Title: Spectroscopic characterization and crystal structures of four hydrochloride cathinones : N-ethyl-2-amino-1-phenylhexan-1-one (hexen, NEH), N-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one (mexedrone), N-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one (ephylone) and N-butyl-2-amino-1-(4-chlorophenyl) propan-1-one (4-chlorobutylcathinone)

Author: Piotr Kuś, Marcin Rojkiewicz, Joachim Kusz, Maria Książek, Aleksander Sochanik

Citation style: Kuś Piotr, Rojkiewicz Marcin, Kusz Joachim, Książek Maria, Sochanik Aleksander. (2019). Spectroscopic characterization and crystal structures of four hydrochloride cathinones : N-ethyl-2-amino-1-phenylhexan-1-one (hexen, NEH), N-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one (mexedrone), N-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one (ephylone) and N-butyl-2-amino-1-(4-chlorophenyl)propan-1-one (4-chlorobutylcathinone). "Forensic Toxicology" (Vol. 37 (2019), iss. 2, s. 456-464), doi 10.1007/s11419-019-00477-y.

Forensic Toxicology (2019) 37:456–464
https://doi.org/10.1007/s11419-019-00477-y

SHORT COMMUNICATION

Spectroscopic characterization and crystal structures of four hydrochloride cathinones: *N*-ethyl-2-amino-1-phenylhexan-1-one (*hexen, NEH*), *N*-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one (*mexedrone*), *N*-ethyl-2-amino-1-(3,4-methylenedioxyphenyl) pentan-1-one (*ephylone*) and *N*-butyl-2-amino-1-(4-chlorophenyl) propan-1-one (*4-chlorobutylcathinone*)

Piotr Kuś[1] · Marcin Rojkiewicz[1] · Joachim Kusz[2] · Maria Książek[2] · Aleksander Sochanik[3]

Received: 30 March 2019 / Accepted: 20 April 2019 / Published online: 14 May 2019

Abstract

Purpose Four compounds found during seizure by drug enforcement agencies were identified and characterized by various instrumental analytical methods.

Methods The samples were analyzed by nuclear magnetic resonance (NMR), infrared and Raman spectroscopies and X-ray crystallography.

Results The four compounds were confirmed as: *N*-ethyl-2-amino-1-phenylhexan-1-one hydrochloride, *N*-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one hydrochloride, *N*-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one hydrochloride and *N*-butyl-2-amino-1-(4-chlorophenyl)propan-1-one hydrochloride; all four were cathinone derivatives available on the designer drug market.

Conclusions X-ray crystallography is especially useful for identifying the new and unknown designer drugs and their enantiomeric forms.

Keywords *N*-Ethylhexedrone · Mexedrone · Ephylone · 4-Chlorobutylcathinone · X-ray crystallography · Raman and NMR spectroscopies

Introduction

During our ongoing studies of compounds available on the illegal market that may have potential psychostimulatory effects, we characterized four further substances using spectroscopic methods and determined their crystallographic structures. As stated previously, crystallographic examination of drug substances generally dubbed "designer drugs" is a rapid and unequivocal determination method, especially when crystal particles are present in specimens found on suspects. The sole problem that may arise is the unavailability of crystallographic data of numerous compounds available on the drug market. Therefore, it seems reasonable to determine basic cell parameters for as many compounds of this type as possible, using the roentgenographic methods. Compounds shown in Fig. 1 have been distributed on the

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11419-019-00477-y) contains supplementary material, which is available to authorized users.

✉ Piotr Kuś
pkus@ich.us.edu.pl

[1] Department of Chemistry, University of Silesia, 9, Szkolna Street, 40-006 Katowice, Poland

[2] Present Address: Institute of Physics, University of Silesia, 1, 75 Pułku Piechoty, 41-503 Chorzów, Poland

[3] Center for Translational Research and Molecular Biology of Cancer, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, 44-100 Gliwice, Poland

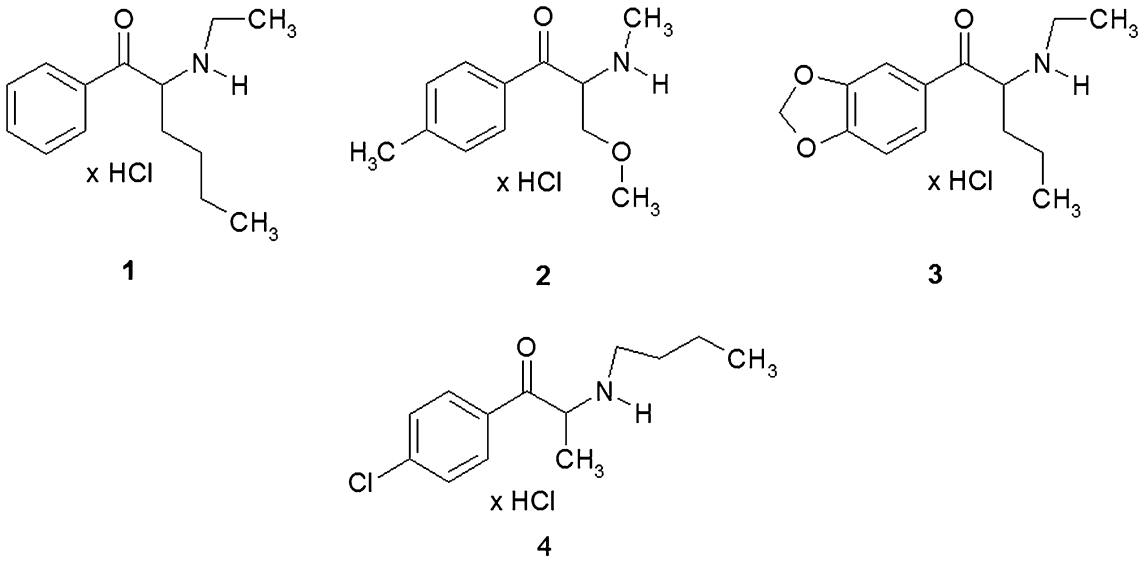

Fig. 1 Structures of *N*-ethyl-2-amino-1-phenylhexan-1-one (*hexen*, *NEH*) (**1**), *N*-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one (*mexedrone*) (**2**), *N*-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one (*ephylone*) (**3**) and *N*-butyl-2-amino-1-(4-chlorophenyl)propan-1-one (*4-chlorobutylcathinone*) (**4**)

