Research Article

Rapid Communications in Mass Spectrometry

Received: 12 July 2013 Revised: 20 August 2013 Accepted: 21 August 2013 Published online in Wiley Online Library

*Rapid Commun. Mass Spectrom.* **2013**, *27*, 2551–2558
(wileyonlinelibrary.com) DOI: 10.1002/rcm.6716

# Gas chromatography/mass spectrometry analysis of the six-ring regioisomeric dimethoxybenzyl-*N*-methylpiperazines (DMBMPs)

**Karim M. Abdel-Hay[1,2], Jack DeRuiter[1] and C. Randall Clark[1]***

[1]Department of Pharmacal Sciences, Harrison School of Pharmacy, Auburn University, Auburn, AL 36849, USA
[2]Dept. of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Alexandria University, Alexandria, 21521, Egypt

**RATIONALE:** Piperazine-based designer drugs represent a novel class of substances found in illicit drug samples in the US and abroad. The clandestine production of these substances often makes use of piperazine as a key commercially available precursor substance. The commercial availability of 1-methylpiperazine suggests additional designer modification based on this additional precursor material.
**METHODS:** This study focuses on the electron ionization mass spectrometric (EI-MS) fragmentation of the dimethoxybenzyl-*N*-methylpiperazines as potential designer modifications of the general benzylpiperazine drug skeleton and explores the gas chromatography (GC)/MS properties of all six of these regioisomeric substances.
**RESULTS:** Fragmentation of the bond between the benzylic carbon and the adjacent piperazine nitrogen provides the base peak in all six spectra. The internal fragmentation within the piperazine ring produces a number of unique ions in the mass spectra of these dimethoxybenzyl-N-methylpiperazines. The migration of methyl groups from nitrogen and oxygen were confirmed by deuterium-labeling experiments.
**CONCLUSIONS:** The six regioisomeric dimethoxybenzyl-*N*-methylpiperazines yield equivalent fragment ions and deuterium labeling confirmed the elemental composition of the characteristic fragments in their mass spectra. Mixtures of the dimethoxybenzyl-*N*-methylpiperazines were successfully resolved via capillary gas chromatography using a relatively polar stationary phase and temperature-programming conditions. 

A number of synthetic piperazine compounds have appeared in illicit drug samples in the US and abroad in recent years and these compounds represent a novel class of designer drugs. The most common piperazines encountered in clandestine drug samples to date include benzylpiperazine (BZP), *m*-chlorophenylpiperazine (mCPP) and 1-(3-trifluoromethylphenyl)piperazine (TFMPP) and these compounds appear to be obtained from commercial sources.[1] These drugs are often found in combination and the most common product combination appears to be BZP with TFMPP,[2] sometimes mixed with other illicit drugs such as amphetamine, cocaine, ketamine and MDMA.[3,4] BZP produces stimulant effects similar to d-amphetamine although only one-tenth as potent. The phenylpiperazines such as TFMPP appear to produce their effects by interacting with serotonergic receptors, and their affinity and selectivity for these receptors are dependent on the nature and position of the aromatic substituents.[5–7] Both BZP and TFMPP were placed in Schedule 1 of the United States Controlled Substance Act in 2002, and have been controlled in other countries as well. With this heightened control it is anticipated that clandestine chemists will continue to explore the development of designer derivatives to obtain novel psychoactive piperazines that are not specifically controlled by existing regulation. This phenomenon has been observed in the phenethylamine-type drugs of abuse including amphetamine,[8] MDMA,[9] bath salts[10] and other clandestine drug series,[11] where legislative control has stimulated the development of numerous designer drug derivatives.

Structural modifications of drugs of abuse are well known for the phenethylamines or amphetamine-derived designer drugs. The most common variations are the introduction of a methylenedioxy or dimethoxy moiety into the aromatic ring of amphetamine leading to 3,4-methylenedioxyamphetamine (MDA) or 2,5-dimethoxyamphetamine (2,5-DMA), respectively. Structural modifications similar to those found in the phenethylamines have already been encountered in the piperazine compounds. Recently, 1-(3,4-methylenedioxybenzyl)piperazine (3,4-MDBP) – the methylenedioxy analogue of *N*-benzylpiperazine (BZP) – has been reported in clandestine samples. This compound has been described as producing psychoactive effects similar to those of 3,4-methylenedioxymethamphetamine (MDMA).[5–7] Furthermore, a clandestine sample of 4-bromo-2,5-dimethoxybenzylpiperazine (a dimethoxybenzylpiperazine derivative) was seized in Germany in 2006.[12] It is likely that additional designer derivatives in this series will appear, and probably include methoxy and dimethoxy ring substituted analogues since this substitution pattern has yielded enhanced psychoactive substances in other drug classes. Additionally, the starting materials for the clandestine synthesis of such designer analogues are readily available and include dimethoxybenzaldehydes, piperazine and 1-methylpiperazine. This could result in the production of a number of novel regioisomeric drugs of abuse (Fig. 1).

