JOURNAL OF MASS SPECTROMETRY
J. Mass Spectrom. **35**, 705–710 (2000)

Regioisomeric differentiation of 2,3- and 3,4-methylenedioxy ring-substituted phenylalkylamines by gas chromatography/tandem mass spectrometry

Swantje Borth,[1]* Wolfram Hänsel,[1] Peter Rösner[2] and Thomas Junge[2]
[1] Pharmazeutisches Institut, Christian Albrechts Universität Kiel, Gutenbergstrasse 76, D-24118 Kiel, Germany
[2] Landeskriminalamt Schleswig-Holstein, Sachgebiet Toxikologie/Betäubungsmittel, Mühlenweg 166, D-24116 Kiel, Germany

Numerous abused drugs of the 3,4-methylenedioxymetamphetamine (MDMA; Ecstasy; *N*-methyl-1-(3,4-methylenedioxyphenyl)-2-propaneamine) type and various alkyl chain- and aromatic ring-substituted isomers give very similar electron ionization (EI) mass spectra. This seriously affects the analysis of especially ring regioisomeric drug variants. Using collision-induced dissociation (CID) (argon) under EI and chemical ionization, the mass spectra of 18 2,3- and 3,4-methylenedioxy ring-substituted phenylethylamines were recorded. These techniques permitted an unequivocal differentiation of all studied ring regioisomeric methylenedioxyphenylethylamines. CID mass spectrometry therefore appear to be a reliable tool to establish the kind of ring substitution pattern in regioisomeric methylenedioxyphenalkylamines.

KEYWORDS: 3,4-methylenedioxymetamphetamine; Ecstasy; collision-induced dissociation; tandem mass spectrometry; phenylethylamines; abused drugs

INTRODUCTION

Since Spiteller's work in 1972,[1] many studies have shown that electron ionization (EI) mass spectrometry (MS) is often insufficient to discriminate between structurally closely related phenylethylamine drug variants because of their often virtually identical mass spectra.[2–9] This seriously affects the ability to detect novel controlled amphetamine analogues ('designer drugs'),[10] such as 3,4-methylenedioxymetamphetamine (MDMA; Ecstasy; **2b**), the most popular compound.[11–13] The differentiation of some side-chain regioisomeric methylenedioxyamphetamines can be achieved by means of derivatization such as acetylation using various chromatographic methods.[8,14–16] Rösner and Junge reported the differentiation of side-chain regioisomers by the structural elucidation of the alkylamino groups of phenylalkyl drug variants by gas chromatography/tandem mass spectrometry (GC/MS/MS).[10,17] Differentiation of the ring isomers 2,3- and 3,4-methylenedioxyamphetamine by EIMS was reported by Soine *et al.*[4] and Casale *et al.*[18] Attempts to differentiate 2,3- and 3,4-methylenedioxyphenylalkylamines by derivatization proved to be unsuccessful.[19]

Our intention here was to identify and differentiate 18 ring regioisomeric 1-(methylenedioxyphenyl)-2-propaneamines (Fig. 1; **1a–d**, **2a–d**) and 1-(methylenedioxyphenyl)-2-butanamines (Fig. 1; **3a–d**, **4a–f**) by low-energy collision-induced dissociation (CID) using EI and methane chemical ionization (CI).

EXPERIMENTAL

Instrumentation

For GC/MS, the EI mass spectra were obtained with a Finnigan TSQ 70 instrument (Finnigan MAT, equipped with a DEC-Station 2100) coupled to a Varian 3400 CX gas chromatograph. A DB1 fused-silica capillary column (30 m × 0.32 mm, i.d., film thickness 0.25 μm) was used. The temperature programme consisted of an initial temperature of 80 °C held for 1 min, followed by a linear ramp to 280 °C at 15 °C min^{-1}, the final temperature being held for 15 min. The split/splitless injector and detector temperatures were kept at 280 °C. Helium was used as the carrier gas.

The mass spectrometric parameters were set as follows: EI mode, ionization voltage 70 eV, scan time 1 s and scan range 40–600 Da; CI mode, ionization voltage 70 eV, source temperature 150 °C, reactant gas methane, source pressure 0.2 Pa, scan time 1 s and scan range 60–600 Da; MS/MS, ionization voltage 70 eV, collision gas argon, collision energy 22 eV, collision gas pressure 0.2 Pa and the exact target thickness was regulated by the intensity ratio of the peaks at m/z 92/91 (0.2) and 91/65 (20) of n-butylbenzene.[20]

---

* *Correspondence to*: S. Borth, Pharmazeutisches Institut, Christian Albrechts Universität Kiel, Gutenbergstrasse 76, D-24118 Kiel, Germany.
E-mail: sborth@pharmazie.uni-kiel.de

