Solvent/Sample Interaction in the GC/MS Analysis of Amines

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Introduction

During a study of the fragmentation of aliphatic amines with an aromatic functionality attached to the amino carbon so that the amino carbon and the benzyl carbon were the same or separated by a single atom of carbon, it was found that the mass spectrum of 3,4-methylenedioxyphenethylamine (MDOPEA) in the NIST/EPA/NIH Mass Spectral Database, NIST08, exhibited no ion current below *m/z* 40 (Fig. 1, right). This resulted in the base peak being at *m/z* 136. The four mass spectra in the NIST08 DB for an analogous compound, phenethylamine (PEA), all exhibited peaks below *m/z* 30. Each of these four spectra had *m/z* 30 as the base peak (Fig. 1, left). Examination of all the mass spectra of amphetamine (structural analogues to PEA) and its MDOPEA analog (3,4-methylenedioxyamphetamine, a.k.a. MDA) showed the base peak in the mass spectra of both of these compounds to be at *m/z* 44 (Fig. 2).

Based on the comparison of the mass spectra of amphetamine and 3,4-methylenedioxy-amphetamine, it was hypothesized that the base peak in the mass spectrum of MDOPEA would be at *m/z* 30, as it was in the mass spectrum of PEA. A sample of the hydrochloride salt of MDOPEA was obtained and analyzed by GC/MS.

A 1.0 µL sample of MDOPEA at a concentration of 1 ng μL^{-1} in a methanol (MeOH) solution was injected in the splitless mode with an injection port temperature of 290 °C. To our surprise, the mass spectrum shown in Fig. 3 was obtained for a single RTIC chromatographic peak.

The only resemblance the spectrum in Fig. 3 had to the spectrum of MDOPEA in the NIST08 Database was that the most intense peaks were at *m/z* 135 and 136. A quick search of the scientific literature resulted in a publication by Clark, DeRuiter, and Noggle[1] reporting the formations of imines when samples of HCl salts of arylethylamine hydro-chlorides in MeOH and EtOH were analyzed by GC/MS. We have published the formation of these same types of compounds being formed from primary straight-chain aliphatic amines in dichloro methane (DCM) at room temperature.[2]

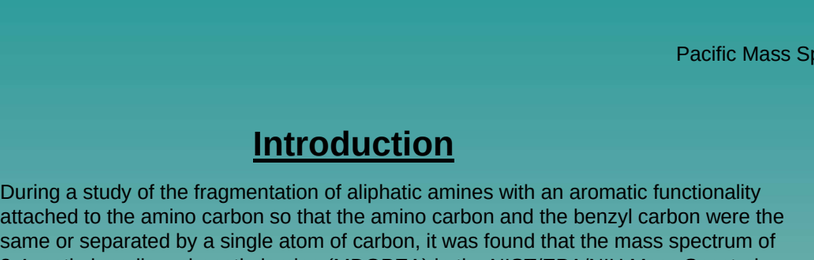

Figure 1. EI mass spectrum from NIST08 of phenethylamine (left) and 3,4-methylenedioxyphenethylamine (right).

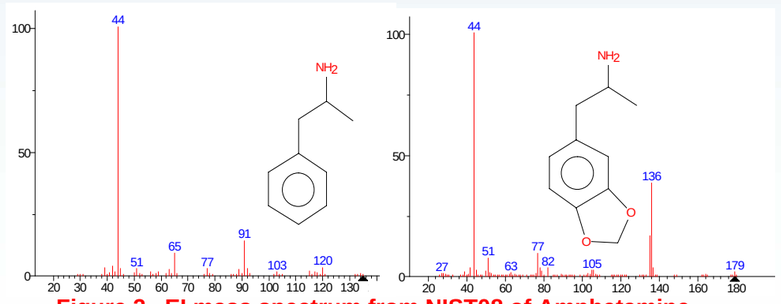

Figure 2. EI mass spectrum from NIST08 of Amphetamine (left) and 3,4-methylenedioxyamphetamine (right).