* *Correspondence to*: C. R. Clark, Department of Pharmacal Sciences, Harrison School of Pharmacy, Auburn University, Auburn, AL 36849, USA.
E-mail: clarkcr@auburn.edu

 

Gas chromatography/mass spectrometry (GC/MS) is the most widely used technique in the analysis of controlled substances in forensic laboratories. However, the identification of psychoactive drugs in a number of structural categories by this method is complicated by the possibility of regioisomeric substances.[8–11] Many regioisomeric and isobaric substances yield essentially identical mass spectral fragments in addition to equivalent molecular weights. Previous studies[13,14] have shown that chemical derivatization methods (primarily acylation) can be applied to solve these analytical challenges for primary and secondary amines. However, in some cases, derivatization does not yield any additional characteristic mass spectral fragments.[15] Thus, identification of structurally related substances such as regioisomers remains a challenge to forensic analyses that depend heavily on mass spectrometry for confirmation level data. The commercial availability of many regioisomeric forms of the synthetic precursor chemicals makes differentiation of potential regioisomeric forms of designer substances a critical issue in forensic drug chemistry.

This study focuses on the EI-MS fragmentation of the dimethoxybenzyl-*N*-methylpiperazines as potential designer modifications of the general BZP drug skeleton and explores the GC/MS properties of these regioisomeric substances. All six precursor dimethoxybenzaldehydes are commercially available as well as *N*-methylpiperazine. The structures for the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines in this study are shown in Fig. 1.

## EXPERIMENTAL

### Instrumentation

GC/MS analysis was performed using a model 7890A gas chromatograph and a model 7683B auto injector coupled with a 5975C VL mass-selective detector (all from Agilent Technologies, Santa Clara, CA, USA). The mass spectral scan rate was 2.86 scans/s. The GC instrument 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 mass spectrometer was operated in the EI mode using an ionization voltage of 70 eV and a source temperature of 230°C. The GC injector was maintained at 250°C and the transfer line at 280°C.

GC/MS chromatographic separations were carried out on a column (30 m × 0.25 mm i.d.) coated with 0.5 µm 100% trifluoropropyl methyl polysiloxane (Rtx-200; Restek Corporation, Bellefonte, PA, USA). The separations were performed using a temperature program 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 5.0 min.

The GC/time-of-flight (TOF) analysis was carried out at the Mass Spectrometry Center, Auburn University. The analysis utilized a 6890N gas chromatograph with a 7683B auto injector purchased (Agilent Technologies, Santa Clara, CA, USA) coupled to a Waters GCT Premier benchtop orthogonal acceleration time-of-flight (oa-TOF) mass spectrometer.

Chromatographic separation was carried out using a DB5-MS capillary column (30 m × 0.25 mm i.d., coated with a stationary phase film thickness of 0.50 µm; J&W Scientific). The temperature program consisted of an initial temperature of 70°C for 1 min, ramped up to 250°C at a rate of 15°C/min followed by a hold at 250°C for 7 min. The identification was confirmed by elemental composition analysis using accurate mass measurement with an internal calibrant (lockmass 118.9919 *m/z*, heptacosafluorotributylamine, Sigma) with an acceptable error of less than 5 ppm and by isotope modeling comparing the experimental and theoretical isotope distribution.

### Drugs and reagents

The general procedure for the synthesis of these six regioisomeric dimethoxybenzyl-*N*-methylpiperazines begins with the appropriate aldehyde, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethoxybenzaldehyde, as starting materials. All six of these precursor aldehydes were obtained from Aldrich Chemical Co. (Milwaukee, WI, USA). The desired regioisomeric dimethoxybenzyl-*N*-methylpiperazines were synthesized by stirring a solution of the appropriate aldehyde in methanol with *N*-methylpiperazine and sodium cyanoborohydride. Isolation of the basic fraction gave the dimethoxybenzyl-*N*-methylpiperazines, which were converted into the corresponding hydrochloride salts using gaseous HCl. All laboratory reagents and chemicals were obtained from Aldrich Chemical Co. (Milwaukee, WI, USA) or Fisher Scientific (Atlanta, GA, USA).

## RESULTS AND DISCUSSION

The structures for the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines are shown in Fig. 1. All six of the corresponding dimethoxybenzaldehyde presursors, as well as *N*-methylpiperazine, are commercially available materials and a one-step reductive amination process yields the desired compounds for this study. The selectivity of the reagent sodium cyanoborohydride allows for the reduction of the imine intermediate formed between the aldehyde and the

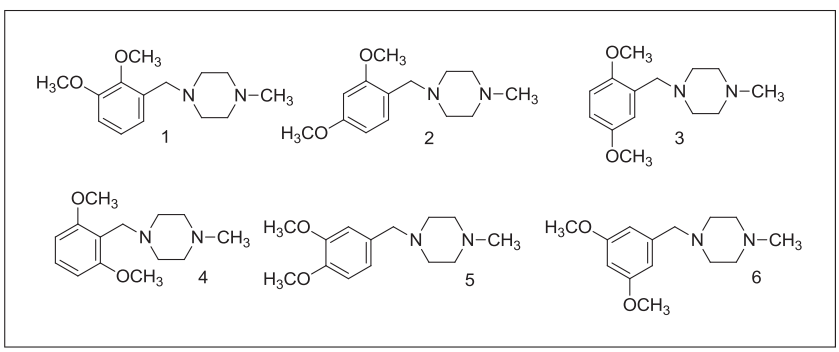


**Figure 1.** Structures for the dimethoxybenzyl-*N*-methylpiperazines studied.

  

