



Two thiazolyindoles and a benzimidazole: Novel compounds on the designer drug market with potential cannabinoid receptor activity



Folker Westphal^{a,*}, Frank D. Sönnichsen^{b,1}, Siegfried Knecht^c, Volker Auwärter^d,
Laura Huppertz^d

^aState Bureau of Criminal Investigation Schleswig-Holstein, Section Narcotics/Toxicology, Mühlenweg 166, D-24116 Kiel, Germany

^bOtto-Diels-Institute of Organic Chemistry, Christian-Albrechts-University Kiel, Olshausenstr. 40, 24098 Kiel, Germany

^cCenter for Education and Science of the Federal Finance Administration, Laboratory Frankfurt, Gutleutstr. 185, 60327 Frankfurt a.M., Germany

^dInstitute of Forensic Medicine, Department of Forensic Toxicology, Medical Center–University Freiburg, Albertstr. 9, 79104 Freiburg, Germany

ARTICLE INFO

Article history:

Received 21 September 2014

Received in revised form 27 December 2014

Accepted 22 January 2015

Available online 29 January 2015

Keywords:

3-([1,3]-thiazol-2-yl)indole

Benzimidazole

Cannabimimetic

Structure elucidation

Analytical data

ABSTRACT

In a seizure of German custom authorities two 3-([1,3]-thiazol-2-yl)indoles (*N*-(2-methoxyethyl),*N*-isopropyl-2-(1-pentyl-1*H*-indol-3-yl)-4-thiazolemethanamine (**1**) and *N,N*-diethyl-2-(1-pentyl-1*H*-indol-3-yl)-4-thiazolemethanamine (**2**)) and one benzimidazole (1-(cyclohexylmethyl)-2-[(4-ethoxyphenyl)methyl]-*N,N*-diethyl-1*H*-benzimidazole-5-carboxamide (**6**)) were seized as pure compounds. The compounds have been detected in Germany for the first time, and no analytical data had been previously published. Mass spectrometric (MS), infrared (IR) spectroscopic, and nuclear magnetic resonance (NMR) spectroscopic data are presented and the way of the structure elucidation of these rather uncommon compounds is discussed.

© 2015 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Cannabimimetics are the compound class with the largest structural diversity of new psychoactive substances (NPS) presently appearing on the market. Many of them show high binding activities to CB₁ and/or CB₂ receptors and are known to mimic the effects of Δ⁹-tetrahydrocannabinol (THC), the major psychotropic active ingredient of cannabis. The effects of THC are mediated by binding to and activation of CB₁ receptors. In recent years, a very large variety of cannabimimetics entered the illegal drug market [1–8]. Starting with naphthoyl-, benzoyl-, phenacetyl-, adamantoyl-, and cyclopropoylindols now indolamides, indazoles, indazol(di)amides and indol(chinoliny)esters have appeared, occasionally combined with other rare or less common structures. With increasing frequency, even pharmaceuticals are entering the designer drug market in large quantities not in

typical pharmaceutical packaging but in pure state for misuse purposes [9].

Besides three already known cannabimimetics (JTE-907, A-834,735 and A-836,339) two brown oily compounds (**1** and **2**, each of them about 10 g) and a beige-colored powder (**6**, about 5 g) were seized from a mail package from China by German custom authorities. The three substances were not identifiable by comparison with IR- and MS-spectra of the available databases. Thus, for structure elucidation high resolution mass spectrometry (HRMS) and NMR spectroscopy were performed in addition to IR and GC–MS and GC–MS/MS analysis.

2. Methods

2.1. Chemicals

Diethylether and ethanol were purchased from Merck (analytical grade, Darmstadt, Germany). CDCl₃ was obtained from Euro-Isotope (Saint Aubin, France). Formic acid (Rotipuran[®] ≥ 98%, p.a.) and 2-propanol (Rotisol[®] ≥ 99.95%, LC–MS grade) were purchased from Carl Roth (Karlsruhe, Germany). Sodium hydroxide (volumetric solution, 1 mol/L) was supplied by Riedel-de Haën

* Corresponding author. Tel.: +49 0431 160 4724; fax: +49 0431 160 4444.

E-mail address: Dr.Folker.Westphal@polizei.landsh.de (F. Westphal).

¹ Manuscript prepared in equal parts with corresponding author.

(Seelze, Germany), acetic acid (Emsure[®], glacial, anhydrous, 100%) was from Merck (Darmstadt, Germany), and ammonium formate (99.995%) as well as methanol (LC-MS-grade) were purchased from Sigma-Aldrich (Steinheim, Germany). A cartridge deionizer (Memtech, Moorenweis, Germany) was used for the preparation of deionized water.

2.2. Gas chromatography mass spectrometry and product ion spectrometry (GC-MS and GC-MS/MS)

2.2.1. Sample preparation

For the analysis of the seized compounds **1** and **2** approximately 2 mg of the oils were dissolved in 1.5 mL ethanol. Approximately 2 mg of the powder (**6**) were dissolved in 2 mL of deionized water, alkalized with 5% NaOH, and extracted with 2 mL diethylether. For analysis 1 μ L of the ethanolic solution/the ethereal extract was injected into the GC-MS system.

2.2.2. Equipment

Electron ionization (EI) and chemical ionization (CI) mass spectra were obtained with a Finnigan TSQ 7000 triple stage quadrupole mass spectrometer (Thermo Scientific, Dreieich, Germany) coupled to a gas chromatograph (Trace GC Ultra,

Thermo Scientific, Dreieich, Germany) with an auto sampler CTC CombiPAL (CTC Analytics, Switzerland).

