JOURNAL OF FORENSIC SCIENCES

*J Forensic Sci,* September 2012, Vol. 57, No. 5
doi: 10.1111/j.1556-4029.2012.02142.x
Available online at: onlinelibrary.wiley.com

**TECHNICAL NOTE**

**CRIMINALISTICS**

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# The Characterization of 3,4-Dimethylmethcathinone (3,4-DMMC)

**ABSTRACT:** Analogs and derivatives of traditional illicit drugs are ever increasing in variety and creativity. Staying abreast of the new developments is a constant challenge for every forensic laboratory. Recently, a seizure from Australian Customs Service presented our laboratory with the designer cathinone 3,4-dimethylmethcathinone (3,4-DMMC). Gas chromatography/mass spectrometry (GC/MS), liquid chromatography/mass spectrometry (LC/MS), nuclear magnetic resonance (NMR) spectroscopy, infrared (IR) spectroscopy, and ultraviolet (UV) spectrophotometry were employed to analyze the spectroscopic characteristics of this cathinone. As an analog, 3,4-DMMC exhibits similar if not identical IR and UV profiles to mephedrone (4-MMC) and methcathinone; however, the retention time from GC is unique as expected, and the electron impact fragmentation pattern is consistent with the fragmentation pattern of other cathinones. The chemical shifts of the carbons and hydrogens were assigned by both one- and two-dimensional NMR techniques, while the molecular weight was confirmed by LC/MS.

**KEYWORDS:** forensic science, cathinones, phenethylamines, gas chromatography mass spectrometry, liquid chromatography mass spectrometry, nuclear magnetic resonance, infrared spectroscopy, ultraviolet

Amphetamine-type stimulants (ATS) belong to the larger alkaloid class of $\beta$-phenethylamines and are responsible for the second largest number of drug-related arrests in Australia in 2008–2009 (1). The ATS class of drugs incorporates naturally occurring stimulants such as ephedrine, cathine (and cathinone), and psychedelics, such as mescaline, but also a constantly increasing number of synthetic analogs of the natural materials, which are often abused for their additional psychedelic and entactogenic effects or their differing potency and duration (2).

Traditionally, cathinone intake has been prevalent in Eastern Africa and Arabia via consumption of plant *Catha edulis Forsk* or khat (3). The structures of cathinone and various cathinone derivatives are shown in Fig. 1. While it has been observed less in Western countries, especially when compared to the non-$\beta$-keto-amphetamines, cathinone and its derivatives methcathinone and methylmethcathinone (mephedrone) have been listed in the most restrictive schedules in the United States (schedule I) (4) and Australia (schedule 9) (5), while the United Kingdom has cathinone listed as a class C drug and methcathinone and mephedrone as class B drugs under the Misuse of Drugs Act 1971 (6,7). However, more designer derivatives of cathinone have surfaced recently in drug-related seizures (8), including dimethylcathinone (9), methylone, butylone, and 3-fluoromethcathinone (10) among a suite of others. These have largely been synthesized (11,12) owing to researcher's interest in their detection (13–15), physical properties (16), and biological effects (17).

One cathinone derivative that appears not to have received much attention but was recently seized by the Australian Customs Service in Western Australia is 3,4-dimethylmethcathinone (3,4-DMMC). Other than 3-fluoromethcathinone, cathinones substituted in the 3-position have not been reported upon or are relatively nonexistent. Interestingly, while a correlation in the effect of the drug has been drawn between amphetamine and cathinone analogs (18), the amphetamine analog of 3,4-DMMC also has received little attention. In light of this and the increase in the number of cathinone derivatives surfacing recently, we were interested in elucidating the spectroscopic characteristics of 3,4-DMMC.

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Received 7 Feb. 2011; and in revised form 27 July 2011; accepted 13 Aug. 2011.

## Experimental

### *Infrared Spectroscopy*

The infrared (IR) spectrum was acquired using a Thermo Scientific Nicolet 6700 FTIR with smart iTR diamond ATR accessory (Thermo Fisher Scientific Singapore, Singapore). Data were collected between 4000 and 550 /cm with a resolution of 4 /cm for 16 scans.