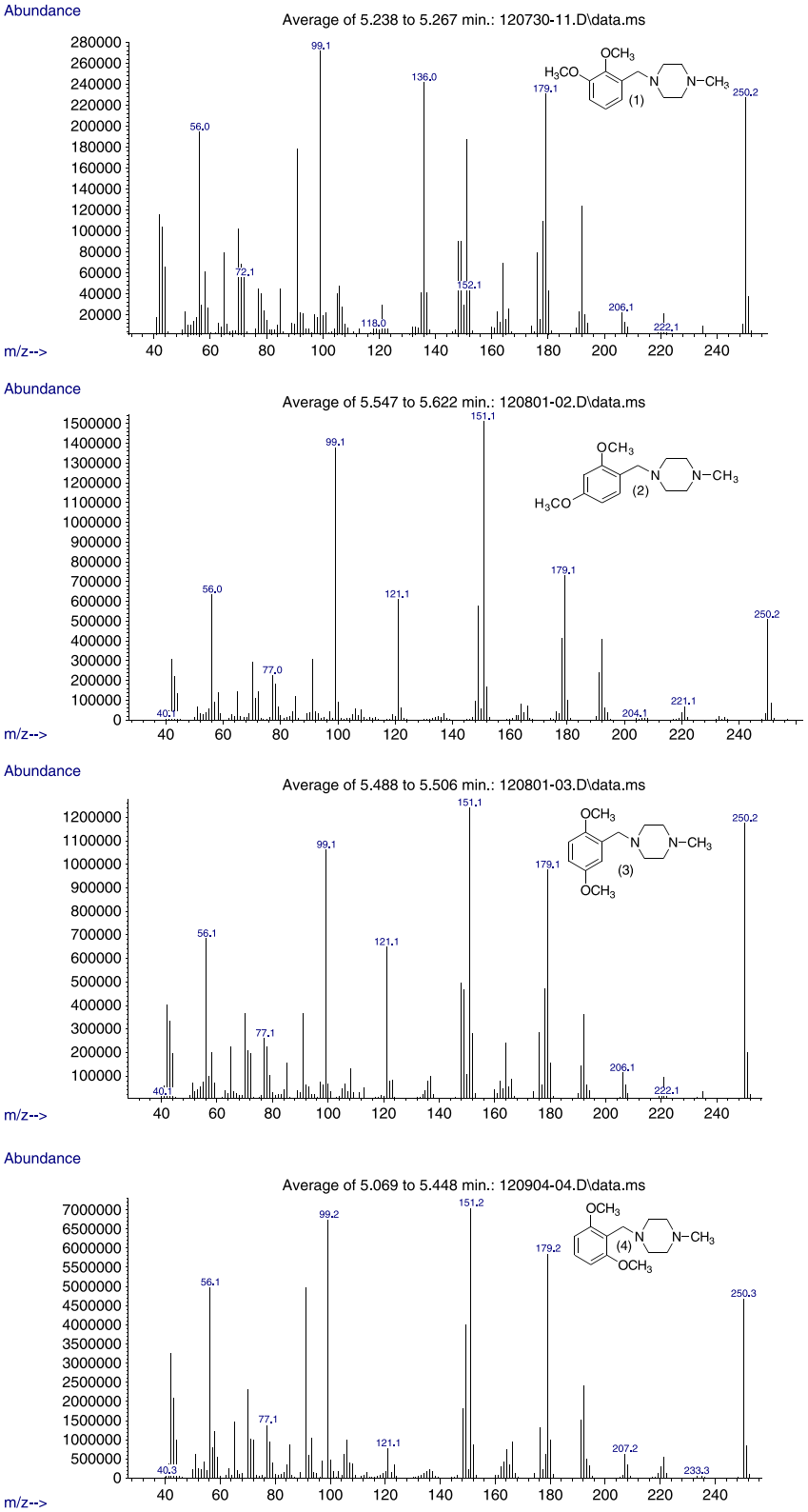


**Figure 2.** Mass spectra for the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines.



  

