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GC-MS and GC-IRD studies on brominated dimethoxyamphetamines: Regioisomers related to 4-Br-2,5-DMA (DOB)

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A series of regioisomeric bromodimethoxyamphetamines have mass spectra essentially equivalent to the controlled drug substance 4-Br-2,5-dimethoxyamphetamine (4-Br-2,5-DMA; DOB); all have molecular weight of 274 and major fragment ions in their electron ionization mass spectra at *m/z* 44 and *m/z* 230/232. The trifluoroacetyl, pentafluoropropionyl and heptafluorobutyryl derivatives of the primary regioisomeric amines were prepared and evaluated in gas chromatography–mass spectrometry (GC-MS) studies. The mass spectra for these derivatives did not show unique fragment ions for specific identification of individual isomers. However, the mass spectra do serve to divide the compounds into three groups, depending on their base peak. Gas chromatography with infrared detection (GC-IRD) provides direct confirmatory data for the identification of the designer drug 4-bromo-2,5-dimethoxyamphetamine from the other regioisomers involved in the study. The perfluoroacylated derivatives of the six regioisomeric bromodimethoxyamphetamines were successfully resolved on non-polar stationary phases such as a 100% dimethylpolysiloxane stationary phase (Rtx-1) and 50% phenyl – 50% methyl polysiloxane (Rxi-50). Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: Br-DMA; brominated dimethoxyamphetamines; regioisomers; GC-MS; GC-IRD; perfluoroacylation

Introduction

Amphetamine derivatives with ring-substituted electron-donating groups such as 4-bromo-2,5-dimethoxyamphetamine (DOB) are serotonin $5HT_2$ receptor agonists and have psychoactive properties reportedly inducing hallucinations even in small doses.[1,2] Studies on structure–activity relationships have revealed that the hallucinogen-like activity is attributed to the primary phenethylamine structure augmented by the presence of methoxy groups in positions 2 and 5, and a hydrophobic 4-substituent, especially a halogen atom.[3] The methyl group alpha to the nitrogen is responsible for increased *in vivo* potency and duration of action compared to unbranched phenethylamines, the so-called 2Cs such as 4-bromo-2,5-dimethoxyphenethylamine (2 C-B).[2]

The most likely method for the synthesis of DOB is via nitroalkane condensation with 2,5-dimethoxybenzaldehyde followed by hydride reduction and ring bromination. All six regioisomeric dimethoxybenzaldehydes are commercially available and uncontrolled, thus any of the six (or more) monobrominated dimethoxyamphetamines can be prepared by the same synthetic methodology[4] from readily available precursors. The psychoactive properties of the 4-bromo-2,5-dimethoxyamphetamine isomer were first described by Shulgin *et al*. in 1971.[5] The pharmacological effects for the other regioisomers have not been extensively described. Thus, analytical differentiation among the brominated derivatives of the six regioisomeric dimethoxyamphetamines is an important issue in forensic drug chemistry. A compilation of literature reports covering the various regioisomeric forms of bromodimethoxyamphetamines has been published recently.[6]

Amphetamines and related designer drugs have been successfully analyzed for clinical and forensic application by a number of techniques.[3,4,7–12] In general, regioisomeric and isobaric substances are considered a significant challenge for the analytical techniques used to identify specific substances. The regioisomer issue is extremely important when some of these molecules are legally controlled drugs or controlled precursor substances.[13–15] This study is concerned with the differentiation of the monobrominated products resulting from the six possible regioisomeric dimethoxyamphetamines. Such compounds have mass spectral equivalency and similar chromatographic elution properties. Those substances co-eluting in the chromatographic system and having common mass spectra could be misidentified. The ability to distinguish between these regioisomers directly enhances the specificity of the analysis for the target molecules.

Previous studies[13,15,16] have shown that chemical derivatization methods (primarily acylation) can be used to add analytical specificity to the analysis of regioisomeric primary and secondary amines of varying side-chain structure. Derivatization can alter major fragmentation pathways often providing additional structural information about an individual isomer as well as altered chromatographic properties.[13,15,16] However, amine acylation is less successful for the

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identification of regioisomeric ring-substitution patterns and not useful for tertiary amines that do not form stable acylation products.

Infrared spectroscopy is a useful confirmation method in the forensic analysis of organic drug compounds. The GC-IR techniques produce a spectrum by rapidly scanning the peaks eluting from the capillary columns. Thus, the technique combines the separation power of capillary GC with the identification power of IR. GC-IR has been successfully applied to the confirmation of drug identification in forensic drug chemistry.[17,18] Previous studies on the differentiation of some ring- and side-chain-substituted regioisomeric phenethylamines related to the drug of abuse 3, 4-MDMA have made use of this method.[18,19] Additionally, the regioisomeric 2, 3, and 4-trifluoromethylphenylpiperazines have been differentiated by GC-IR.[20]

Analytical differentiation of the regioisomeric monobrominated dimethoxyamphetamines (Compounds 1–6, Figure 1) is a significant issue in forensic drug chemistry since all these isomers are not reported to be psychoactive drugs. The aim of this study is to evaluate analytical methods using GC-MS and GC-IRD to characterize and differentiate among this set of ring regioisomeric compounds.

Experimental

Instrumentation

GC-MS analysis was performed using an Agilent Technologies (Santa Clara, CA, USA) 7890A gas chromatograph and an Agilent 7683B auto injector coupled with a 5975 C VL Agilent mass selective detector. The mass spectral scan rate was 2.86 scans /s. The GC was operated in splitless mode with a helium (grade 5) flow rate of 0.7 ml/min and the column head pressure was 10 psi. The MS was operated in the electron impact (EI) mode using an ionization voltage of 70 eV and a source of temperature of 230 °C. The GC injector was maintained at 250 °C and the transfer line at 280 °C.

