TECHNICAL NOTE

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Impurity Profiling Analysis of Illicit Methamphetamine by Capillary Gas Chromatography

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ABSTRACT: The characterizations of methamphetamine samples illegally marketed in Japan were examined by capillary gas chromatographic impurity profiles. The ethyl acetate-extract under basic condition showed the most characteristic and diagnostic gas chromatographic profiles. Most tested samples showed different impurity profiles, though expected similarities existed between some samples found at the same places and times. These profiles were not influenced by the storage of samples. The comparison of impurity profiles obtained by the reported procedure provides very useful information for determining the common and different origin of methamphetamine seizures.

KEYWORDS: forensic science, methamphetamine, impurity profiles, gas chromatography, discrimination, statistical analysis

The differentiation of illicit drug samples is one important objective for intelligence purposes, establishing relationships between seizures or providing evidence of links between dealers and users. Heroin and cocaine samples have been derived from natural origin (opium poppy via morphine and coca leaves) and characterization of certain natural products or their derivatives present in exhibits can provide useful information for establishing a common or different origin of the samples. On the other hand, amphetamine/methamphetamine samples have been synthesized chemically and they contain by-products and residual chemicals. Samples from various manufacturing processes and batches may be characterized by the detection and quantification of impurities, such as starting materials and by-products, diluents and adulterants. Gas chromatographic and high-performance liquid chromatographic procedures have been reported for comparative analysis of illicit abused drugs such as amphetamine/methamphetamine [*1–6*], heroin [*7–13*] and cocaine [*14–20*].

One of the most frequently abused drugs in Japan is methamphetamine. Amphetamine/

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methamphetamine abused in the United States and Europe are usually prepared by the Leuckart reaction and sometimes contain diluents and adulterants. Several studies have been reported on impurity patterns and identification of impurities in Leuckart produced amphetamine/methamphetamine [*1–6*]. Methamphetamine used in the Japanese illicit trade is the *d*-isomer most often synthesized from ephedrine. Samples consist of clear, colorless and relatively big crystals without diluents and/or adulterants. Purities are very high without any appreciable impurities. Although some impurities have been reported in methamphetamine prepared from ephedrine [*21–25*], comparison of impurity profiles of methamphetamine obtained via reduction of ephedrine has not been performed.

In this paper, the most effective extraction method for impurity profiling analysis of methamphetamine seized in Japan is examined by gas chromatography and a statistical approach for comparative analysis is discussed.

Materials and Methods

Instruments and Chromatographic Condition

The gas chromatograph (GC) used was a Hewlett-Packard 5890 series II equipped with a flame ionization detector. Injections of 2 microliter (μL) were made at the splitless mode using Hewlett-Packard 7673 autosampler. The column was a fused-silica wide-bore capillary column, DB-1 (15 m × 0.53 mm i.d., film thickness 1.5 μm, J & W, Cal). The injector and detector temperatures were maintained at 270°C and 250°C, respectively. The column oven temperatures was held at 100°C for 1 min, programmed to 200°C and ramped at 15°C/min, then programmed to 208°C and ramped at 2°C/min, then increased to 300°C and ramped at 10°C/min, and finally held at 300°C for 18 min. The carrier gas was helium at a flow rate of 7 mL/min.

Sample Preparation

A sample of 100 mg of seized methamphetamine hydrochloride was dissolved in 1 mL of 0.1 M phosphate buffer (pH 7.0). The solution was made basic with 0.25 mL of 10% Na_2CO_3 and extracted by vigorous shaking for 10 min with 0.2 mL of extracting solvent, containing tetratriacontane (0.05 mg/mL) as an internal standard. After centrifuging the sample, the organic layer was transferred into the inserts of microvials (Hewlett-Packard) for the autosampler with a disposable pipette. As the extracting solvents, *n*-hexane, *n*-octane, toluene and ethyl acetate were examined. For extraction under acidic condition, each sample was dissolved in 1 mL of 0.1 M acetate buffer (pH 6.0) and extracted with 0.2 mL of *n*-hexane in a similar manner as described.

