4-Methoxyphencyclidine: An Analytical Profile

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ABSTRACT: The synthesis and characterization of 4-methoxyphencyclidine (commonly referred to as methoxydine) is discussed. Analytical data (mass spectrometry, infrared spectroscopy, and nuclear magnetic resonance spectroscopy) are presented.

KEYWORDS: 4-methoxyphencyclidine, 1-[1-(4-methoxyphenyl)cyclohexyl]piperidine, methoxydine, designer drug, synthesis, characterization, forensic chemistry

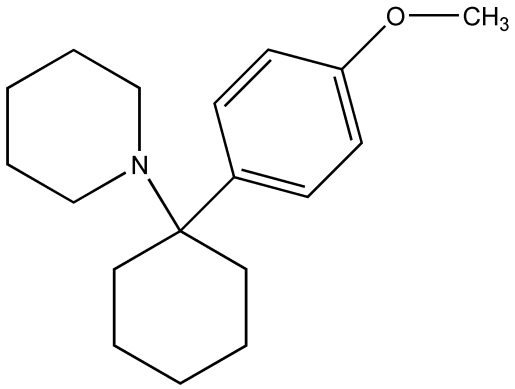

Figure 1 - Structural formula of 4-methoxyphencyclidine.

Internet companies are advertising the sale of large quantities (up to 2 kg) of 4-methoxyphencyclidine, commonly referred to as methoxydine, as a "*research chemical.*" It can be considered a derivative of phencyclidine (PCP) [1], having a *para*-substituted methoxy group on the aromatic ring. Although spectral data for 4-methoxyphencyclidine are available in the literature, unfortunately they are in tabular form [2]. Analytical (spectral) data is presented on its analytical profile to assist forensic chemists who may encounter this substance in casework.

Experimental

Chemicals, Reagents, and Materials

All solvents were distilled-in-glass products of Burdick and Jackson Labs (Muskegon, MI, USA). All other chemicals were of reagent-grade quality and products of Aldrich Chemical (Milwaukee, WI). The intermediate, 1-(piperidin-1-yl)-cyclohexane carbonitrile was part of an authentic reference collection maintained by the DEA Special Testing and Research Laboratory.

Synthesis

A solution of 4-bromoanisole in dry diethyl ether was reacted with magnesium turnings to form a Grignard reagent. A solution of 1-(piperidin-1-yl)cyclohexane carbonitrile in methylene chloride/diethyl ether (1:1) was slowly added to the Grignard with stirring. The reaction was quenched with ice and NH_4Cl, rendered basic with aqueous NaOH, and extracted with diethyl ether. The ether was acidified with methanolic HCl. The resulting hydrochloride crystals were captured via suction filtration and dried. The purity of the final product exceeded 99.0%. The synthetic procedure is outlined in Figure 2; the yield is not reported.

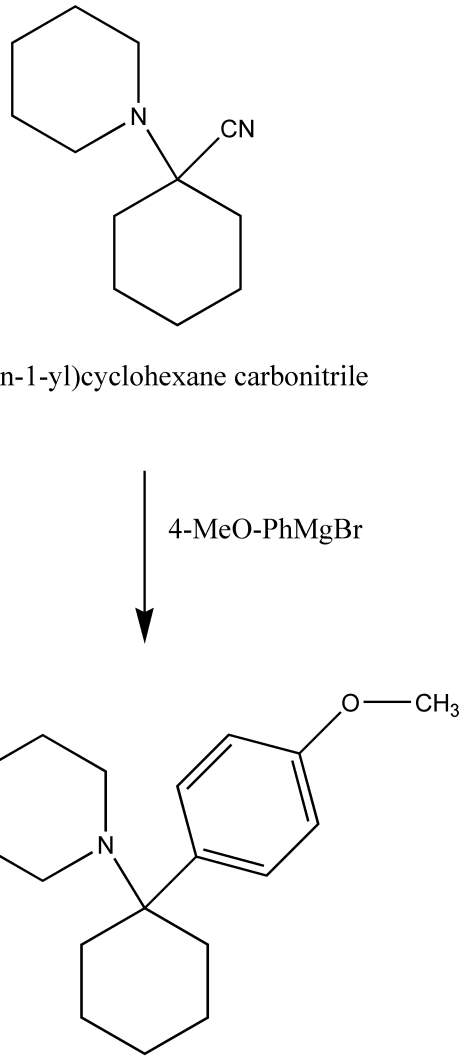

Figure 2 - Synthetic route for 4-methoxyphencyclidine.