GC-MS chromatographic separation was carried out on two different stationary phases; a column (30 m × 0.25 mm i.d.) coated with 0.25 μm 100% dimethyl polysiloxane (Rtx-1) and a column (30 m × 0.25 mm i.d.) coated with 0.50 μm 50% phenyl – 50% methyl polysiloxane (Rxi-50). Both columns were purchased from Restek Corporation (Bellefonte, PA, USA). The separation was performed using a temperature programme consisting of an initial hold at 100 °C for 1.0 min, ramped up to 180 °C at a rate of 9 °C/min, held at 180 °C for 2.0 min then ramped to 200 °C at a rate of 10 °C/min and held at 200 °C for 10.0 min.

GC-IRD studies were carried out on a Hewlett-Packard 5890 Series II gas chromatograph and a Hewlett-Packard 7673 auto-injector coupled with an IRD-II infrared detector obtained from Analytical Solutions and Providers, Covington, Kentucky. The vapor phase infrared detector (IRD) spectra were recorded in the range of 4000–550 cm^{-1} with a resolution of 8 cm^{-1} and a scan rate 1.5 scans per second. The IRD flow cell temperature as well as the transfer line was 280 °C and the GC was operated in the splitless mode with a carrier gas (helium grade 5) flow rate of 0.7 mL/min and a column head pressure of 10 psi. The column used was (Rxi-50). The temperature programme involved in this study consisted of an initial temperature of 70 °C for 1 min, ramped up to 250 °C at a rate of 30 °C/min followed by a hold at 250 °C for 20 min.

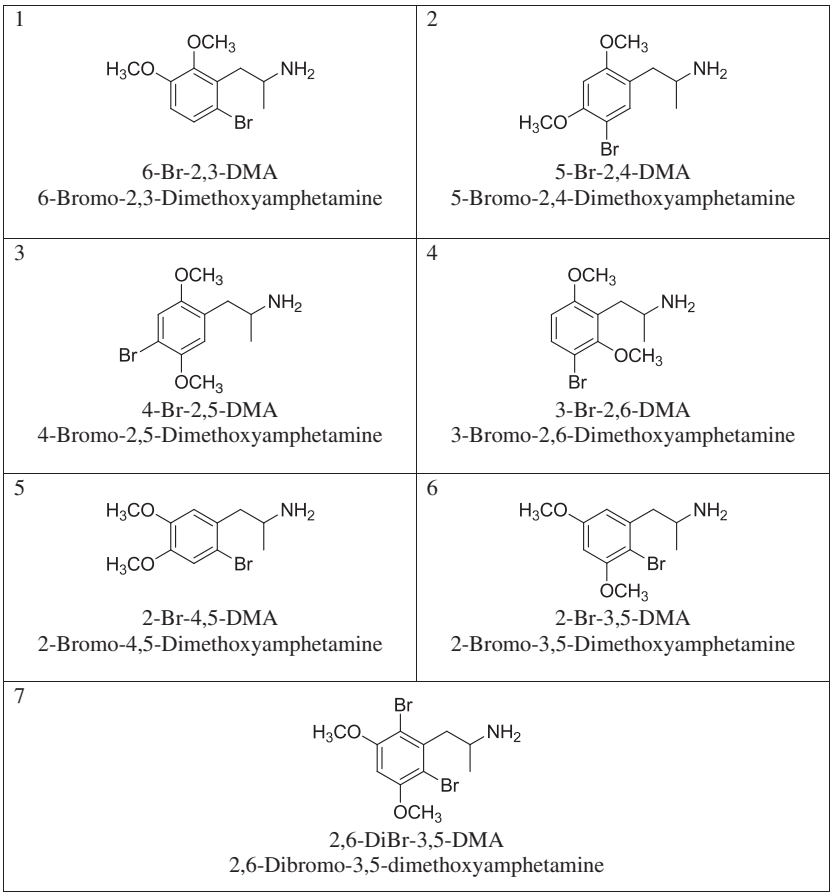

Figure 1. Structures of the brominated dimethoxyamphetamines in this study.

In both GC-MS and GC-IRD analyses, samples were dissolved and diluted in high performance liquid chromatography-grade acetonitrile (Fisher Scientific, Fairlawn, NJ, USA) and introduced via the auto injector using an injection volume of 1 μl.

Drugs and reagents

The six regioisomeric monobrominated dimethoxyamphetamines (Br-DMA), (Figure 1), used in this study were synthesized in our lab. The six regioisomeric dimethoxyamphetamines were prepared by the same general procedure using the appropriately substituted dimethoxybenzaldehyde. The benzaldehyde was treated with butylamine and nitroethane to yield the nitropropene intermediate. Upon reduction with LAH, the phenethylamine was obtained in high yield. Bromination of the amine hydrochloride produced the corresponding Br-DMA. The structures of all products were confirmed by standard spectroscopic techniques (NMR, IR and MS).[4]

All laboratory reagents and chemicals were obtained from Aldrich Chemical Co. (Milwaukee, WI, USA) or Fisher Scientific (Atlanta, GA, USA). The derivatizing agents trifluoroacetic anhydride, pentafluoropropionic anhydride and heptafluorobutyric anhydride were purchased from Sigma-Aldrich, Inc (Milwaukee, WI, USA).

Derivatization procedure

Each perfluoroamide was prepared individually from each of the six regioisomers by dissolving approximately 0.3 mg (1.09×10^{-6} mol) of each amine in 50 μl of ethyl acetate, followed by addition of a large excess (250 μl) of the appropriate derivatizing agent and the derivatization reaction mixtures were incubated in capped tubes at 70°C for 20 min. Following incubation, each sample was evaporated to dryness under a stream of air at 55 °C and reconstituted with 200 μl of ethyl acetate and 50 μl of pyridine. A portion of each final solution (50 μl) was diluted with HPLC grade acetonitrile (200 μl) to give the working solutions.

