JPM

Detailed Examination of Polychlorinated Dibenzofurans in PCB Preparations and Kanemi Yusho oil

M. Morita[1], J. Nakagawa[1], K. Akiyama[1]
S. Mimura[1], and N. Isono[2]

[1]*Tokyo Metropolitan Research Laboratory of Public Health, 3-24-1 Hyakunin-cho, Shinjuku-ku Tokyo, 160 Japan*

[2]*Tokyo Metropolitan University, Megro-ku, Tokyo, Japan*

Polychlorinated dibenzofurans(PCDFs) are known to be highly toxic substances. (HOFMANN 1958) Through chick embryo bioassays, Vos at al. (1970) identified two kind of PCDFs as toxic components in PCBs. Subsequent investigations have revealed that several PCDFs are present in a number of PCB preparations. (BOWES et al. 1973, ROACH and POMERANTZ 1974, NAGAYAMA et al. 1976) However, only limited informations are available on the isomer components of this toxic material.

PCDFs were recently reported to be present in Yusho oil which gave rise to a large scale of human intoxication. (NAGAYAMA et al. 1976) "Yusho", namely oil disease, is a peculiar skin didease characterized by clinical manifestations as follicular accentuation, acneform eruption, pigmentation of the skin and nail and hypersecretion of Meibonian gland. The cause has been considered to be PCB poisoning (Kuratsune et al. 1972) but it was recently suggested that the toxic role of PCDFs was not negligible in the causation of Yusho. Hence, detailed characterization of PCDF components seemed to be necessary in Yusho oil.

The present paper will describe detailed analytical result of PCDF components as to the numbers and compositions in Yusho oil and sixteen PCB preparations.

Materials and Method

Samples Yusho oil was the product of 12th Feb. 1968. PCB samples examined were Kanechlor KC300, KC400, KC500, KC600, Aroclor T64, T241, T1242, T1248, T1254, T1260, Clophen A30, A40, A50, Phenoclor DP4, DP5, DP6. All PCB samples were not specified in lot number. Used PCB sample was Aroclor T1248 used as a heat transfer agent in chemical factory during two years. Operation condition was not specified.

Analysis PCB sample(1g) was dissolved in 2 ml of n-hexane and chromatographed over Florisil column. The size of the column was 1 cm in diameter and 30 cm in length. 20 grams of Florisil(80/100) preactivated at the temperature of 630°C for four hours, was packed. After the first absorption, 200 ml of n-hexane was passed the column in order to remove most of the PCBs and then 50 ml of hexane acetone mixture (95:5) was passed. PCDFs were recovered from the column by eluting with 100 ml of acetone. The recovery was more than 90 %. The acetone fraction was condensed

Bulletin of Environmental Contamination & Toxicology, Vol. 18, No. 1 © 1977 by Springer-Verlag New York Inc.

to the volume of 500 µl with Kundera-Danish condenser and nitrogen gas flashing. An aliquot of the condensed solution was injected to gaschromatography-mass spectrometer (Shimadzu-LKB 9000). The following condition was employed.

Column Dexil 3% on Chromosorb WAW DCMS(100/120) 3mmx2m
Carrier gas He 30ml/min. Ion. Vol. 70eV
Temperatures. Column 270°C Injection 300°C
Separator 300°C Ion source 310°C

Mass spectra were taken at every five second with a computer system (MS-PAC). 192 spectra were obtained from 2 to 18 minutes after injection and the selected mass numbers were plotted on section papers for qualitative and quantitative analysis. Quantification was made on the assumption that each PCDF specimen was ionized to the same extent by the electron of 70eV regardless to the difference of the degree or the positions of chlorine substitution. Amounts of PCDFs were calculated by comparing their peak areas with those of known amount of the standard sample.

Result and Discussion

Mass fragmentgrams of chlorinated dibenzofurans in commercial PCBs and in Yusho oil are shown in Fig. 1 along with our standard sample. Standard sample was synthesized through chlorination of dibenzofuran by chlorine gas under the presence of ferric chloride and iodine. Average chlorine number was 4.7.

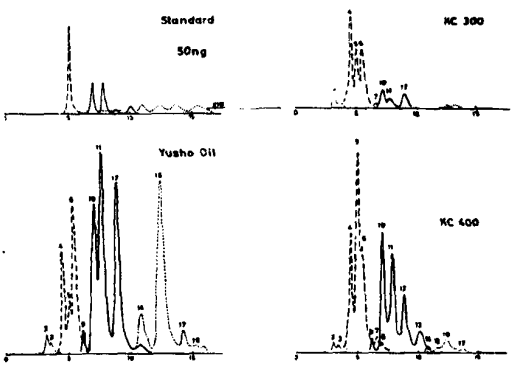


Fig.1. Mass fragmentgrams of PCDFs in PCBs and Yusho oil monitered by parent peaks(270, 304, 338, 372).

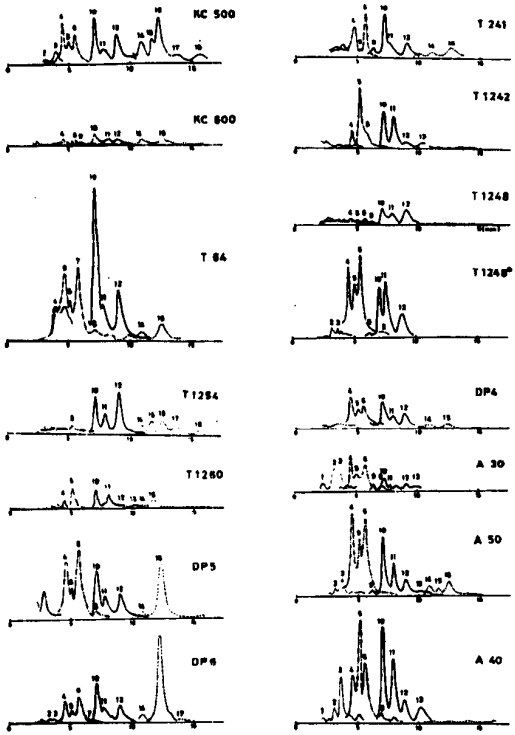
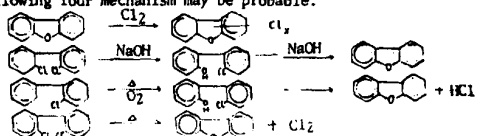


Fig. 1 Continued.

Eighteen PCDF isomers (three trichloro-, five tetrachloro-, five pentachloro- and five hexachlorodibenzofurans) were demonstrable in these samples. Peak 6 was tentatively assigned to 2,3,7,8-tetrachlorodibenzofuran from the coincidence of the retention time with the authentic sample. Other isomers were not identified in their chlorine positions. It is worthy to

note that almost all PCBs have similar PCDF isomers. PCDF concentrations are listed in Table 1.

In regard to the occurence of PCDF in PCB preparations, the following four mechanism may be probable.



Reaction (1) means that dibenzofuran contained as an impurity in technical grade biphenyl is chlorinated to PCDFs in the process of PCB synthesis. Gaschromatographic pattern of our standard sample, however, is fairly different from that of PCDFs in PCB preparations. Therefore, mechanism (1) may not be the major route of PCDFs. Vos et al (1970) suggested the mechanism 2) as a possible route. However, gaschromatographic pattern of PCDFs produced by heating PCB(Aroclor 1248) with sodium hydroxide were different from that of PCDFs in PCB preparations. Thus, the mechanism (2) may also not a major route for the formation of PCDFs. On the other hand, mechanisms (3) and (4) seem more probable because used PCB has a profound PCDFs with similar isomerism.

When PCBs (Aroclor 1248) were sealed with air in glass tube and heated at 300°C for two weeks, increased amount of PCDFs were found. Produced PCDFs had a similar gaschromatographic pattern as shown in Fig.1. At the same time, the formation of hydrogen chloride and polychlorinated biphenylols was observed. This reaction was catalysed by transition metals or their salts. Detailed investigation is now in progress concerning to this reaction.

PCDFs were concentrated in Yusho oil. The ratio PCDF/PCB reaches to about 1.1% which may be five hundred times higher than that originally contained in KC 400. Nagayama et al. and Miyata et al(private communication) recently identified PCDFs independently in Yusho oil and reported the PCDF/PCB ratio as 0.5% and 1.2% respectively. Both results are comparable to our result. PCBs which had been originally used for the heat transfer agent was KC 400, however, the gaschromatographic pattern of PCBs in Yusho oil was rather resembled to that of KC 500. This indicates that lower chlorinated biphenyls were removed by evaporation in the deodouration process of vacuum distillation to result the concentration of PCDFs which are less volatile than PCBs. Furtheremore severe temperature conditions employed in the company might give rise to the profound formation of PCDFs. Metals presented in the heat trnsfer tubing (stainless steel) might catalysed the reaction.

Yusho disease is a chronic intoxication caused by the consumption of rice bran oil (Yusho oil) contaminated by heat transfer oil (KC400). Yusho patients are considered to have ingested about 2 grams of PCBs in average. Assuming that the

Table 1 PCDF concentrations in Yusho oil and PCB samples (ppm)

	Yusho Oil	DP4	DP5	DP6	KC300	KC400	KC500	KC600
1	-	-	-	-	-	-	-	-
2	0.02	-	-	0.1	-	0.2	-	-
3	-	-	-	0.1	-	0.1	0.2	-
4	0.15	0.7	2.0	0.7	2.6	3.4	0.7	0.1
5	0.09	0.3	0.3	0.4	1.8	6.9	0.3	-
6	0.28	0.7	2.2	0.9	2.2	1.6	0.7	0.1
7	-	-	0.1	0.1	0.1	0.2	-	-
8	-	-	-	-	-	0.1	-	-
9	0.03	-	-	-	-	0.3	-	0.1
10	0.53	0.9	1.4	1.5	0.6	4.5	0.1	0.2
11	0.33	0.3	0.5	0.5	0.4	3.9	0.3	0.1
12	0.42	0.4	0.8	0.6	0.6	0.9	0.7	0.1
13	0.02	-	-	-	-	0.8	-	-
14	-	0.2	0.1	0.3	-	0.2	0.5	0.2
15	0.12	0.3	2.5	5.1	-	0.1	0.5	-
16	0.64	-	-	0.1	-	0.4	1 4	0.2
17	0.04	-	-	0.1	-	0.2	0.2	-
18	0.01	-	-	-	-	-	0.5	-
Tri-	0.02	-	-	0.2	-	0.3	0.2	-
Tetra-	0.52	1.7	4.6	2.1	6.7	12.2	1.7	0.2
Penta-	1.33	1.6	2.7	2.6	1.6	10.4	1.1	0.5
Hexa-	0.81	0.5	2.6	5.6	-	0.9	3.1	0.4
Total	2.68	3.8	9.9	10.5	8.3	23.8	6.1	1.1

* Used PCB
Peaks 1-3,4-8,9-15 and 14-18 correspond to trichloro-, tetrachloro-, pentachloro- and hexachlorodibenzofurans, respectively.

ratio PCDF/PCB is one percent, the total intake of PCDFs reaches to 20mg for average patients. Although there is no way of knowing the toxicity of PCDFs in association with the various symptoms of the Yusho disease, there is a possibility that PCDFs were potentially contributed to the Yusho disease.

It is also noteworthy that a crude rice bran oil of the same origin as the Yusho oil had given rise to a large scale of chick death several months before the outbreak of human intoxication. More than five hundred thousand chicks were died in similar symptoms of chick edema disease through the intake of food prescribed with the crude rice bran oil. (KOHANAWA et al. 1969) Chick edema disease is known to be caused by several

Continued (ppm)

T64	T241	T1242	T1248	T1248*	T1254	T1260	A30	A40	A50
-	-	-	-	-	-	-	0.3	0.1	-
-	-	-	-	0.2	-	-	0.6	0.3	0.2
-	-	-	-	0.1	-	-	0.7	1.1	0.5
1.7	1.1	0.3	0.2	1.9	-	0.2	0.7	0.5	3.0
0.3	0.2	1.8	0.1	1.1	0.1	0.6	0.4	2.7	1.7
2.4	1.1	0.2	0.2	2.7	-	-	1.0	2.1	3.6
0.3	-	-	-	-	-	-	-	-	-
0.1	-	-	-	0.1	-	-	0.2	0.1	-
-	0.2	-	0.2	0.1	-	-	0.2	-	0.2
6.3	1.5	1.0	0.7	1.8	1.3	0.5	0.5	3.1	2.2
0.8	0.6	1.0	0.6	2.3	0.7	0.2	0.1	2.2	1.0
2.3	0.4	0.1	0.8	1.4	1.6	0.1	0.1	0.7	0.6
-	-	0.1	-	-	-	0.1	0.1	0.9	0.1
0.5	0.2	-	-	-	0.3	0.1	-	-	0.7
-	-	-	-	0.2	0.5	0.4	-	-	0.3
1.5	0.6	-	-	0.5	0.7	-	-	-	0.8
-	-	-	-	-	0.3	-	-	-	-
-	-	-	-	-	0.1	-	-	-	-
-	-	-	-	0.3	-	-	1.6	1.5	0.7
4.8	2.4	2.3	0.5	5.8	0.1	0.8	2.3	5.4	8.3
9.4	2.7	2.2	2.3	5.6	3.6	0.9	1.0	6.9	4.1
2.0	0.8	-	-	0.7	1.9	0.5	-	-	1.8
16.2	5.9	4.5	2.8	12.4	5.6	2.2	4.9	13.8	14.9

chlorinated dibenzodioxines. (CANTRELL 1967) We failed to find a detectable amount of chlorinated dibenzodioxines in the rice bran oil. Polychlorinated dibenzofurans might have played a serious role to the large scale chick death in Japan.

There is no evidence that PCDFs are present in ecosystems. It is reported that octachlorodibenzofuran is less rapidly absorbed from food than PCBs. (Zikto and Choi 1973) Di- and Tri- and tetrachlorodibenzofuran were not detectable in juvenile atlantic salmon fed with PCDF containing food. While, some isomers of PCDFs were noticed to be very persistent in the body of mouse to which PCDFs were administered intraperitoneally. Detailed investigation seems to be necessary to elucidate the

distribution and the biological impact in the environment of these highly toxic substances if we consider that at least several ppms of PCDFs were discharged to the environment concomittantly with PCBs.

