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ORIGINAL ARTICLE

Identification of new NBOH drugs in seized blotter papers: 25B-NBOH, 25C-NBOH, and 25E-NBOH

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Abstract

Purpose The recreational drug market remains dynamic. After the introduction of 25I-NBOH, an *N*-benzylphenethylamine and new psychoactive substance, as option for LSD and NBOMe drugs, new NBOH substances have been identified in recent years. Herein, we report our efforts for the identification and structural elucidation of three new NBOHs detected in seized blotter papers: 25B-NBOH, 25C-NBOH, and 25E-NBOH.

Methods Blotter papers seized between 2017 and 2018 by local police force in Brazil were submitted to extraction, purification, identification and characterization using attenuated total reflectance-Fourier transform infrared spectroscopy, gas chromatography—mass spectrometry, liquid chromatography—tandem mass spectrometry, and one- and two-dimensional nuclear magnetic resonance spectroscopy.

Results Three new NBOHs were characterized: 2-(((4-ethyl-2,5-dimethoxyphenethyl)amino)methyl)phenol (25E-NBOH, 2C-E-NBOH), 2-(((4-chloro-2,5-dimethoxyphenethyl)amino)methyl)phenol (25C-NBOH, 2C-C-NBOH), and 2-(((4-bromo-2,5-dimethoxyphenethyl)amino)methyl)phenol (25B-NBOH, 2C-B-NBOH).

Conclusions To our knowledge, this is the first report for identification and detailed characterization of 25B-NBOH, 25C-NBOH, and 25E-NBOH in seized samples. NBOH substances are not under United Nations Conventions control. The identification of seized blotter papers between 2014 and beginning of 2019 showed that NBOH substances have become the main hallucinogenic drug in the region. These group are thermolabile under gas chromatographic conditions, demanding other analytical approaches of analysis to avoid misidentifications. Unfortunately, the knowledge about toxicology of NBOHs are limited.

Keywords NBOH · 5-HT_{2A} receptor agonist · New psychoactive substances · Phenethylamines · Seized material · Chemical characterization

Introduction

New psychoactive substances (NPS) have become a global and continuously growing phenomenon over the last decade, posing a risk to public health while remaining a challenge to law enforcement agencies [1, 2]. From 2009 to 2017, over 800 NPS have been reported in 111 countries and territories, most of them being classified as phenethylamines, synthetic cathinones or synthetic cannabinoids [3].

Phenethylamines are agonists of the serotonin (5-HT, 5-hydroxytryptamine) receptors [4]. The *N*-benzyl substitution in phenethylamines (usually from the 2C-X family, such as 2C-I and 2C-B) improve the binding and functional activity in 5-HT receptors, with *N*-(2-hydroxybenzyl) substituted substances usually presenting the highest affinities to the 5-HT_{2A} receptor [4–6].

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Since 2015, a new NPS group based on *N*-benzyl-2,5-dimethoxyphenethylamines (Fig. 1), commonly described as NBOHs, emerged as recreational drugs. NBOHs, substances structurally closely related to NBOMes, are usually found on blotter papers and have become an option for LSD (lysergic acid diethylamide) users. Self-reported use of NBOHs has been reported in United States [7], Australia [8], and Germany [9]. These substances were already identified for street samples seized in Brazil [10], Finland, Germany, and Slovenia [11].

Like most NPS, knowledge about the toxicology of NBOHs is very limited or virtually nonexistent. According to information gathered from user forums (not to be considered as canon), the effects include tachycardia, and auditory and visual hallucinations [12, 13]. While both NBOHs and NBOMes apparently taste bitter, thus providing a simple way for users to distinguish them from LSD [14], NBOHs are reported to induce weaker effects and to last less than NBOMes, being unaccompanied with "body load", an unpleasant physical sensation reported by drug users [14].

Together with usual difficulties associated with the identification of NPS (unknown substance, never before reported, not present in reference spectral libraries, no certified standards available, etc), detection of NBOHs present yet another important trait: thermal degradation under standard gas chromatography, which seriously increases the risk of misidentification [15, 16] and demands the development of other detection methods [17–21].

Herein, we report our efforts for the identification and structural elucidation of three new NBOHs detected in seized samples submitted to our forensic laboratory: 25B-NBOH, 25C-NBOH and 25E-NBOH.

Materials and methods

Chemicals and reagents

Acetone, chloroform, diethyl ether, methanol, sodium hydroxide, and hydrochloric acid were purchased from Synth (Diadema, SP, Brazil); methanol LC grade from Merck (Darmstadt, Germany); ammonium formate and methanol-d_4 with 99.8% isotopic purity, containing 0.03% (v/v) tetramethylsilane (TMS), from Sigma-Aldrich (St. Louis, MO, USA); the ultrapure water from Milipore Direct Q3 (Billerica, MA, USA); silica gel 60 (70–230 mesh) from Merck.