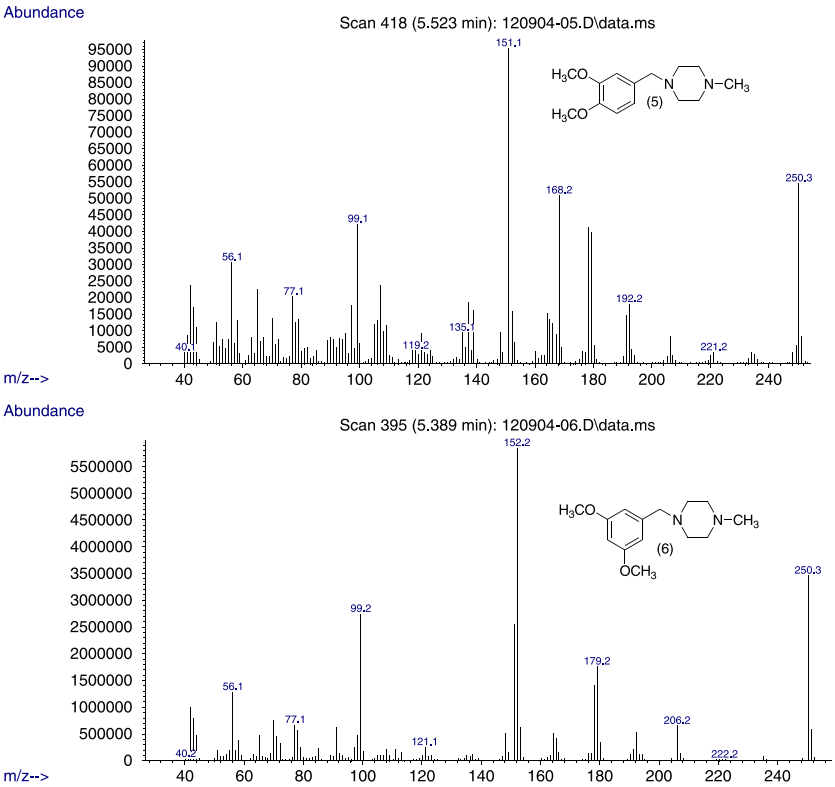


**Figure 2.** (Continued)

secondary nitrogen of *N*-methylpiperazine to yield the desired dimethoxybenzyl-*N*-methylpiperazines. This reduction occurs without the potential competitive reduction of the precursor aldehyde to the corresponding alcohol.

Mass spectrometry is the primary method for confirming the identity of drugs in forensic samples. Figure 2 shows the EI mass spectra of the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines (compounds 1–6) in this study. All six regioisomers show molecular ions at *m/z* 250 and these ions are of significant relative intensity. Major fragment ions of equivalent mass occur in the spectra for these six compounds with only the relative intensity of the individual ions as the major spectral variation. Fragmentation of the bond between the benzylic carbon and the adjacent piperazine nitrogen provides the base peak in all six spectra. The dimethoxybenzyl cation at *m/z* 151 is the base peak for compounds 2, 3, 4, and 5 while the dimethoxybenzyl radical cation (*m/z* 152) resulting from a hydrogen migration rearrangement pathway is the base peak for compound 6. Fragmentation of the same bond between the benzylic carbon and the adjacent piperazine nitrogen with charge retention on the *N*-methylpiperazine group yields the cation at *m/z* 99, the base peak for compound 1. The structures for the base peaks and other characteristic fragment ions in the mass spectra for these regioisomeric dimethoxybenzyl-*N*-methylpiperazines are shown in Fig. 3.

The internal fragmentation within the piperazine ring produces a number of unique ions in the mass spectra of these dimethoxybenzyl-*N*-methylpiperazines. The low-mass ion of highest relative abundance in these spectra is the *m/z* 56 cation. This ion is a characteristic fragment for the piperazine ring and is almost universal in all *N*-1-monosubstituted piperazines (N-4 substituent is hydrogen). This *m/z* 56 ion yielded a mass shift of +6 Da when $d_8$-piperazine was used to label all the four carbons of the piperazine ring.[16] Thus, the *m/z* 56 ion was confirmed to contain six hydrogen atoms and three of the carbons from the original piperazine portion of these molecules; this confirmation was based on studies in the dimethoxybenzylpiperazines (N-4 = H). The formation of the *m/z* 56 ion in the previous series of dimethoxybenzylpiperazine (N-4 = H) regioisomers involved an initial migration of the hydrogen on nitrogen at N-4 to the tertiary N-1 nitrogen followed by a radical site alpha cleavage initiated by the N-4 nitrogen to break the carbon–carbon bond of the piperazine ring. The last step in the formation of the *m/z* 56 ion is the heterolytic breaking of the N-1 to carbon bond to yield the $C_3H_6N^+$ cation. The equivalent mechanistic pathway is illustrated for the N-4 = $CH_3$ compounds in this study in Fig. 4.

The formation of the $C_3H_6N^+$ *m/z* 56 ion for the N-4 = $CH_3$ series of regioisomers involves methyl group migration from N-4 to N-1 of the piperazine ring. The N-4 = $CD_3$ labeled form of 2,3-dimethoxybenzyl-*N*-methylpiperazine was prepared by reacting the monosubstituted dimethoxybenzylpiperazine (N-4 = H) with $CD_3I$. The mass spectrum for this labeled compound is presented in Fig. 5(A) and shows that the *m/z* 56 species did not undergo a mass shift as a result of the N-$CD_3$ group. Thus, the N-4 methyl group is not a part of the *m/z* 56 ion and indicates that the methyl group migration is consistent with the N-H migration in the monosubstituted series.[16] The use of piperazine-$D_8$ in the monosubstituted series produced a mass shift of +6 Da

