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Isolation of Methamphetamine from 1-(1',4'-Cyclohexadienyl)-2-methylaminopropane (CMP) Using Potassium Permanganate

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ABSTRACT: Methamphetamine illicitly prepared via active metal/ammonia (Birch) reduction of ephedrine or pseudoephedrine is commonly contaminated with 1-(1',4'-cyclohexadienyl)-2-methylaminopropane (CMP), often in significant amounts. Large percentages of CMP in methamphetamine samples result in poor quality (mixed) FTIR spectra. Preliminary treatment/cleanup of CMP-contaminated samples with potassium permanganate gives “clean” methamphetamine for FTIR analysis.

KEYWORDS: Methamphetamine, 1-(1',4'-Cyclohexadienyl)-2-methylaminopropane, Ephedrine, Pseudoephedrine, Birch Reduction, Potassium Permanganate, Forensic Chemistry

Introduction

One of the primary methods of clandestine methamphetamine synthesis is the reduction of ephedrine or pseudoephedrine utilizing an alkali metal such as lithium or sodium, and liquefied ammonia. During a typical reduction of (pseudo)ephedrine, only the hydroxyl group is reduced, producing methamphetamine. With excess alkali metal, and in the presence of an additional proton source [1-8], the aromatic ring is additionally reduced to form a cyclohexadiene (Figure 1). This product is readily generated and is consistent with Birch (Na, EtOH, NH_3) type reactions. The product produced in this reaction is known as 1-(1',4'-cyclohexadienyl)-2-methylaminopropane (CMP), or more simply, the Birch reduction product. On occasion, the CMP to methamphetamine ratio is very high in the final product of this synthesis, which can yield an undesirable, mixed infrared spectrum (Figure 2 - second pane). Separation and identification of methamphetamine and CMP is easily accomplished by gas chromatography/mass spectroscopy, but some scientists prefer infrared spectroscopy, as it provides easy differentiation of the various phenethylamines. This paper will describe a quick, qualitative method for the elimination of CMP commonly found with methamphetamine manufactured from (pseudo)ephedrine using the lithium - ammonia reduction method [9-11].

Experimental

Reagents and Solutions:

* A 2% solution of potassium permanganate was prepared by dissolving 0.5 grams $KMnO_4$ > in 25 mL water (use caution, potassium permanganate is a moderately strong oxidizing corrosive).
* Aqueous base (sodium hydroxide, sodium bicarbonate, etc.).
* Organic solvent (hexane, diethyl ether, or similar).
* Hydrogen chloride (HCl).
* Mixture of Methamphetamine - CMP (60:40).

Instrumentation:

* Nicolet Avatar 370 DTGS-Thermo Electron Corporation. Smart Golden Gate Diamond ATR with KRS-5 Lenses. Number of scans 16, resolution 4 cm^{-1}, and range 400 - 4000 cm^{-1}.

* Agilent 5973 GC-MSD quadrupole electron impact mass spectrometer system with a 30 m HP-5 MS, 0.25 mm, 0.25 µm column. Carrier gas is ultra pure Helium. Instrument parameters: Temperature 90°C to 300°C at 30°C/minute, initial time 1 minute, final hold time 6 minutes, injection port temperature 260°C, transfer line 280°C.

* LCQ Advantage Max ThermoFinnigan quadrupole ion-trap mass spectrometer equipped with an electrospray ionization source (ESI) and interfaced to a Surveyor HPLC system. Phenomenex Luna column C18 - 2.0 x 30 mm x 3 µm. Gradient flow of 95:5 to 5:95 Solvent A/Solvent B over a 10 minutes run. Solvent A is H_2O with 0.1% (v/v) formic acid, while Solvent B is acetonitrile with 0.1% (v/v) formic acid. The flow rate

was 200 mL/minute. Samples were prepared using Solvent A. Mass spectrometry data were collected in the positive ion mode using the full-scan mode in order to provide molecular weight information.

Procedure:

1. Place 25 mg of the sample (methamphetamine/CMP) in a test tube.
2. Dissolve the sample in 3 mL of water and add 0.5 mL of 2% $KMnO_4$ solution, then agitate with vortex.
3. Add aqueous base (e.g., sodium hydroxide, sodium bicarbonate, or similar) to the test tube to make a basic solution (pH > 12).
4. Add organic solvent (3 mL hexane) to the test tube, shake, and isolate the organic layer in a new, clean vessel.
5. Bubble HCl gas through the organic extract.
6. Isolate the precipitate (filtration, evaporation, or similar), dry, and obtain an IR spectrum.