References

BOWES,G.W., SIMONEIT,B.R., BURLINGAME,A.L., deLAPPE,B.W. and RISEBROUGH,R.W. : Environ.Health Perspect. No.5,191 (1973)
BOWES,G.W., MULVIHILL,M.J. DeCamp,M.R. and KENDE,A.S. :J. Agr. Food Chem. 23, 1223 (1975)
CANTRELL,J.S. : Chem. Engin. News 45(5), 10 (1967)
HOFMANN,H.Th.: Arch.Exp. Path. Pharmak. 232,228 (1958)
KOHNAMA,M., SHOYA,S., OGURA,Y., MORIWAKI, M. and KAWASAKI,M. : Nat. Inst. Anim. Hlth Quart. 9, 213 (1969)
KURATSUNE, M. YOSHIMURA,., MATSUZAKA,J. and YAMAGUCHI,A.: Environ. Health Perspect. No. 5, 87 (1973)
NAGAYAMA,J., KURATSUNE,M. and MASUDA,Y. : Bull. Environ. Contam. Toxicol. 15, 9 (1976)
ROACH,J.A.G. and POMERANTZ,I.H. :Bull. Environ. Contam. Toxicol. 12,330 (1974)
VOS,J.G., KOEMAN,J.H., VAN DER MAAS,H.L., TEN NOEVER DE BRAUW,M.C. and DE VOS,R.H.: Food Cosmet. Toxicol. 8, 625 (1970)

CHLORODIBENZOFURANS IN PCBs

	CONCENTRATION (PPM)
AROCLOR 1254	
ANNISTON	2-3
NEWPORT (1974)	4-6
KRUMMRICH	
AK - 38	6-7
1974-75 RANGE	5-33
RHESUS FEEDING STUDY (K1-02-602)	10-12
YUSHO OIL	5
KANECHLOR-400 BASIS	5,000

Compiled 10-3-77

Chlorodibenzofurans in PCBs (Estimated)

	Concentration (PPM)
Aroclor 1254	
Anniston	2-3
Newport (1974)	4-6
Kummerick	
AK-38	6-7
1974-75 range	5-33
Rhesus feeding study (KI-02-602)	10-12
Yusho oil	5
Kanechlor-400 basis	5,000
Used Thermino[illegible]	90

DBF

Chemosphere 8, 843 (1979)

p167

FORMATION OF POLYCHLORINATED DIBENZOFURANS (PCDFs) FROM THE PYROLYSIS OF SOME PCB ISOMERS

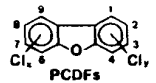
Hans Rudolf Buser
Swiss Federal Research Station
CH - 8820 Wädenswil, Switzerland

and

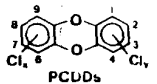
Christoffer Rappe
Department of Organic Chemistry, University of Umeå
S - 901 87 Umeå, Sweden

Introduction

The polychlorinated dibenzofurans (PCDFs, structure see below) are a series of tricyclic aromatic compounds, in chemical, biological and toxicological respects very similar to the polychlorinated dibenzo-p-dioxins (PCDDs, see below).



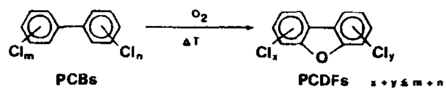
PCDFs



PCDDs

The PCDFs have been identified as undesired trace contaminants in chlorophenols,[6] their derivatives like phenoxy acids[7] and in polychlorinated biphenyls (PCBs).[8] Most recently, PCDFs have been identified in fly ash and flue gases of municipal incinerators and industrial heating facilities.[9,10] They might be ubiquitous products of combustion processes.[11,12]

PCBs are industrial chemicals of wide use and they are now known to be widely distributed in the environment. Although the thermal conversion of PCBs into PCDFs under pyrolytic conditions could be expected, experimental evidence to our knowledge was not reported prior to our previous thesis.[10,13]

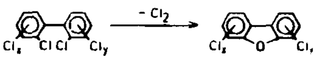


However, increased levels of PCDFs (ppm-range) were observed in a PCB heated to 300° for a week in the presence of air, and in a PCB used in a heat exchange system for extended periods of time.[14,15]

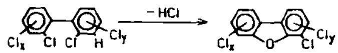
In our previous papers we have reported on the formation of PCDFs from the pyrolysis of commercial PCBs (Aroclor [illegible]).[10,13] These pyrolyses were carried out in sealed quartz mini-ampoules in the presence of air at temperatures of 500-700° C. The yields of the PCDFs were in the [illegible] range. In addition to PCDFs, unreacted PCBs, chlorinated benzenes, naphthalenes and other chlorinated compounds were also observed, [illegible] hydroxybiphenyls were found as possible intermediate products.

By using high-resolution GC and MS, we have further shown that most of the major PCDF isomers found in [illegible] samples were the same as those formed in the pyrolysis of the most common commercial PCBs, giving strong support that these PCDFs originate from the uncontrolled burning of PCBs. Using individual PCB isomers, we have found that the cyclization processes in these pyrolyses are intramolecular and we have described the following three reaction routes leading to different PCDF isomers from the same PCB:

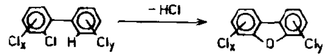
reaction route 1
(loss of ortho-Cl_2)



reaction route 2:
(loss of HCl involving a 2,3-chlorine shift)

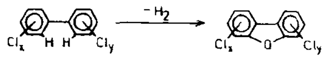


reaction route 3:
(loss of ortho-HCl)



In this paper now the occurrence of these reaction routes in the pyrolysis of individual PCBs is further documented. The formation of PCDFs was investigated in pyrolysis experiments using 3 tetra-, 5 penta-, 7 hexa-, 2 hepta- and 1 octachlorobiphenyl. Our experiments show the generality of the above reactions, and these can be used to predict the formation of specific PCDFs. A fourth, additional reaction route was found to occur with some PCB isomers:

reaction route 4:
(loss of ortho-H_2)



Experimental

MONS 003357

Polychlorinated biphenyls used for pyrolysis

Eighteen PCB isomers were obtained from various sources as listed in Table [illegible]. All isomers were checked for isomeric purity and absence of PCDFs [illegible] described. Single peaks were obtained and purity was found to be generally [illegible] of the PCBs contained detectable quantities of PCDFs (< 0.01 [illegible]) [illegible] were prepared at concentrations of [illegible] benzene.

Microppyrolysis of PCBs

Individual PCB isomers (100 µg each) were pyrolyzed at [illegible] °C in [illegible] [illegible] The [illegible] pyrolysis conditions were as previously [illegible] [illegible] was taken to [illegible] [illegible] of [illegible] was [illegible]

Table 1. List and sources of PCB isomers investigated

Compound	Source	Compound	Source
2,3,4,5-tetrachlorobiphenyl	a	2,4,5,2',4',5'-hexachlorobiphenyl	b
2,3,5,6-	a	2,4,6,2',4',6'-	b
2,6,2',6'-	b	2,4,5,2',4',6'-	c
		2,3,4,2',3',4'-	a
		2,3,5,2',3',5'-	a
		2,3,6,2',3',6'-	a
2,3,4,5,6-pentachlorobiphenyl	c	3,4,5,2',4',5'-	a
2,4,5,2',5'-	c	2,3,4,5,2',3',4'-heptachlorobiphenyl	e
2,4,5,3',4'-	c	2,3,4,5,2',4',5'-	e
2,4,6,2',4'-	c		
2,3,6,2',5'-	c	2,3,4,5,2',3',4',5'-octachlorobiphenyl	c

a = Dr. J. McKinney, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

b = Dr. K. Andersson, University of Umeå, Umeå, Sweden

c = RFR Corp., Hope, RI, USA, courtesy of Dr. J. McKinney

d = Dr. C.A. Wachtmeister, University of Stockholm, Stockholm, Sweden

e = Dr. Y. Masuda, Daiichi College of Pharmaceutical Sciences, Furuoka, Japan

GC-MS Analysis

A Finnigan 4000 quadrupole GC-MS instrument with EI source and coupled to a 50 m 0.36 mm ID OV-17 glass capillary column was used. The column was interfaced to the MS via a platinum capillary interface. The operating conditions were as previously described.[10] However, the column proved somewhat higher elution temperatures for PCDFs (same order of elution) than a comparable OV-17 column interfaced via a glass lined stainless steel tube.

In a first phase, complete mass spectra were recorded using the data system. In a second phase, the samples were reanalyzed with optimal isomer separation using mass specific detection (mass fragmentography) of PCDFs by monitoring molecular ions at m/e 270, 304, 338, 372, 406 and 440 for the tri- to octachloro compounds.

Standard and reference PCDFs used

The PCDF isomers utilized as standard compounds for the present investigation are listed in Table 1. They were the gift of Dr. Masuda, McKinney, Morris and Poland, and of Mr. Garå to Mr. Lindahl. In Figure 1, we give mass fragmentograms of a GC-MS run of the 1,2,3,4,6,7,8-heptachlorodibenzofuran and hexa-PCDFs (peak identifications in Table 2).

In addition, we established the elution order of the 4 hepta-PCDFs (1,2,3,4,6,7,8-; 1,2,3,4,6,8,9-; 1,2,3,4,7,8,9- and 1,2,3,6,7,8,9-), all separated on OV-17, by [illegible] of the [illegible] of 1,2,3,4,6,7,8-hepta-PCDF was assumed

Table 2. Standards and reference PCDFs used in the present study

Compound	Peak number (see Fig. 1)	Source and remarks
2,3,8-tri-CDF	-	a
1,3,6,8-tetra-CDF	1	a,b
1,3,7,9-	2	b
2,4,6,8-	3	b,c
1,3,6,7-	4	a
1,2,4,6-	5	a
2,3,6,8-	6	a,d
2,3,7,8-	7	e
1,3,6,7-	8	a
1,2,4,6,8-penta-CDF	9	c,f
1,3,4,7,8-	10	b (contains also 1,3,4,8,9-penta-CDF)
1,2,4,7,8-	11	d,b (contains also 1,2,4,8,9-penta-CDF)
1,3,4,7,9-	12	b
1,2,3,7,8-	13	g
2,3,4,6,8-	14	c,f
1,2,3,4,8-	15	f
1,2,3,6,7-	16	d
2,3,4,8,9-	17	d
2,3,4,7,8-	18	e
1,3,4,8,9-	19	b (contains also 1,3,4,7,8-penta-CDF)
2,3,4,6,7-	20	d
1,2,4,8,9-	21	b (contains also 1,2,4,7,8-penta-CDF)
1,2,3,4,6,8-hexa-CDF	22	c,f
1,2,4,6,7,8-	23	c,f
1,2,4,6,8,9-	24	c
1,2,3,4,7,8-	25	d
1,2,3,6,7,8-	26	d
1,2,3,4,6,7,8-	27	c,f (contains also 1,2,3,4,6,7,8-hepta-CDF)
1,2,3,4,6,7,8-hepta-CDF	-	c,f (contains also 2,3,4,6,7,8-hepta-CDF)

a = Dr. M. Morita, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan

b = Mr. R. Lindahl, University of Umeå, Sweden; prepared through Pschorr cyclization of polychlorinated diphenylether [16]

c = Mr. A. Garå, University of Umeå, Sweden; prepared from 3,7-diaminodibenzofuran by acetylation, chlorination and reduction [17]

d = Dr. Y. Masuda, Daiichi College of Pharmaceutical Sciences, Furuoka, Japan

e = Dr. J. McKinney, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

f = Mr. A. Garå, University of Umeå, Sweden, prepared through Pschorr cyclization of polychlorinated diphenylether [16]

g = Dr. A. Poland, McArdle Laboratory, Madison, Wisc., USA

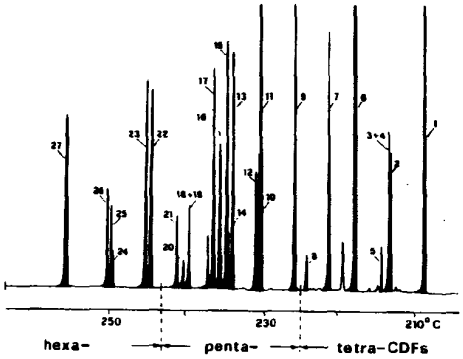


Figure 1. Mass fragmentograms [illegible] and 330 [illegible] of a composite sample of [illegible] perchlorodiphenylether showing the elution of tetra-, penta- and hexa-CDFs (for identification see [illegible]). Column: [illegible] at 20° min, [illegible] at 2°/min.

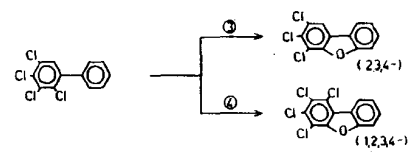
[illegible] discussion

Pyrolysis of tetrachlorobiphenyls

The pyrolysis of three [illegible] studied (see Table 1). Mass fragmentograms of [illegible] and the elution of tetra- and tetra-CDFs.

The pyrolysis of [illegible] a mixture of a tri- and tetrachloro [illegible] Figure 2a). The [illegible] identified to be 1,2,3,4-tetrachloro [illegible] via reaction route 3 (see Scheme 1). The formation of a tetra-CDF from this PCB has to [illegible] a [illegible] reaction route 1, 2 and 4 [illegible] dechlorination reaction [illegible] see [illegible].

and in fact only very minor amounts of additional isomers were observed.



As shown in Figure 2b, the pyrolysis of 2,3,5,6-tetrachlorobiphenyl lead to the formation of a tri-CDF. The product expected is 1,2,4-tri-CDF formed via reaction route 3. The formation of di-, tri- and tetra-CDFs from this PCB via reaction routes 1, 2 and 4 is not possible and in fact no additional PCDFs were observed.

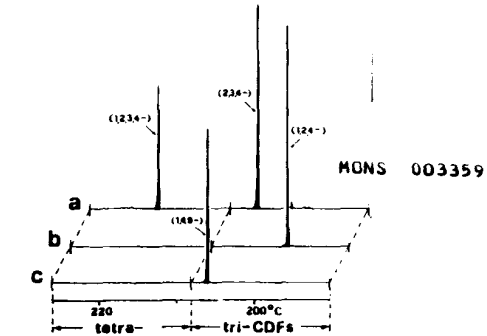
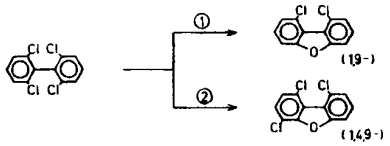


Figure 2. Mass fragmentograms m/e 273 and 305 of pyrolysis [illegible] showing the elution of tri- and tetra-CDF from [illegible] and 2b) and [illegible] (for [illegible] see [illegible]).

