A STUDY ON METHODS FOR DETECTION IN CLANDESTINE METHAMPHETAMINE LABORATORIES

LEE KHAI

UNIVERSITI SAINS MALAYSIA

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A STUDY ON METHODS FOR DETECTION IN CLANDESTINE METHAMPHETAMINE LABORATORIES

by

LEE KHAI

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LIST OF SYMBOLS

A_X	Absorbance
a	Charge transfer constant
C	Concentration
E_p	Peak potential
F	Faraday constant
I_X	Intensity
I_p	Peak current
n	Number of electrons
pA	Peak area
pKa	Acid dissociation constant
R	Ideal gas constant
R_X	Reflectance
R^2	Linear coefficient
S	Slope
T	Temperature
V	Scan rate
λ	Wavelength

LIST OF UNITS

%	percent
°C	degree Celcius
µA	microampere
µg	microgram
µL	microliter
µm	micrometre
µm	micrometre
cm	centimetre
cm^2	square centimetre
g	gram
m	meter
m^3	cubic metre
mg	milligram
min	minute
mL	millilitre
mm	millimetre
mol	mole
ms	millisecond
ng	nanogram
nm	nanometre
s	second
V	volt

LIST OF ABBREVIATIONS

%Recovery	Percentage of recovery
Ad-Tip	Adsorption tip
AOAC	Association of Official Analytical Chemists
ATS	Amphetamine-type stimulant
AuNP	Gold nanoparticle
BDD	Boron-doped diamond
BRBS	Britton Robinson buffer solution
BSTFA	Bis(trimethylsilyl)-trifluoroacetamide
C-14	n-Tetradecane
CAS	Chemical Abstracts Service
CCH	Caring Community House
CCSC	Cure & Care Service Centre
CMV	Capillary microextraction of volatiles
CMY	Cyan-Magenta-Yellow
CV	Cyclic voltammetry
DAINAP	Drug Abuse Information Network for Asia and the Pacific
DCE	Dichloroethane
DCM	Dichloromethane
DDA	Dangerous Drugs Act
DMA	2,5-dimethoxy amphetamine
DMF	N,N-dimethylformamide
DMMA	Dimethoxymethamphetamine
DOB	4-bromo-2,5-dimethoxy amphetamine
DOC	Department of Chemistry
DOET	2,5-dimethoxy-4-ethyl amphetamine
DOM	2,5-Dimethoxy-4-methyl amphetamine
DPV	Differential pulse voltammetry
EA	Ethyl amphetamine
ESR	Zealand Institute for Environmental Science and Research
FFT-SWV	Fast Fourier transform square wave voltammetry
FID	Flame ionisation detector

FTIR	Fourier transform infrared spectroscopy
GC	Gas chromatography
GCE	Glassy carbon electrode
GC-FID	Gas chromatography-flame ionisation detector
GC-MS	Gas chromatography-mass spectrometry
GCS	Glassy carbon sphere
GI	Graphene ink
GIMP	GNU Image Manipulation Program
GLP	Good laboratory practice
GNP	Graphene nanoplatelet
GO	Graphene oxide
GpI	Graphite ink
HFBA	Heptafluorobutyric anhydride
HMWMD	Hazardous Materials and Waste Management Division
HP-5	(5%-Phenyl)-methylpolysiloxane
HPLC	High performance liquid chromatography
i.d.	Internal diameter
ICP-MS	Inductive coupled plasma-mass spectrometry
idPAD	Paper analytical device for illicit drugs
INCSR	International Narcotics Control Strategy Report
IR	Infrared
IRD	Infrared detection
ISCC-NBS	Inter-Society Colour Council and the National Bureau of Standards
IUPAC	International Union of Pure and Applied Chemistry
LC	liquid chromatography
LOD	Limit of detection
LOQ	Limit of Quantification
LSV	Linear sweep voltammetry
m/v	Mass/volume ratio
MBDB	Methylbenzodioxolylbutanamine
MBTFA	N-methyl-bis-trifluoroacetamide
MDA	3,4-methylenedioxy amphetamine
MDE	N-ethyl-3,4-methylenedioxy amphetamine
MDMA	3,4-methylenedioxy methamphetamine

MIP	Molecularly imprinted polymers
MMDA	3-methoxy-4,5-methylenedioxy amphetamine
MOHA	Ministry of Home Affairs
MPCA	Minnesota Pollution Control Agency
MS	Mass spectrometry
MTBSTFA	N-methyl-N-t-butyldimethylsilyl trifluoroacetamide
MWCNT	Multi-walled carbon nanotube
NADA	National Anti-Drug Agency
NCID	Narcotic Crime Investigation Department
NIDA	National Institute of Drug Abuse
NIST	National Institute of Standards and Technology
NNDA	N,N-dimethyl amphetamine
N-OH	MDA N-hydroxy-3,4-methylenedioxy amphetamine
NPD	Nitrogen phosphorus detector
NQS	1,2-naphthoquinone-4-sulphonate
ODS	Octadecylsilyl-silica
P2P	Phenyl-2-propanol
PDMS	Polydimethylsiloxane
PDRM	Royal Malaysian Police
PFBCF	o-Pentafluorobenzyl chloroformate
PGE	Pencil graphite electrode
PMA	4-methoxy amphetamine
PMMA	Paramethoxymethamphetamine
Pt	Platinum wire
QC	Quality control
RAL	Reichs-Ausschuß für Lieferbedingungen und Gütesicherung
RfD	Reference dose
RGB	Red-Green-Blue
RMP	Royal Malaysia Police
RRFIA	Reagent regeneration flow injection anlysis
RSD	Relative standard deviation
SCE	Saturated calomel electrode
SD	Standard deviation
SMART	Synthetics Monitoring: Analyses, Reporting and Trends

S_N1	First order nucleophilic substitution
S_N2	Second order nucleophilic substitution
SWGDRUG	Scientific Working Group of the Analysis of Seized Drugs
SWV	Square wave voltammetry
TBPE	Tetrabromophenolphthalein ethyl ester
TFA	Trifluoroacetyl
TFAA	Trifluoroacetic acid anhydrous
TLC	Thin layer chromatography
TMS	Trimethylsilyl
UNODC	United Nations Office on Drugs and Crime
UV	Ultraviolet
UV-Vis	Ultraviolet-visible
v/v	Volume/volume ratio
VUV	Vacuum ultraviolet detection

