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Identification of ten new designer drugs by GC-MS, UPLC-QTOF-MS, and NMR as part of a police investigation of a Danish Internet company

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The ability of forensic laboratories to detect and identify unknown compounds is highly important since new, non-controlled designer drugs are appearing on the market with increasing frequency. In this study, the combined use of gas chromatography-mass spectrometry (GC-MS) and ultra performance liquid chromatography-quadrupole time of flight-mass spectrometry (UPLC-QTOF-MS) was used for screening of new unknowns. In one large seizure from a Danish Internet company, ten different drugs were identified. Several of the compounds were seized for the first time in Denmark. The GC-MS and UPLC-QTOF-MS analyses were supplemented by nuclear magnetic resonance (NMR) spectra for the structural elucidation of *p*-fluoroamphetamine, mephedrone (4-methylmethcathinone), flephedrone (4-fluoromethcathinone), PPP (α-pyrrolidinopropiophenone), MDPV (3,4-methylenedioxypyrovalerone), Bk-MBDB (2-methylamino-1-(3,4-methylenedioxyphenyl)butan-1-one), *p*FBT (3-(*p*fluorobenzoyl)-tropane), and JWH-073 (1-butyl-3-(1-naphthoyl)indol), whereas methylone (3,4-methylenedioxymethcathinone) and N-ethylcathinone matched electron impact-mass spectrometry (EI-MS) library spectra and therefore the screenings were considered sufficient.

EI-MS spectra and the proposed main fragmentation patterns are presented as well as QTOF-MS exact masses and fragments and NMR chemical shifts. For the β-ketophenylethylamines (mephedrone, flephedrone, PPP, MDPV, Bk-MBDB, methylone, and N-ethylcathinone) some general fragmentation patterns observed in the EI-MS and QTOF-MS spectra are further discussed and compared to other β-ketophenylethylamines. Copyright © 2011 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: QTOF; NMR; designer drugs; fragmentation; GC-MS

Introduction

A large number of new, non-controlled designer drugs have appeared on the market in recent years.[1–8] Due to the widespread use of the Internet, these drugs have also become more easily available and easier to distribute.[9]

In December 2008, an Internet company that trafficked in designer drugs was discovered near Copenhagen in Denmark. The forensic analyses of the products sold by the company revealed at least ten different drugs: methylone (3,4-methylenedioxymethcathinone), mephedrone (4-methylmethcathinone), flephedrone (4-fluoromethcathinone), *p*-fluoroamphetamine, *p*FBT (3-(*p*-fluorobenzoyl)tropane), PPP (α-pyrrolidinopropiophenone), *N*-ethylcathinone, MDPV (3,4-methylenedioxypyrovalerone), Bk-MBDB (2-methylamino-1-(3,4-methylenedioxyphenyl)butan-1-one), and JWH-073 (1-butyl-3-(1-naphthoyl)indole). Of these ten compounds, only methylone was a controlled substance in Denmark (since February 2008) at the time of the seizure. All of the compounds were reported to the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction).[10–12]

Several of the new, synthetic drugs that are sold as 'legal highs' belong to one of the classes of phenylethylamines, β-ketophenylethylamines, piperazines[13] and synthetic cannabinoids,[14] so except for *p*FBT, the drugs in the present case are no exception.

Analytical data are published for a number of compounds within these classes. Typically the identification has been carried out by gas chromatography-mass spectrometry (GC-MS), mostly electron impact-mass spectrometry (EI-MS)[1–6,9,15–28] but sometimes supplemented by chemical ionization-mass spectrometry (CI-MS)[3,17,20–25] or other MS techniques such as gas chromatography-tandem mass spectrometry (GC-MS/MS),[4,5] liquid chromatography-(tandem) mass spectrometry (LC-(MS/)MS),[9,26] or high-resolution MS.[28–30] GC-MS may be supplemented by other techniques such as infrared (IR)[1–3,16,21] or Raman spectroscopy,[30] while for the exact structure elucidation, the use of nuclear magnetic resonance (NMR) spectroscopy is unavoidable.[1–6,9,16,21–24,28,29,31]

However, the typical scenario with seizures of very new drugs is that, at the time of the seizure, published analytical data to assist in the identification of the compounds are limited, and reference substances may not yet be commercially available.

In this study, the GC-MS and NMR data were also supplemented by ultra performance liquid chromatography-quadrupole time of flight-mass spectrometry (UPLC-QTOF-MS) data, which

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provides the exact mass of the analyzed compound. From this, the most likely sum formula can be calculated. UPLC-TOF-MS has been introduced in the forensic screening of human blood, urine and hair,[32,33] but is not routinely used for the analysis of seized drugs. The use of UPLC-QTOF-MS instead of UPLC-TOF-MS even provides an additional fragmentation pattern, which makes it more powerful for identification purposes. A toxicological QTOF-MS spectra library was recently published by Broecker *et al*.[34]

For the unequivocal identification of new, unknown drugs in the absence of reference compounds, the combined use of GC-MS, UPLC-QTOF-MS, and NMR has been shown to be a powerful tool. However, for the forensic screening of human tissues in cases of suspected poisoning with a new designer drug, NMR is not easily applied. In such cases, it is necessary to obtain the reference substance, but in order to know which substance(s) to buy or synthesize, a good tentative identification would be useful. The recognition of general EI-MS and QTOF-MS fragmentation patterns for classes of compounds might potentially provide better tentative identification of unknown drugs. General fragmentation patterns for the β-ketophenylethylamines in this study are presented and discussed, including a comparison to published EI-MS spectra for other β-ketophenylethylamines.

Experimental

Chemicals

LCMS grade acetonitrile and methanol was obtained from Fisher Scientific UK (Leicestershire, UK), and formic acid 98-100% GR for analysis was obtained from Merck (Darmstadt, Germany). As internal standard in GC-MS analyses, a 26 mg/l solution of mepivacaine hydrochloride (Sigma-Aldrich, St Louis, MO, USA) in methanol was used. Deuterated methanol (CD_3OD) was obtained from Sigma-Aldrich (Denmark). Cathinone and methcathinone from Cerilliant (Round Rock, TX, USA), *N*,*N*-dimethylcathinone (metamfepramone) and MDPPP (3,4-methylenedioxypyrrolidinopropiophenone) from GM & C (Valencia, CA, USA), and *N*,*N*-diethylcathinone (amfepramone) donated by Pharmacia (Hilleroed, Denmark) were used to obtain QTOF-MS spectra for comparison.

Instrumentation

GC-MS analysis was carried out with a HP 6890 gas chromatograph coupled to a HP 5973 mass spectrometer. The instrument was operated in split mode (1:10) and the injection port temperature was maintained at 250 °C. The injection volume was 1 μl. The column was a HP5MS 19091S-433, 30 m x 0.25 mm i.d., 0.25 μm. The temperature program was an initial temperature of 80 °C, increasing 10 °C/min to 310 °C, and then held at 310 °C for 10 min with a carrier gas (helium) pressure of 8.8 psi. The transfer line, source, and quadrupole temperatures were 280, 230, and 150 °C, respectively. The MS was operated in the full scan mode in the range *m/z* 40–500.

UPLC-QTOF-MS analysis was carried out with an ACQUITY UPLC system (Waters Corp, Milford, Massachusetts, USA) coupled to a SYNAPT G2 (Waters MS Technologies, Manchester, UK) orthogonal acceleration quadrupole time-of-flight mass spectrometer. Chromatographic separations were performed on a 100 x 2.1 mm ACQUITY BEH 1.7 μm C18 column (Waters Corp, Milford, Massachusetts, USA). The mobile phase was composed of solvent A (0.1% formic acid) and B (100% acetonitrile). The column was maintained at 50 °C and eluted with a gradient of 0–20% B (0–4.0 min), 20–95% B (4.0–9.0 min); the column was then flushed with 100% B (9–11 min). The total runtime was 15 min at a flow rate of 0.60 ml/min.

