Discrimination Batches of Methylamphetamine Synthesised via Non-Metal Reductions Method: The Most Common Method Used in Clandestine Drugs Laboratory in Malaysia

Vanitha Kunalan[a*]

[a] *Narcotics Section, Forensic Division, Department of Chemistry, Malaysia, Ministry of Science, Technology and Innovation (MOSTI)*

ABSTRACT: This research involves repetitive synthesis of methylamphetamine using a non-metal reductions method, the three methods most accessible to clandestine chemists in Malaysia. Basic impurities were extracted separately and analysed by gas chromatograph mass spectrometry (GCMS) using DB-5 columns. The GCMS method was able to discriminate all the three routes based on the 'target route specific impurities'. Results indicate that organic impurities allow discrimination by synthetic pathway. Pearson's correlation coefficient was used to the generated data (raw and processed) to investigate the separation of the sample batches/ chromatographic profiles by synthetic route.

Keywords: clandestine drug laboratory, methylamphetamine, non-metal reductions method

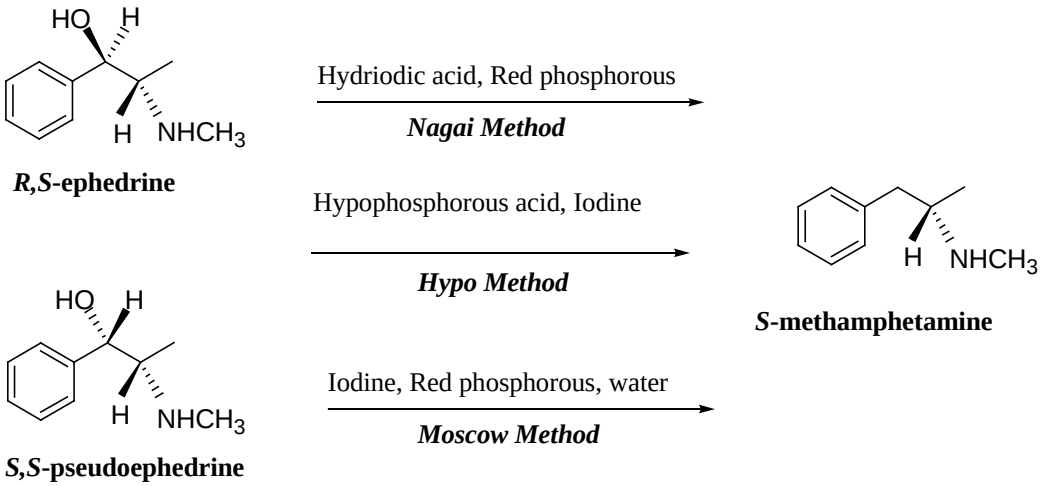
Introduction

The clandestine manufacture of methylamphetamine has recently expanded around the world, particularly in East and Southeast Asia. Compared to such plant-based drugs as heroin, cocaine and cannabis, methylamphetamine is relatively easy to manufacture in clandestine laboratories from commonly available chemicals [1]. Synthesis methods for methylamphetamine can be categorized according to the starting material used. Two major synthetic groups can be distinguished: (a) synthesis starting from 1-phenyl-2-propanone (P2P), which yields racemic methylamphetamine and (b) synthesis using *l*-ephedrine or *d-pseudo*ephedrine as starting materials, which yields *d*-methylamphetamine that is more potent for the central nervous system than the racemic form. Routes most commonly used in Malaysia are a non-metal reductions method such as the Nagai, Moscow and Hypo and all the three routes require ephedrine or pseudoephedrine as starting material.

Each route results in an organic impurity profile that is influenced by the precursors, reagents, and synthetic method used for production. An important goal of this research is the identification of 'route specific' impurities for each of the common methods, in this case, of methylamphetamine manufacture. Route specific impurities are those which, when present in an illicit substance, indicate the use of a particular synthetic pathway. Therefore the impurity profile technique has the potential to be a useful tool for law enforcement authorities for both evidential and intelligence purposes.

Materials and Methods

For this research, methylamphetamine was synthesised in laboratory via the three routes in Scheme 1. Thirty batches of methylamphetamine hydrochloride were synthesised by the Nagai, Moscow and Hypo methods (10 batches per method) using the diastereoisomers pair starting material, (*l*) ephedrine and (*d*) pseudoephedrine. The preparative methods were taken from published materials which are accessible to and used by the clandestine chemist [2].



