analysis, the acid salt of the drug substance was dissolved in hot water and an equivalent quantity of a hot, aqueous solution of dilituric acid was added. The amine diliturates precipitated upon cooling and were recrystallized from water one or more times. The identity and purity of the salts were established by the determination of the nitrogen content by using the micro-Dumas method. All crystalline derivatives analyzed were within 0.3% of the theoretical values and showed sharp melting points.

Photomicrographs

The photomicrographs of the crystalline dilituric derivatives (Fig. 2) supplement the drawings (Fig. 1) and the written descriptions (Tables 1 and 2) as visual aids and represent the more frequently occurring crystalline types for each drug item.

[3]The authors acknowledge supplies of the following drug chemicals: *d*-chlorpheniramine (Chlor-Trimeton®, Schering), diphenhydramine (Benadryl®, Parke-Davis), mephentermine (Wyamine®, Wyeth), methapyrilene (Histadyl®, Lilly), phentermine (Ionamin®, Pennwalt), propoxyphene (Darvon®, Lilly), and pseudoephedrine (Sudafed®, Burroughs Wellcome). The authors express their appreciation and thanks to the manufacturers who supplied the amine salts used in this study.

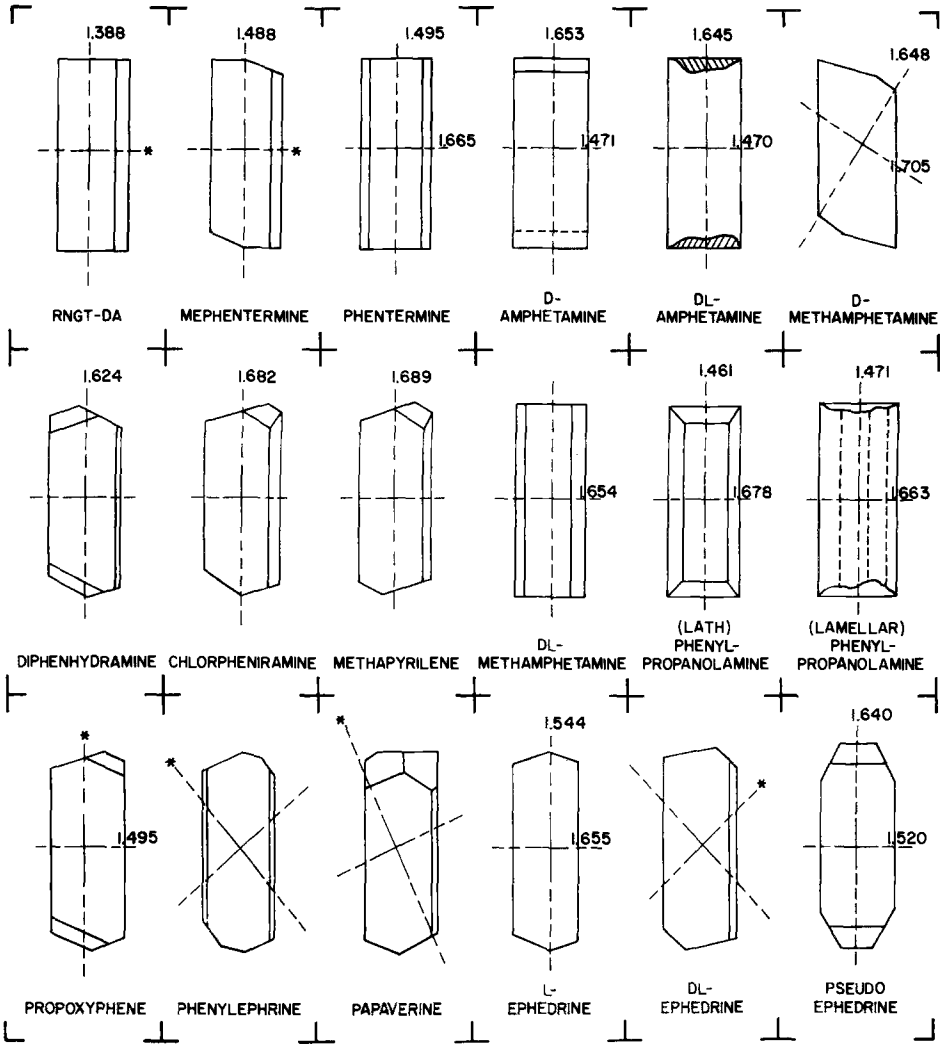

FIG. 1—*Drawings of crystals of amine diliturates (front face).*

Microcrystallography

Microcrystallographic data include the crystal morphology that can be observed with a standard, bright-field microscope and those data studied with the polarizing microscope, such as the refractive indices, the extinction angle, and the sign of elongation. The drawings of the crystals (Fig. 1) and the photomicrographs (Fig. 2) show the crystals in their most frequently occurring front-face orientations.

In Table 1 are listed the refractive indices of each crystal as found on the front face. These indices were obtained by using the Becke line method [*18*]. Briefly, the dried crystals were immersed in liquids having calibrated indices of refraction. If the liquid matched the refractive index of the crystal along the vibration planes (shown as dashed lines in Fig. 1), the crystal would disappear in the liquid. Some of the crystals are not "centered" as they lie on their front faces and the refractive indices of these crystals cannot be obtained within narrow

