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Short Communication

Artifact formation during gas chromatographic–mass spectrometric analysis of a methylsulfinyl-containing metabolite

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ABSTRACT

During gas chromatographic–mass spectrometric analysis using a heated injector, 1-methylthio-4-methylsulfinyltetrachlorobenzene degraded to form tetrachlorothioanisole. Similar reductive defunctionalizations have been reported during *in vivo* metabolisms. Caution should be used to distinguish metabolites from artifacts which may be formed during the analysis of methylsulfoxides.

INTRODUCTION

Methylsulfinyl-containing compounds are common biliary metabolites of pentachlorothioanisole (PCTA) [1] and 1,4-bis-methylthiotetrachlorobenzene (bis-MTTCB) [2] formed by intermediary metabolism of glutathione conjugates. In the course of our studies on the metabolism of PCTA and bis-MTTCB, we have found an interesting degradation which occurs during gas chromatographic–mass spectrometric (GC–MS) analysis of one of these methylsulfinyl-containing compounds.

EXPERIMENTAL

1-Methylthio-4-methylsulfinyltetrachlorobenzene (bis-MTTCBO) was synthesized by the oxidation of bis-MTTCB with one equivalent of *m*-chloroperoxybenzoic acid in methylene chloride. The product was isolated and shown to be 95% pure by reversed-phase high-performance liquid chromatography, ^{1}H nuclear magnetic resonance spectrometry and cool on-column capillary GC. Direct-probe electron-impact MS showed a molecular ion at m/z 322 (four-chlorine cluster). GC–MS analysis of the sample was performed on a Hewlett Packard Model 5890 instrument using a 25 m × 0.3 mm I.D. methyl silicone capillary column. The temperature was programmed from 100 to 280°C at a rate of 10°C/min with an initial 2-min hold time. The split–splitless injector had an untreated borosilicate glass liner with a silanized glass wool plug.

RESULTS

When bis-MTTCBO was analyzed by GC–MS using splitless injection and a heated injector (240°C) and interface (220°C), two product peaks

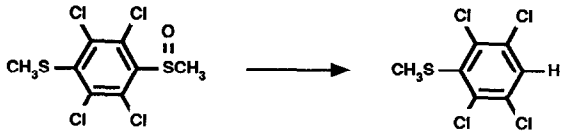

Fig. 1. Formation of tetrachlorothioanisole.

were seen in the total ion current (TIC). The smaller peak, eluting at 19.7 min and accounting for 20% of the TIC area, was bis-MTTCBO, *m/z* 322. The larger peak eluted at 12.5 min and accounted for 80% of the TIC area. The molecular ion at *m/z* 260 (four-chlorine cluster) indicated it was tetrachlorothioanisole (TCTA), formed by replacement of the methylsulfinyl group by hydrogen (Fig. 1). When bis-MTTCBO was again analyzed on the same instrument but using cool on-column injection, only bis-MTTCBO was present in the total ion current. It appeared that formation of TCTA was an artifact due to the heated injector.

DISCUSSION

TCTA has been reported as a metabolite of PCTA [1], bis-MTTCB and other intermediate metabolites of pentachloronitrobenzene and hexachlorobenzene [3]. TCTA is thought to be formed *in vivo* by a reductive desulfurization [3]. Other reductively defunctionalized metabolites have been identified in studies with chlorfenvinphos (a phenacyl chloride) [4], 2-chloro-N-isopropylacetanilide [5] and pentachlorophenol [6]. In each case, the net reaction is replacement of a functional group (Cl or SH) by hydrogen.

We see a similar net reaction (Fig. 1) occurring during GC–MS analysis of bis-MTTCBO using a heated injector. Since methylsulfinyl-containing compounds may be common metabolites formed from glutathione conjugates [7], care should be taken to distinguish reductively defunctionalized metabolites formed *in vivo* and reductive defunctionalization of methylsulfinyl groups which may occur during GC analysis. As yet, we have not investigated whether this degradation is a common feature of methylsulfinyl-containing compounds or unique to bis-MTTCBO. This is the fourth artifact-forming process that has been observed in the manipulation of sulfur-containing metabolites. The others include oxidation by solvent contaminants [8], Pummerer rearrangements [9] and sulfoxide reduction [10].

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