Analytical Profiles for Five "Designer" Tryptamines

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ABSTRACT: Analytical data (Color Tests, GC/FID, GC/MS, FTIR/ATR, ¹H-NMR, and HPLC) for five hallucinogenic "designer" (synthetic) tryptamines is reported. The compounds (5-methoxy-N,N-diisopropyl-tryptamine hydrochloride (5-MeO-DIPT); 5-methoxy-N-methyl-N-isopropyltryptamine base (5-MeO-MIPT), 5-methoxy-α-methyltryptamine hydrochloride (5-MeO-AMT), N,N-dipropyltryptamine hydrochloride (DPT), and 5-methoxy-N,N-dimethyltryptamine base (5-MeO-DMT)) are increasingly encountered in forensic, crime, and toxicology laboratories.

KEYWORDS: Tryptamines, Analogues, Hallucinogens, Color Testing, GC/MS, ¹H-NMR, FTIR/ATR, HPLC, Forensic Chemistry

Introduction

Over the past six months, this laboratory has received over 40 referral drug samples suspected of containing hallucinogenic "designer" tryptamines. Some hallucinogenic tryptamines (e.g., N,N-dimethyltryptamine (DMT), psilocybin, bufotenine, etc.) are naturally produced in fungi, plants, and animals, but these "designer" tryptamines are non-naturally occurring compounds that are produced in laboratories [1]. 5-Methoxy-N,N-diisopropyltryptamine hydrochloride (5-MeO-DIPT), 5-methoxy-N-methyl-N-isopropyltryptamine base (5-MeO-MIPT), 5-methoxy-α-methyltryptamine hydrochloride (5-MeO-AMT), N,N-dipropyltryptamine hydrochloride (DPT), and 5-methoxy-N,N-dimethyltryptamine base (5-MeO-DMT) (Figure 1) are all synthetically produced analogues of known hallucinogenic tryptamines, and have been submitted with increasing frequency to federal, state, and local forensic, crime, and toxicology laboratories throughout the United States. On September 29, 2004, 5-MeO-DIPT (also known by its street names of "Foxy" and "Foxy-Methoxy") became



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Figure 1: Structures of Tryptamine Analogues

federally regulated as a Schedule I Controlled Substance [2]. As of the submission date of this article (April, 2005), 5-MeO-AMT, 5-MeO-MIPT, DPT, and 5-MeO-DMT are not yet specifically listed in the Controlled Substance Act (CSA); however, individuals trafficking in these substances can be prosecuted under the Analogue Statute of the Controlled Substances Act [3]. Herein, we report analytical data (Color Tests, GC/FID, GC/MS, FTIR, NMR, and HPLC) for these five tryptamines.

Experimental

Color Test Reagents

Ehrlich's Reagent: 0.5 g of *para*-dimethylaminobenzaldehyde (p-DMAB) in a mixture containing 50 mL of ethyl alcohol and 50 mL concentrated hydrochloric acid [5]. *Marquis Reagent*: 100 mL formaldehyde in 1000 mL concentrated sulfuric acid [5].

Fourier Transfer Infrared Spectroscopy/Attenuated Total Reflectance (FTIR/ATR)

FTIR spectra were collected on a Thermo Nicolet Nexus 670 FTIR with a potassium bromide (KBr) beam splitter and a deuterated triglycine sulfate (DTGS) KBr detector, equipped with a single bounce Durascope Attenuated Total Reflectance (ATR) accessory. Thirty-two (32) scans were collected between 4000 cm⁻¹ and 400 cm⁻¹, with a resolution of 4.0 cm⁻¹.

Gas Chromatography/Flame Ionization Detector (GC/FID)

GC analyses were performed on an Agilent 6890N gas chromatograph equipped with a flame ionization detector, using a J & W Scientific DB-1 column with a 30 m x 0.25 mm ID and 0.25 μ m film thickness. Instrumental parameters include an injector temperature of 280 °C, hydrogen carrier gas with a flow rate of 1.1 mL/minute, a split ratio of 25:1, and nitrogen make-up gas. The detector temperature was 280 °C. The oven temperature was initially held at 100 °C for 1 minute, then ramped at 12 °C/minute to 280 °C and held for 9 minutes. The concentration for each of the tryptamine analogues was 4 mg/mL in chloroform with a 1 μ L injection.