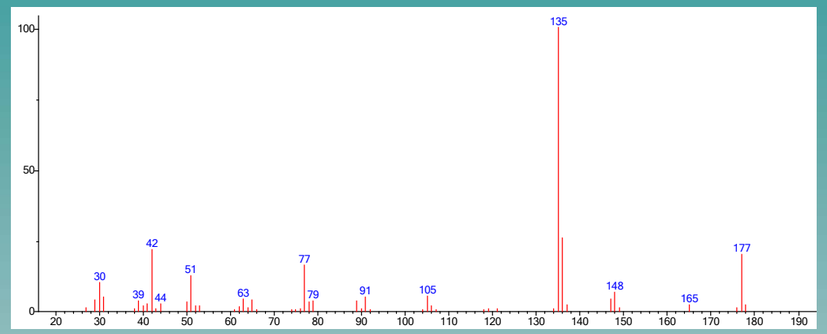

Figure 3. EI spectrum obtained from splitless injection of a 1 ng μL^{-1} sample of 3,4-methylenedioxyphenethylamine HCl in MeOH at 290 °C.

Although the work by Clark, et al. covered primary and secondary amines with aromatic moieties using both methanol and ethanol as solvents and verified that the spectra were not of cyclized tetrahydroisoquinoline, unfortunately it failed to provide information as to the type of injection (split or splitless), injection port temperature, or the concentration of the analyte. When we switched to a split injection using a split ratio of 100:1 of 1.0 µL of a 1 µg μL^{-1} soln., a more expected spectrum was obtained (Fig. 4), and no chromatographic peak appeared for the compound whose mass spectrum is shown in Fig. 3.

Based on the comparison of spectra of amphetamine and MDA with that of PEA, it would have been predicted that the mass spectrum of MDOPEA would have exhibited a base peak at *m/z* 30. As can readily be seen from Fig. 4, this was not the case. The base peak was at *m/z* 135, and the intensity of the peak at *m/z* 30 was about 30% of that of the base peak.

A 1.0 µL splitless injection of 10 ng μL^{-1} solution of PEA in MeOH yielded the RTIC peak with the spectrum shown in Fig. 5 in addition to an earlier-eluting RTIC peak representing the PEA . It should be noted that like the mass spectrum of PEA (Fig. 1), the mass spectrum of the imine artifact has a low intensity $M^{+\bullet}$ peak; however, unlike the mass spectrum of PEA, the mass spectrum of the imine exhibits a strong $[M - H]^+$ peak, which is what was observed in the mass spectra of imine artifacts formed at R.T. by aliphatic amines in DCM solution (spectrum not shown).[2]

The base peak of the spectrum of the PEA imine artifact representing the $H_2C{=}N^+{=}CH_2$ ion was shifted by 12 *m/z* units to *m/z* 42 from that of PEA; finding the corresponding peak in the spectrum of the MDOPEA imine artifact is more of a challenge. The intensity of the *m/z* 42 peak in this spectrum is far less than might be predicted.

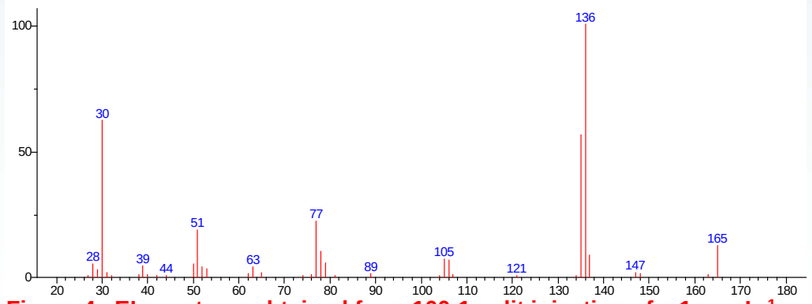

Figure 4. EI spectrum obtained from 100:1 split injection of a 1 µg μL^{-1} sample of 3,4-methylenedioxyphenethylamine HCl in MeOH at 290 °C.