Results and Discussion

Extraction Procedure

Gas chromatograms of *n*-hexane extracts under acidic and basic conditions were shown in Fig. 1.

For impurity profiling studies of methamphetamine prepared by Leuckart reaction, Strömberg et al. [*2*] and Lambrechts et al. [*3*] used a *n*-heptane- and a benzene-extraction respectively under acidic condition. For identification of impurities in methamphetamine, synthesized from ephedrine, Cantrell et al. [*23*] isolated naphthalene-type impurities, 1-benzyl-3-methylnaphthalene and 1,3-dimethyl-2-phenylnaphthalene, by trituration of sample with acetone followed by partition of acetone evaporated residues between dichloromethane and 0.05 M H_2SO_4. Skinner [*24*] also extracted the neutral phenyl-2-

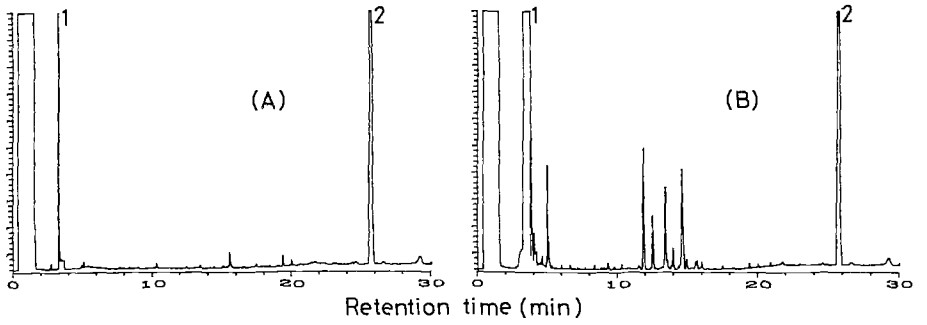

FIG. 1—*Gas chromatograms of* (A) *acidic and* (B) *basic extracts of illicit methamphetamine using* n-*hexane. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

propanone and the naphthalene-type impurities from methamphetamine prepared from ephedrine with ether under acidic condition. However, acidic extracts of methamphetamine seized in Japan showed no significant peaks. While the basic extract exhibited many diagnostic peaks as shown in Fig. 1.

n-Hexane, *n*-octane, toluene, and ethyl acetate were examined as extracting solvents. These organic solvents were selected because of easy handling in transferring after extraction. Each blank extract using these solvents showed no significant peaks on gas chromatograms. Of these solvents, as shown in Fig. 2 ethyl acetate showed the best