LIST OF APPENDICES

KAJIAN ATAS KAEDAH-KAEDAH PENGESANAN DALAM MAKMAL HARAM METAMFETAMIN

ABSTRAK

Masalah metamfetamin telah mengancam secara global, dan lebih dari sepertiga daripada jumlah anggaran pengguna global telah tercatat dalam Asia Timur dan Tenggara. Hal ini merupakan isu keselamatan dan kesihatan yang serius dan potensi bahaya yang terhasil daripada makmal-makmal haram metamfetamin dengan mengambil kira banyak makmal sedemikian yang tidak dapat dikesan. Daripada perspektif sains forensik, penentuan produk haram dan aktiviti-activiti yang berkaitan secara pantas dalam suatu makmal haram terkesan adalah penting. Daripada sudut pandangan orang awam, sesuatu struktur kediaman perlu ditentukan sama ada ia selamat daripada pendedahan sisa-sisa metamfetamin selepas proses penghapusan dan pemulihan. Justeru, kajian ini bertujuan untuk membangunkan satu siri strategi bagi pengesanan metamfetamin yang berpotensi untuk diguna pakai dalam pelbagai penetapan pada situasi makmal haram. Dalam kajian ini, ujian warna, analisis imej digital, spektroskopi ultraungu-nampak (UV-Vis), teknik gas kromatografi, dan pengesanan elektrokimia telah disiasat. Seterusnya, peratusan pemulihan semula bagi sisa metamfetamin pada permukaan daripada permukaan isi rumah lazim telah ditentukan. Keputusan telah menunjukkan bahawa sebagai ujian saringan, ujian Marquis dan Simon masing-masing membenarkan pengesanan metamfetamin sehingga 5 µg dan 10 µg. Dengan bantuan analysis imej digital, intensiti warna Kuning dan Sian telah berjaya diaplikasikan untuk mentaksir keputusan ujian Marquis dan ujian Simon secara objektif dengan membenarkan pengesanan masing-masing pada 1 µg dan 10 µg. Spektroskopi UV-Vis mengesan metamfetamin pada jarak gelombang 469 nm untuk

ujian Marquis dan 580 nm untuk ujian Simon dengan had pengesanan masing-masing pada 1.0 µg/mL dan 2.5 µg/mL. Seterusnya, analisis gas kromatografi terhadap metamfetamin terbitan asid trifluoroasetik telah mempertingkatkan kepekaan yang membolehkan pengesanan positif pada julat linear dari 19.53 ng/mL ke 2.5 µg/mL dan mencapai had pengesanan pada 2.44 µg/mL. Tahap sisa metamfetamin pada 0.5 µg/100 cm^2 telah berjaya dikesan pada empat permukaan. Pemulihan semula yang baik telah dicapai pada permukaan kaca (62.49%), plastik (69.47%) dan keluli tahan karat (72.66%), manakala pemulihan semula yang lebih rendah secara relatif telah dilaporkan daripada permukaan kayu tanpa varnis (33.78%). Teknik pengesanan elektrokimia yang menggunakan elektrod karbon kekaca terubahsuai dengan grafena oksida berupaya mengesan metamfetamin pada kepekatan serendah 0.041 µg/mL. Kesimpulannya, kerangka bagi kaedah-kaedah pengesanan metamfetamin telah berjaya dibangunkan dan sedia diaplikasikan dalam senario makmal haram metamfetamin yang berbeza, berdasarkan kepekaan masing-masing serta adanya dan jenis sampel yang akan dipulih semula. Suatu pengesanan elektrokimia yang baharu selepas pengubahsuaian elektrod juga dibangunkan dan ditubuhkan. Kajian ini akan bermanfaat untuk membantu dalam penyiasatan forensik dan memastikan keselamatan penghuni, dengan itu menggalakkan kesejahteraan sosial yang lebih baik.

A STUDY ON METHODS FOR DETECTION IN CLANDESTINE METHAMPHETAMINE LABORATORIES

ABSTRACT

Methamphetamine-related problems appear to threaten globally, and over one third of the estimated global number of users was recorded in East and South-East Asia. This is a serious security and health issue, as well as the potential hazards arisen from clandestine methamphetamine laboratories, considering many of such laboratories which are not detected. From forensic science perspective, quick determination of illicit products and related activities in a discovered clandestine laboratory is crucial. From the public's perspective, a structure, particular residential structure, must be determined whether it is safe from exposure of methamphetamine residues after dismantlement and remediation. Therefore, this study was aimed to establish a series of strategies for methamphetamine detection potentially applicable in the varying settings of clandestine laboratory situations. In this study, colour tests, digital image analysis, ultraviolet-visible (UV-Vis) spectrometry, gas chromatographic techniques, and electrochemical detection were investigated. Subsequently, the percentage recoveries of residual surface methamphetamine from the common household surfaces were determined. The results show that Marquis and Simon's test allowed detection down to 5 µg and 10 µg of methamphetamine, respectively. Aiding by digital image analysis, the Yellow and Cyan intensities were successfully applied to objectively interpret the Marquis and Simon's test, allowing detection at 1 µg and 10 µg, respectively. UV-Vis spectroscopy detected methamphetamine at wavelength of 469 nm for Marquis test and 580 nm for Simon's test with respective detection limits at 1.0 µg/mL and 2.5 µg/mL. Subsequently, gas chromatography analysis on trifluoroacetic acid anhydride derivatised

methamphetamine had increased the sensitivity, enabling positive detection in a linear range from 19.53 ng/mL to 2.5 µg/mL and achieving detection limit of 2.44 ng/mL. Residual methamphetamine level at 0.5 µg/100 cm^2 were successfully detected on four different surfaces, where good recoveries were achieved on glass (62.49%), plastic (69.47%) and stainless-steel surfaces (72.66%), while relatively lower recovery was reported on unvarnished woof surfaces (33.78%). Electrochemical detection technique using glassy carbon electrode modified with graphene oxide was able to detect methamphetamine as low as 0.041 µg/mL. To conclude, a framework of methamphetamine detection strategies was established and readily applied to different scenarios of clandestine methamphetamine laboratories based on their respective sensitivities as well as the availability and type of samples to be recovered. A novel electrochemical detection upon electrode modification was also developed and established. This study would be beneficial to assist forensic investigation and to ensure the safety of occupants, thus promoting a better societal well-being.

CHAPTER 1

INTRODUCTION

1.1 Methamphetamine

Methamphetamine (Figure 1.1) is the principal member in a group of drugs, known as amphetamine-type stimulants (ATS). It is a highly additive stimulant that acts on the central nervous system by stimulating the excess secretion of dopamine in brain. Note that dopamine plays role in movement, motivation, and reinforcement of rewarding behaviours (NIDA, 2019). Methamphetamine usually appears as usually a white, bitter-tasting powder, or pills with various colours, or crystal with glass fragments or shiny bluish-white rocks (NIDA, 2019). People can take methamphetamine by injecting, ingesting, snorting, and smoking the drug to give the long-lasting effects. Consuming methamphetamine allows users to experience “highs” for hours (NIDA, 2019).

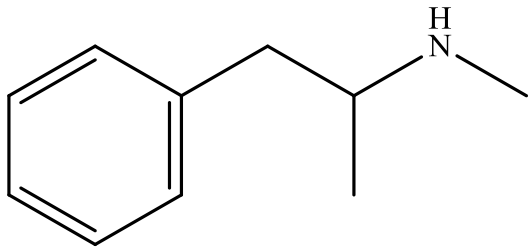


Figure 1.1: Chemical structure of methamphetamine.

Methamphetamine was first synthesised by a German Chemist in 1887. Subsequently, it was synthesised from ephedrine by a Japanese pharmacologist in 1893 (Suwaki et al., 1997). The first medical use of this drug was in 1932 as a nasal spray for the treatment of asthma. It was also reported to provide relief from narcolepsy, reduce activity in hyperactive children, suppress appetite, as well as enable individuals to stay awake for extended periods of time. It was also used to treat a variety of medical

conditions and disorders, namely schizophrenia, morphine addiction, tobacco smoking, low blood pressure, radiation sickness, and persistent hiccups (Julien, 2013). In fact, Methamphetamine was not widely used until World War II when the drug was provided to the military personnel to increase endurance and performance, and to the military support industries to improve productivity of civilian factory workers. After the war, widespread abuse of the drug occurred when methamphetamine from surplus army stocks had occupied the market. Although law restriction had introduced, the abuse of methamphetamine continued to spread among construction workers, truck drivers, and other blue-collar workers, as well as students, housewives, and office workers during that era (Anglin et al., 2000).