Samples and extraction

Blotter papers suspected to contain illicit substances were seized between 2017 and 2018 by police forces from Minas Gerais. These blotters usually represented a colorful side

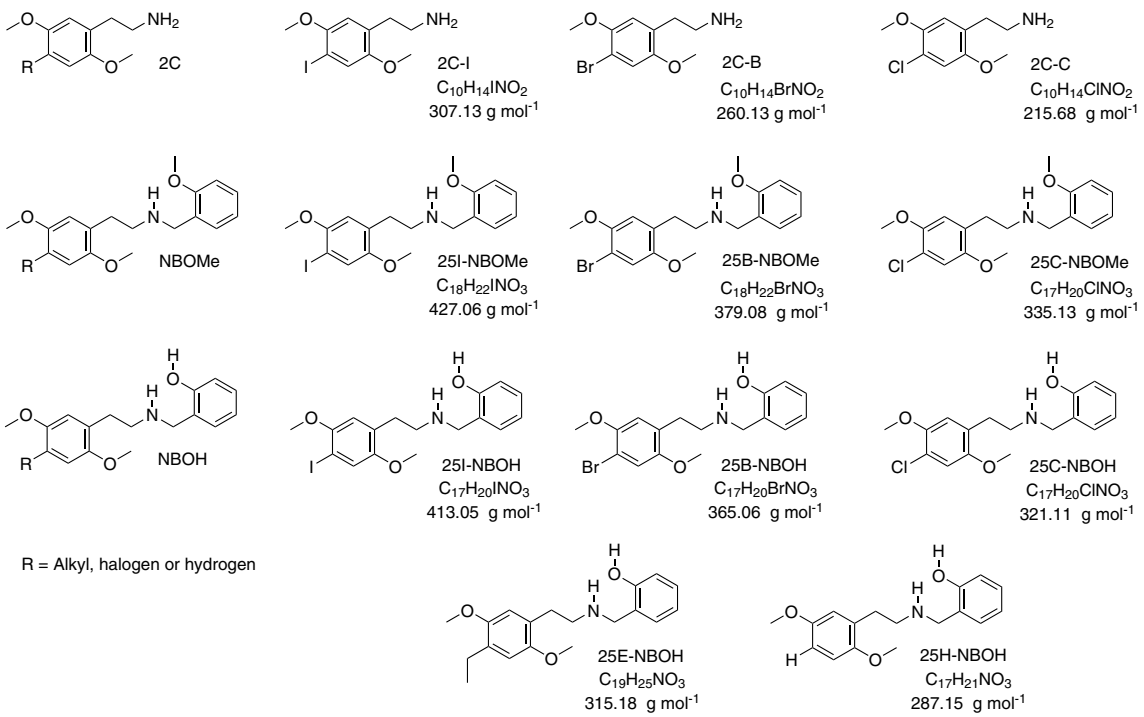


Fig. 1 Structures of *N*-benzylphenethylamines: *2Cs*, 2C-I, 2C-B, and 2C-C; *NBOMes* 25I-NBOMe, 25B-NBOMe, and 25C-NBOMe; *NBOHs* 25I-NBOH, 25B-NBOH, 25C-NBOH, 25H-NBOH, and 25E-NBOH

including drawings of cartoon and game characters, scientists, deities, etc. and a white side (Fig. 2). The samples were grouped according to previous routine analysis, such as gas chromatography–mass spectrometry (GC–MS) and liquid chromatography–tandem mass spectrometry (LC–MS/MS), as follows: one hundred blotter papers for samples named as **01** and **02**, and twenty-five blotter papers for sample named as **03**.

Each sample group (**01**, **02**, and **03**) was submitted to three successive extractions: 30 mL of chloroform (2 ×) and 30 mL of methanol in beakers by 20 min in magnetic stirrer. After mixing the 90 mL of solvent extracted, 1 mL of NaOH solution (1%, w/v) was added. Each solution was evaporated to dryness getting a solid reddish residue. Each residue was submitted to column chromatography using silica gel as stationary phase. The elution was performed with chloroform, acetone, and methanol, in increasing polarity order, providing the corresponding fractions. The acetone fraction was evaporated to dryness and 20 mL of saturated solution of hydrochloric acid in diethyl ether was added to the residue, providing, after new evaporation to dryness, a beige solid labeled as compound **01** (15.1 mg), compound **02** (13.3 mg), and compound **03** (4.5 mg).

Instrumentation

Attenuated total reflectance Fourier transform infrared spectroscopy analysis

Attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) analyses were performed directly from the solids, except for compound **03** due to the small amount available. They were obtained using a NicoletTM iZ10 spectrometer equipped with EverGlo infrared (IR) source, DLaTGS room temperature IR detector under N_2 purge and single-bounce Smart Orbit^{TM} accessory module with diamond ATR crystal (Thermo Fischer Scientific, Madison, WI, USA). Each spectrum was averaged over 16 scans, taken at 4 cm^{-1} resolution, with maximum detector window aperture and minimum interferometer mirror speed, in the range of 400–4000 cm^{-1}.

Gas chromatography–mass spectrometry analysis

Samples were prepared by transferring 1 mg of solid to a microcentrifuge tube and adding 1 mL of LC grade methanol. Each solution was transferred to a vial for analysis. Analysis were performed on an Agilent GC 7890A (Agilent Technologies, Santa Clara, CA, USA) coupled with an Agilent XL MSD 5975C quadrupole mass spectrometer. The chromatographic separation was performed with a 433 HP-1MS capillary column (30 m × 0.25 mm, i.d., film thickness 0.25 µm; Agilent Technologies). A volume of 1 µL of the sample solution was injected with a split ratio of 20:1. Helium was used as carrier gas with a constant flow of 1.0 mL min^{-1}. The temperature of injector and the GC–MS interface was set at 280 and 300 °C, respectively. The oven temperature was initially maintained at 150 °C for 1.5 min; increased to 250 °C at 30 °C min^{-1} and maintained for 1 min; increased to 300 °C at 50 °C min^{-1} and maintained for 3 min (total run time: 11.8 min). The solvent delay was set to 1.5 min. The mass scan range was set to *m/z* 35–550.