Results and discussion

Synthesis of brominated dimethoxyamphetamines

The desired compounds in this study were prepared via bromination of the six individual dimethoxyamphetamines; the structures are shown in Figure 1. The position of bromination is dependent on the pattern of the methoxy group substitutions and typically occurs at only one of the three available ring positions.[4] This reaction proceeds via an electrophilic mechanism, and thus substitution occurs preferentially at ring carbons that are in direct conjugation with the electron-donating methoxy group (the 'ortho' or 'para' positions). In cases involving multiple ring carbons in conjugation, bromination usually occurs at the least sterically hindered site.[4] In each case, only one product was obtained except for 3,5-DMA which gave a mixture of 2-bromo and 2,6-dibromosubstitution products (Structures 6 and 7 in Figure 1, respectively). In this case, the dibromination product predominated, even when minimal amounts of bromine were used in the reaction.[4] The determination of the position of

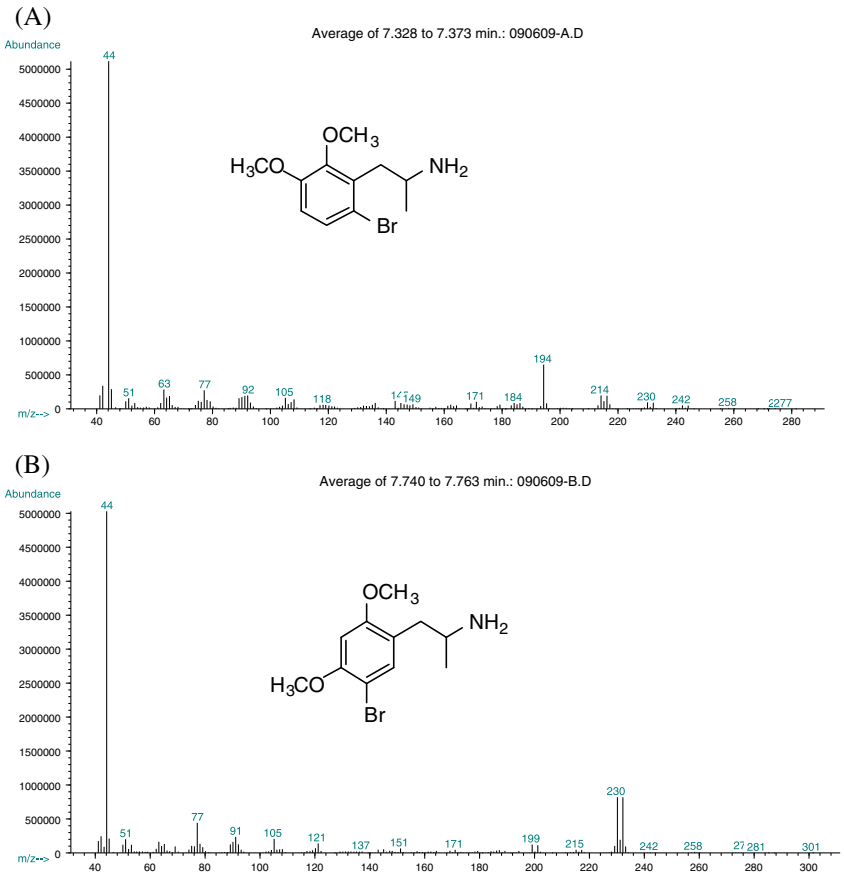

Figure 2. Mass spectra for representative brominated dimethoxyamphetamines. (A) 6-bromo-2,3-dimethoxyamphetamine; (B) 5-bromo-2, 4-dimethoxyamphetamine.

bromine substitution for each of the dimethoxyamphetamines has been described previously.[4]

Mass spectral studies

Mass spectrometry (MS) is the primary method for confirming the identity of drugs in forensic samples. Figure 2 shows the EI mass spectra for two selected examples of the regioisomeric bromodimethoxyamphetamines. These mass spectra indicate that very little structural information is available for differentiation among these isomers since all the major fragment ions occur at equal masses. The mass spectra of all six of the underivatized Br-DMAs were described in a previous report from our lab.[4] Most of these compounds showed only trace amounts of molecular ions; however, bromination of the individual dimethoxyamphetamines was obvious from the abundant fragment ions containing bromine. The mass spectra of the six regioisomers (molecular weight = 273/275) are characterized by the immonium ion base peak (*m/z* 44) and the bromodimethoxybenzyl radical cation at mass 230/232. The loss of the entire alkylamine side-chain yields the substituted benzene carbocation at *m/z* 215/217 and the *m/z* 199/201 ion is likely the loss of CH_2O from the brominated dimethoxybenzyl cation at *m/z* 229/231. The loss of bromine from the molecular ion was observed for those compounds in which the position of the bromine substitution is 'ortho' to the alkylamine side-chain. This ion at *m/z* 194 is present in the mass spectra of bromo-2,3-; 3,5- and 3,4-dimethoxyamphetamines. Thus, the $(M\text{-}Br)^+$ ion at *m/z* 194 can differentiate the 'ortho' brominated positional isomers from the 'non-ortho' brominated isomers. However, no significant fragments are present to individualize a particular isomer within each group. This lack of mass spectral specificity for the individual regioisomers in addition to the possibility of chromatographic co-elution could result in misidentification of individual isomers among this series of compounds. Thus, MS alone does not provide confirmation of identity for a particular isomer (i.e. 4-Br-2,5-DMA) to the exclusion of all other possibilities in this series of Br-DMAs.