The autosampler was maintained at 10 °C. Mass spectrometry was operated in positive ion mode with electrospray ionization (Z-spray). The nebulization gas was set to 750 L/h at a temperature of 350 °C. The cone gas was set to 10 L/h and the source temperature was set to 120 °C. The capillary voltage and the cone voltage were set to 500 and 30 V, respectively. The function 1 voltage was set to 10 V, and the function 2 voltage was set to 20–40 V ramping. The SYNAPT G2 was operated in V optics mode (resolution mode) with >20 000 resolution. The data acquisition rate was set to 0.15 sec/scan, with 0.024 sec inter scan delay; data were collected from 0 min to 9 min. All analyses were acquired using the lock spray to ensure accuracy and reproducibility; leucine-enkephaline was used as the lock mass (*m/z* 556.2771) at a concentration of 300 ng/ml and a flow rate of 50 μl/min. Data were collected in centroid mode from *m/z* 50–1200. The reference spray was automatically sampled with a 30 s interval. There is a difference of around 0.5 mDa between the theoretical mass and the calculated mass, as the software used adds the mass of a hydrogen atom instead of the mass of a proton.

NMR

All NMR spectra were acquired on 1 Bruker Avance av400 WB (Bruker, Rheinstetten, Germany) operating at 400.13 MHz for ^1H using standard pulse program from the Bruker pulse program library. All ^1H NMR spectra were acquired using a 30° pulse, 32 K data points (1 K = 1024), an appropriate number of scans, and a relaxation delay of 2.0 s. Spectra were zero-filled prior to Fourier transformation to 128 K (real part), and apodized with an exponential function (line broadening typically 0.2 Hz).

2D $^1H^1H$ COSY NMR spectra were acquired in the phase sensitive mode (States-TPPI) using 1 K data points for the acquisition dimension and 256–512 increments. Typically 16 to 64 transients were recorded for each increment using 8 dummy scans, and a relaxation delay of 2.0 s. Data were zero-filled and Fourier transformed into 2 K data points in each dimension (real part) using a squared sine bell (phase shift 0, corresponding to echo type signals/dispersive line shapes).

2D $^1H^1H$ NOESY NMR spectra were acquired in the phase sensitive mode (States-TPPI) using 2 K data points for the acquisition dimension and 512 increments. Typically 16 to 64 transients were recorded for each increment using 4 dummy scans, and a relaxation delay of 2.0 s and a mixing time of 300 ms (small molecule general size at 400 MHz). Data were zero-filled and Fourier transformed into 2 K data points in each dimension (real part) using a squared sine bell (phase shift 2, corresponding to an absorptive line shape).

1D ^{13}C NMR spectra were acquired in the power gated mode, using a 30 pulse, 64 K data points, an appropriate number of scans, and a relaxation delay of 2.0 s. Spectra were zero-filled prior to Fourier transformation to 64 K (real part), and apodized with an exponential function (line broadening typically 2.0 Hz). DEPT135 1D ^{13}C NMR spectra were acquired in the power gated mode, 64 K data points, an appropriate number of scans, and a relaxation delay of 1.0 s. Spectra were either not zero-filled or zero-filled prior to 64 K (real part) prior to Fourier transformation, and apodized with an exponential function (line broadening typically 1.0–2.0 Hz). Polarization transfer was optimized for a coupling constant of 145 Hz.

2D $^1H^{13}C$ HMQC NMR spectra (proton detected) were acquired in the phase sensitive mode (States-TPPI) using 4 K data points

for the acquisition dimension and 256 increments. Typically 48 to 256 transients were recorded for each increment using 16 dummy scans, and a relaxation delay of 3.0 s. Data were zero-filled and Fourier transformed into 1–2 K data points in each dimension (real part) using a squared sine bell (phase shift 0, corresponding to absorption type line shapes). Parameters were optimized for a coupling constant of 145 Hz. Linear prediction was applied in the second dimension (forward prediction starting at first data point, 32 coefficients, and 2 K output points).

2D $^{1}H^{13}C$ HMBC NMR spectra (proton detected) were acquired in the phase sensitive mode (States-TPPI) using 4 K data points for the acquisition dimension and 256 increments. Typically 48 to 256 transients were recorded for each increment using 16 dummy scans, and a relaxation delay of 3.0 s. Data were zero-filled and Fourier transformed into 1–2 K data points in each dimension (real part) using a squared sine bell (phase shift 0, corresponding to absorption type line shapes). Two separate spectra were acquired where parameters were optimized for a coupling constant of either 12 Hz or 9 Hz. Linear prediction was applied in the second dimension (forward prediction starting at first data point, 32 coefficients, and 2 K output points).

HMBC

All spectra were data processed using Topspin 1.3 or 3.0 (Bruker, Rheinstetten, Germany).

All ^{1}H NMR spectra and 1D ^{13}C NMR spectra of fluorine-containing compounds were analyzed using gnmr 5.5 (currently not commercially available) using iterative fitting of chemical shifts and coupling constants and full line shape analysis.

Sample preparation

GC-MS

Approximately 50 mg of the unknown drug powder was extracted by 5 ml methanol (10 min rotation in a tube rotator SB1 from Stuart Scientific followed by 5 min centrifugation at 3000 rpm). An aliquot (50 µl) of the extract was diluted by 1000 µl mepivacaine solution in a GC-MS vial.

UPLC-QTOF-MS

Aliquots of 0.2 mg/l were prepared in 20% methanol.

CNMR

All samples were dissolved in 0.60 ml deuterated methanol (CD_3OD).

Case description

In December 2008, the Norwegian police contacted the Danish police because a person known to the Norwegian police had received a parcel from the Internet company Organic-ogc.com, located in Denmark. In this parcel, the police found some white powder, and a letter with the chemical name Bk-MBDB which the police thought was the same as the illegal substance MBDB. The Danish police arrested the owner of the Internet company. They found a safe containing many different powdered substances, each marked with the formula and chemical name. The following compounds were identified: *p*FBT, flephedrone, mephedrone, methylone, PPP, *p*-fluoramphetamine, *N*-ethylcathinone, MDPV, Bk-MBDB and JWH-073 (see Table 1). Nine out of the ten different compounds had been correctly marked with formulae and names, whereas the last powder had been marked "(*R*)-3-((1-methylpyrrolidin-2-yl)methyl)-1*H*-indol-4-ol" (lucigenol), but turned out to be JWH-073. Records recovered from the computer from the site proved that there had been ~2000 sales of the different materials to locations in Norway, Denmark, and Germany. The company did not have any export or import licenses. The police found ~3 kg methylone, 1.4 kg *p*-fluoroamphetamine and 10 kg mephedrone. The police also found a file index of the customers. At the time of the seizure in December 2008, only methylone was (since February 2008) on the Danish list of controlled substances. In September 2009, the owner of the Internet company was sentenced to 18 months in jail and was fined €10 000.

Results and discussion

GC-MS

The GC retention times for the ten compounds are given in Table 1. EI-MS spectra are shown in Figure 1 for eight of the compounds including one phenylethylamine (*p*-fluoroamphetamine) and 7 β-keto-phenylethylamines (mephedrone, flephedrone, methylone, PPP, *N*-ethylcathinone, MDPV and Bk- MBDB). Although the EI-MS spectra have been published elsewhere, the comparison of the spectra revealed a general fragmentation pattern as summarized in Figure 2. Fragment F1 is the base peak fragment. Both of the fragments F1 and F2 have also been described by Dallakian *et al.* [35] Fragment F3 was observed for all of the β-keto-phenylethylamines, but not for phenylethylamines without the β-keto-substitution. The fragments F1, F2 and F3 are summarized for 25 β-keto-phenylethylamines in Table 2.