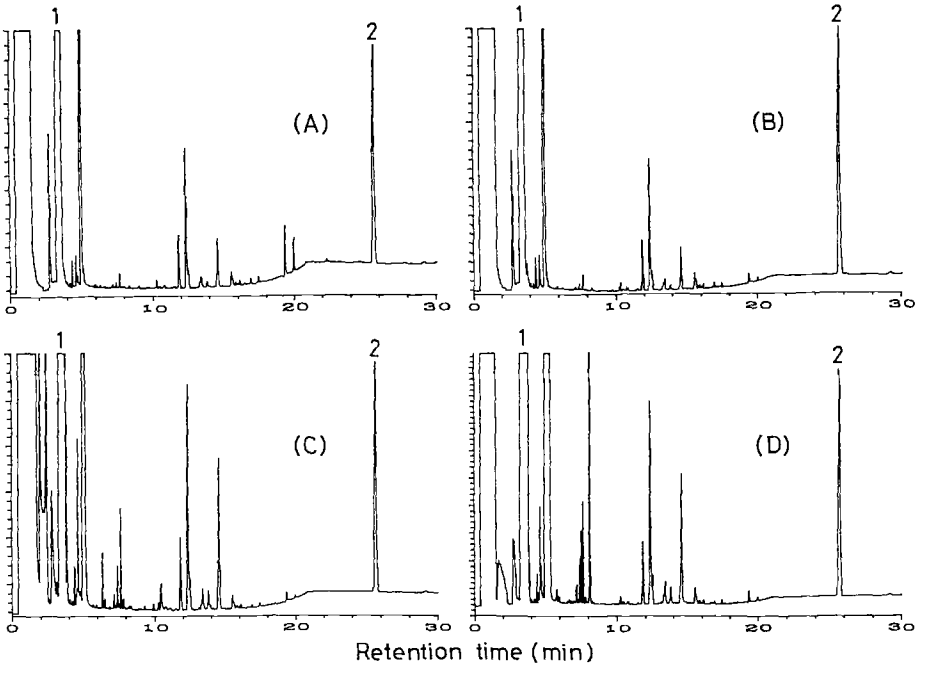

FIG. 2—*Gas chromatograms of extracts of illicit methamphetamine using* (A) n-*hexane,* (B) n-*octane,* (C) *toluene and* (D) *ethyl acetate. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

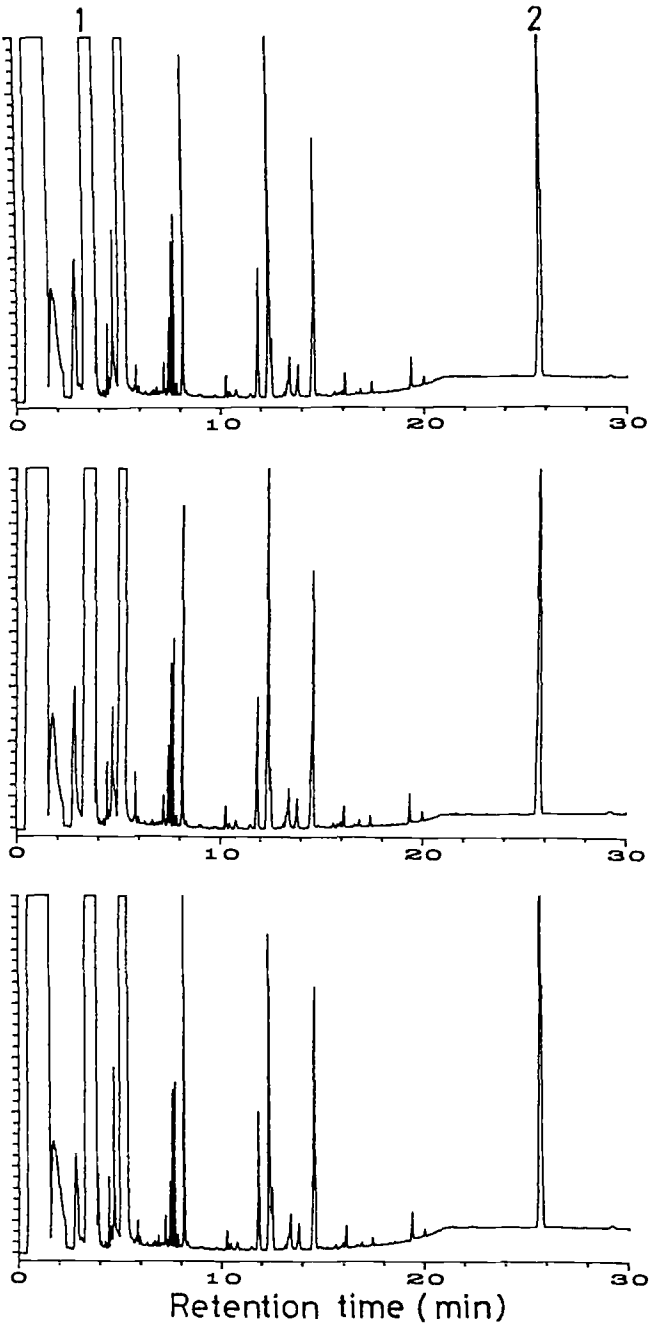

FIG. 3—*Gas chromatograms obtained from three random samples originating from the same package. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

