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The Identification of Unreacted Precursors, Impurities, and By-Products in Clandestinely Produced Phencyclidine Preparations

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ABSTRACT: The typical phencyclidine sample found in clandestine laboratories can be contaminated by the presence of unreacted precursors and large amounts of impurities and by-products. Although this may involve an extensive "cleanup" procedure before phencyclidine identification, the additional analysis of the sample for the impurities will often confirm the synthetic process employed. A gas chromatography/mass spectrometry procedure has been developed in which the 13 major components, including phencyclidine and piperidinocyclohexane carbonitrile, found in these typical clandestine mixtures, may be screened for and identified. The data obtained from this analysis are consistently used as an aid to the successful prosecution of "intent to manufacture" cases.

KEYWORDS: toxicology, criminalistics, controlled substances, phencyclidine

Phenylcyclohexylpiperidine, commonly referred to as PCP or phencyclidine, continues to be a major drug of abuse in this country [*1*]. Most of the PCP obtained is synthesized in crude clandestine laboratories [*2*]. The popularity of these laboratories is due, in part, to the fact that PCP is easy to manufacture and the starting materials are relatively inexpensive in terms of the ultimate profit. Frequently, it is found that the laboratory operator has little knowledge or experience in chemistry. Due in part to this inexperience, the final product is often contaminated with starting materials, reaction intermediates, and by-products.

One of the most beneficial aids in the successful prosecution of clandestine laboratory operators is the forensic chemist's thorough knowledge of their manufacturing procedure. Frequently, the synthesis route is inferred from evidence of precusor chemical purchases. Showing the fact that these chemicals were purchased by the clandestine laboratory operator and were found on the laboratory premises is perforce important to the prosecution. An equally beneficial approach is to establish that laboratory procedures such as mixing and extracting of essential ingredients were employed. One way that this may be accomplished is by analyzing the contaminants found in PCP samples. If there is no finished product available, the same end may be accomplished by analyzing unwashed

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laboratory equipment found on the premises. With this information, it is often possible to verify that there was a controlled substance being manufactured, or that an attempt was made for its production. In a number of cases it is even possible to establish the synthetic route that was being employed.

Synthesis

Although a number of synthetic routes are possible for the manufacture of PCP, only two of them are commonly employed by clandestine laboratory operators [*3–9*]. The first and most popular method used is the "nitrile intermediate" method. In this procedure, piperidine, cyclohexanone, and a cyanide salt are reacted to form the intermediate 1-piperidinocyclohexane carbonitrile (PCC). The PCC intermediate is then added to the phenylmagnesium bromide, Grignard reagent, to form the final product PCP (Fig. 1).

The second method used is the "enamine intermediate." This procedure employs a dehydration reaction of piperidine and cyclohexanone to form the intermediate 1-piperidinocyclohexene. This intermediate is then reacted with *para*-toluenesulfonic acid to form the tosylate salt. The phenylmagnesium bromide, Grignard reagent, is then added to this slurry, producing PCP (Fig. 2).

Instrumental

The gas chromatography (GC) data for the packed column data were obtained on a Hewlett-Packard Model 5840A gas chromatograph with a flame ionization detector (FID). The columns used were: (*a*) a 6-ft by ⅛-in. (1.8-m by 3-mm) inner-diameter glass column packed with 10% OV-101 on 100–120 mesh Gas-Chrom Q, and (*b*) a 6-ft by ⅛-in. (1.8-m by 3-mm) inner-diameter glass column packed with 3% OV-17 on 100–120 mesh Gas-Chrom Q. The parameters were the same for both columns. The injector temperature was 275°C; the detector temperature was 300°C; and the initial column

