Synthesis of 2,3- and 3,4-methylenedioxyphenylalkylamines and their regioisomeric differentiation by mass spectral analysis using GC-MS-MS

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Abstract

3,4-methylenedioxyamphetamine (MDA) derivatives are increasingly abused central nervous system stimulants with neurotoxic properties. In recent years a number of controlled substance analogs (designer drugs) with high structural variety reached the illegal market making their identification an arduous task. The underivatized compounds give very similar or even virtually identical electron impact mass spectra containing mainly intense $C_nH_{2n+2}N^+$ immonium ions. Using tandem mass spectrometry (MS-MS) the additional structural information contained in the collision induced dissoziation (CID) mass spectra of molecular ions using electron impact (EI) and especially chemical ionization (CI) allowed an unequivocal differentiation of 18 studied regioisomeric 1-(methylenedioxyphenyl)-2-propanamines and 1-(methylenedioxyphenyl)-2-butanamines.

Further synthetic methods are presented for 1-(3,4-methylenedioxyphenyl)-N-propyl-2-butanamine, N-isopropyl-1-(3,4-methylenedioxyphenyl)-2-butanamine and four 1-(2,3-methylenedioxyphenyl)-2-butanamine compounds (e.g. MBDB) are also known to be abused psychoactive agents (entactogenes) without the sympatomimetic effects of the 3,4-methylenedioxyamphetamine.

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1. Introduction

The detection and identification of unknown drugs is usually performed by gas chromatography-mass spectrometry (GC-MS) due to the high sensitivity and ability of this method to separate organic compounds in complex mixtures. Using electron impact (EI) this technique is often insufficient to discriminate between structurally closely related phenethylamine drug variants because of their often virtually identical mass spectra with extremely poor molecular and fragment ions [1–4]. This seriously affects the ability to detect novel amphetamine controlled substance analogs [5] which often have neurotoxic properties [6].

Some phenylethylamines such as 1-(3,4-methylenedioxyphenyl)-2-propanamine derivatives (see Fig. 1, 2a–2d) are increasingly abused psychoactive drugs and well documented in the literature [3]. The most popular compound of the various clandestine pro-
Products is N-methyl-3,4-methylenedioxyamphetamine (MDMA; 2b), also known as Ecstasy. The continuing designer drug exploration of the homologous series and their widespread consumption results in an increasing number of reports regarding abuse and intoxication [7]. Some of these novel 3,4-methylenedioxyphenylamphetamine have a complete different psychoactive spectrum [8] compared to the classical hallucinogenic amphetamines and rather induce facilitated communication and introspective states [9–15]. These compounds were described as representing a new pharmacological class, the entactogenes [16].

Phenylethylamine derivatives with a 1-(3,4-methylenedioxyphenyl)-2-butanamine structure (Fig. 1, 4a–4f) produce emphasizing and enhancing effects on empathy without any sympathomimetic side effects of the amphetamines with a 2-propanamine substructure (Fig. 1, 1a–1d, 2a–2d) [16].

The differentiation of some methylenedioxyamphetamine was only achieved by means of derivatization like acetylation and various chromatographic methods [17–19].

Rösner et al. reported the structural elucidation of the alkyl group attached to the α-C-atom and to the nitrogen and α-position of phenylethylamine drug variants by GC-MS-MS [5,20] without using a masking derivatization of the original structure.

Our intention was to identify and differentiate 18 regioisomeric 1-(methylenedioxyphenyl)-2-propanamines (Fig. 1; 1a–1d, 2a–2d) and 1-(methylenedioxyphenyl)-2-butanamines (Fig. 1; 3a–3d, 4a–4f). In the following the methodical synthesis of four 1-(2,3-methylenedioxyphenyl)-2-butanamine derivatives (3a–3d) is presented. The differentiation of regioisomeric 2-propanamine and 2-butanamine derivatives using the additional information contained in the collision-induced dissociation (CID) mass spectra by GC-MS-MS is described. CID mass spectra are obtained by parent ions colliding with an inert gas during the passage through the reaction chamber of a tandem mass spectrometer (MS-MS). During this collision a part of the translational energy of the parent ion is converted into internal energy allowing to overcome higher energy barriers. This leads to new

Fig. 1. Chemical structures of the analyzed methylenedioxyphenylalkylamine derivatives.
analytically valuable reaction channels. The resulting decomposed ions form the CID mass spectrum. All fragment ion spectra were recorded under standardized operating conditions using n-butylbenzene as a reference compound to adjust collision energy and collision gas pressure as described in the literature [20].