The mass spectrum of an imine artifact formed from a splitless injection of 1.0 µL of a 10 ng μL^{-1} soln. of PEA in MeOH at 290 °C was identical to that reported by Clark, et al. The experiment was repeated using both PEA and MDOPEA (HCl salt and free base) in EtOH, IPA, *n*PrOH, and sec-BuOH, and *n*-BuOH. The splitless injection always produced the corresponding imine artifact over a temperature range of 185 to 290 °C. The spectra were analogues to those resulting from the MeOH solutions for both PEA and MDOPEA. The imine artifacts of these two compounds did not produce analogous spectra as did amphetamine and MDA in the Clark, et al. paper. No artifact was observed in the data resulting from the injection of the free base in an *iso*-octane solution or when much higher concentration solutions in the tested alcohols were made using a split injection with a high split ratio.

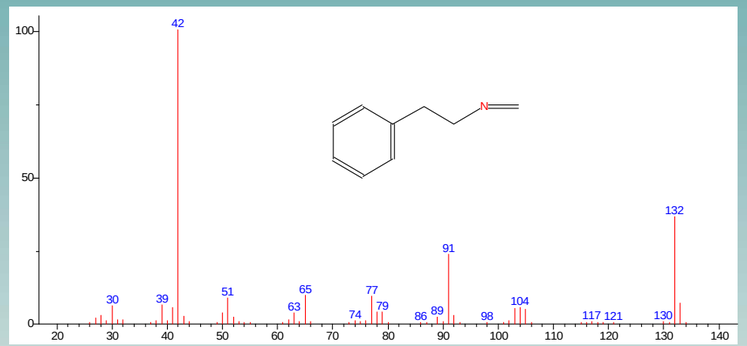

Figure 5. EI spectrum obtained from splitless injection of a 10 ng μL^{-1} sample of phenethylamine HCl in MeOH at 290 °C.

Experimental

All GC/MS analyses were carried out using an Agilent Model 7890A GC interfaced to a Model 5975 Inert XL MSD EI mass spectrometer using a 30-m x 250-µM i.d. column with a 0.25-µm film thickness of XE-52 (SGE, Austin, TX). The GC was fitted with the Agilent split/splitless injector. The mass spectrometer was tuned using the Standard Spectrum Tune provided by Agilent for use with PFTBA. Data analyses were carried out using GC/GCMS ChemStation software Version E.02.00493, the NIST MS Search Program along with the NIST/EPA/NIH Database NIST08. Elemental composition of various ions were determined by acquiring mass spectral data in the Raw Spectrum (Profile) mode (10 recorded measurements for each *m/z* value) and using the *Cerno Bioscience* ***MassWorks*** software for accurate mass analysis. Data acquisition was carried out over a range of *m/z* 20 to *m/z* 300 at a rate of 2.6 spec sec^{-1} (2^3 samples). A threshold of 150 was used for centroided data and 0 for profile data. Different temperature program ramps and injection port temperatures were used. Helium mobile phase at a linear velocity of 25 cm sec^{-1} was used for all experiments. Spectra of PFTBA were acquired over a range of *m/z* 20 to *m/z* 625 @ ~1 spec sec^{-1}, daily, to verify performance.

Conclusion

Two important results came out of this study. First, based on the differences in the mass spectra of PEA and MDOPEA, analogous structures don't necessarily produce analogous EI mass spectra. Additional work is necessary to explain the differences in these spectra. Second, it appears that solvent interactions must be considered when performing splitless injections. This is especially important in looking at substance purity. What may appear to be an impurity may be a solvent reaction artifact occurring in the GC injection port.

References

1 Clark, C. Randall; DeRuiter, Jack; Noggle, FT "GC_MS Identification of Amine-Solvent Condensation Products Formed During Analysis of Drugs of Abuse" *J. Chrmatog. Sci.*, **1992**, *30*, 399–404.
2 Sparkman, OD; Curtis, M; Jones, PR "Interaction of Dichloromethane Solvent with *n*-Alkylamines Analyzed by Electron Ionization GC/MS" *Current Trends in Mass Spectrometry* March 2010, Supplement to *Spectroscopy* and *LCGC* 8–14.