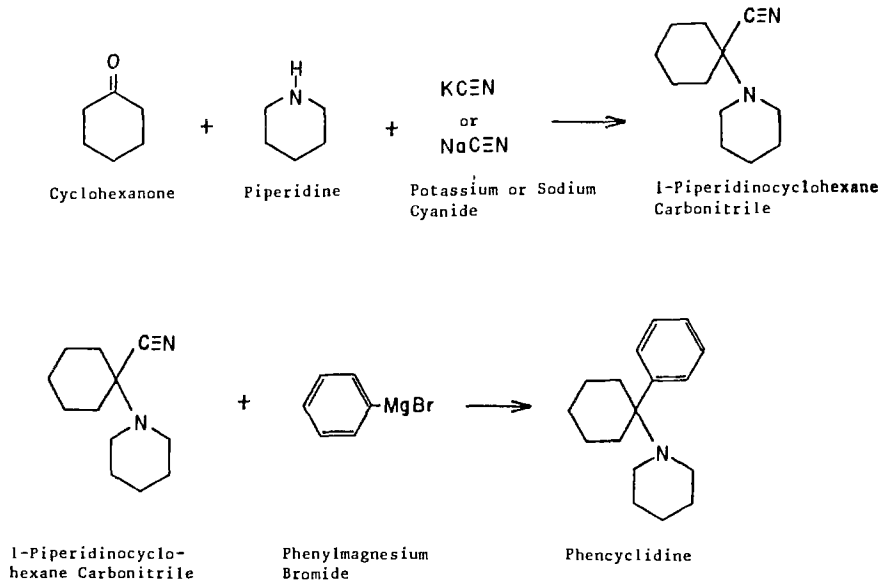

FIG. 1—*PCP synthesis by the carbonitrile method.*

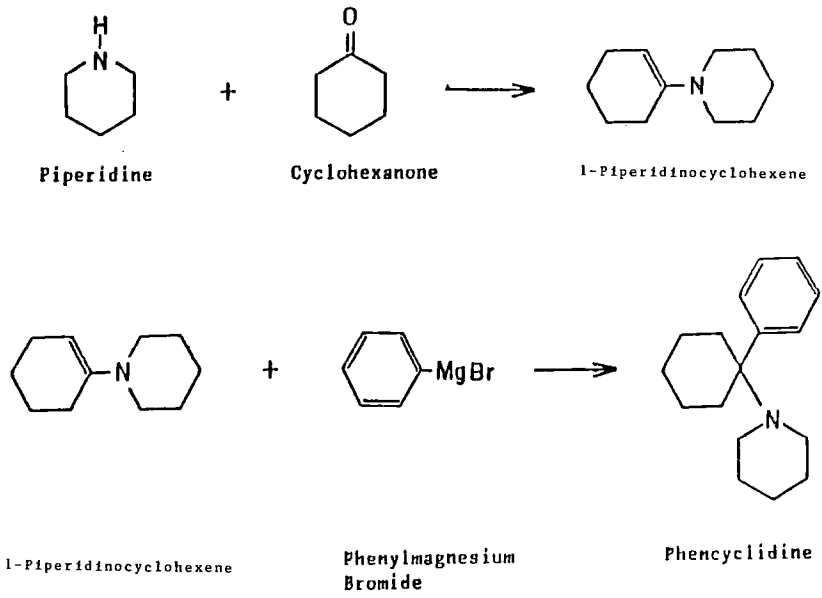

FIG. 2—*PCP synthesis by the enamine method.*

temperature was set at 90°C for 3 min, with a rate of 10°C/min for 16 min up to a final temperature of 250°C, which was held for 2 min.

The gas chromatography/mass spectrometry (GC/MS) was performed on a Hewlett-Packard Model 5970 mass selective detector. The capillary column used was a 12-m by 0.20-mm fused silica HP-1, which has a 0.33-μm film coating of 100% dimethyl polysiloxane gum. The parameters were as follows: the injector temperature was 275°C; the split injection ratio was 45:1; the detector temperature was 280°C; and the current was 70 eV.

Results and Discussion

To establish a system for the routine analysis of samples seized from laboratories producing PCP by either of these methods, it was first necessary to determine what by-products were formed in a typical synthesis. To obtain this information, a number of PCP samples seized from clandestine laboratories were analyzed by GC/MS. Thirteen major low-molecular-weight components were identified which were indicative of routine syntheses. Some of these are obvious intermediates and by-products [*10–13*], while others needed to be synthesized or purchased. No consideration was given to low-concentration, high-molecular-weight components previously identified [*14*]. Using these standards, a mixture was then prepared at an approximately 1-mg/mL concentration of each component. Table 1 lists the individual components.

The first GC results obtained were performed using packed columns. Due to the rapid elution of the low-boiling-point components, a temperature program was employed. This procedure was first attempted on the "nitrile intermediate" synthesis. All of the components are sufficiently resolved for screening purposes on both columns except for the following: phenylcyclohexene and biphenyl coeluted on the OV-101 column, while cyclohexanone and bromobenzene coeluted on the OV-17 column [*15*]. In addition, a possible coelution based on the relative retention times of piperidinocyclohexene and

TABLE 1—*Components of the procedural standard.*

Component	Molecular Weight	Synthesis[a]
Starting reagents		
Cyclohexanone	98	B
Piperidine	85	B
Bromobenzene	157	B[b]
Reaction intermediate		
1-Piperidinocyclohexene[c]	165	E[d]
1-Piperidinocyclohexane carbonitrile	191	N
By-products		
1-Cyclohexylpiperidine	167	B
Biphenyl	154	B
1-Phenylcyclohexene	158	B
1-Phenycyclohexanol	176	B
Phenol	94	B
1-Phenylethanol	122	B
2-(1-Cyclohexenyl)cyclohexanone	178	E
Final product		
1-Phenylcyclohexylpiperidine	243	B

[a]E = enamine method; N = nitrile method; B = both methods.
[b]May not be present if phenylmagnesium bromide is purchased.
[c]Alternately named 1-(1-cyclohexenyl)piperidine.
[d]May also be formed by thermal degradation of PCC from the nitrile method.

