Technical Pentachlorophenol: Origin and Analysis of Base-Insoluble Contaminants

by Jack R. Plimmer*

A long history of toxicological problems has been associated with chlorinated aromatic compounds. Schulz (*1*) has given the clinical picture and an account of many episodes recorded since the initial description of chloroacne by Herxheimer in 1899. In addition to the history of human hazards, agriculture has been concerned with several episodes in which animal feeds were contaminated. Considerable losses of livestock in the 1950's were ascribed to the contamination of feed by chlorinated hydrocarbons. The nature of chick edema disease, responsible for the deaths of millions of broiler chicks in the late 1950's, has been the subject of a long series of chemical and toxicological studies. Chick edema disease is characterized by fluid accumulation in the hydropericardium among other symptoms. It had been suggested that the cause of the disease was a toxic factor present in fats added to the feed; however, its chemical nature was not elucidated until 1966, when 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin was identified by x-ray crystallography as a component of the factor isolated from toxic fats (*2, 3*).

Toxic fats were originally recognized by a bioassay technique (*4*), since it was required that food-grade fatty acids should be free of the toxic factor (*5*). A more rapid method of detection was required, and a gas-chromatographic (GLC) method was developed (*6–8*). This technique required that a characteristic pattern of peaks detected by electron-capture or microcoulometric detector be compared with reference samples of toxic fat supplied to the Food and Drug Administration. It was later recognized that many of the peaks were due to a complex mixture of chlorinated dibenzo-*p*-dioxins present in toxic fat.

Speculation as to the origin of these contaminants ranged over a variety of sources. Some commercial chlorinated phenols were found to contain chlorinated dioxins and other impurities (*9, 10*). Industrial processes that involved heating of chlorophenols were also suspect, since under certain conditions pyrolysis of chlorophenols gave rise to dioxins. Chlorinated phenols are used as starting materials for a variety of industrial chemicals, notably pesticides, and it became clear that if these pesticides were dispersed in the environment undesirable effects could originate from any contaminant dioxins. The controversy surrounding the use of the herbicide, 2,4,5-T, has been linked with the problem of its potential contamination by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (*11*).

The manufacture of 2,4,5-trichlorophenol,

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a component used for synthesis of 2,4,5-T was accomplished by base hydrolysis of 1,2,4,5-tetrachlorobenzene at elevated temperature and high pressure. Tetrachlorodibenzo-*p*-dioxin was formed in this reaction if the temperature rose above an optimum value. Thus 2,4,5-trichlorophenol manufacture involved greater potential for dioxin formation than manufacture of other lower chlorinated phenols made by chlorination of phenol under mild conditions.

1,2,3,7,8,9-Hexachlorodibenzo-*p*-dioxin was the first chlorinated dioxin to be isolated from toxic fat. Subsequently, other dioxins of different degrees of chlorination were identified in the fat samples (*2, 12*). It was deduced that this group of contaminants might be associated with the higher chlorinated phenols, since thermal treatment of the latter could yield dioxins under certain conditions. Higginbotham et al. (*9*) found that the pyrolyzate from 2,3,4,6-tetrachlorophenol showed a GLC peak pattern resembling that displayed by some of the components of toxic fat having long retention times.

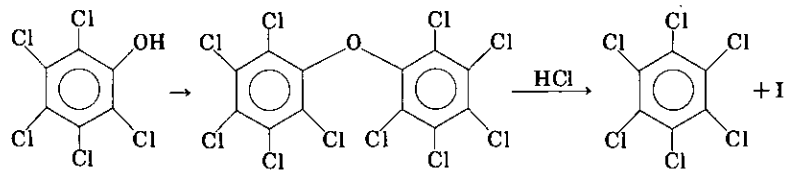
Pentachlorophenol was widely used in industry and appeared to be the most probable source of dioxin contaminants. The presence of pentachlorophenol in a fraction obtained in the cleanup of toxic fat has been reported (*12*). Hides treated with pentachlorophenol have been implicated as the source of contamination. The practice of preserving hides with pentachlorophenol before shipping was adopted by several packers. Excess fats trimmed from these hides were ultimately sold as "fleshings grease" and were used as feed additives. It has been suggested that another source of the toxic factor may have been fat contamination from sodium pentachlorophenate contained in a glue emulsion used in a dry rendering operation (*12*).

