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Short communication

Determination of epichlorohydrin by sulfite derivatization and ion chromatography: characterization of the sulfite derivatives by ion chromatography–mass spectrometry

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Abstract

This work is an upgrade of a previously developed method [J. Chromatogr. A 884 (2000) 251] for epichlorohydrin determination by ion chromatography (IC) and conductivity detection. Here, an ion chromatography–mass spectrometry (IC–MS) coupling has been employed for the separation and the identification of products of epichlorohydrin when reacted with the nucleophilic agent SO_3^{2-}. The high capacity column (IonPac AS11-HC) used for separation provided good resolution. This allowed evaluation of the IC behavior and mass spectrometric identification of epichlorohydrin sulfite derivatives. By using atmospheric pressure interfaces (ESI and APCI) the following species were tentatively identified: 2,3-dihydroxy-1-propanesulfonic, 2,3-epoxy-1-propanesulfonic, 1,3-dihydroxy-2-propanesulfonic and 3-oxetanesulfonic acids and 2-hydroxy-1,3-propanedisulfonic acid (or its isomer 3-hydroxy-1,2-propanedisulfonic acid). The study showed that chlorine atoms are displaced from epichlorohydrin during the reaction, while mass spectrometry confirmed that none of the products formed contains chlorine atoms.

Keywords: Derivatization, LC; Epichlorohydrin; Sulfite

1. Introduction

Epichlorohydrin (1-chloro-2,3-epoxypropane) is used mainly for the manufacture of glycerol, unmodified epoxy resins and, to a lesser extent, elastomers, water-treatment resins, surfactants, ion exchange resins, plasticizers, dyestuffs, pharmaceutical products, oil emulsifiers, lubricants, and adhesives [1]. Limited data are available on the occurrence of epichlorohydrin in occupational and ambient air, water and food. Migration into food and drinking water of epichlorohydrin used as a cross-linking agent in packaging materials and epoxy resins is possible but is expected to be low [2]. Epichlorohydrin can enter drinking-water supplies through the use of flocculating agents in which there are epichlorohydrin residues and through leaching from epoxy resin coatings on pipes [3].

The rate of disappearance from water or aqueous media is expected to be rapid through hydrolysis or evaporation, while in the troposphere, epichlorohydrin is probably photodegraded [2,4]. Hydrolysis is the most probable first reaction in the metabolic pathway of epichlorohydrin, and it results in the formation of the much less toxic 3-chloro-1,2-propanediol [2,5]. Epichlorohydrin is mutagenic in most short-term assays and the maximum contaminant level goal for epichlorohydrin has been set at zero by the US EPA. A review about the mutagenic and clastogenic effects of epichlorohydrin is available [6]. The main analytical methods available for epichlorohydrin quantification in water involve purge-and-trap GC with mass spectrometric, flame ionization, or electron-capture detection [7,8]. An indirect GC determination of epichlorohydrin as dichlorohydrin, formed in the presence of HCl and HBr, has also been proposed [9].

A new anion-exchange based method, developed by our group [10], allowed the analysis of <100 ng/l epichlorohydrin in water. The method exploited the products of a nucle-

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ophilic attack of the epoxide ring by S(IV) from a sodium sulfite solution of optimized composition. In this work, a tentative identification of the reaction products was performed by coupling IC and MS. After derivatization and separation, the compounds formed were studied by electrospray (ESI) and by atmospheric pressure chemical ionization (APCI). Although ESI is preferred for most applications because of its superior sensitivity, APCI offers advantages for analytes with low to medium polarity and lower molecular mass [11].

This study pointed out that none of the products contains chlorine atoms, that are shown to be indeed released through the nucleophilic attack.