PCC was observed on both columns. It was later determined that PCC was not coeluting but was instead thermally degrading to piperidinocyclohexene in the injection port [*16*].

The procedure was then performed on clandestine laboratory samples synthesized by the "enamine intermediate" process. All the components were again sufficiently resolved for screening purposes on both columns, as previously stated. For example, the analysis indicated that biphenyl and phenol, by-products of the Grignard reaction, were present in the mixture, and yet, no bromobenzene was detected. The conclusion was reached that the clandestine laboratory operator purchased phenylmagnesium bromide rather than preparing it from bromobenzene and magnesium turnings [*17*].

A more comprehensive examination was performed by GC/MS with a capillary column. All of the twelve components observed on the packed columns were resolved, and the PCC which decomposed on the packed columns could now be detected intact from the capillary column [*18*]. For example, if PCC is detected, the "nitrile intermediate" synthesis route is definitely established. If no PCC is detected and piperidinocyclohexene is found, then the "enamine intermediate" synthesis was used by the clandestine laboratory operator. Table 2 provides the GC analytical data. Figure 3 shows the total ion current (reconstructed chromatogram) from the GC/MS. Mass spectra of each of the 13 components are not included since most are readily available either from the literature or from standards.

Procedural Standard

The procedural standard is composed of the individual components listed in Table 1, with each diluted to a concentration of approximately 1 mg/mL in methanol. Solid PCP samples are prepared by taking 1 to 3 mg samples and diluting them with methanol.

TABLE 2—*GC relative retention time of the components of the procedural standard.*

Compound	Relative Retention Time		
	OV-101	OV-17	HP-1
Piperidine	0.11	0.06	0.09
Cyclohexanone	0.21	0.15	0.16[a]
Bromobenzene	0.26	0.15	0.19
Phenol	0.3	0.22	0.24[b]
1-Phenylethanol	0.38	0.33	0.27
1-Cyclohexylpiperidine	0.62	0.5	0.47
1-Piperidinocyclohexene	0.66	0.58	0.53
1-Piperidinocyclohexane carbonitrile (PCC)	0.66	0.58	0.77
Biphenyl	0.66	0.64	0.52
1-Phenylcyclohexene	0.68	0.64	0.55
1-Phenylcyclohexanol	0.73	0.73	0.67
2-(1-Cyclohexenyl)cyclohexanone	0.76	0.76	0.71
Phencyclidine (PCP)	1.00	1.00	1.00

[a]Two peaks on this column at 0.158 and 0.166.
[b]Two peaks on this column at 0.239 and 0.242.

Liquid PCP samples are prepared by diluting 1 mL of sample with 4 mL of methanol. Due to the varying concentrations of clandestine laboratory mixtures, the dilution of the sample with methanol will not be consistent.

Several minor components have been observed which are impurities in the various standards.

Conclusions

The work described is the result of an ongoing effort to elicit the maximum amount of information necessary for successful prosecution of clandestine PCP laboratory operators. With the packed column data it was not possible to establish a definite synthetic

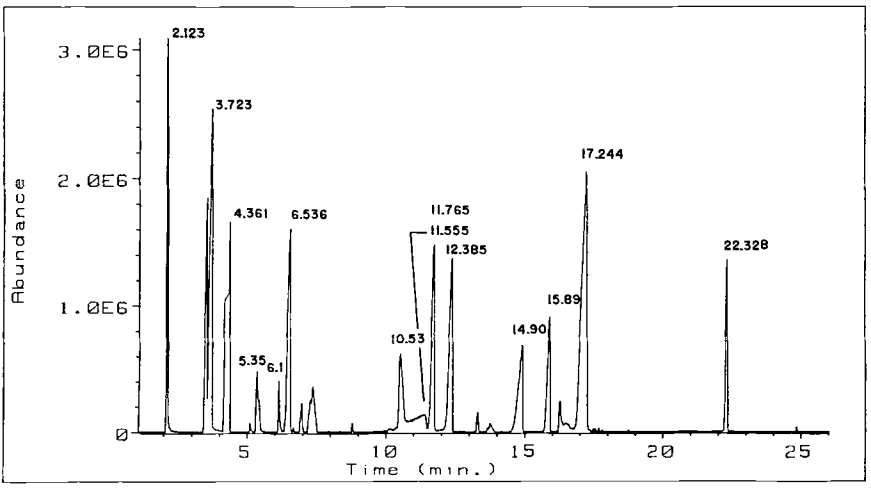

FIG. 3—*GC/MS total ion current of the procedural standard.*

route. It was only possible to establish that certain precursors had been mixed together and that these mixtures could produce PCP.