Gas Chromatography/Mass Spectrometry (GC/MS)

Mass spectra were obtained on an Agilent Model 5975C quadrupole mass-selective detector (MSD) that was interfaced with an Agilent Model 7890A gas chromatograph (GC). The MSD was operated in the electron ionization (EI) mode with an ionization potential of 70 eV, a scan range of 34-600 amu, and at a scan rate of 2.59 scans/s. The GC was fitted with a 30 m x 0.25 mm ID fused-silica capillary column coated with 0.25 µm 100% dimethylpolysiloxane, DB-1 (J & W Scientific, Rancho Cordova, CA). The oven temperature was programmed as follows: initial temperature, 100°C; initial hold, 0.0 min; program rate, 6°C/min; final temperature, 300°C; final hold, 5.67 min. The injector was operated in the split mode (21.5:1) at 280°C. The MSD source was operated at 230°C.

Infrared Spectroscopy (FTIR)

Infrared spectra were obtained on a Thermo-Nicolet Nexus 670 FTIR equipped with a single bounce attenuated total reflectance (ATR) accessory. Instrument parameters: resolution = 4 cm^{-1}; gain = 8; optical velocity = 0.4747; aperture = 150; and scans/sample = 16.

Nuclear Magnetic Resonance Spectroscopy (NMR)

A proton (^1H) NMR spectrum was obtained on an Agilent VNMRS 600 MHz NMR using a 5 mm Protune broad band detection, variable temperature, pulse field gradient probe (Agilent, Palo Alto, CA). The product was dissolved in deuterochloroform ($CDCl_3$) containing 0.03% v/v tetramethylsilane (TMS) as the 0 ppm reference compound. The sample temperature was maintained at 26°C. A standard Agilent proton pulse sequence was used. Data processing was performed using software from Applied Chemistry Development (ACD/Labs, Toronto, Canada).

Results and Discussion

The FTIR spectrum of 4-methoxyphencyclidine HCl (Figure 3) displays absorbances (2000-2700 cm^{-1}) which are consistent with an amine halogen (HCl) ion-pair and significant aliphatic CH absorbance in the region of 2800-3000 cm^{-1}. The 500-1600 cm^{-1} region is peak (band) enriched for discriminative purposes. The ^1H-NMR spectrum (Figure 4) is distinguished from PCP, by the presence of the methoxy resonance at 3.85 ppm and the aromatic doublets at 7.0 and 7.4 ppm (indicating *para*-substitution of benzene). The mass spectrum of 4-methoxyphencyclidine (Figure 5) is fragment ion rich, with mass fragments of *m/z* 188 as the base peak and *m/z* 273 as the molecular ion. Analogous to PCP, an M-1 ion at *m/z* 272 is consistent with the loss of an *ortho* hydrogen from the aromatic ring and subsequent C-N bond formation, which retains the charge on the nitrogen [3].

Conclusions

Analytical data is presented to assist forensic laboratories that encounter 4-methoxyphencyclidine in case exhibits. The three presented spectral techniques each provide unequivocal characterization.