2. Experimental

According to the schematic representation of Fig. 1, the set-up contains a HPLC pump Spectra System P4000 (Spectra-Physics), an anion-exchange precolumn ATC-1 (Dionex, Sunnyvale, CA), an electrolytic cell for the eluent generation EG40-KOH (Dionex), an adjustable current source (SC20-Suppressor Controller, Dionex), a high-pressure degassing unit for the eluent (Dionex), a six-way injection valve (Labpro PR750-100-01, Rheodyne, USA), with a sample loop of 50 μl, a guard (50 mm × 4 mm) and a separation (250 mm × 4 mm) anion-exchange column: IonPac AG11-HC and IonPac AS11-HC (Dionex), a suppressor unit (ASRS-ULTRA, Dionex), a mass spectrometer (LCQ MS system, Finnigan, MAT, San Jose, CA, USA). The eluent was 2.5 mM KOH, for the initial 7 min of run and a linear gradient from 7 to 20 min from 2.5 to 40 mM KOH (flow rate 1.5 ml/min).

Derivatization was performed as discussed later. Procedural blanks were processed in the same way as the epichlorohydrin solutions.

For preconcentration BondElut® C18 (Varian, CA, USA) cartridges were employed. As previously optimized [10], the substrate was washed and conditioned with 5 ml CH_3OH and 10 ml H_2O. Sample volumes of 25 ml were preconcentrated at a flow rate of 1.0 ml/min and eluted with 2.5 ml of CH_3OH/H_2O (50:50 (v/v)) (preconcentration factor: 10). For optimization of the procedure 2.36 μg/ml epichlorohydrin samples were used.

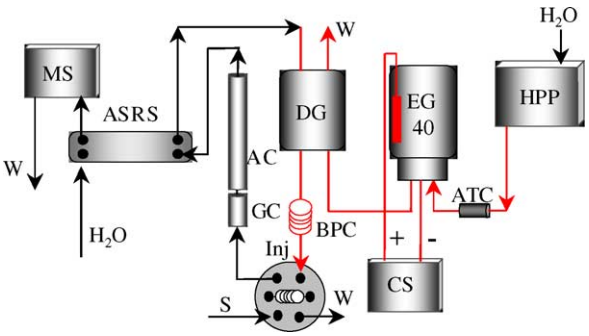

Fig. 1. Scheme of IC–MS manifold. HPP: pump, ATC: anion-exchange precolumn, EG40: eluent generator, CS: adjustable current source, DG: degassing unit, BPC: back-pressure coil, Inj: six-way injection valve, GC: guard column, AC: separation column, ASRS: suppressor unit, MS: mass spectrometer, S: sample, W: waste.

For MS analysis the sample was prepared as follows: 2.0 ml of epichlorohydrin (8.3×10^{-3} M) was added to 0.25 ml of NaOH (1.0 M) and 1.0 ml of Na_2SO_3 (0.1 M) into a 25 ml flask and diluted to the volume with water. The mixture was thermostated at 30 °C for 24 h prior to analysis.

For ESI–MS, the conditions were: source voltage 4.21 kV, source current 80.3 μA, sheath gas (N_2) flow rate 0.75 MPa, AuX gas (N_2) flow rate 0.18 MPa, capillary voltage −9.66 V, capillary temperature 250 °C, sheath liquid 10% NH_4OH, 50 μl/min. For APCI–MS, the conditions were: source voltage 1.60 kV, source current 4.88 μA, vaporizer temperature 302 °C, sheath gas (N_2) flow rate 0.69 MPa, AuX gas (N_2) flow rate 0.18 MPa capillary voltage −9.74 V, capillary temperature 150 °C.

(±)Epichlorohydrin, anhydrous sodium sulfite and methanol were from Fluka (Buchs, Switzerland), sodium hydroxide was from Merck (Darmstadt, Germany). High-purity water was obtained with a Milli-Q system (Millipore, Bedford, MA, USA). Before use, eluents were filtered with 0.22 μm cellulose acetate filters (Millipore).