Gas Chromatography/Mass Spectrometry (GC/MS)

GC/MS spectra were collected on an Agilent 6890N GC interfaced with an Agilent 5973N Mass Selective Detector (MSD) using a scan acquisition from 34 to 550 amu. A J & W Scientific DB-1 column with a 30 m x 0.25 mm ID and 0.25 μ m film thickness was utilized. The injection port temperature was set at 280 °C. The

carrier gas was Helium with a split ratio of 25:1 and constant flow of 1 mL/minute. The oven temperature was initially held at 100 $^{\circ}$ C for 1 minute, then ramped at 12 $^{\circ}$ C/ minute to 300 $^{\circ}$ C and held for 7 minutes. A volume of 1 μ L containing a concentration of 4 mg/mL of each tryptamine analogue in chloroform was injected.

High Performance Liquid Chromatography (HPLC)

HPLC analyses were performed on a Hewlett Packard (HP) Series 1100 HPLC equipped with an ultraviolet lamp and diode array detector (DAD). A volume of 20 μ L containing a concentration of 0.4 mg/mL of each tryptamine analogue diluted in phosphate buffer was injected onto a Whatman Partisil 5 ODS 3, 3.2 x 125 mm column, and scanned from 220 nm – 340 nm with a threshold of 1.0 mAU. An HPLC gradient program was utilized with an initial 20 minute ramp from 95:5 phosphate buffer/methanol to 70:30 phosphate buffer/methanol. This was held for 6 minutes. This was followed by a 10 minute ramp from 70:30 phosphate buffer/methanol to 20:80 phosphate buffer/methanol and held for 4 minutes. The pump flow was 0.76 mL/minute with a total run time of 45 minutes.

Nuclear Magnetic Resonance (¹H-NMR)

Proton NMR analyses were performed on a Varian Mercury 400 MHz NMR using a 5 mm Nalorac Indirect Detection probe, or on a Varian Unity 500 MHz NMR with a 5 mm Varian Indirect Detection probe. The samples were prepared at 10 - 30 mg/mL in deuterium oxide (D₂O) containing 3-(trimethylsilyl) propionic-2,2,3,3- d_4 acid, sodium salt (TSP) as the reference at 0 ppm (Aldrich Chemical Co., Milwaukee, WI). The proton spectra were obtained with 8 scans using a 45 second delay and 90° pulse.

Results and Discussion

Color Testing

Testing each of the tryptamine analogues with the Ehrlich's reagent produced the same change in color from purple to blue, except for DPT HCl, which produced a violet color change and 5-MeO-MIPT which changed from purple to a faint blue. In the presence of the Marquis reagent, each tryptamine analogue produced the same color change from yellow to black, except for DPT HCl which gave a yellow color only, as shown in Table 1.

"Designer" Tryptamine	Ehrlich's Reagent	Marquis Reagent
N,N-DPT HCl	violet	yellow
5-MeO-DMT	purple to blue	yellow to black
5-MeO-MIPT	purple to faint blue	yellow to black
5-MeO-DIPT HCl	purple to blue	yellow to black
5-MeO-AMT HCl	purple to blue	yellow to black

Table 1: Results of Color Testing.

<u>GC/FID</u>

The tryptamine analogues were first injected separately to establish an absolute retention time, followed by an injection of a mixture containing the tryptamine analogue and tryptamine itself (as an internal standard) to establish a relative retention time. Based upon the relative retention times, each tryptamine was fully resolved, as shown in Table 2.

HPLC

The HPLC chromatograms show that each tryptamine has the same ultraviolet spectra (UV) and molar absorptivity due to the UV detection of identical chromophores. The retention time is utilized to distinguish each tryptamine, noting that in aqueous acid, each one has a λ max at 276 nm. DPT HCl has a λ max at 280 nm, as shown in Table 3.