The acylated derivatives of the regioisomeric Br-DMA were evaluated in an effort to individualize their mass spectra and identify marker ions that would allow discrimination among these isomeric compounds. Acylation lowers the basicity of nitrogen and can allow other fragmentation pathways to play a more prominent role in the resulting mass spectrum.[13,15,16] The trifluoroacetyl (TFA), pentafluoropropionyl (PFPA), and heptafluorobutryl (HFBA) derivatives were evaluated for their ability to individualize the mass spectrum of 4-Br-2,5-DMA to the exclusion of the other five regioisomeric compounds. The mass spectra for the six PFPA amides are shown in Figure 3 and these spectra are representative of all the amides evaluated in this study. From these spectra, a common peak occurs at *m/z* 190 which corresponds to the loss of 229/231 mass units from the molecular ions at 419/421 for the PFPA derivatives. The ions at *m/z* 190 are the PFPA immonium ion species, likely formed from the α-cleavage of the amide nitrogen to eliminate the corresponding bromodimethoxybenzyl radical. Thus, these fragments at *m/z* 190 are analogous to *m/z* 44 in the underivatized species because all these ions represent the

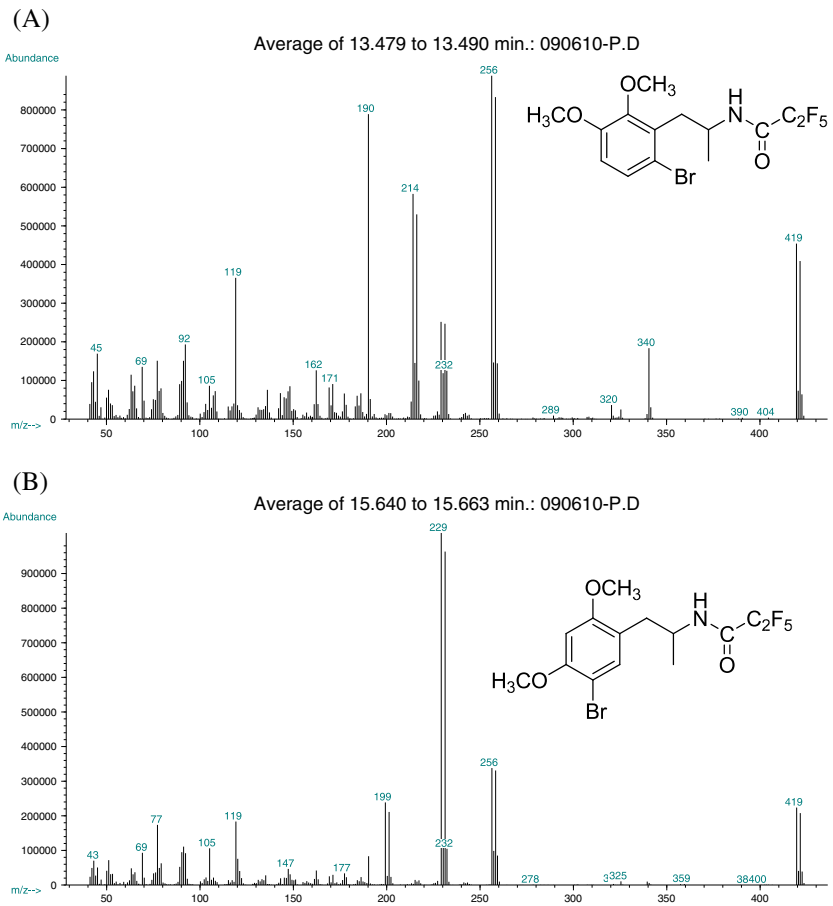

Figure 3. Mass Spectra of the PFPA derivatives of the regioisomeric brominated dimethoxyamphetamines (Compounds 1–7).

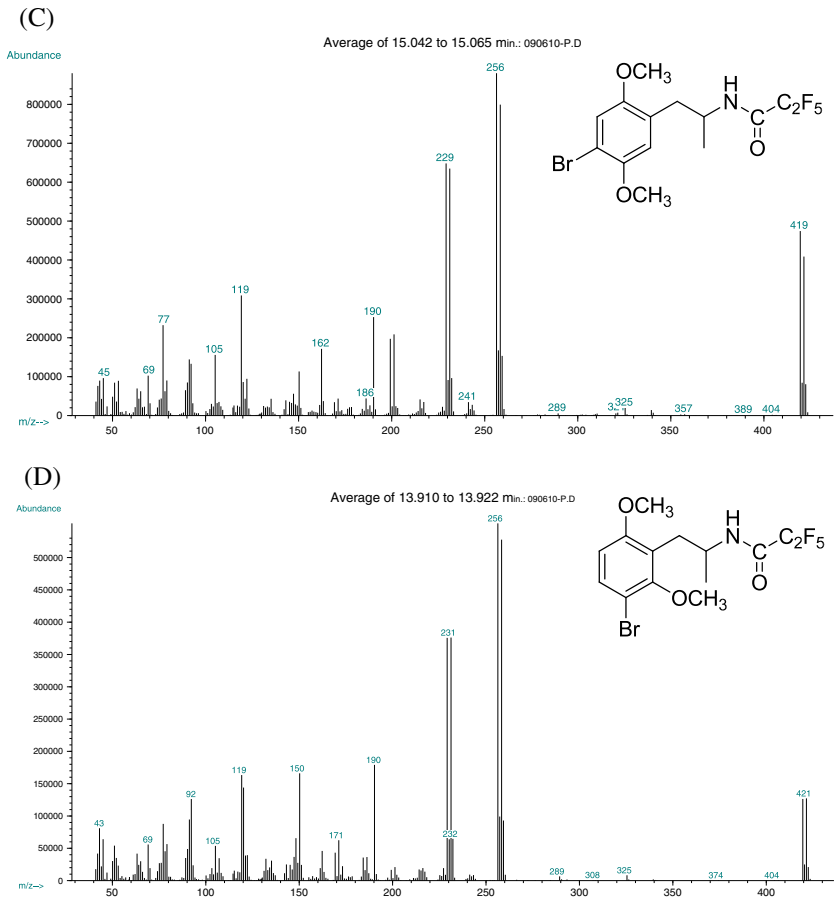

Figure 3. Continued

$(M–229/231)^+$ species. The bromodimethoxybenzyl cations (*m/z* 229/231) are also major fragments in the spectra of some of the isomeric amides. The structures for these ions are shown in Figure 4 and the analogous ions occur in the spectra of the TFA and HFBA derivatives.