2. Instrumentation

GC-MS: electron impact mass spectra were obtained with a Finnigan TSQ 70 (Finnigan MAT, Bremen) with a DEC-Station 2100, coupled to a Varian 3400 CX gas chromatograph. A fused silica capillary column DB1 (30 m×0.32 mm, thickness 0.25 μm) was used. The temperature program consisted of an initial temperature of 80°C held for 1 min, followed by a linear ramp to 280°C at 15°C/min. The final temperature was held for 15 min. The split/splitless injector and detector temperature were 280°C, the carrier gas was helium. EI-mode: ionization voltage 70 eV, scantime 1 s, scan range: 40–600 Da.

CI-mode: ionization voltage 70 eV, source temperature 150°C, reactant gas: methane, source pressure: 0.2 Pa, scantime: 1 s, scan range: 60–600 Da.

MS-MS: ionization voltage 70 eV, collision gas: argon, collision energy 22 eV, collision gas pressure: 0.2 Pa. The exact target thickness was regulated by the intensity quotient of the peaks 92/91 (0.2) and 91/65 (20) of n-butylbenzene.

2.1. Materials

2,3-Propanamine derivatives (1a–1d) were synthesized according to Casale and co-workers [21], the 3,4-isomers (2a–2d) were kindly provided from the reference collection of the Landeskriminalamt (LKA) Schleswig-Holstein, Germany. 3,4-Butanamine derivatives (4a–4d) were synthesized according to Noggle and co-workers [2].

2,3-Methylenedioxybenzaldehyde and lithium aluminium hydride were obtained from Aldrich Chemical Co. KG. (Steinheim, Germany). All other chemicals and solvents were from E. Merck (Darmstadt, Germany) and were of reagent grade or better quality.

2.2. Synthesis

2.2.1. Preparation of β-ethyl-2,3-methylenedioxy-β-nitrostyrene (6)

2,3-Methylenedioxybenzaldehyde (5) (3.0 g, 22 mmol), nitropropane (3.0 g, 34 mmol) and cyclohexylamine (2.2 g, 22 mmol) were dissolved in 20 ml of glacial acetic acid and heated to 95°C. After 6 h, the hot, yellow-brown solution was poured on crushed ice, stirred and acidified with concentrated HCl, whereby the crude product precipitated. Recrystallization from isopropanol provided 2.3 g (47% yield) of the nitrostyrene as bright yellow crystals. mp: 62°C.

1H NMR (300 MHz, CDCl3): 7.97 (s, 1H, CH); 6.88 (m, 3H, aromatic CH); 6.03 (s, 2H, OCH2O); 2.89–2.84 (q, J=7.3 Hz, 2H, CH2); 1.27–1.22 (t, J=7.3 Hz, 3H, CH3). 13C NMR (75 MHz, CDCl3): 153.98; 147.85; 146.88; 126.25; 122.10; 121.31; 114.53; 109.98; 101.40; 21.20; 12.28. Anal. calc. for C11H11NO4 (221.21): C 59.70, H 4.98, N 6.30; found: C 60.08, H 4.91, N 6.26.

2.2.2. Preparation of 1-(2,3-methylenedioxyphenyl)-2-butanamine hydrochloride (3a·HCl)

A solution of 2,3-methylenedioxy-β-ethyl-β-nitrostyrene (3.7 g, 17 mmol) in 20 ml of THF was added for 30 min to a solution of LiAlH4 (4.2 g, 110 mmol) in 50 ml of THF and then heated to reflux. After 5 h, the excess LiAlH4 was quenched with dropwise water and the precipitated inorganic salts were removed via suction filtration. The filtrate was evaporated in vacuo to a yellow oil which was treated with etheral HCl and white crystals precipitated to give 2.8 g (85% yield) of 3a·HCl. mp: 168°C.

1H NMR (300 MHz, d6DMSO): 8.28 (br, 3H, NH3); 6.84–6.76 (m, 3H, aromatic CH); 6.01 (s, 2H, OCH2O); 3.31 (m, 1H, CH); 2.96–2.77 (AB-part of an ABX system, 3JAX=5.7 Hz, 3JBX=8.5 Hz, 2J=13.9 Hz, 2H, CH2CH3); 1.59–1.50 (m, 2H, CH2CH3); 0.94–0.89 (t, J=7.4 Hz, 3H, CH3). 13C NMR (75 MHz, d6DMSO): 146.90; 145.73; 123.16; 121.72; 117.88; 107.29; 100.63; 51.83; 31.81; 24.40; 9.33. Anal. calc. for C11H16NO2Cl (229.69): C 57.50, H 6.97, N 6.10; found: C 57.82, H 7.14, N 6.12.

