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FURTHER STUDIES ON IMPURITIES IN CHLOROPHENOLS

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SUMMARY

Impurities in three chlorinated phenol formulations manufactured from phenol by direct chlorination were investigated. The impurities were separated by means of gas and thin-layer chromatography and analyzed with a combined gas chromatograph–mass spectrometer.

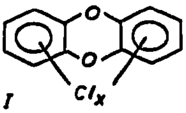
The main impurities (1–5%) were chlorinated 2-hydroxydiphenyl ethers (predioxins), precursors to chlorinated dibenzo-*p*-dioxins, and 4-hydroxydiphenyl ethers (isopredioxins).

Further impurities, such as chlorinated dihydroxybiphenyls, chlorinated diphenyl ethers and chlorinated dibenzofurans, were identified. The levels of chlorinated dibenzofurans were high (10–100 ppm) in relation to their toxicity.

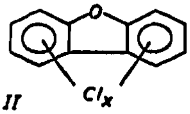
INTRODUCTION

The widespread use of chlorophenols as fungicides, bactericides, etc., is well known. Recently, attention has been drawn to the chlorophenols as precursors to chlorinated dibenzo-*p*-dioxins (chlorinated dioxins), a group of toxic and chemically stable compounds.

Previous investigations[1,2] have shown that chlorinated dioxins (I), chlorinated dibenzofurans (II) and chlorinated diphenyl ethers (III) (*i.e.*, non-phenolic compounds) are common impurities in technical chlorophenols and their derivatives.



I



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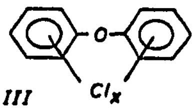
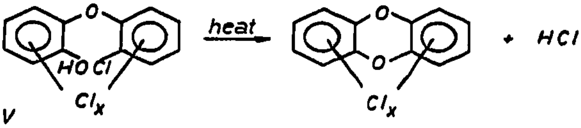


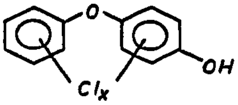
III

The existence of phenolic precursors to chlorinated dioxins, chlorinated 2-hydroxydiphenyl ethers, has been reported[3,4]. These predioxins (IV) are converted into dioxins when heated:



IV

Isomers of predioxins, chlorinated 4- or 3-hydroxydiphenyl ethers, have also been identified[3]. These substances, called isopredioxins (V), do not undergo the same ring closure to form dioxins. Also, 2-hydroxydiphenyl ethers with no chlorine in the 2'-position do not undergo the same ring closure to form dioxins, and these isomers are also called isopredioxins.



V

The investigation has now continued with other commercial chlorophenols used in Sweden as wood preservatives. The formulations are 2,4,6-trichlorophenol, potassium 2,3,4,6-tetrachlorophenate and 50% aqueous solution of potassium 2,4,6-trichlorophenate. These are all manufactured by the catalytic chlorination of phenol, while the previously investigated pentachlorophenols[3,4] are normally manufactured by alkaline treatment of hexachlorobenzene.

EXPERIMENTAL

Reagents

n-Hexane (p.a.), diethyl ether (p.a.), diazomethane[5], diazoethane[6] and, for the concentration determinations, 2-hydroxy-2',4,4'-trichlorodiphenyl ether, were used.

Gas chromatographic system

A Pye-Unicam Model 84 gas chromatograph equipped with a flame ionization detector (FID) was used. It was equipped with a glass column (2.7 m, I.D. 0.40 cm) filled with 1% Apiezon M on acid-washed, dimethyldichlorosilane-treated Chromosorb W (100–120 mesh). The operating conditions were: injector temperature, 275°; column temperature, 240°; detector temperature, 275°; carrier gas, helium at a flow-rate of 25 ml/min.

Gas chromatographic–mass spectrometric system

An LKB 9000 mass spectrometer equipped with a Pye-Unicam Model 84 gas chromatograph and a split to a FID was used. The column and operating conditions for the gas chromatograph were as above and the temperature of the connection between it and the mass spectrometer was 250°. The operating conditions for the mass spectrometer were: separator temperature, 255–270°; ion source temperature, 270°; electron energy, 70 eV.

Thin-layer chromatographic system

The plates were covered with a 0.25-mm layer of silica gel HF_{254}, nach Stahl, and activated for 1 h at 120° before use. The two developing systems were *n*-hexane and *n*-hexane–diethyl ether (65:35). For gas chromatographic–mass spectrometric (GC–MS) identification the bands, which were rendered visible under UV light (254 nm), were scraped off and eluted with diethyl ether.