  

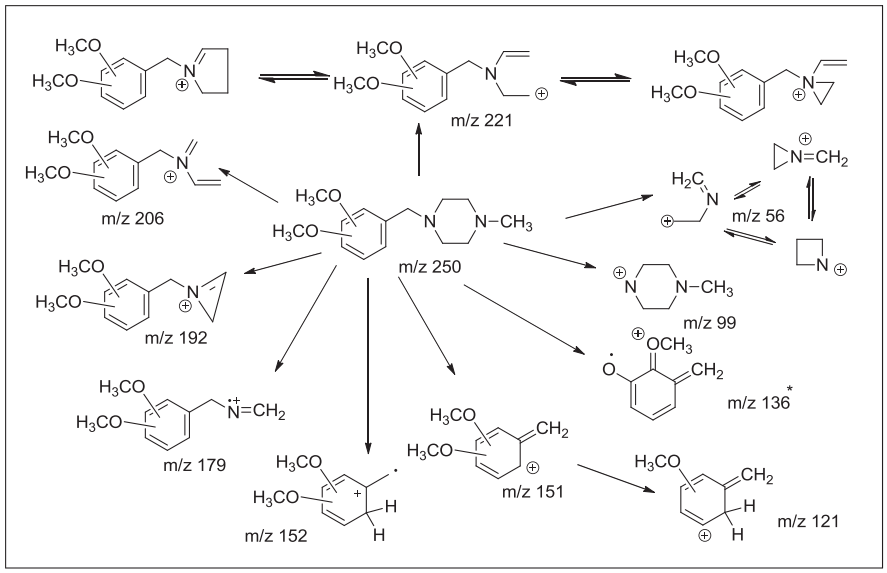


**Figure 3.** Mass spectral fragmentation for the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines (*2,3-isomer only).

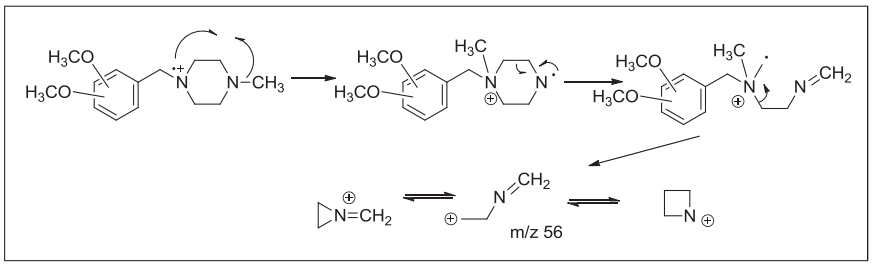


**Figure 4.** Mechanism for the formation of the *m/z* 56 cation in the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines.

for the ion in question yielding the $C_3D_6N^+$ cation at *m/z* 62. The mass spectrum for 2,3-dimethoxybenzylpiperazine-$D_8$ is shown in Fig. 5(B). When the *N*-4-methyl ($CH_3$) group is added to the 2,3-dimethoxybenzylpiperazine-$D_8$, the resulting mass spectrum (Fig. 5(C)) continues to show a mass shift of +6 Da for the $C_3D_6N^+$ cation at *m/z* 62. The mass spectrum for the 2,3-dimethoxybenzyl-*N*-$CD_3$-piperazine-$D_8$ in Fig. 5(D) also shows the +6 Da mass shift for this ion further confirming the structure for this characteristic fragment. The mass shifts for the molecular ions in Figs. 5(A)–5(D) provide validation of the structures of the labeled species. Furthermore, the fragment ions for the individual piperazine species at *m/z* 102, 93, 107 and 110 in Figs. 5(A)–5(D) respectively confirm the position of the deuterium labels in the model compounds.

The mass spectrum for the 2,3-dimethoxybenzyl-*N*-methylpiperazine regioisomer in Fig. 2 as well as all the deuterium-labeled derivatives of this compound in Fig. 5 show a unique fragment at *m/z* 136. This ion does not undergo any deuterium-initiated mass shifts; thus, this fragment does not come from the piperazine portion of the molecule. Exact mass analysis shows this ion to be $C_8H_8O_2$, a radical cation species. This ion essentially represents the molecular equivalent of a methyl group loss from the *m/z* 151 cation to form a peak of intensity approximately equal to the base peak for the 2,3-dimethoxybenzyl regioisomer. Previous carbon-13- and deuterium-labeling studies in the monosubstituted (N-4 = H) dimethoxybenzylpiperazines[16] showed that the methyl group lost to form the *m/z* 136 species is from the methoxy group at the 3-position of the aromatic ring. The resonance-stabilizing effects of the 2-methoxy group favor the loss of the methyl group from the 3-position. A possible mechanistic pathway for the formation of the *m/z* 136 ion has been described.[16] The mass spectrum in Fig. 6 provides support that the fragmentation pathway for these *N*-methylpiperazines in this study is equivalent to the previously reported monosubstituted dimethoxybenzylpiperazines.[16] The mass spectrum in Fig. 6 is for the deuterium-labeled benzylic carbon of 2,3-dimethoxybenzyl-*N*-methylpiperazine and the results show a mass shift of +1 Da at *m/z* 137. These data indicate that the benzylic carbon remains a part of the ion in question and leaves only the methyl group from one of the two methoxy ring substituents as the source for the elimination fragmentation. Thus, the formation of the *m/z* 136 radical cation in this *N*-methylpiperazine series is the same process as the previously reported[16] 2,3-dimethoxybenzylpiperazine series. The deuterium labeling of the benzylic carbon followed the previously described synthetic method using sodium cyanoborodeuteride ($NaBD_3CN$) as the reducing reagent.

