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Rapid communication

Single-crystal X-ray diffraction analysis of designer drugs: Hydrochlorides of metaphedrone and pentedrone

Damian Trzybiński [a,*], Paweł Niedziałkowski [a], Tadeusz Ossowski [a], Anna Trynda [b], Artur Sikorski [a]

[a] University of Gdańsk, Faculty of Chemistry, J. Sobieskiego 18/19, 80-952 Gdańsk, Poland
[b] Forensic Laboratory of Gdańsk, Police Headquarters, Biskupia 23, 80-875 Gdańsk, Poland

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ABSTRACT

This article, written as a result of cooperation between a police forensic laboratory and an academic institution, outlines the possibility of applying single-crystal X-ray diffraction analysis as an effective method of identifying designer drugs in forensic analysis. This technique allows crystalline samples to be determined with full assurance about their identity, even in the case of new substances for which no reference standards yet exist. Here, single-crystal X-ray diffraction measurements of single-crystal specimens obtained from two samples were performed. Solution and refinement of the structures demonstrated that the target compounds were metaphedrone and pentedrone hydrochlorides – synthetic cathinone derivatives used as recreational stimulants. In addition to the identification of the title compounds, this paper gives a first report on their crystal structures. Once the *CIF*-files containing the crystal structure data of the title compounds have been deposited in the *Cambridge Structural Database* – the world repository of small molecule crystal structures – it will be possible to identify single crystals of the title compounds quickly on the basis of simple parameters (lattice parameters $a, b, c, \alpha, \beta, \gamma$ and unit cell volume). This description of the relationship between the geometrical parameters of moieties and the analysis of intermolecular interactions occurring in crystals of the title compounds extends knowledge about the synthetic derivatives of cathinone and may play a role in future studies, leading to a better understanding of their characteristic properties.

1. Introduction

In recent years a record number of new compounds that can be used as "legal highs" have been detected in Europe [1]. These substances, usually produced by modifying the structure of existing drugs in order to by-pass the provisions of existing laws, are known as designer drugs [2,3]. In Poland, these chemicals – increasingly popular among young people – were mass-produced from legal ingredients and offered for sale as "collector's items", "plant fertilizers", "scented sachets" or even Christmas decorations. However, the product labels did not state that they were suitable for human consumption, nor did they list any psychoactive substances among the ingredients. One of the most popular of these were synthetic derivatives of cathinone (2-amino-1-phenylpropan-1-one) (Fig. 1), a compound contained in a plant called *khat*, especially 4-methyl methcathinone (2-(methylamino)-1-(*p*-tolyl)propan-1-one), known as mephedrone and its salts [4,5]. This compound is now specifically listed as prohibited in most European countries, including Poland, so its availability has been substantially limited [6,7]. However, other cathinone-related compounds, such as metaphedrone (2-(methylamino)-1-(*m*-tolyl)propan-1-one) or pentedrone (2-(methylamino)-1-phenylpentan-1-one) are still readily available [8–10].

Like amphetamines, derivatives of cathinone are basically central nervous system stimulants [11]. Detailed studies of this group of compounds have demonstrated their mechanism of action, which lies in binding to monoamine transporters for dopamine, serotonin and noradrenaline in the brain, which causes deliverence of these [12,13]. Synthetic cathinones are often sold in crystalline form. Single-crystal X-ray diffraction analysis – a non-routine method – can be used in forensic analysis. This technique has a number of advantages: (1) it is non-destructive and enables crystalline samples to be determined with full assurance about their identity, even in the case of new substances for which there are no reference standards; (2) it can be used to determine the structures of elements, simple inorganic and organic compounds, as well as more complex systems like fullerenes, proteins or nucleic acids; (3) only a small amount of the target substance is required for analysis [14] – crystals much less than 0.5 mm in size are generally suitable for X-ray diffraction measurements. The

* Corresponding author. Tel.: +48 58 523 5425; fax: +48 58 523 5464.
E-mail address: trzybinski@chem.univ.gda.pl (D. Trzybiński).

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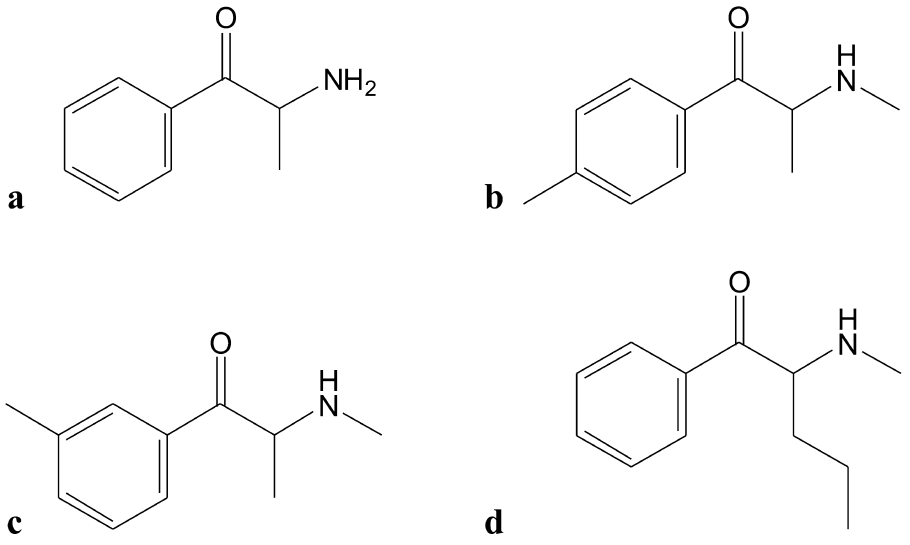

Fig. 1. Molecular diagrams of cathinone (a) and its synthetic derivatives: mephedrone (b), metaphedrone (c) and pentedrone (d).