Extraction procedure

Trichlorophenol (1 g), potassium 2,3,4,6-tetrachlorophenate (1 g) and potassium 2,4,6-trichlorophenate (2 g of the 50% aqueous solution) were dissolved in 100 ml of 1 *M* aqueous potassium hydroxide. The aqueous solutions were extracted with three 50-ml volumes of *n*-hexane–diethyl ether (1:1) and the combined organic layers were washed once with 50 ml of 1 *M* potassium hydroxide solution and once with 50 ml of water. After drying over magnesium sulphate, the extracts were evaporated to dryness (before and after treatment with ethereal diazomethane solution in order to check for remaining phenolic impurities in the extracts), dissolved in 2 ml of acetone and analyzed by combined GC–MS (5-μl injection volume).

The remaining aqueous phases were acidified with dilute sulphuric acid (to pH 1), extracted with three 50-ml volumes of *n*-hexane–diethyl ether (1:1), washed with 50 ml water and dried over magnesium sulphate. The extracts were treated with an ethereal solution of diazomethane or diazoethane and evaporated to dryness and the residues were dissolved in 2 ml of acetone and analyzed by combined GC–MS.

Levels of different impurities

In order to determine the levels of the phenolic impurities, the acidified solutions of the formulations were extracted with diethyl ether followed by the addition of 2-hydroxy-2′,4,4′-trichlorodiphenyl ether (trichloropredioxin) as an internal standard. The solutions were treated with diazomethane and injected into the gas chromatograph. The peak areas were measured with a dish integrating recorder and the determination was made on the assumption that all phenolic compounds (*i.e.*, predioxins, isopredioxins and dihydroxybiphenyls) had the same or almost the same response to the FID as the methylated standard, after treatment with diazomethane. The determinations of the concentrations of non-phenolic impurities (*i.e.*, dibenzofurans and diphenyl ethers) were made in a corresponding manner using the same internal standard.

RESULTS

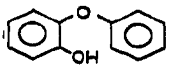
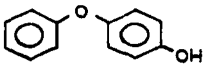
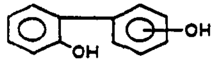
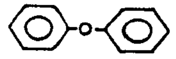
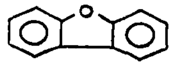
In all of the formulations investigated, high levels of different impurities were found. After extraction, the fractions were analyzed by means of combined GC–MS (see Table I and Figs. 1–3).

Phenolic impurities

The main impurities in all three formulations (ranging between 1 and 5%) were the chlorinated predioxins and isopredioxins (IV and V), which were detected as their methyl ethers. Their structures were determined by MS according to earlier investigations[3,4]. In agreement with Jensen and Renberg[3], the methylated predioxins

TABLE I

ANALYSIS OF FRACTIONS BY COMBINED GAS CHROMATOGRAPHY-MASS SPECTROMETRY

*Compound**	*No. of chlorine atoms*	*Formulation*		
		*2,3,4,6-Tetrachlorophenate (Nos. refer to peaks in Fig. 1)***	*2,4,6-Trichlorophenol (Nos. refer to peaks Fig. 2)***	*2,4,6-Trichlorophenate (Nos. refer to peaks in Fig. 3)***
Acidic fraction				
Chlorinated predioxins	4	—	1	—
	5	3	3, 6	3, 6
	6	6, 7, 8, 9	6, 9, 11, 12	6, 9, 11, 12
	7	14, 17	t	17
	8	18	—	—
Chlorinated*** isopredioxins	4	2	2	2
	5	4	4, 5	4, 6
	6	7, 8, 10	8, 10, 12	8, 10, 11, 12
	7	16	t	16
Chlorinated dihydroxybiphenyls§	4	1	1	1
	5	2	3	3
	6	5, 8	—	5, 13
	7	16	—	—
Neutral fraction				
Chlorinated diphenyl ethers	4	—	+	+
	5	—	+	+
	6	—	+	+
	7	—	+	—
Chlorinated dibenzofurans	5	—	—	+
	6	—	—	+
				

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* Hydroxylic compounds detected as their methyl ethers.

** + = Present in the neutral fraction; — = not present; t = traces.

*** The hydroxy group in the isopredioxin is indicated in the *para*-position as this seems to be the most logical, but this does not exclude the presence of the *meta*-isomer.

§ In all dihydroxybiphenyls but one (peak 13), at least one hydroxyl group is in the *ortho*-position because of the MS fragment M^+-50, *i.e.*, M^+-CH_3Cl.

preferentially lose CH_3Cl and the methylated isopredioxins lose CH_3. As an example, the MS fragmentations for one pentachlorinated predioxin ($C_{12}H_5Cl_5O_2$) and one isopredioxin are given in Table II.