Since 1970, the United States (US) government intensified the restriction and made methamphetamine use in most circumstances (Anglin et al., 2000). Black market which illegally supplied mainly from pharmaceutical companies, distributors, and physicians, as well as American motorcycle gang, known as Bay Area motorcycle gangs took over majority of the manufacture and distribution of methamphetamine, and subsequently spread its use along the Pacific Coast (Miller, 1997). In the 1990s, while large laboratories were set up by Mexican drug trafficking organisation in California (Morgan and Beck, 1997), smaller “stove top” laboratories were also appeared. From there, it spread across the United States and into Europe through the Czech Republic. Today, manufacture of methamphetamine continues to dominate and the global methamphetamine market is expanding but remains mainly concentrated in North America, as well as East and South-East Asia (UNODC, 2020a).

1.2 Methamphetamine abuse and manufacture

Despite harsh penalties imposed on drug users as well as drug smugglers or distributors, methamphetamine-related problems appear to record an increasing trend. According to the World Drug Report (UNODC, 2020b), signs of increasing in the usage of methamphetamine is seen in the United States, Europe countries, Australia, and New Zealand. In East and South-East Asia, specifically, the abuse of methamphetamine and its threat remains prevalent. These regions consist of more than one third of the estimated global number of users of amphetamine-type substances (ATS), referring to amphetamine, methamphetamine, and pharmaceutical stimulants (UNODC, 2020b).

Global seizure of methamphetamine, particularly, had increased sevenfold in the past two decades (UNODC, 2020a). However, the domestic methamphetamine manufactures, mainly in the United States, China, and Islamic Republic of Iran, had dropped sharply in recent years. Such situation was also reflected in the decreased number of dismantled laboratories (UNODC, 2020a). On the other hand, seizures of methamphetamine were highly reported and signs of marked expansions of methamphetamine trafficking in the region were noticed in Mexico, as well as East and South East Asia (UNODC, 2020a). It was evident that the methamphetamine market had been shifted from the "traditional" countries in North America to East and Southeast Asia. In context of Malaysia, methamphetamine seizures in 2018 had contributed to approximately 8% (nearly 7,000 kg) of the seizures in East and South East Asia (UNODC, 2020a). A three-folds was marked as compared with the previous year (NADA, 2020).

1.2.1 Methamphetamine users in Malaysia

In global setting, the use of methamphetamine tablets is more common than the use of crystalline methamphetamine (UNODC, 2020b). Yet, in Malaysia, the majority

of people seeking drug treatment were users of crystalline methamphetamine (NADA, 2020; UNODC, 2020b). In 2019, 16,154 methamphetamine users were recorded among a total of 27,811 drug addicts (NADA, 2020). Figure 1.2 illustrates the trend of drug addicts based on types of drugs used in six years period (2014–2019).

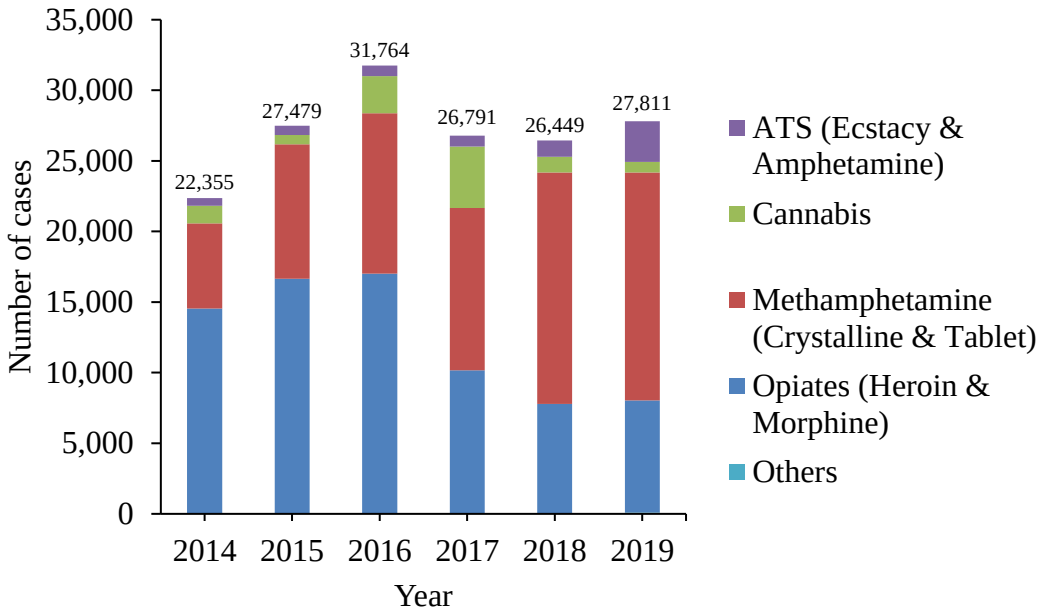


Figure 1.2: Trend of drug addicts based on type of drug used, 2014–2019 (NADA, 2020).

As reported by the National Anti-Drug Agency (NADA, 2020), methamphetamine (crystalline and tablet) had surpassed opiates since 2017, and became the most widely used illegal drugs in Malaysia (Figure 1.2). The number of users has drastically increased from 11,485 (42.86%) in 2017 hiking up to 16,384 (61.12%) in 2018, and 16,154 (58.08%) last year. In addition, the reported price of crystalline methamphetamine had dropped at approximately 30% in 2018 from RM 70,000 to RM 50,000 (NADA, 2020). The trend had also indirectly reflected the demands of synthetic drugs by the increased number of drug users, particularly methamphetamine in illicit drug market and regional supply. Subsequently, the illicit

manufacturing and trafficking activities of methamphetamine had been triggered (Hamdan et al., 2015; UNODC, 2020a).

1.2.2 Manufactures of methamphetamine in Malaysia

To date, methamphetamine is known to be the most commonly manufactured ATS and well established in the illicit drug markets worldwide (UNODC, 2019). Over the period between 2014 – 2018, the majority of clandestine laboratories (95%) dismantled worldwide synthesised illicit methamphetamine (UNODC, 2020a). Unlike heroin or cocaine, methamphetamine manufacturing does not require the extraction of active compounds from plants that have to be cultivated under certain growth conditions in a period. Due to this simplicity, such drug can be manufactured in either small scale using simple "ingredients" in any closed apartments for local consumption; or produced in large scale with sophisticated manufacturing equipment in clandestine laboratories, utilising a range of precursor chemicals and synthetic routes (UNODC, 2016). Such relatively simple procedure had resulted in creations of manufacturing sites in a variety of premises and structures (Granholm and Olszewski, 2007; Owens, 2017; UNODC, 2019), deserving forensic investigation.

Quantity of amphetamine-type stimulant seized at the global level has quadrupled over the past two decades (UNODC, 2020a). However, it is difficult to estimate the global production of methamphetamine based on seizures and dismantled laboratories (UNODC, 2019), as the amount of illicit drugs that successfully enter the black market remains unknown. Furthermore, limited data and information that available from the world drug markets on the trend of abuse in addition to the appearance of new psychoactive drugs had restrict the accurate interpretation on the current drug status, particularly the illicit methamphetamine (UNODC, 2019). Also, specifically in Asia, the difficulties for the authorities to access the remote areas that

operate the clandestine laboratories due to the security issues and high rate of violence crime, had caused the uneven records of cases across countries (UNODC, 2020a).