illegal drug market in Poland. During the preparation of this manuscript, the crystallographic structures of two designer drugs, **2** (The Cambridge Crystallographic Data Centre, CCDC 1452166) [1] and **3** (CCDC1504573) [2] were reported. We show here data obtained in our laboratories in order to compare the results of examining differently sourced crystals of the same designer drug; the results unequivocally showed that we dealt with the same compounds of the same enantiomeric compositions. Our results for compounds **2** and **3** additionally included Raman data. Raman spectroscopy proved very useful and has been extensively employed for rapid determination of drugs of abuse, for example, during hand luggage control for aircraft passengers [3–6]. In all likelihood, such a portable equipment could also be used for rapidly checking the presence of compounds, which have not been tested so far in this way, including cathinones.

Materials and methods

Chemicals

Deuterated dimethyl sulfoxide (DMSO-d_6) was purchased from Sigma-Aldrich (Poznań, Poland). *N*-Ethyl-2-amino-1-phenylhexan-1-one hydrochloride (**1**), *N*-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one hydrochloride (**2**), *N*-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one hydrochloride (**3**) and *N*-butyl-2-amino-1-(4-chlorophenyl)propan-1-one hydrochloride (**4**) salts were provided in pure form by drug enforcement agencies as materials seized on the illicit drug market. Crystals suitable for crystallography were obtained by slow evaporation of DMSO-d_6 solutions used in nuclear magnetic resonance (NMR) spectroscopic studies (compounds **1, 3**, and **4**) or directly from provided crystalline materials (compound **2**).

Gas chromatography–mass spectrometry analysis

Gas chromatography–mass spectrometry (GC–MS) analyses were performed using a Thermo Trace Ultra chromatograph coupled to a mass spectrometer (Thermo DSQ; Thermo Scientific, Warsaw, Poland). The injector was maintained at 260 °C. Sample injection (1 µL) was in the splitless mode. Separation of sample components was conducted using the Rxi®-5Sil MS column (30 m length, 0.25 mm inner diameter, 0.25 µm film thickness; Restek, Bellefonte, PA, USA). Helium was used as a carrier gas at the flow rate of 1.2 mL min^{-1}. The mass detector was set to positive electron ionization (EI) mode and the electron beam energy was 70 eV. The mass detector was operating in a full scan mode in the 40–450 amu range.

NMR spectroscopy

The NMR spectra were recorded using UltraShield 400 MHz apparatus (Bruker, Bremen, Germany) with DMSO-d_6 as a solvent. The peaks were referenced to the residual DMSO (2.49 and 39.5 ppm) resonances in ^{1}H and ^{13}C NMR, respectively.

Fourier transform infrared and Raman spectroscopies

The infrared (IR) spectra of each compound were obtained using a Nicolet iS50 Fourier transform (FT)-IR spectrometer (Thermo Scientific) and the attenuated total reflectance technique. Raman measurements were performed using a Thermo Scientific™ DXR™ 2xi Raman imaging microscope equipped with a 780 nm laser (Thermo Scientific).

Differential scanning calorimetry

Differential scanning calorimetry (DSC) was performed with a DSC Pyris 1 (Perkin Elmer, Waltham, MA, USA) using aluminum sample pans. The DSC experiments were carried out in a nitrogen atmosphere with a temperature range from 20 °C to over the melting point and with scanning rate at 10 °C min^{-1}.

X-ray spectroscopy

Single-crystal X-ray experiments were performed at 200 K (**1**), 100 K (**2** and **4**) or 290 K and 100 K for (**3**). The data were collected using a SuperNova kappa diffractometer with Atlas CCD detector (Agilent Technologies, Santa Clara, CA, USA). Collected data were integrated with CrysAlis^{Pro} software (version 1.171.38.41q, 2015; Rigaku Oxford Diffraction, Rigaku, Tokyo, Japan). The solving and refining procedures were similar for all compounds. The structures were solved using direct methods with the SHELXS-2013 software and the solutions were refined using SHELXL-2014/7 program [7]. CCDC 1905624 for **1**, CCDC 1905623 for **2**, CCDC 1905622 (290 K) and CCDC 1906036 (100 K) for **3**, and CCDC 1905621 for **4** contain supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via: www.ccdc.cam.ac.uk/data_request/cif.

Results and discussion

Analyzed substances were seized by police; they were presented as unlabeled white powder samples. Three of them had been characterized chromatographically (compounds **1** [8], **2** [9], and **3** [10]). Compound **4** has not been characterized yet (chromatographically or spectroscopically).

Melting points

Melting points were measured for compounds **1**–**4** by both DSC method and hot-plate analysis, and are shown in Table 1. All compounds melted with decomposition. DSC for all compounds showed a rather wide melting range. The values given in the table are maximum endothermic peak values related to the melting process (e.g., Fig. S1). When using a classical measurement method (hot-plate), rather sharp melting temperature ranges were observed for compounds **1** and **2**, whereas for compounds **3** and **4** the melting process entailed partial decomposition bringing change of color, wide melting temperature range and, finally, decomposition.