3. Results and discussion

In our previous study, epichlorohydrin was analyzed after derivatization with sodium sulfite by separation of its reaction products (arbitrary labeled as *Epi 1* and *Epi 2*) on a IonPac AS11 column (capacity: 45 μeq per column). It was shown that *Epi 1* eluted close to the void volume. When the method is coupled to a preconcentration step, *Epi 2* is not completely resolved from CH_3OH (the eluent for the recovery of epichlorohydrin from the C18 cartridge). In order to improve the resolution between the solvent peak and *Epi 2*, this study, aimed at identifying the reaction products, was performed on a higher capacity column, IonPac AS11-HC (290 μeq per column).

For each reaction product, the repeatability and linearity of the method were studied at different concentrations (see Table 1). In order to check for any catalytic effects, the yields were compared in basic and neutral medium.

As previously optimized, epichlorohydrin was derivatized with 6 mM Na_2SO_3, 10 mM NaOH at 30 °C for 24 h. Fig. 2 shows typical chromatograms obtained. It must be pointed out that the reaction gave four additional products not detected during the first study [10]. The areas for all peaks increased with an increasing epichlorohydrin concentration.

One peak was identified as Cl^- ion by the standard addition method. The linearity of response with an increasing epichlorohydrin concentration indicates that Cl^- ions are released by epichlorohydrin during its derivatization.

If the reaction is performed in NaOH medium, the formation of *Epi 2* is favored over *Epi 1*. Poor linearity and repeatability were observed for *Epi 5*.

Table 1
R.S.D. values of peak areas and correlation coefficient (r^2) for the reaction products in the range of 0.125–30 mg/l (four concentrations; $n = 3$) epichlorohydrin

	6 mM Na_2SO_3, 10 mM NaOH		6 mM Na_2SO_3	
	R.S.D. (%)	r^2	R.S.D. (%)	r^2
12–30 mg/l				
Epi 1	2.8	0.9993	5.8	0.9996
Epi 2	3.0	0.9988	2.4	0.9988
Epi 3	N.C.	–	N.C.	–
Epi 4	8.3	0.9882	1.7	0.9589
Epi 5	N.C.	–	N.C.	–
Cl^-	3.4	0.9983	3.1	0.9952
125–450 μg/l[a]				
Epi 2	5.8	0.9998	4.7	0.9979

Data for two derivatization conditions. N.C.: not calculated.
[a] Other compounds not detected.