Fig. 2 Appearances of blotter papers containing illicit substances

Liquid chromatography coupled to tandem mass spectrometry analysis

LC–MS/MS analyses were performed on a Prominence UFLC system (Shimadzu Corporation, Kyoto, Japan) coupled with a Shimadzu LCMS 8030 triple quadrupole mass spectrometer with electrospray ionization source (ESI) set in the positive ionization mode. LabSolutions™ (Shimadzu Corporation) was used for data acquisition and processing.

Direct flow injections were performed with a total flow rate of 0.4 mL min^{-1}. The mobile phase consisted of 50% of ultra-pure water (A) and 50% of acetonitrile (B), both containing ammonium formate (0.024%, w/v). The injection volume was 1 µL and the total run time was 1 min.

The MS conditions were as follows: desolvation line temperature, 250 °C; heat block temperature, 400 °C; nebulizing gas flow, 3 L min^{-1}; drying gas flow, 15 L min^{-1}; collision-induced dissociation (CID) gas pressure, 230 kPa; dwell time, 100 ms; and interface voltage, 4.5 kV. A Q3 full scan were set from *m/z* 110 to 500 to seek out the protonated molecule ($[M+H]^+$), and product ion scan (PIS) were performed with collision energies of − 10, − 20, − 30, and − 40 eV for the purpose of analyzing the fragmentation pattern.

Nuclear magnetic ressonance spectroscopy analysis

The nuclear magnetic resonance (NMR) experiment was conducted using 12 mg of compound **01**, 12 mg of compound **02** and 3.5 mg of compound **03**. Each solid was dissolved in 0.6 mL methanol-d_4 with tetramethylsilane (TMS) as internal standard. ^{1}H, ^{13}C, DEPT 135 (Distortionless Enhancement by Polarization Transfer), HSQC (Heteronuclear Single Quantum Coherence) and HMBC (Heteronuclear Multiple-Bond Correlation) experiments were recorded using a Bruker Avance DRX 600 MHz spectrometer (Bruker, Ettlingen, Germany). Acquisition was conducted by TopSpin software 4.0.6 version (Bruker) and processing was conduct by MestReNova 12.0 (MestreLab Research, Santiago de Compostela, Spain).

Results

ATR-FTIR analysis

ATR-FTIR spectra of compounds **01** and **02** indicated the presence of small impurities that were not eliminated during the purification processes. The single infrared spectral profile analysis using available forensic libraries (SWGDRUG and Europe Response infrared library) indicated presence of signals matching with NBOH drugs [22, 23]. Interpretation of the ATR-FTIR spectra indicated the same findings from our previous work [15]: the higher degree of similarity with 25R-NBOMe when compared with 2C-R and a systematic decrease of the spectral band centered around 1250 cm^{-1}, characteristic of asymmetric C–O–C vibrations of NBOMe compounds, indicating the substitution of OCH_3 by OH (Fig. 3).

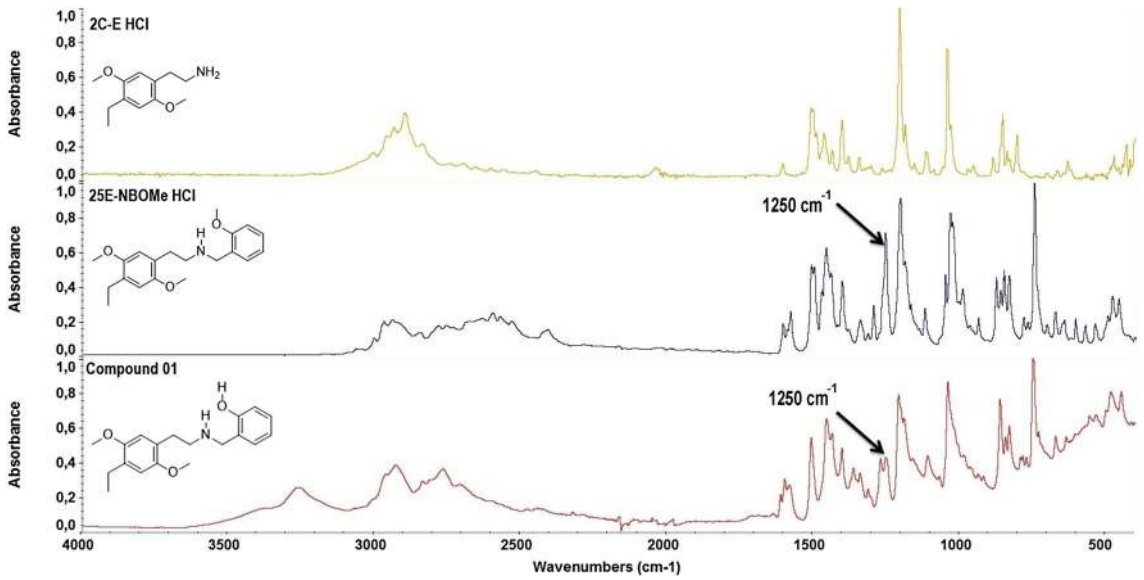


Fig. 3 Comparison of infrared (IR) spectrograms for 2C-E (from SWGDRUG IR library), 25E-NBOMe (from SWGDRUG IR Library version 2.0), and compound **01**, identified as 25E-NBOH. The arrows show the decrease of spectral band indicating the substitution of OCH_3 by OH in the 25E-NBOH