Table 1 Melting points of compounds **1**–**4**

Compound	DSC °C	Hot-plate °C	Literature °C
1	188.9	184–186	171–175 [11]
2	187.4	184–186	190–192 [1]
3	204.9	205–211	–
4	235.5	> 200 dec.	–

Melting point measured using hot-plate are uncorrected

DSC differential scanning calorimetry

GC–MS analysis

Chromatographic analyses of compounds **1**–**4** were reported earlier [12–15]. Figure 2 shows GC–MS spectra for compound **4**, which were obtained in our laboratories. This spectrum contained all the peaks reported in [15], and additionally, the molecular ion was of the greatest intensity (100%). It is rare to measure the mass spectra of cathinone hydrochlorides under these conditions.

Iminium ions arising in the process of bond cleavage between carbons α and β in the side chains were ions with greatest intensity for compounds **1**–**3** (*m/z* 114 for **1**, *m/z* 88 for **2**, and *m/z* 100 for **3**) and with 82% intensity for compound **4** (*m/z* 100).

NMR spectra

The N–H protons of all compounds appeared as a double broad singlet at: $\delta = 9.61$ and 9.18 ppm for compound **1**, $\delta = 9.76$ and 9.26 ppm for compound **2**, $\delta = 9.61$ and 9.05 ppm for compound **3** and $\delta = 9.81$ and 9.19 ppm for compound **4**. These protons are diastereotopic (chemically inequivalent). The NMR spectra of compounds **2** and **4** confirmed the presence of di-substituted *para*-benzene rings; spectrum of compound **1** confirmed monosubstituted benzene ring and spectrum of compound **3** a three-substituted benzene ring at 1, 3 and 4 positions. The methinic protons appeared as a triplet at $\delta = 5.28$ ppm for compound **1**, broad singlet at $\delta = 5.39$ ppm for compound **2**, broad singlet at $\delta = 5.18$ ppm for compound **3** and

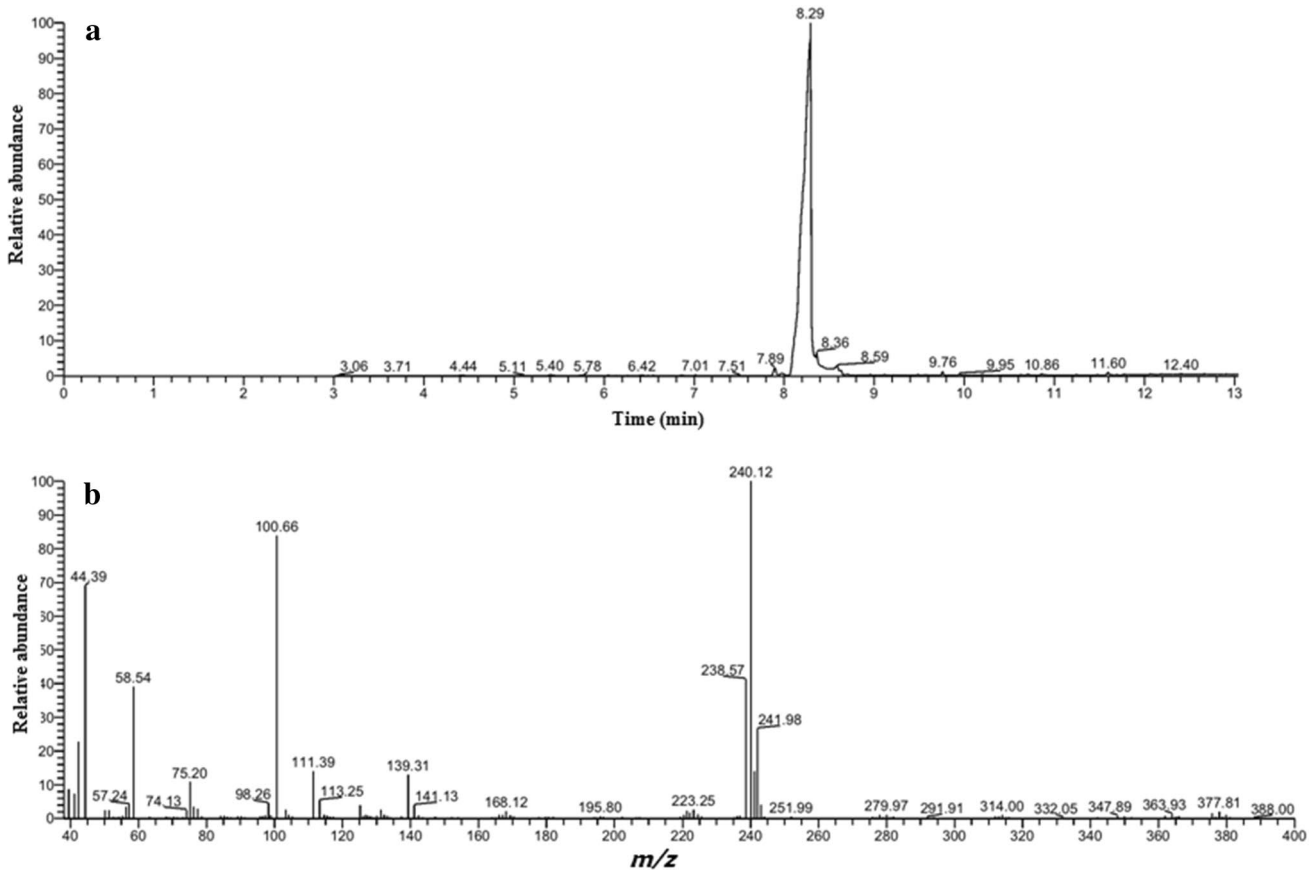

Fig. 2 Gas chromatography (**a**) and mass spectrometry data (**b**) of 4-chlorobutylcathinone **4**

multiplet at $\delta = 5.22$ ppm for compound **4**. The *N*-methyl protons for **2**, and *N*-methylene protons of compounds **1**, **3** and **4** yielded two chemically inequivalent broad singlets.