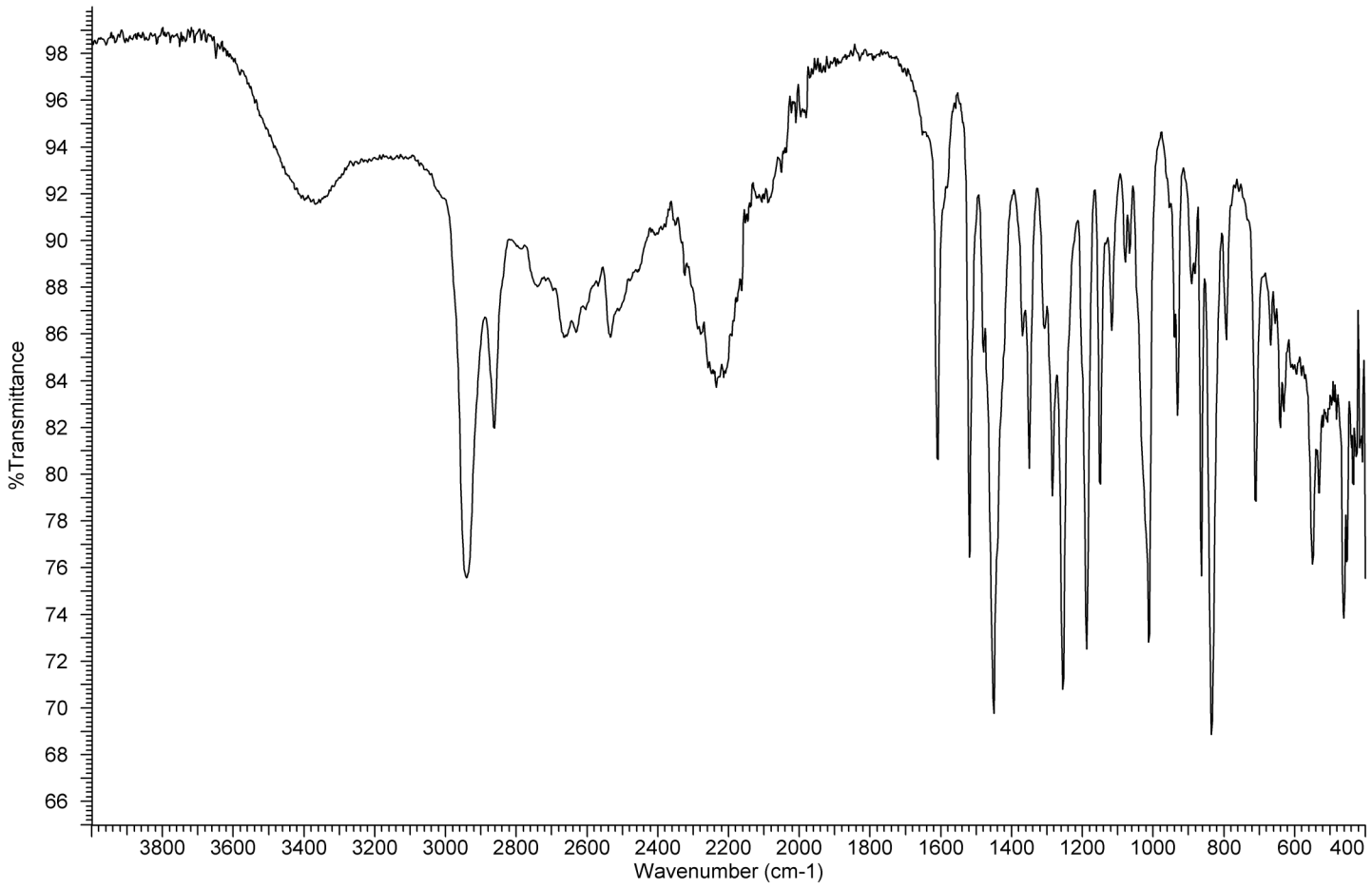

Figure 3 - Infrared spectrum (FTIR) of 4-methoxyphencyclidine HCl.

