Isotope Ratio Mass Spectrometry (IRMS) Profiling of Methylamphetamine Synthesized using Precursors Extracted from Proprietary Cold Medication via Hypo and Moscow Routes

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ABSTRACT: Isotope ratio mass spectrometry provides an 'isotope fingerprint' of a chemical molecule which may be useful in discriminating between precursor source for the methylamphetamine synthesised and this is explored in detail. Isotope ratio mass spectrometry (IRMS) was used to specifically address the potential to link the methylamphetamine product to either of the synthetic routes (Hypophosphorous or Moscow) or to link the final product by precursor extraction solvent. We also address the ability IRMS to discriminate inter and intra batch variations of methylamphetamine synthesised from both clandestine routes.

Keywords: firearm fatality, suicidal, shotgun, Kronlein

Introduction

This work exposes the variation in light stable isotopic values (C,H,N) derived from the analysis of methylamphetamine synthesised from two popular clandestine routes, namely the Hypophosphorous and Moscow routes, as shown in Figures 1 and 2. The final products were repetitively synthesised using precursors, catalysts and reducing agents that were derived from house hold products and cold medications [1-7]. Pseudoephedrine was extracted using three different solvent systems, from Sudafed which is an over the counter cold medication widely available in the United Kingdom [8-13]. Methylamphetamine was also prepared from laboratory grade pseudoephedrine. Six repetitive batches of the final products were produced in each case to provide within and between batch variations and providing a total of 48 samples (i.e. 24 for each route).

Figure 1: Scheme of methamphetamine synthesis via Hypophosphorous (Hypo) route

Figure 2: Scheme of methamphetamine synthesis via Moscow route

Materials and Methods

Hypophosphorous (Hypo) route

Pseudoephedrine hydrochloride (2.0 g), iodine (4.0 g) and 3.6 mL of hypophosphorus acid were mixed together in a flask and the mixture refluxed for 8 hours then allowed to cool. The basification and salting procedure is similar to the process detailed in the Moscow route synthesis detailed below. Confirmation of the target compound was determined using H NMR and FTIR which was in agreement of published literature [7-9].

Moscow route

Pseudoephedrine hydrochloride (2.0 g), red phosphorous (0.6 g), iodine (4.0 g) and distilled water (2 mL) were mixed and refluxed for 24 hours. The cooled mixture was diluted with an equal volume of water and the red phosphorus filtered out. A few grams of thiosulfate were placed into a beaker and 25% sodium hydroxide solution (8 mL) were added. This mixture was added to the filtered reaction mixture, and swirled to reveal methylamphetamine free base as oil which was then extracted into toluene. Anhydrous hydrogen chloride gas was bubbled through to reveal a white preciptitate, which was washed with toluene [7-8]. The solid was dried under high vacuum. Confirmation of the target compound was determined using H NMR and FTIR which was in agreement of published literature [7-9].

Isotope ratio mass spectrometry (IRMS) analysis

^{13}C and ^{15}N Isotope analysis by EA-IRMS

Carbon and nitrogen isotope abundances analyses were carried out using an automated nitrogen-carbon analyser (ANCA) coupled to an automated breath analyzer (ABCA) isotope ratio mass spectrometer (SerCon Ltd, Crewe, United Kingdom). Typically 0.4 mg of sample material was weighed into tin capsules (Elemental microanalysis, Devon, United Kingdom) and introduced via a solid Costech Zero-Blank autosampler (Pelican Scientific Limited, Alford, United Kingdom). The elemental analyser (EA) reactor tubes were comprised of two quartz glass tubes filled with chromium (III) oxide/copper oxide and reduced copper, held at 1020 °C and 620 °C for combustion and reduction respectively. A water trap filled with magnesium perchlorate was used to remove water from combustion gases thus generated, and post reactor gas chromatograpy(GC) column was kept at 65 °C for separation of evolved N_2 and CO_2. Data were processed using proprietary software (SerCon Limited, Crewe, United Kingdom). Measured isotope ratios are expressed in the δ notation [$^{o}/_{oo}$] relative to the appropriate international standard material anchoring the isotope scale (e.g., VPDB for ^{13}C or VSMOW for ^{2}H).

