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Short Communication

Determination of 3-chloropropanediol and related dioxolanes by gas chromatography☆

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ABSTRACT

3-Chloropropanediol has been derivatized with N,O-bis(trimethylsilyl)trifluoroacetamide and determined by capillary gas chromatography in extracts of resins and in solvents containing ketones and the corresponding ketals (dioxolanes). *n*-Tetradecane was used as the internal standard.

Underivatized 3-chloropropanediol reacts with ketones and forms the corresponding ketals (dioxolanes). Ketones interfere therefore with the determination of underivatized 3-chloropropanediol. The reaction between 3-chloropropanediol and acetone in excess obeys pseudo-first-order kinetics.

The precision of gas chromatography, expressed as the standard deviation, was found to be 0.43 μg/ml or (relative standard deviation) 0.42%.

INTRODUCTION

3-Chloropropanediol is a toxic compound [1–5] which has been shown to be an antifertility agent in male rats [1,2] and mutagen in bacterial assays [3,4]. Although there is no direct evidence for toxic effects in humans, the results of animal tests dictate that 3-chloropropanediol must be monitored. When used as an intermediate, unreacted 3-chloropropanediol in the product has to be determined and removed if present in amounts above the allowable limit. The determination of 3-chloropropanediol by gas chromatography (GC) is difficult [6]. 3-Chloropropanediol can react during GC with other components of the sample, to form hydrochloric acid in the presence of water, react with active sites on the column and non-volatile residues in the column inlet. As a result, the peak shape deteriorates with repeated injections and the precision is poor.

GC of 3-chloropropanediol derivatized with *n*-butaneboronic acid and phenylboronic acid has been reported [6–8]. We have been using in our laboratory N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), a more powerful derivatization agent, along with an internal standard for the determination of 3-chloropropanediol in extracts of resins and in solvents containing ketones and the corresponding ketals (dioxolanes). Trimethylsilylation with BSTFA has been used for the characterization of aliphatic diols [9] and dihydroarenediols [10] by GC–mass spectrometry.

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EXPERIMENTAL

Chemicals

3-Chloropropanediol and n-tetradecane were purchased from Aldrich. BSTFA was purchased from Kodak Laboratory Chemicals. Acetonitrile, distilled in glass, was purchased from Burdick & Jackson Labs.

2-Isobutyl-2-methyl-4-(chloromethyl)-1,3-dioxolane, formed by reacting 3-chloropropanediol with methyl isobutyl ketone (MIBK), was prepared by E. Pechold (Jackson Lab., Du Pont) and purified by distillation (b.p. 79–80°C/7 mmHg).

Instrumentation

A Varian Model 6000 chromatograph was equipped with an autosampler and a flame ionization detector. A 30 m × 0.75 mm I.D. SPB-5 megabore borosilicate glass capillary column, or alternatively a SPB-5 0.25 mm I.D. capillary fused-silica column was used. The SPB-5 columns (purchased from Supelco, Bellefonte, PA, USA) have a bonded 1.0 μm thick film of 94% dimethyl–5% diphenyl–1% vinyl polysiloxane and correspond to DB-5 capillary columns obtainable from other suppliers.

Carrier gas (helium) flow was for the megabore column 5 ml/min and for the 0.25 mm capillary column 0.8 ml/min. The make up gas flow was 30 ml/min for both columns. The injector was held at 220°C, the detector at 300°C. The oven temperature program was a 3 min hold at 60°C, then a 6°C/min temperature rise to 265°C and no post-program hold.