1.2.3 Clandestine laboratories dismantled in Malaysia

Methamphetamine seized in Malaysia is thought to be manufactured within the national boundaries (INCSR, 2014; Reych, 2016), based on simple synthesise pathway (Frank, 1983; Burgess and Chandler, 2003; Christian, 2004; Abdullah et al., 2014; INCSR, 2014). In Malaysia, a seizure of 23 clandestine laboratories was reported in 2019, bringing up the number of such laboratories to 261 within ten years period, 2011 – 2019 (Figure 1.3) (Hamdan et al., 2015; UNODC, 2015, 2020c; NADA, 2020).

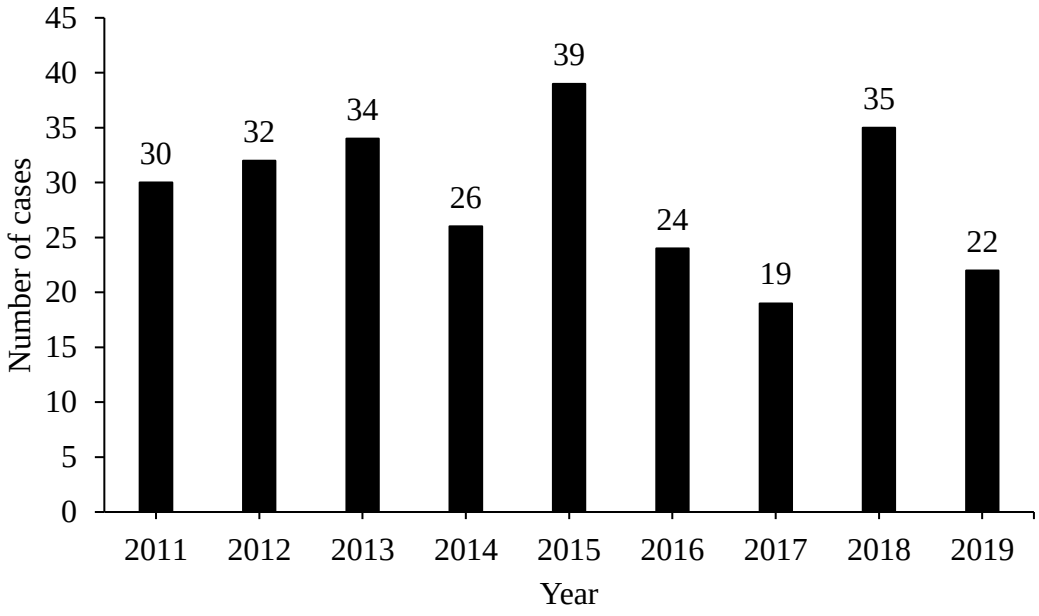


Figure 1.3: Number of cases for dismantled clandestine laboratories, 2011–2019 (Hamdan et al., 2015; UNODC, 2015, 2020c; NADA, 2020).

A decrease in number of cases for clandestine laboratory discoveries from 35 in 2018 to 23 in 2019 by approximately 34.28% had indirectly showed that the success of law enforcement in Malaysia in deterring the manufacture activities (NADA, 2020).

However, the data could be underestimated. As reported by the Royal Malaysian Police (RMP) recently (Ismail, 2020; Omar, 2020; Hamid, 2020; Ramli, 2020), the manufacturing sites were found in remote areas, rental room, and underground of a house which are not easily identified if the activities are concealed well. With that, there might be other clandestine methamphetamine laboratories that have been operated in areas that are yet to be noticed by the authorities and law enforcement agencies.

1.2.4 Control and legislation of methamphetamine in Malaysia

As efforts to respond to the expanding illegal methamphetamine supply, methamphetamine is listed in Dangerous Drugs Act (DDA) 1952 under the First Schedule (Dangerous Drugs Act, 1952). Poison Act 1952 meanwhile monitors the marketing, as well as the trafficking of related precursors and other essential chemicals (Poison Act, 1952). DDA 1952 is the main regulation against the drug-related offences, including trafficking, importation, manufacturing, selling, possessing, exporting and self-administration of all types of drugs. It also provides the punishment for various drugs offences under the Act. For methamphetamine, specifically, the punishments are subjected as follows:

a) Any person who found with possession of less than 5 g in weight of methamphetamine will be liable to a fine not exceeding RM 5,000 or to imprisonment up to 2 years or both.

b) Any person who found with possession of 5 g or more but less than 30 g in weight of methamphetamine will be punished with imprisonment for 2-5 years and whipping of 3-9 strokes.

c) Any person who found with possession of more than 30 g in weight of methamphetamine will be subjected to more than 5 years or lifetime imprisonment, as well as with whipping of more than 10 strokes.

d) Any person who has involved in trafficking, or preparatory for the purpose of trafficking of methamphetamine will be convicted with death penalty.

Narcotic Crime Investigation Department (NCID), Royal Malaysian Police enforces Dangerous Drug Act (Special Preventive Measures) 1985 against drug traffickers or liable individuals that had involved in illegal drugs activities (MOHA, 2019). It implements the right of Royal Malaysian Police to detain any suspected individuals for not more than 60 days. This is followed by detention under Home Ministry involving the movement restriction and monitored by electronic monitoring device for up to two years (Dangerous Drugs (Special Preventive Measures) Act, 1985). Dangerous Drugs Act (Forfeiture of Property) 1988 is also enforced to provide authorities the powers to trace, freeze and forfeit the assets of drug traffickers, including vehicles and questioned properties (Dangerous Drugs (Forfeiture of Property) Act, 1988).

Lastly, Drug Dependents Act (Treatment and Rehabilitation) 1983 is specialised for drug addicts with treatment and rehabilitation (Drug Dependants (Treatment and Rehabilitation) Act, 1983). All the drug dependents' cases are now investigated under the NADA of Ministry of Home Affairs to relieve the burden on the police department. Instead of compulsory drug rehabilitation including arrests, court orders and legal implication, NADA has adopted paradigm shift in transforming the Act into more accessible and voluntary-based services in government clinics. This application had proved to be effective in Malaysia. According to the statistics compiled by NADA

(2020), the number of drug addicts that received treatment and rehabilitation in the community centres such as Cure & Care Service Centre (CCSC) and Caring Community House (CCH) had increased about 24.86% in 2019 (NADA, 2020).

1.3 Problem Statements

In operational level during the investigation of dismantled methamphetamine manufacturing and packaging sites, an investigative officer is required to determine the identity of the illicit drug. On the other hand, they are requested to detect the possible presence of residual methamphetamine, especially when dealing with an inactive laboratory (Martyny et al., 2007). Additionally, complex scenes with large number of items also make forensic investigation difficult to trace the manufacturing, trafficking, packaging, distribution, and sale of such illicit drugs. Available colour tests that currently used as routine procedures (*i.e.* Marquis and Simon's test) can be applied for detection of trace amount of surface methamphetamine but the sensitivity is in questioned (Harper et al., 2017). In such situations, subjective interpretation of conventional colour screening tests shall carry advantages to assist the investigation. A more objective screening strategy is crucial to allows on-the-spot screening on identity of illicit drugs, as well as the presence of residual drug on the contaminated surfaces.