Each batch of samples was bracketed by two blanks (empty tin capsules) and two sets of laboratory certified standards of known isotopic composition (Iso-Analytical, Crewe, United Kingdom). This standard was leucine ($\delta^{13}C_{VPDB}$ = -30.52 $^{o}/_{oo}$, $\delta^{15}N_{AIR}$= +10.77 $^{o}/_{oo}$).

^{2}H Isotope analysis by TC/EA-IRMS

A Delta^{Plus}-XP isotope ratio mass spectrometer (IRMS) coupled to a high-temperature conversion/elemental analyser (TC/EA; both Thermo-Fischer Corporation, Bremen, Germany) was used for $^{2}H/^{1}H$ isotope ratio measurement of synthesised methylamphetamine samples. Typically, 0.2 mg of solid sample was weighed into a silver capsule and placed in a desiccator for one week before the samples were introduced into the TC/EA by means of a solid Costech Zero-Blank solid autosampler (Pelican Scientific Ltd, Alford , United Kingdom). The reactor tube was self packed and comprised of an Alsint ceramic tube, containing a glassy carbon tube filled with glassy carbon granulate, silver and quartz wool (SerCon, Crewe, Cheshire). The reactor temperature was set at 1425 °C while the postreactor gas chromatograph column was maintained at 85 °C. Helium (99.99% purity, Air Products plc,Crewe, Cheshire) pressure was set at 1.45 bar. The run time per analysis was 350s. Measured $^{2}H/^{1}H$ isotope ratios are expressed as δ values in $^{o}/_{oo}$ relative to VSMOW.

The working reference gas, H_2 (BOC, Guilford, Surrey, United Kingdom), was calibrated against VSMOW ($\delta^{2}H$=0.00 $^{o}/_{oo}$) and checked against international reference material (IRM), IAEA-CH-7 polyethylene ($\delta^{2}H_{VSMOW}$= -100.3 $^{o}/_{oo}$; IAEA, Vienna, Austria). Cross checking the $\delta^{2}H_{VSMOW}$-value obtained for the working reference gas H_2 against a further international reference material (IRM) for H^2 isotope analysis, GISP, yielded a measured $\delta^{2}H_{VSMOW}$-value for GISP of -194.6 $^{o}/_{oo}$ (accepted $\delta^{2}H_{VSMOW}$ = -189.73 $^{o}/_{oo}$; IAEA, Vienna Austria). A typical batch analysis comprised of 10 samples run in triplicate, preceded and followed by a set of standards as reported previously [1]. This consisted of in-house standards (coumarin, $\delta^{2}H_{VSMOW}$= +62.56 $^{o}/_{oo}$) and one IRM (IAEA-CH-7) as calibration controls at the beginning and end of the set. Each batch was preceded and followed by a blank silver capsule. Precision of ^{2}H isotope analysis as monitored by the IRMs and lab standards was $\pm$1.15 $^{o}/_{oo}$ or better.

IRMS Sample preparation

Aliquots sufficient for stable isotope analysis were weighed out and dried in a desiccator to remove any traces of moisture (*in vacuo* over P_4O_{10}). To prepare samples for isotope

analysis, drug aliquots were removed from the desiccator and approximately 0.2 and 0.4 mg samples were weighed out in triplicate into silver and tin capsules (SerCon Limited, Crewe, United Kingdom) for analysis by TC/EA-IRMS and EA-IRMS respectively. Capsules were subsequently crimped and placed into 96 well-plates already prepared with blanks and appropriate reference materials. Batch run ready well-plates were placed into another desiccator, where they were kept *in vacuo* over P_4O_{10} until analysis.

Results and Discussion

Figures 1 and 2 represent the light element stable isotopic values derived from samples of methylamphetamine synthesised from laboratory grade precursors (PS-LG) using the moscow and hypo routes (ML and HL). A clear discrimination between both routes using laboratory grade precursor is apparent for $\delta^{13}C$ vs $\delta^{2}H$ and $\delta^{15}N$ vs $\delta^{2}H$.