Chlorophenols have been used for many years as antiseptics, disinfectants, and fungicides. Higher chlorinated phenols are particularly valuable as fungicides and wood preservatives. Several tri-, tetra-, and pentachlorophenols have been manufactured for these uses under commercial brand names. Pentachlorophenol is used extensively as a wood preservative and was introduced for this purpose during the 1930's. It is also employed as a herbicide and in the preservation of starches, dextrins and glues. U.S. production in 1969 was 46 million lb, and more than 25 million lb of this was used as a wood preservative (*13, 14*). Pentachlorophenol is used in water solutions as the sodium salt (solubility 33 g in 100 g water), mineral oil solutions, or in solutions in other carriers.

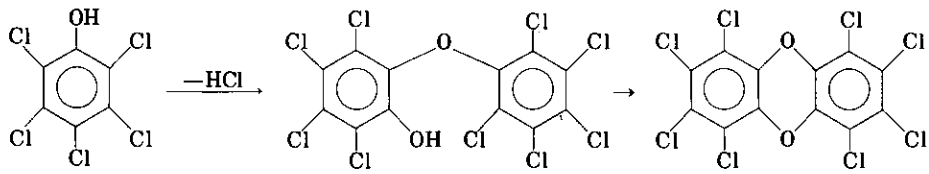
There are two major routes for the manufacture of pentachlorophenol: direct liquid-phase chlorination of phenol, and hydrolysis of hexachlorobenzene at 125–275°C. According to Sittig (*15*), a temperature in the range 65–130°C with an optimum at 105°C is used in the primary reactor stage until 3 or 4 chlorine atoms have been introduced. The temperature is then increased at such a rate that the reactant mixture is held 10°C above the melting point of the product. Solvents are not needed, but a catalyst such as aluminum chloride is added (*16, 17*). The technical product is a mixture of pentachlorophenol and tetrachlorophenol and usually contains about 12% of the latter. It melts in the range 180–185°C, and pure pentachlorophenol has mp 190–191°C(*18*).

The vigorous thermal conditions employed may favor many side reactions. These result in the formation of condensation products, including chlorinated ethers, dibenzofurans, and dibenzo-*p*-dioxins. When pentachlorophenol is heated alone to 300°C, a poor yield of octachlorodibenzo-*p*-dioxin is obtained, but the major product is hexachlorobenzene. This is explained by formation of an intermediate decachlorodiphenyl ether (II) which on cleavage in the presence of HCl gives pentachloropenol and hexachlorobenzene (III) (*19*), although heating of I for 6 hr in refluxing benzene while chlorine was bubbled through the solution gives octachlorodibenzofuran (VI) in 52% yield.

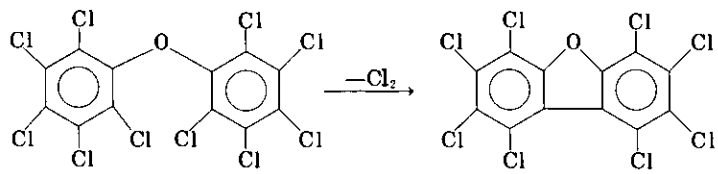
The formation of octachlorodibenzo-*p*-dioxin (V) may take place by loss of a molecule of HCl from two molecules of penta-



(I) (II) (III) (1)



(IV) (V) (2)



(II) (VI) (3)

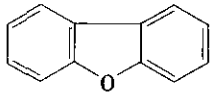
chlorophenol. The ether (IV) thus formed can lose a second molecule of HCl to give a dioxin (V). Elimination of chlorine from the diphenyl ether (II) would yield octachlorodibenzofuran (VI).