Current methods of detection and quantitation of residual methamphetamine at the suspected clandestine laboratories and illicit samples recovered from dismantled laboratories rely heavily on instrumental analyses. The methods included gas chromatography (GC) coupled with mass spectrometry (MS) or flame ionisation detector (FID) for the confirmation and quantitation by forensic analysts. Although these methods were suggested by the Scientific Working Group for the Analysis of

Seized Drugs (SWGDRUG, 2013), not all of these methods may be suitable for on-the-spot setting. Recoveries of methamphetamine from common surfaces in clandestine laboratory had been established by Abdullah and Miskelly (2010b), but its applicability and suitability in Malaysian settings shall be tested and investigated.

In overseas, analysis is conducted merely to establish whether methamphetamine is present in the structure. Note that the colour tests might not be a good choice in such scenario where they should not be directly tested on some surfaces due to corrosiveness nature of reagents, such as sulphuric acid in Marquis reagent. If a testing is requested, GC-MS is undoubtable the gold standard as described in the EPA Method 8270 (EPA, 2013). However, when a potential tenant or buyer wishes to have a quick safety check on possible methamphetamine contamination in a room, to make them feel comfortable and secured, random surface sampling was carried out, resulting in large number wipe samplings to be analysed, to establish the safety of the questioned property. Although GC-MS possesses the required sensitivity level, it can be costly and timely. Therefore, a relatively more portable, rapid and cost-effective detection method, which is able to provide complementary results to GC analyses, is necessary for public health and safety purposes.

Owing to the relatively simple synthesis method, manufacture of methamphetamine could take place in any space using common household materials. The activities of illicit drug production and packaging could have contaminated the surfaces of a structure. Either in active or inactive state, contaminated sites or properties that involved “cooking” of methamphetamine may possess physical, chemical, and environmental hazards to the successive tenants (Martyny et al., 2007; Abdullah and Miskelly, 2010c; Kuhn et al., 2019). Forensic investigators who visited a scene require

the knowledge on the appropriate sampling and testing strategies to maximise the investigative information. As a general public, a thorough screening and confirmatory procedure for safety check on all possible methamphetamine contamination surfaces followed by remediation of the whole room or property (if necessarily) is particular important to ensure the security and comfortable of the occupants (Owens, 2017).

With that, the varying scenarios of clandestine laboratories possess different purposes of analysis, leading to different significance and outcome of the analytical results. This study hence aims to address the key issues in forensic analysis of illicit methamphetamine. Figure 1.4 illustrates the three main scenarios arisen from the clandestine laboratories and the relevant key issues. Based on the different settings of clandestine laboratories, it was noted that the questions addressed are different and shall be responded through different strategies. In other words, appropriate detection methods and strategies shall be applied on the case-by-case basis, aiding to save the cost and time, as well as to properly plan the sampling and evidence collection for benefit of forensic science communities and the societies.

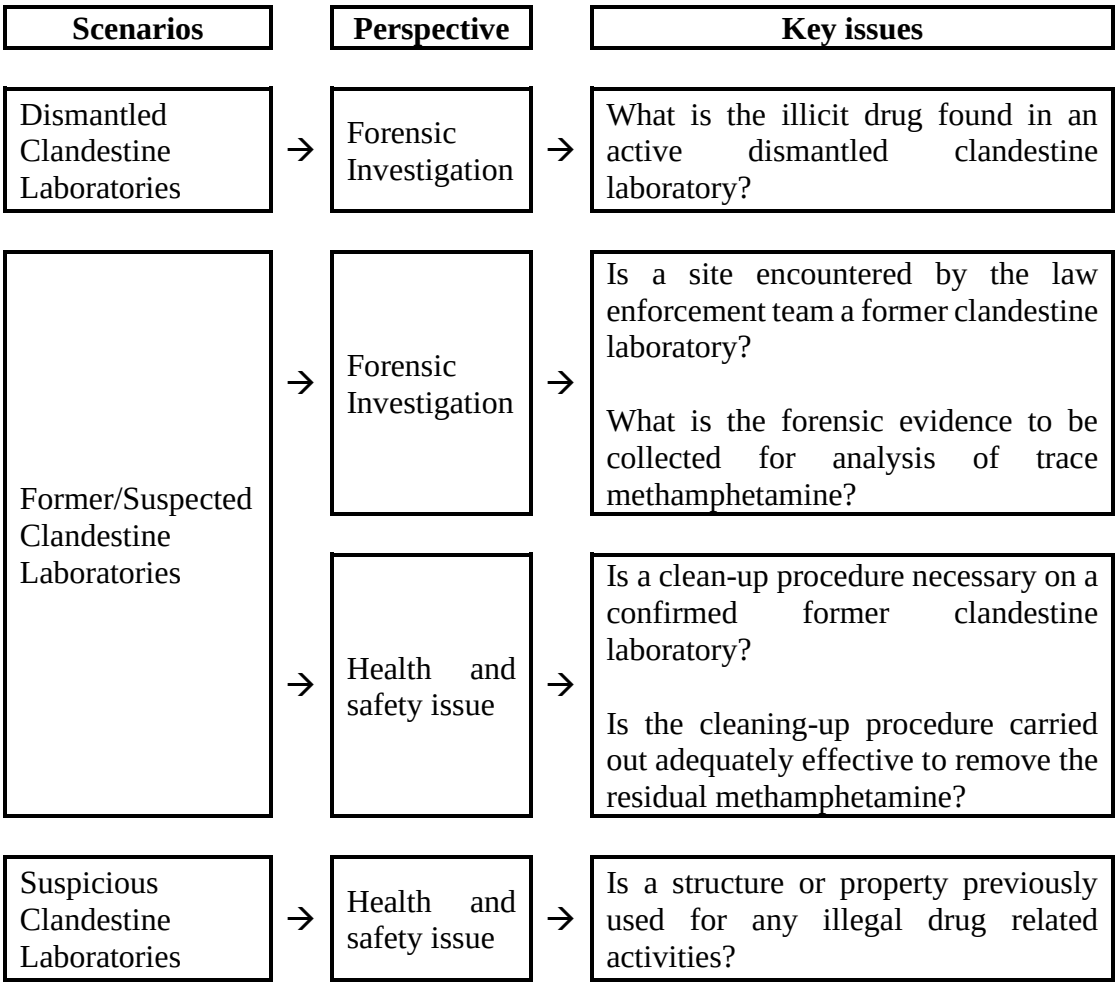


Figure 1.4: Clandestine laboratory scenarios and key issues to be addressed in this study.

1.4 Scope of Study

Most guidelines used the surrogate approach to monitor the level of methamphetamine contamination as a marker for decision making (EPA, 2013; enHealth, 2017; WA Health, 2020). It is assumed that cleaning methamphetamine to a particular level is also simultaneously cleaning other chemicals, immediate products or co-products potentially appeared on any surface in the setting of clandestine laboratories, given that the cleaning procedure is adequately effective. Hence, the present study focuses on the detection of methamphetamine to confirm the presence of

methamphetamine-related activities in simulation of clandestine laboratories, as well as to determine the necessary of remediation and its effectiveness.

The detection methods that were selected in the study included the common routine procedures in forensic investigation, namely colour tests (Marquis and Simon's tests for methamphetamine) and GC techniques. Digital image analysis and UV-Vis spectroscopy were applied to achieve objective colour determination of Marquis and Simon's test. Chemical derivatisation was conducted prior to increase sensitivity of GC techniques.