As previously reported,[16] the pyrolysis of 2,6,2',6'-tetrachlorobiphenyl formed a di- and a tri-CDF (elution of tri-CDF shown in Figure 2C). The expected di-CDF, the 1,9- substituted isomer formed via reaction route 1. The formation of a tri-CDF from this tetrachlorobiphenyl has to involve a rearrangement reaction; the isomer expected is 1,4,9-tri-CDF (reaction route 2). This PCB cannot form tri- and tetra-CDFs via reaction routes 3 and 4, and again no additional PCDFs were observed.

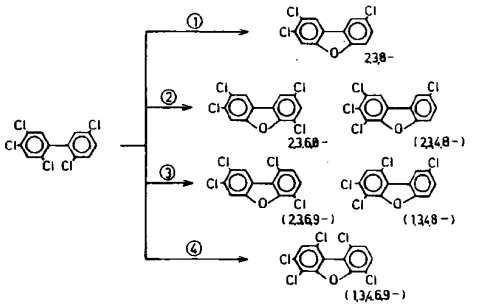


Pyrolysis of pentachlorobiphenyls

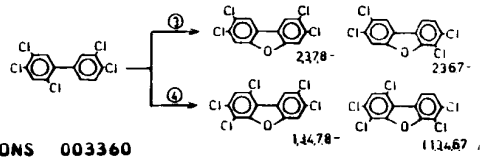
The pyrolysis of five pentachlorobiphenyls was investigated (see Table 1). Mass fragmentograms showing the elution of tri-, tetra- and penta-CDFs are given in Figure 3.

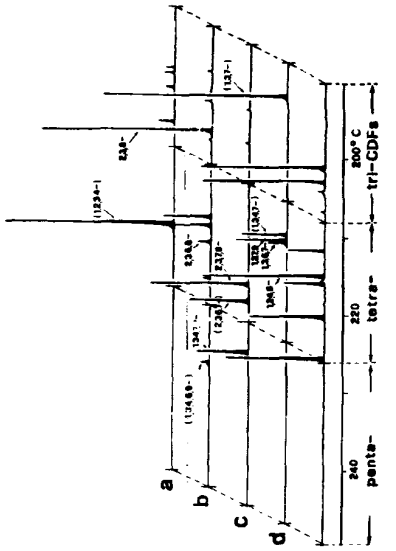
The pyrolysis of 2,3,4,5,6-pentachlorobiphenyl lead to the formation of a tetra-CDF as the major product and smaller amounts of four tri-CDFs (see Figure 3a). The tetra-CDF expected is the 1,2,3,4-substituted isomer formed via reaction route 3; the same isomer was also observed from the pyrolysis of 2,3,4,5-tetrachlorobiphenyl. The formation of PCDFs via reaction routes 1, 2 and 4 is not possible from this PCB. The finding of small amounts of tri-CDFs could mean that these PCDFs are formed in a non specific dechlorination process of 1,2,3,4-tetra-CDF or of pentachlorobiphenyl prior to cyclization. In either case, the expected PCDFs contain Cl-substituents exclusively in one of the two carbon rings of the dibenzofuran nucleus (4 possible isomers). Two of these tri-CDFs were tentatively identified as [illegible] tri-CDFs, pyrolysis products of 2,3,4,5- and 2,3,5,6-tetrachlorobiphenyl (see Figure 2a and b).

As shown in Figure 3b, 2,4,5,2',3'-pentachlorobiphenyl formed a major tri-CDF and smaller amounts of 6 tetra-CDFs and a penta-CDF. This number of PCDFs can be expected from the pyrolysis of this PCB via reaction routes 1, 2, 3 and 4 (see Scheme below). PCDFs identified by co-chromatography, with reference compounds (see Table 2) were 2,3,4-tri- and 2,3,7,8-tetra-CDF from via reaction routes 1 and 3, respectively. So far, no attempts have been made to identify the remaining tetra-CDFs. A small amount of a [illegible]-CDF was observed. The [illegible] compound is 1,3,4,6,9-tri-CDF formed via reaction



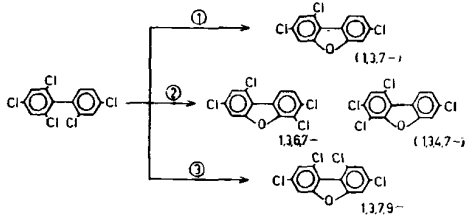
The pyrolysis of 2,4,5,3',4'-pentachlorobiphenyl lead to the formation of two tetra- and a penta-CDF (see Figure 3c). No tri-CDFs can be expected from this PCB via reaction route 1. The two tetra-CDFs were identified by co-chromatography with reference compounds (see Table 2) as the 2,3,7,8- and 2,3,6,7- substituted isomers, formed via reaction route 3. This PCB cannot form tetra-CDFs via reaction route 2 and in fact no additional tetra-CDFs were observed. Pyrolysis of this PCB is expected to form two penta-CDFs via reaction route 4, namely 1,3,4,7,8- and 1,3,4,6,7-penta-CDF (see Scheme below). However, only the formation of 1,3,4,7,8-penta-CDF could be confirmed



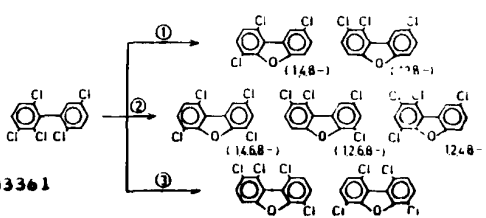


Mass fragmentograms (m/e 270, 304 and 338) of pyrolyzed pentachlorobiphenyls showing elution of tri-, tetra- and penta-CDFs from (a) 2,3,4,5,6-, (b) 2,4,5,2',5'-, (c) 2,4,5,3',4'-, (d) 2,4,6,2',4'- and (e) 2,3,6,2',5'-pentachlo-
Estimated isomer identities as in Figure 1.

Pyrolysis of 2,4,6,2',4'-pentachlorobiphenyl gave a tri- and three tetra-CDFs as shown in Figure 3d. This number of isomers can be expected from this PCB *via* reaction routes 1, 2 and 3 (see Scheme below). The formation of a penta-CDF *via* reaction route 4 is not possible and in fact no penta-CDF was observed. The tri-CDF expected is the 1,3,7- substituted isomer. Two of the tetra-CDFs were confirmed as 1,3,6,7- and 1,3,7,9-tetra-CDF formed *via* reaction routes 2 and 3, respectively; the third tetra-CDF (first eluting) is expected to be 1,3,4,7-tetra-CDF, an additional isomer formed *via* reaction route 2.



The pyrolysis of 2,3,6,2',5'-pentachlorobiphenyl lead to the formation of two tri- and five tetra-CDFs (see Figure 3e) as expected from this PCB *via* reaction routes 1, 2 and 3 (see Scheme below). Again, the formation of a penta-CDF *via* reaction route 4 is not possible and in fact no penta-CDF was observed.



One of the main products was tentatively identified as 1,2,4,8-tetra-CDF, a pyrolysis product of 2,4,5,4'-tetrachlorodiphenylether [18]. Two of the tetra-CDFs (1,2,6,9- and 1,4,6,9-) are also expected pyrolysis products of 2,3,6,2',3',6'-hexachlorobiphenyl (see later).

Pyrolysis of hexachlorobiphenyls

The pyrolysis of seven hexachlorobiphenyls was investigated (see Table 1). Mass fragmentograms of pyrolyzed samples are given in Figure 4. They show the elution of tetra-, penta- and hexa-CDFs.

The results of the pyrolysis of 2,4,5,2',4',5'- and 2,4,6,2',4',6'-hexachlorobiphenyl were previously reported.[10,13] However, the identity of some of the resulting PCDFs was tentative and could not be confirmed at that time for lack of reference compounds. Additional standards available now made it possible to confirm these tentative identifications. In case of 2,4,5,2',4',5'-hexachlorobiphenyl, the formation of a tetra- and two penta-CDFs was observed (see Figure 4a). These PCDFs were identified as 2,3,7,8-tetra-, 2,3,4,7,8- and 1,3,4,7,8-penta-CDF formed via reaction routes 1, 2 and 3, respectively. In case of 2,4,6,2',4',6'-hexachlorobiphenyl, a tetra- and a penta-CDF were found (see Figure 4b) and identified as 1,3,7,9-tetra- and 1,3,4,7,9-penta-CDF formed via reaction routes 1 and 2. The formation of a penta-CDF via reaction route 3 is not possible with this PCB and in fact no additional penta-CDF was observed. None of the two hexachlorobiphenyls showed the formation of significant amounts of hexa-CDFs.

From the pyrolysis of 2,4,5,2',4',6'-hexachlorobiphenyl, the formation of a major tetra- and some minor penta-CDFs was observed (see Figure 4c). The tetra-CDF expected is the 1,3,7,8- substituted isomer formed via reaction route 1. The expected penta-CDFs are 2,3,4,7,9- and 1,3,4,7,8-penta-CDF (reaction route 2), and 1,3,4,7,9-penta-CDF (reaction route 3). However, only the formation of 1,3,4,7,8- and 1,3,4,7,9-penta-CDF could be confirmed. The formation of 2,3,4,7,9-penta-CDF remained unclear.

The pyrolysis of 2,3,6,2',3',6'-hexachlorobiphenyl lead to the formation of a tetra- and a penta-CDF (see Figure 4d). They were identified as 1,3,6,7-tetra- and 1,2,3,6,7-penta-CDF, the isomers expected from the pyrolysis of this PCB via reaction routes 1 and 3, respectively. The formation of 1,2,3,7,9-penta-CDF via reaction route 2 is not possible with this hexachlorobiphenyl. The formation of a hexa-CDF could not be confirmed.

The pyrolysis of 2,3,5,2',3',5'-hexachlorobiphenyl gave a major and a minor tetra-CDF and a major penta-CDF (see Figure 4e). The major PCDFs were identified as 2,3,7,8-tetra- and 1,2,4,6,8-penta-CDF, the expected products from the pyrolysis of this PCB via reaction routes 1 and 3, respectively. Again, the formation of a penta-CDF via reaction route 2 is not possible with this PCB and in fact no additional isomer was observed. The identity and source of the additional, minor tetra-CDF remained unclear.

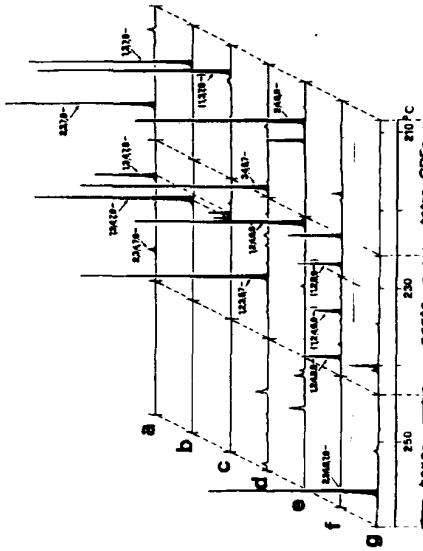
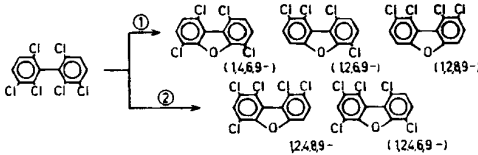
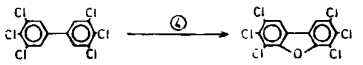


Figure 4: Mass fragmentograms (m/e 304, 330 and 372) of pyrolyzed hexachlorobiphenyls showing elution of tetra-, penta- and hexa-CDFs from (a) 2,4,5,2',4',5'-, (b) 2,4,6,2',4',6'-, (c) 2,4,5,2',4',6'-, (d) 2,3,6,2',3',6'-, (e) 2,3,5,2',3',5'- and (g) 3,4,5,3',4',5'-hexachlorobiphenyl. Column conditions as in Figure 1.

Pyrolysis of 2,3,6,2',3',6'-hexachlorobiphenyl yielded three tetra- and two penta-CDFs (see Figure 4f), the number of isomers expected via reaction routes 1 and 2 (reaction route 3 and 4 not possible for this PCB). In case of the tetra-CDFs, the expected isomers are 1,4,6,9- , 1,2,6,9- and 1,2,8,9-tetra-CDF. The first two eluting isomers were also observed from the pyrolysis of 2,3,6,2',3',5'-pentachlorobiphenyl (see earlier). Therefore, the last eluting tetra-CDF was tentatively identified as the 1,2,3,9-substituted isomer. In case of the penta-CDFs, the expected isomers are 1,2,4,8,9- and 1,2,4,6,9-penta-CDF. The formation of 1,2,4,6,8,9-penta-CDF could be confirmed by co-chromatography with a reference sample (see Table 2); the identification of 1,2,3,6,9-penta-CDF as the first eluting isomer remains tentative.



The major pyrolysis product of 2,3,4,5,3',4',5'-heptachlorobiphenyl was identified as 2,3,4,6,7,8-hexa-CDF (see Figure 4g). This PCDF is formed via reaction route 4. The formation of tetra- and penta-CDFs via reaction routes 1, 2 and 3 is not possible for this PCB isomer. Nevertheless, small amounts of penta-CDFs were observed, but the identity and source of these compounds remained unclear.

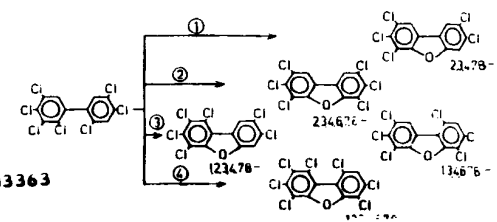


Pyrolysis of hepta- and octachlorobiphenyls

The pyrolysis of two hepta- and one octachlorobiphenyl was investigated (see Table 1). All three isomers are main components of higher chlorinated commercial PCBs.[19] Mass fragmentograms of pyrolyzed samples are given in Figure 5.

The pyrolysis of 2,3,4,5,2',3',4'-heptachlorobiphenyl lead to the formation of penta-, hexa- and hepta-CDFs (see Figure 5a). A single penta-CDF is formed; it was confirmed as 2,3,4,6,7-penta-CDF, the expected product from the pyrolysis of this PCB via reaction route 1. In case of the hexa-CDFs, the formation of two isomers was observed (not completely separated from each other). The expected isomers are 1,2,3,4,6,7- and 1,2,3,6,7,8-hexa-CDF (reaction route 3). The formation of the latter was confirmed by comparison to a reference sample (see Table 2). In addition, Figure 5a shows the elution of three hepta-CDFs. The main isomer was confirmed as 1,2,3,4,7,8,9-hepta-CDF, the product expected via reaction route 4. However, significant amounts of 1,2,3,4,6,7,8- and 1,2,3,4,6,7,9-hepta-CDF were also found. The formation of these isomers is unexpected but was so far not further investigated.