Received 20 December 1999
Accepted 3 March 2000

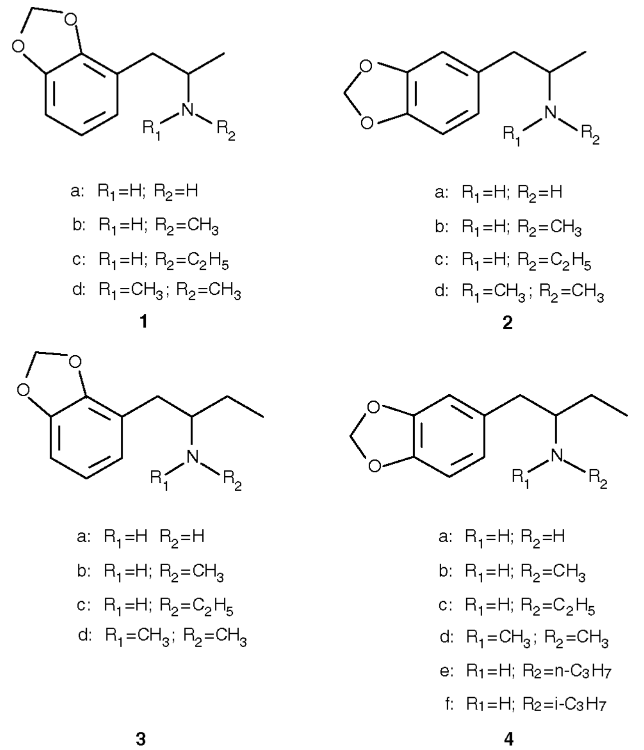


Figure 1. Structures of methylenedioxy ring-substituted phenylethylamine derivatives.

All fragment ion spectra were recorded under standardized operating conditions using *n*-butylbenzene as a reference compound to adjust the collision energy and collision gas pressure as described in the literature.[20]

Materials

The 1-(2,3-methylenedioxyphenyl)-2-propaneamine derivatives (**1a–d**) were synthesized according to Casale *et al.*[18] The 3,4-methylenedioxy ring-substituted propanamine isomers (**2a–d**) were kindly provided from the reference collection of the Landeskriminalamt (LKA) Schleswig-Holstein, Germany.

The syntheses of the previously unreported 1-(2,3-methylenedioxyphenyl)-2-butanamine compounds (**3a–d**) and of *N*-propyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (**4e**) and *N*-isopropyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (**4f**) have been published elsewhere (Borth S, Hänsel W, Rösner P, Junge T. *Forensic Sci.* 2000; in press). The 1-(3,4-methylenedioxyphenyl)-2-butanamine derivatives (**4a–d**) were synthesized according to Noggle and co-workers.[2]

RESULTS AND DISCUSSION

The low-energy CID parent ion ($M^{+\bullet}$ and $[M+H]^+$) mass spectra of the 2,3- and 3,4-ring regioisomers (Fig. 1, **1a–4f**) showed fragmentation pathways with very different abundances (Tables 1 and 2). Using EI-CID, the molecular ions of **4e** and **f** did not have sufficient abundance for recording fragment ion mass spectra for the unequivocal identification of the regioisomeric 2,3- and 3,4-substitution patterns. CI, however, gave abundant protonated molecular ($[M+H]^+$) ions, thus allowing the recording of fragment ion mass spectra in all cases. Therefore, this method is advantageous for establishing the substitution pattern of the methylenedioxy group of methylenedioxyphenylethylamine drug variants at submicrogram levels where other methods, such as NMR spectroscopy, lack sufficient sensitivity.

EI-CID mass spectra of 2,3- and 3,4-methylenedioxyphenyl-2-propanamine and -2-butanamine derivatives

The EI-CID mass spectra of all 2,3-methylenedioxyphenylethylamine derivatives (**1a–d** and **3a–d**) are dominated by immonium base peak ions with the general

Table 1. Structurally significant fragment ions in the low-energy EI-CID molecular ion $M^{+\bullet}$ mass spectra of 1a–4d