2.2.3. Preparation of N-formyl-1-(2,3-methylenedioxyphenyl)-2-butanamine (7)

A solution of 3a (2.24 g, 12 mmol) and 1.0 ml of formic acid 98% (1.0 g, 22 mmol) were added to
100 ml of toluene and heated to reflux with a soxhlet containing 4 Å molecular sieve. After 48 h the resulting solution was evaporated in vacuo to give a colored oil, which was dissolved in 100 ml of dichloromethane and washed several times with dilute HCl. The organic layer was dried over anhydrous sodium sulfate and evaporated in vacuo to give 2.1 g (82% yield) of N-formyl-1-(2,3-methylenedioxyphenyl)-2-butanamine as a yellow oil.

2.2.4. Preparation of N-methyl-1-(2,3-methylenedioxyphenyl)-2-butanamine hydrochloride (3b-HCl)

A solution of 7 (2.0 g, 9 mmol) in 10 ml of THF was added over 15 min to 60 ml of a solution of 2.28 g LiAlH₄ in THF and heated to reflux. After 4.5 h the excess LiAlH₄ was quenched dropwise with water in the usual manner. The oil was dissolved in dilute HCl and washed with dichloromethane, alkalinized with concentrated NaOH and then extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate and evaporated in vacuo to a light yellow oil, which was diluted with ethereal HCl to give 0.8 g (41% yield) 3b-HCl. mp 139°C. ³¹H NMR (300 MHz, d₆DMSO): 9.13 (br, 2H, NCH₂); 6.85–6.72 (m, 3H, aromatic CH); 5.95 (s, 2H, OCH₂O); 3.33–3.29 (m, 1H, CH); 3.07–2.88 (AB-part of an ABX system, 3JAₓ=4.7 Hz, 3JBₓ=9.2 Hz, 3JCₓ=14.48 Hz, 2J=14 Hz, 2H, CH₂CH); 2.56 (s, 3H, NCH₃); 1.66–1.53 (m, 2H, CH₂CH₃); 0.93–0.88 (t, J=7.4 Hz, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): 146.84; 145.62; 122.97; 121.74; 117.83; 107.26; 100.61; 58.78; 29.82; 29.03; 22.04; 8.79. Anal. calc. for C₁₃H₂₀NO₆Cl (321.76): C 48.70, H 6.34, N 4.67. Found: C 48.53, H 6.26, N 4.35.

2.2.5. Preparation of N-acetyl-1-(2,3-methylenedioxyphenyl)-2-butanamine (8)

A solution of 3a (1.0 g, 6.2 mmol) in 2 ml of acetic anhydride (1.16 g, 11 mmol) was heated in a 10 ml glass tube to 75°C with continuous stirring. After 24 h the cooled mixture was dissolved in 30 ml of dichloromethane, washed several times with dilute HCl, dilute NaOH, water and then dried over anhydrous sodium sulfate. Evaporation under vacuum afforded 1.0 g (82% yield) of N-acetyl-1-(2,3-methylenedioxyphenyl)-2-butanamine as an amber solid. mp: 93°C.