The last two compounds, *p*FBT and JWH-073, belonged to other classes of compounds. Their EI-MS spectra are shown in Figure 3.

UPLC-QTOF-MS

The UPLC-QTOF-MS gives the same kind of data as a UPLC-TOF-MS. The ions are then further fragmented in the additional collision cell. The UPLC retention times for the ten compounds are given in Table 1.The protonated molecules and the most abundant fragments for each of the ten compounds are listed in Tables 3–6 along with the calculated most likely sum formulae (smallest mass error, isotope pattern for proposed MH + confirmed, sum formula of fragment should be a subset of the mother ion). For the full spectra we refer to the supplemental material. For *p*-fluoroamphetamine significant source fragmentation occurred, while for the other

Table 1. CAS-numbers, GC and UPLC retention times of the ten compounds

Compound	CAS no.	RT (GC) (min)	RT (UPLC) (min)
p-fluoroamphetamine	459-02-9	5.37	2.72
Mephedrone	1189805-46-6/ 1189726-22-4 (HCl)	9.53	3.13
Flephedrone	7589-35-7	7.83	2.37
Methylone	186028-79-5 (HCl)	12.51	2.32
PPP	19134-50-0	11.58	2.69
N-ethylcathinone	18259-37-5/ 51553-17-4 (HCl)	8.79	2.46
MDPV	687603-66-3/ 24622-62-6 (HCl)	16.91	4.31
Bk-MBDB	17762-90-2 (HCl)	13.26	2.98
*p*FBT	96920-56-8	14.75	4.44
JWH-073	208987-48-8	24.60	7.96

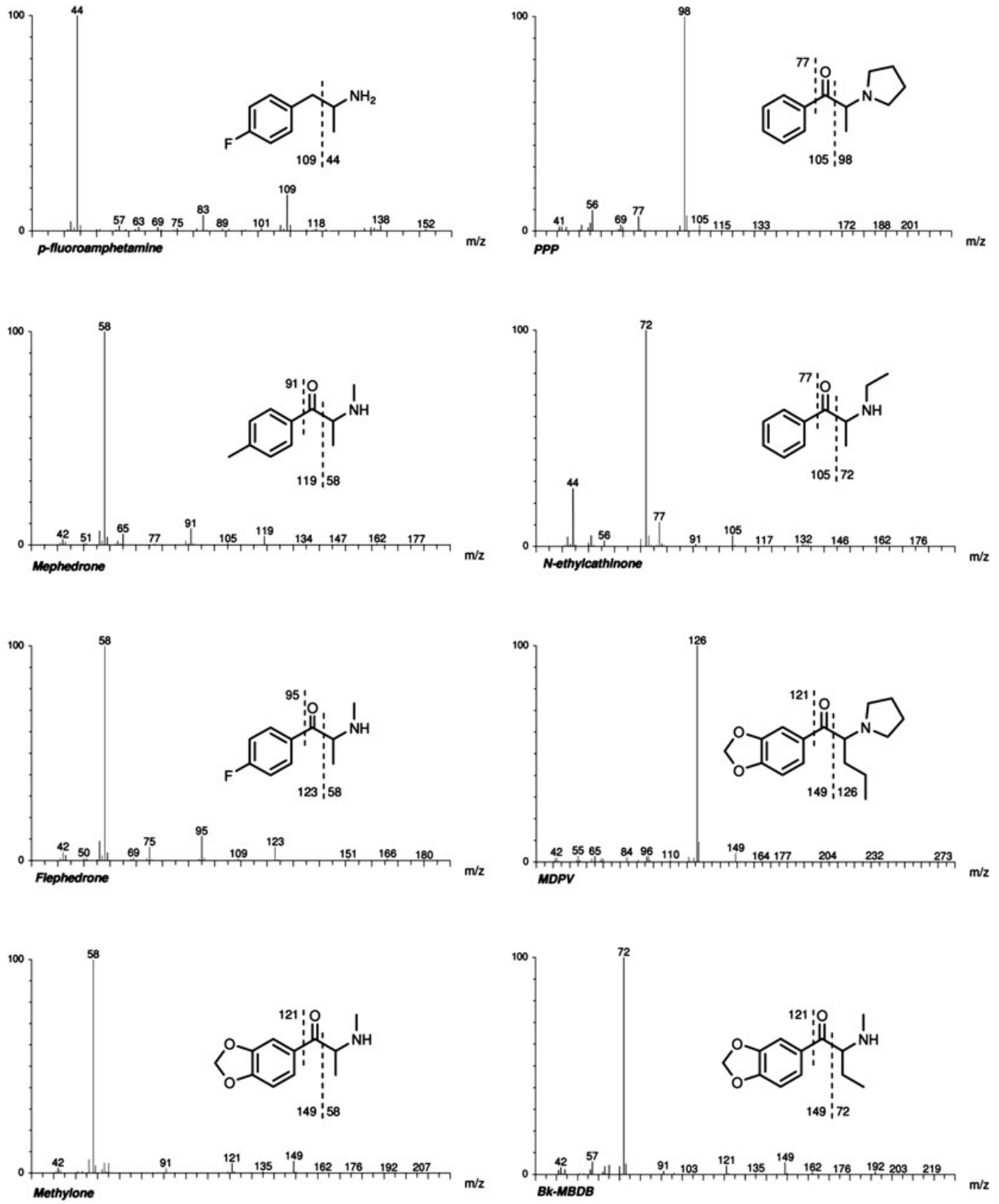


Figure 1. EI-MS spectra and proposed fragmentation for the eight phenylethylamines, of which seven are β-keto-phenylethylamines.

compounds no source fragmentation or only some loss of water occurred, see supplemental material. Isolation of the MH + ion from the source resulted in the same fragments formed in the collision cell.

Although the fragmentation mechanisms of EI and QTOF mass spectrometry are different, some of the same fragments can be observed (marked with an asterisk in Tables 3–6). A general QTOF fragmentation pattern for all 7 β-keto-phenylethylamines

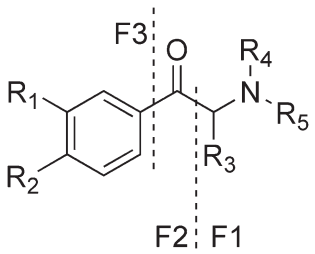


Figure 2. Proposed EI-MS fragmentation pattern for a general β-keto-phenylethylamine, fragments F1, F2, and F3.

(mephedrone, flephedrone, methylone, PPP, *N*-ethylcathinone, MDPV, and Bk-MBDB) could not be identified, as opposed to the data obtained from EI-MS spectra (Figure 2), but differentiation into subclasses gave rise to some interesting speculations, although a study of fragmentation mechanisms was not included in this investigation. Comparison to reference compounds of some other β-keto-phenylethylamines, run under the same conditions, were also made (cathinone, methcathinone, *N,N*-dimethylcathinone (metamfepramone), *N,N*-diethylcathinone (amfepramone), and MDPPP (3,4-methylenedioxypyrrolidinopropiophenone), included in Tables 4 and 5).