Results and Discussion

The potassium permanganate reaction was performed on a mixed (60:40) sample of methamphetamine and CMP. Prior to performing the potassium permanganate reaction, this sample was analyzed by mass spectrometry for confirmation of sample components (Figures 3, 4A, and 4B). Potassium permanganate was then reacted with the mixture. When CMP is reacted with potassium permanganate, the double bonds on CMP are hydroxylated. By applying this technique with an aqueous base/organic solvent extraction, the CMP sodium salt formed remained in the aqueous phase while methamphetamine passed into the organic phase, where it was isolated by precipitation as the hydrochloride salt form. The final product was then sufficiently pure to be identified by infrared spectroscopy (Figure 2). Again a mass spectrometer was used to determine the effectiveness of the reaction, and the analysis confirmed that methamphetamine had been fully isolated from CMP (Figure 5 and 6).

To verify the hydroxylation of CMP and to show that no methamphetamine is produced by this reaction, a pure sample of CMP was reacted with potassium permanganate using the described technique and then analyzed by LC/MS (Figure 7). The presence of the 186 and 220 fragments in the mass spectrum obtained indicate that a mixture of dihydroxylated and tetrahydroxylated derivatives of CMP are produced by reaction with aqueous potassium permanganate (pH > 8) [12]. There is no indication in the mass spectrum that CMP is converted to methamphetamine (no significant molecular ion at m/z 150). Methamphetamine is left unaffected when reacted with potassium permanganate (Figure 8).

Conclusions

In mixtures where the ratio of CMP to methamphetamine is high, the isolation of methamphetamine can be achieved by reacting CMP with potassium permanganate and an aqueous base. The procedure facilitates the isolation of methamphetamine from its primary by-product associated with the lithium - ammonia method of methamphetamine synthesis. It is rapid and straightforward, with few steps, and allows for convenient identification of methamphetamine using infrared spectroscopy.

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* Law Enforcement Restricted Publication.

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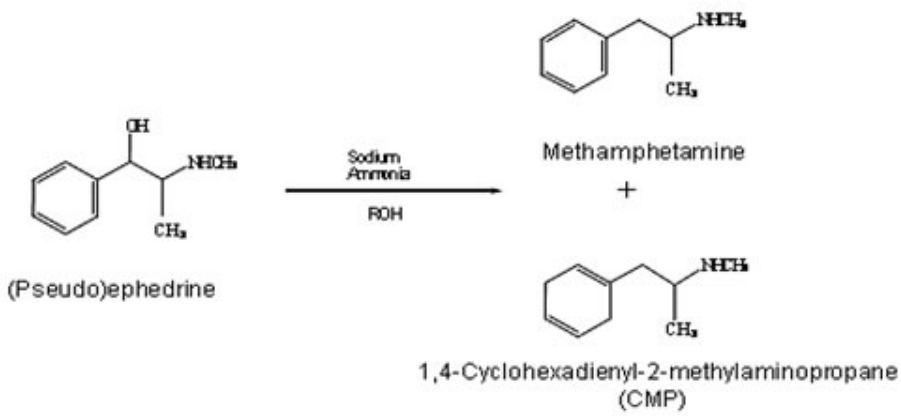

Figure 1. Classic Birch Route of Production with Excess Alkali Metal and Additional Proton Source.