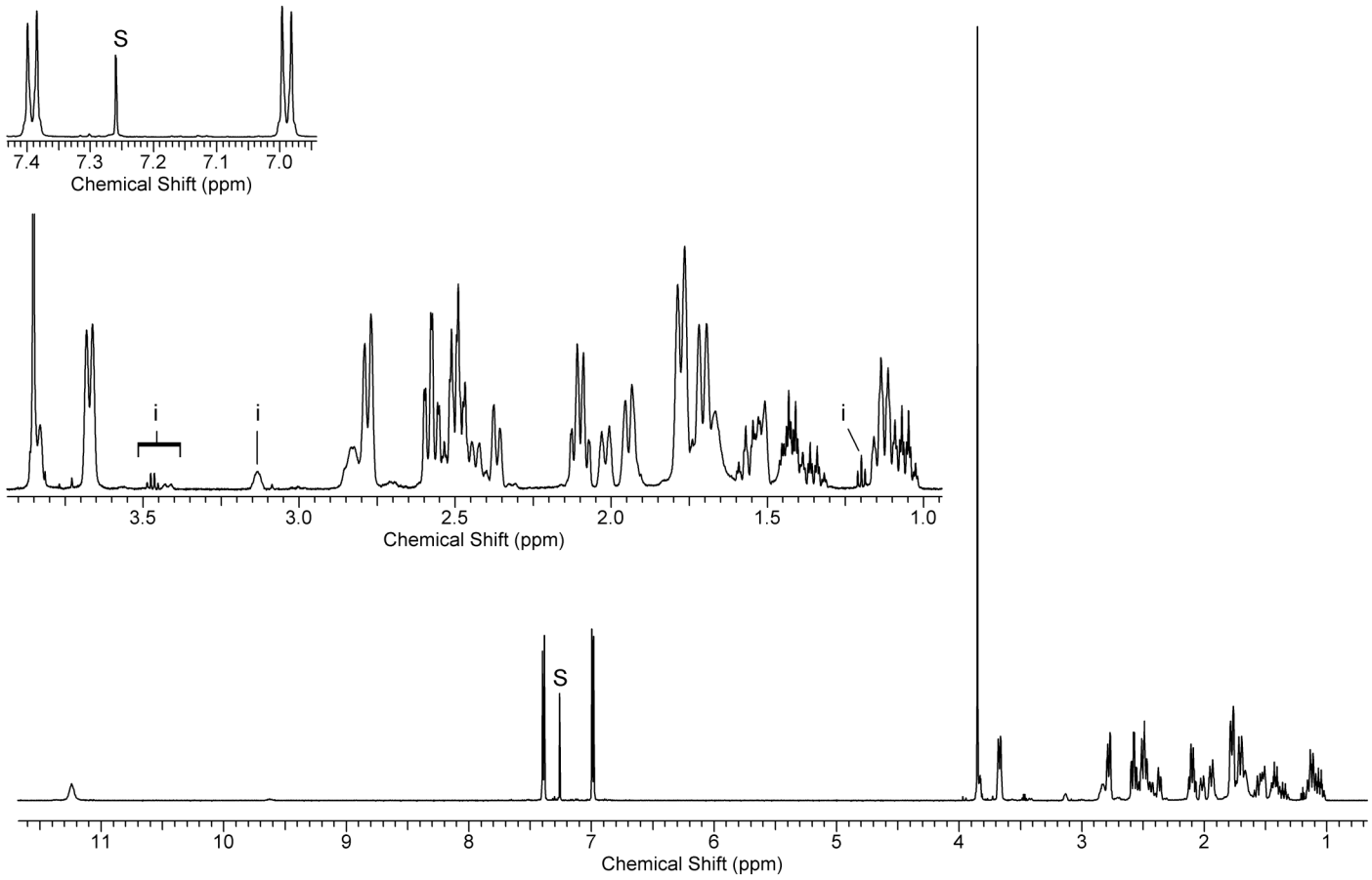

Figure 4 - Proton NMR spectrum of 4-methoxyphencyclidine HCl. S = trace $CHCl_3$ from $CDCl_3$, i = trace impurity.