Compound	Ring-substitution pattern	Parent ion (P)[a] (*m/z*)	Relative abundance of ions (% base peak)[b,c] of fragment ions (*m/z*)										
			44	58	72	86	135	136	147	177	192	207	221
1a	2,3-	179	100	—	—	—	3.0	33.6	—	—	—	—	—
1b	2,3-	193	—	100	—	—	6.8	1.2	—	—	—	—	—
1c	2,3-	207	—	—	100	—	11.7	7.4	—	8.9	2.4	5.4	—
1d	2,3-	207	1.5	—	100	—	1.7	2.9	—	1.2	3.1	—	—
2a	3,4-	179	3.1	—	—	—	30.9	100	—	—	—	—	—
2b	3,4-	193	—	24.3	—	—	15.3	100	1.9	—	—	—	—
2c	3,4-	207	3.5	—	72.9	—	30.9	100	—	2.2	2.7	1.4	
2d	3,4-	207	—	—	100	—	3.7	8.1	—	—	5.6	4.9	—
3a	2,3-	193	—	100	—	—	3.0	11.3	—	—	—	—	—
3b	2,3-	207	—	1.2	100	—	—	—	—	—	1.7	—	—
3c	2,3-	221	—	8.4	—	100	22.7	35.5	20.3	10.7	28.7	—	2.1
3d	2,3-	221	—	—	—	100	—	—	—	—	—	—	9.0
4a	3,4-	193	—	7.7	—	—	19.1	100	—	—	—	—	—
4b	3,4-	207	1.1	—	57.5	—	28.8	100	—	2.0			—
4c	3,4-	221	—	—	—	100	5.0	6.4	1.1	54.4	12.1	—	6.9
4d	3,4-	221	—	—	—	100	6.3	3.6	—	—	3.1	—	—

[a] P refers to the parent ions, i.e. the ion undergoing CID ($M^{+\bullet}$) (*m/z*).
[b] Relative abundance is expressed as a percentage of the base peak (100%).
[c] For experimental details, see text.

Table 2. Structurally significant fragment ions in low energy CI-CID protonated molecule $[M+H]^+$ mass spectra of 1a–4f

Compound	Ring-substitution pattern	Parent ion (P)[a] (*m*/*z*)	Relative abundance of ions (% base peak)[a,b] of fragment ions (*m*/*z*)															
			58	72	77	105	119	123	133	135	137	145	147	163	177	194	208	222
1a	2,3-	180	—	—	2.3	44.5	—	51.6	29.6	100	0.1	4.0	—	39.4	—	—	—	—
1b	2,3-	194	—	—	1.7	30.7	—	18.6	24.0	100	0.6	3.8	—	35.3	—	12.2	—	
1c	2,3-	208	2.7	1.1	2.6	32.9	—	18.3	25.4	100	1.4	2.2	—	29.0	—	—	6.0	—
1d	2,3-	208	14.6	7.4	3.0	36.2	—	0.3	22.6	100	5.4	3.2	—	25.8	—	1.3	—	—
2a	3,4-	180	—	—	—	64.7	2.7	1.6	97.0	100	19.6	—	—	93.5	—	—	—	—
2b	3,4-	194	16.5	—	4.9	72.7	—	0.4	100	92.8	16.1	1.6	1.1	60.5	—	10.2	—	—
2c	3,4-	208	—	9.5	2.9	61.7	—	0.1	100	84.7	35.4	—	—	70.8	—	—	4.3	—
2d	3,4-	208	4.5	20.2	2.9	52.6	—	0.2	71.3	59.2	17.6	—	—	100	—	—	7.5	—
3a	2,3-	194	—	—	—	1.4	1.2	20.7	—	100	0.3	—	—	—	2.0	5.4	—	—
3b	2,3-	208	—	—	—	1.3	1.5	4.6	—	100	0.6	—	2.3	—	—	—	5.6	—
3c	2,3-	222	—	—	—	—	1.5	3.8	—	100	0.7	—	2.8		—	—	—	5.5
3d	2,3-	222	—	—		1.4	1.6	0.2	—	100	3.2	—	2.8	—		—	—	8.1
4a	3,4-	194	4.3	—		—	1.7	1.0		100	1.5	—	2.8	—	3.7	1.6	—	—
4b	3,4-	208		3.0	—	—	1.9	0.1	—	100	8.5	—	3.3	—	2.1	—	1.8	—
4c	3,4-	222	—	—	—	—	2.7	0.02	—	100	31.9	—	5.0	—	3.0	—		3.0
4d	3,4-	222	—	—	—		2.9	0.01		100	40.5	—	5.6	—	3.0	—	—	3.4
4e	3,4-	236	—	—		—	3.0	—	—	100	31.0	—	5.2	—	2.1	—	—	—
4f	3,4-	236	—	—	—	—	3.3	—	—	100	29.4	—	5.0	—	2.0	—	—	—

[a] a–c See Table 1.