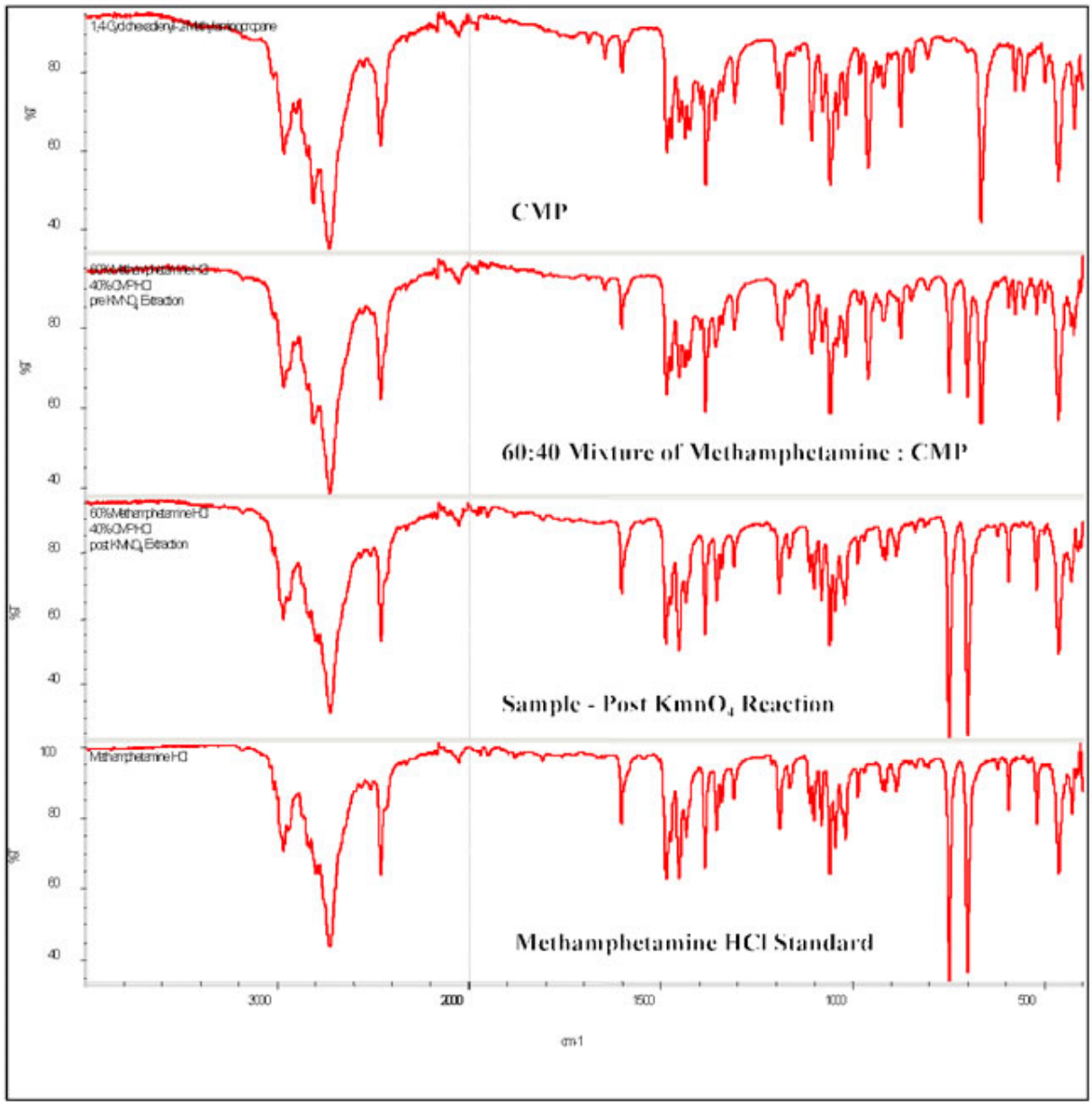

Figure 2. IR Spectra - Pre and Post Potassium Permanganate Reaction Versus Reference Standards.