The pyrolysis of 2,3,4,5,2',4',5'-heptachlorobiphenyl again lead to the formation of penta-, hexa- and hepta-CDFs (see Figure 5b). The penta-CDF was confirmed as the 2,3,4,7,8- substituted isomer formed via reaction route 1. In case of the hexa-CDFs, the formation of two major and a minor isomer was observed. One of the major isomers is confirmed as 1,2,3,4,7,8-hexa-CDF, the minor as 2,3,4,6,7,8-hexa-CDF; they are products formed via reaction routes 3 and 2, respectively (see Scheme below). The other major hexa-CDF is expected to be 1,3,4,6,7,8-hexa-CDF, another product expected via reaction route 3. The mass fragmentogram also shows the elution of hepta-CDFs. The main isomer was confirmed as 1,2,3,4,6,7,9-hepta-CDF, the expected product from this PCB via reaction route 4. However, smaller amounts of additional hepta-CDFs were also observed.



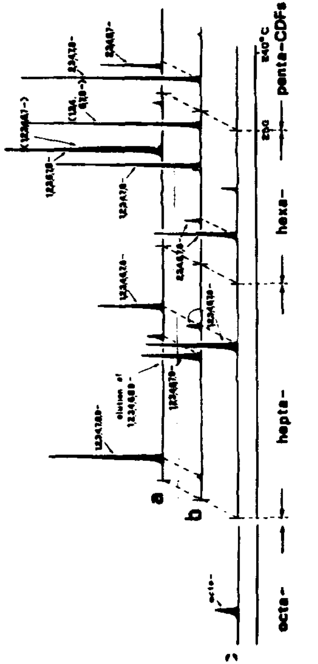


Figure 5: Mass fragmentograms (m/e 338, 372, 406 and 440) of pyrolyzed hepta- and octachlorobiphenyls showing elution of penta-, hexa-, hepta- and octa-CDF from (a) 2,3,4,5,2',3',4'-, (b) 2,3,4,5,2',4',5'-hepta- and (c) 2,3,4,5,2',3',4',5'-octachlorobiphenyl. Column conditions as in Figure 1.

The pyrolysis of 2,3,4,5,2',3',4',5'-octachlorobiphenyl yielded hexa-, hepta- and octa-CDFs (see Figure 5c). The main hexa-CDF was confirmed as the 2,3,4,6,7,8-substituted isomer formed via reaction route 1. In addition, a minor hexa-CDF was also observed, the identity and source of which remained unclear. The hepta-CDF was confirmed as the 1,2,3,4,6,7,8- substituted isomer, the expected product formed via reaction route 3. The mass fragmentogram also shows the elution of octa-CDF, the pyrolysis product formed via reaction route 4.

Conclusions

The pyrolysis of 18 individual PCBs was studied and shown to result in the formation of PCDFs via intramolecular cyclizations. The yields of PCDFs were estimated to be in the range of 0.1% up to several %. Again the application of high-resolution GC and MS is documented as a necessity for the separation and identification of the PCDFs formed. Pyrolysis of individual PCBs has proven to be useful for the preparation of individual PCDFs in situations where only minute amounts of isomers are required for reference purposes, mainly in GC-MS analyses.

The formation of the PCDFs was found to follow four general reaction routes involving the loss of Cl_2, H_2, and HCl with or without a 2,3-chlorine migration (see introduction). Due to the observed generality, it is possible to predict the structure of the resulting PCDFs.

The results support our earlier conclusion that pyrolysis of PCBs is resulting in the formation of highly toxic compounds. Consequently, the uncontrolled burning of PCBs is a threat to the environment and should be avoided.

Acknowledgements

We thank Mr. A. Gară and Mr. R. Lindahl, Drs. K. Andersson, Y. Masuda, J. McKinney, M. Morita, A. Poland and C.A. Wachtmeister for making available the PCBs and the PCDF reference compounds used in the present investigation.

References

1. C. Rappe, H.R. Buser and H.-P. Bosshardt, Ann. New York Acad. Sci., in press.
2. A. Poland, E. Glover and [illegible], J. Biol. Chem., 251, 4936 (1976).
3. J.A. Moore, E.E. McConnell, U.A. Gaagard and M.W. Harris, Ann. New York Acad. Sci., in press.
4. M. Kuroki and Y. Masuda, Chemosphere, 7, 771 (1978).
5. H.R. Buser, C. Rappe and A. Gara, Chemosphere, 7, 439 (1978).
6. C. Rappe, A. Gara and H. Buser, Chemosphere, in press.
7. C. Rappe, H.R. Buser and H.-P. Bosshardt, Chemosphere, 7, 431 (1978).
8. J.G. Vos, J.H. Koeman, H.L. van der Maas, M.C. ten Noever de Brauw and R.H. de Vos, Food Cosmet. Toxicol., 8, 625 (1970).
9. K. Olie, P.L. Vermeulen and O. Hutzinger, Chemosphere, 6, 455 (1977).
10. H.R. Buser, H.-P. Bosshardt, C. Rappe and R. Lindahl, Chemosphere, 7, 419 (1978).
11. Dow Chemical Company, Tetrachloroethanes of Fire, Report, November, 1978.
12. R.J. Smith, Science, 204, 1166 (1978).
13. H.R. Buser, H.-P. Bosshardt and C. Rappe, Chemosphere, 7, 109 (1973).
14. M. Morita, J. Nakagawa, [illegible], S. Hirata and K. Isono, Bull. Environ. Contam. Toxicol., 18, 67 (1977).
15. M. Morita, J. Nakagawa, [illegible], Bull. Environ. Contam. Toxicol., 19, 861 (1978).
16. R. Norstrom, K. Andersson and C. Rappe, Chemosphere, 5, 419 (1976).
17. A.S. Kende, J.J. Wade, [illegible], D. Ridge and A. Poland, 167th National Meeting of the American Chemical Society, Los Angeles, 1974.
18. H.R. Buser, [illegible], University of Stockholm, Sweden, 1975.
19. M. Zell, H. Hagenmaier and [illegible], Chemosphere, 6, 179 (1977).

(Received in UK 8 February 1979)

ENVIRONMENT INTERNATIONAL

A Journal of Science, Technology, Health, Monitoring and Policy

Previously announced as International Journal of the Environment

Editor A.A. Moghissi, *U.S. Environmental Protection Agency, Washington D.C., U.S.A.*
Managing Editor Barbara Moghissi

Contents of Volume 1 Number 3
SPECIAL UNEP ISSUE FOR WORLD ENVIRONMENT DAY
Guest Editors Margaret R. Biswas and Asit K. Biswas
Foreword
M.K. TOLBA, *Executive Director, United Nations Environment Programme, Nairobi, Kenya*
MARGARET R. BISWAS and ASIT K. BISWAS, *Biswas & Associates, Ottawa, Canada*
Editorial
REPORT OF THE EXECUTIVE DIRECTOR, *United Nations Environment Programme, Nairobi, Kenya*
Environmental Impact of Irrational and Wasteful Use of Natural Resources
REPORT OF THE EXECUTIVE DIRECTOR, *United Nations Environment Programme, Nairobi, Kenya*
The State of the Environment: Selected Topics – 1978
M.K. TOLBA, *Executive Director, United Nations Environment Programme*
Environment Management
UNEP SECRETARIAT
Environment and Development

The new bi-monthly publication *Environment International* is a multidisciplinary forum for environmental literature. Vital issues of pollution and methods for protection are all covered. Encompassing essentially the entire field of environmental protection, EI covers:

- concentration of elements and compounds including pollutants
- release rates of pollutants from various sources
- transport of pollutants in the environmental media
- health and ecological effects of pollutants
- [illegible] effects
- identification and interpretation of laws, regulations, and standards
- [illegible] which will contribute to the understanding of environmental behavior of pollutants and to promote environmental protection

[illegible] EI will include [illegible] topics. For instance certain issues will [illegible] specific pollutants (mercury, [illegible] environmental concepts (air [illegible] ecological effects, environmental [illegible] production and regulatory [illegible] approaches, control technologies [illegible] and other containment [illegible]. Other special issues will be devoted to [illegible] in selected geographical areas. We welcome suggestions for [illegible]

Subscription Information
Published [illegible]
[illegible] Subscription [illegible] $76.00
[illegible]
Regular [illegible]
Airmail [illegible] $144.00
Air/surface [illegible]
FREE SPECIMEN COPY [illegible]
SUBSCRIPTION REQUEST [illegible]
Send [illegible]
[illegible]

Transportation Committee. Both committees have jurisdiction over the superfund.

Breaux said that the liability provisions in the superfund "should be interpreted narrowly" to cover only third party damages for economic loss, not for medical injuries. Breaux said that he agreed with the Administration's proposal not to award third party damages to victims of abandoned hazardous waste sites because such claims would drain the superfund.

Fee Not A Penalty

Regarding industry assertions that the fee assessed against the petroleum and chemical industries to finance the superfund is unfair and is a "penalty" for past disposal practices, Breaux said that he does not regard the fee as a penalty, but rather as a fee on a product. He said that industry can add the fee onto the cost of its products, ultimately passing the added cost on to the consumer.

In addition, Breaux said he did not agree with industry assertions that the liability concept in the superfund is an ex post facto denial of due process.

Litigation

U.S. SUPREME COURT TO HEAR BENZENE ARGUMENTS OCTOBER 10

The U.S. Supreme Court will hear oral arguments October 10 on the validity of the Occupational Safety and Health Administration's standard governing worker exposure to benzene.

The arguments before the Court will come more than a year after the U.S. Court of Appeals for the Fifth Circuit struck down the standard on the ground that OSHA failed to show that the standard's benefits bear a "reasonable relationship" to its costs.

OSHA and the AFL-CIO, both of which are seeking to have the appeals court decision overruled, attacked the concept of balancing costs against benefits in setting an exposure level for toxic substances.

Oil producers and users who successfully challenged the standard in the Fifth Circuit Court accused OSHA of exaggerating the appeals court ruling. The producers and users insist that the court did not require OSHA to conduct an elaborate cost-benefit analysis but only that it consider a "rough but educated estimate" of benefits expected from reducing the permissible exposure level from 10 parts per million to one ppm.

The Court scheduled one and a half hours for argument of the benzene case.

Litigation

OCCIDENTAL EMPLOYEE CLAIMS DBCP CAUSED CHILD'S DEFORMITIES

An employee of the California plant which manufactured the pesticide dibromochloropropane (DBCP) filed suit against the company charging that his exposure to the chemical caused his child's deformities.

The action, filed August 28 by attorneys for Frank Arnett, an employee of Occidental Chemical Company, Lathrop, Calif., charged Occidental with "carelessly, negligently, and recklessly" failing to prevent employees' contact with DBCP, allowing Arnett to become seriously injured.

The suit asks more than $6 million in punitive damages and $2 million in compensatory damages.

According to attorney Duane Miller, the suit is the first one filed by an Occidental employee against the company itself. Worker's compensation laws prohibit a worker from suing his or her employer for work-related injuries or illnesses.

But the attorneys for Arnett said that recent evidence, which indicates Occidental knew DBCP was in the drinking water supply of the plant, but did nothing about it, provides cause for action against the firm for intentional and willful injury.

A high rate of sterility among workers at the Lathrop plant was first discovered in September 1977 and resulted in the issuance of an emergency temporary standard by the Occupational Safety and Health Administration (Current Report, September 16, 1977, p. 893).

Arnett charged in his suit that his DBCP exposure caused his sterility, which was reversed when the plant ceased manufacturing the pesticide.

The complaint was filed as an amendment to an earlier suit against several chemical companies and researchers which alleged the defendants failed to publicize their research on the harmful effects of DBCP.

Spokesmen for Occidental Chemical said they had not yet been informed of the suit, and therefore had no comment.

Hazardous Substances

CHLORINATED AROMATIC COMPOUNDS SOURCE OF DIOXINS, FURANS IN COMBUSTION PRODUCTS

Highly toxic polychlorinated dioxins and furans found in combustion products from municipal and industrial incinerators, come primarily from burning of certain chlorinated aromatic compounds, according to European researchers.

This finding was reported by Christoffer Rappe, of the University of Umea, Sweden, and Hans-Rudolf Buser, of the Swiss Federal Research Station, Waedenswil, Switzerland, during the American Chemical Society meeting held in Washington, D.C., September 9-14.

The researchers identified chlorinated phenols, polychlorinated biphenyls (PCBs), chlorinated diphenyl ethers, and chlorinated benzenes as the major precursors of the toxic dioxins and furans.

Their findings draw attention to the possible environmental hazard from polychlorinated dibenzofurans. The furans are similar in chemical structure and toxic effects to the dioxins, but are somewhat less toxic and have received less attention from environmentalists and the public.

However, Rappe told Chemical Regulation Reporter he considers the furans to be more worrisome than the dioxins. He said the dioxins found in combustion products consist largely of the less toxic members of the dioxin family. The most toxic furan isomers, however, are major constituents of the furans found in fly ash and flue gas, Rappe said.

Rappe said one study indicates that 2,3,7,8-tetrachlorodibenzofuran (TCDF) is about one-fifth as toxic as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the most toxic of the dioxins.

Rappe and Buser recommended that the burning of PCBs and of chlorinated phenols, benzenes, and diphenyl ethers be carefully controlled by monitoring chlorinated dioxins and furans in fly ash and flue gases.

PCBs

The researchers said burning of commercial PCBs was found to produce a variety of chlorinated furans, with yields of between 3 and 25 percent. They said the most toxic furan,

TCDF, was a main constituent of the furans produced from PCBs.

Rappe said the pattern of isomers formed from burning PCBs showed a close match with the pattern found in fly ash samples. He concluded that uncontrolled burning of materials containing PCBs may be an important source of hazardous furans in the environment.

Chlorophenols

The researchers also said burning wood shavings impregnated with chlorophenols produced significant quantities of furans. They said their results suggest that chlorophenols are important precursors to dioxins found in fly ash.

This finding may have serious implications for the future status of pentachlorophenol, a common wood preservative which is currently being reviewed by the Environmental Protection Agency for possible regulatory restrictions (Current Report, May 16, p. 230).

Polychlorinated Diphenyl Ethers

The scientists also said chlorinated furans are produced from combustion of any of the various chlorinated diphenyl ethers. In addition, they said, some of the ethers also yield varying amounts of dioxins, including TCDD.