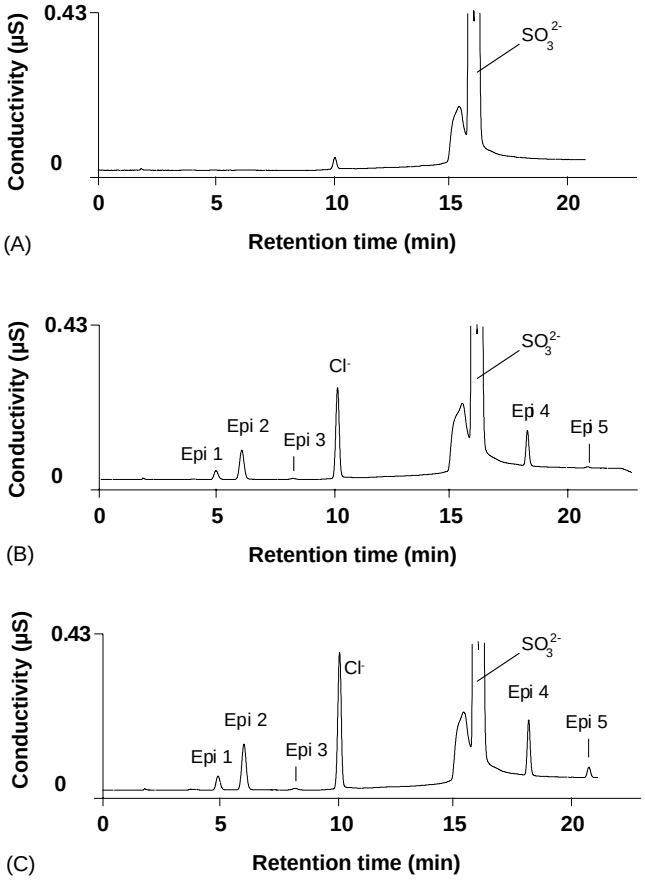

Fig. 2. Separation of the reaction products of epichlorohydrin with sodium sulfite and NaOH. Derivatization conditions: 6.0 mM Na_2SO_3, 10 mM NaOH, 1 h at 30 °C. (A) Blank, (B) epichlorohydrin: 23.6 mg/l, (C) epichlorohydrin: 35.4 mg/l. Column: IonPac AG11-HC and AS11-HC. Eluent: $t = 0$–7 min, 2.5 mM KOH; $t = 7$–20 min, from 2.5 to 40 mM KOH. Flow rate: 1.5 ml/min. Loop: 50 μl.

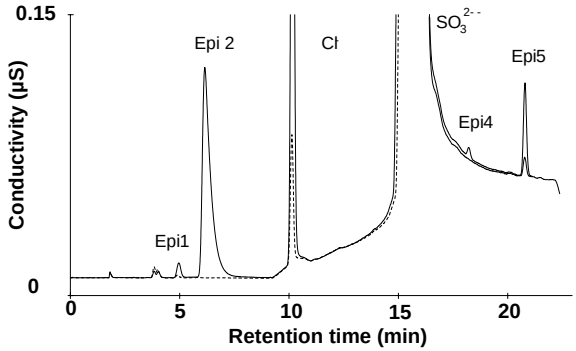

Fig. 3. Separation of the reaction products of epichlorohydrin with sodium sulfite. Derivatization conditions: 6.0 mM Na_2SO_3, 1 h at 30 °C. Dot line: blank, solid line: epichlorohydrin 23.6 mg/l. IC conditions as in Fig. 2.

Comparing the reaction yields obtained with and without NaOH, it is noted that in neutral conditions, the formation of *Epi 2* increases, whilst the formation of *Epi 1* decreases (Fig. 3). The data showed that when derivatizing without NaOH, the peak of *Epi 4* is only the 25% of what can be obtained when adding OH^- ions.

The detection limit for E*pi 2*, evaluated as three times the noise signal, was 2 μg/l. It is important to note that the *Epi 2* peak was free from interferences.

4. Optimization of the preconcentration procedure

Due to the interference problems experienced in the previous study, the preconcentration procedure was optimized for this anion-exchange system. Known amounts of epichlorohydrin were preconcentrated, exploiting its neutral form, before derivatization. Preconcentration and elution were performed as detailed in Section 2. After elution from the C18 cartridge, epichlorohydrin was derivatized with 6 mM Na_2SO_3. Due to the poor linearity of peaks *Epi 4* and *Epi 5*, the discussion is limited to *Epi 1* and *Epi 2*, the most stable species formed by epichlorohydrin.

The results showed a strong interference from CH_3OH which prevented the identification of both *Epi 1* and *Epi 2*. The decrease of the eluent strength has only minor benefits. Evaporation of CH_3OH (30 min at 65 °C) both before and after derivatization was tested. Although the boiling point of epichlorohydrin is about 120 °C, loss of epichlorohydrin occurred if evaporation was performed before derivatization. Detection of *Epi 1* and *Epi 2* was possible only if the evaporation was performed after the derivatization. Recovery data were 86 and 87%, respectively (R.S.D. = 3.7%, $n = 4$).

The optimized procedure was applied for the analysis of a drinking water sample from Ljubljana (Slovenia). The sample was filtered and injected without preconcentration and preconcentrated both with 6 mM Na_2SO_3 and with 10 mM NaOH, 6 mM Na_2SO_3, and after spiking with 250 μg/l epichlorohydrin. None of the original samples processed revealed the presence of epichlorohydrin.

5. Characterization of the reaction products by MS

In order to obtain well-defined mass spectra for each reaction product, concentrated solutions of epichlorohydrin (62 mg/l) were used. Due to the larger number of species found, the reaction was performed with 6 mM Na_2SO_3, 10 mM NaOH. The eluent composition was optimized to reduce re-conditioning times, while still ensuring good separation. The new eluent composition was 13 mM KOH (EG40, $I = 20$ mA). The conductimetric detection was verified also for these conditions (Table 2). Two ionization procedures (ESI and APCI) were studied.