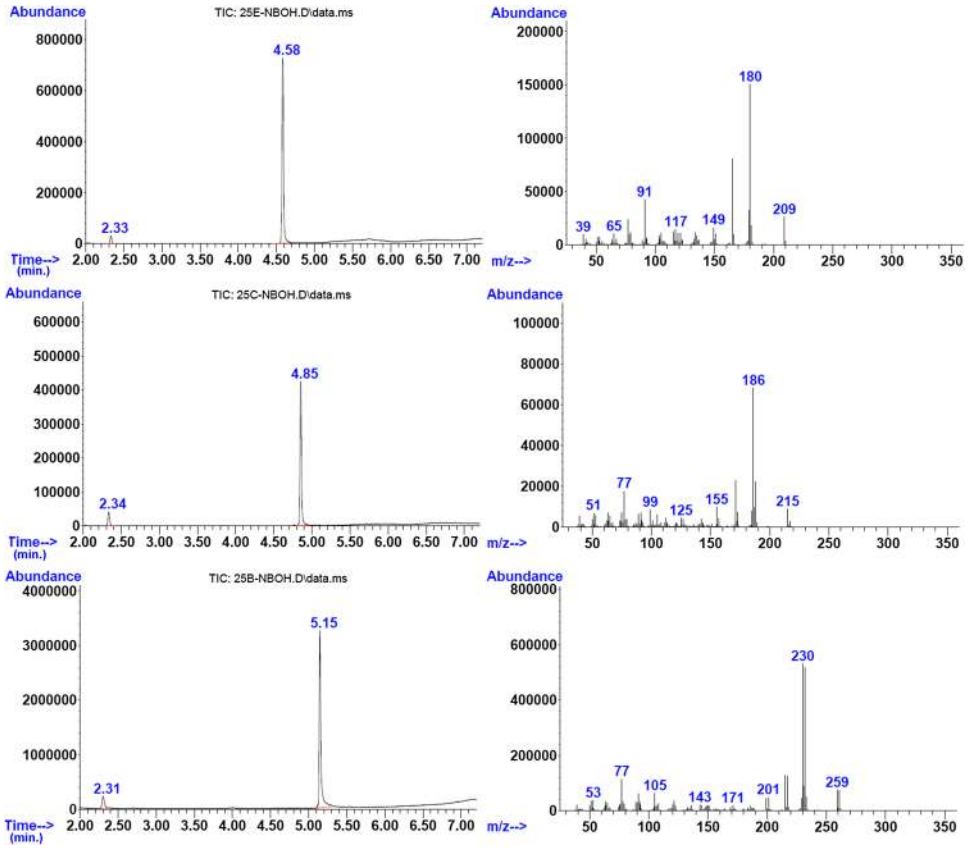


Fig. 4 Total ion chromatograms by gas chromatography–mass spectrometry (GC–MS) for samples **01** (25E-NBOH), **02** (25C-NBOH) and **03** (25B-NBOH), and respective mass spectra of the main peaks

Table 1 Gas chromatography–mass spectrometry ion data for analyzed samples

Formula	Proposed ion	Ion (*m/z*)			
		–R			
		$–CH_2CH_3$ (25E-NBOH)	–Cl (25C-NBOH)	–Br (25B-NBOH)	–I (25I-NBOH)
$C_{10}H_{14}NO_2R^{+\cdot}$	180 + R	209	215	259	307
$C_9H_{11}O_2R^{+\cdot}$	151 + R	180	186	230	278
$C_8H_8O_2R^+$	136 + R	165	171	215	263
$C_8H_8OR^+$	120 + R	149	155	199	247

Also see Fig. 6

GC–MS analysis

The GC–MS analysis of compounds **01**, **02** and **03** (Fig. 4) indicated the presence of, respectively, 2C-E (RT: retention time = 4.58 min), 2C-C (RT = 4.85 min) and 2C-B (RT = 5.15 min) as most intense peaks according to mass spectra library available (Table 1). The mass spectra for the secondary peaks (RTs = 2.33, 2.34, and 2.31 min, respectively; Fig. 5) were all similar but they had no reasonable match on MS libraries currently. These results have already been predicted for other NBOHs corroborating the finding that this group of substances are thermolabile under the GC temperature conditions [16]. Considering the results of mass spectrum libraries and the presence of secondary peaks, there was an indication that substances **01**, **02** and **03** were 25E-NBOH, 25C-NBOH, and 25B-NBOH, respectively. The thermal fragmentation reactions and proposed mass fragmentation pathways for these substances are presented in Fig. 6 according to the previous works [16, 24].