### *Gas Chromatography/Mass Spectrometry*

*Sample Preparation*—The sample was dissolved in water which was basified to *c.* pH 9 and extracted with dichloromethane containing a bupivacaine internal standard.

Gas chromatography/mass spectrometry (GC/MS) was run using an Agilent model 6890N GC equipped with an Agilent model 5975 mass-selective detector (MSD; Agilent Technologies Pty Ltd, Mulgrave, VICTORIA). The GC was fitted with a 12 m × 0.2 mm I.D. silicate column coated with 0.33 μm 100% dimethylpolysiloxane (HP-1 Ultra; Agilent Technologies Pty Ltd). The injection port was maintained at 240°C, and injections were performed in splitless mode. The oven temperature program was as follows: Initial temperature 60°C (0.5 min) ramped to 310°C at 25°C/min (final hold 3.5 min). Helium was used as the carrier gas at 2.5 mL/min. The MSD was tuned to operate at 69.9 eV for the electron impact energy and 20.4 V for the repeller plate. The method used to elute the sample was retention time-locked to bupivacaine.

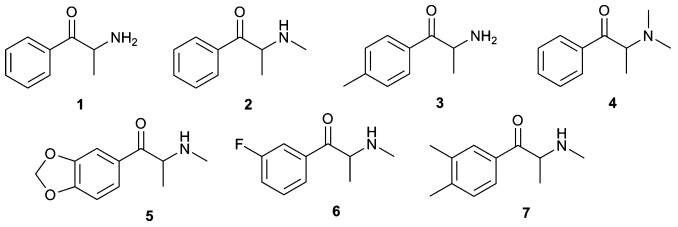



FIG. 1—*Structures of various cathinones.*

### *Liquid Chromatography/Mass Spectrometry*

Liquid chromatography/mass spectrometry (LC/MS) was performed using an Agilent 1100 HPLC coupled with an Agilent 1100 Ion Trap and an electrospray ionization (ESI) source. The HPLC was fitted with a 4.5 × 150 mm Zorbax Extend C-18 reverse-phase column (Agilent Technologies Pty Ltd) with a 5-µm particle size. The sample was chromatographed using an isocratic elution of a 4:1 10 mM ammonium formate buffer/methanol solution with a flow rate of 0.500 mL/min at 40°C. The ESI source was maintained at 350°C with the nebulizer gas set to 60.0 psi and the dry gas flowing at 10 L/min. Nitrogen was used as both the nebulizing and dry gas. Mass spectra were accrued over a range of 70–700 m/z with a 50.00-msec acquisition time. Multiple reaction monitoring was set to auto.

### *Nuclear Magnetic Resonance Spectroscopy*

*Sample Preparation*—The sample was dissolved in water which was basified to *c.* pH 9 and extracted with deuterated chloroform ($CDCl_3$). The $CDCl_3$ was passed through a plug of sodium sulfate before being subjected to nuclear magnetic resonance (NMR).

$^{1}H$, $^{13}C$, and 2D NMR spectra were acquired at 24°C on a Bruker 400 MHz instrument using a 5-mm PABBO–BB probe (Bruker BioSpin Pty Ltd, Alexandria, NSW). Proton spectra were collected using a carrier frequency of 400.132 MHz, while carbon spectra were proton decoupled and collected using a carrier frequency of 100.620 MHz. The chemical shifts ($\delta$) are reported in parts per million (ppm) using chloroform ($CHCl_3$, 7.26 ppm) as the reference (in $CDCl_3$).

### *Ultraviolet Spectrophotometry*

Ultraviolet (UV) spectra were acquired on a Perkin Elmer Lambda 25 UV-Visible spectrometer (Melbourne, VICTORIA), using a 1 cm path length. The sample was diluted to six known concentrations in water and scanned over a range of 210–350 nm at a rate of 450 nm/min.