The decreased role for the α-cleavage fragmentation process in these amides allows the formation of ions more diagnostic of each individual isomer. Acylation, and in particular perfluoroacylation, weakens the bond between nitrogen and the α-carbon of the substituted phenethyl group, allowing the formation of charged hydrocarbon species of increased relative abundance. The alkene fragment observed at *m/z* 256/258 occurs in the spectra of all the TFA, PFPA, and HFBA derivatives, indicating that the perfluoroacyl moiety is not a component of these ions. These alkene fragments which are the bromodimethoxyphenylpropene radical cations result from cleavage of the bond between nitrogen and the alkyl carbon of the hydrocarbon side chain. This bond cleavage occurs following an initial hydrogen rearrangement likely from the benzylic carbon to the carbonyl oxygen (Figure 4).

An important fragmentation pathway, which is characteristic of the ortho-methoxy regioisomers is described in Figure 5. Those bromodimethoxyamphetamines with the methoxy group in the ortho position relative to the side chain are characterized by a significant fragment at *m/z* 199/201 ion. This ion likely arises from the loss of mass 30 (CH_2O) from the initial bromodimethoxybenzylic cation at *m/z* 229/232. The *m/z* 199/201 ion is a significant fragment only when the methoxy-group is ortho to the alkyl side chain and therefore the site of initial benzylic cation formation. This *m/z* 199/201 ion can be formed by migration of hydrogen from the methoxy group to the benzyl carbocation followed by loss of formaldehyde (Figure 5). This fragment occurs in all spectra of TFA, PFPA, and HFBA for ortho methoxy Br-DMAs. The suggested mechanism for the loss of CH_2O from the ortho-methoxy benzyl cations was previously described.[14]

A major fragment at *m/z* 214/216 occurs in the mass spectra of all three perfluoroacyl derivatives of 6-Br-2,3-DMA. This fragment corresponding to $C_8H_8O_2Br$ and represents the loss of the propyl side chain from the previously described alkene radical cation at *m/z* 256/258. This ion can arise by hydrogen migration from the methoxy group to the benzylic carbon radical site followed by loss of propene. The proposed mechanism for this fragmentation process is shown in Figure 6.

The TFA, PFPA, and HFBA derivatives of all six regioisomeric amines show essentially equivalent fragments with only relative abundance differences. However, these six regioisomers could be divided into three groups with respect to the base peak. The first group consisting of 6-Br-2,3-, 4-Br-2,5- and 3-Br-2, 6-DMA shows the alkene radical cation at *m/z* 256/258 as the base peak. The second group includes 5-Br-2,4- and 2-Br-4, 5- DMA and these compounds show the benzyl cation fragment at *m/z* 229/231 as the base peak. The third group of compounds which includes 2-Br- and 2,6-DiBr-3,5-DMA shows the immonium ion fragment resulting from an α-cleavage reaction as the base peak. This occurs at *m/z* 140, 190 and 240 for the TFA, PFPA, and HFBA derivatives, respectively.