LC–MS/MS analysis

The positive full scan and PIS mass spectra of compounds **01**, **02**, and **03** are presented in Fig. 7. For compound **02**, the relative intensity of the ion at *m/z* 322 was 3:1 of signal at *m/z* 324. For compound **03**, the relative intensity of the ion

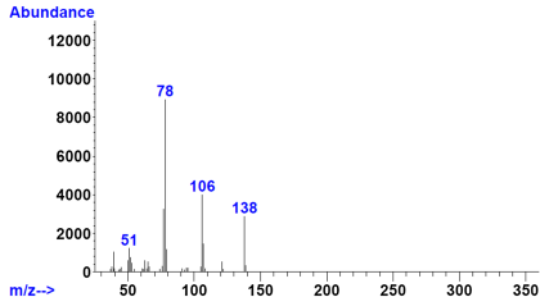


Fig. 5 GC–MS spectra of secondary peaks

at *m/z* 368 was 1:1 of signal at *m/z* 370. These isotopologue patterns indicate the presence of chlorine and bromine atoms in chemical structures of **02** and **03**, respectively. The precursor ion and product ions of the analyzed substances (Fig. 8) are compatible with mass fragmentation pathway proposed in the previous works [15, 25] and can be summarized as shown in Table 2.

NMR analysis

NMR spectroscopic results of **01**, **02**, and **03** are presented in Tables 3, 4, and 5, respectively. Minor impurities were detected in the three spectra without prejudice to the data interpretation. All experiments (^{1}H, ^{13}C, DEPT 135, HSQC and HMBC) were used for characterizing **01** and **02**. However, due to the limited amount of **03**, ^{13}C signals were assigned only by HSQC and HMBC experiments.

It was observed thirteen types of H-signal (two of these signals were overlapped) and nineteen types of C-signal for compound **01**; eleven types of H-signal and seventeen types of C-signal for compound **02** and **03**. In general, these signals, supported by HSQC and HMBC experiments, were attributed to one 1,2,4,5-tetra-substituted aromatic ring containing two methoxy, one ethylmethylamine group and an ethyl (**01**), chlorine (**02**) or bromine group (**03**). It was observed that the amine group was attached to one (2-hydroxyphenyl)methyl group. Based on structural elucidation using NMR, compound **01** was

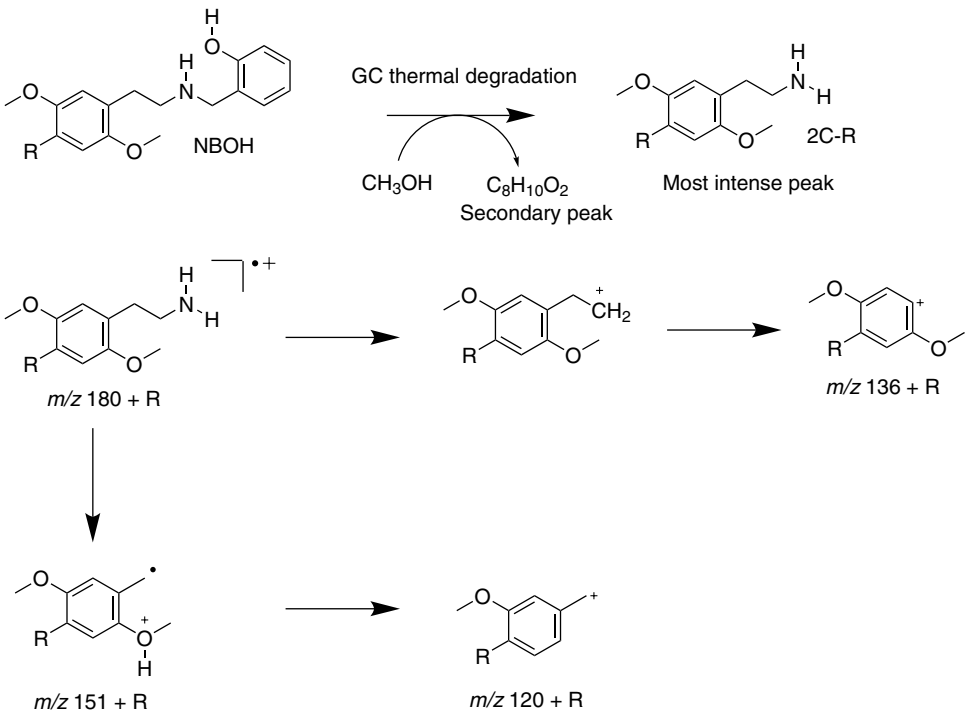


Fig. 6 Thermal fragmentation reaction produced by GC–MS, and proposed mass fragmentation pathways for 25R-NBOH/2C-R