Similar reactions of tetrachlorophenols or lower chlorinated phenols might be expected to give a mixture of related chlorinated compounds. Polymeric compounds might also be anticipated.

The presence of such compounds in samples of commercial pentachlorophenol has been confirmed. Firestone et al. (*10*) identified tetrachlorodibenzofuran, octa-, and nonachlorodiphenyl ethers, hexa-, hepta-, and octachlorodibenzo-*p*-dioxins in a typical pentachlorophenol sample by electron capture–gas–liquid chromatography (EC–GLC). The identity of these compounds (except for the tetrachlorodibenzofuran and octachlorodibenzo-*p*-dioxin) was confirmed by combined gas chromatography–mass spectrometry (GC–MS). Hexa- and heptachlorodibenzofurans were also identified by this technique since authentic compounds were unavailable and EC/GLC data were lacking. Many dibenzofurans having 4 to 8 chlorine atoms and ethers with 4 to 10 chlorine atoms

were found in tetra- and pentachlorophenol samples. There was evidence for the presence of tetrachlorodibenzofuran and pentachloroanisole in some pentachlorophenol samples (Tables 1–4).

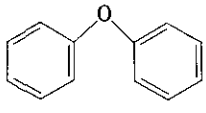
Table 1. Occurrence of chlorinated dibenzofuran in eight pentachlorophenol samples.[a]



	No. of Cl atoms				
Sample	4 Cl	5 Cl	6 Cl	7 Cl	8 Cl
1			+	+	
2		+	+	+	
3			+	+	
4			+		
5					
6	+	+	+	+	
7			+	+	+
8			+		

[a] Data of Firestone et al. (*10*).

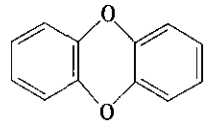
Table 2. Occurrence of chlorinated diphenyl ethers in eight pentachlorophenol samples.[a]



	No. of Cl atoms						
Sample	4 Cl	5 Cl	6 Cl	7 Cl	8 Cl	9 Cl	10 Cl
1							
2		+	+	+	+	+	+
3				+	+	+	
4		+	+	+	+	+	
5							
6	+	+	+	+			
7			+	+	+	+	
8				+	+	+	

[a] Data of Firestone et al. (*10*).

Table 3. Occurrence of chlorinated dibenzo-*p*-dioxins in eight samples of pentachlorophenol.[a]



	No. of Cl atoms		
Sample	6 Cl	7 Cl	8 Cl
1	+	+	+
2	+	+	+
3	+	+	+
4	+	+	
5	+		
6	+	+	+
7	+	+	+
8	+	+	+

[a] Data of Firestone et al. (*10*).

Table 4. Levels of chlorinated dioxins by EC/GLC.[a]

	Dioxin, ppm[b]					
Sample	6 Cl		7 Cl		8 Cl	
1	14		5.4	9.1	3.8	
2	20		1.3	10	3.3	
3	0.96	38	10	39	15	
4	35		23			
5	0.03	0.14				
6	13		12		35	
7	0.91		0.50	1.6	5.3	
8	15		23		15	

[a] Data of Firestone et al. (*10*).

[b] Figures in double columns refer to isomers detected but not identified.

Levels found by these investigators (*10*) were 0.17–39 ppm of hexachlorodioxin in all eight pentachlorophenol samples examined. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was not found in any of the 11 tetra- and pentachlorophenol samples. Similar findings were reported from other laboratories. Woolson et al. (*20*) examined 11 samples of pentachlorophenol and found that 10 were contaminated with chlorodioxins. No 2,3,7,8-tetrachlorodibenzo-*p*-dioxin was found. Seven samples had hexachlorodibenzo-*p*-dioxin contents in the range of 10–100 ppm. The

heptachlorodibenzo-*p*-dioxin content of four samples lay between 10 and 100 ppm and that of six samples between 100 and 1000 ppm. Four samples had octachlorodibenzo-*p*-dioxin contents between 10 and 100 ppm and six had octachlorodibenzo-*p*-dioxin contents between 100 and 1000 ppm. Three samples of tetrachlorophenol examined were contaminated with hexa-, hepta-, and octachlorodibenzo-*p*-dioxins at levels below 100 ppm. In addition to dimeric compounds, polymers were formed in manufacture, and mass spectrometry of the neutral fraction by use of the solids inlet showed that compounds of high molecular weight were present in some samples.