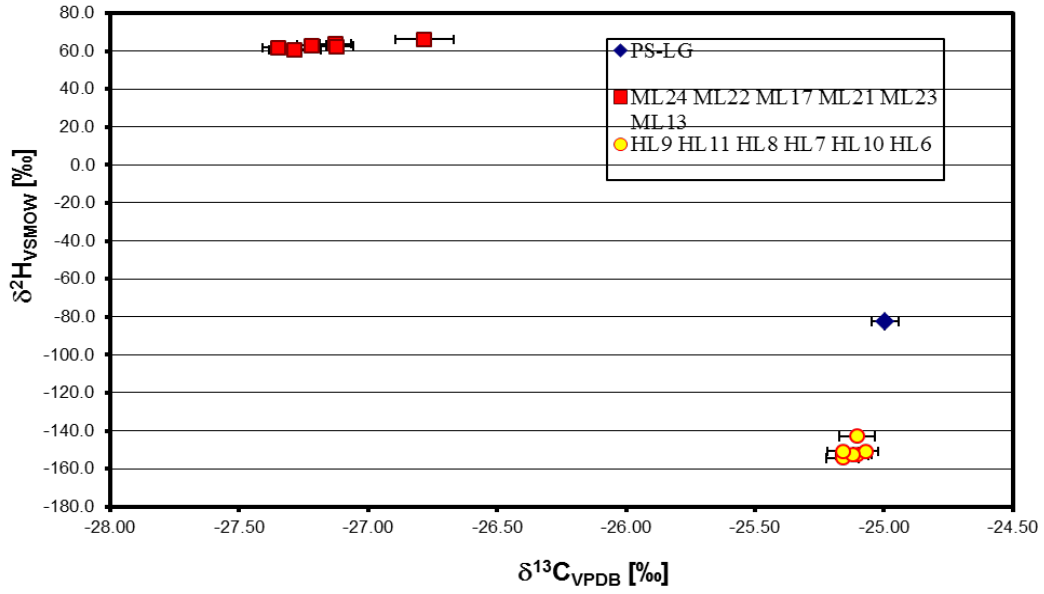

Figure 1: Light element stable isotopic values ($\delta^{13}C$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from laboratory grade precursors using the Moscow and Hypo routes

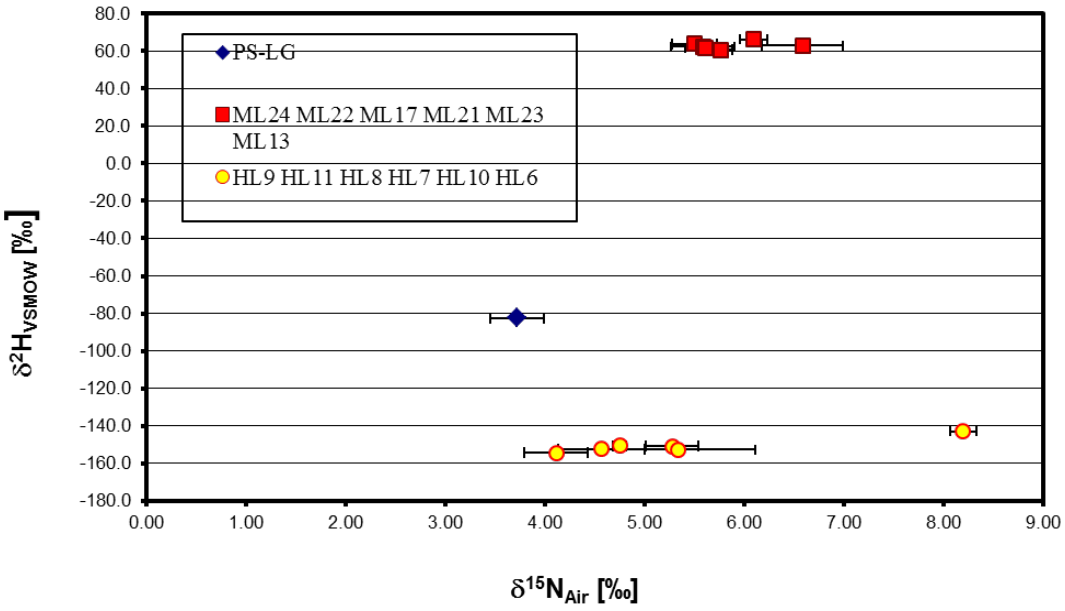

Figure 2: Light element stable isotopic values ($\delta^{15}N$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from laboratory grade precursors using the Moscow and Hypo routes