One subclass could be the *N,N*-dialkylcathinones including the pyrrolidino-compounds (PPP, MDPV, MDPPP, *N,N*-diethylcathinone, and *N,N*-dimethylcathinone), whose fragmentation patterns had the common feature of a loss of the *N*-substituent (#1a, Table 4, e.g. the pyrrolidine-ring). Another common feature was that the ion corresponding to water loss was not observed for these compounds, except a trace for *N,N*-dimethylcathinone. PPP, MDPV, MDPPP and *N,N*-diethylcathinone also showed a cleavage between the keto- and the alkyl-groups (#1b, Table 4). For PPP, MDPPP, *N,N*-diethylcathinone and *N,N*-dimethylcathinone the loss of the *N*-substituent seems to be followed by loss of CO (#1c), while for MDPV and MDPPP it seems, that the pyrrolidine-loss is followed by the loss of CH_2O (#1 d), probably at the methylenedioxy function. The *N*-monoalkylcathinones could be another subclass (Table 5).

Their main fragments are speculated to arise from water loss (#2a) followed by the loss of the *N*-alkyl group during ring formation into an indole-structured radical cation (#2b), which, in turn, can lose a hydrogen-radical (#2c). This can explain the two fragments that differ only by one mass unit (shown for mephedrone in Figure 4). *N,N*-dimethylcathinone shows traces of the same fragments (Table 4), but the subclass 1 fragments are more abundant.

Methylone and Bk-MBDB, for which water loss was also observed, did not fragment like this to a significant degree. Probably, the formation of a 5,6-dioxymethylene-indole was not favorable (although a small peak at 188.0712 Da, corresponding to 2-ethyl-5,6-dioxymethylene-indole after loss of hydrogen ($C_{11}H_{10}NO_2$) was observed for Bk- MBDB). The 3,4-methylenedioxycathinones must therefore be categorized as even another subclass (Table 6). They were characterized by the common (gross) loss of CH_4O_2, $C_2H_4O_3$, and $C_3H_7O_3$, which possibly are fragments arising from a series of subsequent losses of H_2O (#3a), CH_2O (#3b), CO (#3c) and ·CH3 (#3 d). Since the keto-oxygen and the methylenedioxy-oxygens are separated by 4 and 5 carbons, it is obvious that the gross losses of $C_2H_4O_3$ and $C_3H_7O_3$ must occur in multiple steps,

Table 2. EI-MS fragments of β-keto-phenylethylamines corresponding to F1, F2, and F3 in Figure 2

Compound (β-ketophenylethylamines)	EI-MS fragment			Reference
	F1	F2	F3	
cathinone	44	105	77	NIST MS library
Bk-MDA (3,4-methylenedioxycathinone)	44	149	121	[21]
methcathinone	58	105	77	NIST MS library
mephedrone	58	119	91	present case, [2,30]
flephedrone	58	123	95	present case, [1,23]
methedrone (*p*-methoxymethcathinone)	58	135	107	[37]
methylone	58	149	121	present case, [21,30]
N-ethylcathinone	72	105	77	present case, [16]
N,N-dimethylcathinone (metamfepramone)	72	105	77	[16]
Bk-MBDB (butylone)	72	149	121	present case, [9,15,30]
Bk-MDDMA (3,4-methylenedioxy-*N,N*-dimethylcathinone)	72	149	121	[15]
Bk-MDEA/ ethylone (3,4-methylenedioxy-*N*-ethylcathinone)	72	149	121	[15,21]
3,4-methylenedioxy-*N,N*-dimethylcathinone	72	149	121	[21]
Bk-MBDP/ pentylone (2-methylamino-1-(3,4-methylenedioxyphenyl)pentan-1-one)	86	149	121	[23]
PPP	98	105	77	present case, [17]
MPPP (*p*-methyl-α-pyrrolidinopropiophenone)	98	119	91	[17,23,25]
MDPPP (3,4-methylenedioxypyrrolidinopropiophenone)	98	149	121	[20]
N,N-diethylcathinone (amfepramone)	100	105	77	NIST MS library
3,4-methylenedioxy-N,N-diethylcathinone	100	149	121	[21]
MPBP (*p*-methyl-α-pyrrolidinobutiophenone)	112	119	91	[4]
MDPBP (3,4-methylenedioxypyrrolidinobutiophenone)	112	149	121	[23]
MDPV	126	149	(121)	present case, [5,9,23]
β-naphyrone (1-naphthalen-2-yl-2-pyrrolidin-1-yl-pentan-1-one)	126	155	127	[22,24,26]
α-naphyrone (1-naphthalen-1-yl-2-pyrrolidin-1-yl-pentan-1-one)	126	155	-	[22]
MPHP (*p*-methyl-α-pyrrolidinohexiophenone)	140	119	91	[4,27]
α-phtalimidopropiophenone	174	105	77	[2]

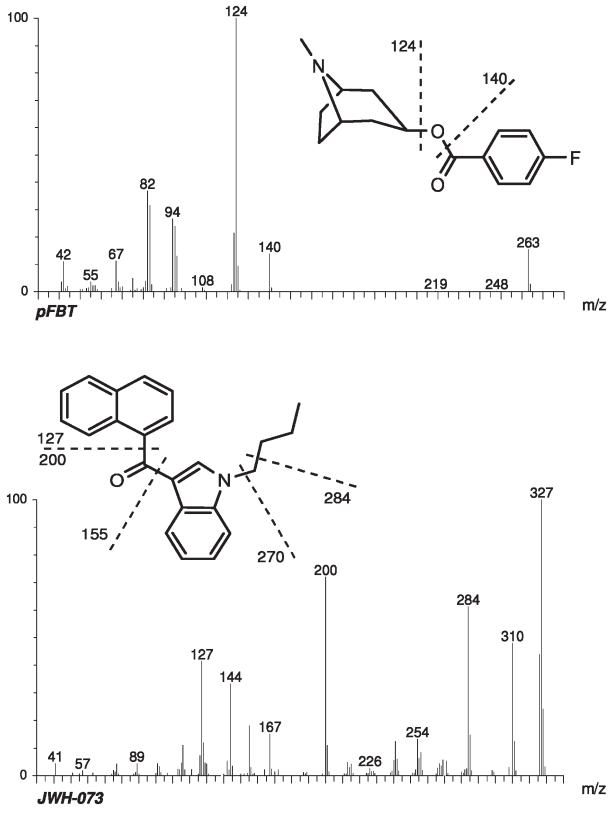


Figure 3. EI-MS spectra and proposed fragmentation for *p*FBT and JWH-073.

but also the loss of CH_4O_2 could reasonably be a two-step fragmentation. A mechanism including an initial water loss would also explain why these losses were not observed for MDPV and MDPPP (although a closer inspection revealed small traces of the ion corresponding to the gross loss of $C_2H_4O_3$), since MDPV and MDPPP did not undergo a significant water loss.

p-Fluoroamphetamine

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the spectrum reported by Rösner *et al.*[3] and the fragments F1 and F2 (Figure 2) were observed at m/z 44 and m/z 109, respectively. The $[M-1]^+$ ion was seen at m/z 152 and the $[M-15]^+$ ion at *m/z* 138. As for amphetamine, the molecular ion itself is not observed. The chromatogram showed a small impurity of amphetamine eluting just ahead of *p*-fluoroamphetamine. The impurity may originate from an impure precursor in the synthesis.

UPLC-QTOF-MS

See Table 3. The observed fragment (109.0450 Da) was similar to the EI-MS fragment at *m/z* 109 (F2), while the fragment of 137.0766 Da corresponded to loss of ammonia.

NMR

From GC-MS data, the compound was known to be a fluoroamphetamine isomer. Examining the ^{1}H NMR spectrum, it is immediately obvious that the aromatic ring is para-substituted. Chemical shifts and coupling patterns are consistent with the compound being p-fluoroamphetamine. This is confirmed by the ^{13}C NMR spectrum where again the spectrum is that of a para-substituted aromatic compound, where one substituent is fluorine. The aromatic signals of the ^{13}C NMR spectrum can be unequivocally assigned by the diminishing $^nJ_{CF}$ (ipso > ortho > meta > para). A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems (both ^{1}H and ^{13}C). The results are in reasonable agreement with literature data[3] considering the different solvent used (see supplemental data).