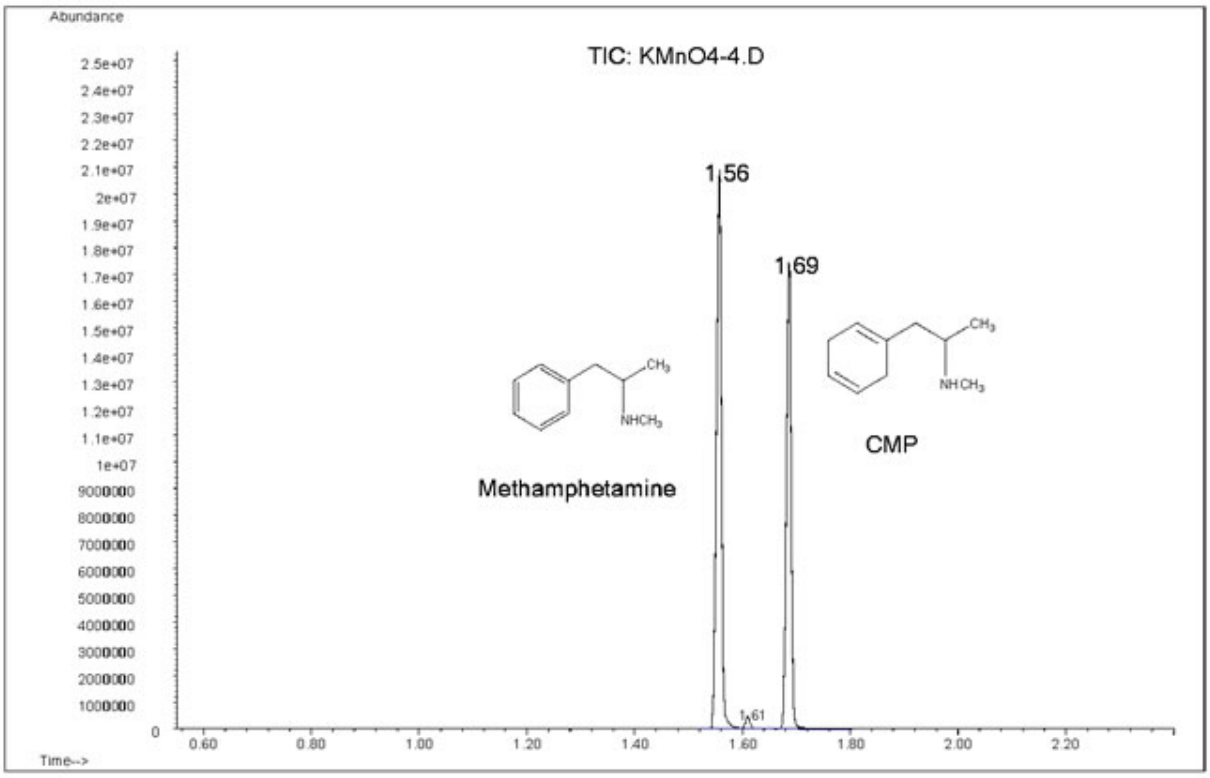

Figure 3. Mass Spectrometer TIC Post Adding Methamphetamine Standard to CMP for a 60:40 Mixture.

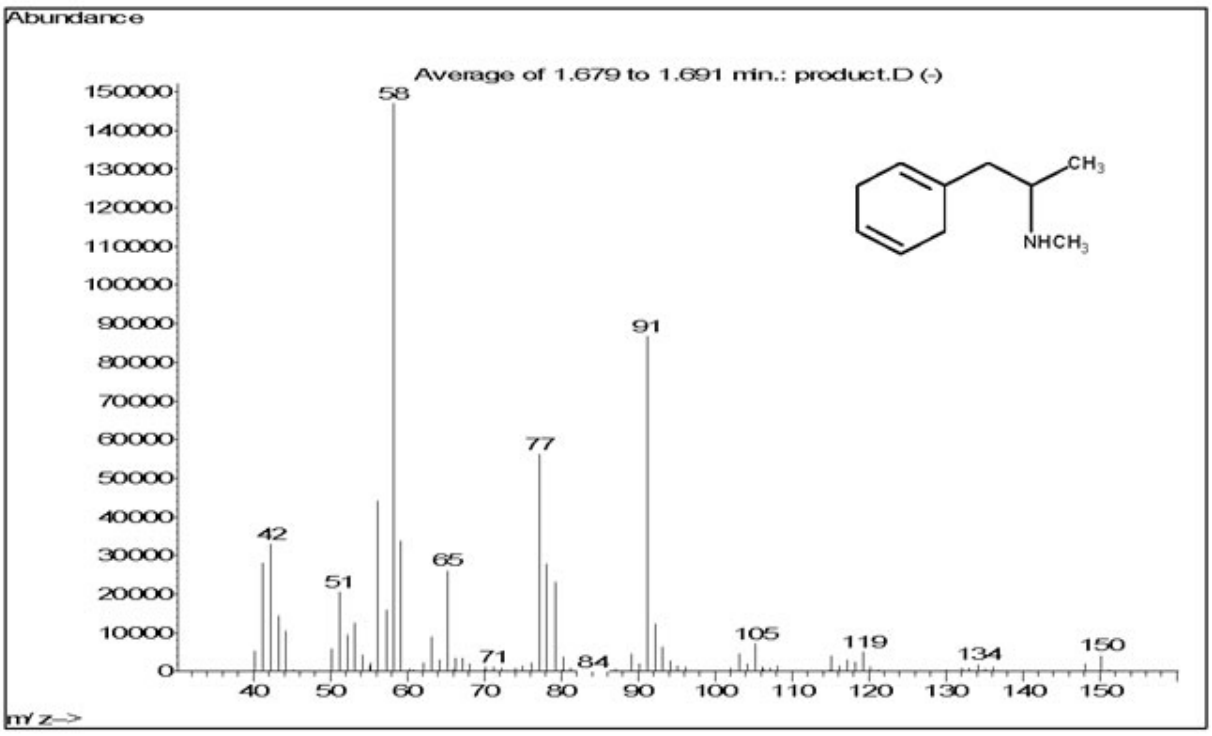

Figure 4a. Mass Spectrum of CMP.