Figures 3 to 8 represent the $\delta^{13}C$ vs. $\delta^{2}H$ and $\delta^{15}N$ vs. $\delta^{2}H$ stable isotopic values of Moscow and hypophosphorous methylamphetamine. These samples were synthesized from precursors extracted using ethanol (PS-E) and commercial methylated spirits (PS-MMS) and an mixture of ethanol:methanol in a ratio of 90%:10% (PS-DA). The synthetic routes could be readily discriminated when the cold medication was extracted using methylated spirits, in particular when plotting $\delta^{13}C$ vs. $\delta^{2}H$ (Figure 5) though a $\delta^{15}N$ vs. $\delta^{2}H$ also shows some separation as illustrated in Figure 6.

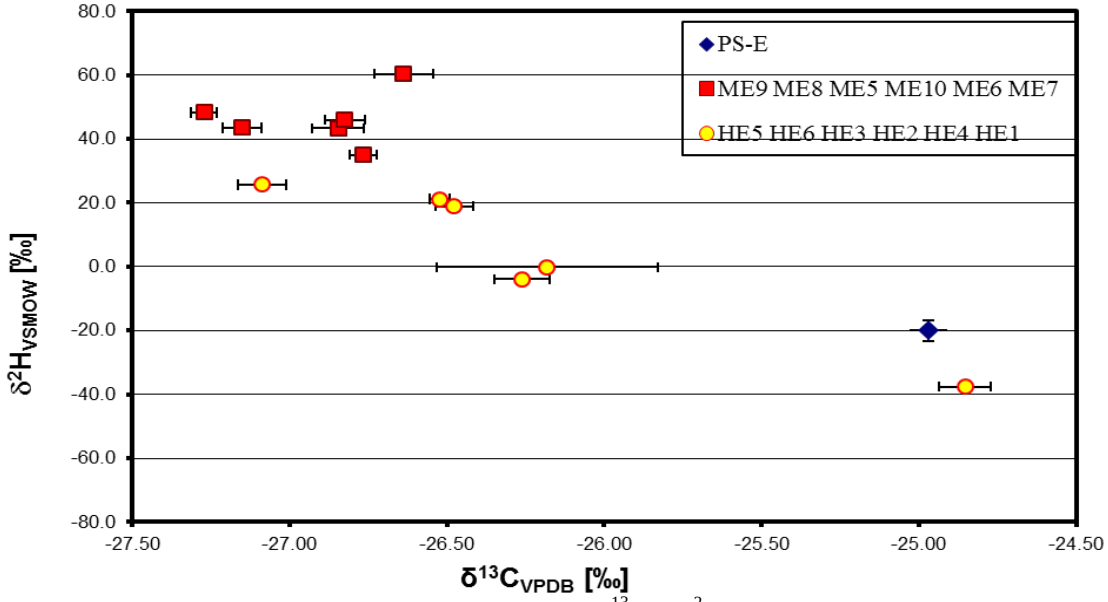

Figure 3: Light element stable isotopic values ($\delta^{13}C$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by ethanol (PS-E) using the Moscow and Hypo routes