2.2.6. Preparation of N-ethyl-1-(2,3-methylenedioxyphenyl)-2-butanamine perchlorate (3c-HClO₄)

A solution of 8 (1.0 g, 4.3 mmol) in 10 ml of THF was added for 5 min to a solution of LiAlH₄ (0.6 g, 15.8 mmol) in 20 ml of THF and heated to reflux. After 3.5 h the excess LiAlH₄ was quenched in the usual manner. The extracted oil was evaporated in vacuo to a light yellow oil, which was dissolved in a solution of isopropanol, concentrated perchloric acid and diethyl ether (3:1:20) to get a spontaneous crystallization of 0.5 g (53% yield) 3c-HClO₄. mp: 126°C. ¹H NMR (300 MHz, CD₃OD): 6.85–6.72 (m, 3H, aromatic CH); 5.95 (s, 2H, OCH₂O); 3.50–3.42 (m, 1H, CH); 3.07–2.88 (AB-part of an ABX system, 3JAₓ=5.6 Hz, 3JBₓ=8.2 Hz, 3JCₓ=14.3 Hz, 2H, CH₂CH); 1.72–1.62 (q, J=7.4 Hz, 2H, CH₂CH₃); 1.32–1.27 (t, J=7.1 Hz, 3H, NCH₂CH₃); 1.02–0.97 (t, J=7.4 Hz, 3H, CH₂CH₃). ¹³C NMR (75 MHz, CDCl₃): 146.51; 145.48; 123.21; 121.10; 120.73; 106.22; 100.16; 58.30; 40.58; 33.53; 25.76; 15.40; 9.44. Anal. calc. for C₁₃H₂₀NO₆Cl (321.76): C 48.53, H 6.26, N 4.35; found: C 48.70, H 6.34, N 4.67.
NMR (75 MHz, CD3OD): 149.05; 147.33; 124.06; 123.44; 118.43; 108.94; 102.39; 68.76; 40.82; 40.00; 29.70; 23.26; 10.76. Anal. calc. for C13H19NO2Cl (271.31): C 61.74, H 7.93, N 5.39. Found: C 61.46, H 8.08, N 5.17.

2.2.8. Preparation of 1-(3,4-methylenedioxyphenyl)-N-propyl-2-butanamine hydrochloride (4e·HCl)

The synthesis scheme from Noggle [2] with conversion of the nitrostyrene in a ketone followed by reductive amination with the corresponding alkylation or chloridation chloride was employed starting with 9-propylamine (140 mmol). The oil was treated with ethereal hydrochloric acid to get spontaneous crystallization of 1.4 g (52%) 4e·HCl. mp: 137 °C. 1H NMR (300 MHz, d6DMSO): 8.55 (br, 2H, NH2); 6.91–6.73 (m, 3H, aromatic CH); 6.05 (s, 2H, OCH2O); 3.35–3.29 (m, 1H, AB-part of an ABX system, 3JAB=9.07 Hz, 3JAX=7.64 Hz, 3JBX= 13.29 Hz, 2H, CH2CH(CH3)); 1.58 (m, 2H, CH2CH3); 1.28 (m, 6H, CHCH2CH3); 0.92–0.88 (t, J=7.2 Hz, 3H, CH3). 13C NMR (75 MHz, d6DMSO): 147.36; 145.90; 130.77; 122.22; 109.38; 108.20; 100.84; 56.53; 56.50; 47.30; 22.08; 18.62; 8.87. Anal. calc. for C14H22NO2Cl (271.78): C 61.99, H 8.10, N 5.10; found: C 61.46, H 8.08, N 5.17.

3. Results and discussion

The 3,4-methylenedioxyphenyl-2-butynamines may be readily prepared via a number of synthetic routes [2]. However, the preparation of 4e and 4f and of all 2,3-butanamine derivatives (3a–3d) have not been described previously.

The general synthetic scheme for the preparation of the 2,3-(methylenedioxyphenyl)-2-butynamine isomers (3a–3d) is presented in Scheme 1. In summary, 2,3-Methylenedioxybenzaldehyde was condensed with nitropropane to give β-ethyl-2,3-methylenedioxy-β-nitrostyrene. Reduction with LiAlH4 gave 1-(2,3-methylenedioxyphenyl)-2-butamine (3a). Formylation, acetylation and subsequent reduction turned it to N-methyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3b) and N-ethyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3c). N,N-dimethyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3d) was prepared from 3a by reduction of the formimine and the following formylation and reduction of the N-methylformamid. All compounds were isolated as their hydrochloride or perchlorate salts. The purity of each product was controlled by GC and exceeded 97%.

The preparation of N-alkylated amines followed a trend of decreasing yields: 1-(2,3-methylenedioxyphenyl)-2-butamine (3a)= 82%, N-methyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3b)= 41%, N-ethyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3c)= 53%, N,N-dimethyl-1-(2,3-methylenedioxyphenyl)-2-butamine (3d)= 5%; the results suggest that steric hindrance plays a significant role in the overall stabilities of N-substituted compounds.

For the preparation of 4e the synthesis scheme from Noggle [2] was extended to n-propylamine. The analog synthesis of 4f with isopropylamine failed. 4f was therefore synthesized by reduction of the condensation product of 4a with acetone.
3.1. Mass spectrometry

A mixture consisting of all the compounds except 1d and 2d shown in Fig. 1 was analyzed by gas chromatography (GC) and the insufficient separation of the isomers due to their structural similarities is presented in the total ion chromatogram (Fig. 2). As can be seen in Fig. 2 several compounds (e.g. 3a and 1c or 4a, 2c and 3b) are coeluted. Using conventional EI mass spectrometry the compounds under investigation showed very similar spectra with a dominant immonium ion base peak and only few minor peaks making a differentiation of regiosomeric compounds by this method alone is impossible.