They said chlorinated benzenes were found to yield both dioxins and furans when burned, but at lower yields than the PCBs and diphenyl ethers.

Wood Preservatives

Rappe and Buser reported experiments with a variety of fire retardant chemicals. They said a number of the chemicals tested yielded dioxins or furans. One flame retardant, hexabromobiphenyl, yielded 3 to 5 percent of the most toxic furan isomer.

They recommended that halogenated phenols, biphenyls, and diphenyl ethers should not be used as flame retardants.

Chlorinated Furans Found in Fish

In a related development, David L. Stalling, of the U.S. Fish and Wildlife Service's National Fisheries Research Laboratory, reported the discovery of chlorinated dibenzofurans in fresh water fish in the central and northeastern United States.

Speaking at an ACS press conference September 10, Stalling said the furans have been detected at levels of about one part per billion in carp, catfish, coho salmon, and lake trout taken from the Connecticut, Hudson, and Ohio rivers, and from Lake Michigan.

Stalling related the finding of furans in fish to Rappe and Buser's discovery that furans are created by combustion of PCBs.

He said the furans are as much as 500 times as toxic as their PCB precursors.

Transformer fires in locomotive or in electrical generation equipment could cause the conversion of PCBs to the highly toxic furans, Stalling said. Use of PCBs in hydraulic systems also could cause the conversion, he added, as could low temperature incineration of PCB-contaminated industrial wastes by municipal incineration plants.

He cautioned that careful analysis and investigation should be done before any heating or incineration of PCBs is permitted.

Hudson River Lowest

Stalling said furan levels in fish taken from the Hudson River were lower than the levels found in fish from the other waterways. He said much of the PCB found in the Hudson, which is believed to contain more PCBs than any other U.S. waterway, came from original production of the chemical rather than from its use in industrial processes.

Stalling said the level of furans in manufactured PCBs is less than one part per million.

PCBs and Dioxin

Initial interpretation of the new data showed that there is little relationship between PCBs and dioxin formation, Stalling said.

Dioxin, for example, was found in the only body of water where no furan contamination of fish was found, Stalling said.

The data presented by Stalling was found by testing 16 fish samples collected at five sites between 1970 and 1979. He said 25 to 50 more sites will be tested for furans in the coming year.

He and co-workers also hope to identify which of 135 furan isomers are present in waterways and whether they are harmful to aquatic life, Stalling said.

He said that, for the time being, people can protect themselves against consumption of furans by following advisories against consumption of fish taken from waters contaminated by PCBs.

No Dioxins From Coal-Fired Power Plant

The amount of dioxin in particulate emissions from coal-fired power plants "is so small as to escape detection with the finest scientific equipment available, U.S. researchers said at a September 13 ACS press conference.

Brenda Kimble, of the Department of Energy's Radiobiology Laboratory, and Michael L. Gross, director of the Midwest Center for Mass Spectrometry, at the University of Nebraska, described their analysis of fly ash particles collected from the stack of "a typical power plant burning low-sulfur, high-ash coal."

They said they found no dioxin at the lowest level of detection, corresponding to one millionth of a gram of TCDD from the burning of 200 tons of coal.

They contrasted their findings with results reported by the Dow Chemical Company. Dow researchers found dioxins in emissions from a wide variety of common combustion sources, including fossil-fueled power plants (August 31, p. 889). Kimble and Gross suggested that Dow's conclusions cannot be applied to all fossil-fueled power plants.

Donald Townsend of Dow, who was also present at the press conference, said the power plant tested by Dow had burned primarily fuel oil, with a small amount of coal. He said Dow had found dioxins all over the Midwest. Townsend said dioxins, including TCDD, were even found in a U.S. Bureau of Standards standardized sample of urban particulate matter.

Gross said he would not want to extrapolate his findings to all power plants, including those not burning western coal.

Buser said the European researchers had not studied emissions from coal-burning power plants, since coal is not used to generate electricity in Switzerland.

Sterility Linked by Researcher to PCBs

Functional sterility significantly correlates with the level of PCBs found in human males, according to Ralph C. Dougherty, a Florida State University (FSU) research chemist.

He said 23 percent of the males he tested were functionally sterile because their seminal fluids contained low numbers of sperm.

The lowest sperm densities were found in men with the highest levels of PCBs in their bodies, Dougherty said at a September 10 ACS session.

9-14-79

0148-7973/79/500.50

Since 1974, there has been a greater than 100 percent increase in the number of males with low sperm densities, indicating functional sterility, Dougherty said.

His research shows that PCB contamination accounts for about 25 percent of the shift toward lower sperm counts, he said, adding that he believes other toxic substances eventually will be implicated in the decline.

Dougherty said his study of 132 men at FSU showed that 23 percent were functionally sterile because they had sperm densities of less than 20 million per milliliter.

In a 1929 study, only about 7 percent of the men tested were functionally sterile, while, in 1974, about 10 percent were, Dougherty's statistics showed.

Dougherty said several identified toxic substances were found in the seminal plasma of his volunteers, but that only PCBs correlated with low sperm densities.

Among the substances found, but not tied by Dougherty to sperm density, were pentachlorophenol, hexachlorobenzene, and various metabolites of DDT.

He said some other chemicals found correlated with the low sperm densities, but that he and his coworkers were unable to identify the substances.

None of them, however, seemed to have the significant correlation which PCB had, Dougherty said.

Fertility Declining

Dougherty said median sperm density has declined from 90 million per milliliter in 1929, to 65 million per milliliter in 1974, and to 60 million per milliliter in 1979.

The most common sperm density found in volunteers, however, illustrates the steep decline in the fertility rate, Dougherty said.

Plotting the sperm densities on a graph shows that the largest number of men in the 1929 study had sperm densities of 100 million per milliliter, according to Dougherty.

In 1974, the largest number of men had a density of 60 million per milliliter, while in the 1979 study, the most common density had fallen to 20 million per milliliter, Dougherty said.

The researcher said he believes college students may have lower than normal sperm densities because of such factors as stress and sexual activity.

He added, however, that the lower densities found in his study could not be accounted for by the makeup of the study group alone.

To validate his study, he has recruited a number of workers in an electrical plant. Because these workers have been exposed to PCBs on a regular basis in their jobs, their sperm counts should confirm his findings with college students, he said.

PCBs Degrading Health

Dougherty said there is "a strong presumption" that PCBs are "responsible for depressing the health parameters of people in the United States."

Further study will show, he said, that PCBs and all of the polychlorinated aromatics are too dangerous to be used or manufactured.

Significance to Cancer Study

Dougherty said his study has major significance for detecting hazardous substances and for carcinogen detection programs.

Because it takes eight cell divisions to create a sperm, a lowered sperm count shows that something is inhibiting cell division, Dougherty said.

Most substances that slow cell division are found to be carcinogenic or mutagenic, he said.

For that reason, evaluation of sperm count and seminal plasma could provide a method of correlating impeded cell division with the amounts of toxic substances in the donor, he said.

Those substances which seem to be lowering sperm count should be considered too hazardous for use and should be banned, he said.

PCBs Increasing in Great Lakes

The contamination of the Great Lakes by PCBs may continue to increase in spite of the EPA ban on further production or use of the chemicals, researchers told ACS September 11.

The researchers said the atmosphere is the major source of PCBs presently entering the lake, and therefore, the contamination cannot be prevented by eliminating municipal and industrial discharges of PCBs into the lakes.

Thomas J. Murphy, of DePaul University, Chicago, said levels of PCBs found in Great Lakes fish have declined only slightly since the early 1970s, despite a great reduction in PCB use. He contrasted this with earlier experience with DDT. He said DDT levels in fish declined rapidly after the pesticide was banned.

Present concentrations of PCBs in many fish exceed the Food and Drug Administration limit of two parts per million, Murphy said (June 29, p. 471). FDA recently stayed the new two ppm action level (August 31, p. 890).

Murphy said known pollution from municipal, industrial, and tributary sources do not seem to account for the present PCB levels in the Great Lakes. He said he and other researchers set out to determine whether fallout from the atmosphere could be an important source of PCB contamination.

They measured rates ranging from 15 to 75 grams per square kilometer per year at various points in Lake Michigan and Lake Huron. Assuming an average rate of 25 grams per square kilometer, Murphy said, the contribution of PCBs from the atmosphere would be about 2,500 pounds per year in each of the two lakes. This is greater than the contribution from all other known sources, he said.

Murphy said the PCBs in the atmosphere probably come from such sources as municipal incinerators and evaporation from landfills, from PCBs discarded in the past, and from PCBs used in paints and as preservatives.

Lake Superior

S. J. Eisenreich of the University of Minnesota reported research on PCB contamination of Lake Superior. He said atmospheric deposition from rain, particles, and PCB vapor account for over 80 percent of the total PCBs presently entering the lake.

Eisenreich estimated that 20 thousand to 23 thousand pounds of PCBs enter Lake Superior each year, while only 2,300 to 3,500 pounds are removed by outflow and sedimentation. Consequently, 16 thousand to 21 thousand pounds apparently accumulate in the lake each year, he said.

Level Has Not Peaked

Eisenreich said he believes the atmospheric contamination of Lake Superior has not yet reached its peak, although PCB production has been dropping since 1969. He said PCB-containing materials and products such as electrical equipment are being disposed of continuously. He said there is a substantial time lag between the disposal of PCBs and their appearance in the Great Lakes.

Eisenreich said the importance of atmospheric deposition as a source of PCB contamination is demonstrated by the

presence of PCBs in small lakes on islands isolated from any source of direct PCB contamination.

He said fish caught in the island lakes had PCB levels as much as 100 times higher than those caught in the Great Lakes. He attributed the higher contamination levels in the island fish to the shallowness of the island lakes, which makes them more sensitive to atmospheric contamination.

Eisenreich said the Great Lakes have low sedimentation rates. PCBs which settle out of the lake water remain close to the surface of the bottom where they are available to bottom-feeding marine life, he said. He estimated that it would take about 175 years for PCBs to be buried in sediments so deeply that they cannot reenter the lake.

Chemicals and Bacteria

The presence of bacteria in drinking water increases its ability to carry pesticides and PCBs by up to 100 percent, according to John Duck, a research chemist with NUS Corporation, Pittsburgh, Pa..

While the findings mean bacteria in drinking water may pose a greater health hazard than originally thought, they also mean that bacteria could be used to remove hazardous substances from ambient water systems, the researcher said.

Duck said his research shows that the presence of bacteria in water increases the amounts of pesticides and PCBs that the water can hold.

The chemicals seem to attach themselves to the cell membranes of the bacteria and are resistant to removal, Duck said.

The implications of the study are that pesticides, PCBs, and possibly other toxic substances could be removed from drinking and ambient water supplies by passing bacteria coated plates through the water, Duck said.

The researcher said he found that bacteria form a major mode of transport for PCBs and pesticides in water environments.

Without the bacteria, the PCBs and pesticides tend to settle out of water or tend to be adsorbed, Duck said.

Bacteria, along with the attached hazardous substances, tend to remain suspended in the water and are difficult to filter out, Duck said.

He said that he found destruction of the bacteria cell had little effect on its ability to hold the hazardous substances.

The chemicals tested, aldrin and PCBs, seem to attach to the cell membrane or possibly to combine with the lipoproteins in the membrane and thus are resistant to destruction, he said.

For that reason, chlorination or other means of sterilization do "not necessarily eliminate" the potential hazard that finished drinking water supplies might contain PCBs or pesticides, Duck said.

Duck said that filtering the water may remove some of the bacteria and consequently the hazardous substances, but that more testing needs to be done before a definite judgment can be made on the efficiency of filtering.

He said further work will be done to determine the exact method by which the bacteria carry the hazardous substances and to find out the feasibility of using bacteria-laden plates or membranes to remove hazardous substances from water.

He said his study has significance because treated drinking water contains between 100 and one million microorganisms per milliliter. Those microorganisms, which are resistant to normal treatment processes, serve as convenient carriers for hazardous substances, he said.

Litigation

COURT PARTIALLY BARS CLAIM AGAINST ALLIED CHEMICAL IN KEPONE SUIT

A former officer and director of a Virginia firm which manufactured the pesticide kepone was partially barred in his attempt to collect damages for emotional distress and defamation from Allied Chemical Company, which contracted to buy the pesticide.

The U.S. District Court for the Eastern District of Virginia, in *William P. Moore v. Allied Chemical Corporation, The Travelers Indemnity Company, and Hooker Chemicals & Plastic Corporation*, determined that Moore was barred in the emotional distress claim but could proceed in his defamation suit to recover damages.

Moore's former company, Life Science Products, produced kepone purchased by Allied. At issue was whether Moore had an opportunity to litigate the matter fully during Occupational Safety and Health Review Commission proceedings following an inspection of the Life Science Products, Hopewell, Va., plant August 11 to 18, 1975.

Allied contended that admissions in the former litigation prohibited Moore from alleging that he was unaware of the full dangers of kepone and thereby pursuing his claims against Allied. Moore contended that Allied knew of the devastating physiological effects which kepone could have on its workers, but that the firm deliberately failed to warn him of these dangers, and that, consequently, he suffered severe emotional distress.

In determining that Moore was estopped on the emotional distress count, the court adopted Allied's argument. However, as to the defamation claim, the court found that the facts and issues determined in the OSAHRC proceedings were not substantively the same.

Writing for the court, Judge Calvitt Clarke, Jr., said that the truth of Allied's statements and their defamatory nature were matters to be determined at trial.

Pesticides

ROHM & HAAS ASKS EPA TO CANCEL REGISTRATIONS OF VACOR RODENTICIDE

The Rohm & Haas Company voluntarily requested that the Environmental Protection Agency cancel U.S.registrations of its rat and mouse pesticides containing the active ingredient Vacor (*N-3-pyridylmethyl-N-p-nitrophenylurea*), the agency announced September 12.

The company said it stopped sale of the rodenticides worldwide and has begun a recall of the products, according to the agency.

EPA was already in the process of reviewing the registrations of Vacor because of concerns expressed by the California Department of Food and Agriculture, which banned the rodenticide for home use March 1, the agency said.

Vacor has been the cause of several human deaths in South Korea, most classified as suicides, EPA said. California reported nine adult poisoning cases, two of which resulted in death, the agency said. California was also concerned that the packaging of Vacor products appeared to be attractive to children, according to EPA.

The products involved were sold to consumers under the name "Vacor Rat Killer" and "Vacor Rat and Mouse Killer," and to pest control operators as "DLP-787 House Mouse Killer" and "DLP 787," the agency said.