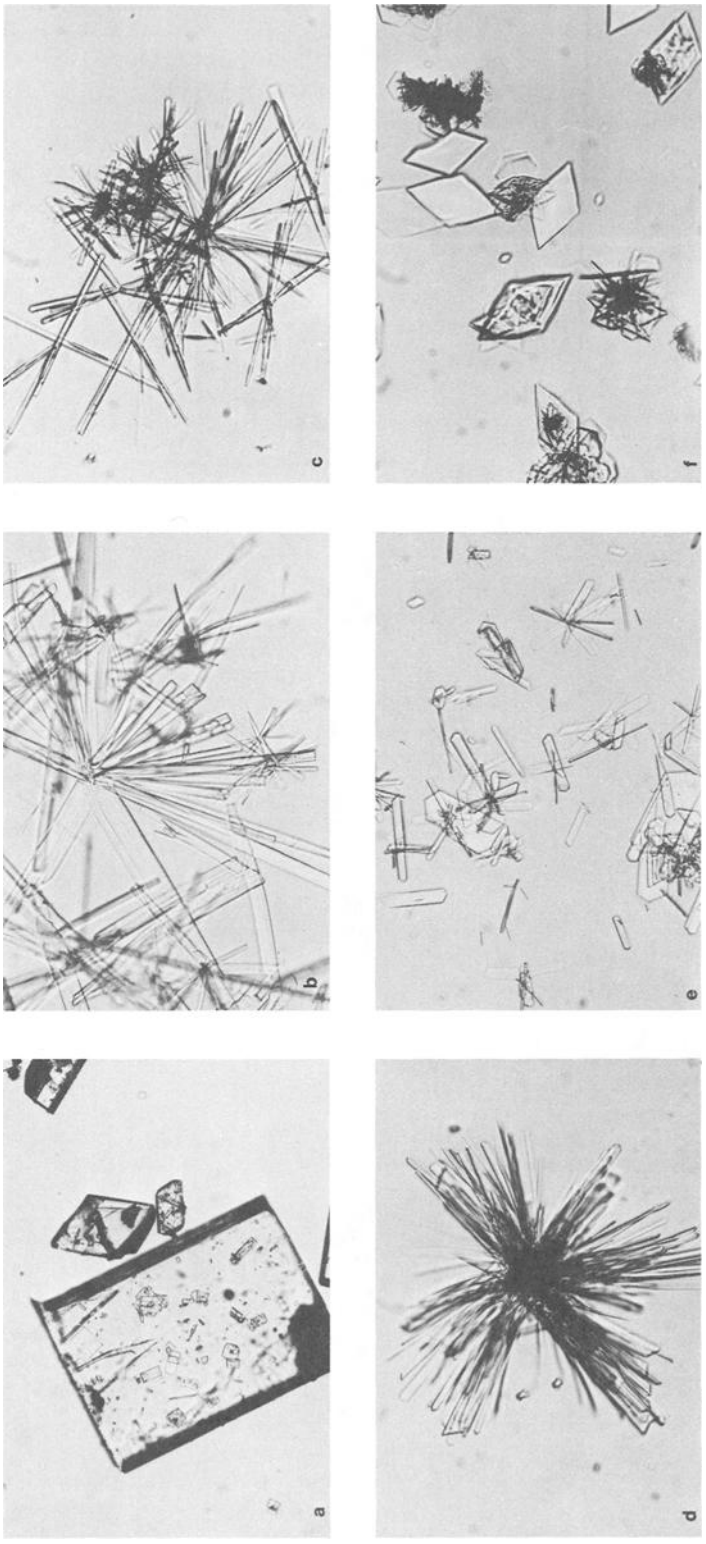

FIG. 2—*Photomicrographs of amine dilliurates:* (a) *reagent, dilituric acid;* (b) *mephentermine;* (c) *phentermine;* (d) *diphenhydramine;* (e) *chlorpheniramine; and* (f) *methapyrilene.*