Procedure

The SPB-5 column with a bonded 1.0 μm thick film of 94% dimethyl–5% diphenyl–1% vinyl polysiloxane exhibited less peak tailing than the moderately polar SPB-20 (20% diphenyl–80% dimethylpolysiloxane phase) column or the polar Supelcowax-10 (polyethylene glycol phase) column with similar dimensions.

n-Tetradecane, 1.0 mg/ml in acetonitrile, was used as the internal standard because its retention time was sufficiently long to exceed that of components found in extracts of the material analyzed. A 4-ml sample of the 3-chloropropanediol solution in acetonitrile (or another solvent) was transferred to a septum vial and 0.5 ml of BSTFA were added. (If an alcohol is used to extract 3-chloropropanediol from a sample, more BSTFA is needed). The closed septum vial was heated for 10 min at 80°C. After allowing the reaction mixture to cool, 0.5 μl of the reaction mixture was injected in a splitless mode (megabore column) or 1.0 μl in a 1:50 split mode (0.25 mm capillary column).

RESULTS AND DISCUSSION

A 1-mol amount of 3-chloropropanediol reacts with 2 mol of BSTFA in two steps. Presumably the primary hydroxyl group reacts at a faster rate than the secondary hydroxyl:

$$HOCH_2CH(OH)CH_2Cl \xrightarrow{BSTFA} (CH_3)_3SiOCH_2CH(OH)CH_2Cl$$

$$(CH_3)_3SiOCH_2CH(OH)CH_2Cl \xrightarrow[\text{heat}]{\text{BSTFA}} (CH_3)_3SiOCH_2CH(OSi(CH_3)_3)CH_2Cl$$

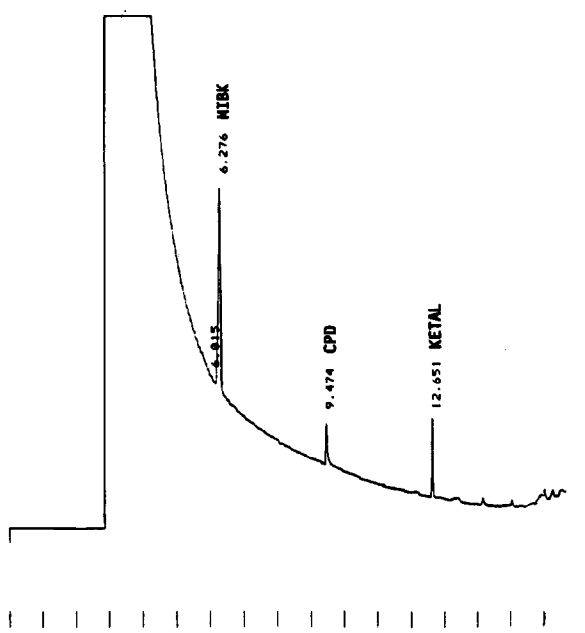


Fig. 1. Gas chromatogram of an equimolar mixture of underivatized 3-chloropropanediol (CPD) and methylisobutylketone (MIBK). Megabore 30 m × 0.75 mm I.D. SPB-5 capillary column. Splitless injection. Numbers at peaks indicate retention times in min.

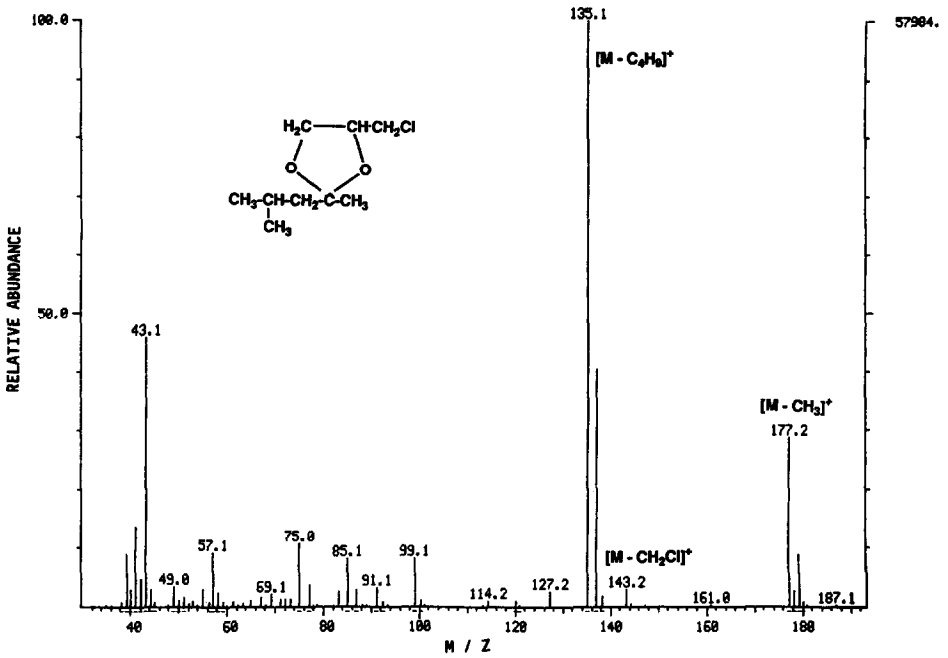
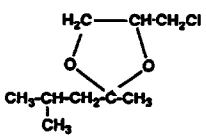