Mephedrone (4-methylmethcathinone):

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the spectrum reported by Camilleri *et al.*[2] and showed the fragments F1, F2, and F3 (Figure 2, Table 2) at *m/z* 58, *m/z* 119, and *m/z* 91, respectively.

UPLC-QTOF-MS

See Table 5. We suggest the observed fragment of 145.0880 Da is a 2,6-dimethylindole radical cation (Figure 4) arising from loss of water followed by loss of a methyl-radical. The radical cation can lose a hydrogen-radical, resulting in the fragment of 144.0809 Da. Fragmentation of radical cations is known from EI mass spectrometry, and indeed a library EI-MS spectrum (NIST mass spectral library) of 2,6-dimethylindole does have $[M]^{+\cdot}$ and $[M-1]^+$ as the main peaks.

Table 3. UPLC-QTOF-MS data for *p*-fluoroamphetamine, *p*FBT and JWH-073. Fragments also found in the EI-MS spectra are marked by an asterisk

Compound	Observed m/z (Da)	Abundance (%)	Likely formula	Theoretical m/z (Da)	m/z error (mDa (ppm))
p-Fluoro-amphetamine	154.1028	1	MH + = C9H13FN+	154.1032	−0.4 (−2.6)
	137.0766	1	C9H10F+	137.0767	−0.1 (−0.7)
	109.0450	100	C7H6F + (*)	109.0454	−0.4 (−3.7)
	83.0284	7	C5H4F+	83.0297	−1.3 (−15.7)
*p*FBT	264.1394	93	MH + = C15H19FNO2+	264.1400	−0.6 (−2.3)
	124.1121	100	C8H14N + (*)	124.1126	−0.5 (−4.0)
	93.0695	28	C7H9+	93.0704	−0.9 (−9.7)
	91.0539	13	C7H7+	91.0548	−0.9 (−9.9)
JHW-073	328.1705	17	MH + = C23H22NO+	328.1701	0.4 (1.2)
	200.1069	19	C13H14NO + (*)	200.1075	−0.6 (−3.0)
	155.0492	100	C11H7O + (*)	155.0497	−0.5 (−3.2)
	144.0444	9	C9H6NO+	144.0449	−0.5 (−3.5)
	127.0545	46	C10H7+ (*)	127.0542	−0.3 (2.4)

* Similar fragment observed in the EI-MS spectrum

Table 4. UPLC-QTOF-MS data for the suggested subclass 1 of β-keto-phenylethylamines (*N,N*-dialkylcathinones). Fragments also found in the EI-MS spectra are marked by an asterisk, and fragments used for subclassification are marked by #no

Compound	Observed m/z (Da)	Abundance (%)	Likely formula	Theoretical m/z (Da)	m/z error (mDa (ppm))
PPP	204.1385	45	MH + = C13H18NO+	204.1388	−0.3 (−1.5)
	184.1118	5	C13H14N+	184.1126	−0.8 (−4.3)
	133.0651	18	C9H9O + (#1a)	133.0653	−0.2 (−1.5)
	105.0699	100	C8H9+ (#1c)	105.0704	−0.5 (−4.8)
	98.0960	54	C6H12N + (*, #1b)	98.0970	−1.0 (−10.2)
MDPV	276.1596	42	MH + = C16H22NO3+	276.1600	−0.4 (−1.4)
	205.0856	30	C12H13O3+ (#1a)	205.0865	−0.9 (−4.4)
	175.0744	62	C11H11O2+ (#1d)	175.0759	−1.5 (−8.6)
	149.0229	76	C8H5O3 + · (*)	149.0239	−1.0 (−6.7)
	135.0435	82	C8H7O2+	135.0446	−1.1 (−8.1)
	126.1276	100	C8H16N + (*, #1b)	126.1283	−0.7 (−5.5)
MDPPP	248.1288	746	MH + = C14H18NO3+	248.1287	0.1 (0.4)
	177.0546	40	C10H9O3+ (#1a)	177.0552	−0.6 (−3.4)
	149.0600	51	C9H9O2+ (#1c)	149.0603	−0.3 (−2.0)
	147.0443	124	C9H7O2+ (#1d)	147.0446	−0.3 (−2.0)
	119.0495	34	C8H7O+	119.0497	−0.2 (−1.7)
	98.0966	61	C6H12N + (*, #1b)	98.0970	−0.4 (−4.1)
N,N-diethyl-cathinone	206.1548	100	MH + = C13H20NO+	206.1545	0.3 (1.5)
	133.0649	7	C9H9O + (#1a)	133.0653	−0.4 (−3.0)
	105.0699	17	C8H9+ (#1c)	105.0704	−0.5 (−4.8)
	100.1119	8	C6H14N + (*, #1b)	100.1126	−0.7 (−7.0)
N,N-dimethyl-cathinone	178.1237	100	MH + = C11H16NO+	178.1232	0.5 (2.8)
	160.1123	1	C11H14N + (#2a)	160.1126	−0.3 (−1.9)
	144.0807	1	C10H10N + (#2c)	144.0813	−0.6 (−4.2)
	133.0651	20	C9H9O + (#1a)	133.0653	−0.2 (−1.5)
	105.0707	29	C8H9+ (#1c)	105.0704	0.3 (2.9)

#1a-d: Subclass 1 fragments expected to be #1a: Loss of N-substituent, #1b: cleavage, #1c: loss of CO from fragment #1a,
#1d : loss of CH2O from fragment #1a
#2a-c: Subclass 2 fragments expected to be #2a: Water loss, #2b : Subsequent indole-structured radical-cation, #2c: Loss of hydrogen from #2b.
*: Similar fragment observed in the EI-MS spectrum

NMR

Examining the ^{1}H NMR spectrum, the following fragments are immediately identified: A para-substituted, aromatic fragment with a polarized double bond as one substituent and an aliphatic chain as the other. A methyl group with an olefinic substituent, an *N*-methyl group, and a CH_3CH fragment with at least one electronegative substituent.

A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems. The results are in reasonable agreement with literature data[29] considering the different solvent used (see supplemental data).

Flephedrone (4-fluoromethcathinone)

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the literature [1,23] and showed the fragments F1, F2 and F3 (Figure 2, Table 2) at *m/z* 58, *m/z* 123 and *m/z* 95, respectively.

UPLC-QTOF-MS

See Table 5. We suggest a fragmentation similar to that of mephedrone is responsible for the fragments of 148.0558 Da and 149.0630 Da.

NMR

Examining the ^{1}H NMR spectrum immediately leaves the following fragments: No CH_2 group is present, and a CH_3-group at the nitrogen atom. Furthermore, the chemical shift of the aromatic protons indicates a substituent with a polarized double bond, and a CH_3-CH fragment is evident. The coupling pattern of the aromatic protons can only arise from a para-substituted phenyl group where one of the substituents is fluorine (given the symmetry and the extra splittings), since a general idea of the structure was known from GC-MS. A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems. These results are in reasonable agreement with literature data[1] considering the different solvent used (see supplemental data).

Methylone (3,4-methylenedioxymethcathinone)

GC-MS

The EI-MS spectrum (Figure 1) matched a known library spectrum, and the fragments F1, F2, and F3 (Figure 2, Table 2) were recognized at *m/z* 58, *m/z* 149, and *m/z* 121, respectively.

UPLC-QTOF-MS

See Table 6. Fragments possibly corresponding to a sequential loss of H_2O, CH_2O, CO and ·CH3 were observed (190.0854, 160.0753 Da, 132.0804 Da, and 117.0569).