In a simple clandestine laboratory setting, glass surfaces were usually found on various lab apparatus; trays or common containers for storage or transportation were often found with stainless steel or plastic surfaces; while wood surfaces were commonly seen on benches or working tables where synthesis processes may take place. Therefore, four household surfaces, namely glass, stainless steel, plastic, and unvarnished wood surfaces were selected for recovery study.

Electrochemical detection had gained popularity in rapid and cost-effective detection of methamphetamine sample in various matrices (Švorc et al., 2014; Oghli et al., 2015; Akhoundian et al., 2019; Haghighi et al., 2020). Hence, a novel electrochemical detection based on glassy carbon electrode was developed for methamphetamine detection. Carbon materials were chosen for electrode modification due to its good electrical conductivity and lower price.

1.5 Aim and Objectives

The present study aims to study the detection of illicit methamphetamine using a series of detection strategies in clandestine laboratory settings. To achieve the aim, the specific objectives were set as follows:

i. To explore the detection of illicit methamphetamine using Marquis and Simon's tests with naked-eye observation and digital image analysis.

ii. To explore the detection of illicit methamphetamine using Marquis and Simon's tests followed by ultraviolet-visible (UV-Vis) spectroscopy.

iii. To determine underivatised and derivatised illicit methamphetamine using gas chromatography-flame ionisation detector (GC-FID) and gas chromatography-mass spectrometry (GC-MS).

iv. To investigate the recovery of illicit methamphetamine from common household surfaces using gas chromatography-flame ionisation detector (GC-FID).

v. To investigate the electrochemical detection of illicit methamphetamine with differential pulse voltammetry (DPV).

vi. To compare the applicability of established detection strategies in different scenarios of clandestine laboratories.

1.6 Significance of Study

This study would benefit the law enforcement agencies in both forensic intelligence and public health and safety perspective. The novelty of this study would be the proposal on the different strategies for the detection of methamphetamine and its residues based on the various types of clandestine laboratory scenario. It was important

to note the appropriate detection strategies shall be selected in a clandestine laboratory scenario as the conditions of these structure would not be the same. For example, detection strategies for preliminary investigation on the confirmed or suspected site, the availability of seized illicit drug, as well as appropriate sampling methods at the crime scene shall be taken into consideration during forensic investigation.

No two crime scenes are exactly the same and forensic investigator must always prepare for the worst scenario. To maximise the chance of true positive detection and to enhance the percent recovery of residual methamphetamine, an investigative team must be able to carry out the most appropriate strategies, adjusted for the conditions of dismantled or suspected clandestine laboratories. Rapid and relatively sensitive detection strategy could play important role in the detection of both bulk and residual methamphetamine at the scene of clandestine laboratories. The continuously dismantlement of clandestine laboratories also justifies the need for cost effective approach to perform field testing before the routine instrumental analyses.

From the perspective of public, there are instances where the owners or tenants of properties are suspicious regarding the activities that had been carried out in these properties. A readily available and established screening and testing procedure shall be carried out to determine the presence of residual illicit methamphetamine, the necessary of remediation, as well as the suitability of a property to be occupied. This is important for security check by the owners to manage their properties and ensure the safety of their tenants from health hazards. Besides, the findings could serve for both intelligence and evidential purposes to link the sources of seizures. It could also help to disclose the distribution network in the illegal drug market by elucidating the possible sites of

manufacturing, packaging, and storing illicit methamphetamine along with the route of drug trafficking in Malaysia.

The current study investigates a series of detection strategies for on-the-spot testing of surface methamphetamine, including colorimetric-based detection with both digital image analysis and UV-Vis spectroscopy, as well as the electrochemical detection with a simple electrode sensor. Digital image analysis and UV-Vis spectroscopy aids in objective determination of colour tests to prevent false results, as well as to minimise inter-rater variation. Development of a novel electrochemical detection based on commercial electrode modified with low-cost materials would assist the detection of residual methamphetamine. Adequate sensitivity achieved by electrochemical detection also demonstrates the potential in providing testing outcomes that complement with GC analyses.

In addition to the sensitivity, the potential to be modified into portable devices for convenience field testing based on the outcome of this research study shall assist the investigative procedure. It requires low amount of reagent and the sample analyte that could effectively save cost and time. With that, the suggested methods could serve as an alternative to the conventional screening tests which are subjective in nature. They could also help to reduce the workload of investigators at the scene, and to minimise the backlog of samples prior to analytical analyses in the forensic laboratories.

CHAPTER 2

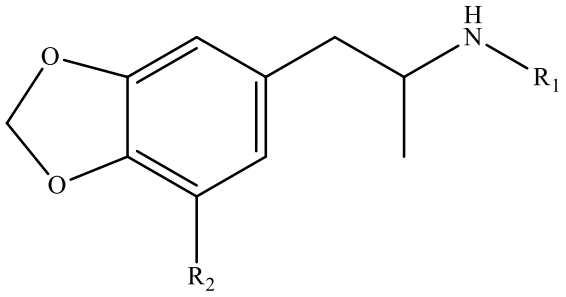
LITERATURE REVIEW

2.1 Overview

The literature review describes the properties of methamphetamine, including both physical and chemical aspects. The situations of clandestine laboratories, their contamination as well as the remediation strategies and standards are reviewed. In addition, various analytical methods of illicit methamphetamine detection, covering the colorimetric detection, UV-Vis spectroscopy, electrochemistry, as well as gas chromatographic methods, are also critically discussed. Lastly, the sampling method of surface methamphetamine is also covered.

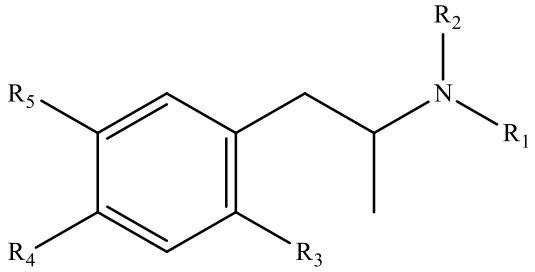
2.2 Physical and chemical properties of methamphetamine

ATS are phenethylamines that consists of the principal members, namely amphetamine, methamphetamine and other ring-substituted, carbon-substituted, or nitrogen-substituted compounds. The compounds resemble the chemical structure of amphetamine (UNODC, 2009b; NIDA, 2019). This group of illicit substances can also be categorised into another two groups, *i.e.* methylenedioxyamphetamine type compound (Figure 2.1) and amphetamine type compound (Figure 2.2), depending on the site of substitution occurs (UNODC, 2006; UNODC, 2009b).



MDE	$R_1=C_2H_5$; $R_2=H$
N-OH MDA	$R_1=OH$; $R_2=H$
MMDA	$R_1=H$; $R_2=OCH_3$
MDMA	$R_1=CH_3$; $R_2=H$
MDA	$R_1=H$; $R_2=H$

Figure 2.1: Examples of methylenedioxyamphetamine type compounds (MDE: N-ethyl-3,4-methylenedioxy amphetamine; N-OH MDA: N-hydroxy-3,4-methylenedioxy amphetamine; MMDA: 3-methoxy-4,5-methylenedioxy amphetamine; MDMA: 3,4-methylenedioxy methamphetamine; MDA: 3,4-methylenedioxy amphetamine).