Fig. 2. Mass spectrum of 2-isobutyl-2-methyl-4-(chloromethyl)-1,3-dioxolane.

Although BSTFA reacts with 3-chloropropanediol at ambient temperature, heating for 10 min at 80°C assures complete silylation, especially when other less reactive species may be present in the sample. As an added benefit, trimethylsilylation increases the flame ionization detector response by adding three carbons to each hydroxyl group derivatized.

Underivatized 3-chloropropanediol reacts with ketones during GC, as shown in Fig. 1 with an equimolar mixture of MIBK and 3-chloropropanediol dissolved in acetonitrile. A peak corresponding to the reaction product was identified by mass spectrometry (Fig. 2) as the ketal of MIBK (2-isobutyl-2-methyl-4-(chloromethyl)-1,3-dioxolane):



Consequently, ketones interfere with the determination of underivatized 3-chloropropanediol by GC. Derivatized 3-chloropropanediol, however, does not react with ketones. Kinetics of the reaction between 3-chloropropanediol and ketones can be determined therefore by using BSTFA to terminate the reaction. This is illustrated with a pseudo-first order plot (Fig. 3) of 3-chloropropanediol in acetone. The rate of the reaction is fairly rapid and the use of acetone as the solvent for preparing analytical standards of 3-chloropropanediol [8] is therefore not advisable.

Ketals of 3-chloropropanediol do not react with

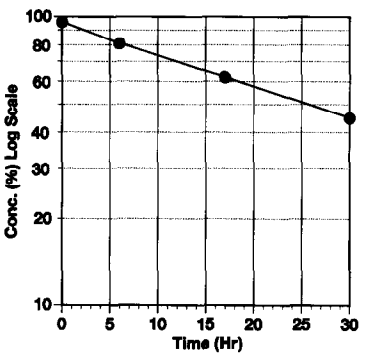


Fig. 3. A pseudo-first order plot of 3-chloropropanediol reacting with acetone at 25°C. Initial concentration of 3-chloropropanediol in acetone 3.11 g/l.

TABLE I

ANALYSIS OF MIXTURES OF 3-CHLOROPROPANEDIOL AND 2-METHYL-2-ISOBUTYL-4-(CHLOROMETHYL)-1,3-DIOXOLANE

3-Chloropropanediol			2-Methyl-2-isobutyl-4-(chloromethyl)-1,3-dioxolane		
Prepared concentration (mg/ml)	Found concentration (mg/ml)	Recovery (%)	Prepared concentration (mg/ml)	Found concentration (mg/ml)	Recovery (%)
0.412	0.405	98.3	0	0	
0.330	0.337	102.2	0.161	0.158	98.1
0.247	0.249	100.7	0.321	0.311	96.9
0.165	0.161	97.3	0.482	0.476	98.8
0	0		0.803	0.797	99.3