formula $[C_nH_{2n+2}N]^+$ (*m*/*z* 44, 58, 72, etc.) resulting from an α-cleavage reaction (Table 1; see Fig. 2).[10,17,21,22] The EI-CID mass spectra of 3,4-methylenedioxy isomeric compounds **2a–c** and **4a** and **b** show significant ions at *m*/*z* 136. This signal could be due to a rearrangement of nitrogen H atoms to the aromatic *ortho* position eliminating an imine, as shown by many phenylethylamine derivatives.[22,23] The peak at *m*/*z* 136 could also be generated by a specific six-centre H-rearrangement (rH) similar to that in alkylbenzenes.[23–26] This second pathway may be responsible for the fragment at *m*/*z* 136 of the *N*,*N*-dimethylated compounds having no nitrogen H atom. Substituents in the *ortho* position should decrease both rearrangements. Consequently, the 2,3-ring isomers with only one free *ortho* position show the ion at *m*/*z* 136 with lower abundance. Further, an intermolecular hydrogen bond between NH and the ether oxygen may lead to an unfavourable conformation for the discussed rearrangements.[27,28] Compounds **4e** and **f** do not form molecular $M^{+\bullet}$ ions with sufficient abundance for recording EI-CID mass spectra.

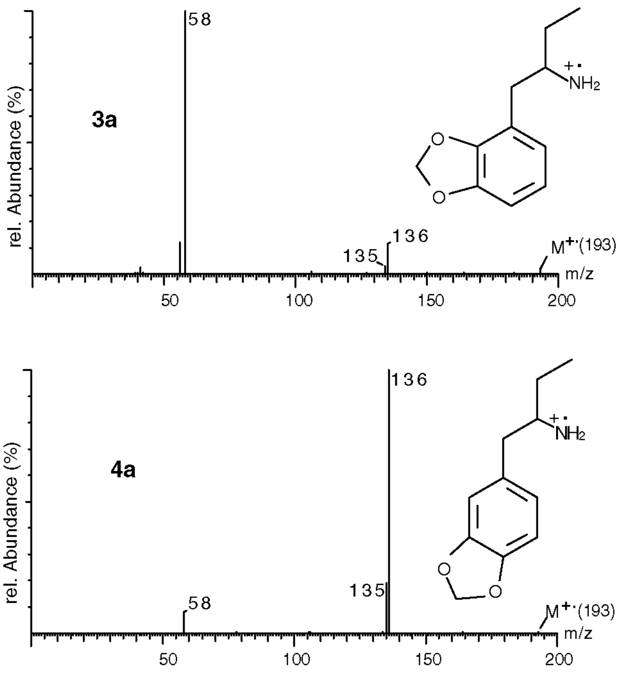


Figure 2. Comparison of the low energy EI-CID mass spectra of $M^{+\bullet}$ ions (*m*/*z* 193) of 1-(2,3-methylenedioxyphenyl)-2-butanamine (**3a**) and 1-(3,4-methylenedioxyphenyl)-2-butanamine (**4a**).

CI-CID mass spectra of 2,3- and 3,4-methylenedioxyphenyl-2-propanamine and -2-butanamine derivatives

The CI-CID spectra of all protonated methylenedioxy ring-substituted regioisomers (see Fig. 1, **1a–4f**) show very abundant benzyl cations or the corresponding tropylium cations at *m*/*z* 135 (Table 2, e.g. **3a** and **4a**; see Fig. 3) via cleavage of the benzyl bond by the charge of the ammonium cation. The CI-CID mass spectra of the homobenzyl cations, generated by the elimination of amines, also show a fragment ion at *m*/*z* 135 (see Fig. 4) (P. Rösner, unpublished CID results on homobenzyl cations with *m*/*z* 163 and 177). This indicates, that, in addition to other fragmentation processes, the ion at *m*/*z* 135 might be generated by a two-step fragmentation path (Scheme 1). From the protonated molecule an amine is eliminated to give a homobenzyl cation,[23,29] which further eliminates an alkene after an H rearrangement (rH) and an inductive cleavage reaction.[23,30,31] The 2,3-methylenedioxy isomeric compounds **1a–d** and **3a–d** form a significant $[C_7H_7O_2]^+$ ion at *m*/*z* 123 (Table 2; Scheme 2) with the mass of a protonated methylenedioxybenzene. It is known that $CI(CH_4)$ spectra of alkylbenzenes show protonated benzene ($[C_6H_7]^+$) ions, generated by olefin displacement reactions by breaking phenyl bonds via ion–molecule complexes.[30,32–34] We suggest that an analogous fragmentation path forms the $[C_7H_7O_2]^+$

