

4-Bromo-2,5-dimethoxyphenethylamine (2C-B): a review of the public domain literature

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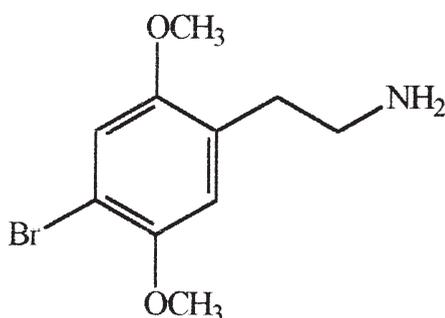
Introduction

There has been a considerable increase in the use of 'recreational' drug taking in general and the use ring substituted amphetamines in particular [1]. Amongst these latter is included 4-bromo-2,5-dimethoxyphenethylamine (also known as 2C-B, Venus, Bromo, Erox, Bees and/or Nexus) (Figure 1), which is a synthetic drug with hallucinogenic activity similar to LSD, mescaline and psilocybin [2]. It is subject to control in a number of countries. That it is of significance is illustrated by the fact that in 1998, in England and Wales, of the ring substituted phenethylamines, it was the third most reported, following MDMA and MDEA [3]. Unlike amphetamine, methylamphetamine, MDA, MDMA and MDEA, for which there is a great deal of collated information concerning analysis and profiling, there is no collated information for 2C-B. This paper collates and critically reviews the available literature and suggests directions for research involving this drug.

Prevalence and use

2C-B gained popularity during the mid 1980s as a replacement of choice for LSD and psilocybin [4]. It is encountered by the forensic scientist in powdered and tablet forms. It may be consumed orally, in tablets which typically contain 5 mg, in doses of between 10 and 50 mg. A light dose is considered to be 5–15 mg, a strong dose 20–50 mg [5]. Following an onset period of 20–90 minutes, the effects may last for two to five hours and after-effects may last between two and four hours. It may also be insufflated in powdered form, the doses for this route of administration being approximately one third of the oral dose. It is reportedly excreted, in urine, as native drug for up to three hours after ingestion, along with the metabolites 4-bromo-2,5-dimethoxyphenylacetic acid, 4-bromo-2,5-dimethoxybenzoic acid and 4-bromo-5-hydroxy-2-methoxyphenethylamine.

Figure 1 4-Bromo-2,5-dimethoxyphenethylamine (also known as 2C-B, Venus, Bromo, Erox, Bees and/or Nexus).



Qualitative and quantitative identification

There is little information on the definitive identification of this drug from street samples [6]. The forensic scientist is likely to encounter the drug as tableted or powdered dose forms. As with many drug samples where sufficient material is available, these would be subjected to presumptive (colour) tests, possibly TLC (for which there does not appear to be any reported information) and then confirmatory analysis.

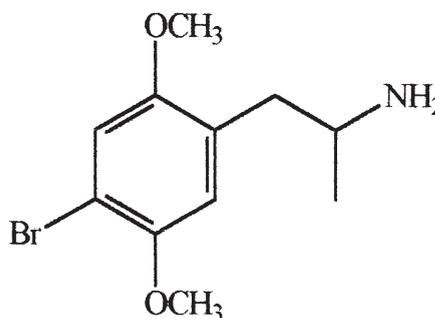
Presumptive tests

2C-B is reported to yield a positive colour reaction with the Marquis reagent. The reported colour obtained is yellow, turning green [3,7]. This is the same colour as obtained for DOB (2,5-dimethoxy-4-bromoamphetamine) (Figure 2) and further analysis is subsequently required to prove the identity of the drug. This requires chromatographic, mass spectroscopic, IR and NMR analysis [6].