"Designer"		Relative Retention Time vs.
<u>Tryptamine</u>	Absolute Retention Time	Tryptamine (10.547 minutes)
5-MeO-AMT	12.732 minutes	1.207
5-MeO-DMT	12.946 minutes	1.227
DPT	13.625 minutes	1.292
5-MeO-MIPT	14.272 minutes	1.353
5-MeO-DIPT	15.195 minutes	1.441

Table 2: Results of GC/FID Analyses.

Table 3: Results of HPLC Analyses.

"Designer" Tryptamines	Retention Time	<u>λmax in Aqueous Acid</u>
5-MeO-AMT	9.325 minutes	276 nm
5-MeO-DMT	10.280 minutes	276 nm
5-MeO-MIPT	11.961 minutes	276 nm
5-MeO-DIPT	17.051 minutes	276 nm
DPT	17.016 minutes	280 nm

FTIR/ATR

The infrared spectra of 5-MeO-AMT HCl (Figure 2) is a primary amine salt which shows N-H stretching in the region of 3256 cm⁻¹. 5-MeO-DIPT HCl (Figure 3) and DPT HCl (Figure 5) are tertiary amine hydrochlorides which exhibit a N-H stretch in the region of 3156 cm⁻¹ to 3186 cm⁻¹. In the region of 3000 cm⁻¹ to 3035 cm⁻¹, 5-MeO-MIPT (Figure 4) and 5-MeO-DMT (Figure 6) exhibit an aromatic C-H stretch.

<u>GC/MS</u>

The mass spectra are displayed in Figures 7 - 11. Each of the base peaks are attributed to *alpha* cleavage of the amine side chain, with the exception of 5-MeO-AMT (Figure 7). 5-MeO-AMT produces a base peak at m/z 161 due to *alpha* cleavage and proton transfer to the indole moiety. 5-MeO-AMT has a molecular ion at m/z 204 and a prominent peak at m/z 44. 5-MeO-MIPT (Figure 8) gives a molecular ion at m/z 246 with a base peak at m/z 86. The ion at m/z 160 suggests the loss of the methyl-isopropylamine side chain (C₅H₁₂N). 5-MeO-DIPT (Figure 9) gives a molecular ion at m/z 174 with a base peak at m/z 114 (C₇H₁₆N⁺). The fragmentation at m/z 160 suggests the loss of 114 from the molecular ion. DPT (Figure 10) gives a molecular ion at m/z 244 and a base peak at m/z 114, with fragments at m/z 130 due to a loss of C₇H₁₆N and m/z 144 due to the loss of C₆H₁₄N from the molecular ion. 5-MeO-DMT (Figure 11) gives a molecular ion at m/z 160 due to the loss of the base peak at m/z 180 due to the loss of C₇H₁₆N and m/z 144 due to the loss of C₆H₁₄N from the molecular ion. 5-MeO-DMT (Figure 11) gives a molecular ion at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the base peak at m/z 160 due to the loss of the bas

<u>NMR</u>

The NMR spectra are displayed in Figures 12 -16. All five compounds were easily distinguishable by proton NMR. The 5-methoxy substituted tryptamines have the same peak patterns and very similar chemical shifts in the aromatic region and methoxy region: 4 aromatic protons (2 doublets, a singlet, and a doublet of doublets) and 3 protons at 3.9 ppm (singlet for the methoxy group). DPT is not substituted at position 5, giving a different aromatic peak pattern for 5 protons (2 doublets, 2 triplets, and one singlet), and these signals have different chemical shifts from the 5-methoxy compounds, as shown in Figure 1.

All five compounds have unique and easily interpretable peak patterns. A singlet at 2.8 - 2.9 ppm indicates an N-CH₃; integration will determine if the peak represents a mono- or di-methyl group. Doublets at 1.2 - 1.3 ppm indicate methyls bonded to a methine that are *beta* to the amine nitrogen (Figures 12-14). Integration of these doublets and their associated methines will determine if the group is a diisopropylamine, monoisopropylamine, or a simple N-CHR-CH₃. The spectrum of DPT (Figure 15) contains a triplet at 0.9 ppm integrating to 6 protons, indicating 2 methyls bonded to 2 methylenes (multiplets at 1.6-1.7 ppm) bonded to 2 more methylenes (multiplet at 3.1 ppm); i.e., an N,N-dipropyl group. Ethyl amine protons are found as triplets or multiplets above 3 ppm.