Chlorinated dioxins may be characterized by mass spectral fragmentation. The stability of the molecular ion in electron impact-induced fragmentation was indicated by its high relative abundance, and the base peak in the dibenzo-*p*-dioxin spectra (21–23) was a member of the cluster of peaks associated with the molecular ion. The presence of ^{35}Cl and ^{37}Cl isotopes results in a series of peaks at M, M+2, M+. . .; the number and relative intensity of these peaks indicates the degree of chlorination of the molecular ion (Figs. 1 and 2). Fragmentation took place by loss of Cl and (CO+Cl). Doubly charged molecular ions were also observed. Chlorinated dibenzofurans also possess a

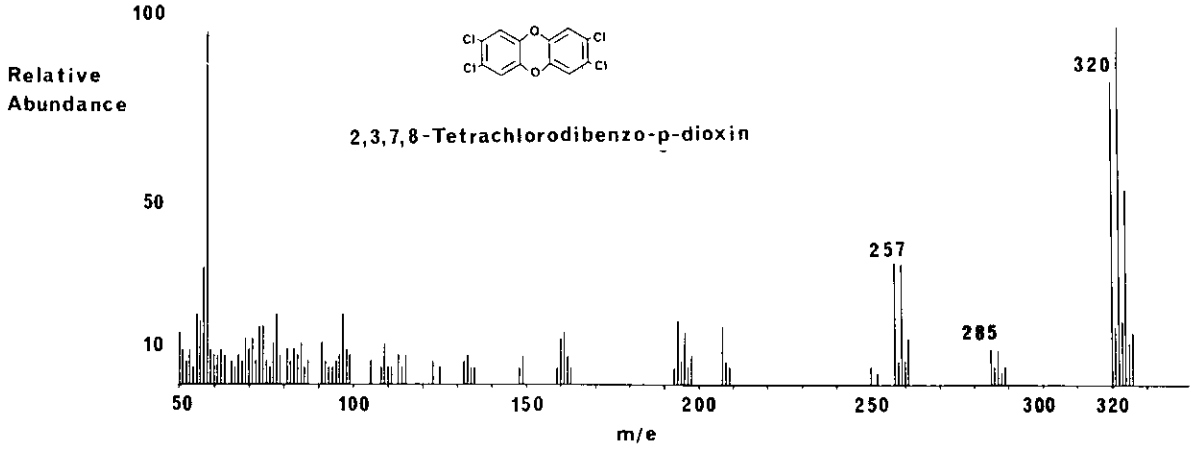


FIGURE 1. Mass spectrum of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

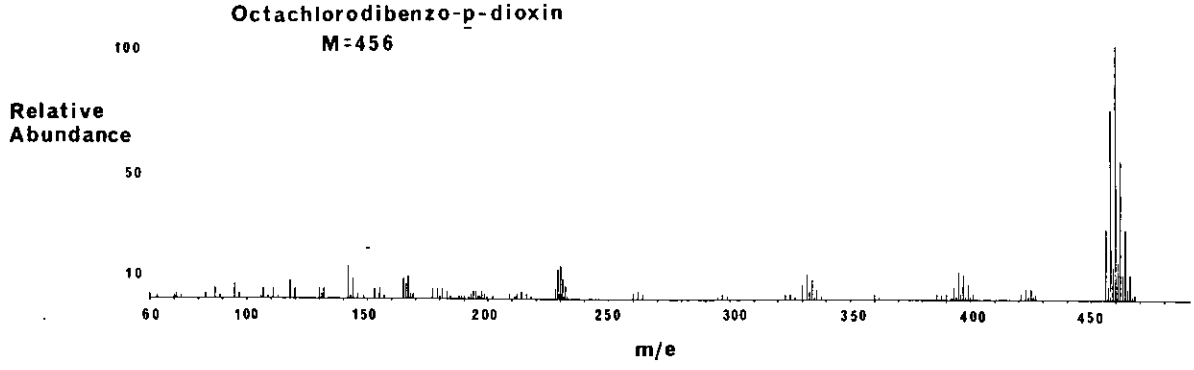


FIGURE 2. Mass spectrum of octachlorodibenzo-*p*-dioxin.