The spectra for these six regioisomeric dimethoxybenzyl-*N*-methylpiperazines in Fig. 2 show two major high-mass fragment ions at *m/z* 179 and 192 of variable relative



  

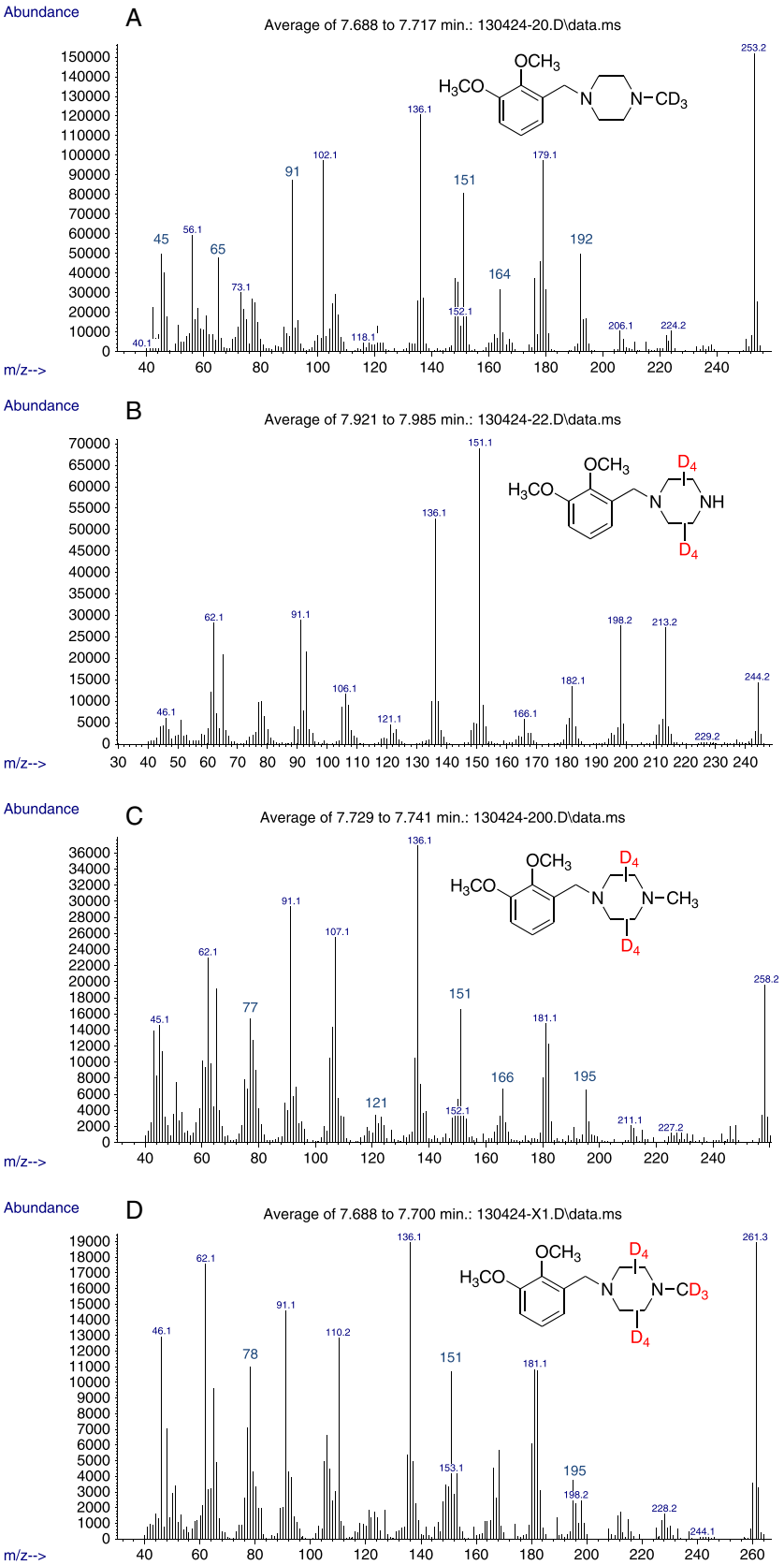


**Figure 5.** Mass spectra for deuterium-labeled 2,3-dimethoxybenzyl-*N*-methylpiperazines.

  