[redacted]own into a cocked hat last week when U. S. Fish & Wildlife scientist Dr. David Stalling reported at the American Chemical Society meeting that polychlorinated dibenzofurans, 1,000 times more potent than polychlorinated biphenyls and a probable carcinogen and teratogen, accompanies PCBs and is often masked by the parent chemical. Meanwhile, EPA officials were at Midland, Mich., this week receiving part of the information the agency subpoenaed in connection with Dow Chemical's production of monochloro biphenyl (See Sept. 5, Page 10).

THE WHITE HOUSE Regulatory Analysis Review Group, established to make certain that government regulations make economic sense, has so far left TSCA implementation alone and has not commented on any TSCA proposals.

EPA SCIENCE ADVISORY BOARD's subcommittee on toxic substances will meet Sept. 19 at Waterside Mall to review health effects tests standards proposed by the Office of Toxic Substances.

HEXACHLOROCYCLOPENTADIENE was inadvertently left off of the list of chemicals for which the Interagency Toxic Testing Committee recommended epidemiological studies (See May 16, Page 27), EPA corrected in a Sept. 4 Federal Register announcement.

EPA'S JOAN Z. BERNSTEIN, Office of General Counsel, will serve as Acting Assistant Administrator for Enforcement until EPA finds a replacement for Marvin Durning. Swep T. Davis, formerly Deputy Assistant Administrator for Water Standards and Planning and James N. Smith, formerly a Special Assistant to Thomas C. Jorling, have been appointed to the positions of Associate Assistant Administrators for Water and Waste Management. Davis will focus on strategy development and "superfund" while Smith will work on program operations.

EPN RPAR NOTICE is scheduled to be published by EPA in the Sept. 19 Federal Register with an Oct. 29 deadline for filing rebuttals. The deadline will probably be extended to early January. The RPAR is based on delayed neurotoxicity (See Aug. 29, Page 21).

HOELON 3 E C, diclofop, (See Aug. 1, Page 2) slides from animal studies were scheduled for a side-by-side review Sept. 12 at a meeting of EPA scientists, Dr. Melvin Dwaine Reuber, National Cancer Institute-Frederick Research Center, and scientists with American Hoechst Corp. It is understood that Dr. Reuber's earlier review of the slides noted carcinogenic effects.

NOTICE that Mobil Chemical Co. has applied to the EPA to register Hefty Dog/Cat Repellent containing 16.4% of the new active ingredient cinnamic aldehyde was published in the Sept. 6 Federal Register. The company proposed the pesticide be classified for general use to repel dogs and cats from garbage bags and cans. Comment deadline is Oct. 9.

PESTICIDE PETITION filed by American Cyanamid, and noted Sept. 6 would set tolerances for residues of pendimethalin of 0.1 p.p.m. in or on sorghum grain, fodder, and forage. The herbicide is N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine and its metabolite 4-((ethylpropyl)amino)-2-methyl-3,5-dinitrobenzyl alcohol. EPA on Sept. 4 made further editorial changes in its alphabetical list of pesticide chemicals (See July 11, Page 5), deleting extraneous listings and adding those that were inadvertently omitted.

applicant relies on Monsanto data either by "cite-all" or specific reference; notice to company and to above named law firm; registration cannot be issued until 20 days from the date of the notification letter; the requirement does not apply if the applicant submits his own data or data other than Monsanto's to support the application or is authorized by Monsanto to use Monsanto's data.

The Diamond Shamrock stipulation procedures include: (1) above with 30 days notice to the company; registrations cannot be issued until 35 days from the date of the notice letter; and, essentially (4) above.

The Merck and Company, Inc. stipulation procedures included: 30 days notice as in (1) above to the company's counsel, Patrick M. Raher of the law firm of Hogan & Hartson, Washington, D.C.; registration cannot be issued until 35 days from the date of the notice letter; and, essentially (4) above.

Provisions of the Petrolite Corporation stipulation compliance procedures: 15 days notice of intent to "register any product or accept an amendment containing gluteraldehyde as an active ingredient if the product is labeled for use in oil field operations" sent to Raher, Hogan & Hartson as above; registration cannot be issued for 20 days from the date of the notice letter; and, substantially (4) above.

In complying with the provisions of the injunctions and stipulations, the Registration Division will find all registration actions covered by them on ever-changing lists, inform the applicants, tell them how to comply, wait for their response, notify parties to the injunctions and stipulations, wait for their responses before acting. Delay and error seem unavoidable.

copies for Callis, Weber, Wilson, [redacted], Kaley

Fish contaminated with polychlorinated dibenzofurans (PCDFs), a by-product of polychlorinated biphenyls (PCBs), have been found in the Ohio, Connecticut, and Hudson rivers and Lake Michigan, near Saginaw, Mich., a federal Fish and Wildlife Service researcher reported Sept. 10 at the American Chemical Society (ACS) national meeting in Washington, D.C. (See Page 2).

Dr. David Stalling, the Interior Department researcher, said PCDF can be formed by the oxidation of PCBs, especially when they are burned at relatively low temperature. "We know that very high temperature burning, if done for long enough, will completely destroy PCBs," Stalling said. "However, Dr. Christopher Rappe, University of Umea, Sweden, has demonstrated that low temperature combustion in the 400 degree to 600 degree Celsius range can convert 25 percent of PCBs to PCDFs."

The PCDFs, at concentrations up to 2 parts per billion (p.p.b.), were found in carp, catfish, lake trout and coho salmon in areas where there has been a historic problem with PCB contamination, Stalling said.

"We have not yet identified the individual chemical structures of the PCDFs in our (fish) samples," he said, "so we cannot be sure which of the 135 possible compounds are present or whether they might have toxic effects."

"Once specific PCDFs in fish are identified, laboratory scientists will have a better idea how they are formed, and which structures should be tested for possible toxic effects in fish and other aquatic organisms," the USDI researcher concluded.

ebate continues over Dow's dioxin theory

sults of several recent dies don't jibe with Dow's ntention that dioxins enter vironment from combustion; t, agreement is emerging

1979
Washington, D.C.

king potshots at Dow Chemical's ory that polychlorinated di--*p*-dioxins are formed by all combustion processes and are, refore, ubiquitous in the environ- nt has become a popular sport ong some analytical chemists, ecially when there are reporters sent. The most recent opportunity this activity, the symposium and ss conference on the chemistry of nzodioxins and dibenzofurans, nsored jointly by the divisions of sticide Chemistry and of Chemical alth & Safety (Probationary), had share of shooters. But the sessions so seemed to show, perhaps for the st time, an emerging common und shared by scientists on all es of the issue.

The issue is Dow's theory, first posed last November, that poly- lorinated dibenzo-*p*-dioxins, di- nzofurans, and biphenyls are med in trace amounts in all forms combustion. Therefore, they are t only ubiquitous in the environ- nt, but have been there since the vent of fire. It is only their detec- n that is recent, due to advances in alytical techniques (C&EN, Feb. , page 23).

The theory has gained so much attention because one of the polychlo- nated dibenzo-*p*-dioxins, the 3,7,8-tetrachloro species (2,3,7,8-CDD), is an extremely toxic com- und that also is a carcinogen and a ratogen in laboratory animals. This mpound is a trace contaminant in e herbicide 2,4,5-trichlorophenox- cetic acid (2,4,5-T) produced by ow and others.

The herbicide is currently under an emergency suspension for many uses from the Environmental Protection Agency because of an alleged association between its use and increased miscarriages in a group of women living near forests that had been sprayed with the herbicide in Alsea, Ore. Detectable levels of 2,3,7,8-TCDD also have been found in fish taken from the Tittabawassee River, which flows by Dow's production plant for the herbicide in Midland, Mich. Presence of the compound in fish led Michigan's Department of Natural Resources to suspect the company of illegally contaminating the river with this compound.

So Dow's theory that combustion is a major source of polychlorinated dioxins in the environment is more than interesting chemistry. If true, it goes a long way toward absolving the company's product and its manufacturing process from responsibility for contamination of the environment by these very toxic compounds.

Among the potshots the theory received at the symposium, two are most prominant: Brenda J. Kimble of the Department of Energy's Radiobiology Laboratory at the University of California, Davis, and Michael L. Gross, director of the Midwest Center for Mass Spectrometry at the University of Nebraska, Lincoln, have analyzed the smokestack emissions of a coal-fired power plant in California. They find no TCDD's in the emissions, down to their detection level of 0.6 ppt of fly ash. The Dow study looked specifically at the smokestack emissions of a power plant and concluded that this was a source of dioxins.

Also, David L. Stalling of the U.S. Fish & Wildlife Service and associates analyzed 16 samples of fish and other aquatic animals for polychlorinated dibenzofurans and dibenzodioxins. They found dibenzo-*p*-dioxins in only two samples, both from the Tittabawassee River. Further, 2,3,7,8-TCDD was the most common isomer in these samples, an isomer distribution that would not be expected if the source of the isomer were ordinary combustion. The most likely explanation, Stalling says, is that the Dow plant is the source of the isomer found in the fish.

C&EN staff photo

Crummett: complex and expensive

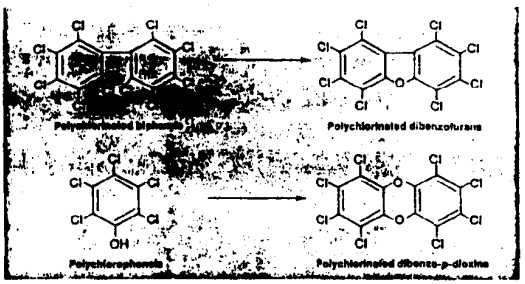
Even these reports may be at least partially compatible with Dow's findings. For example, Warren B. Crummett, a research scientist with Dow's analytical laboratories, explained that the power plant where Dow found dioxins in the stack emissions was on Dow's Midland facility. During the sampling period it was burning primarily fuel oil, with a small amount of coal. Various scientists at the press conference suggested that possibly the fuel oil, or even the air in Midland, contains chemical precursors to the dioxins found in the stack emissions that are not found in the California power plant.

Crummett criticized the California study in two ways. He says the samples were taken from too low in the smokestacks and that the particulates that were analyzed were primarily siliceous, whereas Dow had found that the dioxins in such emissions were associated with carbonaceous particulates.

"The particulates we sampled were the same as those that come out the top of the smokestack," Kimble says. The Dow study made sweeping claims about power plants being sources of environmental dioxins based on extremely limited evidence, she says. What she and Gross have shown is that at least one important class of power plants, those that burn western coal, can be free of dioxin contamination.

The question of the need to have

Dioxins, dibenzofurans can form from burning precursors



Note: These polychlorinated compounds contain one or more, but not necessarily all, of the chlorine atoms pictured in these structures.

precursors present in the material being burned in order to generate chlorinated dioxins or dibenzofurans in combustion has become a central point of dispute. Something, of course, has to provide the atoms that eventually end up in the dioxins and dibenzofurans. Dow contends, based on its widespread finding of these compounds in combustion products, that just about anything that will burn can serve as a precursor. Others, particularly Christoffer Rappe of the University of Umea, Sweden, and Hans-Rudolf Buser of the Swiss Federal Research Station, Wädenswil, think that synthetic chlorinated compounds must be present before combustion will yield chlorinated dioxins and dibenzofurans.

Here, too, there seems to be some middle ground emerging. Crummett, for instance, seems to acknowledge that some materials produce more dioxins when they are burned than do others. He maintains, however, that precursor compounds are so widespread in the environment that tracking them down via combustion data is a task of such complexity and expense as to be infeasible. He reported two new examples of how widespread 2,3,7,8-TCDD is in the environment. Detectable levels of this compound now have been found in commercial sludge fertilizer made from treated sewage. It also has been detected in the National Bureau of Standards' standard sample of urban particulate matter.

Buser and Rappe now say that the synthetic chemical precursors for both dioxins and diobenzofurans can be found "practically everywhere" in the environment at low levels. They maintain, however, that, except in special circumstances, such as the combustion of chemical wastes or accidental fires involving stores of certain kinds of chemicals, such combustion presents very little health hazard. And, like Dow, they think that the use of 2,4,5-T is a very much less important contributor of dioxins to the environment than is combustion.

Even the dioxins that enter the environment from pesticide use seem to be much less hazardous than laboratory tests would lead one to believe, says Capt. Alvin L. Young of the U.S. Air Force's Occupational & Environmental Health Laboratory, Brooks Air Force Base, Tex. Young and his associates have analyzed the soil and animals at Eglin Air Force Base in Florida where 73,000 kg of 2,4,5-T was sprayed between 1962 and 1970. Much of this material contained much higher levels of 2,3,7,8-TCDD than are now found in the herbicide.

Some 2,3,7,8-TCDD was still present in soil samples taken in 1978. Concentrations ranged from less than 10 ppt to 1500 ppt. (Young's analytical method cannot distinguish 2,3,7,8-TCDD from all other chlorinated dibenzo-*p*-dioxins. The concentration he reports is for the combination of isomers that includes the 2,3,7,8-TCDD isomer.)

The Air Force chemists did not find detectable levels of 2,3,7,8-TCDD in any plants taken from the site. However, they did find it in nine species of animals, including mammals, birds, fish, and reptiles. Levels varied from several hundred parts per trillion in the livers of beach mice and meadowlarks to 12 ppt in the whole bodies of two kinds of fish.

Beach mice, which contained the highest concentrations of the compound, were singled out for further study. Eighteen types of tissue from 300 animals were examined for toxic effects, but none of the tissues were significantly different from those of control group animals.

Just how important the trace quantities of dioxins that are being found in the environment are likely to be is a point that was raised frequently during the symposium. Rappe, Buser, and Stalling all seemed to agree that the polychlorinated dibenzofurans, though less toxic in an absolute sense than the most toxic dioxins, are of more concern because they are present in higher concentrations. They can be formed by combustion of polychlorinated biphenyls (PCB's), which earlier work has shown are very widespread in the environment.

Stalling, along with Donald W. Kuehl of EPA's Duluth, Minn., research laboratory, Ralph C. Dougherty of Florida State University, and Rappe, finds polychlorinated dibenzofurans and naphthalenes in aquatic animals living in waters that contain PCB's and their breakdown products. The results are somewhat preliminary, since only 16 samples have been analyzed and, so far, no samples have been checked from pristine waters. However, animals taken from the Ohio River and Lake Michigan, where contamination comes from used PCB's, show higher levels and more complex mixtures of these compounds than do fish taken from the Hudson River, which is contaminated by newly manufactured PCB's but contains low levels of PCB combustion products.