Scheme 1: Three routes for the syntheses of methylamphethamine in laboratory

For each analysis, impurities were extracted from 100 mg of methylamphetamine hydrochloride. Since the extraction of impurities is pH dependent, buffer was used to maintain a specific pH. For this study, basic (phosphate buffer, pH 10.5) extraction was used in order to see the full spectrum of the impurities. Aqueous buffer was used to dissolve the methylamphetamine sample before extraction into ethyl acetate. Basic impurities was extracted and analysed by gas chromatography mass spectrometry (GCMS) [3].

An Agilent 6890 GC and 5973 mass selective detector (MSD) were used with a non-polar column (DB-5MS); the oven temperature programme started at 50 ºC for 1 min and then increased at 10 ºC/min until 300 ºC, where it was held for 10 min; the injector and detector (transfer line) temperatures were set at 250 and 300 ºC respectively; helium was used as a carrier gas at a constant flow rate of 2 mL/min; 1µL of extract was injected in the splitless mode [3,4].

Results and Discussion

Dimethylphenylnaphthalene and benzylmethnaphthalene were found in batches of methylamphetamine synthesized via the Nagai and Moscow routes. N-methyl-N-(α-methylphenethyl)-3-phenylpropenamide was found in all batches of methylamphetamine, regardless of whether the Nagai (Figure 1), Moscow (Figure 2) or Hypo (Figure 3) routes were used.Using basic extract, it has been possible to identify two and one unknown compounds respectively for the Moscow and Hypo (Figure 2 and 3) present in the pH 10.5 extract.