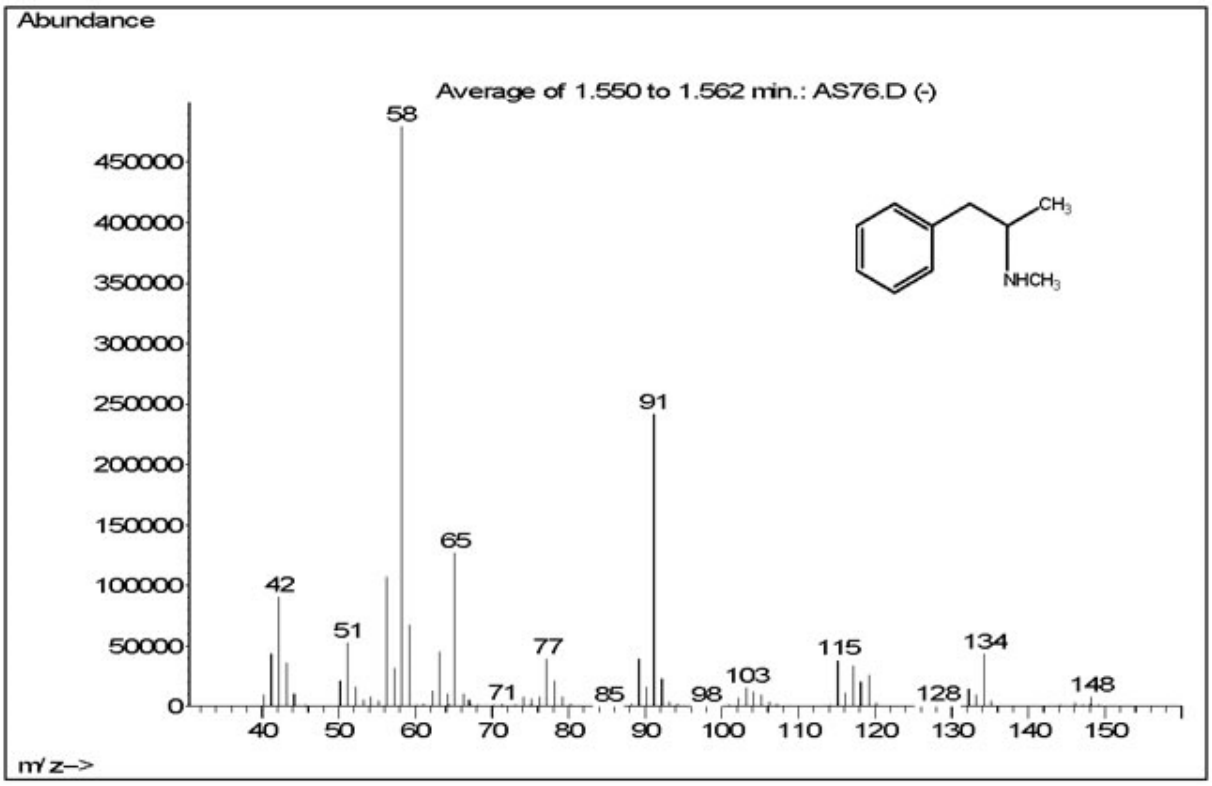

Figure 4b. Mass Spectrum of Methamphetamine.