Rappe and Buser have been studying the combustion products of chlorophenols, PCB's, and chlorinated diphenyl ethers and benzenes. All of these compounds can be converted to polychlorinated dibenzodioxins and dibenzofurans in high yield, they find. However, 2,3,7,8-TCDD, the most toxic of the dibenzodioxins, is a minor product of combustion under the conditions found in municipal incinerators. 2,3,7,8-tetrachlorodibenzofuran, the most toxic of this class of compounds, is the major isomer formed under these conditions. PCB's can yield chlorinated dibenzofurans as high as 25%, they find.

Nevertheless, except for a few special cases, they do not see even the dibenzofurans as health hazards. They do recommend that polychlorinated phenolic chemical wastes be very carefully incinerated in ovens that allow for high-temperature incineration and long residence times to make sure that toxic products are destroyed. And halogenated phenols, biphenyls, and diphenyl ethers should not be used as flame retardants because of the high toxicity of their combustion products. C

Chemosphere, Vol. 12, No. 4/5, pp 669-680 1983
Printed in Great Britain

0045-6535/83/050669-12$03.00/0

CONTAMINATION OF AN OFFICE BUILDING IN BINGHAMTON, NEW YORK BY PCBS, DIOXINS, FURANS AND BIPHENYLENES AFTER AN ELECTRICAL PANEL AND ELECTRICAL TRANSFORMER INCIDENT.

Arnold Schecter, M.D., M.P.H., Professor and Coordinator, Department of Preventive Medicine, Clinical Campus, Upstate Medical Center, State University of New York at Binghamton, Binghamton, New York, 13901, USA; formerly Director, Broome County Health Department, Binghamton, New York

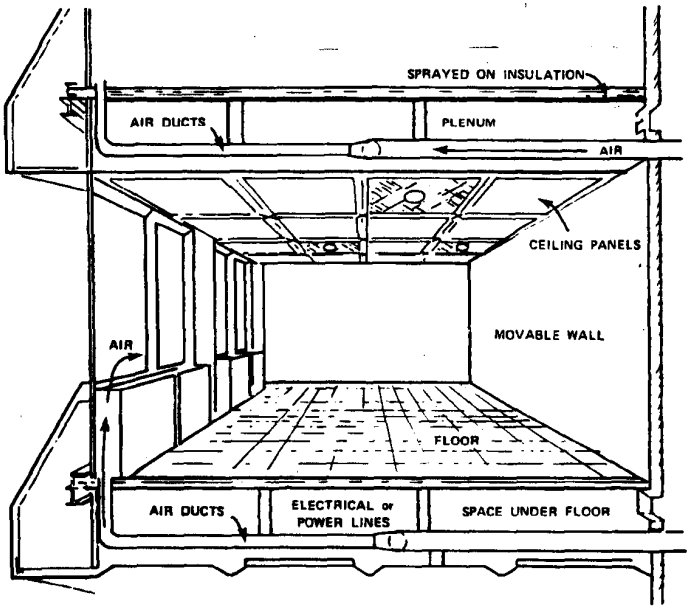
INTRODUCTION

Binghamton, New York is located approximately 200 miles north northwest of New York City in Broome County. The city population is approximately 53,000 persons, the tri city area 154,000, and the county population is about 213,000. On Thursday morning, February 5, 1981, at approximately 5:30 AM a malfunction occurred causing overheating of an electrical panel and a nearby electrical transformer within the State of New York's Office building in Binghamton. This overheating led to the release of between 180 to 200 gallons of transformer fluid originally containing 65% PCBs (Arochlor 1254), and 35% tri and tetra chlorinated benzenes. Pyrolytic conversion of these compounds led to the formation of numerous furan and dioxin isomers, which, along with the PCBs contaminated every floor of the office building. Biphenylenes were also produced during this event. Twenty-one months later the building has still not been reoccupied. Cleaning with water and detergent continues as do efforts to set standards for the presence of PCBs, furans, dioxins, and biphenylenes in soot and also in air. It is believed that this incident is the first to document formation and contamination of a non industrial building with these chemicals after an otherwise somewhat prosaic electrical system malfunction. Because electrical system fires, explosions, overheating with the involvement of PCBs and in some cases the chlorinated benzenes is probably relatively common, what has been learned in Binghamton may have general public health relevance elsewhere in both a prospective as well as retrospective fashion.

Thursday, February 5, 1982

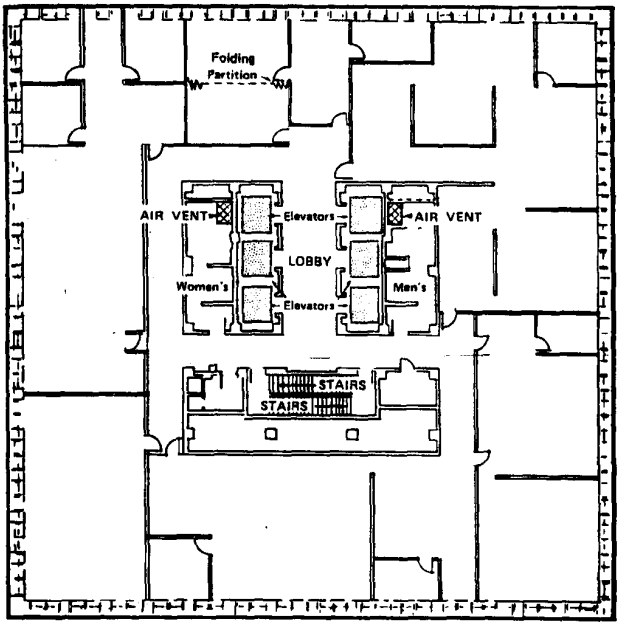
At 5:30 in the morning Binghamton firemen and police responded to a fire alarm at the Binghamton State Office Building (BSOB), a 22 story modern office building, located in downtown Binghamton, which was and is part of a one block governmental complex. This consists of Binghamton City Hall, the Broome County Office Building, the BSOB and a common plaza as well as two levels (basement and subbasement) of common parking garage. An electrical panel, one of two in the basement, was found to have overheated. This overheating which created loud noises, like explosions, was estimated to have lasted 5-30 minutes. The nearby transformer, which had originally contained approximately 1,060 gallons of transformer fluid, leaked an estimated 180 to 200 gallons of fluid onto the floor. Dense smoke was present in the area around the transformer. Smoke had been previously vented from the building through two safety doors on the roof at the top of each of two staircases which had opened in response to the smoke or heat. Doors leading to the outside and into the basement level of the parking garage, were opened and large fans used to remove smoke. It was later noted that there were two air shafts beginning in the ceiling of the area housing the two panels and transformers which vented the men's and women's rooms located on each floor and which terminated at the top of the building. Smoke was later found to have passed through these shafts, through metal

TYPICAL ROOM
STATE OFFICE BUILDING
BINGHAMTON, NEW YORK



MONS 003375

TYPICAL FLOOR PLAN*
STATE OFFICE BUILDING
BINGHAMTON, NEW YORK



*Most inner walls are movable.

gratings on the wall of each bathroom,into the bathrooms,and was then distributed in a non homogeneous fashion throughout the usual working areas as well as hidden spaces, including air ducts, elevator shafts, plenums above the ceilings, desk drawers, inside file cabinets, as well as in typewriters and other office equipment.

For reasons which are not clear at this time the usual circuit breakers and other safety devices designed to prevent overheating did not prevent the overheating which occurred. The transformer room, as previously mentioned, was not sealed off from the rest of the building. There was probably also a significant pressure and temperature differential which assisted the distribution of chemical contaminants. At the time of the accident the temperature outside was below zero fahrenheit and the building temperature in the sixties except for the overheated transformer and electrical panel which was estimated to have been overheated to up to several thousand degrees fahrenheit.

A strong chemical odor was immediately noticed by firemen and policemen a security guard and an engineer involved in the incident. This same odor was also easily noticed in the basement and first floor of the nearby City Hall, including the basement jail area as well as the police headquarters located in the first floor and basement. The fire department in a portion of City Hall also had a chemical odor. Outside of the BSOB a strong odor consistent with the presence of PCBs or polychlorinated benezenes persisted for several days.

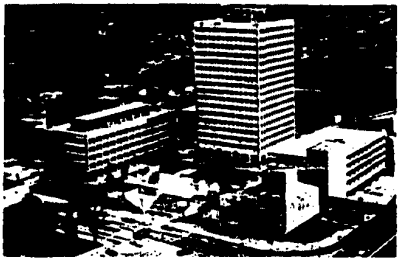
The firemen and policemen went to Binghamton City Hospital for emergency department evaluation of their chemical exposure. Within hours a representative of the General Electric Company, the manufacturer of the damaged transformer, informed medical personnel of the composition of the transformer fluid. A health emergency was declared and all personnel except for emergency workers, including fire and police personnel, evacuated the entire governmental complex. This ban on the use of the City and County Buildings continued for a total of 4 days, through the weekend. The State Office building could not be used because of loss of electrical power. The parking garage under the governmental complex was contaminated with levels of PCBs, as high as 2,000 to 4,000 micrograms per square meter, employing hexane soaked wet wipes on the concrete floor. After its contamination was appreciated, it was closed, steam and detergent cleaned twice, tested for PCBs, dioxins, and furan levels, and then reopened several months later.

A command post was set up on the fourth floor of the adjacent City Hall which was used for the next few weeks by workers involved in the incident until the recognition of toxic chemicals lead to the use of a trailer and portable toilets nearer the building and geographically removed from non involved workers.

Within days cleanup work began on the BSOB to remove the soot covered material found throughout the building. Both experts in toxic chemical removal were employed as well as janitorial workers of the State of New York who began washing and vacuuming the building. Electrical system repair was begun during the first week after the incident. The goal initially set by the State of New York, the owner of the polluted building, was to open the building within days or, if necessary, weeks. This goal was set on day two of the incident. This initial goal assumed that contamination of the air with PCBs and chlorinated benzenes constituted the totality of the chemical contamination. Because of the electrical failure venting of the building to the outside air was not possible. The windows of the building do not open.

CHEMICAL ANALYSIS

Initial chemical sampling and analysis performed by Mr. Charles Garner, an industrial hygienist on loan from the nearby IBM Corporation factory confirmed the presence of chemicals consistent with those in the transformer in the air of the basement and first floor of City Hall. Later study revealed air ducts running from the BSOB into the basement area of the immediately adjacent City Hall. Air and soot samples collected several days after the incident and analyzed by Galson Laboratory and separately by Dr. James Carnahan of the General Electric Company revealed PCBs present within soot as well as air levels as high as 80 micrograms per cubic meter within the BSOB and many floors above the transformer several days after the incident. Air levels of PCBs fell to a level of 1-3 micrograms per cubic meter, and these levels persisted for over a year when



Photographs of the Governmental Complex in Binghamton New York, from top left, clock-wise: The Governmental Complex with the County Building of the left, then the State Office Building, followed by City Hall and the City Council Chambers. A desk with soot on it and a window, photographically darkened, in the State Office Building. A worker in the polluted building apparently wearing an asbestos protective mask rather than a NIOSH approved mask protective against organic vapors and particulate matter. The damaged electrical panel (left), the damaged transformer and an apparently undamaged electrical panel. Soot is apparent. A cleanup worker in February, 1981, in the contaminated building, not wearing his gloves or mask and with an open protective suit exposing his own clothes.

measured by standard methods sampling and analyzing PCBs in air. Analysis of soot samples collected in a number of floors in the building revealed levels of Arochlor 1254 as high as 10 to 20% by weight. There was not a readily apparent pattern to the soot or PCB distribution. PCBs were measured in elevated amounts even where no visible soot existed, as in the first floor cafeteria. Sampling of the fourth through seventh floors, and the corresponding stairwells where soot of a flocular nature as well as heavy despositions of soot were found, revealed PCB contamination in all areas initially sampled. These included, floors, walls, light fixtures, ceiling panels, sprayed on insulation and beams within hidden aspects above the false ceiling (plenums), within file cases and desk drawers, and later, within air ducts and elevator shafts. The area of visibly most obvious soot was in the men's bathrooms especially in the middle floors such as the fourth through seventh floors where soot was noted to have flowed from the air vent areas through the metal grating into the bathrooms and under the bathroom doors into the general office work areas. According to verbal accounts from Binghamton firemen they did not find this distribution of soot remarkable. Sampling for PCBs from other buildings in downtown Binghamton, revealed levels from 0.1 to 0.7 micrograms per square meter in older buildings to non detectable in some newer buildings employing a dry (filter paper) wipe sampling technique on floors, desks and walls. Within seven days after the incident Dr. James Carnahan of the General Electric Company Laboratory at Schenectady, New York notified us that furan isomers were present in the B50B soot in amounts above what might have existed from trace contamination of the original transformer fluid. This suggested pyrolytic conversion of the PCBs as previously found under laboratory and industrial conditions. It also raised the possibility of similar pyrolytic conversion of the polychlorinated benzenes to the somewhat more toxic dioxin isomers. An elequent isomer analysis of a sample of soot was performed by Dr. David Stalling of the US Fish and Wildlife Bureau which extended the previous furan findings by providing confirmation of specific furan isomers and also described the finding of dioxins and biphenylenes. The presence of the dioxins including the highly toxic 2,3, 7,8 tetra chlorinated dioxin isomer was later described by Dr. Patrick O'Keefe and colleagues at the New York State Health Department as well as by Dr. Christoffer Rappe and Dr. Hans Buser. Each laboratory and each sample led to somewhat different values as would be expected given the non homogeneous nature of the soot and the technical difficulty of the chemical separations and analysis. Later analysis confirmed the differing amount of these various chemicals in various locations within the building.

Later analysis of the concrete parking garage floor after two slow detergent cleanings showed small amounts of total furan and dioxin isomers at levels as high as 127 nanograms total for those isomers measured, with the furans markedly predominating. An adjacent building's parking garage, also less than 12 years old, had essentially non detectable levels of furans and dioxins present; hexane or benzene extraction type wipe technique was employed in the latter instances in order to extract a higher percent of the total amount of chemicals present, usually we found from 1:1 to 10:1 ratios of PCBs on adjacent sections of contaminated floor or concrete by "wet" (solvent) wiping or dry wipe technique, respectively. Analysis performed by Prof. James Spalik of B.C.C.