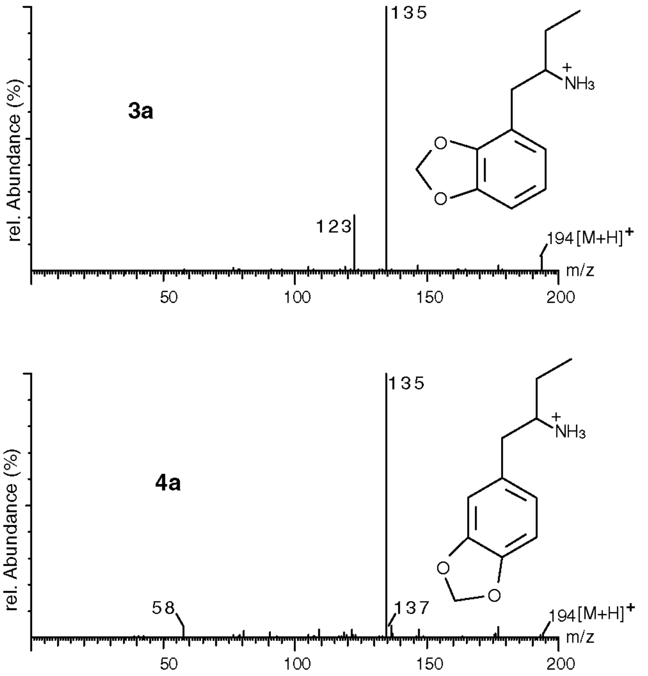


Figure 3. Comparison of the low energy CI-CID mass spectra of $[M + H]^+$ ions (*m/z* 194) of 1-(2,3-methylenedioxyphenyl)-2-butanamine (**3a**) and 1-(3,4-methylenedioxyphenyl)-2-butanamine (**4a**).

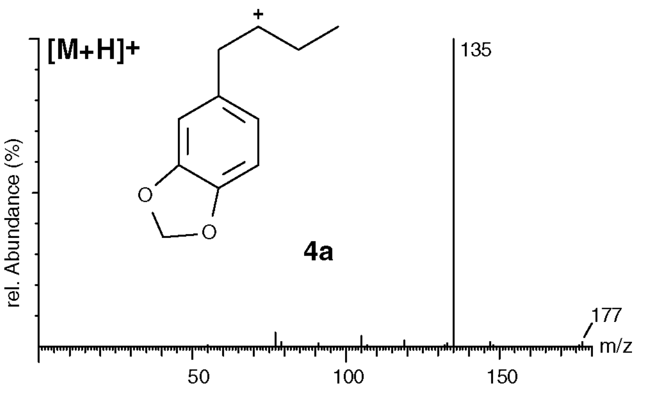
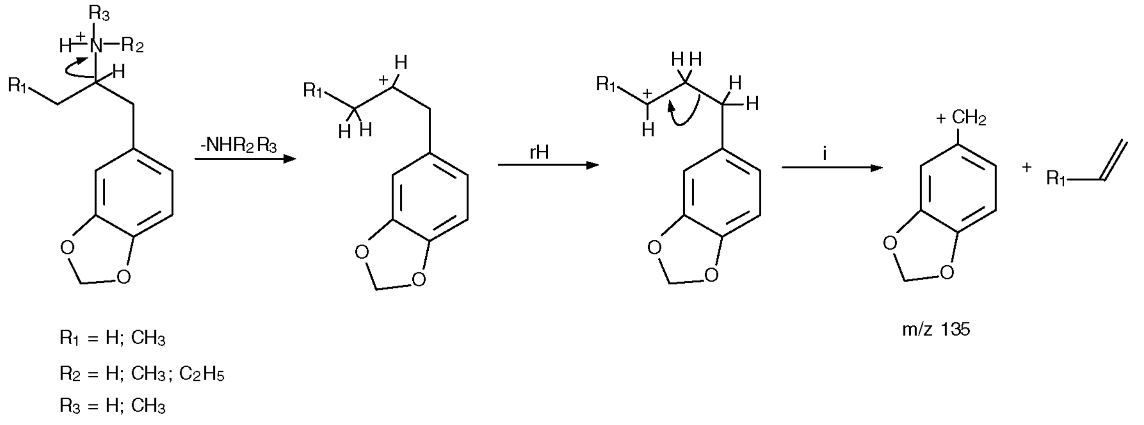


Figure 4. CI-CID mass spectrum of the homobenzyl cation (*m/z* 177) of 1-(3,4-methylenedioxyphenyl)-2-butanamine (**4a**) showing the main fragment with *m/z* 135.