When ESI–MS detection was used, the ionization of molecules originating from the reaction of epichlorohydrin was too low; hence, chromatograms did not show relevant signals; i.e. sensitivity was poor. Nevertheless, it was possible to record a signal at mass 219. This species, strongly retained by the IC column, was probably related to the $[M - H]^-$ ion of either:

- HSO_3–CH_2–CH(OH)–CH_2SO_3H, 2-hydroxy-1,3-propanedisulfonic acid;
  or its isomer
- HSO_3–CH_2–CH(SO_3H)–CH_2(OH), 3-hydroxy-1,2-propanedisulfonic acid.

Since two sulfonic groups (that can strongly interact with the anion-exchange column) are present, this compound is probably one of the last eluted species.

Further experiments were performed by IC–APCI–MS and using the same experimental conditions. The mass spectra showed the presence of four main species at retention times 0.2 min longer than with conductivity detector (Table 2).

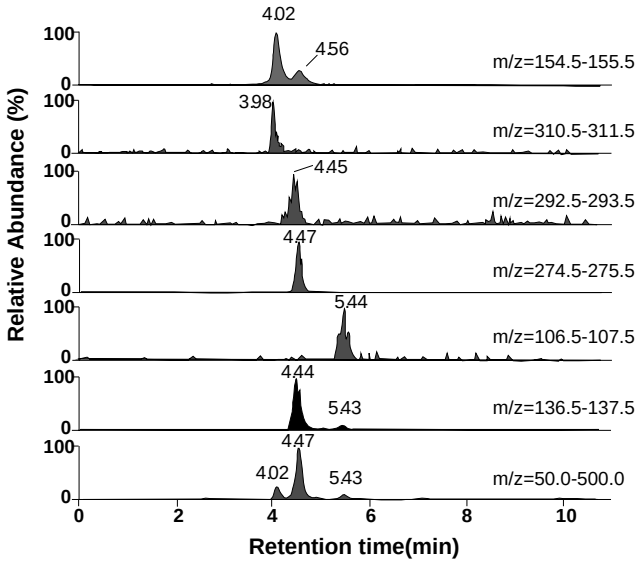

Fig. 4. Chromatograms obtained with the IC–APCI–MS method for different *m*/*z* values. Eluent: 13 mM KOH, flow rate 1.0 ml/min.

Due to its low molecular mass, chloride ion cannot be detected with this type of MS detector. Moreover, in order to prevent clogging and damage for the MS detector due to the conversion of SO_3^{2-} and SO_4^{2-} to S_2 on the heated capillary, these anions were not detected. The mass 219 compound detected with ESI–MS was not detected by APCI–MS. The main reason for this is the highly ionic character of this compound that prevents detection in APCI where neutral to slightly ionic substances can be detected. Fig. 4 shows the chromatograms obtained at defined mass ranges and the main results for the identified species are summarized in Table 2.

The LC-peaks in the $m/z = 155$ mass chromatogram show an area ratio of about 2:1, supporting the actual probability of a faster deprotonation of the more acidic molecule. The mass 293 compound ($t_r = 4.45$ min) corresponds to