DOB	$R_1,R_2=H$; $R_3,R_5=OCH_3$; $R_4=Br$
DMA	$R_1,R_2,R_4=H$; $R_3,R_5=OCH_3$
DOET	$R_1,R_2=H$; $R_3,R_5=OCH_3$; $R_4= C_2H_5$
NNDA	$R_1,R_2=CH_3$; $R_3,R_4,R_5=H$
PMA	$R_1,R_2,R_3,R_5=H$; $R_4= OCH_3$
DOM	$R_1,R_2=H$; $R_3,R_5=OCH_3$; $R_4=CH_3$

Figure 2.2: Examples of methylenedioxyamphetamine type compounds (DOB: 4-bromo-2,5-dimethoxy amphetamine; DMA: 2,5-dimethoxy amphetamine; DOET: 2,5-dimethoxy-4-ethyl amphetamine; NNDA: N,N-dimethyl amphetamine; PMA: 4-methoxy amphetamine; DOM: 2,5-Dimethoxy-4-methyl amphetamine).

Methamphetamine, with an IUPAC name of (2S)-N-methyl-1-phenylpropan-2-amine, is a base with chemical formula of $C_{10}H_{15}N$ and molecular mass of 149.23 g/mol. It can be sticky waxy base (McKetin et al., 2005) or colourless volatile oil (EMCDDA, 2013). However, methamphetamine seizures is usually encountered in solid form either as powder, crystals, or tablets (McKetin et al., 2005). The hydrochloride salts are the commonly encountered as salt form, which appear heavier (molecular mass = 185.69 g/mol), less volatile (melting point = 170–175 °C), and typically encountered as racemic mixture, *i.e. d,l*-methamphetamine (UNODC, 2006). The proportion of these two optical isomers is closely related to the chemical precursors

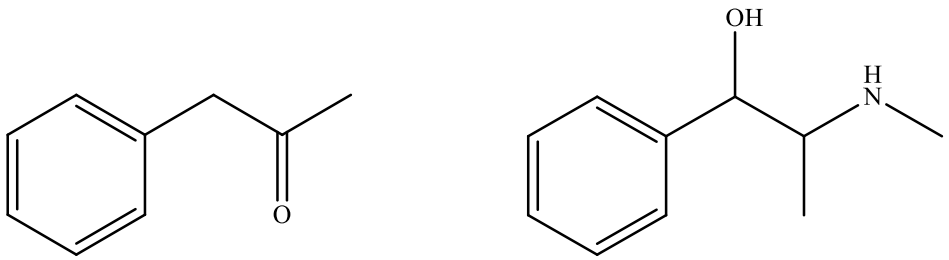
and synthetic pathway (Stojanovska et al., 2013; Kunalan, 2014; Hamdan et al., 2015; Onoka et al., 2020). Use of hydrochloric acid (HCl) as the conjugate of methamphetamine base could be due to the performance of HCl-protonated amine group in terms of oxidation stability and water solubility (Thomas and Rubino, 1996; Park et al., 2019). Its relatively better recrystallisation favours the production during manufacture of methamphetamine (Park et al., 2019).

In term of solubility, methamphetamine base is slightly soluble in water but miscible with diethyl ether. Methamphetamine hydrochloride salt, meanwhile, practically insoluble in diethyl ether but dissolves well in water. Both forms of methamphetamine are soluble in methanol, dichloromethane (DCM) and chloroform (UNODC, 2006). Therefore, methanol, DCM and chloroform are commonly used as solvents for sample extraction and instrumental analysis of methamphetamine.

2.3 Manufactures of Illicit Methamphetamine

2.3.1 Introduction to methamphetamine synthesis

Methamphetamine is normally illegally synthesised in clandestine laboratories for domestic use as well as illegal drug trade (Scott and Dedel, 2006). Generally, 1-phenyl-2-propanol (P2P) and ephedrine/pseudoephedrine (Figure 2.3) are the two main precursors used in the manufacture of methamphetamine (Allen and Cantrell, 1989; Stojanovska et al., 2013; Onoka et al., 2020). Different pathways can be implemented to produce the end product of illicit methamphetamine utilising these two precursors.



(a) (b)

Figure 2.3: Chemical structure of (a) P2P and (b) ephedrine/pseudoephedrine.

There are many methods which can be used to synthesise methamphetamine through one or several basic chemical reactions. Several precursors or intermediates can be chemically reacted to form methamphetamine through various organic chemical processes, including heterogeneous catalysis, dissolving metals, metal hydrides and non-metal reductions (Allen and Cantrell, 1989). The variations of these methods that would be discussed in the following sections. As rightly pointed out by Frank (1983), it is vital for forensic chemists to be familiar with the synthesis methods being used by clandestine laboratory operators to assist in the investigations of clandestine laboratories and their related activities.

According to Frank (1983), the knowledge of drug synthesis pathway is important at least for four reasons, namely (i) safety reasons where the forensic scientists must be able to readily able to recognise the reactions in progress, and more importantly to handle them, as well as to be able to deal with the hazardous situation; (ii) evidentiary reasons where the forensic scientists must be able to demonstrate to the court of law that a particular drug is being synthesised, (iii) prosecutive reasons where the forensic scientists need to be able to explain the synthesis steps involved to the court of law, and (iv) intelligence reasons where the forensic scientists shall be able to identify key chemicals likely to be used and this allow for the decision makers to reduce or

control supply or availability in the market, thus making clandestine manufacturing of illicit drug difficult. In addition to those for the reasons outlined by Frank (1983), the literature search also indicated that decontamination purposes would be the fifth reasons which is important from the perspective of making decision on the remediation of contaminated laboratories, which are explored in this study. Contaminated laboratories are those sites which had been contaminated by the manufacturing and packaging activities of illicit drugs.

Historically, in 1970s and 1990s, forensic science literatures reported the three major methods of synthesis, namely the Amalgam Method, the Red Phosphorous Method, and the Anhydrous Method (Frank, 1983; Allen and Cantrell, 1989; Ely and McGrath, 1990; erowid.org, 2004). These methods could then be further explained using different terms of synthesis routes.

2.3.1(a) The Amalgam method

Literature search showed that the most common method of methamphetamine synthesis in the early days was the Amalgam method, or also known as the Mercuric method (Frank, 1983; Irvine and Chin, 1997). Among the variations reported, reaction of P2P with methylamine, mercuric chloride and aluminium in alcohol was the most popular method before 1980 (Frank, 1983). In general, the reaction mechanism can be summarised as shown in Figure 2.4 (Christian, 2004; Abdullah, 2007).

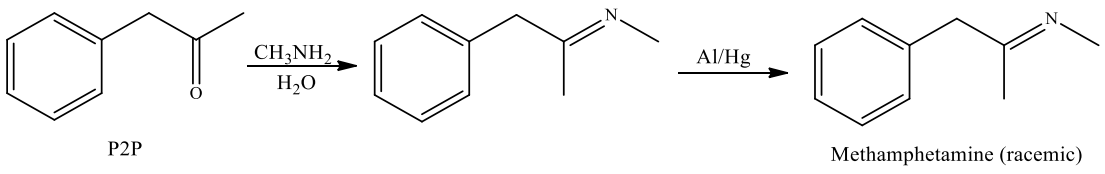


Figure 2.4: Methamphetamine synthesis using Amalgam method.