2.2.3. GC parameters

Samples were introduced via the gas chromatograph with splitless injection using a fused silica capillary column DB-1 (30 m \times 0.25 mm, film thickness 0.25 μ m). The temperature program started with an initial temperature of 80 $^{\circ}$ C, held for 2 min, followed by a ramp to 310 $^{\circ}$ C with 20 $^{\circ}$ C/min. The final temperature was held for 25 min. The injector temperature was 250 $^{\circ}$ C. The transfer line temperature was maintained at 300 $^{\circ}$ C. The carrier gas was helium in constant flow mode at a flow rate of 1.2 mL/min.

2.2.4. MS parameters

The electron ionization (EI) energy was 70 eV with an emission current of 200 μ A. The scan time was 1 s and the scan range was m/z 29–700. The ion source temperature was maintained at 175 $^{\circ}$ C.

The chemical ionization (CI) energy was 70 eV with an emission current of 200 μ A and a source temperature of 175 $^{\circ}$ C. The reactant gas was methane and the source pressure was 1.5 mTorr (0.2 Pa). The scan time was 0.5 s and the scan range was m/z 50–600.

In the EI-MS/MS-product-ion-mode the ionization energy was 70 eV with an emission current of 200 μ A and a source

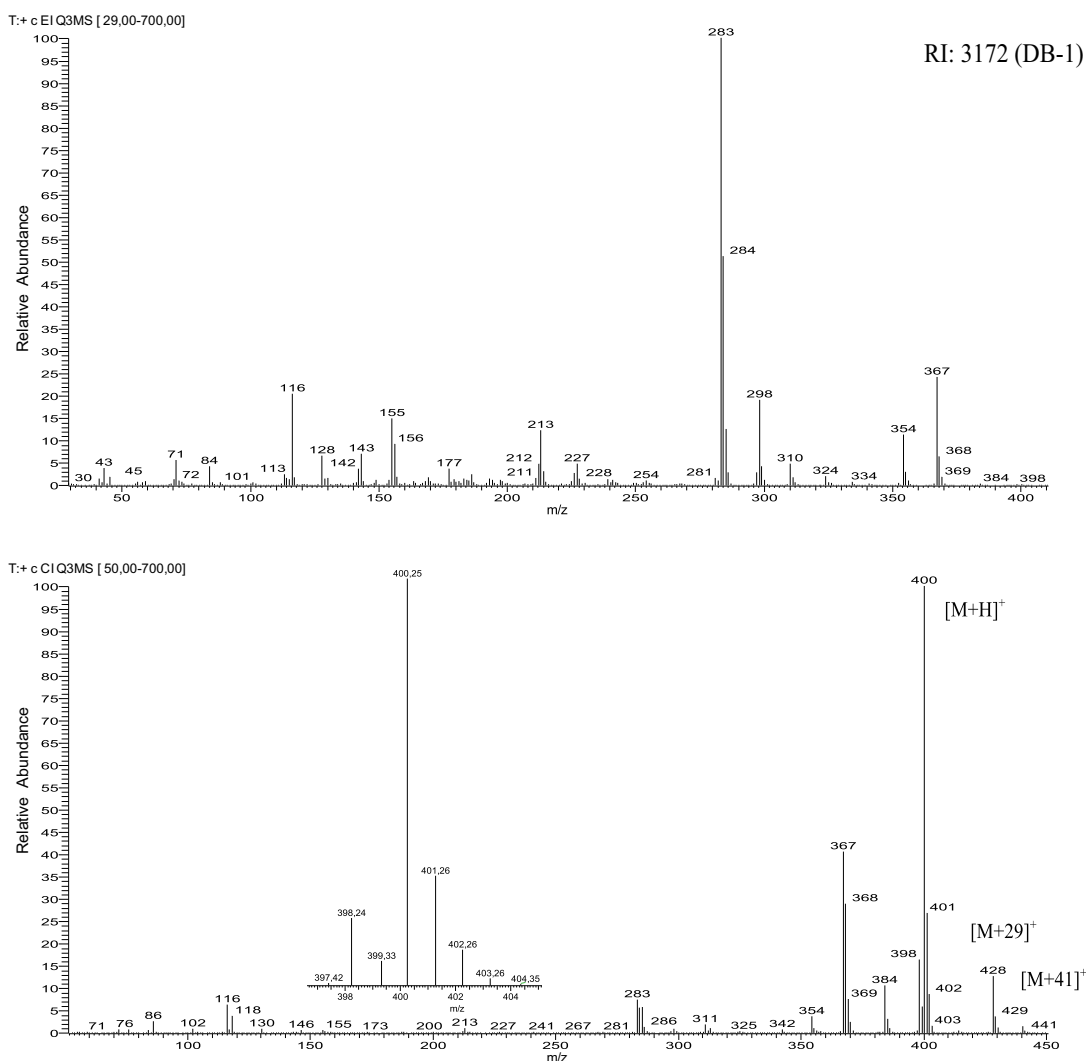


Fig. 1. EI-MS spectrum (top) and CI-MS spectrum of **1** (bottom).

Download English Version:

<https://daneshyari.com/en/article/95416>

Download Persian Version:

<https://daneshyari.com/article/95416>

[Daneshyari.com](https://daneshyari.com)