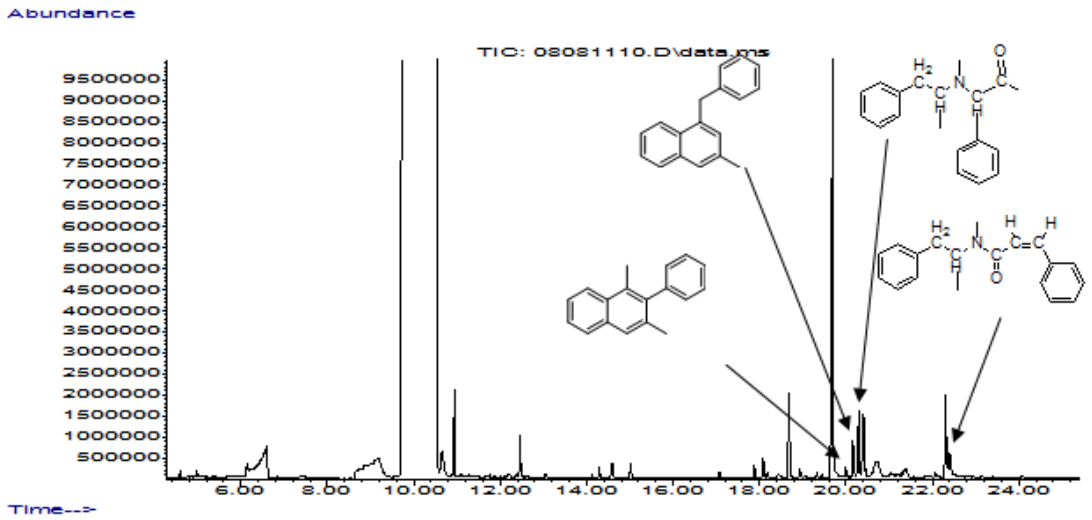


Figure 1: Nagai method

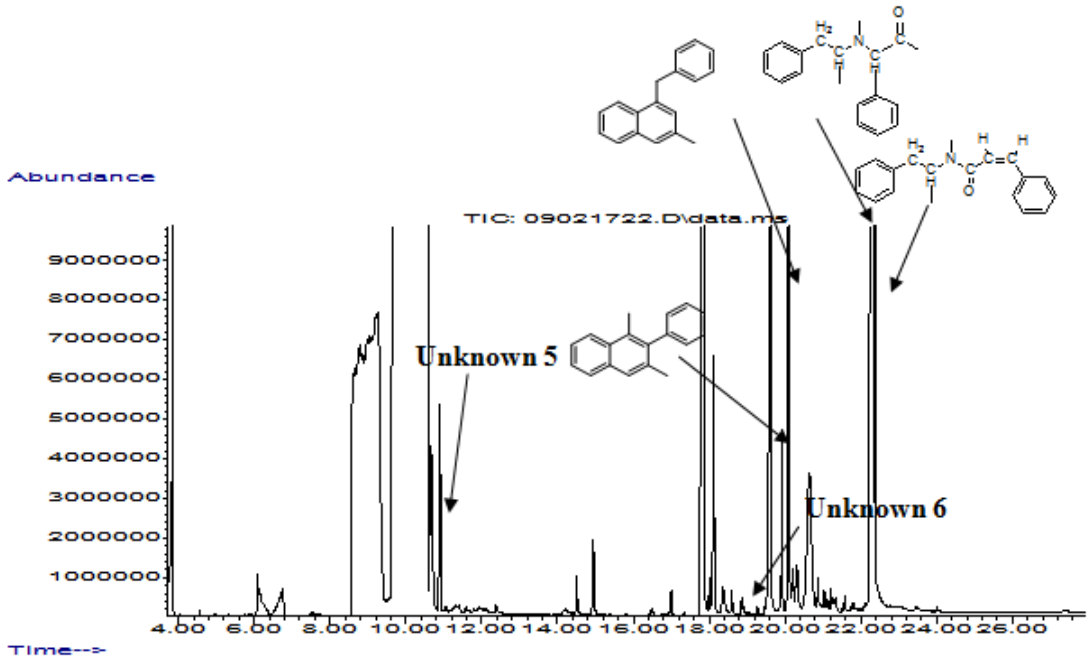


Figure 2: Moscow method

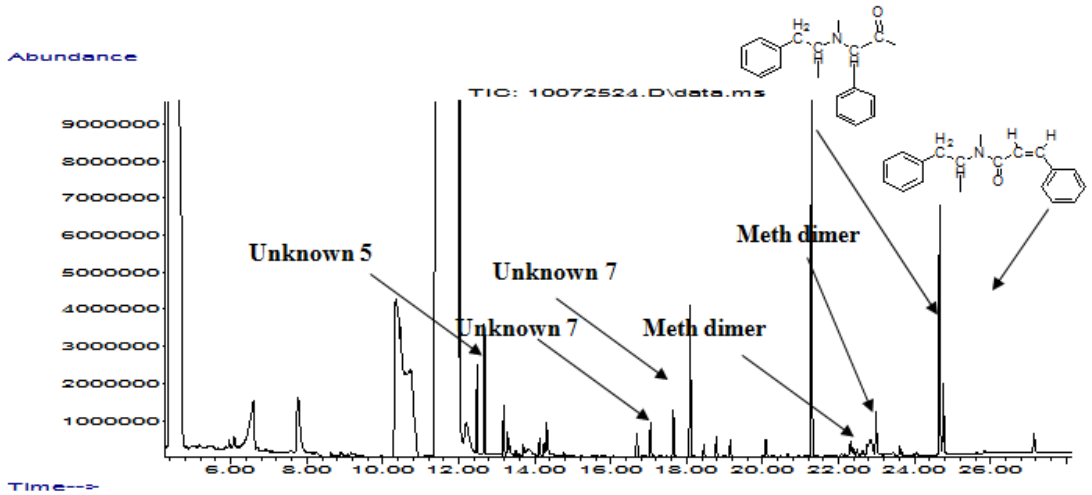


Figure 3: Hypo method

After interrogation of each of the 30 methylamphetamine samples analysed for target impurities, 19 of impurities were identified within the analytical results derived from the samples together with the route specific impurities across the three synthetic routes. To compare the profiles, Pearson correlation coefficients were calculated for the data set. The Pearson correlation coefficients were calculated for each pair of samples using the data set. The peak areas were normalised to the sum of the peak area of the targets impurities. The sixteenth root data pre-treatment method was chosen. As a set point, the 95.00 threshold value was chosen across the data set. Accurate discrimination by synthetic route of the 30 batches was achieved using the target impurities from this study normalised to the sum of the targets and pre-treated by the sixteenth root method. The lowest coefficient calculated for a pair of samples from within a synthetic route was 98.01 and the maximum threshold that would allow the 30 samples within each route to be deemed similar was 99.94.

Conclusion

This work has reported the impurities found in methylamphetamine hydrochloride synthesised in-house in repetitive batches of samples from the diastereoisomers pair starting material, via a non-metal reductions method, the three preparative methods. Basic

extraction was used in order to see the full spectrum of impurities by DB5-MS column. There were distinct differences in the organic impurity profiles of the three routes. Pearson correlation coefficients have proved that accurate discrimination between chromatographic profiles of synthetic routes is achievable when target impurities data is considered.

References

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Additional information and reprint request:
Vanitha Kunalan
Narcotics Section, Forensic Division
Department of Chemistry, Malaysia
Ministry of Science, Technology and Innovation (MOSTI)
Kuala Lumpur, Malaysia