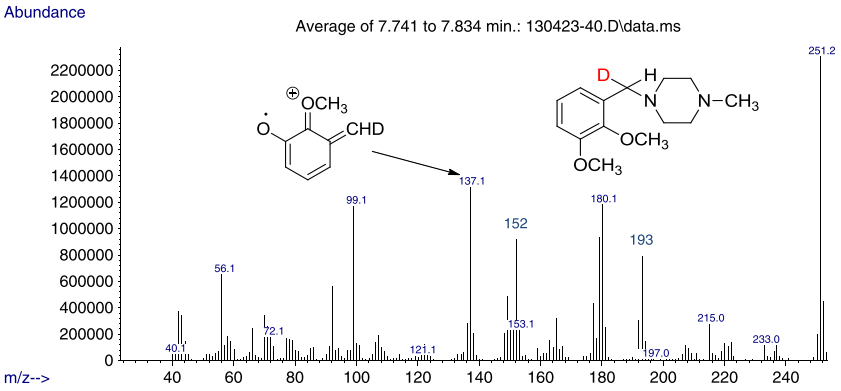


**Figure 6.** Mass spectrum the benzylic carbon deuterium-labeled 2,3-dimethoxybenzyl-*N*-methylpiperazines.

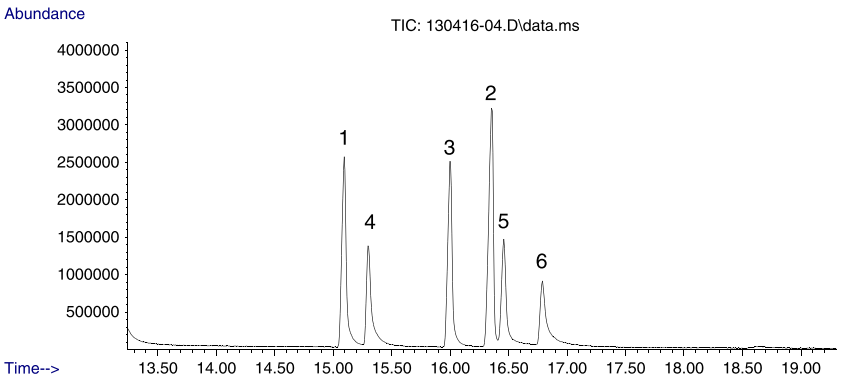


**Figure 7.** Gas chromatographic separation of the six regioisomeric dimethoxybenzyl-*N*-methylpiperazines.

abundance. A comparison of the fully deuterium-labeled 2,3-dimethoxybenzyl-*N*-$CD_3$-piperazine-$D_8$ in Fig. 5(D) with the spectrum for the equivalent unlabeled isomer in Fig. 2 supports the proposed structures for the *m/z* 179 and 192 fragments in Fig. 3. Furthermore, the spectrum in Fig. 5(D) for the $D_{11}$ derivative supports the proposed structures for the minor high-mass ions at *m/z* 206 and 221 observed in many of the spectra in Fig. 2.

### Gas chromatography

Gas chromatographic separation of the dimethoxybenzyl-*N*-methylpiperazines was accomplished using an Rtx-200 (100% trifluoropropyl methyl polysiloxane) stationary phase in a capillary column (30 m × 0.25 mm) of 0.5-µm film thickness. Several temperature programs were evaluated and the most efficient program (see Experimental section) was used to generate the representative chromatogram shown in Fig. 7. This chromatogram shows the separation of the six dimethoxybenzyl-*N*-methylpiperazine regioisomers and the elution order appears related to the degree of substituent crowding on the aromatic ring. Compounds 1 and 4 elute first and these two isomers contain substituents arranged in a 1,2,3-pattern on the aromatic ring. Three isomers (compounds 2, 3 and 5) have two groups substituted 1,2 with one isolated substituent. The 1,3,5-trisubstituted pattern in compound 6 provides minimum intramolecular crowding and elutes last in this group of compounds. The two compounds with maximum crowding substituted in a 1,2,3-manner on the aromatic ring show the 2,3-dimethoxy substitution pattern to elute first followed by the 2,6-dimethoxy isomer eluting second. The relative position of the methoxy groups appears to determine the elution order in the three compounds having two groups substituted in a 1,2-pattern. Within this group of three compounds the first to elute is the 1,4-relationship for the two methoxy groups in compound 3. This is followed by the 1,3-pattern for compound 2 and lastly the 1,2-pattern for compound 5.

In previous studies on the chromatographic properties of the monosubstituted piperazines (N4 = H), these secondary amines showed severe chromatographic tailing on a number of stationary phases. This issue was overcome by acylation of the secondary amine nitrogen with perfluoroacyl groups such as the pentafluoropropionyl group and others. Adequate peak shape and resolution were obtained for these tertiary amines (compounds 1–6) in this study.