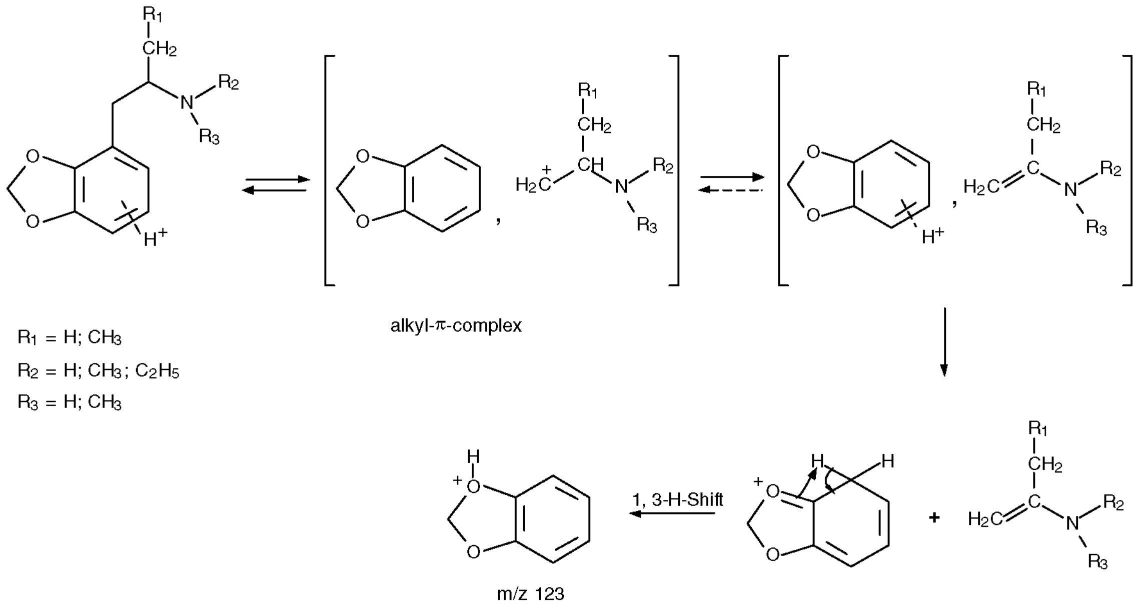
ions in the CID mass spectra of the 2,3-ring isomeric compounds **1a–d** and **3a–d** (Scheme 2). The charge of the protonated aromatic ring leads to cleavage of the aminoalkylphenyl bond and forms an benzene alkyl π-complex. Within this complex an H-atom transfer from the alkyl side-chain to the aromatic part forms a second ion–neutral complex consisting of a protonated methylenedioxybenzene ($[C_7H_7O_2]^+$, *m/z* 123) and an enamine or isomers which dissociate irreversibly to the products. From our experiments it is known that the CI-CID spectra of the nitrogen dideuterated compounds of **1a** and **3a** show an ion at *m/z* 124 (P. Rösner, unpublished results on nitrogen dideuterated compounds). This suggests participation of the H atoms of the alkyl side-chain[26,34] and also the H atoms of the nitrogen atoms in the discussed ion–molecule complex pathway (P. Rösner, unpublished results on nitrogen dideuterated compounds). This view is supported by the significantly lower abundance of the *m/z* 123 ion in the spectra of the *N*,*N*-dimethylated compounds (**1d**, **3d**; see Table 2). This possible ion–molecule complex pathway to a protonated methylenedioxybenzene demands further investigation.

The 3,4-methylenedioxy ring-substituted compounds **2a–d** and **4a–f** do not show this protonated methylenedioxybenzene ($[C_7H_7O_2]^+$) ion to a significant extent. Obviously the neighbouring *ortho* oxygen of 2,3-methylenedioxyphenylethylamines with its proton-accepting properties supports the cleavage of the phenyl bond by lowering the critical energy barrier by forming the intermediate benzene alkyl π-complex.[32–34] Such oxygen participation is in agreement with the observation that neighbouring proton-accepting groups play an important role in the fragmentation of collisionally activated protonated amides through intermediate ion–neutral complexes.[35]