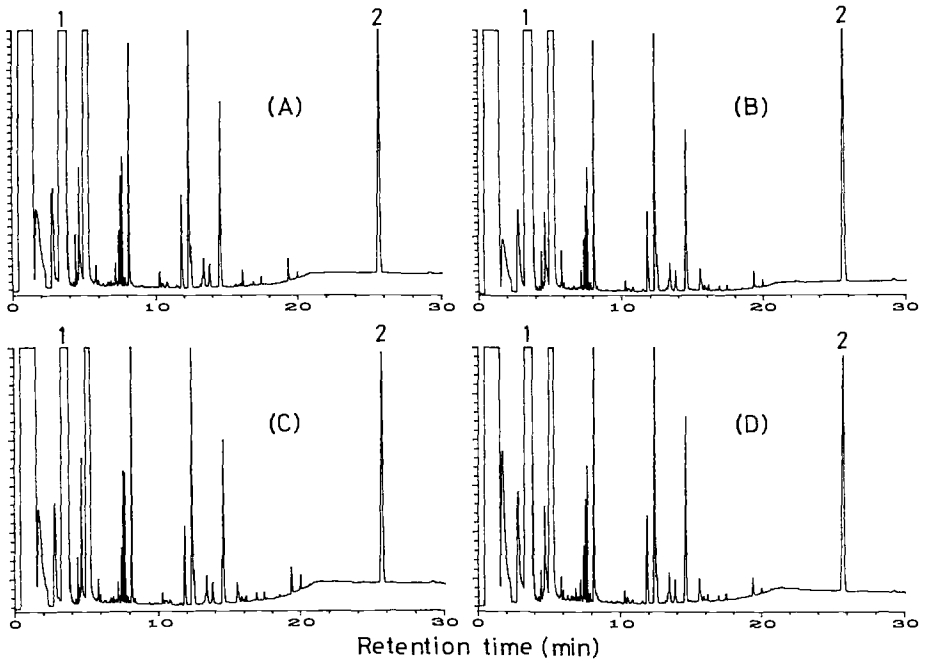

FIG. 4—*Change of impurity profiles after storage of samples at room temperature for various periods.* (A), *original;* (B), *1 week;* (C), *3 weeks;* (D), *8 weeks. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

extraction efficiency, that is, ethyl acetate-extract gave higher and more peaks on the gas chromatogram than other extracts. In particular, the impurity having the retention time at approximately 8 min could be extracted only with ethyl acetate.

From those results, the extractions were carried out with ethyl acetate under basic condition in the subsequent experiments.

Intra-Sample Variation

The establishment of a "common source" of drugs is dependent on the difference between the magnitude of inter- and intra-batch variation in their impurity profiles. As mentioned in the Introduction, methamphetamine samples illegally marketed in Japan consist of relatively big crystals, and heterogeneity of impurities is anticipated in the same batch.

Three random samples from the same plastic bag seized in 32 caseworks were analyzed. Each of the three samples originating from the same package showed very similar chromatograms. Figure 3 shows typical gas chromatograms obtained from three samples originating from the same bag. It indicates that the variation of impurities within the packages is very small.

Stability of the Impurities

The stability of impurities in methamphetamine samples was examined by storing the ground and homogenized sample in closed glass containers in darkness at room temperature.