## CONCLUSIONS

The six regioisomeric dimethoxybenzyl-*N*-methylpiperazines yield the same fragment ions in their mass spectra. Deuterium labeling was successful in confirming the elemental composition of the characteristic fragments in the mass spectra



  

of all the dimethoxybenzyl-*N*-methylpiperazines. Methyl-group migration from the N-4 position allows for the formation of the major low-mass fragment at *m/z* 56 in these spectra. Mixtures of the dimethoxybenzyl-*N*-methylpiperazines were successfully resolved via capillary gas chromatography using a relatively polar stationary phase and temperature-programming conditions. The elution order appears related to the degree of substituent crowding on the aromatic ring with the most crowded 1,2,3-substitution patterns eluting first and the highest retention for the compound with minimum intramolecular crowding (the 1,3,5-trisubstitution pattern).

## Acknowledgement

This project was supported by Award No. 2011-DN-BX-K530, awarded by the National Institute of Justice, Office of Justice Programs, U.S. Department of Justice. The opinions, findings, and conclusions or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect those of the Department of Justice.

## REFERENCES

[1] R. A. Glennon, R. M. Slusher, R. A. Lyon, M. Titeler, J. D. McKenney. 5-$HT_1$ and 5-$HT_2$ binding characteristics of some quipazine analogues. *J. Med. Chem.* **1986**, *29*, 2375.
[2] R. A. Glennon. Central serotonin receptors as targets for drug research. *J. Med. Chem.* **1987**, *30*, 1.
[3] D. de Boer, I. J. Bosman, E. Hidvégi, C. Manzoni, A. A. Benkö, L. J. A. L. dos Reys, R. A. A. Maes. Piperazine-like compounds a new group of designer drug-of-abuse on the European Market. *Forensic Sci. Int.* **2001**, *121*, 47.
[4] R. F. Staack, L. D. Paul, D. Schmid, G. Roider, B. Rolf, Proof of a 1-(3-chlorophenyl)piperazine (mCPP) intake – Use as adulterant of cocaine resulting in drug–drug interactions? *J. Chromatogr. B* **2007**, *855*, 127.
[5] Drug Enforcement Administration – Department of Justice. Schedules of controlled substances: temporary placement of benzylpiperazine and trifluoromethylphenylpiperazine into schedule I. *Fed. Regist.* **2002**, *67*, 161.
[6] H. Tsutsumi, M. Katagi, A. Miki, N. Shima, T. Kamata, M. Nishikawa, K. Nakajima, H. Tsuchihashi. Development of simultaneous gas chromatography–mass spectrometric and liquid chromatography–electrospray ionization mass spectrometric determination method for the new designer drugs, *N*-benzylpiperazine (BZP), 1-(3-trifluoromethylphenyl) piperazine (TFMPP) and their main metabolites in urine. *J. Chromatogr. B* **2005**, *819*, 315.
[7] R. Haroz, M. I. Greenberg. New drugs of abuse in North America. *Clinics Lab. Medicine* **2006**, *26*, 147.
[8] H. M. Maher, T. Awad, J. DeRuiter, C. R. Clark. GC–MS and GC-IRD studies on brominated dimethoxyamphetamines regioisomers related to 4-Br-2,5-DMA (DOB). *Drug Test. Anal.* **2012**, *4*, 591.
[9] K. M. Hegadoren, G. B. Baker, M. Bourin. 3,4-Methylenedioxy analogues of amphetamines: defining the risks to humans. *Neurosci. Biobehav. Rev.* **1999**, *23*, 539.
[10] Y. F. Hamad Abiedalla, K. Abdel-Hay, J. DeRuiter, C. R. Clark. Synthesis and GC-MS analysis of a series of homologs and regioisomers of 3,4-methylenedioxypyrovalerone (MDPV). *Forensic Sci. Int.* **2012**, *223*, 189.
[11] P. Jankovics, A. Váradi, L. Tölgyesi, S. Lohner. Detection and identification of the new potential synthetic cannabinoids 1-pentyl-3-(2-iodobenzoyl)indole and 1-pentyl-3-(1-adamantoyl)indole in seized bulk powders in Hungary. *Forensic Sci. Int.* **2012**, *214*, 27.
[12] F. Westphal, T. Junge, U. Girreser, S. Stobbe, S. B. Péres. Structure elucidation of a new designer benzylpiperazine: 4-Bromo-2,5-dimethoxybenzylpiperazine. *Forensic Sci. Int.* **2009**, *187*, 87.
[13] T. Awad, J. DeRuiter, C. R. Clark. GC-MS analysis of acylated derivatives of the side chain and ring regioisomers of methylenedioxymethamphetamine. *J. Chromatogr. Sci.* **2005**, *43*, 296.
[14] T. Awad, J. DeRuiter, C. R. Clark. GC-MS analysis of the ring and side chain regioisomers of ethoxyphenethylamines. *J. Chromatogr. Sci.* **2008**, *46*, 671.
[15] T. Awad, C. R. Clark, J. DeRuiter. Chromatographic and mass spectral studies on methoxy methyl methamphetamines related to 3,4-methylenedioxymethamphetamine. *J. Chromatogr. Sci.* **2007**, *45*, 468.
[16] K. M. Abdel-Hay, J. DeRuiter, C. R. Clark. GC-MS and GC-IRD studies on the six ring regioisomeric dimethoxybenzylpiperazines (DMBPs). *Drug Test. Anal.* **2013**, *5*, 560.

  