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3-Naphthoylindazoles and 2-naphthoylbenzoimidazoles as novel chemical groups of synthetic cannabinoids: Chemical structure elucidation, analytical characteristics and identification of the first representatives in smoke mixtures

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ABSTRACT

By means of gas chromatography with mass spectrometry detection (GC–MS), including high resolution mass spectrometry (GC–HRMS) together with ultra-high performance liquid chromatography in combination with high resolution tandem mass spectrometry (UHPLC–HRMS), nuclear magnetic resonance spectroscopy (NMR) and Fourier transform infrared spectroscopy (FT-IR), structure of novel synthetic cannabinoids, namely, 1-(5-fluoropentyl)-1*H*-indazol-3-yl(naphthalen-1-yl)methanone, naphthalen-1-yl(1-pentyl-1*H*-benzo[*d*]imidazol-2-yl)methanone and 1-(5-fluoropentyl)-1*H*-benzo[*d*]imidazol-2-yl(naphthalen-1-yl)methanone was established. Analytical data obtained in the paper enable reliable identification of these compounds during qualitative analysis of seizures, including smoke mixtures.

1. Introduction

Synthetic cannabinoids are one of the most widely spread classes of designer drugs nowadays [1–30]. Meanwhile not only new structural modifications of known types of compounds but also new groups of synthetic cannabinoids [17,21–30] regularly appear in illicit market. Therefore, determination of the structure of new psychoactive compounds remains the most important task, in the field of qualitative analysis of designer drugs.

Peculiar feature of the second half of the year 2013 became massive expansion of synthetic cannabinoids where traditional indol-3-ylcarbonyl core was modified. Main contribution in this process was done by significant broadening of the list of derivatives of indazole-3-carboxamide which were first detected in smoke mixtures as far as in March 2012 [22,23,26,27,29]. In October 2013, we have found new compound, comprising indazol-3-ylcarbonyl moiety, namely, 1-(5-fluoropentyl)-1*H*-indazol-3-yl(naphthalen-1-yl)methanone (**1**, Table 1). Compound **1** is a structural modification of 1-(5-fluoropentyl)-1*H*-indol-3-yl(naphthalen-1-yl)methanone (AM-2201) [15–20,25], cannabimimetic of 3-naphthoylindole group.

At the same time, we have identified another two compounds, namely naphthalen-1-yl(1-pentyl-1*H*-benzo[*d*]imidazol-2-yl) methanone (**2**, Table 1) and 1-(5-fluoropentyl)-1*H*-benzo[*d*] imidazol-2-yl(naphthalen-1-yl)methanone (**3**, Table 1) which could be referred to 2-naphthoylbenzoimidazole group. The structure of compound **3** (given short name FUBIMINA) was discovered in the paper [30] independently and in parallel with our work which served additional proof of our findings. The paper [30] report electron ionization (EI) mass-spectrum and NMR spectrum for compound **3**, but our data supplement analytical characteristics for this compound (which favor reliable distinguishing of compounds **1** and **3**, having very similar EI spectra) significantly. As for compound **2**, we were the first to identify it.

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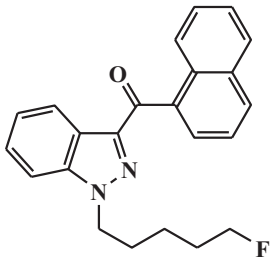
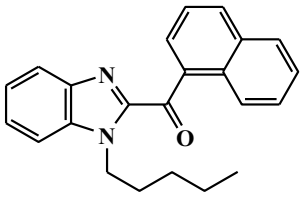
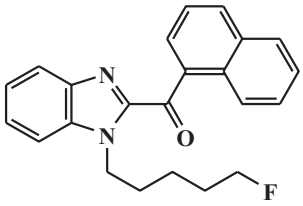
Table 1
Structures and chemical names of compounds **1**–**3**.

Compound	Conventional name	Structure	Chemical name
1	AM(N)-2201 (THJ-2201)		1-(5-fluoropentyl)-1*H*-indazol-3-yl(naphthalen-1-yl)methanone
2	BIM-018 (JWH-018 benzimidazole analog)		naphthalen-1-yl(1-pentyl-1*H*-benzo[*d*]imidazol-2-yl)methanone
3	BIM-2201 (FUBIMINA)		1-(5-fluoropentyl)-1*H*-benzo[*d*]imidazol-2-yl(naphthalen-1-yl) methanone

Structures, chemical names and authors' conventional names for compounds under discussion are given in Table 1. Short names used by Internet-dealers and in scientific literature are also given (in brackets).

2. Materials and methods

2.1. Materials

Compounds **1**–**3** either as individual microcrystalline powders or as applications to a plant matrix were sampled from real evidences brought for examination to the forensic laboratories of several cities in Russian Federation and Belarus. Preliminary control of uniformity of samples before being subjected to structural investigations by means of NMR and IR spectroscopy was performed by GC/MS and ultra-high performance liquid chromatography (UHPLC) with MS and UV detection.

2.2. Solvents and reagents

For investigations we used methanol ('for liquid chromatography' grade) purchased from Merck KGaA (Darmstadt, Germany), water ('for GC, HPLC and spectrophotometry' grade) from Honeywell, Burdick and Jackson (Muskegon, USA), acetonitrile ('HPLC-gradient' grade) from Panreac (Barcelona, Spain), formic acid (98.0% min.) from Sigma–Aldrich (Steinheim, Germany). For NMR spectroscopy, DMSO-d_6 with isotopic purity $\geq$99.8% ('A' grade, by Russian TU 95-1893-89, St. Petersburg, Russia) was used. For determination of generalized log-linear retention indices (GI), a set of individual *n*-alkanes (Fluka, Sigma–Aldrich, Steinheim, Germany) was applied as a standard. For recording FT-IR spectra, potassium bromide (IR grade, Panreac, Barcelona, Spain) was used.

2.3. Preparation of sample solution

For qualitative analyses, *ca.* 1 mg (for GC–MS) or *ca.* 0.5 mg (for GC–HRMS) of each product was dissolved in methanol (1 ml). After dissolving, solution was passed through a cellulose membrane filter (5064-8222, Agilent Technologies, USA) to serve as a sample solution for analysis. For UHPLC–HRMS, the solution thus obtained was diluted with additional methanol to attain 5 μg/ml. For all the analyses, the solution was diluted with methanol to a suitable concentration before instrumental analysis if necessary.

2.4. Instruments and methods

GC–MS analysis of compounds in their solutions in methanol was performed with 'Agilent 7820A' gas chromatograph equipped with 'Agilent 5975' quadrupole mass selective detector (all – from Agilent Technologies, USA). For chromatographic separation, capillary column HP-5ms with chemically immobilized (5%-biphenyl)-95%-dimethylpolysiloxane (30.0 m × 0.25 mm × 0.25 μm, 19091S-433, Agilent Technologies, USA) was used. The oven temperature program consisted of: (i) an initial temperature of 100 °C; held for 2.0 min; (ii) a ramp to 290 °C with 20 °C/min; (iii) final temperature (290 °C) was held for 25 min. Injector temperature was 280 °C, detector interface was 290 °C. Helium in constant flow mode was used as a carrier gas with flow rate 1.0 ml/min. Detector was equipped with EI source (70 eV), mass range of total ion current of 20–550 amu. Calibration of detector was performed automatically in 'Autotune' mode using perfluorotributylamine standard (PFTBA,