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Figure 2: FTIR Spectrum of 5-Methoxy-α-methyltryptamine HCl.



Figure 3: FTIR Spectrum of 5-Methoxy-N,N-diisopropyltryptamine HCl.



Figure 4: FTIR Spectrum of 5-Methoxy-N-methyl-N-isopropyltryptamine Base.



Figure 5: FTIR Spectrum of N,N-Dipropyltryptamine HCl.



Figure 6: FTIR Spectrum of 5-Methoxy-N,N-dimethyltryptamine Base.



Figure 7: Mass Spectrum of 5-Methoxy-α-methyltryptamine.





Abundance

Abundance



Figure 9: Mass Spectrum of 5-Methoxy-N,N-diisopropyltryptamine.



Abundance

Figure 10: Mass Spectrum of N,N-Dipropyltryptamine.





Figure 11: Mass Spectrum of 5-Methoxy-N,N-dimethyltryptamine.

[Figures 12 - 16 Follow]



Figure 12: Proton NMR (400 MHz) of 5-Methoxy-α-methyltryptamine (with Insets).

¹H NMR (400 MHz, D₂O) δ ppm 7.45 (d, J=8.90 Hz, 1 H) 7.30 (s, 1 H) 7.18 (d, J=2.45 Hz, 1 H) 6.94 (dd, J=8.90, 2.45 Hz, 1 H) 3.91 (s, 3 H) 3.65 - 3.74 (m, J=7.50, 6.65 (x3) 6.50 Hz, 1 H) 3.10 (dd, J=14.80, 6.50 Hz, 1 H) 3.03 (dd, J=14.80, 7.50 Hz, 1 H) 1.38 (d, J=6.65 Hz, 3 H).



Figure 13: Proton NMR (500 MHz) of 5-Methoxy-N,N-diisopropyltryptamine (with Insets).

¹H NMR (500 MHz, D_2O) δ ppm 7.43 (d, J=8.80 Hz, 1 H) 7.25 (s, 1 H) 7.07 (d, J=2.42 Hz, 1 H) 6.92 (dd, J=8.88, 2.42 Hz, 1 H) 3.88 (s, 3 H) 3.53 - 3.77 (m, J=6.40 (x6) Hz, 1 H) 3.20 (dd, J=10.50, 6.00 Hz, 2 H) 3.08 (dd, J=10.50, 6.00 Hz, 2 H) 1.35 (d, J=6.64 Hz, 6 H) 1.32 (d, J=6.55 Hz, 6 H).



Figure 14: Proton NMR (400 MHz) of 5-Methoxy-N-methyl-N-isopropyltryptamine (with Insets).

¹H NMR (400 MHz, D₂O) δ ppm 7.45 (d, J=8.90 Hz, 1 H) 7.30 (s, 1 H) 7.17 (d, J=2.45 Hz, 1 H) 6.96 (dd, J=8.80, 2.45 Hz, 1 H) 3.90 (s, 3 H) 3.55 - 3.69 (m, J=6.70 (x6) Hz, 1 H) 3.37 - 3.55 (m, 1 H) 3.05 - 3.33 (m, 3 H) 2.81 (s, 3 H) 1.31 (d, J=6.46 Hz, 3 H) 1.23 (d, J=6.26 Hz, 3 H).



Figure 15: Proton NMR (400 MHz) of N,N-Dipropyltryptamine (with Insets).



Figure 16: Proton NMR (400 MHz) of 5-Methoxy-N,N-dimethyltryptamine (with Insets).

 $^{1}\text{H NMR (400 MHz, D}_{2}\text{O}) \delta \text{ ppm 7.47 (d, J=8.90 Hz, 1 H) 7.32 (s, 1 H) 7.20 (d, J=2.45 Hz, 1 H) 6.97 (dd, J=8.90, 2.45 Hz, 1 H) 3.91 (s, 3 H) 3.46 (t, J=7.43 Hz, 2 H) 3.20 (t, J=7.43 Hz, 2 H) 2.92 (s, 6 H).}$