## Results and Discussion

Figure 2 shows the total ion chromatogram (TIC) and electron impact mass spectrum of 3,4-DMMC. Under the conditions used,

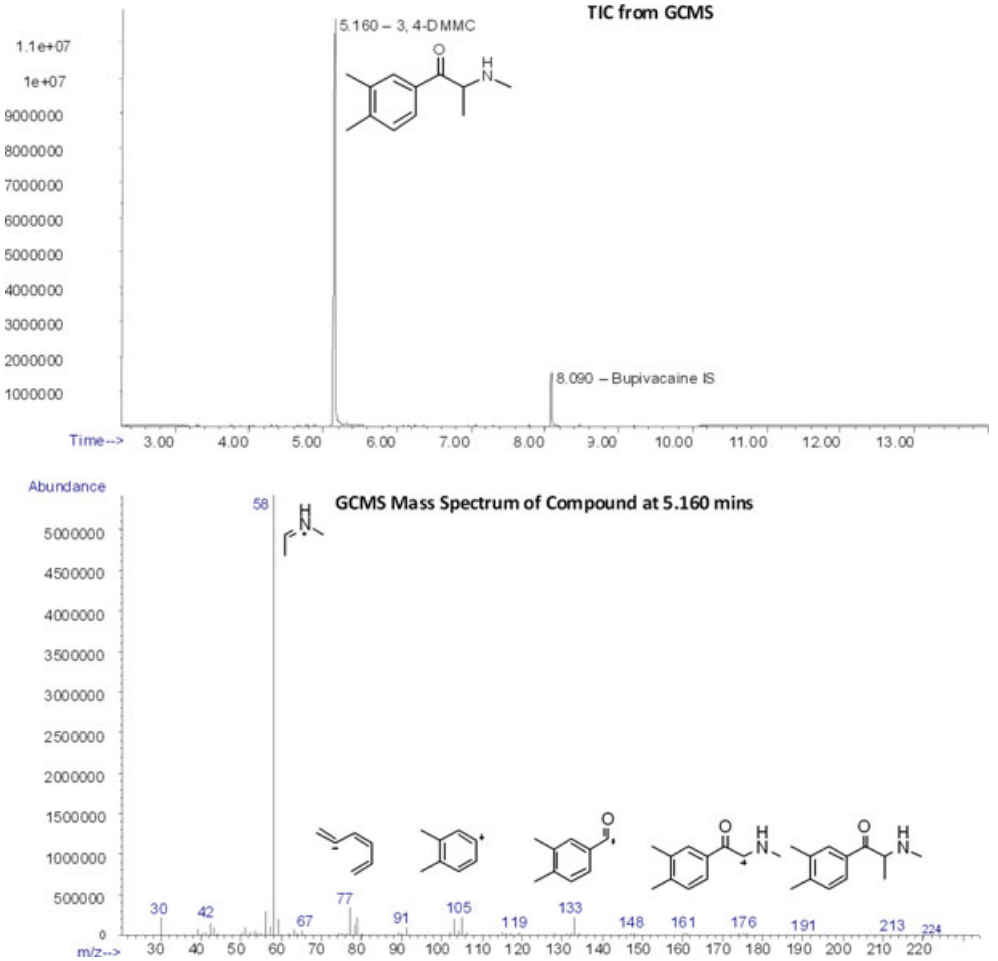



FIG. 2—*Gas chromatography/mass spectrometry total ion chomatogram and electron impact mass spectrometry spectrum of 3,4-DMMC.*