prominent molecular ion and fragmented by loss of (CO+Cl) and Cl. Dioxins and dibenzofurans were characterized in the crude base-insoluble extract derived from pentachlorophenol by accurate mass measurement of the molecular ion (*21*). They can be distinguished from the related polychlorohydroxydiphenyl ethers by differences in fragmentation patterns. However, the mass spectrum of (IV) shows the loss of two Cl atoms to give a peak coincident with the molecular ion of hexachlorodibenzofuran. The presence of the latter compound is indicated by a molecular ion at *m/e* 476. The spectrum of 4,6-dichloro-2-(2′,4′-dichlorophenoxy) phenol, for example, showed an abundant ion corresponding to the loss of 2Cl from the molecular ion (Fig. 3). The base peak was at *m/e* 146, but this fragment arose from a hydrogen-transfer process limited to 2-hydroxydiphenyl ethers. Loss of HCl was important but the loss of (CO+Cl) or CO alone was negligible. The methyl ether gave a similar pattern but loss of (CH_3+Cl) gave the most abundant fragment. An octachlorodiphenyl ether gave an abundant ion by loss of 2Cl. Rappe and Nillson (*23*) determined the mass spectrum of a methylated fraction obtained from pentachlorophenol. This fraction contained only base-insoluble compounds but nevertheless reacted with diazomethane (*24*). Such behavior is a characteristic of polychlorohydroxydiphenyl ethers which are sterically hindered. The presence of *O*-methylated octachloro- and nonachlorohydroxydiphenyl ethers was indicated by fragmentation patterns similar to those discussed above, i.e. peaks at M, M-CH_3, M-Cl, M-(CH_3 + Cl) and M-2Cl. On this evidence, Rappe and Nillson (*23*) were led to suggest that ring closure of nonachlorohydroxydiphenyl ether occurred in the heated inlet system of the mass spectrometer and was responsible for the appearance of octachlorodibenzo-*p*-dioxin in the neutral fraction.

In spite of the findings of Rappe and Nillson, data obtained through the use of the direct inlet of the mass spectrometer provides evidence for the occurrence of chlorinated dioxins and dibenzofurans per se in the base-insoluble fraction (*20*). Some thermal elimination of HCl from nonachlorohydroxydiphenyl ether might be expected but the fragmentation pattern of the mixture would be expected to show a large peak at *m/e* (M-2Cl) by analogy with the spectrum of 4,6-dichloro-2-(2′,4′-dichlorophenoxy) phenol (Fig. 3) (*25, 26*), in addition to the molecular ion.

It is to be expected that the composition of the neutral fraction will vary with its origin, and the results cited (Tables 1–4) indicate wide variability. However, some