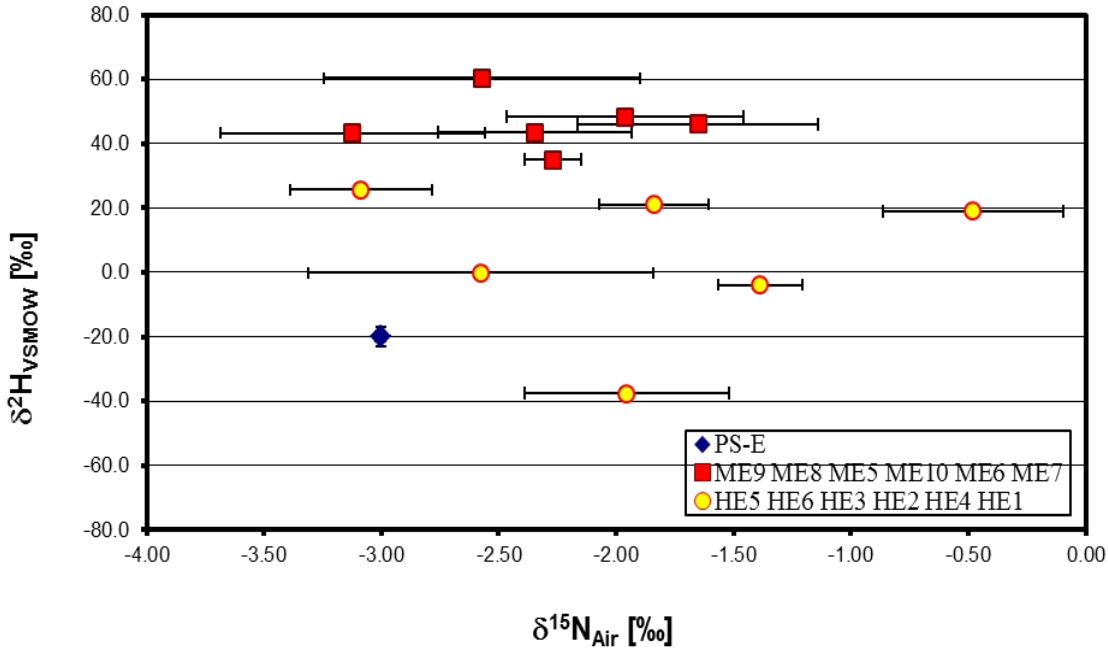

Figure 4: Light element stable isotopic values ($\delta^{15}N$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by ethanol (PS-E) using the Moscow and Hypo routes

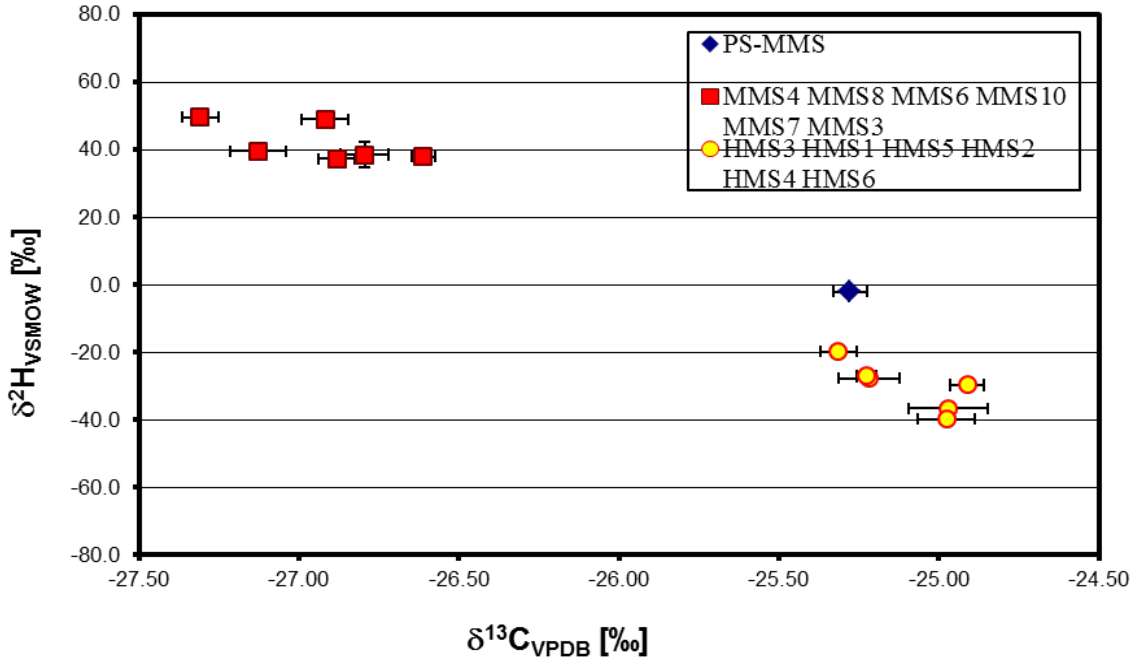

Figure 5: Light element stable isotopic values ($\delta^{13}C$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by commercial methylated spirits (PS-MMS) using the Moscow and Hypo routes