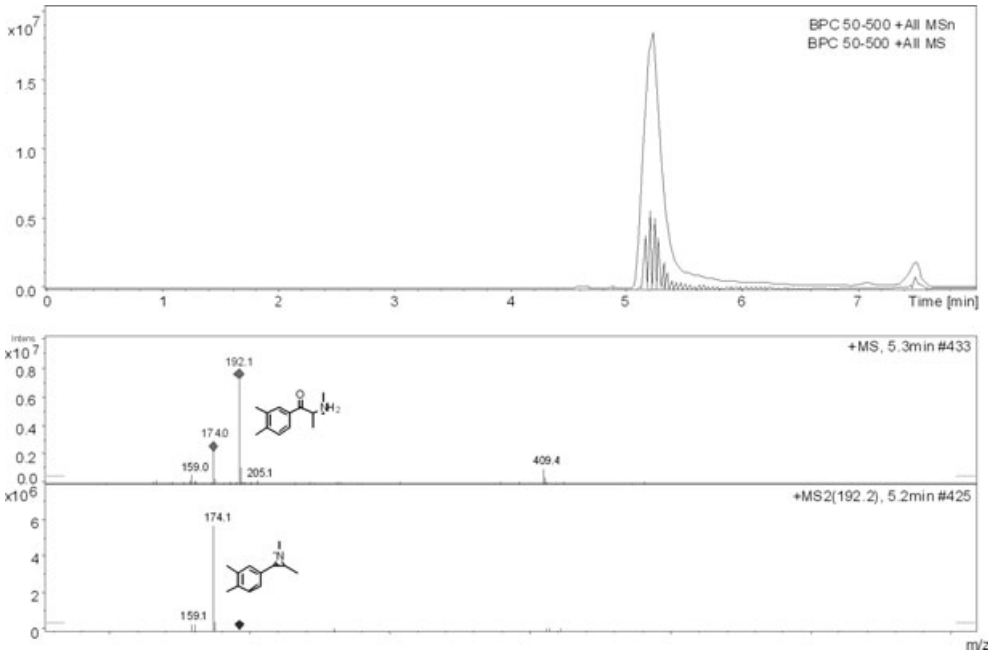



FIG. 3—*Liquid chromatography/mass spectrometry total ion chromatogram and electrospray + mass spectrometry spectrum.*

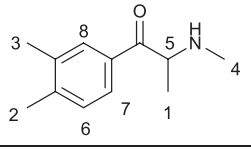
3,4-DMMC was eluted at 5.060 min, which is consistent with the cathinone family, as cathinone, methcathinone, and mephedrone elute at 3.69, 3.86, and 4.58 min, respectively. The fragmentation of methcathinones has been described in earlier studies (16,19), and as expected, the molecular ion at 191 *m/z* is barely present. The base peak at 58 *m/z* is indicative of the N-methyl phenethylamine structure and is of an immonium ion formed from the α-cleavage of the benzylic bond, which is initiated by the amine (also Fig. 1). The 3,4-dimethylbenzoyl cation is observed at *m/z* 133, while the cation at *m/z* 105 is a xylene cation resulting from the subsequent loss of the carbonyl functional group. The further loss of an acetylene group from the xylene cation explains the 79 *m/z* ion. The minor ion at *m/z* 176 is the result of another α-cleavage initiated by the amine, causing the loss of the α-methyl group.

The molecular weight of 191 for 3,4-DMMC was confirmed by running the sample through ESI LC/MS in positive ion mode (Fig. 3). The TIC illustrated that the sample was relatively clean, and the ESI + MS displayed the expected *m/z* 192 ion as well as an *m/z* 174 ion, which is most likely an azirine intermediate resulting from the loss of $H_2O$ from the parent molecule.

NMR analysis showed that the hydrogen at the chiral center was easily identified in the proton spectrum because of its chemical shift of 4.19 ppm and its coupling to the α-methyl at 1.28 ppm to produce the characteristic quartet–doublet splitting pattern. The 1,3,4 trisubstitution pattern on the phenyl ring was confirmed by a combination of the modified distortionless enhancement by polarisation transfer (DEPT) spectrum showing three quaternary aromatic carbons and the splitting pattern of two doublets at 7.74 ($^4J$ 1.7 Hz) and 7.23 ppm ($^3J$ 7.7 Hz) and a double doublet at 7.70 ppm ($^3J$ 7.7 Hz, $^4J$ = 1.7 Hz). All hydrogen couplings were confirmed by a correlation spectroscopy (COSY) experiment.

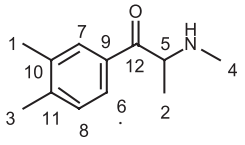
To assign the remaining methyl proton and the carbon chemical shifts, heteronuclear single quantum coherence spectroscopy (HSQC) and heteronuclear multiple bond correlation spectroscopy (HMBC) experiments were conducted and their correlations mapped (see additional information for the two-dimensional NMR spectra). From these correlations, the hydrogens and carbons could be assigned according to Tables 1 and 2.