Table 5. UPLC-QTOF-MS data for the suggested subclass 2 of β-keto-phenylethylamines (*N*-monoalkylcathinones). Fragments also found in the EI-MS spectra are marked by an asterisk, and fragments used for subclassification are marked by #no

Compound	Observed m/z (Da)	Abundance (%)	Likely formula	Theoretical m/z (Da)	m/z error (mDa (ppm))
Mephedrone	178.1221	1	MH + = C11H16NO+	178.1232	−1.1 (−6.2)
	160.1125	12	C11H14N + (#2a)	160.1126	−0.1 (−0.6)
	145.0880	85	C10H11N + · (#2b)	145.0891	−1.1 (−7.6)
	144.0809	100	C10H10N + (#2c)	144.0813	−0.4 (−2.8)
	119.0862	8	C9H11+	119.0861	0.1 (0.8)
	91.0543	6	C7H7+ (*)	91.0548	−0.5 (−5.5)
Flephedrone	182.0971	2	MH + = C10H13FNO+	182.0981	−1 (−5.5)
	164.0869	18	C10H11FN + (#2a)	164.0876	−0.7 (−4.3)
	149.0630	100	C9H8FN + · (#2b)	149.0641	−1.1 (−7.4)
	148.0558	81	C9H7FN + (#2c)	148.0563	−0.5 (−3.4)
	103.0541	15	C8H7+	103.0548	−0.7 (−6.8)
N-Ethyl-cathinone	178.1220	2	MH + = C11H16NO+	178.1232	−1.2 (−6.7)
	160.1127	9	C11H14N + (#2a)	160.1126	0.1 (0.6)
	132.0802	44	C9H10N+	132.0813	−1.1 (−8.3)
	131.0718	50	C9H9N + · (#2b)	131.0735	−1.7 (−13.0)
	130.0648	100	C9H8N + (#2c)	130.0657	−0.9 (−6.9)
	117.0572	41	C8H7N + ·	117.0578	−0.6 (−5.1)
	105.0694	22	C8H9+	105.0704	−1.0 (−9.5)
Meth-cathinone	164.1071	9	MH + = C10H14NO+	164.1075	−0.4 (−2.4)
	146.0966	100	C10H12N + (#2a)	146.0970	−0.4 (−2.7)
	131.0730	64	C9H9N + · (#2b)	131.0735	−0.5 (−3.8)
	130.0657	38	C9H8N + (#2c)	130.0657	0.0 (0.0)
	105.0699	7	C8H9+	105.0704	−0.5 (−4.8)
Cathinone	150.0927	9	MH + = C9H12NO+	150.0919	0.8 (5.3)
	132.0823	100	C9H10N + (#2a)	132.0813	1.0 (7.6)
	117.0584	28	C8H7N + ·	117.0578	0.6 (5.1)
	105.0712	11	C8H9+	105.0704	0.8 (7.6)

#2a-c: Subclass 2 fragments expected to be #2a: Water loss, #2b: Subsequent indole-structured radical-cation, #2c: Loss of hydrogen from #2b.
*: Similar fragment observed in the EI-MS spectrum

Table 6. UPLC-QTOF-MS data for the suggested subclass 3 of β-keto-phenylethylamines (3,4-methylenedioxy-compounds). Fragments also found in the EI-MS spectra are marked by an asterisk, and fragments used for subclassification are marked by #no

Compound	Observed m/z (Da)	Abundance (%)	Likely formula	Theoretical m/z (Da)	m/z error (mDa (ppm))
Methylone	208.0971	3	MH + = C11H14NO3+	208.0974	−0.3 (−1.4)
	190.0854	5	C11H12NO2+ (#3a)	190.0868	−1.4 (−7.4)
	160.0753	100	C10H10NO + (#3b)	160.0762	−0.9 (−5.6)
	132.0804	81	C9H10N + (#3c)	132.0813	−0.9 (−6.8)
	117.0569	21	C8H7N + · (#3d)	117.0578	−0.9 (−7.7)
	91.0545	8	C7H7+	91.0548	−0.3 (−3.3)
Bk-MBDB	222.1125	3	MH + = C12H16NO3+	222.1130	−0.5 (−2.3)
	204.1026	8	C12H14NO2+ (#3a)	204.1024	0.2 (1.0)
	175.0625	61	C10H9NO2 + ·	175.0633	−0.8 (−4.6)
	174.0914	100	C11H12NO + (#3b)	174.0919	−0.5 (−2.9)
	146.0966	43	C10H12N + (#3c)	146.0970	−0.4 (−2.7)
	131.0732	46	C9H9N + · (#3d)	131.0735	−0.3 (−2.3)

#3a-d: Subclass 3 fragments suggested to be #3a: Water loss, #3b: Subsequent loss of CH2O, #3c: Subsequent loss of CO,
#3d: Subsequent loss of a CH3 radical
*: Similar fragment observed in the EI-MS spectrum

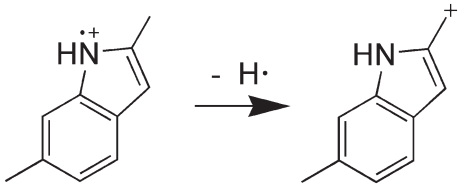


Figure 4. Proposed structure of two QTOF-MS fragments of the *N*-alkylcathinones, shown for mephedrone.

PPP (α-pyrrolidinopropiophenone)

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the spectrum reported by Springer *et al.*[17] and the fragments F1, F2, and F3 (Figure 2, Table 4) were observed at *m/z* 98, *m/z* 105, and *m/z* 77, respectively.

Table 7. NMR data for PPP including comparison to published data for the homologue pyrovalerone

Peak		δ ^{13}C (ppm)	DEPT 135	Litt.[35] (Analog)	δ ^{1}H (ppm), (multiplicity) J	Litt.[35] (Homologue)
1	C(1) = O	197.4	no	196.7		
2	C(4′)H	136.3	u	134.9	7.745, (adt) 7.23 Hz	7.78
3	C(1′)	134.4	no	134.5		
4	C(3′)H + C(5′)H	130.6	u	129.2	7.611, (adt) 8.04, 7.23 Hz	7.64
5	C(2′)H + C(6′)H	130.2	u	128.8	8.092, (add) 8.04 Hz	8.11
6	C(2)H	66.8	u	67.3	5.436, (t) 7.07 Hz	5.62
7	C(2″)H_2 + C(5″)H_2	55.8	d	53.6	3.743 & 3.108, (m)	3.64 & 3.49
8		53.4	d	51.9	3.386 & 3.759, (m)	3.26 & 3.10
9	C(3″)H_2 + C(4″)H_2	24.5	d	31.7	2.176 & 2.090, (m)	2.15–1.85
10		24.4	d	31.7	2.22 8 & 2.064, (m)	

no: not observed, m: multiplet, s: singlet, t: triplet, add: apparent double doublet, adt:apparent double triplet

Structure:

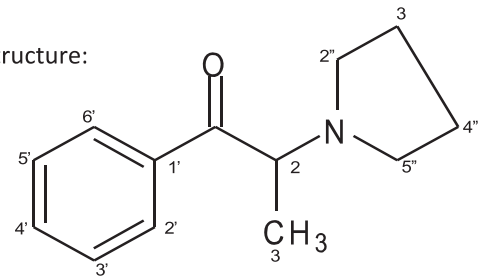
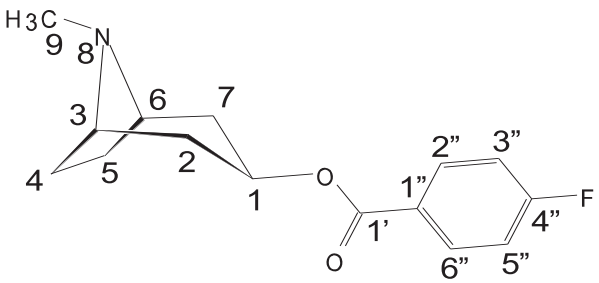