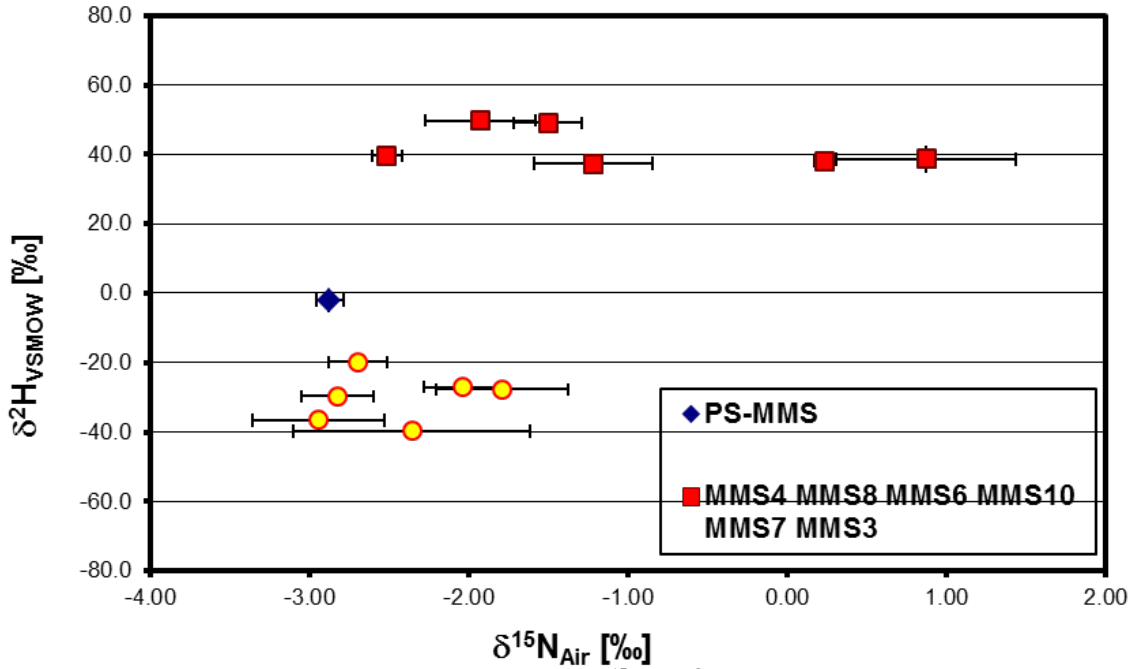

Figure 6: Light element stable isotopic values ($\delta^{15}N$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by commercial methylated spirits (PS-MMS) using the Moscow and Hypo routes

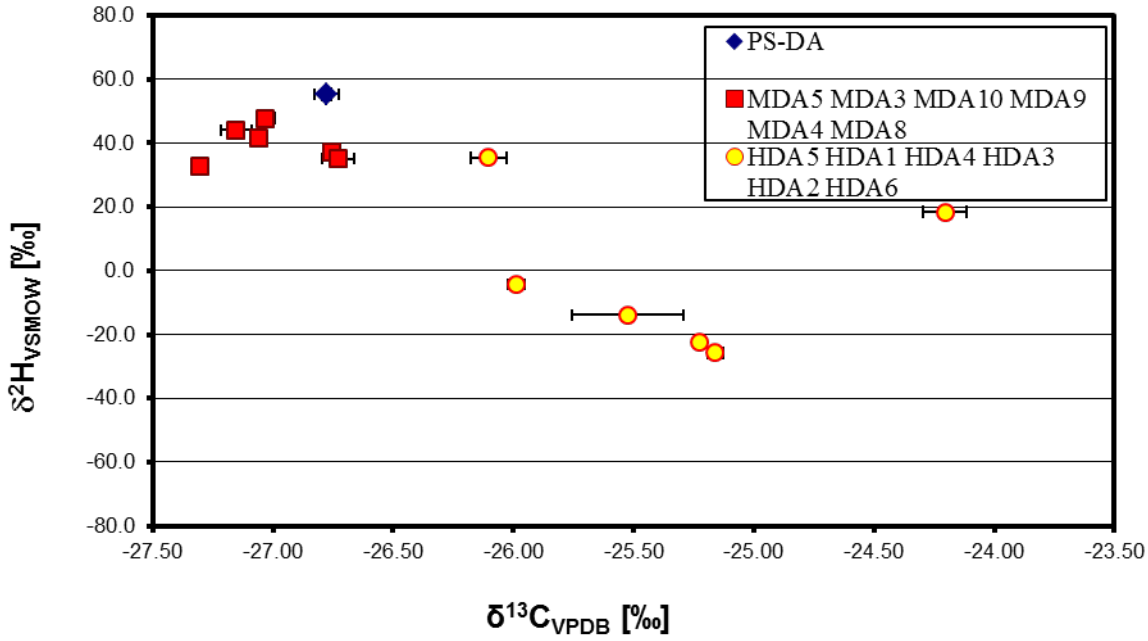

Figure 7: Light element stable isotopic values ($\delta^{13}C$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by a mixture of ethanol:methanol in a ratio of 90%:10% (PS-DA) using the Moscow and Hypo routes