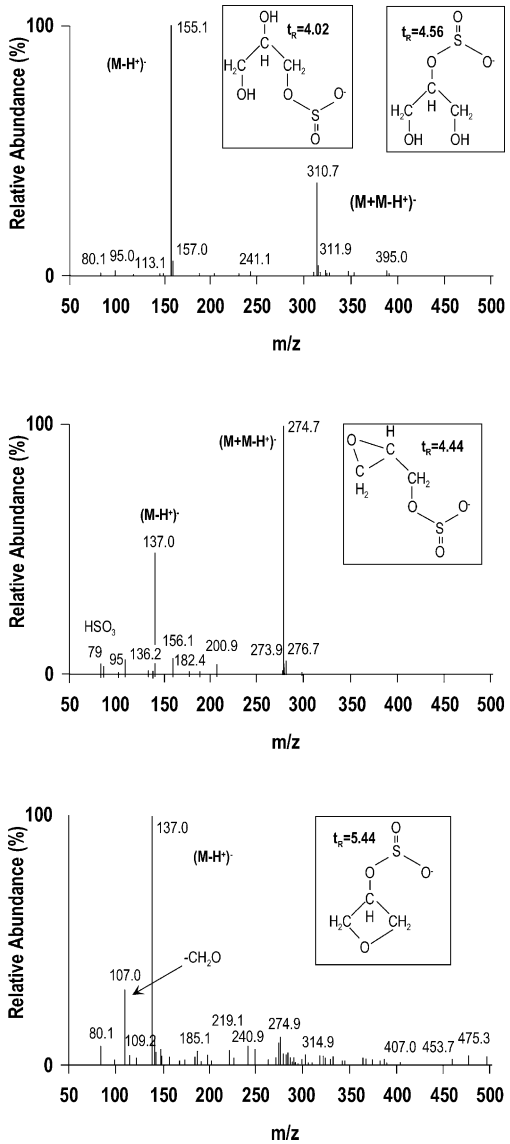

Fig. 5. Mass spectra of the most abundant peaks at retention times 4.02, 4.44 and 5.44 min. IC conditions as in Fig. 4.

Table 2
Molecular masses and possible structures for the reaction products of epichlorohydrin detected by IC–APCI–MS and IC conductivity

m/*z*	Species	Retention time (min)		Name
		APCI–MS	Conductivity	
155	$[M-H]^-$	4.02	3.80	*Epi 1*. 2,3-Dihydroxy-1-propanesulfonic acid
311	$[M-H]^-$	4.02	3.80	*Epi 1*. 2,3-Dihydroxy-1-propanesulfonic acid
137	$[M-H]^-$	4.44	4.26	*Epi 2*. 2,3-Epoxy-1-propanesulfonic acid
155	$[M-H]^-$	4.56	4.36	*Epi 3*. 1,3-Dihydroxy-2-propanesulfonic acid
275	$[M-H]^-$	5.44	5.19	*Epi 4*. 3-Oxetanesulfonic acid

a mixed adduct ion of 2,3-epoxy-1-propanesulfonic acid and 1,3-dihydroxy-2-propanesulfonic acid, the isomer of 2,3-dihydroxy-1-propanesulfonic acid. It is noted that the isomers with the sulfonic group on the second carbon of the chain (i.e., 1,3-dihydroxy-2-propanesulfonic and 3-oxetanesulfonic acids, see structures in Fig. 5) do not form the adduct ions among themselves; in facts, no peaks were detected at the retention times 5.44 and 4.56 min at the *m*/*z* values of 275 and 311, respectively. It is likely that the sulfonic group in the middle of the chain prevents the simple adhesion of two similar molecules in order to form the adduct ion. If the sulfonic group is placed on one side of the molecule, the adduct can appear if two molecules orientate their sulfonic groups in opposite directions and form a stable adduct ion.

6. Conclusions

IC–MS has been used for the separation and identification of reaction products of epichlorohydrin with the nucleophilic agent SO_3^{2-}. The use of a high-capacity separation column allowed us to solve co-elution problems experienced during previous research and to better evaluate the chromatographic behavior of the reaction products. ESI–MS allowed the last eluting species to be tentatively identified as 2-hydroxy-1,3-propanedisulfonic acid or its isomer 3-hydroxy-1,2-propanedisulfonic acid. APCI–MS helped to identify four derivatives and confirmed the release of chloride ions. Their increase is linearly dependent on the increase of the epichlorohydrin concentration, which suggests that chlorine atoms are displaced from epichlorohydrin during the reaction.

Possible structures of the other products are 2,3-dihydroxy-1-propanesulfonic, 2,3-epoxy-1-propanesulfonic, 1,3-dihydroxy-2-propanesulfonic and 3-oxetanesulfonic acids.

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