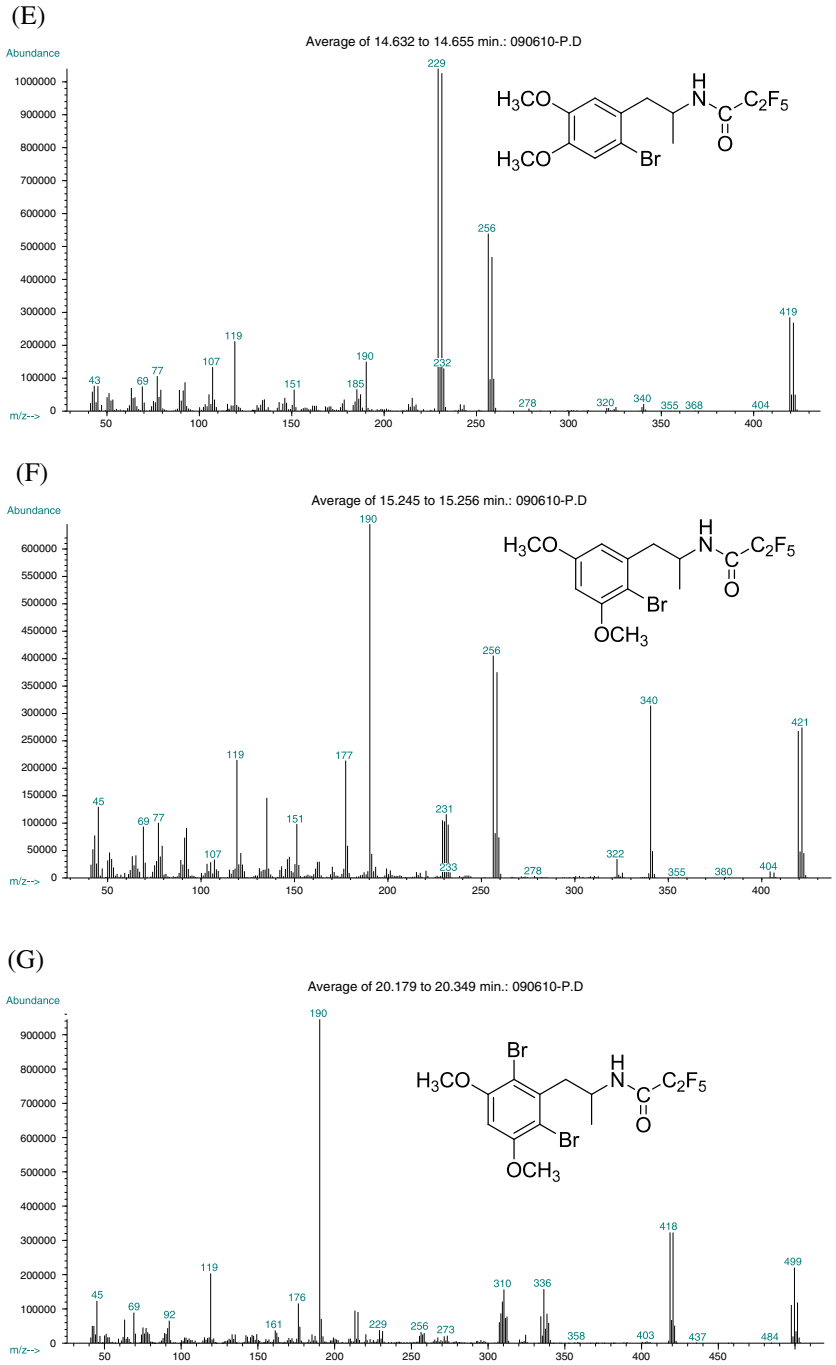

Figure 3. Continued

Vapor-phase infrared spectrophotometry

IRS is often used as a confirmatory method for drug identification in forensic drug analysis. GC-IRD was evaluated for differentiation between 4-Br-2,5-DMA and its ring regioisomers. The vapor-phase IRS could provide compound specificity without the need for chemical modification of the parent molecule. The vapor-phase IRS for the six studied compounds are shown in Figure 7. These spectra were generated in the vapor-phase following sample injection into the gas chromatograph and each compound shows absorption bands in the regions 700–1700 cm^{-1} and 2700–3100 cm^{-1}. Variations in the side-chain composition results in differences in the IR spectrum in both regions [18–20] while changes in the aromatic ring substitution results in unique IR bands in the region 700–1700 cm^{-1}. Thus, these six Br-DMA ring regioisomers could be readily distinguished from each other through differences in their IR spectra in the region 700–1700 cm^{-1}.

The MS of these compounds, even after acylation, does not provide characteristic fragments (except for *m/z* 214 in case of 6-Br-2,3-DMA) for the differentiation of these isomers from one another. However, the mass spectra for the acylated derivatives divide these compounds into three groups depending on their base peak. GC-IRD provides critical information to complete the individual identification of these ring regioisomers. Among

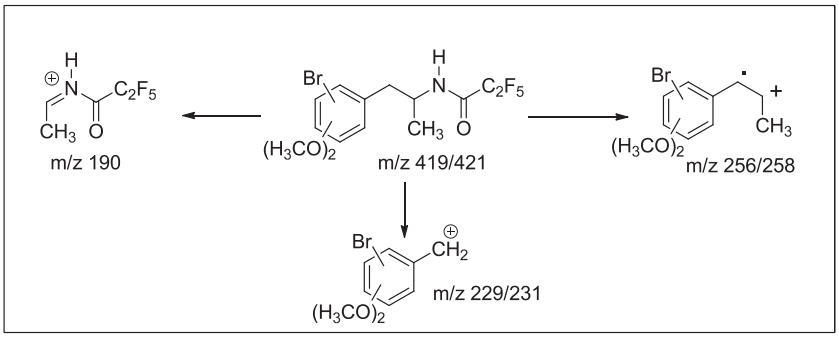

Figure 4. Proposed structures for major mass spectral fragment ions for the perfluoroacyl derivatives of the regioisomeric bromodimethoxyamphetamines.

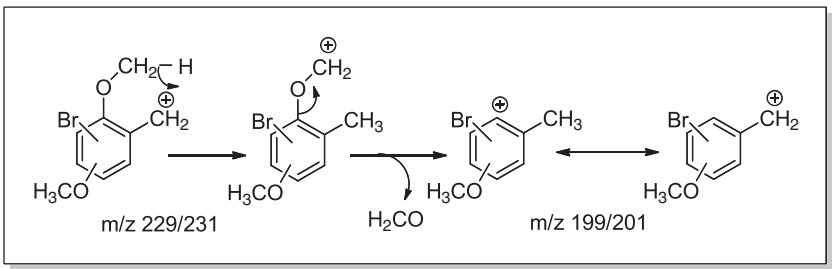

Figure 5. Mechanism for the formation of the *m/z* 199/201 ions in the spectrum of the perfluoroacyl derivatives of the 2-methoxy regioisomers of the studied compounds.

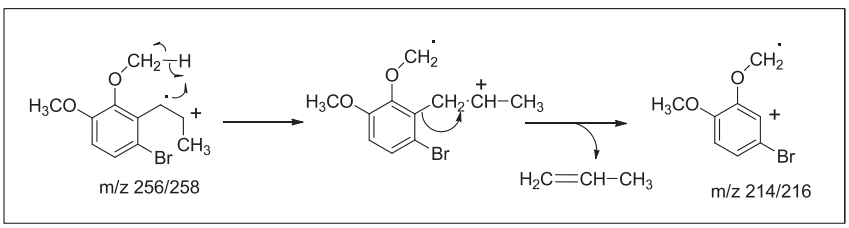

Figure 6. Mechanism for the formation of the *m/z* 214/216 ions in the spectrum of the perfluoroacyl derivatives of the 6-Br-2,3-DMA.

members of the first group; 6-Br-2,3-, 4-Br-2,5- and 3-Br-2,6-DMA which shows the base peak at *m/z* 256, at least five IR absorption bands of different intensities can be used to differentiate among these three isomers. The first is the two adjacent peaks appearing at 1019 and 1084 cm^{-1} in the IR spectrum of 6-Br-2,3-DMA, of which the first is a strong absorption band. These peaks are converted into a singlet peak at 1038 cm^{-1} in case of 4-Br-2,5-DMA. The second is the two adjacent peaks appearing at 1223 and 1273 cm^{-1} in case of 6-Br-2,3-DMA, of which the latter is a strong absorption band. These peaks appear as a singlet at 1212 cm^{-1} in case of 4-Br-2,5-DMA. 3-Br-2,6-DMA is characterized by having a multiplet peak in the region 1020-1275 cm^{-1}. The third is the sharp absorption peak at 1381 cm^{-1} which is unique to 4-Br-2, 5-DMA since it is missing in the other two regioisomers. The fourth is the three adjacent bands appearing in the IR spectrum of 6-Br-2,3-DMA at 1408, 1439, and 1466 cm^{-1}, of which the latter is a strong absorption band. These bands appear as two adjacent bands at 1447 and 1489 cm^{-1} for 4-Br-2,5-DMA or at 1405 and 1462 cm^{-1} for 3-Br-2,6-DMA. The fifth is the sharp absorption band of intermediate intensity at about 1575 cm^{-1} which is characteristic to 3-Br-2,6-DMA since it is of much lower intensity in the other two isomers.