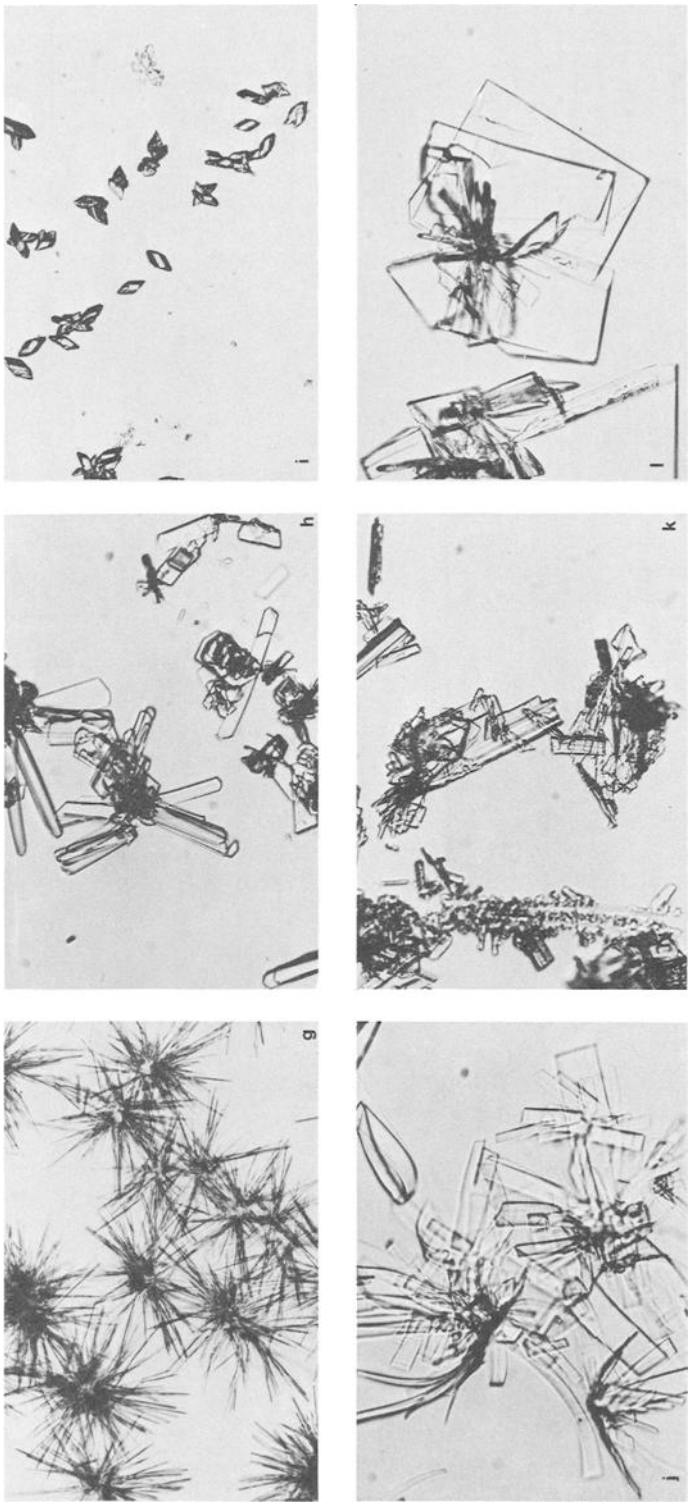

FIG. 2—*Continued:* (g) *propoxyphene;* (h) *phenylephrine;* (i) *papaverine;* (j) d-*amphetamine;* (k) dl-*amphetamine; and* (l) d-*methamphetamine.*