TABLE 1—*$^1$H chemical shifts in 3,4-DMMC.*



| $^1$H Spectrum | | | |
|---|---|---|---|
| Peak No. | δ (ppm) | Profile | Integration |
| 1 | 1.28 | d | 3 |
| 2 | 2.32 | s | 3 |
| 3 | 2.32 | s | 3 |
| 4 | 2.35 | s | 3 |
| 5 | 4.19 | q | 1 |
| 6 | 7.23 | d | 1 |
| 7 | 7.70 | dd | 1 |
| 8 | 7.74 | d | 1 |

TABLE 2—*$^{13}$C chemical shifts in 3,4-DMMC.*



| $^{13}$C Spectrum | |
|---|---|
| Peak No. | δ (ppm) |
| 1 | 19.9 |
| 2 | 20.1 |
| 3 | 20.2 |
| 4 | 34.8 |
| 5 | 59.4 |
| 6 | 126.1 |
| 7 | 129.5 |
| 8 | 130.1 |
| 9 | 133.7 |
| 10 | 137.3 |
| 11 | 143.2 |
| 12 | 203.4 |

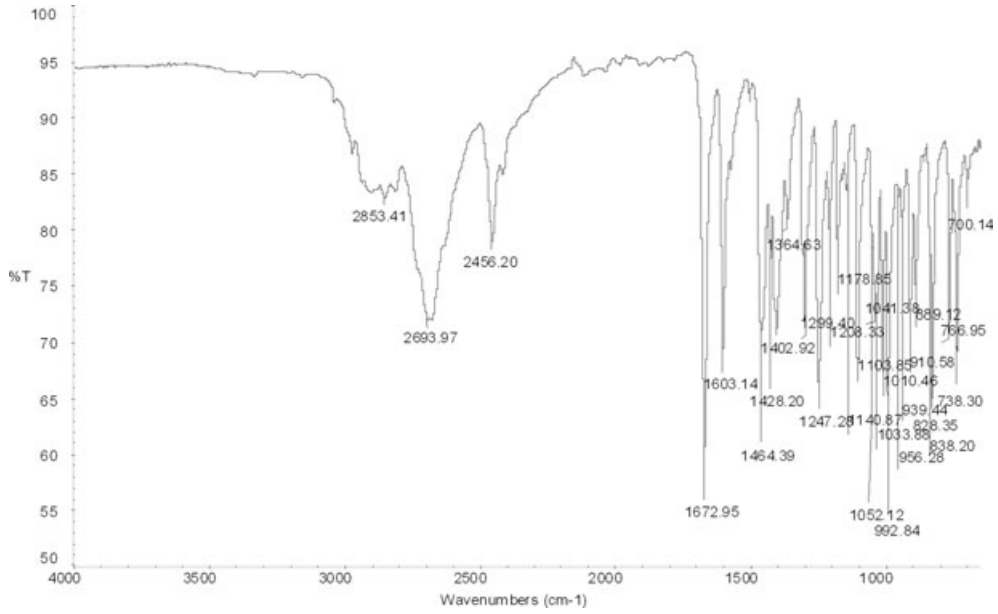



FIG. 4—*Infrared spectrum of 3,4-DMMC.*

Measuring the absorption of 3,4-DMMC in the UV region, a maximum was observed at 266 nm, which is bathochromically shifted by 16 nm in comparison with methcathinone but is virtually identical to mephedrone. Measuring the absorption spectrum at six different concentrations allowed us to calculate that 3,4-DMMC possesses a molar absorptivity ($\varepsilon$) of *c*.12 000 when taking into consideration that the cathinone derivative was in the hydrochloride salt form (evidenced by a $AgNO_3$ anion test on the sample).

The most recognized attributes in the IR spectrum (Fig. 4) of 3,4-DMMC are the NH+ cation stretch at 2456 /cm and the carbonyl stretch at 1672 /cm (20); however, the most characteristic aspect is the elaborate number of stretches observed between 700 and 1700 /cm, which is similar to mephedrone but very different from methcathinone (16,21).

*Acknowledgments*

The authors would like to thank Curtin University Chemistry Department for acquiring the NMR spectra and M. Davies and M. Hoare for the initial analysis of the sample.

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