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Differentiation of methylenedioxybenzylpiperazines (MDBP) by GC–IRD and GC–MS

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ABSTRACT

The substituted benzylpiperazine, 3,4-methylenedioxybenzylpiperazine (3,4-MDBP) and its regioisomer 2,3-methylenedioxybenzylpiperazine (2,3-MDBP) have almost identical mass spectra. Perfluoroacylation of the secondary amine nitrogen of these regioisomeric piperazines gave mass spectra with differences in relative abundance of some fragment ions. However the spectra did not yield any unique fragments for specific identification of one regioisomer to the exclusion of the other compound.

Gas chromatographic separation coupled with infrared detection (GC–IRD) provides direct confirmatory data for structural differentiation between the two regioisomers. The mass spectrum in combination with the vapor-phase infrared spectrum provides for specific confirmation of each of the regioisomeric piperazines. The underivatized and perfluoroacyl derivative forms of the ring substituted benzylpiperazines were resolved on a 30-m capillary column containing an Rxi-50 stationary phase.

1. Introduction

Several compounds of the 1-arylpiperazine type are known to have good binding affinity for serotonin receptors of the human central nervous system [1]. This affinity is made more selective with the appropriate aromatic ring substituents [2]. This new class of potential designer drugs includes a variety of benzylpiperazine substitution patterns such as N-benzylpiperazine, 1-(3,4-methylenedioxybenzyl)-piperazine and phenylpiperazines such as 1-(3-trifluoromethyl-phenyl)piperazine, 1-(3-chlorophenyl)piperazine and 1-(4-methoxyphenyl)piperazine [3]. The most commonly abused compounds of this group are reported to be N-benzylpiperazine and 3-trifluoromethylphenylpiperazine (3-TFMPP) [3]. Recently, 3,4-MDBP has been described as producing psychoactive effects similar to those of 3,4-methylenedioxymethamphetamine (MDMA) [4–6]. Some of the piperazine compounds are commercially available and are not yet under specific legal control [7].

Analysis of 3,4-MDBP in biological and forensic samples has been the focus of several studies in recent years [8–11]. Gas chromatography-mass spectrometry (GC–MS) is the most commonly employed technique in the analysis of controlled substances in forensic laboratories [12–17].

The 3,4-methylenedioxybenzylpiperazine has been reported as a potential drug while the pharmacological properties of its 2,3-regioisomer have not been described. These two compounds have the same nominal mass (MW = 220) and yield almost identical EI mass spectra. Without reference standards and with a possibility of chromatographic co-elution the discrimination between these two isomers presents a challenge to forensic drug chemistry. The identification of psychoactive drugs in a number of chemical categories is complicated by the existence of regioisomeric and isobaric substances related to the target drug [8–13]. These isomeric substances are a challenge to forensic analyses that must depend heavily on mass spectrometry for confirmation level data. Many of these regioisomeric and isobaric substances have the same nominal mass and yield essentially identical mass spectra. Previous studies [9,13] have shown that chemical derivatization methods (primarily perfluoroacylation) can be successfully applied to discriminate among many isomerically related compounds. Derivatization can alter major fragmentation pathways often providing additional structural information about an individual isomer as well as altered chromatographic properties [9–13]. However in some cases, derivatization did not yield characteristic mass spectral fragment ions for individual isomers [11].

Infrared spectroscopy is considered a confirmation method for the identification of organic compounds due to the uniqueness of infrared spectra for very similar organic molecules. Gas chromatography with infrared detection (GC–IRD) is characterized by scanning quickly enough to obtain IR spectra of peaks eluting from the

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capillary GC columns. This technique has been successfully used in the identification of amphetamine isomers [18] as well as side chain regioisomers of methamphetamine and phentermine [19]. Recently, GC–IRD studies have been described for the differentiation of ring and side chain substituted ethoxyphenethylamines, methoxymethcathinones and methylenedioxymethamphetamines [20].

This report will describe GC–IRD and GC–MS discrimination studies on the regioisomeric ring substituted methylenedioxybenzylpiperazines.

2. Experimental

2.1. Instrumentation

GC–MS analysis was performed using an Agilent Technologies (Santa Clara, CA) 7890A gas chromatograph and an Agilent 7683B auto-injector coupled with a 5975C VL Agilent mass selective detector. The mass spectral scan rate was 2.86 scans/s. The GC was operated in splitless mode with a helium (grade 5) flow rate at 0.7 mL/min and the column head pressure was 10 psi. The MS was operated in the electron impact (EI) mode using an ionization voltage of 70 eV and a source temperature of 230 °C. The GC injector was maintained at 250 °C and the transfer line at 280 °C.

GC–IRD studies were carried out using a Hewlett-Packard 5890 Series II gas chromatograph and a Hewlett-Packard 7673 auto-injector coupled with an IRD-II infrared detector (IRD) obtained from Analytical Solutions and Providers (ASAP), Covington, KY. The vapor-phase infrared spectra were recorded in the range of 4000–700 cm^{-1} with a resolution of 8 cm^{-1} and a scan rate 1.5 scans/s. The IRD flow cell and transfer line temperatures were maintained at 280 °C and the GC was operated in the splitless mode with a carrier gas (helium grade 5) at a flow rate of 0.7 mL/min and a column head pressure of 10 psi.