The lower chlorine content in the tri- and tetrachlorophenol formulations compared with the pentachlorophenol makes the appearance of a third isomer feasible, *i.e.*, 2-hydroxydiphenyl ether with no chlorine in the 2′-position. It seems most logical to assign this isomer to the isopredioxins because it is unable to undergo ring closure

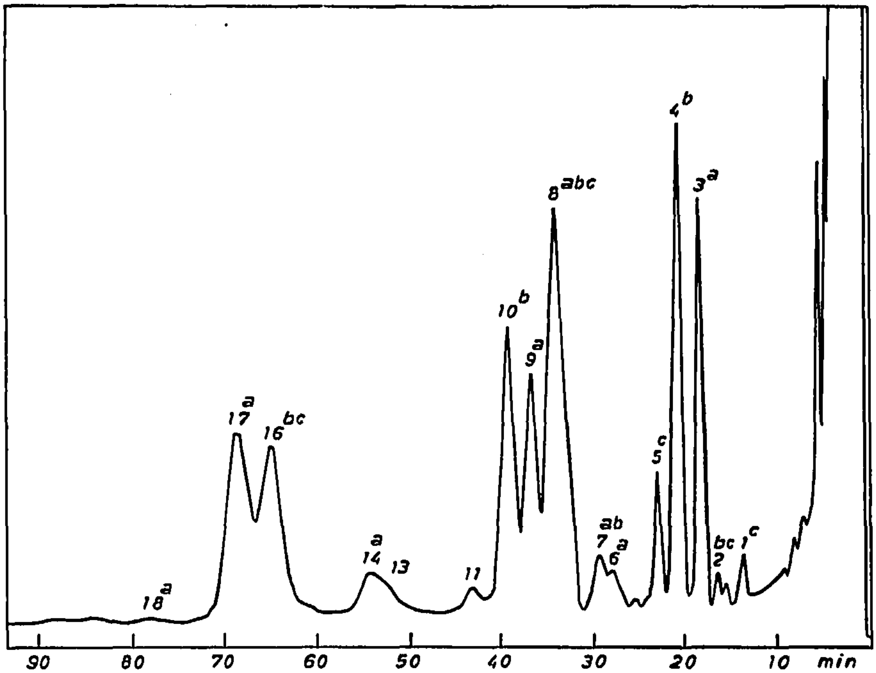


Fig. 1. Gas chromatogram of extract from acidified solution of potassium 2,3,4,6-tetrachlorophenate (Nos. refer to Table I). a = Chlorinated predioxin; b = chlorinated isopredioxin; c = chlorinated dihydroxybiphenyl.

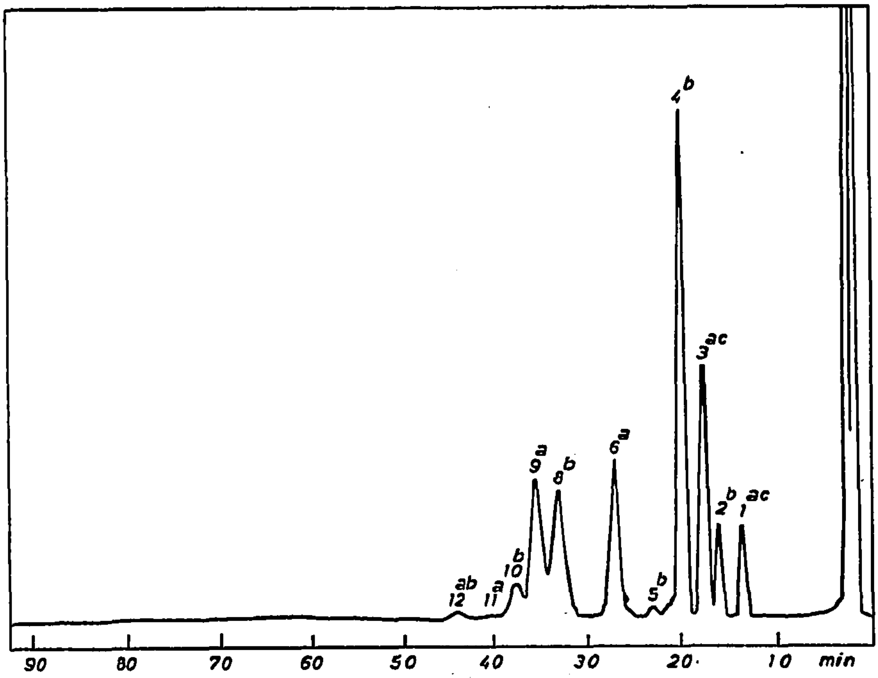


Fig. 2. Gas chromatogram of extract from acidified solution of 2,4,6-trichlorophenol (Nos. refer to Table I). a = Chlorinated predioxin; b = chlorinated isopredioxin; c = chlorinated dihydroxybiphenyl.