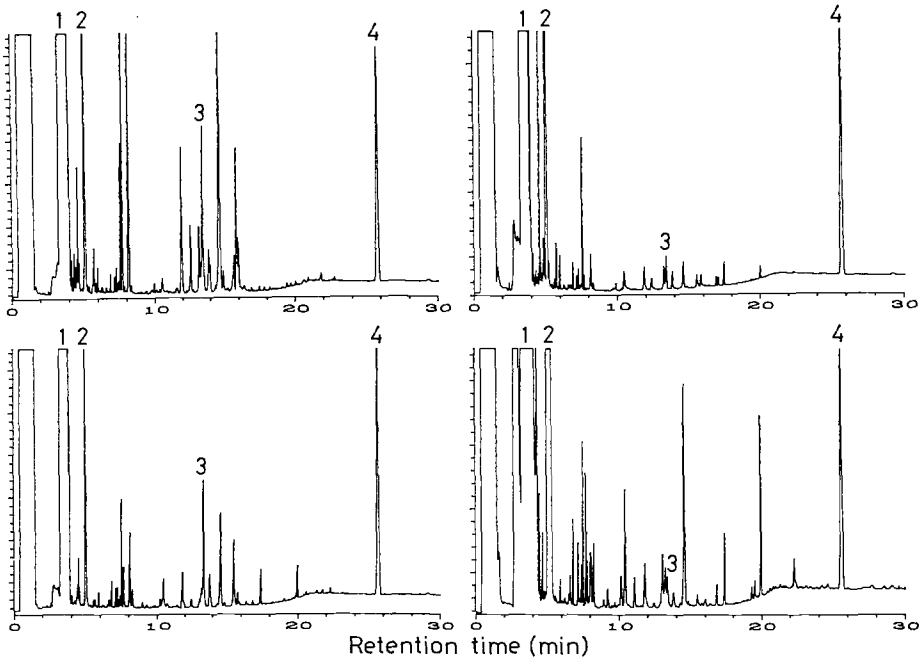

FIG. 5—*Typical impurity profiles of different methamphetamine samples. Peaks: 1 = methamphetamine; 2 = ephedrine; 3 = methamphetamine dimer; 4 = tetratriacontane (internal standard).*