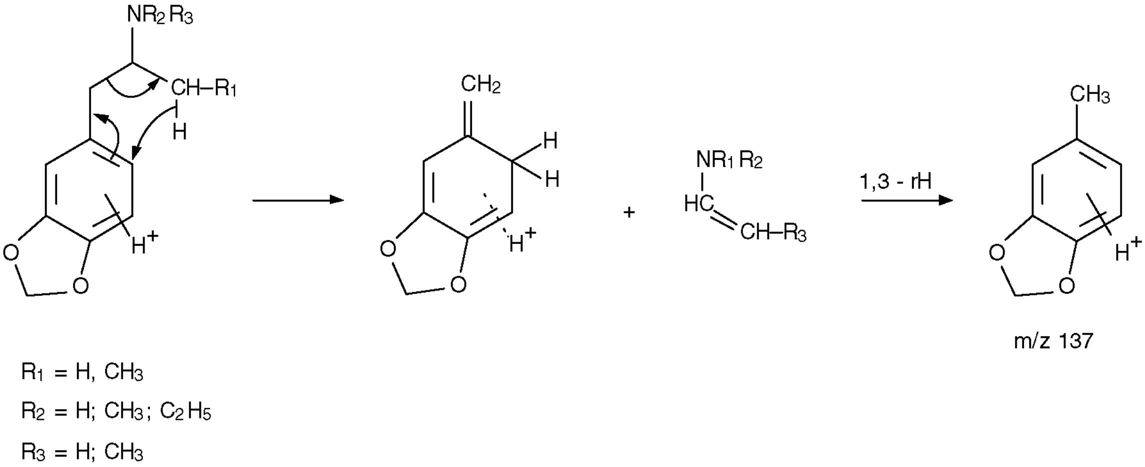
The 3,4-methylenedioxy-substituted compounds **2a–d** and **4a–f** show a significant homologous $[C_8H_9O_2]^+$ ion at *m/z* 137 by a formally benzylic bond cleavage.[30,36,37] We suggest that this ion is formed by an intramolecular hydrogen rearrangement formally analogous to the McLafferty rearrangement, as shown by many odd- and even-electron ions (Scheme 3).[36,38] The protonated collisionally activated 3,4-methylenedioxyphenylethylamines undergo a six-centre γ-H atom rearrangement to the *ortho* ring positions by a β-bond cleavage forming an enamine and a protonated methylidenecyclohexadiene. A following 1,3-hydrogen shift could possibly form a protonated 3,4-methylenedioxytoluene. Using EI it has been shown



Scheme 1. Alkylamine–alkene loss of 3,4-methylenedioxy ring-substituted phenylethylamine compounds **2a–d** and **4a–f** ($CI(CH_4)$).



Scheme 2. Alkene loss of 2,3-methylenedioxy ring-substituted phenylethylamine compounds **1a–d** and **3a–d** generating $[C_7H_7O_2]^+$ ions with *m/z* 123 due to cleavage of the phenyl bond (CI(CH_4)).



Scheme 3. Alkene loss of 3,4-methylenedioxy ring-substituted phenylethylamine compounds **2a–d** and **4a–f** generating $[C_8H_9O_2]^+$ ions at *m/z* 137 due to cleavage of the benzyl bond (CI(CH_4)).

that blocking the *ortho* position in alkylbenzenes prevents such hydrogen rearrangements completely.[3a] This may explain the very low abundance (<1%) of $[C_8H_9O_2]^+$ ions in the CI-CID mass spectra of 2,3-methylenedioxy isomeric compounds with one *ortho* position blocked. Thus, the protonated methylenedioxybenzene at *m/z* 123 and the protonated 3,4-methylenedioxytoluene at *m/z* 137 allow a regioisomeric assignment to the 2,3- and 3,4-methylenedioxyphenylethylamines, respectively.

Comparison of EI- and CI-CID mass spectra

Using EI-CID molecular ion MS, all 2,3-methylenedioxyphenylethylamine derivatives show an immonium ion base peak, whereas the 3,4-ring isomeric compounds show a base peak at *m/z* 136, except for **4c** and both *N*,*N*-dimethylated derivatives **2d** and **4d** (Fig. 2). The immonium ions and the ion at *m/z* 136 are important indicators for the differentiation of the regioisomers.

Using CI-CID molecular ion MS, the 2,3-methylenedioxy ring isomers show significant $[C_7H_7O_2]^+$ ions at *m/z* 123, whereas the 3,4-regioisomers show significant $[C_8H_9O_2]^+$ ions at *m/z* 137 (Fig. 3, Table 2). Therefore, the ion at *m/z* 123 indicates the 2,3-ring-substituted phenylethylamine isomers and the ion at *m/z* 137 the 3,4-ring-substituted isomers. Using CI-CID, an unequivocal differentiation of all the compounds studied is possible. Only CI gives protonated molecular ions $[M + H]^+$ of sufficient abundance in any case and has obviously advantages compared with EI-CID-MS.

CONCLUSION

The CID mass spectra of all the compounds studied, **1a–4f**, using EI and CI(CH_4) ionization show analytically valuable fragmentation processes which allow an unequivocal differentiation of all studied homologues and regioisomers **1a–4f**.

Because of the generally higher abundance of $[M+H]^+$ ions during CI compared with $M^{+\bullet}$ ions, CI-CID-MS has a generally superior sensitivity for the detection of lower substance levels. This method is advantageous for differentiating ring regioisomeric methylenedioxyphenylalkylamines drug variants at submicrogram levels where other methods, such as NMR spectrometry, lack sufficient sensitivity.

Acknowledgement

The authors express their gratitude to Dr Ulrich Girreser for his continuing support and advice on analytical problems.