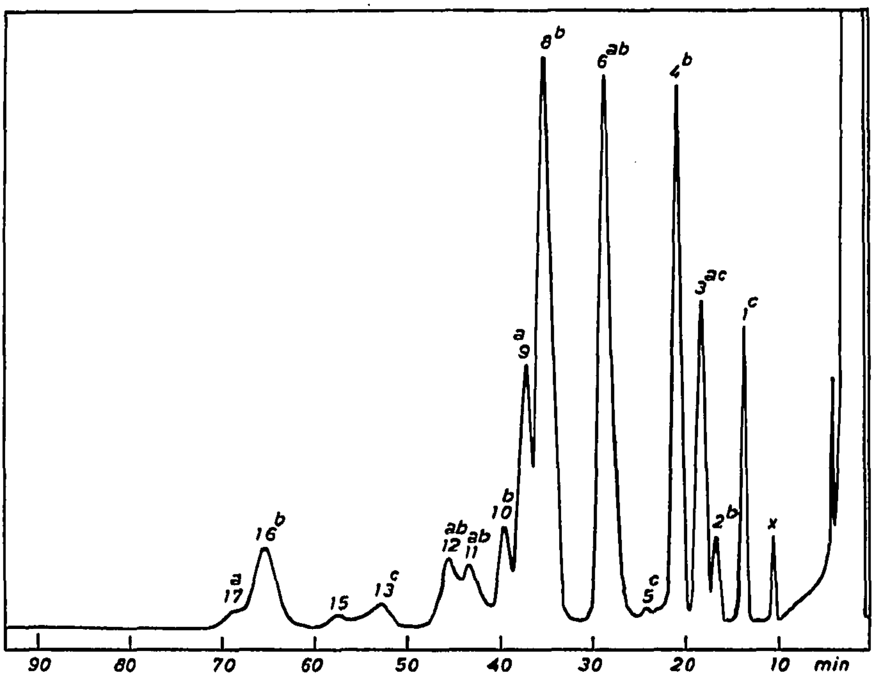


Fig. 3. Gas chromatogram of extract from acidified solution of potassium 2,4,6-trichlorophenate. x = Standard (300 ppm of trichloropredioxin). (Nos. refer to Table I). a = Chlorinated predioxin; b = chlorinated isopredioxin; c = chlorinated dihydroxybiphenyl.

(with displacement of HCl) into dioxins[3,4]. Consequently, the MS fragmentation M^+-CH_3Cl is rare and these compounds will be detected as isopredioxins.

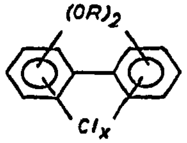
In all three diazomethane-treated formulations, a homologous series of chlorinated compounds with molecular weights of 350, 384, 418 and 452 were found (the isotopic clusters correspond to 4-, 5-, 6- and 7-chlorine, respectively). This makes two series probable (VI and VII) ($R = CH_3$).

TABLE II

EXAMPLE OF MS FRAGMENTATION

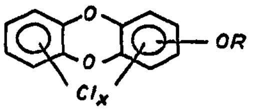
Fragment	*Relative intensity (%)*	
	Pentachloropredioxin	*Pentachloroisopredioxin*
M^+	100	68
M^+-CH_3	19	100
M^+-CH_3Cl	93	1

In order to distinguish between these series, the unmethylated extracts were treated with diazoethane instead of diazomethane. This treatment showed that structure VI is correct, because the molecular weight increases by 28, corresponding to two CH_2CH_3 groups instead of two CH_3 groups. Consequently, the impurities correspond-



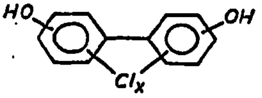
VI

For $X = 4$ and
$R = CH_3$, $M^{+} = 350$
$R = C_2H_5$, $M^{+} = 378$



VII

$M^{+} = 350$
$M^{+} = 364$



VIII

ing to this series are the chlorinated dihydroxybiphenyls (VIII). It seems, however, that these substances have not been observed in earlier studies of the impurities in chlorinated phenols.

Non-phenolic impurities

Two types of non-phenolic compounds were found, chlorinated dibenzofurans and chlorinated diphenyl ethers. The presence of penta- and hexachlorodibenzofurans was established by MS, and the spectra obtained were in agreement with those published by Vos *et al.*[7]. The structures of the chlorinated diphenyl ethers were determined on the basis of mass spectrometric fragmentation according to Firestone *et al.*[1] and Granoth[8]. The levels of the chlorinated diphenyl ethers were high compared with the dibenzofurans and using the same standard the levels were estimated to be in the range 100–1000 ppm.