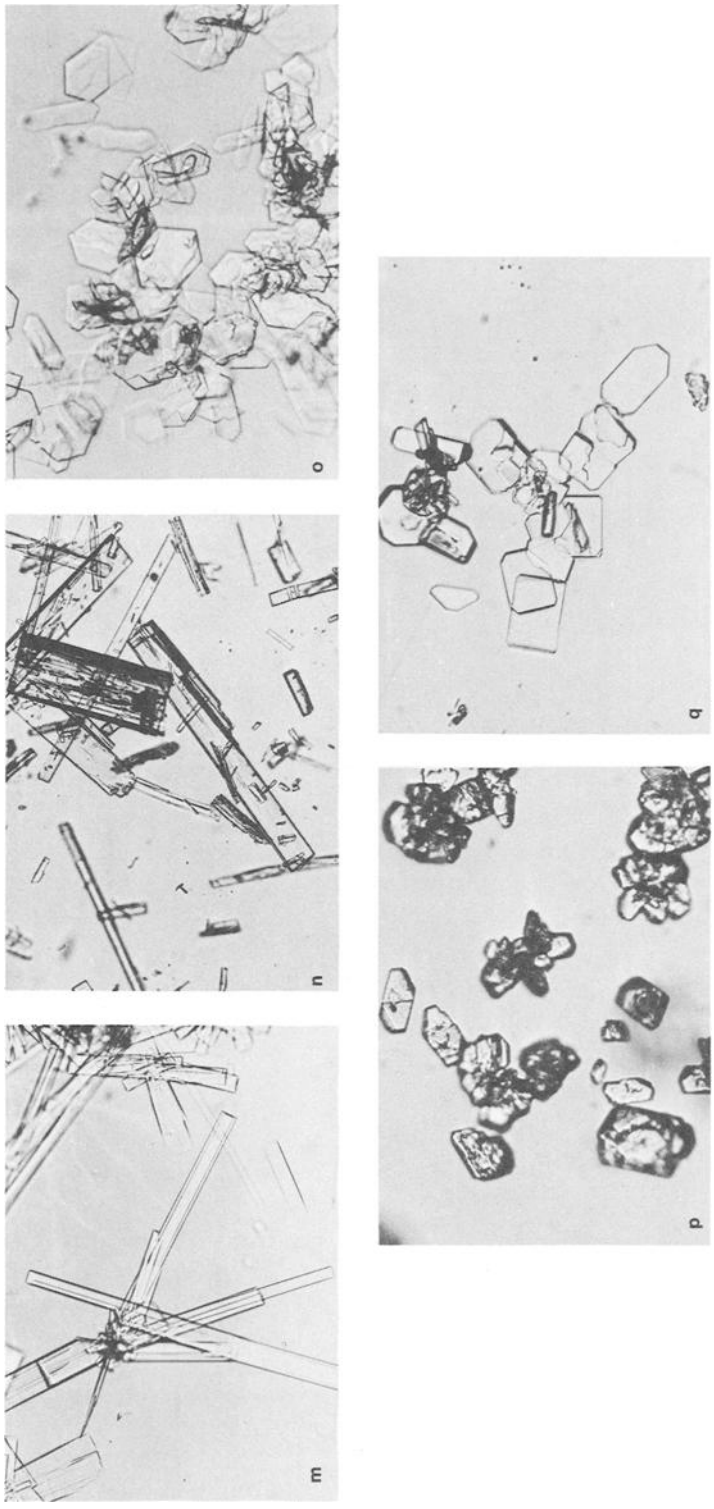

FIG. 2—*Continued:* (m) dl-*methamphetamine;* (n) *phenylpropanolamine (lath-shaped);* (o) l-*ephedrine;* (p) dl-*ephedrine; and* (q) *pseudoephedrine.*

TABLE 1—*Apparent (most frequently observed orientation) properties.*

Drug Dilituarate (Front Face)	Crystal Habit	Extinction Angle	Refractive Indices		Elongation
dl-Amphetamine (Benzedrine®)	platelet	parallel = 0°	1.470	1.645	slow
d-Amphetamine (Dexedrine®)	platelet	parallel = 0°	1.471	1.653	slow
Chlorpheniramine (Chlor-trimeton)	hexagonal platelet	parallel = 0°	variable	1.682	slow
Diphenhydramine (Benadryl)	hexagonal platelet	parallel = 0°	variable	1.624	slow
Ephedrine	hexagonal platelet	parallel = 0°	1.544	1.655	fast
dl-Ephedrine (racephedrine)	hexagonal platelet	front = 38°	variable	variable	fast
Mephentermine (Wyamine)	acicular	parallel = 0°	1.488	variable	fast
dl-Methamphetamine	platelet	parallel = 0°	variable	1.654	fast
d-Methamphetamine (Methedrine®, Desoxyn®)	platelet	front = 33°	1.648	1.705	fast
Methapyrilene (Histadyl)	hexagonal platelet	parallel = 0°	variable	1.689	slow
Papaverine	prismatic	front = 27°	variable	variable	slow
Phentermine (Ionamin)	acicular	parallel = 0°	1.495	1.665	fast
Phenylephrine (Neo-Synephrine®)	prismatic	front = 42°	variable	variable	slow
dl-Phenylpropanolamine (Propadrine®)					
Lath-shaped	lath-shaped	parallel = 0°	1.461	1.678	fast
Lamellar	lamellar	parallel = 0°	1.471	1.663	fast
Propoxyphene (Darvon)	acicular	parallel = 0°	1.495	variable	slow