In general the molecular ion CID mass spectra using EI are distinct (Figs. 3–6). In case of compounds 4e and 4f the molecular ions did not have sufficient intensity for recording daughter ion mass spectra.

Therefore, the CI-CID protonated molecule mass spectra are superior with respect to applicability and sensitivity allowing lower limits of detection.

3.2. Spectral interpretation

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

As the EI mass spectra the EI-CID mass spectra (Fig. 3) of the 2,3-propanamines are dominated by immonium base peak ions with the general formula \( \text{C}_n \text{H}_{2n-2} \text{N}^+ \) (m/z: 44, 58, 72, etc.) resulting from an \( \alpha \)-cleavage reaction (Scheme 2). In contrast the

\[ \text{R}_3 \]
\[ \text{R}_1 \]
\[ \text{R}_2 \]

Scheme 2. The electron-donating ability of the nitrogen atom induces an \( \alpha \)-cleavage reaction (\( \alpha \)) and produces an immonium ion.

Therefore, the CI-CID protonated molecule mass spectra are superior with respect to applicability and sensitivity allowing lower limits of detection.
Fig. 2. GC total ion chromatogram of the mixture of 16 studied compounds (1a–1c, 2a–2c, 3a–3d, 4a–4f). Column: fused silica capillary column DB1 (30 m×0.32 mm, thickness 0.25 μm). Carrier gas: He. Temperature: 1.0 min at 80°C, then to 280°C at 15°C/min. Scantime: 1 s.
3,4-propanamine EI-CID mass spectra (Fig. 4) show significant or base peaks ions at \( m/z \) 136.

This odd electron ion could be formed by a rearrangement of nitrogen H-atoms to the aromatic part eliminating R-CH=NR\(_1\) (Scheme 3A) [22] as shown by many phenylethylamine derivatives. \( m/z \) 136 could also be generated by the well known specific six-centre H-rearrangement (rH) of a \( \gamma \)-H-atom of the alkyl side chain to the aromatic part [23] eliminating a neutral enamine (Scheme 3B). This or analogous processes might be suppressed in 2,3-methylenedioxyphenyl-2-propanamines (1a–1d) by an intramolecular stabilization of the amino group and the ether oxygen in \textit{ortho} position (Fig. 7). Further a statistical

Fig. 3. Low energy EI-CID molecular ion mass spectra of 1-(2,3-methylenedioxyphenyl)-2-propanamines (1a–1d).

Fig. 4. Low energy EI-CID molecular ion mass spectra of 1-(3,4-methylenedioxyphenyl)-2-propanamines (2a–2d).
effect would disfavor H-rearrangements (rH) in 2,3-methylenedioxyphenyl-2-propanamines (1a–1d) which have only one free ortho position.

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

The CI-CID mass spectra of 2,3-propanamines (Fig. 8) show in general less complex fragmentation patterns compared with the 3,4-propanamines (Fig. 9). This could be due to a stabilization by intramolecular hydrogen bonding of an ammonium hydrogen with the ortho ether oxygen.

Both regioisomers generate a very intense or base peak ion at m/z 135 (Figs. 8 and 9). From our investigations it is known that besides a direct inductive cleavage of the benzyl bond by the charge of the ammonium cation a two-step fragmentation process could be discussed [24]. An amine elimination gives a
Scheme 3. 3,4-Propanamine and 3,4-butanamine derivatives (2, 4) show an enamine and an imine loss due to γ-H-atom rearrangements (rH) of both the nitrogen H-atom (A) and the H-atom of the alkyl side chain (B) followed by an α-cleavage of the benzyl bond producing ions with m/z 136.
homobenzyl cation (m/z 163) which eliminates an alkene after an H-rearrangement (rH) and an inductive cleavage reaction [22]. Only the 2,3-propanamine regioisomers (1a–1d) form a significant ion at m/z 123, which therefore is an indicator for the 2,3-methylenedioxy substitution pattern. On the other hand, the 3,4-methylenedioxyphenyl-2-propanamines generate a significant ion at m/z 137 which is missing or has very low intensity in the CI-CID mass spectra of the 2,3-methylenedioxyphenyl-2-propanamines. This ion is formed by an oxygen protonated species and a six-centered H-rearrangement (rH) of a γ-H-atom of the alkyl side chain to the aromatic part (Scheme 4) [22,25]. In 2,3-propanamines, this process might be hindered by the already discussed intramolecular stabilization between the ammonium group and the *ortho* ether oxygen as well as the unfavorable statistical effect. The significant ion with m/z 137 therefore is an indicator for the 3,4-methylenedioxy substitution pattern.