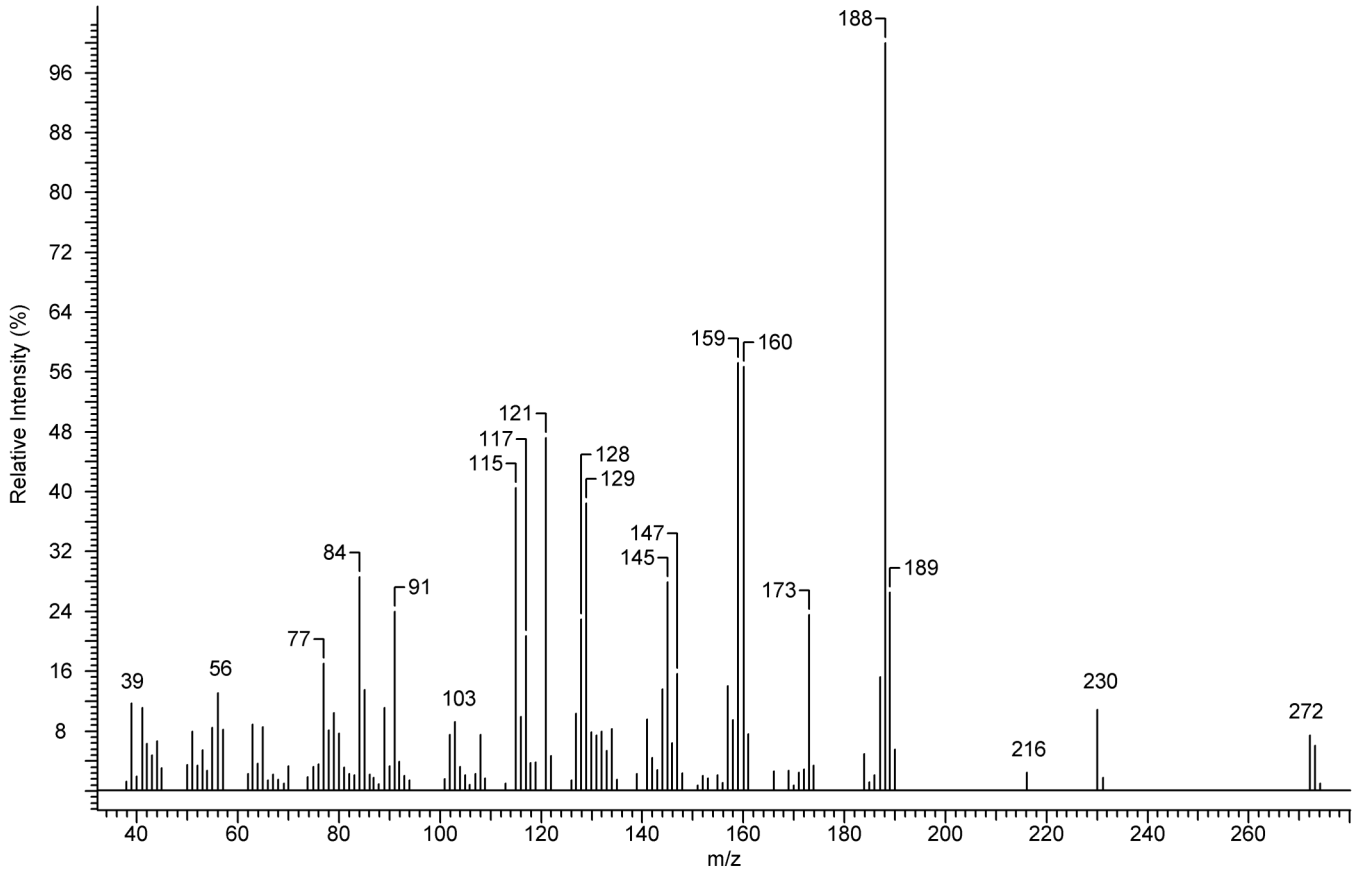

Figure 5 - Electron ionization mass spectrum of 4-methoxyphencyclidine.

References

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2. Costa JF, Speaker TJ. Chromatographic and spectral properties of some aryl-substituted phencyclidine analogs. Journal of Analytical Toxicology. 1983;7(5):252-6.
3. Smith RM. *Understanding Mass Spectra: A Basic Approach, 2nd ed*. John Wiley & Sons, Inc., Hoboken, NJ, 2004, p 278.