The second group consisting of 5-Br-2,4- and 2-Br-4,5- DMA have a base peak at *m/z* 229 for the PFPA acylated derivative and several IR bands can be used to differentiate between these two compounds. The first is the absorption band at 1034 cm^{-1} in the IR spectrum of 5-Br-2,4-DMA which is shifted to 1026 cm^{-1} for 2-Br-4,5-DMA. Then the doublet peak in the IR spectrum of 5-Br-2, 4-DMA appearing at 1158 and 1206 cm^{-1} which is characteristic to this particular isomer. The singlet peak at 1297 cm^{-1} is also unique to this isomer. The 2-Br-4,5-DMA isomer is characterized by a triplet absorption peak at 1158, 1215 and 1273 cm^{-1}. However, these two isomers (5-Br-2,4- and 2-Br-4,5- DMA) show a common singlet peak at about 1378 cm^{-1} and two adjacent peaks at nearly 1443 and 1493 cm^{-1}.

The third group of compounds characterized by a m/z 190 base peak for the PFPA derivative (2-Br-3,5-DMA and 2,6-DiBr-3, 5-DMA) show several unique IR bands to differentiate the two compounds. The first is that the two adjacent bands appearing in the IR spectrum of 2-Br-3,5-DMA at 1023 and 1080 cm^{-1} are shifted to 1053 and 1088 cm^{-1} for 2,6-DiBr-3,5-DMA. Then the doublet peak appearing in the IR spectrum of 2-Br-3,5-DMA at 1158 and 1204 cm^{-1} which is converted into a singlet at about 1208 cm^{-1} for 2,6-DiBr-3,5-DMA. The third is the singlet peak at about 1327 cm^{-1}

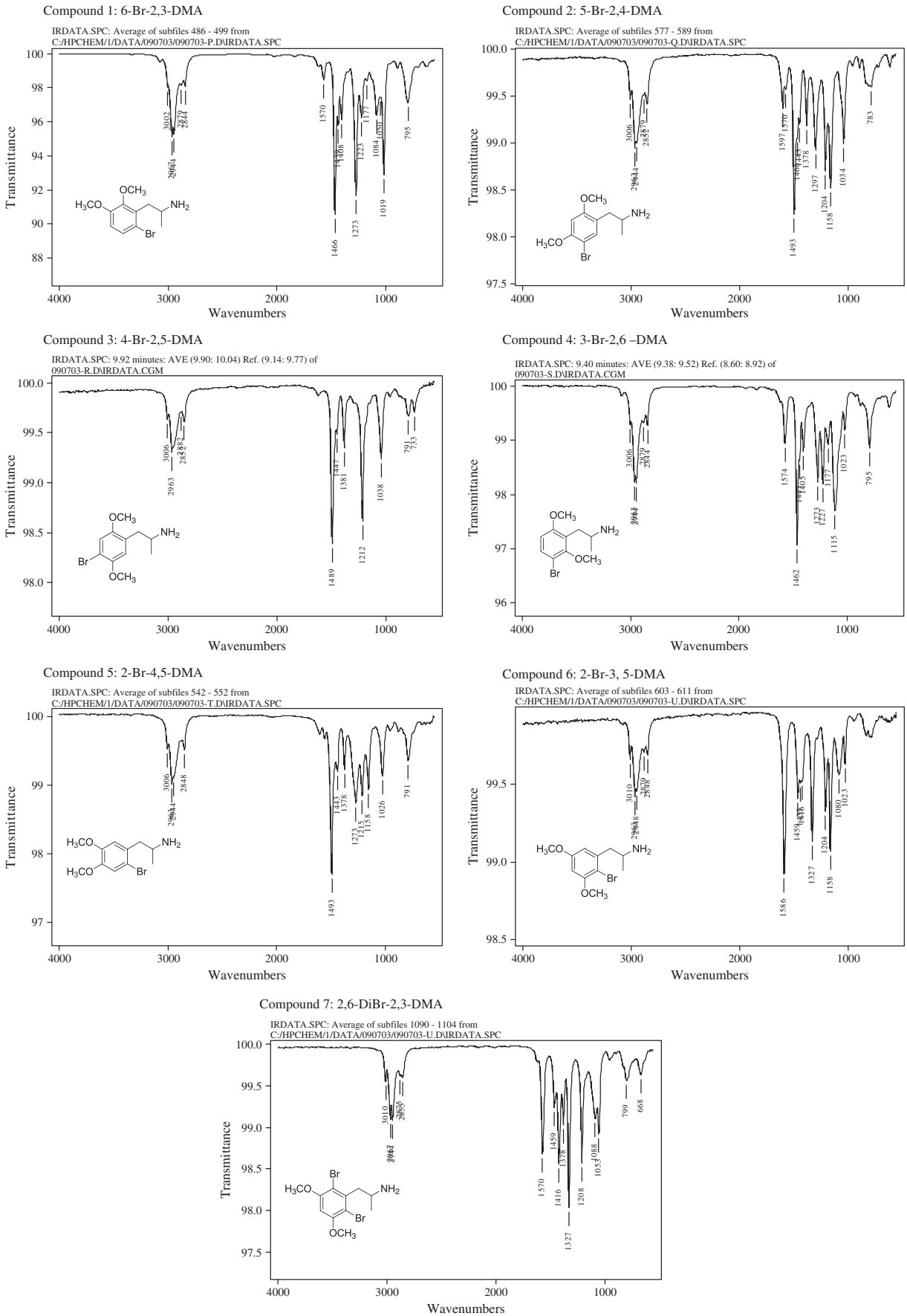

Figure 7. Vapor phase IR spectra of the regioisomeric brominated dimethoxy-amphetamines (Compounds 1–7).