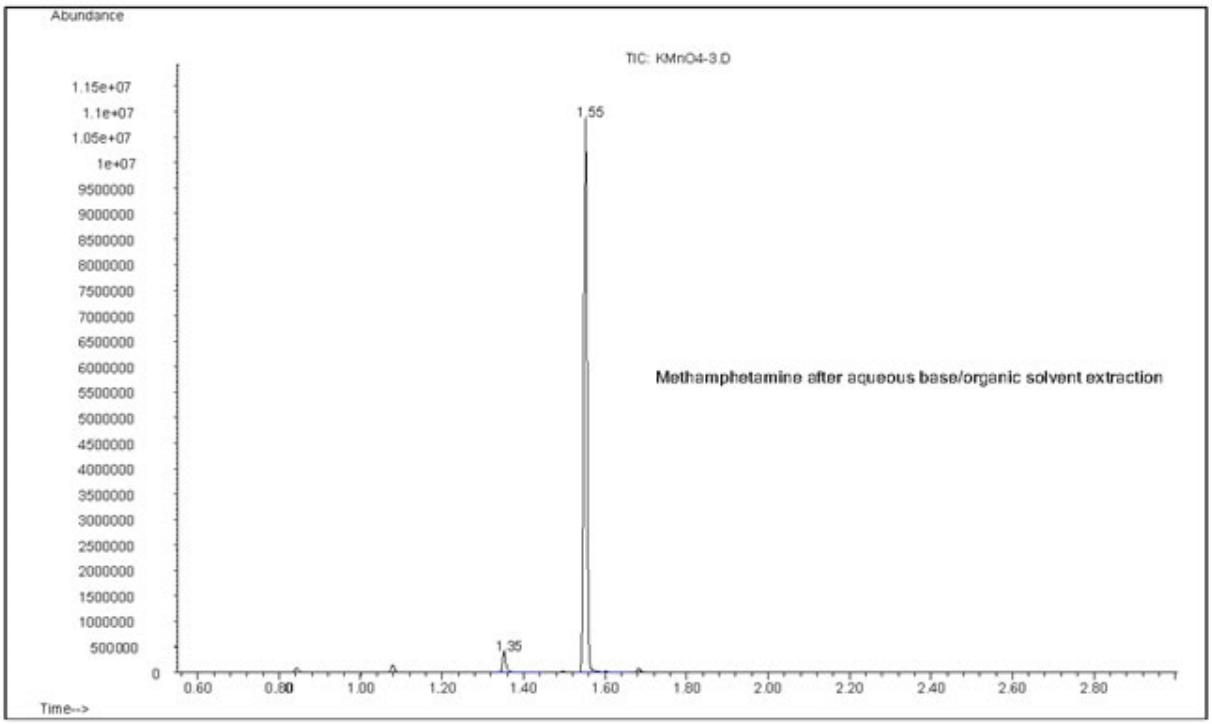

Figure 5. TIC Post Potassium Permanganate Reaction.