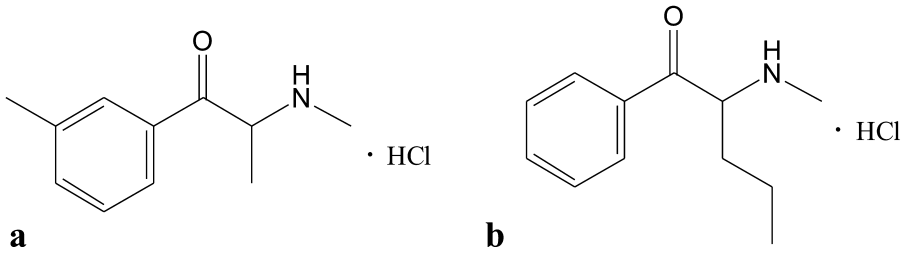

Fig. 2. Molecular diagrams of the target compounds – metaphedrone HCl (a) and pentedrone HCl (b).

method is thus potentially interesting in the context of contemporary forensic analysis.

Here, we present the first report on the crystal structure of the two hydrochloride salts of synthetic cathinone derivatives – metaphedrone and pentedrone (Fig. 2).

To the best of our knowledge, this is the first article on the possible application of single-crystal X-ray diffraction analysis to forensic purposes as an effective method of identifying synthetic cathinone derivatives. To date, moreover, there are only a few crystal structures of cathinones in the *Cambridge Structural Database*, the world repository of small molecule crystal structures [15]. Therefore, apart from the forensically important, certain confirmation of identity, analysis of the relationship between the geometrical parameters of moieties and the intermolecular interactions occurring in crystals of the title compounds may play a role in future studies, leading to a better understanding of their characteristic properties.

2. Experimental

2.1. Materials and methods

The crystals of the target compounds (Fig. 3) were obtained from Polish law enforcement officials.

Good-quality single-crystal specimens were selected for the X-ray diffraction experiments at $T = 295(2)$ K and affixed to the tip of glass capillaries with epoxy glue. Diffraction data were obtained on the *Oxford Diffraction Gemini R Ultra Ruby CCD* diffractometer owned by the Faculty of Chemistry, University of Gdańsk (Fig. 4), using a *MoKα* radiation source ($\lambda = 0.71073$ Å).

The lattice parameters were obtained by least-squares fit to the optimized setting angles of the reflections by means of *CrysAlis CCD* [16]. Data were reduced using *CrysAlis RED* software [16]. The structural resolution procedure was carried out with the *SHELXS-97* package, solving the structure by direct methods and carrying out refinements by full-matrix least-squares on F^2 using the *SHELXL-97* program [17]. The H-atoms at N9 were located on a Fourier-difference map,

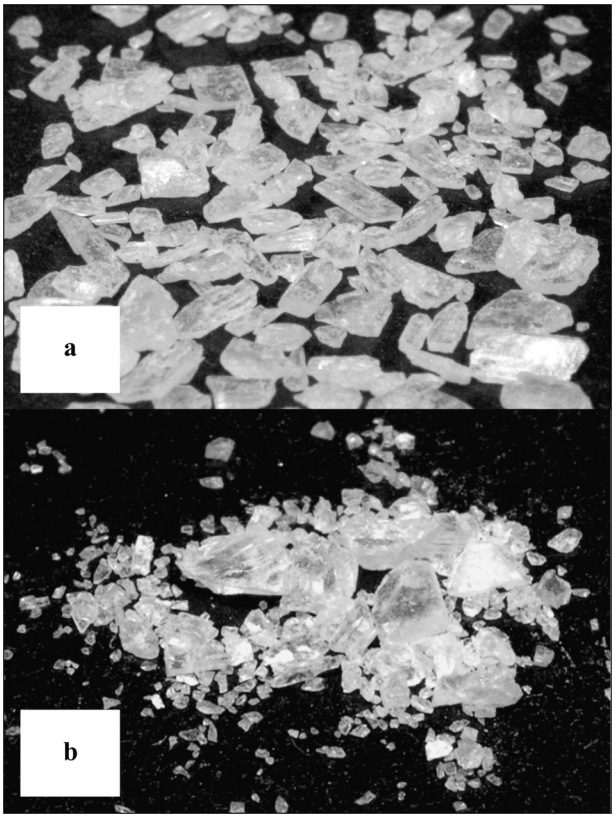

Fig. 3. Crystals of the target compounds – metaphedrone HCl (a) and pentedrone HCl (b).

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