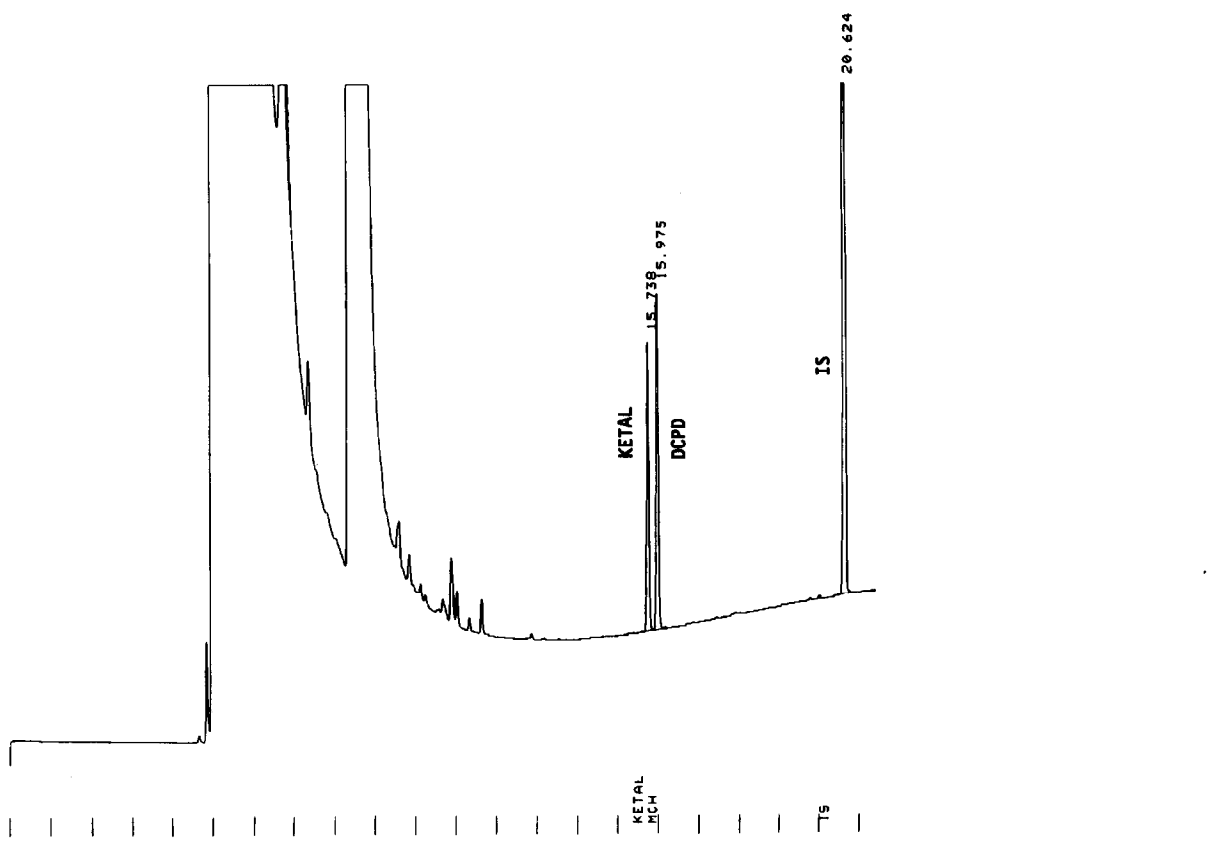


Fig. 4 Gas chromatogram of derivatized 3-chloropropanediol (DCPD) and 2-isobutyl-2-methyl-4-(chloromethyl)-1,3-dioxolane (KETAL) in acetonitrile. Internal standard: *n*-tetradecane (IS). Megabore 30 m × 0.75 mm I.D. SPB-5 capillary column.

BSTFA (Table I) and can be determined in the presence of 3-chloropropanediol by GC (Fig. 4).

The accuracy of the analyses is shown with data in Table I. The precision of gas chromatography was expressed as the standard deviation of five replicate analyses of the same solution containing 103.3 μg/ml 3-chloropropanediol in acetonitrile. The standard deviation was found to be 0.43 μg/ml or (relative standard deviation) 0.42%. The detection limit of 3-chloropropanediol is about 5 μg/ml.

ACKNOWLEDGEMENT

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