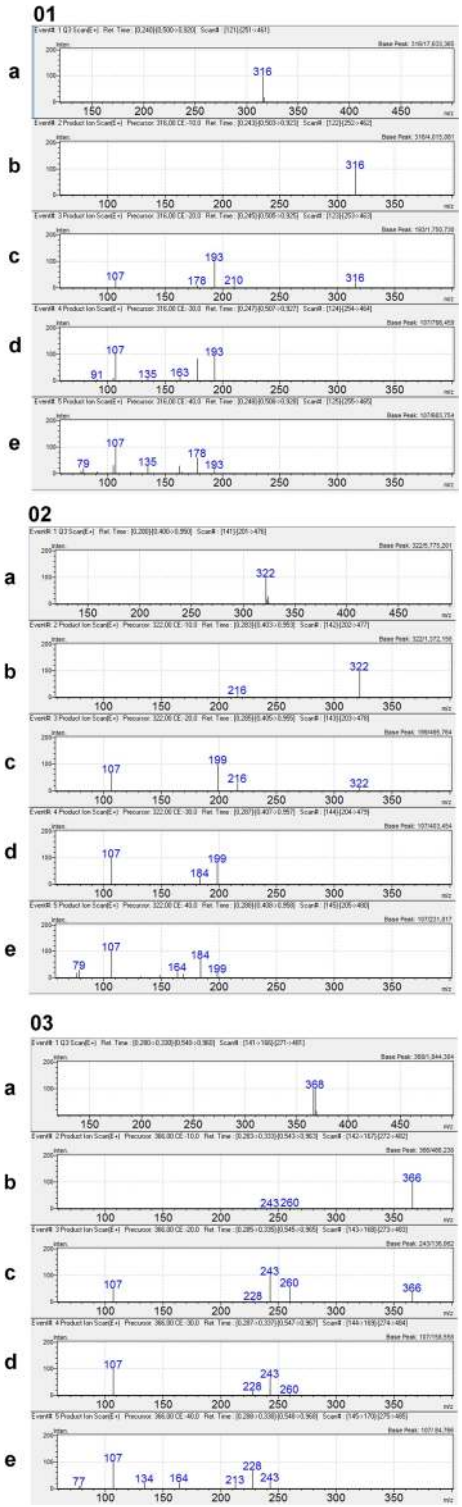


Fig. 7 Full scan mass spectra (**a**) and product ion spectra of **01** (25I-NBOH), **02** (25C-NBOH), and **03** (25B-NBOH) at different collision energies of 10 (**b**), 20 (**c**), 30 (**d**), and 40 eV (**e**) recorded by liquid chromatography–tandem mass spectrometry (LC–MS/MS)

identified as 2-(((4-ethyl-2,5-dimethoxyphenethyl)amino) methyl)phenol (25E-NBOH, 2C-E-NBOH), compound **02** as 2-(((4-chloro-2,5-dimethoxyphenethyl)amino)methyl) phenol (25C-NBOH, 2C-C-NBOH), and compound **03** as 2-(((4-bromo-2,5-dimethoxyphenethyl)amino)methyl) phenol (25B-NBOH, 2C-B-NBOH). These data were in agreement with those observed by ATR-FTIR, GC–MS and LC–MS/MS.

NBOH outlook

The number of identifications of *N*-benzylphenethylamines (NBOMes and NBOHs) and LSD by our laboratory in seized samples between 2014 and the first semester of 2019 is shown in Fig. 9a, updating our previous work [10]. NBOMes dominated the blotter paper drug market up to the beginning of 2016. Starting at this point, NBOH identification has increased, overcoming NBOMes at the second semester of 2016. In contrast, the number of NBOMes identifications has decreased and are, nowadays, less significant than LSD (305 identifications of NBOHs, 86 of LSD and 20 of NBOMes, between July 2018 and June 2019).

From 2015 to 2017, the only NBOH detected was 25I-NBOH. The other NBOHs (Fig. 9b) started appearing in the last two years, with 25B-NBOH first identified in 2017, and 25C-NBOH and 25E-NBOH in 2018, totalizing 376 NBOHs identifications in blotter paper (Jan 2017 to Jun 2019). Although 25H-NBOH has been also identified in 2017, it was considered primarily as a minor component, always associated with other major component NBOHs, and was not included in the number of identifications considered until January 2018.

Discussion

To our knowledge, the present study is the first academical work to identify and to characterize 25B-NBOH, 25C-NBOH, and 25E-NBOH in authentic street seized samples. With the addition of 25I-NBOH, the first substance of these group reported, NBOHs has become a consolidated option in the recreational drug market. Regarding the legal aspect, none of NBOH substances are controlled by any United Nations Conventions. Due to the efforts of local forensic laboratories, some NBOHs are scheduled in Brazil as prohibited substances: 25I-NBOH (October 2016), 25B-NBOH, 25C-NBOH, 25E-NBOH and 25H-NBOH (December 2018) [26]. Scheduling of the *N*-benzylphenethylamines seems to have impact in local drug market, namely decreasing the availability of scheduled drugs. The dynamics

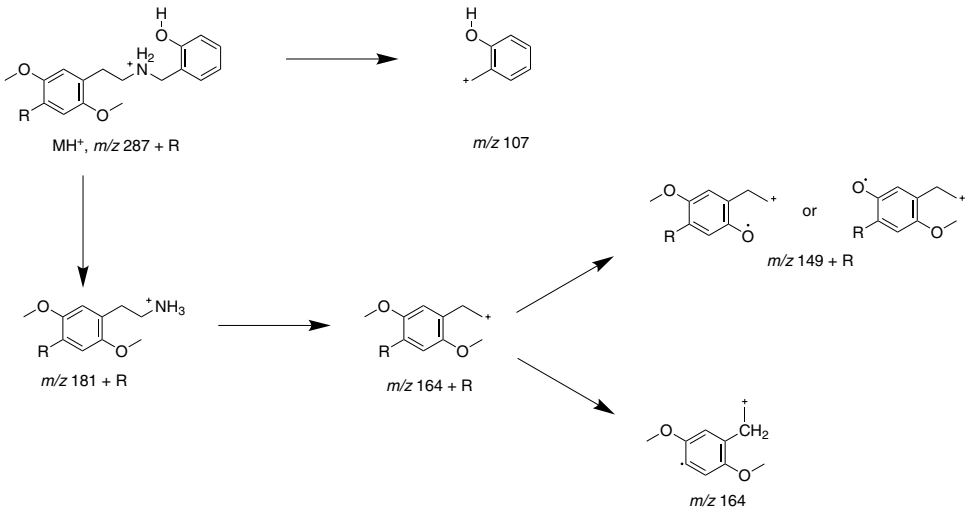


Fig. 8 Proposed mass fragmentation pathways for 25R-NBOH produced by LC–MS/MS

Table 2 Precursor and product ion data by liquid chromatography–tandem mass spectrometry for analyzed samples