Chromatographic separations were carried out using two stationary phases. Column one was a 30 m × 0.25 mm i.d. capillary coated with 0.50 μm of 50% phenyl–50% methyl polysiloxane (Rxi-50). The temperature program consisted of an initial temperature of 100 °C for 1 min, ramped up to 230 °C at a rate of 20 °C/min followed by a hold at 230 °C for 15 min. Column two was a 30 m × 0.25 mm i.d. capillary coated with 0.5 μm of 100% trifluoropropyl methyl polysiloxane (Rtx-200). The separation was performed using a temperature program consisting of an initial hold at 100 °C for 1.0 min, ramped up to 180 °C at a rate of 9 °C/min, held at 180 °C for 2.0 min then ramped to 200 °C at a rate of 10 °C/min and held at 200 °C for 5.0 min. Both GC capillary columns used in this study were purchased from Restek Corporation (Bellefonte, PA).

In both GC–MS and GC–IRD analyses, samples were dissolved and diluted in high-performance liquid chromatography-grade acetonitrile (Fisher Scientific, Fairlawn, NJ) and introduced, individually and in physical mixtures, via the auto-injector using an injection volume of 1 μL.

2.2. Drugs and reagents

The general procedure for the synthesis of these two regioisomeric methylenedioxybenzylpiperazines utilize 2,3-methylenedioxybenzaldehyde and 3,4-methylenedioxybenzaldehyde (piperonal), as starting materials. The preparation of 2,3-methylenedioxybenzaldehyde has been reported previously [21,22]. The two regioisomers were prepared by the reductive amination of the appropriate aldehyde and piperazine in presence of sodium cyanoborohydride. Isolation of the basic fraction gave the corresponding methylenedioxybenzylpiperazine bases, which were converted to the corresponding hydrochloride salts using gaseous HCl and purified by recrystallization. All laboratory reagents and solvents were

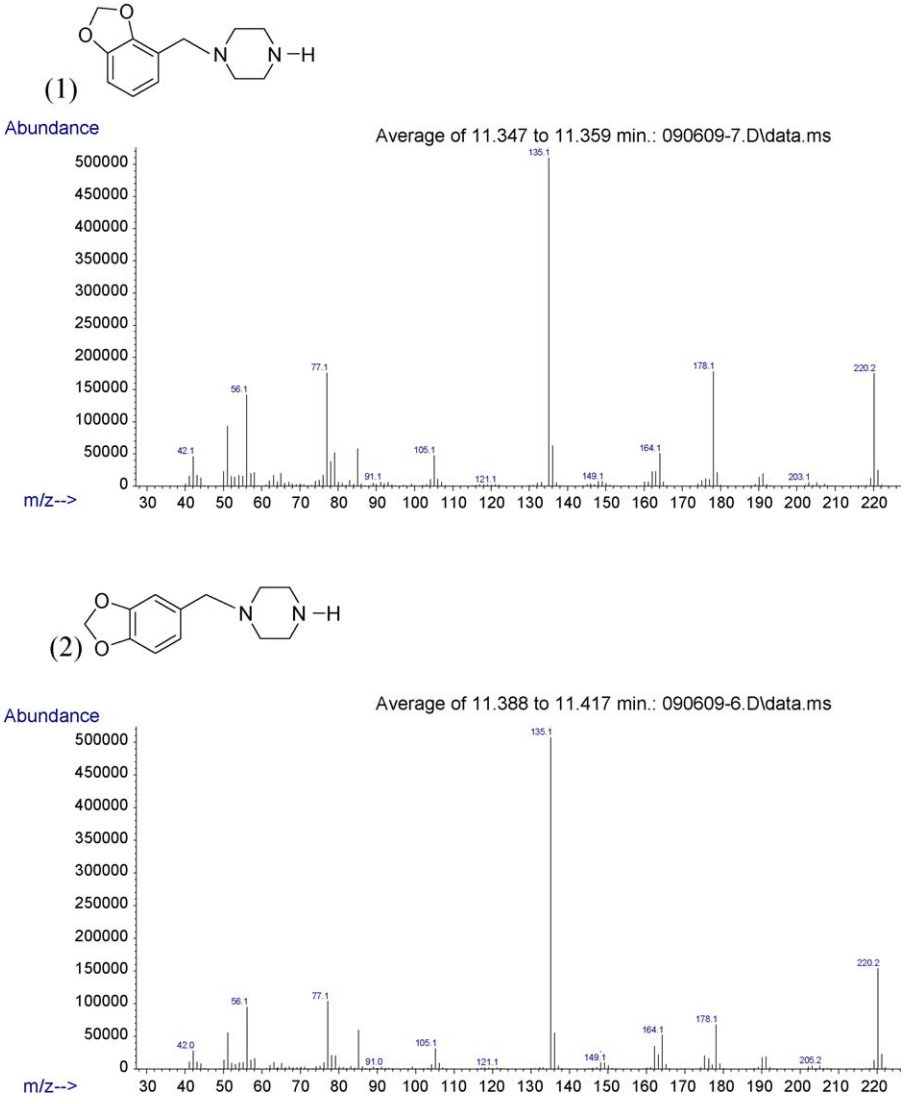

Fig. 1. Mass spectra of the methylenedioxybenzylpiperazines.