Gas chromatography–mass spectrometry

This method can be used to separate components of complex mixtures but does not allow differentiation of the positional isomers of bromo-dimethoxyphenethylamines and hence cannot be used as definitive identification of 2C-B [8]. However, it is a useful starting point for analysis. In this report native drug, methylated (Figure 3) and acetylated (Figure 4) 2C-B were prepared and analysed, using GC–MS in full scan mode, with comparison between standard drugs and street samples analysed in an identical manner [8]. Using GC–MS, it was possible to determine that the drug being analysed in this example was a phenethylamine brominated in the meta or para position with

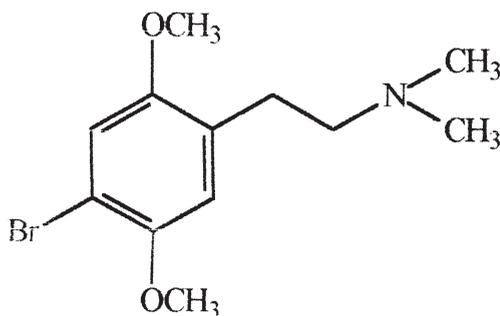
Figure 2 DOB (2,5-dimethoxy-4-bromoamphetamine).



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Figure 3 Methylated 2C-B.

respect to the ethylamine chain but it was not possible to discriminate between the two.

IR and NMR spectroscopy [6]

Using these methods, it ought, in principle, to be possible to identify the drug in the street sample without ambiguity. Prior to analysis using these methods, the samples were subjected to liquid–liquid extraction. The samples were ground in a pestle and mortar and dissolved in 0.1M HCl, sonicated for 30 minutes, basified and extracted into methylene chloride. This mixture was centrifuged, frozen and the organic phase collected. The sample was acidified using HCl dissolved in isopropanol, the organic solvent evaporated under a stream of nitrogen and the residue analysed by IR and NMR.

The IR spectrum of the standard 2C-B and street sample were almost identical, suggesting the identity of the drug. However, there were also differences in the degree of noise in the spectra, suggesting another technique would be of assistance.

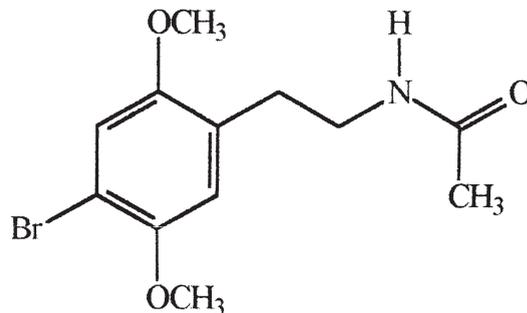
NMR spectra, particularly when 2D methods are used, can be used to achieve identification of drugs, including the identity of positional and stereo isomers. ¹H NMR studies indicated that the two aromatic protons were in the para position and other functional groups of 2C-B were also identified. However, it was necessary to discriminate between the 4-bromo-2,5-dimethoxy compound and the 2-bromo-4,5-dimethoxy compound. Whilst it is possible to use mass spectroscopic data and NOESY experiments to distinguish between these possibilities, it is also possible to arrive at a direct identification using HMBC methods and it was this method that was used in this paper.

High performance liquid chromatography [6]

HPLC was performed using an enrichment column following extraction of the drugs from the street samples, followed by HPLC on a RP-8 column and an acetonitrile/potassium phosphate (pH 3.2) mobile phase, which involved a solvent gradient and diode array detection. HPLC was used for the quantification of the drug in the tablets, which were found to contain 3–8 mg 2C-B per tablet depending upon the source.

Synthesis and drug profiling

In addition to qualitative and quantitative analysis of drugs, it is becoming increasingly necessary to profile amphetamines, for comparison and intelligence purposes [9]. Street samples of

Figure 4 Acetylated 2C-B

2C-B are reportedly very pure [4,6] and success in determining precursors and synthetic impurities has, to date, been reported as being unsuccessful [6].

It is likely that the route of synthesis of street samples follows that described in PIHKAL [2], starting with the reaction of 2,5-dimethoxybenzaldehyde and nitromethane, to form the nitrostyrene, subsequently reducing the product with LiAlH₄ and then brominating the final product. Impurities from such a route might be speculated upon, but attempts are required to develop an optimised method for their extraction and analysis. It is in this area that further studies are being undertaken.

Conclusion

This paper draws together, for the first time, the information that is available for the identification and quantification of 2C-B. It identifies a need for further research (i) in the area of profiling this drug for comparison and intelligence purposes and (ii) identifying possible toxic effects associated with the impurities which may be found in this drug. Studies in this area are ongoing.

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