The ^{13}C NMR spectra displayed carbonyl resonance at: 196.8, 193.4, 194.7 and 195.8 ppm for compounds **1**–**4**, respectively. The characteristic methinic carbons resonated at 61.0, 59.2, 60.5 and 57.6 ppm for compounds **1**–**4**, respectively. All other resonances for all compounds are listed below.

Compound 1 (N-ethyl-2-amino-1-phenylhexan-1-one hydrochloride)

^{1}H NMR (DMSO-d_6): δ (ppm): 9.61, 9.18 (2 × bs, 2H, $=N^+H_2$), 8.08 (d, 2H, Ar*H*), 7.76 (t, 1H, Ar*H*), 7.61 (t, 2H, Ar*H*), 5.28 (t, 1H, C*H*), 3.02, 2.91 (2 × m, 2H, N–CH_2–CH_3), 1.98–1.89 (m, 2H), 1.27 (t, 3H, N–CH_2–CH_3), 1.29–1.20 (m, 1H), 1.20–1.16 (m, 2H), 1.16–1.12 (m, 1H), 0.73 (t, 3H, -CH_3).

^{13}C NMR (DMSO-d_6): δ (ppm): 196.8, 135.3, 134.4, 129.7, 129.2, 61.0, 41.7, 29.9, 26.1, 22.3, 13.9, 11.6.

Compound 2 (N-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one hydrochloride)

^{1}H NMR (DMSO-d_6): δ (ppm): 9.76, 9.26 (2 × bs, 2H, $=N^+H_2$), 7.95, 7.41 (dd, 4H, $J = 8.4$ Hz, Ar*H*), 5.39 (bs, 1H, C*H*), 4.02 (dd, 2H, $J_1 = 11.6$ Hz, $J_2 = 3.2$ Hz), 3.82 (dd, 2H, $J_1 = 11.6$ Hz, $J_2 = 3.2$ Hz), 3.17 (s, 3H), 2.58 (t, 3H, $J = 4.8$ Hz), 2.41 (s, 3H).

^{13}C NMR (DMSO-d_6): δ (ppm): 193.4, 147.8, 131.4, 130.1, 129.3, 69.6, 63.4, 59.2, 31.9, 21.7.

Compound 3 (N-ethyl-2-amino-1-(3,4-methylenedioxyphenyl)pentan-1-one hydrochloride)

^{1}H NMR (DMSO-d_6): δ (ppm): 9.61, 9.05 (2 × bs, 2H, $=N^+H_2$), 7.76 (d, 1H, $J = 8$ Hz, Ar*H*), 7.58 (s, 1H, Ar*H*), 7.13 (d, 1H, $J = 8$ Hz, Ar*H*), 6.20 (s, 2H, –O–CH_2–O–), 5.18 (bs, 1H, C*H*), 3.05–2.92 (m, 1H, N–CH_2–CH_3),

Table 2 Crystal data and structure refinement for compounds **1**–**4**

Parameter	Compound			
	1	**2**	**3**	**4**
Molecular formula	$C_{14}H_{22}NOCl$	$C_{12}H_{18}NO_2Cl$	$C_{14}H_{20}NO_3Cl$	$C_{13}H_{19}NOCl_2$
Molecular weight	255.77	243.72	285.76	276.19
Crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/n$	*Pbca*
Temperature (K)	200	100	290	100
a (Å)	7.6557 (2)	7.2178 (3)	14.6230 (5)	14.0767 (4)
b (Å)	7.1372 (1)	7.5931 (2)	7.3239 (2)	7.0795 (2)
c (Å)	26.9735 (6)	23.5824 (8)	15.0050 (5)	28.9189 (7)
α (°)	90	90	90	90
β (°)	90.936 (2)	91.827 (3)	111.771 (4)	90
γ (°)	90	90	90	90
V (Å^3)	1473.64 (5)	1291.79 (8)	1492.37 (9)	2881.94 (13)
Z	4	4	4	8
*D*x (g cm^{-3})	1.153	1.253	1.272	1.273
Absorption coeff. (mm^{-1})	0.246	0.282	0.260	0.436
F (000)	552.0	520.0	608.0	1168.0
Crystal size (mm)	0.04 × 0.12 × 0.45	0.07 × 00.23 × 0.35	0.03 × 0.12 × 0.17	0.03 × 0.10 × 0.10
Data collection and structure solution:				
Data collected	23,949	9634	11,505	35,917
Independent reflections	3001	2625	3051	2943
Observed reflections [$I > 2\sigma(I)$]	2760	2422	2558	2943
R(int.)	0.025	0.023	0.027	0.0262
Completeness (%)	99.9	99.8	99.9	99.8
T_{max}/T_{min}	1.000/0.725	1.000/0.855	1.000/0.791	1.000/0.889
No. of parameters	156	148	174	156
*R*1[$I > 2\sigma(I)$]	0.0385	0.0284	0.0361	0.0397
wR2 (all data)	0.1079	0.0762	0.1021	0.0944
S	1.043	1.063	1.051	1.172
Largest difference peak and hole (eÅ^{-3})	0.545 and − 0.167	0.344 and − 0.202	0.341 and − 0.214	0.637 and − 0.428

2.92–2.80 (m, 1H, N–CH_2–CH_3), 1.95–1.80 (m, 2H, –CH_2–CH_2–CH_3), 1.35–1.25 (m, 1H, –CH_2–CH_2–CH_3), 1.25 (t, 3H, N–CH_2–CH_3), 1.15–1.03 (m, 1H, –CH_2–CH_2–CH_3), 0.79 (t, 3H, –CH_2–CH_2–CH_3).