Table 8. NMR data for *p*FBT

Peak		^{1}H NMR	^{13}C NMR
#	nH	δ, ppm. J, Hz	δ, ppm. J, Hz
1	1	5.307. t, $^{3}J_{1\_2a} = {}^{3}J_{1\_7a} = 5.0$	66.53
2a, 7a	2	2.287. bd, $^{3}J_{1\_2a} = {}^{3}J_{1\_7a} = 0.0$, $^{2}J_{2a2e} = -16.2$	36.07
2e and 7e	2	2.650. dt, $^{3}J_{1\_2e} = {}^{3}J_{1\_7a} = 5.0$, $^{2}J_{2a2e} = -16.2$	
3, 6	2	3.998. bs.	63.84
4e,4a,5e,5a	4	2.453. bs.	25.06
9	3	2.875 bs.	39.67
1′		-	165.86
1″		-	127.67. $^{4}J_{CF} = 3.3$
2″,6″	2	8.083. AA′, $^{3}J_{2''-3''} = 8.6$ $^{4}J_{2''-6''} = 2.36$, $^{5}J_{2''-5''} = 0.0$, $^{4}J_{H-F} = 5.8$	133.28. $^{3}J_{CF} = 9.53$
3″,5″	2	7.262. AA′, $^{3}J_{2''-3''} = 8.6$ $^{4}J_{3''-5''} = 2.6$, $^{5}J_{3''-6''} = 0.0$ $^{3}J_{H-F} = 8.7$	116.85. $^{2}J_{CF} = 22.44$
4″		-	167.36. $^{1}J_{CF} = 252.98$

In this solvent (CD3OD) at this field (400.13 MHz, 1H) at this temperature (298.2 K) a large part of the signals from the Tropane system are exchange broadened. s: singlet. q: quartet. d: doublet. bs: exchange broadenen singlet. bd: exchange broadened doublet. AA′: AA′ system of a parasubstituted (aromatic) spin-system. 2J2a2e = 2J7a7e.



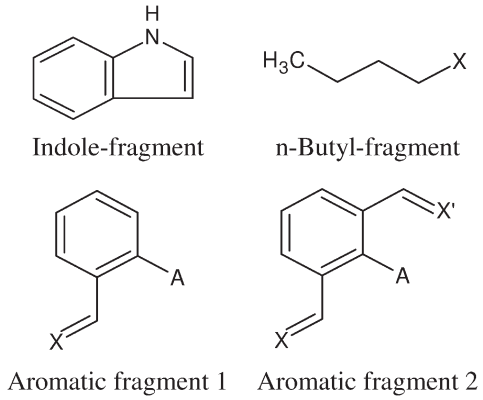


Figure 5. Major fragments identified from the first series of NMR spectra of JWH-073.

UPLC-QTOF-MS

See Table 4. We suggest that the fragment of 133.0651 Da corresponds to the loss of the pyrrolidine ring. The same loss was observed for MDPV. A fragment corresponding to the EI-MS fragment F1 was observed.

NMR

See Table 7. A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems. The results are in reasonable agreement with literature data for the homologue pyrovalerone[36] considering the different solvent used (see Table 7). NMR data for PPP has not been published before.

N-Ethylcathinon

GC-MS

The EI-MS spectrum (Figure 1) matched a known library spectrum, and it was consistent with the spectrum reported by Dal Cason.[16] Fragmentation like that of the β-keto-phenylethylamines (Figure 2, Table 4) was observed, i.e. a base peak at *m/z* 72 (F1), and the fragments F2 and F3 at *m/z* 105 and *m/z* 77, respectively.

UPLC-QTOF-MS

See Table 5. We propose that a fragmentation similar to that of mephedrone is responsible for the fragments of 130.0648 Da and 131.0718 Da.

MDPV (3,4-methylenedioxypyrovalerone)

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the fragmentations reported by Uchiyama *et al.*[9] The fragments F1, F2, and F3 (Figure 2, Table 4) were observed at *m/z* 126, *m/z* 149, and *m/z* 121, respectively.

UPLC-QTOF-MS

See Table 4. The fragments F1 and F2 were even found in the QTOF-MS spectrum (126.1276 Da and 149.0229 Da, respectively). The fragment of 205.0856 Da may arise from loss of the pyrrolidine ring, similar to the fragmentation observed for PPP as described above.

NMR

A full line shape iterative analysis (gNMR version 5.05) of ^{1}H NMR spectrum confirmed the spin systems. The results are in reasonable agreement with literature data[5] considering the different solvent used (see supplemental data).

Bk-MBDB (2-methylamino-1-(3,4-methylenedioxyphenyl) butan-1-one)

GC-MS

The EI-MS spectrum (Figure 1) was consistent with the fragmentations reported by Uchiyama *et al.*[9] The fragments F1, F2, and F3 (Figure 2, Table 4) were observed at *m/z* 72, *m/z* 149, and *m/z* 121, respectively.

UPLC-QTOF-MS

See Table 6. We suggest that Bk-MBDB undergoes a fragmentation similar to that of methylone, since fragments corresponding

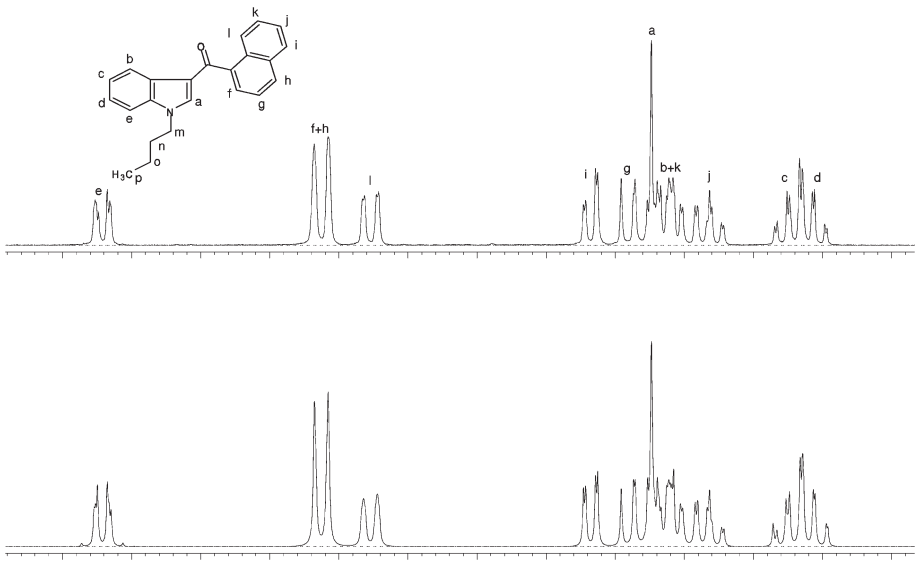
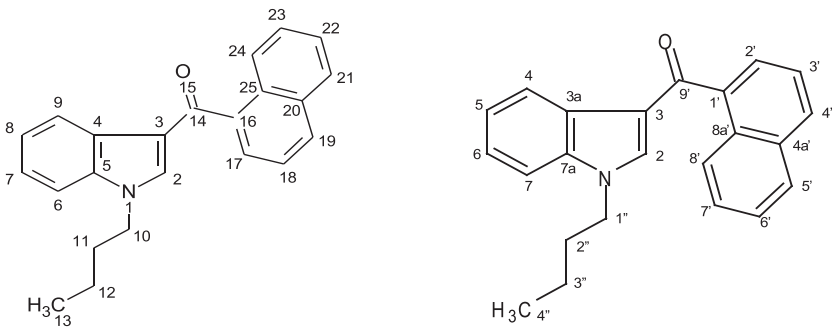


Figure 6. Expansion of the aromatic region of the 1D ^{1}H NMR spectrum for JWH-073. Upper trace: Experimental spectrum. Lower trace: calculated spectrum full line shape analysis.