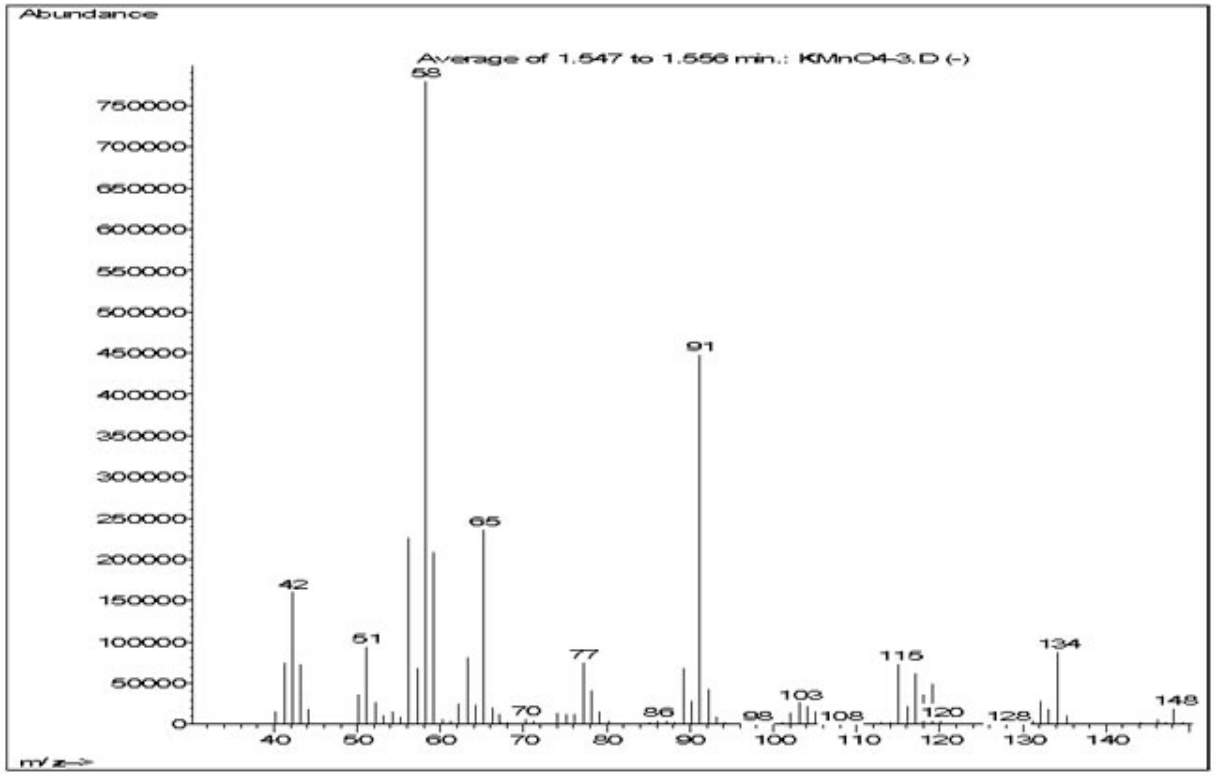

Figure 6. Mass Spectrum of Methamphetamine Post Potassium Permanganate Reaction.

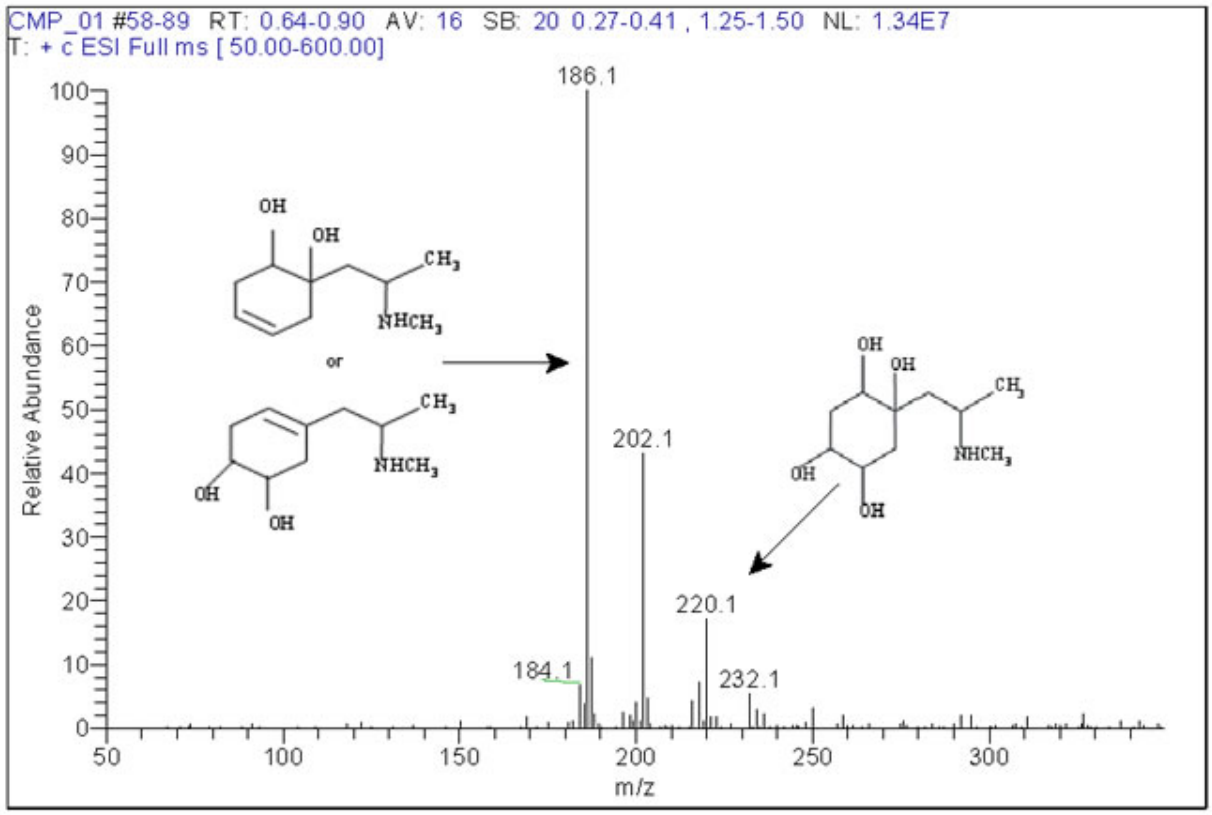

Figure 7. ESI-MS Spectrum Indicating the Presence of both Dihydroxylated and Tetrahydroxylated Derivatives of CMP.