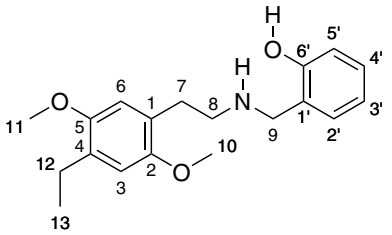
Formula	Proposed ion	Ion (*m/z*)			
		–R			
		$–CH_2CH_3$ (25E-NBOH)	–Cl (25C-NBOH)	–Br (25B-NBOH)	–I (25I-NBOH)
$C_{17}H_{21}NO_3R^+$	287 + R	316	322	368	414
$C_{10}H_{15}NO_2R^+$	181 + R	210	216	260	308
$C_{10}H_{12}O_2R^+$	164 + R	193	199	243	291
$C_9H_9O_2R^{+\cdot}$	149 + R	178	184	228	276
$C_{10}H_{12}O_2^{+\cdot}$	164	164	164	164	164
$C_7H_7O^+$	107	107	107	107	107

Also see Fig. 8

of such process, specially its rate, however, is not clearly enough; while an NBOH was first identified in a seized sample about 1.5 years after the ban of the corresponding NBOMe, newer NBOHs emerged only seven months after the ban of 25I-NBOH. Although these numbers help us to illustrate the dynamics of the drug market, they should not be considered accurately because they are significantly influenced by the agility of police investigation, seizures of drug materials and the ability of forensic laboratories to establish the identity of new substances.

The knowledge about pharmacology and toxicology of these NBOHs, as well others NPS, are limited. 25I-NBOH showed a higher selectivity for the 5-HT_{2A} receptor when compared to 5-HT_{2C} (449.8-fold higher) followed by 25C-NBOH (43.7-fold higher), 25E-NBOH (31.0-fold higher), and 25B-NBOH (8.7-fold higher) [5]. Many studies on toxicokinetics and toxicodynamics of NBOHs remain to be explored.

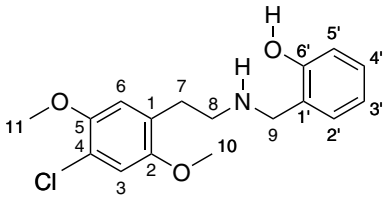
Table 3 ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectral data for compound **01** (25E-NBOH) obtained at 600 MHz (methanol-d_4)



Position	^{1}H [δ (ppm), M, J (Hz), Integral]	^{13}C [δ (ppm)]	DEPT 135	HMBC	
				^{2}J	^{3}J
1	–	122.0	C	–	–
2	–	151.3	C	–	–
3	6.79, s, 1H	112.1	CH	–	C1, C12
4	–	132.6	C	–	–
5	–	151.4	C	–	–
6	6.78, s, 1H	113.1	CH	–	C4, C7,
7	2.99, t, J = 7.5, 2H	27.0	CH_2	C1, C8	C2, C6
8	3.21, t, J = 7.5, 2H	47.0	CH_2	C7	C1, C9
9	4.21, s, 2H	46.9	CH_2	C1′	C8, C2′, C6′
10 / 11	3.77, s, 3H; 3.88, s, 3H	55.0; 55.1	CH_3	–	C2 ; C5
12	2.60, q, J = 7.5, 2H	23.0	CH_2	C4, C13	C3, C5
13	1.15, t, J = 7.5, 3H	13,5	CH_3	C12	C4
1′	–	117.4	C	–	–
2′	7.31–7.26, m, 1H	131.2	CH	–	C9, C4′, C6′
3′	6.92–6.87, m, 1H	119.3	CH	–	C2′, C5′
4′	7.31–7.26, m, 1H	131.0	CH	–	C6′
5′	6.92–6.87, m, 1H	115.0	CH	–	C3′
6′	–	156.1	C	–	–

DEPT distortionless enhancement by polarization transfer, *HMBC* heteronuclear multiple-bond correlation, *J* coupling constant, *M* multiplicity, *s* singlet, *t* triplet, *q* quartet, *m* multiplet

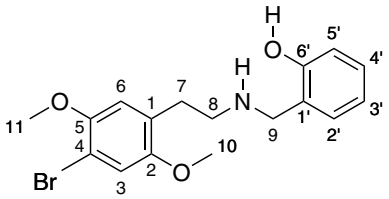
Table 4 ^{1}H and ^{13}C NMR spectral data for compound **02** (25C-NBOH) obtained at 600 MHz (methanol-d_4)