^{13}C NMR (DMSO-d_6): δ (ppm): 194.7, 153.3, 148.7, 129.1, 126.3, 109.0, 108.3, 103.0, 60.5, 41.6, 32.6, 17.7, 14.1, 11.6.

Compound 4 (N-butyl-2-amino-1-(4-chlorophenyl)propan-1-one hydrochloride)

^{1}H NMR (DMSO-d_6): δ (ppm): 9.81, 9.19 (2 × bs, 2H, = N$^+H_2$), 8.09, 7.70 (dd, 4H, $J = 8$ Hz, Ar*H*), 5.22 (m, 1H, C*H*), 2.97, 2.51 (2 × m, 2H, N–CH_2–CH_2–), 1.7 (m, 2H, N–CH_2–CH_2–CH_2–), 1.48 (d, 3H, C–CH_3), 1.36 (m, 2H, N–CH_2–CH_2–CH_2–CH_3), 0.90 (t, 3H, N–CH_2–CH_2–CH_2–CH_3).

^{13}C NMR (DMSO-d_6): δ (ppm):195.8, 140.1, 132.2, 131.2, 129.8, 57.6, 45.4, 28.1, 19.8, 16.0, 13.9.

IR and Raman spectra

IR and Raman spectra for all analyzed compounds confirmed the structures of the examined samples. They did not diverge from spectra of cathinones previously characterized by us.

In IR spectra, characteristic carbonyl stretches occurred at: 1691, 1690, 1681 and 1696 cm^{-1} for compounds **1**–**4**, respectively. The aromatic C=C ring stretch vibrations appeared at 1598, 1599 and 1588 cm^{-1} for compounds **1**, **2** and **4**, respectively, while the value for **3** was shifted to 1609 cm^{-1}. This effect is the result of an additional dioxa ring system present in the molecule. The IR spectra for compounds **1**–**4** are available in the supplementary material (Figs. S2–S5).

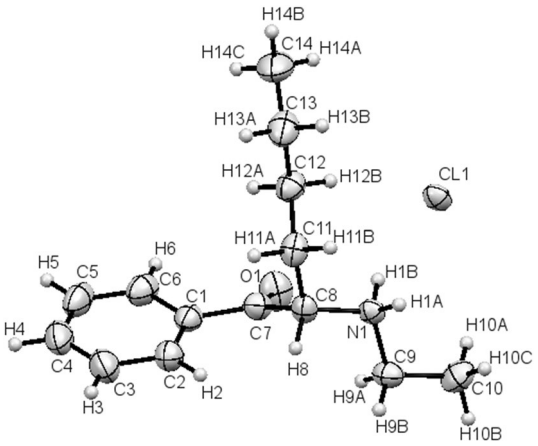

Fig. 3 (*S*)-Enantiomer molecule of compound **1** in the crystal. Ellipsoids correspond to 50% probability levels

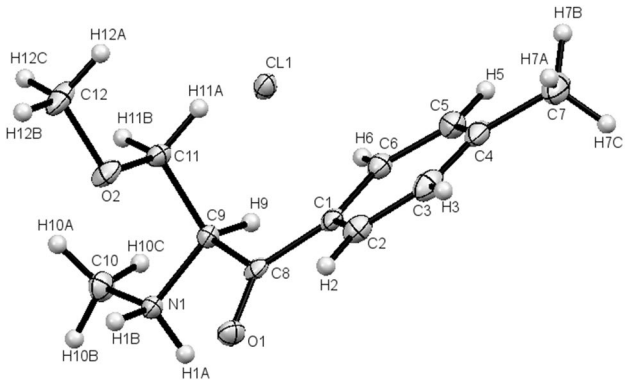

Fig. 5 (*S*)-Enantiomer molecule of compound **2** in the crystal. Ellipsoids correspond to 50% probability levels

Carbonyl stretches in Raman spectra are also characteristic: they occur at 1692 cm^{-1} for **1** and **2** as well as at 1679 and 1697 cm^{-1} for **3** and **4**, respectively. Likewise, the aromatic C=C ring stretch vibrations appeared at 1598 cm^{-1} for compounds **1** and **2**, and at 1586 cm^{-1} for **4**, respectively. For compound **3**, vibrations were shifted to 1610 and 1601 cm^{-1}. All other absorption peaks are shown in the spectra available in the supplementary material (Figs. S6–S9).

X-ray crystallography

Compounds **1**–**3** formed monoclinic crystals in the $P2_1/n$ space group. Compound **4** formed orthorhombic crystals in the *Pbca* space group. All compounds occurred as the enantiomers in the examined crystals. Crystal data and structure refinement for all four compounds are summarized in Table 2. The molecular structures and packing diagrams of compounds **1**–**4** are shown in Figs. 3, 4, 5, 6, 7, 8, 9 and 10. All distances and angles in the molecular structures were typical.

Characteristic features of cathinone hydrochlorides were short distances between NH_2 groups and two chlorine ions. They lay within 2.204–2.358 Å distance range (at Θ angles: 149.21–173.96°) for N–H···Cl and within 3.084–3.154 Å distance range for N···Cl. These values are in accordance with data reported in [16]. The cited paper analyzed various N–H donors in ionic bonds with halide anions.