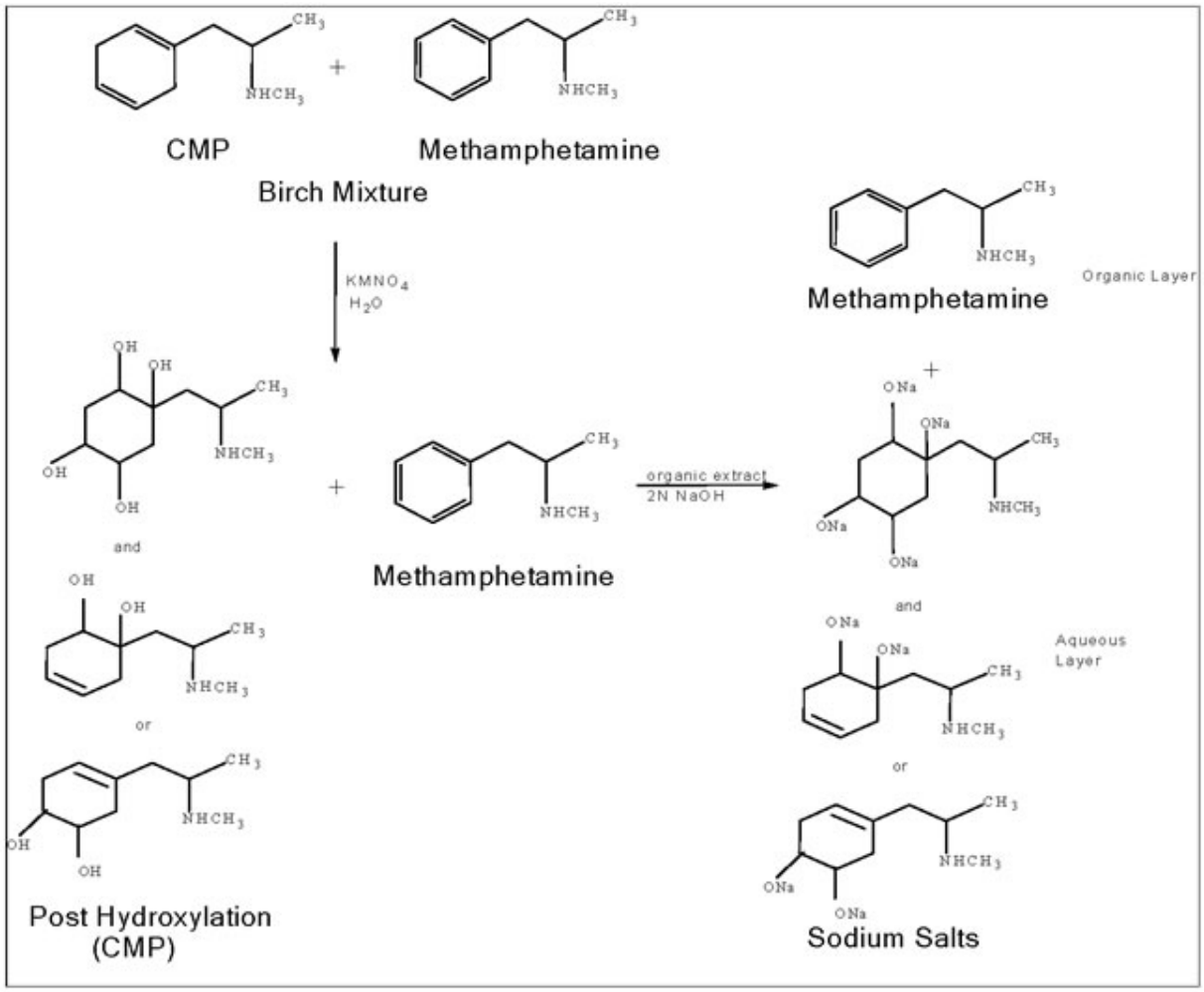

Figure 8. Proposed Potassium Permanganate Reaction.

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