Position	^{1}H [δ (ppm), M, J (Hz), Integral]	^{13}C [δ (ppm)]	DEPT 135	HMBC	
				^{2}J	^{3}J
1	–	123.9	C	–	–
2	–	151.6	C	–	–
3	7.03–7.00, br, 1H	113.0	CH	C2, C4	C1, C5
4	–	121.5	C	–	–
5	–	149.3	C	–	–
6	6.99–6.96, brs, 1H	115.2	CH	C5	C2, C4, C7
7	3.02, t, J = 7.7, 2H	26.8	CH_2	C1, C8	C2, C6
8	3.21, t, J = 7.7, 2H	46.5	CH_2	C7	C1, C9
9	4.23, s, 2H	46.7	CH_2	C1′	C8, C2′, C6′
10	3.78, s, 3H	55.2	CH_3	–	C2
11	3.83, s, 3H	56.0	CH_3	–	C5
1′	–	117.3	C	–	–
2′	7.34–7.25, m, 1H	131.2	CH	C9, C4′	C6′
3′	6.93–6.87, m, 1H	119.6	CH	C2′, C4′	C1′, C5′
4′	7.34–7.25, m, 1H	131.0	CH	–	C2′, C6′
5′	6.93–6.87, m, 1H	114.9	CH	C6′	C3′
6′	–	156.1	C	–	–

For abbreviations except *br* broad and *brs* broad singlet, see Table 3

Table 5 ^{1}H and ^{13}C NMR spectral data for compound **03** (25B-NBOH) obtained at 600 MHz (methanol-d_4)



Position	^{1}H [δ (ppm), M, J (Hz), Integral]	^{13}C [δ (ppm)]	HMBC	
			^{2}J	^{3}J
1	–	124.8	–	–
2	–	151.9	–	–
3	7.16, s, 1H	115.8	C4	C1, C5
4	–	110.0	–	–
5	–	150.0	–	–
6	6.96, s, 1H	114.7	–	C2, C4, C7
7	3.01, t, J = 7.6, 2H	27.0	C1, C8	C2, C6
8	3.22, t, J = 7.6, 2H	46.5	C7	C1, C9
9	4.23, s, 2H	47.0	C1′	C8, C2′, C6′
10	3.79, s, 3H	55.3	–	C2
11	3.83, s, 3H	55.9	–	C5
1′	–	117.3	–	–
2′	7.33–7.25, m, 1H	131.4	–	C9, C4′, C6′
3′	6.93–6.87, m, 1H	120.0	–	C5′
4′	7.33–7.25, m, 1H	131.0	–	C2′, C6′
5′	6.93–6.87, m, 1H	114.6	–	C3′
6′	–	156.1	–	–

For abbreviations, see Table 3

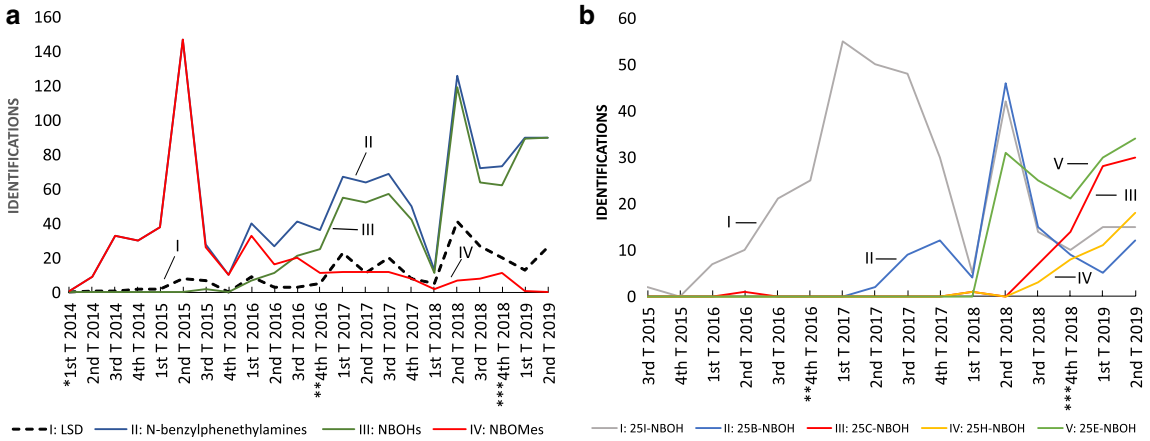


Fig. 9 Changes of *N*-benzylphenethylamine identification between first trimester (T) of 2014 and second trimester of 2019 (**a**) and NBOH identification between third trimester of 2015 and second trimester of 2019 (**b**). Asterisk: local ban of several NBOMe substances; double asterisk: local ban of 25I-NBOH; triple asterisk: local ban of other NBOH substances

Conclusions

The permanent emergence of NPS is, undoubtedly, a result of the efforts of drug dealers in circumventing drug controls. In this context, here we have presented data on the identification and structural characterization of three NPS, members of the NBOH class: 25B-NBOH, 25C-NBOH and 25E-NBOH. To our knowledge, this is the first report to identify and to characterize these three substances in authentic street seized samples which have emerged in the Brazilian market after 25I-NBOH was scheduled. As predicted in a previously published work, we have confirmed that these three substances are thermolabile, degrading into the corresponding 2C-X molecule during its injection in standard gas chromatography, easily leading them to be misidentified as such, a grave error from the forensic point of view.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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