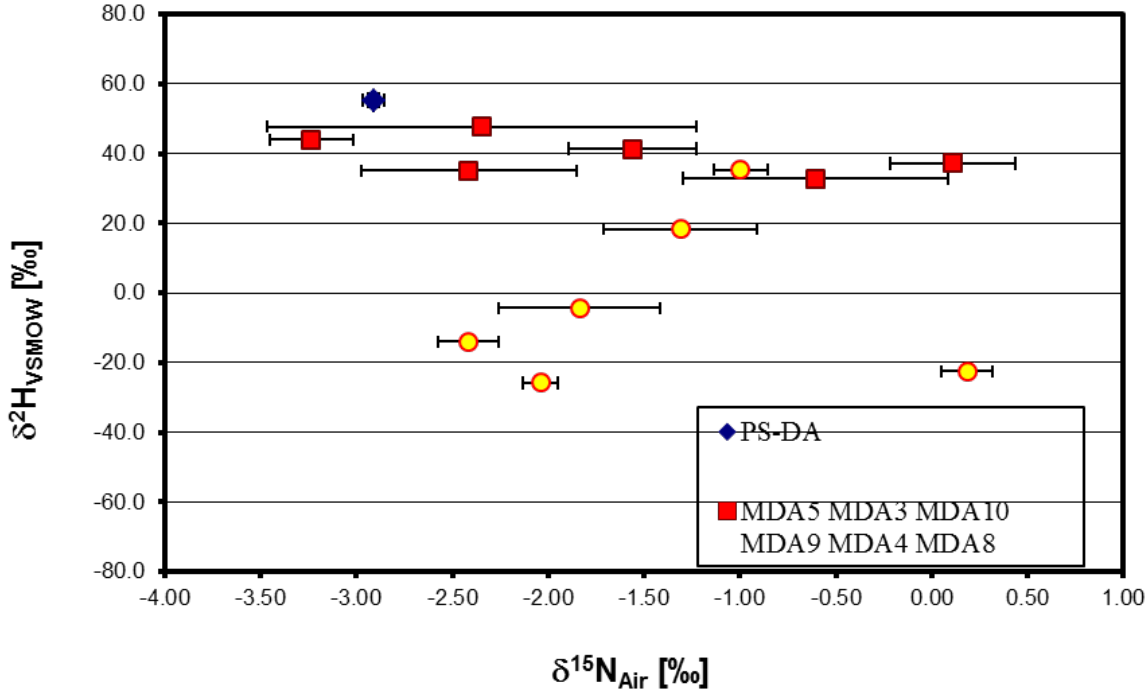

Figure 8: Light element stable isotopic values ($\delta^{15}N$ vs $\delta^{2}H$) derived from samples of methylamphetamine synthesised from extracted precursors by a mixture of ethanol:methanol in a ratio of 90%:10% (PS-DA) using the Moscow and Hypo routes

Extraction of the pseudoephedrine from the cold medication using ethanol or an ethanol: methanol mixture produced a significant convolution of the $\delta^{15}N$ vs $\delta^{2}H$ plot. This convolution was less evident on the plot of $\delta^{13}C$ vs $\delta^{2}H$. In each case, a tighter cluster was

evident within the hypophosphorous samples suggesting less isotopic effects as a consequence of this synthetic method regardless of extracting solvent.

Conclusion

We have demonstrated that isotope ratio mass spectrometry analysis (IRMS) is potentially useful in the comparison and discrimination of batches of methylamphetamine produced from the same precursor materials and different synthetic routes. There appears to be a significant effect encountered as a result of the precursor extracting solvent and to our knowledge this is the first time IRMS has been applied to articulate the differences in such samples.

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