Other substances have been indicated in low concentrations. Their detailed structures have not been determined, but mass spectrometric data suggest the presence of chlorinated phenoxydioxins, chlorinated phenoxybiphenyls and other trimers.

Thin-layer chromatography

For screening purposes, useful information can be given by a combination of TLC and GC. The TLC was carried out both on the complete formulations with *n*-hexane–diethyl ether as eluent in order to check for phenolic impurities and on the extracts from the basic aqueous solutions with *n*-hexane as eluent in order to check for non-phenolic impurities. With the complete formulations, the non-phenolic impurities do not interfere as their concentration is low compared with that of the phenolic compounds. The R_F values are given in Table III. The R_F values for predioxins and isopredioxins are in agreement with those reported by Jensen and Renberg[3].

The TLC scrapings were checked by GC–MS in order to establish their com-

TABLE III

R_F VALUES OF CHLORINATED COMPOUNDS USING DIFFERENT ELUENTS

Chlorinated compound	*Eluent*	
	n-Hexane–diethyl ether	*n-Hexane*
Predioxin	0.49	—
Isopredioxin	0.19	—
Dibenzofuran	—	0.44
Diphenylether	—	0.24–0.32

positions. The results are in agreement with the GC–MS analysis performed of the complete extracts.

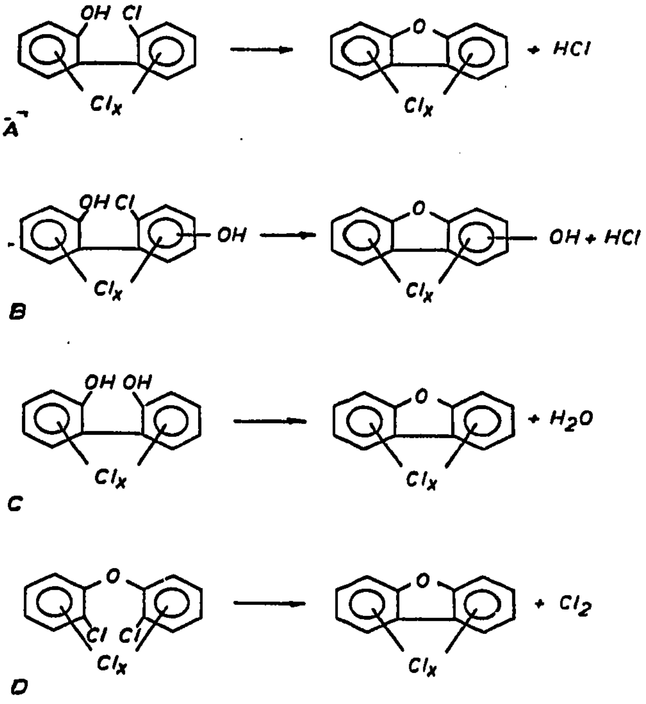
DISCUSSION

The concentrations of predioxins and isopredioxins are unexpectedly high (1–5 %). Dioxins might be present in low concentrations (less than 0.1 ppm) as the possibility of their masking by the diphenyl ethers cannot be excluded. This low dioxin concentration can be explained by the absence of alkali in the manufacturing process, as alkali has been reported to favour the formation of dioxins[9,10]. It must be noted that the chlorophenols investigated have been manufactured without employing high temperatures, and using iron as a catalyst, which may play a role in the formation of dimers.

The large number of isomers may be a result of further chlorination of the predioxins and isopredioxins already formed. Further chlorination would also explain the relatively high amount of hexachloro isomers in the trichloro formulations and hexa- and heptachloro isomers in the tetrachlorophenate.

The concentration of the highly toxic[7] chlorinated dibenzofurans is at the same level as in some polychlorobiphenyl formulations (which is in the range 5–20 ppm, ref. 7), and thus the commercial chlorophenols cannot be ignored as sources of chlorinated dibenzofurans. Furthermore, the occurence of hydroxybiphenyls in chlorophenol formulations has been suggested[1]. These types of substances, the dihydroxybiphenyls found in this work and the diphenyl ethers are possible precursors of chlorinated dibenzofurans both in the industrial process and in the environment. There are at least three possibilities for the ring closure:

(1) the same type as reported for predioxins[3,4] (A and B);
(2) with water displacement (C); and
(3) with chlorine displacement (D).



The last route is probably favoured by the catalyst, and the formation of the chlorinated dihydroxybiphenyls can also be explained by a similar chlorine displacement reaction.

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