Pseudoephedrine (Sudafed)	prismatic	parallel = 0°	1.520	1.640	slow
Reagent: dilituric acid	tabular	parallel = 0°	1.388	variable	fast

TABLE 2—*Dilturate microchemical descriptions.*

Substance	Description
	PLATELETS
d-Amphetamine	thin platelets "S to C" shaped on side edges
dl-Amphetamine	poorly formed, splintered, fragmented, elongated platelets
d-Methamphetamine	thin, square platelets twinned on the broad top face
dl-Methamphetamine	elongated platelets with square ends
dl-Phenylpropanolamine	elongated lamellar platelets with square ends
	HEXAGONAL PLATELETS
l-Ephedrine	benzene ring-like platelets
Racephedrine	large yellow, flat crystals twinned on top face
dl-Chlorpheniramine	crystals thinner and more elongated than ephedrine
Methapyrilene	diamond-shaped platelets often found in rosettes
Diphenhydramine	slim, elongated, hexagonal platelets often forming stellate rosettes
	PRISMATIC FORMS
Phenylephrine	commonly shows three faces on the ends of elongated, narrow prisms
Pseudoephedrine	elongated prisms with truncated square ends
Papaverine	small, thickened, diamond-shaped prisms; sides of crystal may appear as wide as the front face
	ACICULAR FORMS
Propoxyphene	elongated needles found in stellate rosettes; the rosettes appear to be connected by acicular branches forming elongated clusters
Phentermine	short acicular needles in stellate formations united as in a "daisy chain"
Mephentermine	long needles in stellate rosettes with lath-like bases