Table 9. NMR data for JWH-073 including comparison to published ^{13}C data

Peak		δ ^{13}C (ppm)	δ ^{13}C litt[e] (ppm)	δ ^{1}H (ppm)
C(14)	9′	194.77	191.97	
C(2)	2	141.05	137.95	7.548 (s)
C(5)	7a	140.31	136.97	
	1′	138.87	139.01	
	4a′	135.38	133.67	
	8a′	132.12	130.72	
C(17)/C(19)	2′/4′	131.28	129.91	8.025 (d[b], 8.15 Hz)
C(24)	8′	129.55	125.93	7.954 (dd, 8.20 Hz, < 2 Hz[a])
	3	128.31	126.93	
C(22)	6′	127.93	126.23	7.466 (ddd, 8.33 Hz, 7.16 Hz, 1.05 Hz)
C(9)	7	111.80	109.97	7.526 (dd, 8.74 Hz, < 2 Hz[a])
C(21)	5′	127.04	128.11	7.635 (dd, 7.16 Hz, < 2 Hz[a])
C(17)/C(19)	2′/4′	126.67	125.77	8.025 (d[b], 7.08 Hz)
C(18)	3′	125.92	124.51	7.572 (dd, 8.15 Hz, 7.08 Hz)
C(8)	6	124.92	122.79	7.347 (ddd, 8.74 Hz, 7.43 Hz, < 2 Hz[a])
C(7)	5	124.07	123.54	7.315 (ddd, 8.32 Hz, 7.43 Hz, < 2 Hz[a])
C(6)	4	123.48	122.85	8.342 (dd, 8.32 Hz, -2.66 Hz)
	3	118.34	117.44	
C(23)	7′	127.53	126.69	7.523 (ddd, (.33 Hz, 8.20 Hz, < 2 Hz[a])
C(10)	1″	47.86	46.87	4.157 (t[c], 7.82 Hz)
C(11)	2″	33.07	31.75	1.755 (q[d], 7.82 Hz, 7.24 Hz, -9.91 Hz (gem))
C(12)	3″	20.99	19.97	1.256 (q[d], 7.82 Hz, 7.24 Hz, -9.91 Hz (gem))
C(13)	4″	13.97	13.52	0.874 (t, 7.82 Hz)

Notes.
[a]: constant given.
[b]: small unresolved coupling broadens lines.
[c]: Apparent triplet, technically AA′MM′ spinsystem.
[d]: Apparent quintet, technically AA′MM′XX′ spinsystem.
[e]: Lindigkeit *et al.* [28] ^{13}C NMR data for JWH-073. Solvent: $CDCl_3$. referenced to chlororoform (77.01 ppm).
m: multiplet, s: singlet, t: triplet, dd: double doublet, ddd: double double doublet.



to the same sequential losses of H_2O, CH_2O, CO and ·CH3 were observed (204.1026, 174.0914 Da, 146.0966 Da, and 131.0732 Da).

NMR

Examining the ^{1}H NMR spectrum, the following fragments are immediately identified: a 1,2,4 trisubstituted aromatic fragment with a polarized double bond as the substituent between 2 and 4, and substituents 5,6 being electronegative atoms with a lone-pair. A methylene fragment with two electronegative substituents, an *N*-methyl group, and a 1,1-disubstituted propane fragment. A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems. The structure was then deduced by combining information from MS and NMR data. The results are in reasonable agreement with literature data[30] considering the different solvent used (see supplemental data).

*p*FBT (3-(*p*-fluorobenzoyl)tropane)

GC-MS

The EI-MS spectrum (Figure 3) matched an internally shared spectrum for *p*FBT (between forensic institutes), and is in reasonable agreement with the drug profile for synthetic cocaine derivatives from EMCDDA (*p*FBT: *m/z* (% abundance): 82(54.7), 95(54.1), 124 (100.0), 140(6.0), 263(13.7)).[12] The base peak fragments at *m/z* 124 and the fragment at *m/z* 140 may derive from the tropane- and the tropanolate moieties.

UPLC-QTOF-MS

See Table 3. The observed fragment (124.1121 Da) was similar to the EI-MS base peak fragment at *m/z* 124.

NMR

The NMR data (Table 8) showed the expected high degree of symmetry that would be expected from the tropane group as well as the para-substituted phenyl group. A full line shape iterative analysis (gNMR version 5.05) confirmed the spin systems. NMR data for *p*FBT has not been published before.

JWH-073 (1-butyl-3-(1-naphthoyl)indole)

GC-MS

The EI-MS spectrum (Figure 3) was consistent with the literature data.[19,28] It was also highly similar to the spectrum reported for JWH-018 (1-pentyl-3-(1-naphthoyl)indol) by Auwärter *et al.*[18] with some fragments being identical while other fragments as well as the molecular ion displayed mass values of 14 less than those of JWH-018.

UPLC-QTOF-MS

See Table 3. The observed fragments of 155.0492, 127.0545 and 200.1069 Da were similar to those found in the EI-MS spectrum.

NMR

Based the 1D ^{1}H NMR and the COSY spectra the following fragments were identified and analyzed using full line shape iterative analysis (gNMR version 5.05): An n-butyl fragment, an indole or 'tryptophane-like' fragment, a 1,2-disubstituted aromatic system containing four protons, and a 1,2,3-trisubstituted system (Figure 5). To support the analysis of the spin system a J-resolved ^{1}H 2D NMR spectrum was acquired, that confirmed the analysis.

These fragments were confirmed using the ^{13}C NMR spectrum, where furthermore a carbonyl carbon (identified as an aromatic ketone from the chemical shift – 194.8 ppm – since no aldehyde proton was observed in the ^{1}H NMR spectrum) and six quaternary aromatic carbon atoms were identified.

Considering the history of the sample and the above fragments a likely identification of the compound was JWH-073 (Figure 6, where the aromatic region of the 1D ^{1}H NMR spectrum is displayed together with the full iterative line shape analysis).

Due to limitations in the software and the computer system the small coupling constants across the ring systems could not be included in the calculation. However, chemical shifts and large coupling constants are reliable.

These results are in reasonable agreement with literature data[28] (^{13}C data only) considering the different solvent used (Table 9).

Conclusion

This work represents the detection and identification of ten designer drugs. By March 2009, nine of these compounds had been added to the Danish list of controlled substances, and by March 2010 even the last substance, JWH-073, was added. Two drugs, methylone and *N*-ethylcathinone, matched known EI-MS library spectra, and because the identity corresponded to the formula and chemical name marked on the sample, confirmation by UPLC-QTOF-MS was considered sufficient for their identification. The ^{1}H- and ^{13}C-NMR spectra allowed an unequivocal determination of the aromatic substitution pattern and of the aliphatic structure of the eight other compounds, mephedrone, flephedrone, p-fluoroamphetamine, PPP, MDPV, Bk-MBDB, pFBT, and JWH-073.

A general EI-MS fragmentation pattern was recognized for the β-ketophenylethylamines, and some general QTOF-MS fragments were suggested for subclasses of these related substances. The limits of these subclasses need to be explored.

The recognition of fragmentation patterns for classes and subclasses of compounds may be used for prediction of spectra and a better tentative identification of unknown drugs, which could be especially useful in cases where NMR is not easily applied.

Supporting Information

Supporting information may be found in the online version of this article.

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