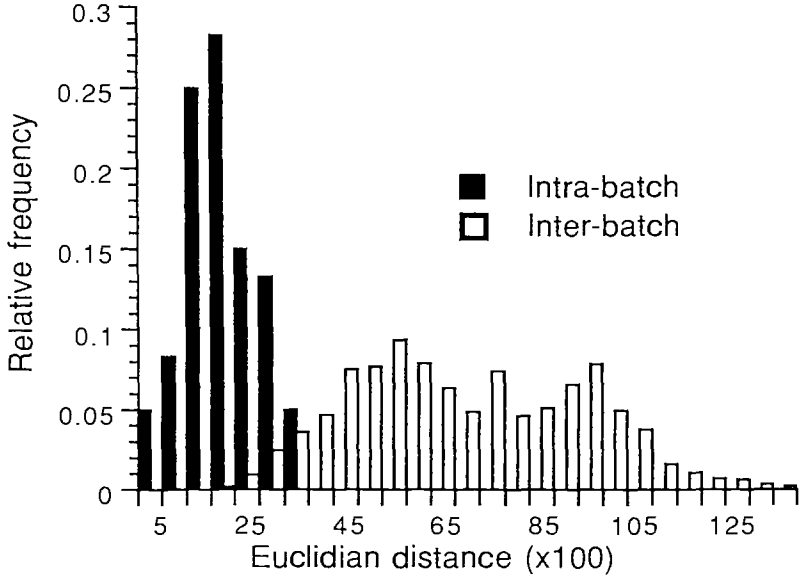

FIG. 6—*Distribution of Euclidian distances among methamphetamine samples.*

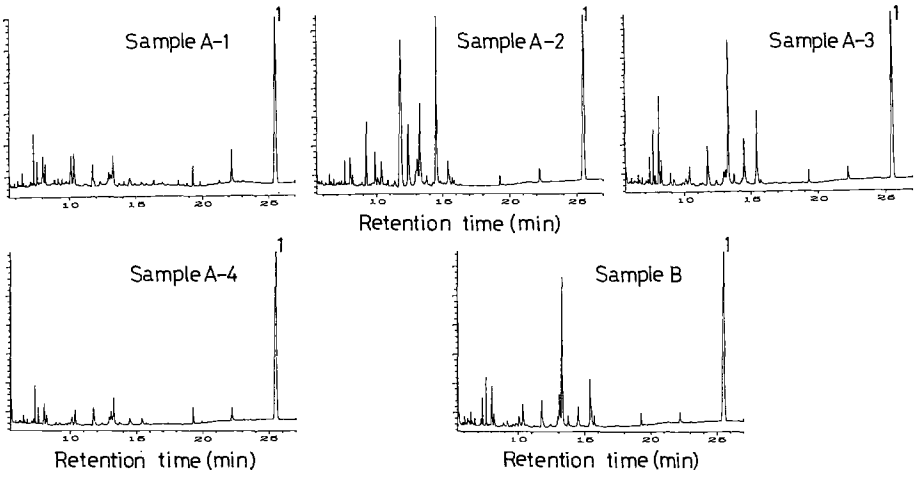

FIG. 7—*Expanded impurity profiles of methamphetamine exhibits in Case 1. Samples A-1~A-4 and Sample B were possessed by Suspect A and B, respectively. Peak 1 is tetratriacontane (internal standard).*

Figure 4 shows the chromatograms of the extracts obtained from the sample after storage for various periods. The impurity profiles remained similar in any storage period of time during 8 weeks. This indicates that the impurities analyzed here are very stable, not lost by vaporization and do not change into other compounds.

Inter-Sample Variation

More than 130 methamphetamine seizures from 24 different places in Japan were analyzed. Some typical gas chromatograms are shown in Fig. 5. Although some samples seized at the same place and time showed very similar chromatograms, most samples exhibited differences and individual characteristics. In order to evaluate the significance of the differences in each chromatogram, the Euclidian distance ($d_{a,b}$) between each of two chromatograms obtained from sample a and b is calculated as follows:

$$d_{a,b} = [\Sigma\ (x_{aj} - x_{bj})^2]^{1/2}$$

x_{aj} : the area ratio of peak j to the internal standard in chromatogram of sample a
x_{bj} : the area ratio of peak j to the internal standard in chromatogram of sample b

We define $d_{a,b}$ as the distance between sample a and b. The distances between samples

TABLE 1—*Euclidian distances among samples seized in case 1.*

	A-1	A-2	A-3	A-4	B
A-1	0.000	0.460	0.487	0.130	0.428
A-2		0.000	0.464	0.454	0.420
A-3			0.000	0.496	0.181
A-4				0.000	0.430
B					0.000