In crystals of compounds **1**–**4**, many weak hydrogen bonds were present between molecules, which determined arrangement and spacing of cathinone molecules in the elementary cell; for example π–π interactions between benzene rings in molecules of compounds **1** and **4**, C–H···π interactions in structures of compounds **2**, **3** and **4**, or

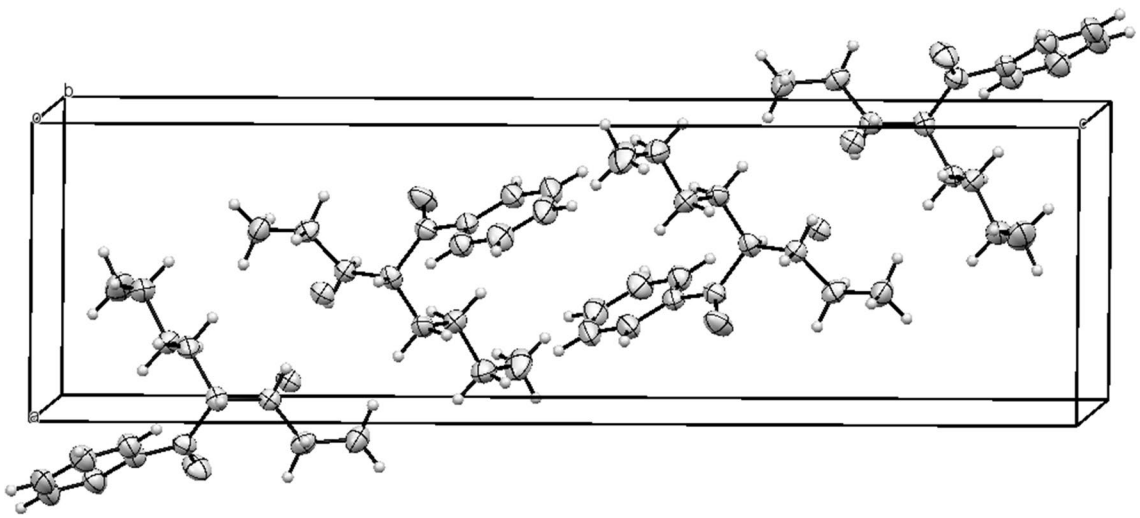

Fig. 4 Packing diagram for compound **1**: view along *b* axis

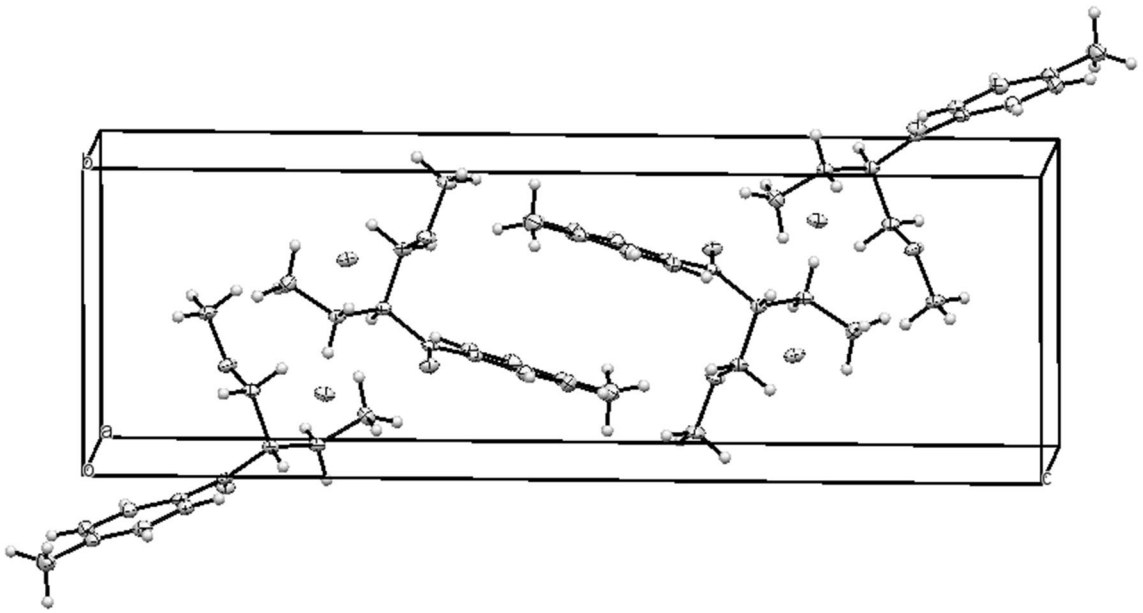

Fig. 6 Packing diagram for compound **2**: view along *a* axis

intramolecular interactions of N–H···O type in compounds **2** and **3** or of C–H···O type in compound **3**. An interaction of C–H···Cl type was also found in compound **2**.

Compound 1

Crystals of *N*-ethyl-2-amino-1-phenylhexan-1-one hydrochloride (**1**) presented a racemic mixture. The compound had two enantiomeric ion pairs in the unit of the crystal lattice (Fig. 4). Torsion angles C7C8N1C9 were identical in both enantiomers (70.65°). The most characteristic weak interaction in the structure of this compound was the intermolecular interaction of hydrogen atom at carbon C14 with a C4 atom of the adjacent molecule phenyl ring (length 2.830 Å), as well as the π–π interaction between phenyl rings separated from each other by 3.835 Å and centroid distance of 4.079 Å (68.59° angle) (Figs. S10, S11).