As reported by UNODC (2006), P2P methods were quickly replaced by methods using ephedrine/pseudoephedrine partly because the product upon such synthesis is a racemic methamphetamine, where *d*- and *l*-methamphetamine isomers are present in 50:50 ratio (Skinner, 1993; Cunningham et al., 2013). It is less potent as compared to the manufacturing method using ephedrine/pseudoephedrine that can result in the production of pure *d*-methamphetamine isomer as illustrated in Figure 2.5 (Mendelson et al., 2006).

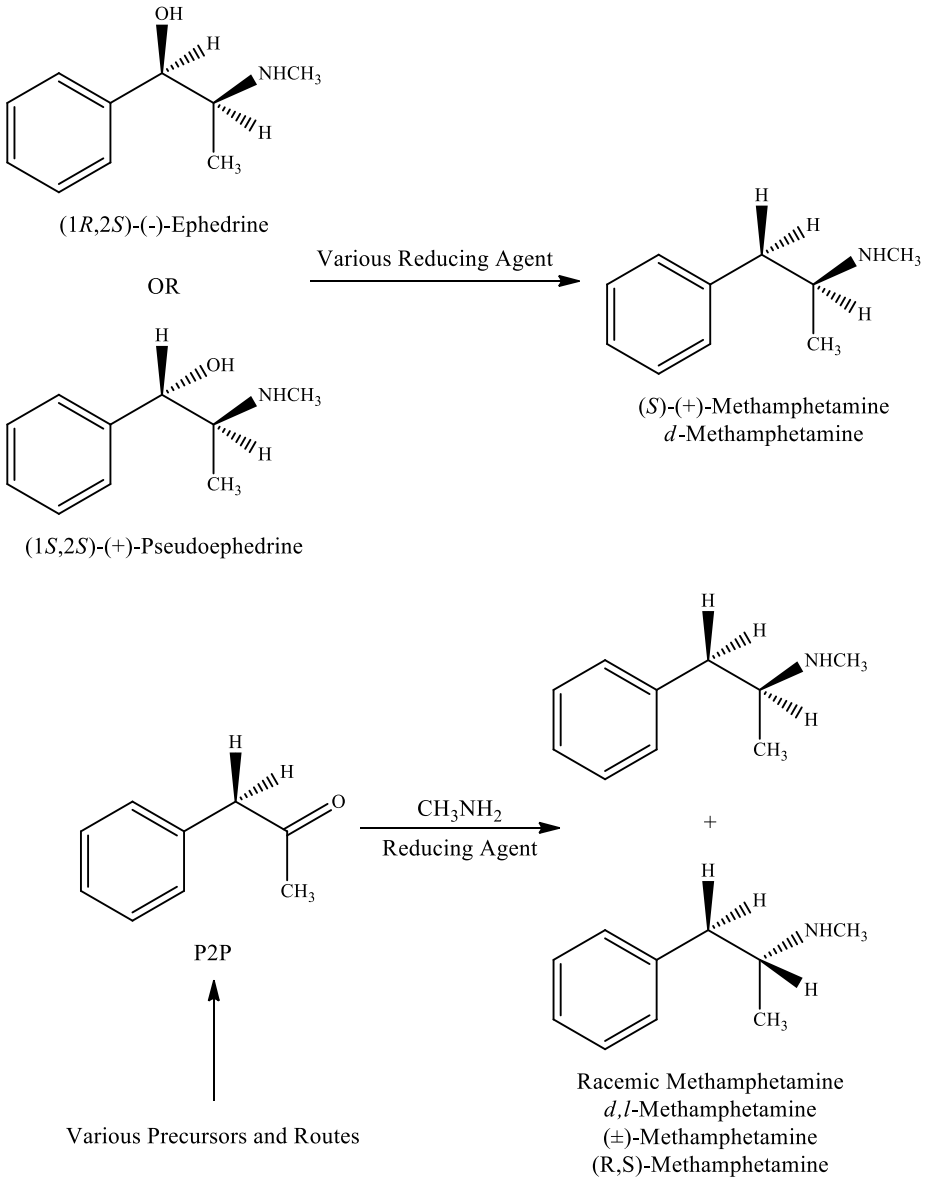


Figure 2.5: Synthesis for *d*-methamphetamine and racemic methamphetamine from ephedrine/pseudoephedrine and P2P respectively.

Note that the findings by Mendelson et al. (2006) indicated that pharmacokinetics of the *d*- and *l*-methamphetamine isomers are similar, but their pharmacodynamic differences between the isomers are substantial. It was also found that both *d*- and *l*-methamphetamine isomers have similar intoxication at high doses. However, the psychodynamic effects of the latter are shorter-lived and less desired by abusers. As *l*-methamphetamine is less potent (Cunningham et al., 2013) and the production of a racemic product is less desired, this could be the contributing factors to the emerging of alternative synthesis method other than P2P pathway. In addition, categorising P2P as a Schedule II controlled substance in 1980 in United States was also an important factor that led to the shift on the choice of precursor (Irvine and Chin, 1997). Internationally, since P2P is a precursor chemical in the manufacturing of methamphetamine, its trade and use are closely monitored for illicit activities (UNODC, 2014). It was also reported that clandestine scientist can synthesis their own P2P, for instance, from phenylacetic acid with acetic anhydride or lead (II) acetate (Allen and Cantrell, 1989). There are also variety of methods reported by methamphetamine "cooking" recipes such as from β-keto esters or *via* the tube furnace (Fester, 1999). However, these methods are unverified street cooking methods with questionable yield.

2.3.1(b) Red Phosphorus methods

Forensic literatures have reported the synthesis of methamphetamine from ephedrine and pyridine with hydrogen iodide and red phosphorous in 1981 in the United States (Frank, 1983). Skinner (1990) also demonstrated the manufacturing of methamphetamine by heating a mixture of ephedrine, red phosphorous, and hydroiodic acid, which was then filtered, made basic, extracted and crystallised as hydrochloride salt from ether/acetone with hydrochloric acid. This method of synthesis was known as the Red Phosphorous method which was preferred in 1980s and 1990s because it was

easy and used readily available precursors either ephedrine or pseudoephedrine to yield *d*-methamphetamine. Note that ephedrine and pseudoephedrine are diastereoisomers as shown in Figure 2.6.

Ephedrine Pseudoephedrine

Figure 2.6: Diastereoisomeric structures of ephedrine and pseudoephedrine.

In late 1980s, the precursor chemicals, ephedrine/pseudoephedrine were listed into the controlled schedules in the United States and alerted worldwide (Cunningham et al., 2013; UNODC, 2014). It is important to point out, as highlighted by Skinner (1990), that hydroiodic acid (HI)/red phosphorous method presents hazards to the manufacturers and the investigators. HI is a toxic and strong irritant while red phosphorous is a flammable and explosive solid. Furthermore, this process could also produce a highly poisonous gas, *i.e.* phosphine, during the heating of HI/red phosphorous mixture, where several fatal cases had been reported in forensic literatures (Willers-Russo, 1999; Burgess, 2001).

It was worth noting the forensic importance of several impurities and intermediates that were detected when red phosphorous method was used in the synthesis of methamphetamine. Besides red phosphorous, incomplete reacted precursors, such as iodoephedrine could have also caused reddish or yellowish final impure methamphetamine (Skinner, 1990). This could be the indicators to differentiate methamphetamine synthesised using other pathways. It is therefore vital to be able to