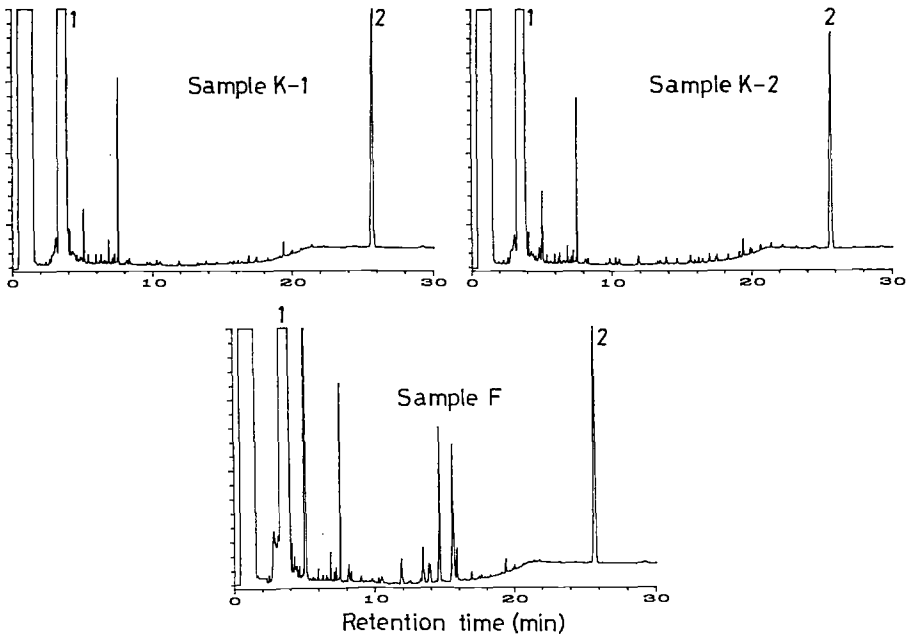

FIG. 8—*Impurity profiles of methamphetamine exhibits in Case 2. Sample K-1 and K-2 were found at the same place and time, while Sample F was seized at another place. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

seized at the same place and time are less than 0.35 (mean = 0.180, range = 0.026–0.349), while distance between samples shown in Fig. 5 are 0.378–1.500 (mean = 0.979). In Fig. 6, the distribution of Euclidian distances among analyzed methamphetamine exhibits are summarized. It indicates that the inter-batch variation of impurity profiles are significantly greater than the intra-batch variation.

From these results, it is confirmed that the impurities analyzed here form a very suitable index for determining the commonality of origin for methamphetamine samples.

With regard to the identification of impurities found by gas chromatography, ephedrine and methamphetamine dimer were confirmed by GC/mass spectrometry as described in the previous paper [*25*]. However, naphthalene-type impurities, which occur in methamphetamine synthesized from ephedrine via reduction with hydroiodic acid [*23,24*], were not detected. Identification of other impurities is under investigation.

Analysis of Casework Samples

Case 1—Suspect A was arrested for possession of methamphetamine samples. He had four packages containing 23.35 g (Sample A-1), 7.08 g (Sample A-2), 6.43 g (Sample

TABLE 2—*Euclidian distances among samples seized in case 2.*

	K-1	K-2	F
K-1	0.000	0.038	0.590
K-2		0.000	0.614
F			0.000

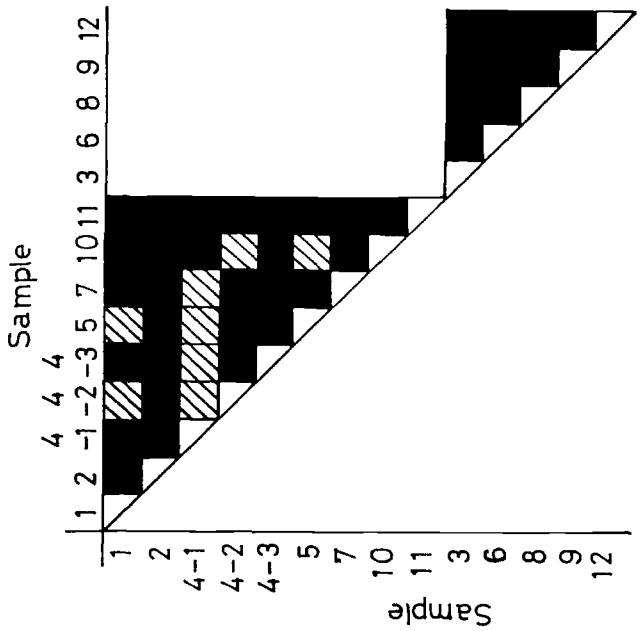

FIG. 9—*Euclidian distances* (d) *among samples seized in Case 3. Samples 1~6 was found in a car and Samples 7~12 in a yacht. Samples 4-1, 4-2 and 4-3 were originated from the same package.* ■, $d \leq 0.15$; □, $0.15 < d \leq 0.25$ →; □, $0.15 < d \leq 0.25$.