Compound 2

Crystals of *N*-methyl-2-amino-1-(4-methylphenyl)-3-methoxypropan-1-one hydrochloride (**2**) presented a racemic mixture. The compound had two enantiomeric ion pairs in the unit of the crystal lattice (Fig. 6). Torsion angles C7C8N1C9 were identical in both enantiomers (178.56°). Discussion concerning interactions in the crystal can be found in [1]. Interactions in the molecule of this compound were of C–H···π type (3.008 Å). Short distance interactions

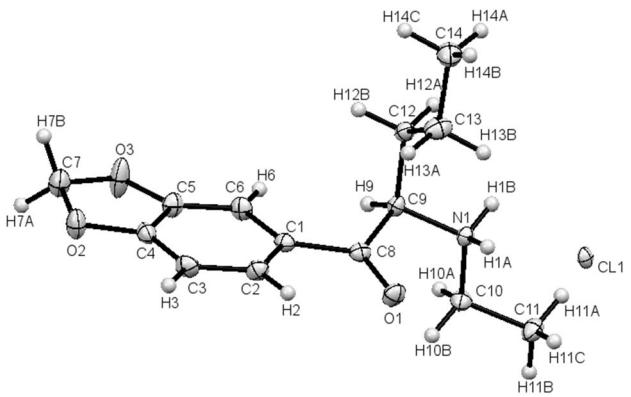

Fig. 7 (*R*)-Enantiomer molecule of compound **3** in the crystal. Ellipsoids correspond to 50% probability levels

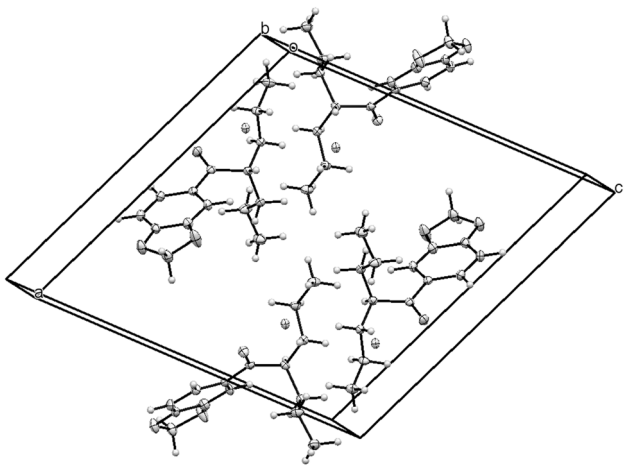

Fig. 8 Packing diagram for compound **3**: view along *b* axis

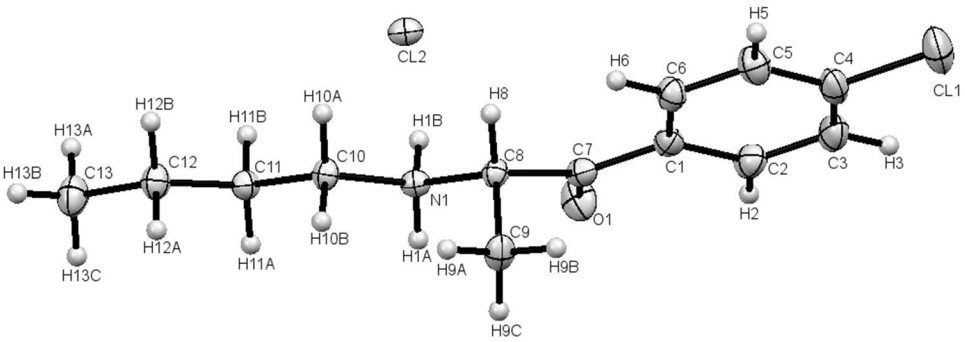

Fig. 9 (*S*)-Enantiomer molecule of compound **4** in the crystal. Ellipsoids correspond to 50% probability levels

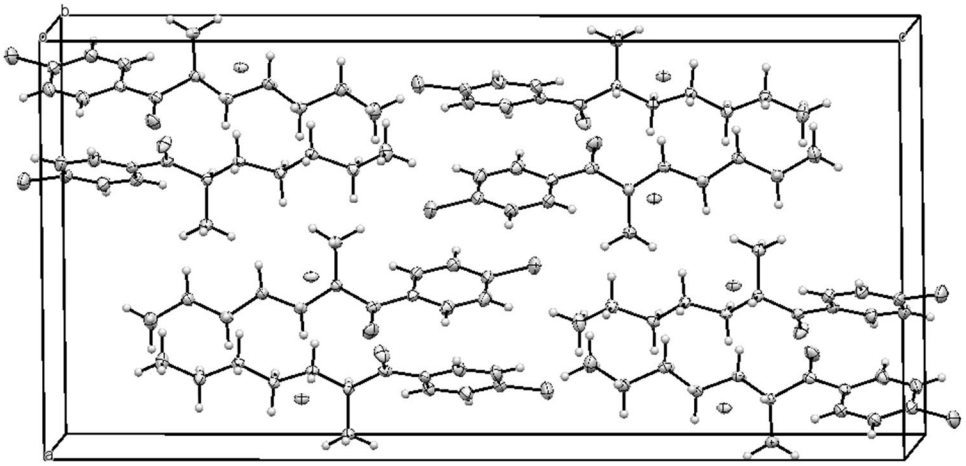

Fig. 10 Packing diagram for compound **4**: view along *b* axis

of C_{Ar}–H···O–CH_3 type (2.581 Å) determined the reverse pair arrangement of molecules (Figs. S12, S13).