Thus, the two ions at m/z 123 and m/z 137 allow the structural assignment to the 2,3-substituted and 3,4-substituted phenylethylamines, respectively.

### 3.2.3. EI-CID mass spectra of 2,3- and 3,4-butanamine derivatives

The EI-CID mass spectra (Fig. 5) of the 2,3-methylenedioxyphenyl-2-butanamine derivatives (3a–3d) show an immonium base peak ion. The isomeric 3,4-butanamines 4a and 4b produce a base peak ion at m/z 136, formed by the same mechanism already discussed for the 3,4-propanamines (Scheme 3). Thus, the base peak with m/z 136 is an indicator for the 3,4-substitution pattern of 4a and 4b. The compounds 4c and 4d generate immonium ion as base peaks (Fig. 6), whereas 4e and 4f do not form molecular M⁺ ions with sufficient intensity for recording EI-CID mass spectra.

### 3.2.4. CI-CID mass spectra of 2,3- and 3,4-butanamine derivatives

The CI-CID mass spectra of all regioisomeric butanamine derivatives (Figs. 10 and 11) show a base peak ion at m/z 135 according to the same amine elimination discussed for the 3,4-propanamines. Only the 2,3-butanamines, except 3d, show the same characteristic peak as the 2,3-propanamines at m/z 123. This ion is

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**Fig. 7.** Stabilization of the conformation of the 2,3-propanamine and 2,3-butanamine derivatives (1, 3) due to the amino group and the oxonium ion.

**Scheme 4.** 3,4-Propanamine and 3,4-butanamine derivatives (2, 4) show an enamine loss probably due to a γ-H-atom rearrangement (rH) followed by an induced cleavage of the benzyl bond producing an ion with m/z 137.
therefore specific for the 2,3-methylenedioxy substitution pattern as well in 2,3-propanamines as in 2,3-butanamines. In the same way the 3,4-regioisomers form a significant fragment at \( m/z \) 137, which is specific for the 3,4-methylenedioxy substitution pattern.

3.3. Comparison of EI- and CI-CID mass spectra

Using EI-CID molecular ion mass spectrometry all 2,3- and 3,4-propanamine (1a–2d) derivatives show the same characteristics as their butanamine homologs (3a–4d). All 2,3-isomers show an immonium ion
basepeak, whereas the 3,4-isomers show a basepeak at m/z 136, except for 4c and both N,N-dimethylated derivatives 2d and 4d. This difference might be explainable by the high N-alkylation grade disfavoring steric pretensions rearrangements (Scheme 3). The immonium ions and the ion at m/z 136 are important indicators for the identification of the regioisomers. In general, the CI-CID molecular ion mass spectra of the both regioisomeric propanamine compounds

Fig. 10. Low energy CI-CID mass spectra of 1-(2,3-methylene-dioxyphenyl)-2-butanamines (3a–3d).

Fig. 11. Low energy CI-CID mass spectra of 1-(3,4-methylene-dioxyphenyl)-2-butanamines (4a–4f).
show a more complex fragmentation pattern as the spectra of the regioisomeric homologue butanamine compounds. The ion \( m/z \) 123 indicates the 2,3-methylenedioxy substructure and the ion \( m/z \) 137 the isomeric 3,4-methylenedioxy substitution pattern. However, the 2,3-\(N\)-dimethylated compounds do not form a fragment with \( m/z \) 123.

Using CI-CID an unequivocal identification of all studied compounds is possible. Only the CI gives protonated molecular ions \([M+H]^+\) of sufficient intensity and has clearly advantages compared with EI-CID mass spectrometry.

4. Conclusion

The CID mass spectra of the (pseudo) molecular ions of compounds 1a–4f using EI and CI ionization show analytically valuable fragmentation processes. Because of the general much higher intensity of the protonated molecules \([M+H]^+\) during CI with respect to \([M]^+\) ions the CI-CID mass spectrometry has a general superior sensitivity for the detection of lower substance levels. The specific fragmentations of the compounds allow an unequivocal identification and differentiation of all studied homologs and regioisomers under investigation.

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