A-3) and 6.71 g (Sample A-4) of the drug, respectively. He confessed that he had sold some methamphetamine packages to Suspect B and 3.41 g of methamphetamine sample (Sample B) was found in Suspect B's house. In order to warrant Suspect A's confession, impurity profiles of these 5 samples were compared. As shown in Fig. 7, a good correspondence between the profiles of Sample A-3 and Sample B was observed, while Samples A-1 and A-4 also showed very similar impurity profiles. The similarity or dissimilarity of each sample was evaluated by calculation of Euclidian distances between the particular samples. The results were shown in Table 1. The distance between Sample A-3 and Sample B is 0.181 and that between Sample A-1 and A-4 is 0.130. These results

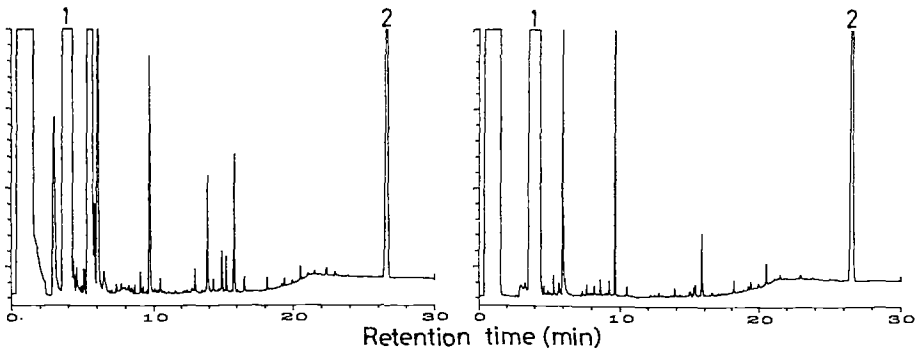

FIG. 10—*Typical impurity profiles of methamphetamine exhibits that seem to belong to different groups in Case 3. Peaks: 1 = methamphetamine; 2 = tetratriacontane (internal standard).*

suggest that Sample A-3 and Sample B originate from the same batch, leading to warrant Suspect A's confession from a scientific standpoint.

Case 2—A sample containing 500 g of methamphetamine hydrochloride (Sample F) was found in a car. The car owner belonged to an organized crime group (Boryokudan) in F prefecture. The Police Intelligence Unit received information that the group had a connection with some Boryokudans in K prefecture. At about the same time, 1.8 kg of methamphetamine, packed in two bags (Sample K-1 and K-2), was seized at an apartment house where a member of a Boryokudan had lived in K prefecture. To examine the links between these two Boryokudans, three seizures were subjected to laboratory analyses. Sample K-1 and K-2 showed very similar impurity profiles to each other, but their profiles were different from that of Sample F (Fig. 8). These observations were supported by calculation of the Euclidian distance among each of the samples (Table 2). From these facts, it was considered that Sample K-1 and K-2 originated from the same batch, but the origin of Sample F was different. More investigation of the intelligence unit has revealed these two Boryokudans have no connections.

Case 3—Forty-nine packages, each containing about 1 kg of methamphetamine sample, were found in a car that was parked in a parking place near a yacht marina. Another 51 packages were found in a yacht anchored at the marina. We were asked to clarify the relationship between these seizures. Six packages (Samples 1 to 6) from the car and six packages (Samples 7 to 12) from the yacht were randomly selected and impurity profiling analysis was performed.

The Euclidian distance between samples (Fig. 9) indicated that the 12 samples were classified into two groups. Very high similarities were observed between Samples 1, 2, 4, and 5 found in the car and Samples 7, 10 and 11 found in the yacht. In addition, similarity was found between Samples 3 and 6 in the car and Samples 8, 9, and 12 in the yacht. From these results, we considered that these seizures belong to the same illegal marketing route and originated from two batches. The typical chromatograms of samples in each group are shown in Fig. 10.

Conclusions

We have examined extraction procedures for characterization of methamphetamine seizures in Japan by gas chromatographic impurity profiles. The extraction with ethyl acetate under basic condition gives characteristic impurity profiles by capillary gas chromatography. The comparison of profiles obtained by this method provides very useful information for determining the common and different origins of methamphetamine exhibits.

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