Compound 3

Crystals of *N*-ethyl-2-amino-1-(3,4-methylenedioxy-phenyl) pentan-1-one hydrochloride (**3**) presented a racemic mixture. The compound had two enantiomeric ion pairs in the unit of the crystal lattice (Fig. 8). Torsion angles C7C8N1C9 were identical in both enantiomers (72.45°). A very detailed discussion of interactions occurring in the crystal can be found in [2]. Crystal packing for this compound was strongly affected by C–H···π bonds between hydrogen atom C7 and the centroid of the adjacent molecule phenyl ring (2.606 Å) (Fig. S14).

Compound 4

Crystals of *N*-butyl-2-amino-1-(4-chlorophenyl)propan-1-one hydrochloride (**4**) presented a racemic mixture. The compound had four enantiomeric ion pairs in the unit of the crystal lattice (Fig. 10). Torsion angles C7C8N1C9 were identical in both enantiomers (173.43°).

Arrangement of molecules in the crystal structure suggested that the determining interactions were those of π···π and C–H···π type. The most crucial ones were interactions of π···π type with phenyl ring centroids' distance equal to 4.287 Å (angle 62.30°) and substantial contribution of C_{Ar}–Cl···C_{Ar} interaction (3.806 Å) (Fig. S15)

Conclusions

In the present study, we have identified and characterized four synthetic cathinones seized on the drug market, by GC–MS, NMR, FT-IR, and Raman spectroscopies, DSC, and X-ray crystallography. Although compounds **1**–**3** had been characterized chromatographically, there has been no report on chemical characterization of compound **4**. Moreover, X-ray crystallographic data of compounds **1** and **4** have not been reported in the scientific context. X-ray crystallography is especially useful for identifying the new and unknown designer drugs and their enantiomeric forms.

Acknowledgements We wish to thank Dr. Barbara Hachuła for IR and Raman spectra measurements and Dr. Sławomir Maślanka for DSC measurements.

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.

References

1. McLaughlin G, Morris N, Kavanagh PV, Power JD, Dowling G, Twamley B, O'Brien J, Talbot B, Walther D, Partilla JS, Baumann MH, Brandt SD (2017) Synthesis, characterization and monoamine transporter activity of the new psychoactive substance mexedrone and its *N*-methoxy positional isomer, *N*-methoxymephedrone. Drug Test Anal 9:358–368
2. Wood MR, Bernal I, Lalancette RA (2017) The hydrochloride hydrates of pentylone and dibutylone and the hydrochloride salt of ephylone: the structures of three novel designer cathinones. Struct Chem 28:1369–1376
3. de Oliveira Penido CAF, Pacheco MTT, Lednev IK, Silveira L Jr (2016) Raman spectroscopy in forensic analysis: identification of cocaine and other illegal drugs of abuse. J Raman Spectrosc 47:28–38
4. Hargreaves MD, Page K, Munshi T, Tomsett R, Lynch G, Edwards HGM (2008) Analysis of seized drugs using portable Raman spectroscopy in an airport environment—a proof of principle study. J Raman Spectrosc 39:873–880
5. West MJ, Went MJ (2011) Detection of drugs of abuse by Raman spectroscopy. Drug Test Anal 3:532–538
6. Burnett AD, Edwards HGM, Hargreaves MD, Munshi T, Page K (2011) A forensic case study: the detection of contraband drugs in carrier solutions by Raman spectroscopy. Drug Test Anal 3:539–543
7. Sheldrick GM (2015) Crystal structure refinement with SHELXL. Acta Crystallogr C 71:3–8
8. Liu C, Jia W, Li T, Hua Z, Qian Z (2017) Identification and analytical characterization of nine synthetic cathinone derivatives *N*-ethylhexedrone, 4-Cl-pentedrone, 4-Cl-α-EAPP, propylone, *N*-ethylnorpentylone, 6-MeO-bk-MDMA, α-PiHP, 4-Cl-α-PHP, and 4-F-α-PHP. Drug Test Anal 9:1162–1171
9. Qian Z, Jia W, Li T, Liu C, Hua Z (2017) Identification and analytical characterization of four synthetic cathinone derivatives iso-4-BMC, β-TH-naphyrone, mexedrone, and 4-MDMC. Drug Test Anal 9:274–281
10. Brandt SD, Freeman S, Sumnall HR, Measham F, Cole J (2011) Analysis of NRG 'legal highs' in the UK: identification and formation of novel cathinones. Drug Test Anal 3:569–575
11. Boehringer Ingelheim GmbH (1968) Patent: GB1069797, 1964. Chem Abstr 68:95537w
12. European project response to challenges to forensic drugs analyses (2016) Analytical report: *N*-ethylhexedrone. www.policija.si/apps/nfl_response_web/0_Analytical_Reports_final/N-ethylhexedrone-ID-1503-16-report_final.pdf. Accessed 2 Oct 2016
13. European project response to challenges to forensic drugs analyses (2016) Analytical report: mexedrone. www.policija.si/apps/nfl_response_web/0_Analytical_Reports_final/Mexedrone-ID-1519-16-report_final.pdf. Accessed 2 Oct 2016
14. European project response to challenges to forensic drugs analyses (2016) Analytical report: *N*-ethyl-norpentylone. www.policija.si/apps/nfl_response_web/0_Analytical_Reports_final/N-Ethyl-norpentylone-ID-1437-16-report_final.pdf. Accessed 15 Jan 2016
15. Cayman chemical (2016) 4-Chloro-*N*-butylcathinone (hydrochloride). www.caymanchem.com/product/19972. Accessed 17 Aug 2016
16. Stainer T (1998) Hydrogen-bond distances to halide ions in organic and organometallic crystal structures: up-to-date database study. Acta Crystallogr B54:456–463