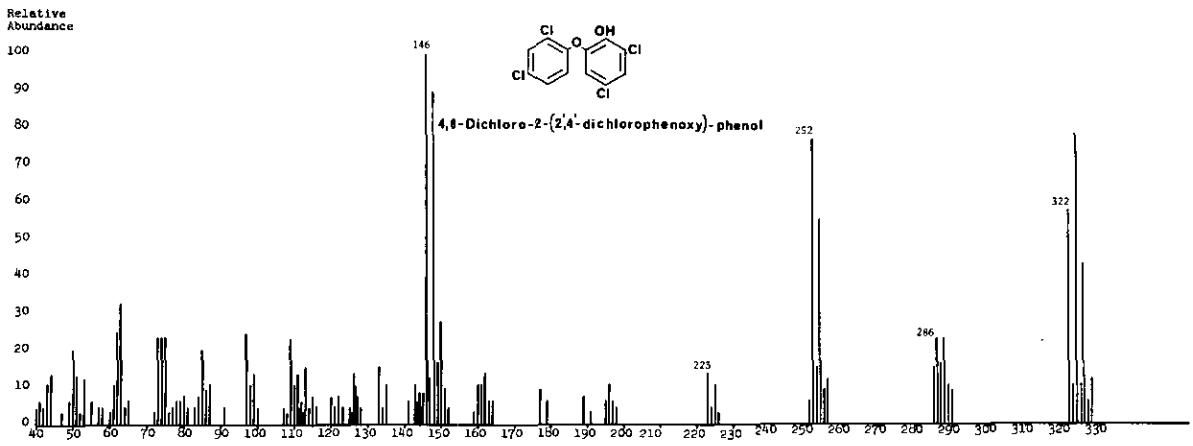


FIGURE 3. Mass spectrum of 4,6-dichloro-2-(2′,4′-dichlorophenoxy)-phenol.

further investigation of the base-insoluble fraction is necessary to assess the role of polychlorohydroxydiphenyl ethers as precursors of dioxins. Methylation followed by GC–MS is required to provide further information on this point.

Some of the reactions of pentachlorophenol that can occur under environmental conditions have been studied and compounds related to the products of thermal treatment were identified. Transformation of pentachlorophenol by light resulted in the formation of dioxins (*26*) or their precursors (*27*). Munakata (*27*) found that an aqueous solution of sodium pentachlorophenate exposed to sunlight for 10 days gave a complex mixture which included polychlorinated diphenyl ethers formed by phenol-coupling reactions. Replacement of chlorine substituents by hydroxyl groups also occurred, and it is conceivable that the products thus formed could potentially cyclize to dioxins if subjected to pryolysis. In a later study of the photochemical reactions of sodium pentachlorophenate, octachlorodibenzo-*p*-dioxin was obtained as a photoproduct in low yield (*26*).

Formation of diphenyl ethers by photolytic coupling of lower chlorinated phenols took place through a sensitized process (*25*). 2,4-Dichlorophenol and 2,4,5-trichlorophenol formed polychlorophydroxydiphenyl ethers, as well as polychlorodihydroxybiphenyls, on irradiation at 310 nm in water in the presence of riboflavin. The reaction involved the formation of phenoxy radicals which coupled through oxygen or carbon atoms to give ethers or biphenyls, respectively. The products are precursors of chlorinated dioxins or dibenzofurans but, if photocyclization to dioxins does occur, the rate of photolysis of the lower chlorinated dioxins is so rapid that they do not accumulate in measurable quantity in the reaction mixture (*28*). None were found among the reaction products, in contrast to the photochemical reaction of pentachlorophenol in which octachlorodibenzo-*p*-dioxin accumulated, presumably because the latter compound is relatively resistant to photodecomposition (*26*).

It is therefore to be anticipated that the composition of the base-insoluble fraction of pentachlorophenol will be altered by exposure to light and air. Thus, "weathering" may produce samples of altered chemistry and toxicity. Exposure to moderately high temperatures may have similar effects. Several analytical techniques have confirmed the presence of chlorinated dibenzodioxins, dibenzofurans, polychlorohydroxydiphenyl ethers and polymeric chlorinated aromatic ethers in the neutral fraction of pentachlorophenol. Although pentachlorophenol has been linked to chick edema disease, the majority of analytical results in the literature indicated only hexachloro and higher chlorinated dioxins present in most samples of pentachlorophenol examined. However, the sample of fleshings grease analyzed by Metcalfe (*12*) contained trichloro- and tetrachlorodibenzo-*p*-dioxins, in addition to pentachloro-and higher chlorinated dioxins.

In view of these findings, few generalizations can be made, except that a strong case exists for continued study of the levels and nature of contaminants in pentachlorophenol and for closer vigilance over its use. These safeguards are necessary for its continued use as a fungicide, particularly in wood treatment, where desirable alternatives are not readily available.

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