REFERENCES

1. Spiteller G. *Z. Rechtsmed.* 1972; **70**: 234.
2. Clark CR, DeRuiter J, Valaer A, Noggle FT. *J. Chromatogr. Sci.* 1995; **33**: 328.
3. Noggle FT, Clark CR, Bondir KH, DeRuiter J. *J. Chromatogr. Sci.* 1991; **29**: 31.
4. Soine WH, Duncan W, Lambert R, Middleberg R, Finley H, O'Neil DJ. *J. Forensic Sci.* 1992; **37**: 513.
5. Spiteller G. *Z. Rechtsmed.* 1973; **71**: 274.
6. Battu C, Marquet P, Fauconnet AL, Lacassie E, Lachatre G. *J. Chromatogr. Sci.* 1998; **36**: 1.
7. Tatsuno M, Nishikawa M, Katagi M, Tsuchikashi H. *J. Anal. Toxicol.* 1996; **20**: 281.
8. Harnbeck CL, Czarny J. *J. Anal. Toxicol.* 1993; **17**: 23.
9. Cody JT. *J. Chromatogr. Sci.* 1992; **77**: 580.
10. Rösner P, Junge T. *Microgram* 1994; **27**: 411.
11. McGuire P, Fahy T. *J. Psychiatr. Res.* 1992; **160**: 276.
12. Henry JA, Jeffrys KJ, Dawling S. *Lancet* 1992; **340**: 384.
13. Enderlin V, Kupferschmidt H, Meier-Abt PJ. *Proceedings of the 18th International Congress of the European Association of Poisons Entres and Clinical Toxicologists*. Swiss Toxicological Information Centre (STIC): Zürich, March 1998; 21.
14. Noggle FT, Clark CR, DeRuiter J. *J. Chromatogr. Sci.* 1996; **34**: 230.
15. Maurer HH. *Ther. Drug. Monit.* 1996; **18**: 465.
16. Ensslin HH, Kovar K-A, Maurer HH. *J. Chromatogr. B* 1996; **683**: 189.
17. Rösner P, Junge T. *J. Mass Spectrom.* 1996; **31**: 1047.
18. Casale JF, Hays PA, Klein RFX. *J. Forensic Sci.* 1995; **40**: 391.
19. Clark CR, Noggle TT, Holston PL, DeRuiter J. *Microgram* 1998; **9**: 244.
20. Dawson PH, Sun WF. *Int. J. Mass Spectrom. Ion Phys.* 1984; **55**: 155.
21. Shannon JS. *Proc. R. Aust. Chem. Inst.* 1964; **31**: 323.
22. Burgers PC, Terlouw JK, Levsen K. *Org. Mass Spectrom.* 1982; **17**: 295.
23. McLafferty FW. *Anal. Chem.* 1959; **31**: 82.
24. Morton TH. *Tetrahedron* 1982; **38**: 3195.
25. Harnish D, Holmes JL. *J. Am. Chem. Soc.* 1991; **113**: 9729.
26. Wesdemiotis C, Schwarz H, Borchers F, Heimbach H, Levsen K. *Z. Naturforsch., Teil B* 1977; **33**: 1150.
27. Kuck D. *Org. Mass Spectrom.* 1989; **24**: 1077.
28. Houriet R, Rufenacht H, Stahl D, Tichy M, Longevialle P. *Org. Mass Spectrom.* 1985; **20**: 300.
29. Dallakian P, Budzikiewicz H, Brzezinka H. *J. Anal. Toxicol.* 1996; **20**: 255.
30. Kuck D. *Mass Spectrom. Rev.* 1990; **9**: 583.
31. Boer FP, Shannon TW, McLafferty FW. *J. Am. Chem. Soc.* 1968; **90**: 7239.
32. Herman JA, Harrison AG. *Org. Mass Spectrom.* 1981; **16**: 423.
33. Berthomieu D, Audier H, Denhez J-P, Monteiro C, Mourgues P. *Org. Mass Spectrom.* 1991; **26**: 271.
34. Leung H-W, Harrison AG. *Org. Mass Spectrom.* 1977; **12**: 582.
35. Tu Y, Harrison AG. *J. Am. Soc. Mass Spectrom.* 1998; **9**: 454.
36. Munson MSB, Field FH. *J. Am. Chem. Soc.* 1967; **89**: 1047.
37. Benoit FM, Harrison AG. *Org. Mass Spectrom.* 1976; **11**: 599.
38. Kingston DG. *Chem. Rev.* 1974; **74**: 215.
39. Gamble AA, Gilbert JR, Tillett JG. *Org. Mass Spectrom.* 1971; **5**: 1093.