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GC–MS studies on acylated derivatives of 3-methoxy-4-methyl- and 4-methoxy-3-methyl-phenethylamines: Regioisomers related to 3,4-MDMA

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Abstract

A series of side chain regioisomers of 3-methoxy-4-methyl- and 4-methoxy-4-methyl-phenethylamines have mass spectra essentially equivalent to the controlled drug substance 3,4-methylenedioxymethamphetamine (3,4-MDMA), all have molecular weight of 193 and major fragment ions in their electron ionization mass spectra at *m/z* 58 and 135/136. The acetyl, propionyl and trifluoroacetyl derivatives of the primary and secondary regioisomeric amines were prepared and evaluated in GC–MS studies. The mass spectra for these derivatives were significantly individualized and the resulting unique fragment ions allowed for specific side chain identification. The trifluoroacetyl derivatives provided more fragment ions for molecular individualization among these regioisomeric substances. These trifluoroacetyl derivatives showed excellent resolution on a non-polar stationary phase such as Rtx-1.

Keywords: GC–MS; Phenethylamines; 3,4-MDMA; Regioisomers; Forensic drug chemistry

1. Introduction

Early studies [1–4] in this series have shown the 10 direct regioisomeric substances, 3,4-methylenedioxymethamphetamine (3,4-MDMA) and its' 9 regioisomeric equivalents, have identical molecular weights and major mass spectral fragments of equivalent mass-to-charge ratios. Therefore direct analysis of these regioisomers by electron ionization mass spectrometry does not provide adequate data for the specific differentiation and identification of any one of these regioisomers (specifically the drug of abuse Ecstasy, 3,4-MDMA) to the exclusion of all the other isomers [1].

All 10 of the direct regioisomeric compounds (5 side chains and 2 ring substitution patterns) of MW = 193 showed major fragment ions for the imine at *m/z* 58 and the substituted benzyl fragment at *m/z* 135/136. Thus, the specific identification of any one of these substances must be based on a combination of mass spectral data as well as chromatographic resolution of these regioisomeric substances. Further studies have demonstrated that some of these compounds have very similar gas chromatographic retention properties, indeed 3,4-MDMA was found to co-elute with one of its non-drug regioisomeric equivalents, *N*-ethyl-2,3-methylenedioxyphenethylamine [1] under common conditions used to identify Ecstasy (3,4-MDMA) in forensic drug samples.

Additional studies [2] have shown that all 10 compounds can be resolved using the more polar gas chromatographic stationary phases and specific temperature programming conditions. Additional background information on the structures of these 10 regioisomeric substances as well as their individual mass spectra and chromatographic properties can be found in references [1,2]. The perfluoroacyl derivatives of the eight primary and secondary amines provide unique mass spectral fragment ions to differentiate among the side chain substitution patterns for the direct regioisomers of MDMA [4].

The preparation and analytical evaluation of the ring substituted methoxy methyl methamphetamines, a series of isobaric compounds related to 3,4-MDMA has been described recently [5]. The 10 methoxy methyl methamphetamines were compared to 2,3- and 3,4-MDMA, all 12 compounds have the same side chain structure generating the *m/z* 58 ion, the base

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peak in the electron ionization mass spectrum for these amines. Mass spectral differentiation of 3,4-MDMA from some of the methoxy methyl methamphetamines was possible after formation of the perfluoroacyl derivatives. Gas chromatographic separation on non-polar stationary phases successfully resolved subsets of the methoxy methyl methamphetamines, based on ring position of the methoxy group, from 2,3- and 3,4-MDMA as the perfluoroacyl derivatives.

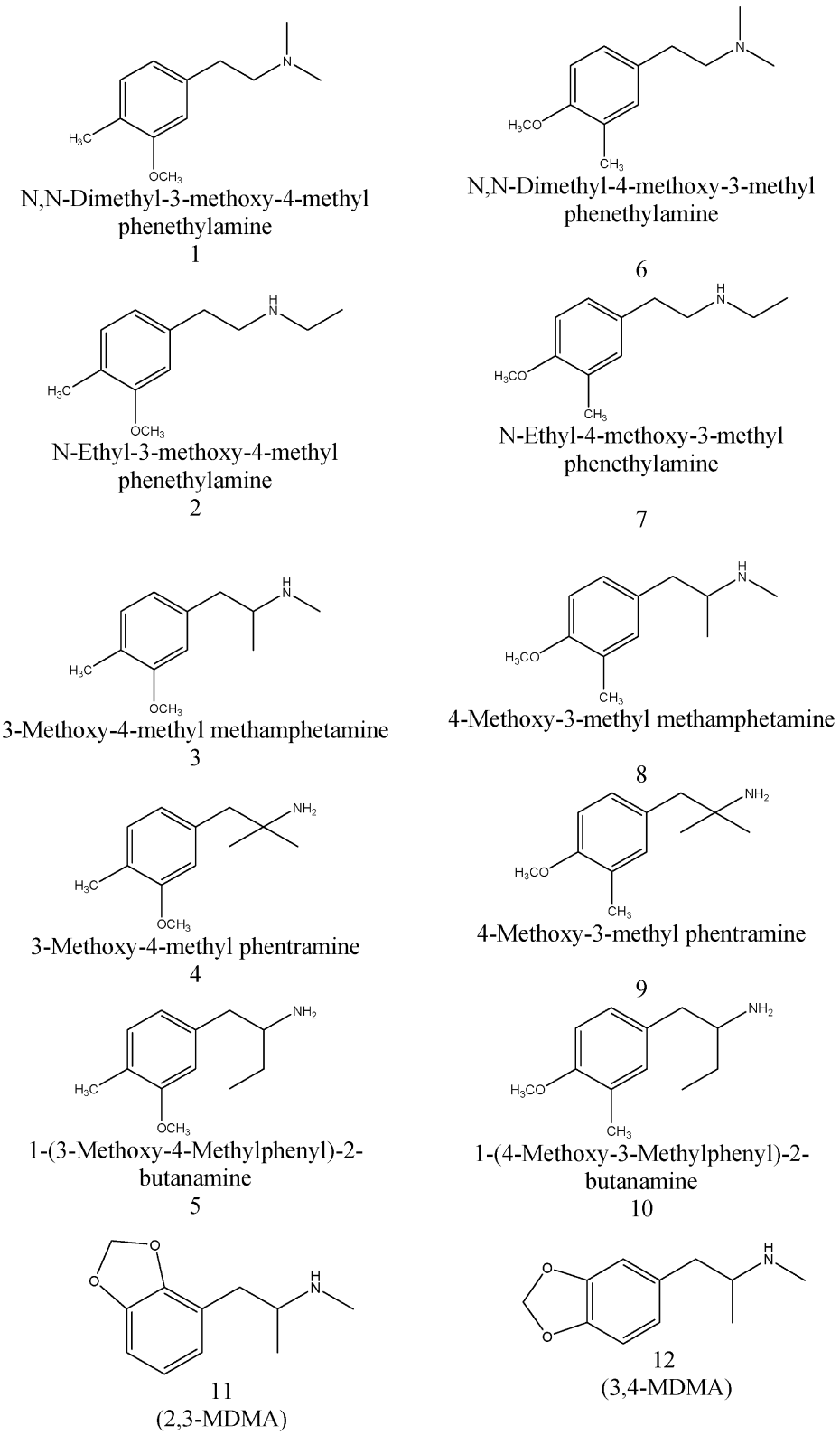

Fig. 1. Structures of the regioisomeric and isobaric compounds in this study.