Since the capillary column will resolve the critical components, it may be used to establish the intermediates and the synthesis route followed by the clandestine laboratory operator.

References

[1] "The Supply of Illicit Drugs to the United States," National Narcotics Intelligence Consumers Committee, Washington, DC, April 1988, pp. 38–51.

[2] Frank, R. S. and Gunn, J. W., Jr., "Clandestine Drug Laboratory Situation in the United States," *Journal of Forensic Sciences*, Vol. 28, No. 1, Jan. 1983, pp. 18–31.

[3] Maddox, V. H., Godefroi, E. F., and Parcell, R. F., "The Synthesis of Phencyclidine and Other 1-Arylcyclohexylamines," *Journal of Medicinal Chemistry*, Vol. 8, March 1965, pp. 231–235.

[4] Kalir, A., Edery, H., Pelah, Z., Balderman, D., and Porath, G., "1-Phenylcycloalkylamine Derivatives: II. Synthesis and Pharmalogical Activity," *Journal of Medicinal Chemistry*, Vol. 12, May 1969, pp. 473–477.

[5] Parke, Davis and Co., "Process for Producing Certain New 1-Phenylcyclohexylamine Compounds," U.S. Patent No. 3 192 219, 29 June 1965.

[6] Godefroi, E. F., Maddox, V. H., and Parcell, R. F., "Process for Producing a Depressant-Like Effect on the Central Nervous System," U.S. Patent No. 3 097 136, 9 July 1963.

[7] Weston, A., "Antispasmodics. Derivatives of 1-Phenylcycloparaffincarboxylic Acids," *Journal of the American Chemical Society*, Vol. 68, Nov. 1946, pp. 2347–2350.

[8] Marvil, C. S. and Lazier, W. A., "Benzoylpiperidine," *Organic Synthesis Collective*, Vol. 1, H. Gilman, Ed., John Wiley and Sons, New York, 1941, pp. 99–101.

[9] Shulgin, A. T. and Maclean, D. E., "Illicit Synthesis of Phencyclidine (PCP) and Several of Its Analogs," *Clinical Toxicology*, Vol. 9, No. 4, 1976, pp. 553–560.

[10] Baker, J. K., "Detection of 1-Piperidinocyclohexane Carbonitrile in Illicit Phencyclidine Samples," *Analytical Chemistry*, Vol. 54, 1982, pp. 347–349.

[11] Cone, E. J., Vaupel, D. B., and Buchwald, W. F., "Phencyclidine Detection and Measurement of Toxic Precursors and Analogs in Illicit Samples," *Journal of Analytical Toxicology*, Vol. 4, May 1980, pp. 119–123.

[12] Cone, E. J., Darwin, W. D., Yousefnejad, D., and Buchwald, W. F., "Separation and Identification of Phencyclidine Precursors, Metabolites and Analogs by Gas and Thin-Layer Chromatography and Chemical Ionization Mass Spectrometry," *Journal of Chromatography*, Vol. 177, 1979, pp. 149–153.

[13] Schnoll, S. H., "Street PCP Scene: Issues on Synthesis and Contamination," *Journal of Psychedelic Drugs*, Vol. 12, No. 3/4, 1980, pp. 229–233.

[14] Jones, L. A., Beaver, R. W., and Schmoeger, T. L., "Isolation, Identification, and Synthesis of Compounds Cosynthesized in the Preparation of Phencyclidine," *Journal of Organic Chemistry*, Vol. 46, 1981, pp. 3330–3333.

[15] Skowronski, G. T., Raney, J. K., and Wagenhofer, R. J., "Analysis of Components found in Clandestinely Synthesized Phencyclidine Samples," paper presented at the 31st Annual Meeting of the American Academy of Forensic Sciences, Atlanta, GA, Feb. 1979.

[16] Helisten, C. and Shulgin, A. T., "The Detection of 1-Piperidinocyclohexanecarbonitrile Contamination in Illicit Preparations of 1-(1-Phenylcyclohexyl) Piperidine and 1[1-(2-Thienyl)-Cyclohexyl] Piperidine," *Journal of Chromatography*, Vol. 117, 1976, pp. 232–235.

[17] Raney, J. K., Skowronski, G. T., and Wagenhofer, R. J., "Identification of Components Found in Phencyclidine Samples Synthesized by the Enamine Intermediate," paper presented at the 32nd Annual Meeting of the American Academy of Forensic Sciences, New Orleans, LA, Feb. 1980.

[18] Angelos, S. A., Raney, J. K., Skowronski, G. T., and Wagenhofer, R. J., "Identification of Clandestine Phencyclidine Mixtures by Capillary Gas Ghromatography/Mass Spectrometry," paper presented at the 39th Annual Meeting of the American Academy of Forensic Sciences, San Diego, CA, Feb. 1987.

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