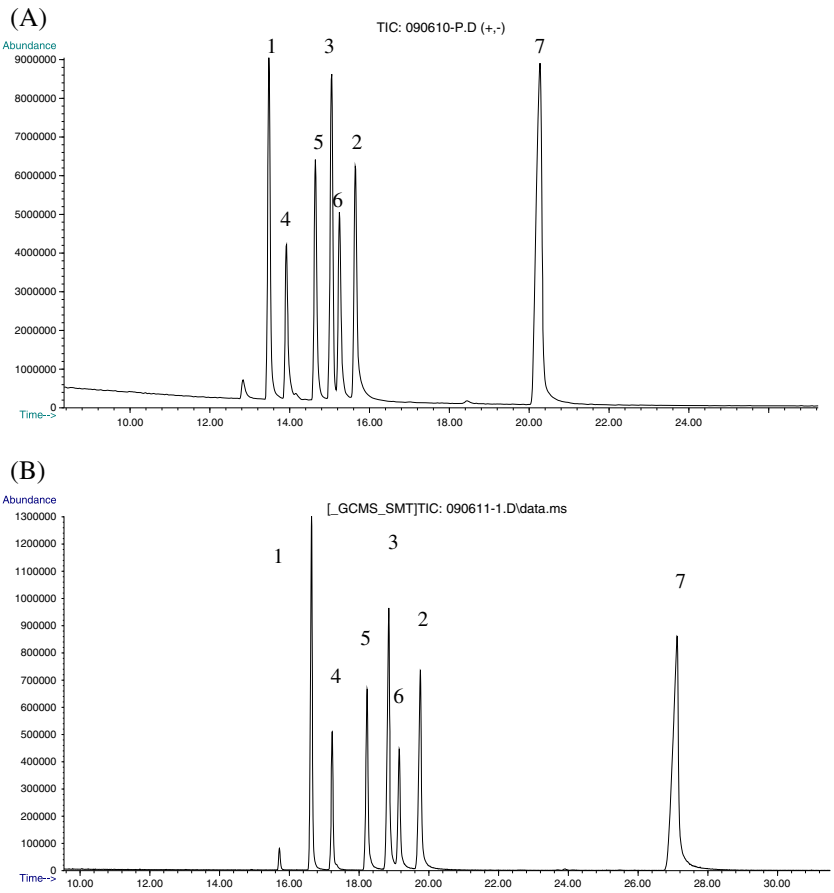

Figure 8. Gas chromatographic separation of PFPA derivatives of the regioisomeric brominated dimethoxyamphetamines (Compounds 1–7). (A) Rxi-50 and (B) Rtx-1 column.

which is characteristic to 2-Br-3,5-DMA and the fourth is the two adjacent peaks at about 1434 and 1459 cm^{-1} which are present only in the 2-Br-3,5-DMA. The fifth is the sharp absorption band at 1586 cm^{-1} in the IR spectrum of 2-Br-3,5-DMA which is shifted to 1570 cm^{-1} for 2,6-Dibromo-3,5-DMA. Additionally, 2,6-DiBr-3,5-DMA is characterized by a multiplet peak in the region 1327–1459 cm^{-1} which differentiates this compound from the monobrominated 2-Br-3,5-DMA.

These studies indicate that vapor phase infrared spectra provide useful data for confirmation and differentiation among these regioisomeric amines of mass spectral equivalence. IR absorption bands provide distinguishing and characteristic information to individualize the amines in this set of uniquely similar compounds which cannot be obtained from their MS spectra even after derivatization.

Gas chromatography

The GC properties of the TFA, PFPA, and HFBA derivatives of the ring regioisomeric bromodimethoxyamphetamines were compared on two stationary phases of similar column dimensions (30 m × 0.25 mm). The stationary phases compared in this study were the relatively non-polar phases, 100% dimethyl polysiloxane (Rtx-1) and 50% phenyl–50% methyl polysiloxane (Rxi-50). Several temperature programmes were evaluated and representative chromatograms for the PFPA derivatives are shown in Figure 8. For all three sets of derivatives, 6-Br-2,3-DMA elutes first followed by 3-Br-2,6-DMA, 2-Br-4,5-DMA, 4-Br-2,5-DMA, 2-Br-3,5-DMA and then 5-Br-2,4-DMA which is the last eluting monobrominated compound. As expected the 2,6-DiBr-3,5-DMA elutes after all the monobrominated regioisomers. A direct comparison of Rtx-1 and Rxi-50 phases showed increasing retention on the less polar Rtx-1 phase (Figure 8B) using an identical temperature programme. This is the same for all three types of derivatives; TFA, PFPA and HFBA. Thus, GC separation studies of the perfluoroacyl derivatives of the regioisomeric Br-DMAs showed satisfactory resolution on both types of stationary phase involved in this study.

Conclusion

Differentiation of the controlled 4-Br-2,5-DMA from the five positional ring methoxy isomers of monobrominated dimethoxyamphetamines was evaluated using a combination of gas chromatography and mass or infrared spectrometry. All six compounds have the same nominal mass and produce similar EI mass spectra under common chromatographic conditions. Thus, the traditional electron impact mass spectrum provides little structural information for differentiating among these compounds. Because of the unique similarity of these compounds by MS, the specific GC-MS identification of a compound such as 4-Br-2,5-DMA requires the use of reference standards of each of the other amines in order to confirm their chromatographic resolution.

Derivatization of the amines with perfluoroacylating agents served to divide the compounds into three groups depending

on their base peaks. However, GC-IRD studies provided additional discrimination and allowed for the specific identification of each isomer. The perfluoroacyl derivatives of the studied compounds were successfully resolved on two different stationary phases.

Acknowledgement

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