limits. These indices are reported as "variable," and asterisks are used in Fig. 1 to indicate the higher refractive index in an orientation unless values are given for it.

The extinction angle data were obtained by aligning the long length of the crystal with the cross hair of the microscope and turning the crystal on the rotating stage to the point of extinction or darkness. The extinction angle ($\leq 45°C$) is then determined on the calibrated microscope stage. The sign of elongation is obtained by aligning the long side of the crystal in the 45° position with the unit retardation plate (Gypsum, 1λ plate) of the microscope. A negative sign of elongation [(−) = fast] is recorded when the polarization colors or birefringence increases in order when the long side of the crystal coincides with the fast ray of the speed plate and conversely.

Results and Discussion

Significant Properties

The most significant chemical microscopical properties are shown in Table 1, Fig. 1, and the photomicrographs (Fig. 2). The crystals of the diliturates are so flattened that, when suspended in a liquid on a microscope slide, nearly all crystals assume the same or nearly the same orientation. Optical properties (Table 1) noted are the crystal morphology (Figs. 1 and 2), the extinction angle, and the refractive indices on the front face of the crystal. These data serve to identify the drug chemical under investigation.

To facilitate the use of the data found in Table 1, the following morphological forms described by Clarke [*19*] are repeated here:

1. A needle, an acicular form, is a long thin crystal with pointed ends.
2. A rod is similar to a needle but with square-cut ends.
3. A blade is a broad needle, becoming a plate when length and breadth are of the same order of magnitude.
4. A tablet is a plate with appreciable thickness, becoming a prism as the thickness increases.
5. For multiple crystal forms, a rosette is a collection of crystals radiating from a single point, while a cluster is a loose complex of crystals termed a bundle when most of the crystals lie in one direction.
6. Dendrites are multibranched crystals.

Descriptions of Crystal Derivatives

Additional descriptions of some of the dilituratates will facilitate identification of them. The reagent, dilituric acid, rarely crystallizes out of solution at the concentration employed; however, small, square to rectangular tablets are characteristic of this chemical. Other descriptions have been summarized in Table 2.

Other drugs found in "white crosses" that do not form microcrystalline derivatives with dilituric acid are the xanthines—caffeine and theophylline. These two drugs form characteristic crystal derivatives with the chlorauric acid reagent of Fulton [*20*]. With this reagent, caffeine appears as acicular needles in rosettes and theophylline as rod-like tablets also in rosettes.

Conclusions and Summary

The role assigned to microcrystallography by many forensic analysts is one of either confirming or refuting information obtained from color tests and other "presumptive" analytical procedures [*21*]. It has also been observed by some analysts that crystal tests, characteristically, have been found to be somewhat subjective in nature. These references probably result from the fact that crystalline morphology was the sole microcrystallographic parameter evaluated. If the other criteria of chemical microscopy presented in this paper, such as the vibration directions, the refractive indices, the extinction angle, and the sign of elongation, are used, microcrystalline data would better serve the analyst as a more reliable and a less presumptive procedure in the analytical scheme.

A procedure for the preparation of crystalline derivatives of drugs found in the illicit street drug preparation termed the "white cross suite" has been presented. The chemical microscopy of the dilituratate derivatives of these drugs has been evaluated, listed, and reviewed. These data serve to identify these drugs and thus can be used as a principal method for drug identification.

Acknowledgments

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