A representative finding among the initial chemical analysis is that of Christoffer Rappe and Hans Buser which showed:

A. PCDD	Total level	20	ppm
2,3,7,8-Tetra-CDD		0.6	ppm
4 other isomers			
(1,3,7,8-, 1,4,7,8-, 1,2,3,7-			
or 1,2,3,8- and 1,2,7,8- 1,4,6,9-)		0.6	ppm
Total level tetra-CDDs		1.2	ppm
1,2,3,7,8-Penta-CDD		2.5	ppm
7 other penta-CDD isomers		2.5	ppm

	Total level penta-CDDs		5.0	ppm
	1,2,3,4,6,8- + 1,2,4,6,7,9-Hexa-CDD		1.2	ppm
	1,2,3,6,8,9-Hexa-CDD		1.3	ppm
	1,2,3,4,7,8-Hexa-CDD		0.7	ppm
	1,2,3,6,7,8-Hexa-CDD		0.6	ppm
	1,2,3,7,8,9-Hexa-CDD		0.4	ppm
	1,2,3,4,6,7-Hexa-CDD		0.5	ppm
	Total level hexa-CDDs		4.7	ppm
	1,2,3,4,6,7,9-Hepta-CDD		4	ppm
	1,2,3,4,6,7,8-Hepta-CDD		3	ppm
	Total level hepta-CDDs		7	ppm
	Octa-CDD		2	ppm
8.	PCDFs	Total level	2160	ppm
	2,3,7,8-Tetra-CDF		12	ppm
	1,3,7,9-Tetra-CDF		1	ppm
	6 other tetra-CDF isomers		15	ppm
	Total level of tetra-CDFs		28	ppm
	1,3,4,7,8-Penta-CDF		65	ppm
	1,2,4,7,8-Penta-CDF		25	ppm
	1,2,4,7,9-Penta-CDF		22	ppm
	1,2,3,7,8-Penta-CDF		310	ppm
	1,2,3,6,7-Penta-CDF		60	ppm
	1,2,6,7,8-Penta-CDF		25	ppm
	2,3,4,7,8-Penta-CDF		48	ppm
	2,3,4,6,7-Penta-CDF		12	ppm
	12 other penta-CDF isomers		110	ppm
	Total level penta-CDFs		670	ppm
	1,2,3,4,6,8-Hexa-CDF		30	ppm
	1,3,4,6,7,8-Hexa-CDF		125	ppm
	1,2,4,6,7,8-Hexa-CDF		50	ppm
	1,2,3,4,7,8-Hexa-CDF		310	ppm
	Total level hexa-CDF		515	ppm

Patrick O'Keefe & Smith New York State Health Department, 1981

2,3,7,8 TCDD & 2,3,7,8 TCDF

Transformer Soot - Binghamton State Office Building

Analytical Result (ppm)

Sample	TCDD(1)	TCDF(2)
Binghamton soot #1	3	273
Binghamton soot #2	4	124
Average Value	3.5	200

Both samples were composite soot taken from floors 3 & 4

(1) 2,3,7,8 TCDD - Tetrachlorodibenzo paradioxin
(2) 2,3,7,8 TCDF - Tetrachlorodibenzo furan

David Stalling, Ph.D., United States Fish and Wildlife Bureau, 1981

Binghamton State Office Building Soot

TCDD 5 ppm	2378 Tetra CDD TCDDS	
Tetra - CDFs	5.4	ppm
Penta - CDFs	105	ppm
Hexa - CDFs	512	ppm
Hepta - CDFs	101	ppm
Octa - CDFs	30	ppm
Total Furans	753.4	ppm
Biphenylenes	50	ppm

WRIGHT STATE UNIVERSITY, BREHM LABORATORY, DAYTON, OHIO 45435
RESULTS OF HRGC/LRMS ANALYSIS OF WIPE SAMPLE BRO-4 (BROOME COUNTY NO. 4) FOR TETRA- THROUGH OCTA-CHLORINATED DIBENZO-p-DIOXINS AND DIBENZOFURANS.

Government Complex Parking Garage (After Cleaning) Dr. Thomas Tiernan, 1982

CDD/CDF	Apparent Isomers	Quantity of CDD/CDF Detedted (ng/wipe)	Minimum Detectable Quantity (ng per isomer)	%Recovery of Internal stds
TEcdd	N.D.	N.D.	0.10	100
	$^{37}Cl_4$-2,3,7,8	----	----	
PCDD	N.D.	N.D.	0.10	
HxCDD	N.D.	N.D.	0.20	
HpCDD	1,2,3,4,6,7,8	0.65	0.20	
	1,2,3,4,6,7,9	0.45	0.20	
	Total	1.1	0.20	
	$^{37}Cl_4$- 1,2,3,4,6,7,8	----	----	100

CDD/CDF	Apparent Isomers	Quantity of CDD/CDF Detected (ng/wipe)	Minimum Detectable Quantity (ng per isomer)	% Recovery of Internal Stds.
OCDD	1,2,3,4,6,7,8,9	1.0	0.20	
	$^{37}Cl_8$OCDD	----	----	100
TCDF	1,2,4,8	2.0	0.10	
	2,3,6,8	3.1	0.10	
	2,3,7,8	9.6	0.10	
	Other isomers (8)	35.8	0.10	
	Total	50.4	0.10	
PCDF	1,2,4,7,8	5.2	0.10	
	Other isomers (13)	11.8	0.10	
	Total	17.0	0.10	
HxCDF	1,2,4,6,7,9	1.6	0.20	
	Other isomers (12)	43.6	0.20	
	Total	45.2	0.20	
HpCDF	1,2,3,4,6,8,9	2.7	0.20	
	Other isomers (4)	4.6	0.20	
	Total	7.3	0.20	
OCDF	1,2,3,4,6,7,8,9	7.3	0.20	

MEDICAL ASPECTS OF THE INCIDENT

Toxic chemicals including those found in the Binghamton electrical panel transformer incident have been implicated in an increasing variety of medical disorders especially in a variety of annual species. These include skin lesions, cancers, adverse reproductive outcomes, central and peripheral nervous system as well as gastrointestinal disorders, immunologic deficiencies, and other pathologic conditions.

Initially, some of those exposed to the Binghamton chemical complex complained of skin rashes, headaches, irritability, anxiety, difficulty sleeping, sexual difficulties, and tingling of the extremities. A collaborative medical surveillance was established which accepted all persons exposed or who thought they were exposed to the toxic chemicals involved. The results of this activity, which includes about 500 persons, are still far from complete at this time. Evaluation included a medical history and physical examination, hematologic tests of blood, blood chemistries for 22 substances including liver enzymes and triglyceride and cholesterol levels from fasting patients. Urine was sometimes taken. Blood PCB tests were ordered but are not yet completely analyzed and available. Special fat analysis for PCBs, furans and dioxin isomers was performed. Lymphocyte function studies and urine porphorin analysis was performed on one patient.

Elevated liver enzymes and triglyceride and cholesterol levels were found in some of the 500 patients without etiology being well characterized. The percent of abnormal laboratory examinations may or may not be above that expected from a matched control population. Estimates of exposure to the chemicals in question proved a problem. Ideally, serum PCB, furan and dioxin levels as well as cytochrome P 450 & 448, liver enzymes, cholesterol triglycerides, liver levels before and immediately after exposure might have proved helpful but were not available. Workers in the building after the initial cleanup effort do in fact have preentry as well as exit medical evaluations including blood PCB levels.

As would be expected from such a large group of persons exposed in this incident a number of medical conditions have arisen, as diverse as malignant melanoma of the skin and transient erythema of the face to fetal damage and wastage where the husband was the exposed partner, to serious psychiatric disorders including an obsession with the exposure to these toxic chemicals followed by a suicide attempt with the patient still comatose months after the attempt. Establishing etiology regarding causation of any of

these medical abnormalities with respect to the toxic chemicals remains as elusive at the present time as establishing exposure levels of individual patients.

It is not the purpose of this paper to review medical aspects of the diagnostic pathologic, and possible treatment options which confront physicians or health officials faced with problems of patients who may have been exposed to toxic chemicals in combinations produced by electrical system incidents such as the one documented in this paper. Likewise, I will not review the various animal toxicologic tests, including rabbit skin, guinea pig LD 50, electron microscopic examinations of guinea pig liver tissue, chick embryo tests and others performed or under way at this time in an attempt to characterize the toxicity of the Binghamton soot. It is important to note that the soot has not inactivated these chemicals as shown by chick embryo fetotoxicity and terotogenicity demonstrated in pilot tests with the Binghamton soot but not with fireplace soot or activated charcoal as well as guinea pig LD 50 testing.

At the present time over one billion dollars in law suits or the intention to file law suits have been filed primarily against the State of New York as the owner of the polluted building. Under New York State Law it is necessary to file an "Intention to Sue" within a given time frame in order not to lose the right at some future date to sue the State of New York for damages recognized at a later date. Such damage derived from an incident might include cancer or other conditions not apparent initially. Damages awarded under the American judicial system might take into account punitive as well as compensatory damages, and include loss of income, medical costs. and other items.

In addition the question of jurisdiction arises. Usually a city or county would declare a potential health hazard through its health department, acting partly under legal powers granted by State Government. The Federal Government has standing in certain instances, through the Environmental Protection Agency (E.P.A.), the Occupational Safety and Health Administration (OSHA) or the National Institute on Occupational Safety and Health (NIOSH) as well as other agencies on certain occasions. Here the State of New York found itself the inadvertant owner of a polluted building. Instead of its customary role in acting as a regulator, the State found itself in the role of pollutor. Questions defining which agency regulates a given governmental agency which becomes a pollutor is an aspect of law and public policy which has not been previously addressed to the best of our knowledge in circumstances similar to the Binghamton incident.

It is however, worthy of note that in the United States at this time a Federal Anency such as the EPA will not enter such disasters without the approval of the State authorities. Because of this entry of the E.P.A. was delayed several months until their aid was sought and obtained by the senior Senator from the State of New York, Senator Patrick Moynihan.

CONCLUSIONS and DISCUSSION

At this early time less than two years after the Binghamton (State Office Building) incident there are some tentative conclusions which may be made:

1. Electrical incidents involving PCB and polychlorinated benzene containing transformers, capacitators, ballasts etc. constitute a previously unrecognized health hazard by exposing persons in non industrial sites including offices and schools to such toxic chemicals as PCB's, furans, dioxins, biphenylenes, and other related compounds. Several similar incidents including a Binghamton City Hall capacitor incident producing air levels of 80 micrograms per cubic meter were noted in Binghamton during the year after the incident.

2. The presence of these chemicals has not been previously documented in similar circumstances so that long term exposure to small or other than small amounts of a combination of toxic chemicals of this kind has probably been occurring in industrial countries since 1929 when widespread use of PCB's began. These incidents may be contributing to environmentally induced or promoted cancers, reproductive abnormalities, immunologic deficiency, and possibly premature death from infection, neurologic and gastrointestinal system pathology and possibly, by elevating serum triglyceride and cholesterol levels, excess or avoidable cardiovascular and cerebrovascular pathology.

3. Prevention of some of these incidents is relatively easily and economically achieved by redesigning and enclosing PCB containing transformers and other PCB containing elect-

rical systems. Many transformers are already in contained areas. Others, like the Binghamton transformer, are placed in a fashion which easily may lead to significant contamination of the building. Future buildings must be constructed with this newly described potential health hazard in mind and preexisting buildings must be evaluated carefully and, if necessary, appropriate safety features added. Improved circuit breakers or fuses are certainly desirable. Adequate fire safety and temperature decreasing devices can be installed to prevent incidents similar to the Binghamton incident.

4. Removal and replacement of PCB and polychlorinated benzene containing transformers, capacitors, ballasts, etc. must clearly be considered if health risks warrant such measures. Refilling transformers as with silicon may diminish the risk. "Dry" transformers, with no fluid, may offer improved safety, at least with respect to toxic chemical exposure. Mineral oil containing transformers, while posing a fire hazard, appear to be less of a toxic chemical threat.

5. There is no unanimity regarding standards for PCB's in gaseous phase even in industry at this time. The current United States OSHA standard for PCB's in air for industry is 500 or 1000 micrograms per cubic meter, depending on the isomer mix. However a National Institute on Occupational Safety and Health (NIOSH) Criteria Document has taken the position, that no exposure to PCB's should be considered safe or desirable. To implement that point of view it was suggested in that document that one microgram per cubic meter, the minimum level of detection at that time, be used as a value to replace the 500 or 1000 micrograms per cubic meter standard. Different values may well have to be established for young children, pregnant women, and other special cases to adequately satisfy conditions as demanding as those found in Binghamton and doubtlessly elsewhere, simply awaiting confirmatory chemical analysis. Standards for PCB's in soot, or for dioxins, furans and biphenylenes in soot or air need to be established.

6. National and international levels for those chemicals must be established not only for buildings and various portions of these buildings, such elevator shafts, air ducts, and elsewhere, but also for human body fluids and organs. At present, serum and fat determinations of PCB, dioxin, and furan isomer levels are in early stages of being used to attempt to document levels of exposure. Individual isomer analysis of body tissues may prove useful. As clinicians we have values to consider for lead, arsenic and other chemicals in body fluids, but we do not currently have clinically meaningful values for dioxins, furans, biphenylenes or PCB's. Determination of metabolic pathways and usefulness of blood, fat, urine or fecal levels of these compounds and their metabolities will doubtlessly lead to data useful to clinicians evaluating and treating patients after related incidents.

7. Because toxic chemical exposure is a rapidly increasing health problem, it may be appropriate that serum be drawn and stored for all willing members of the population at several points in time in order that comparisons be made when indicated to be able to evaluate level of exposure after an individual incident. At the very least, none elevated but low levels of a given chemical found after chemical contamination might prove quite reassuring to a patient. In the Binghamton incident persons without previous blood samples available were exposed to various amounts of PCB's, dioxins, furans, biphenylenes and other pyrolytic byproducts. Because of this, blood PCB and furan and dioxin analysis will be very difficult to interpret. Fish from the Hudson River in New York are frequently high in PCB levels and fish from the Great Lakes have been found to contain significant levels (in parts per trillion, P.P.T.) of dioxins, including 2,3,7,8 TCDD. Previous exposure to industrial chemicals or herbicides containing dioxins, PCB's or furans provides further confounding variables. With a presumed relatively low level exposure for most of the original 500 persons under medical surveillance it will be difficult to differentiate origin of postive but low levels of PCB's found in body tissues. Isomer analysis and fat biopsy data may be of value but these techniques are still experimental and the amounts present, expecially since some samples were taken long after the incident, may be too low to detect accurately at this time. Frozen samples for future analysis may prove useful.

8. Medical surveillance of exposed populations following similar instances from both an occupational medicine standpoint as well as an epidemiologically oriented study is desirable. For the individual patient and his or her physician knowing what to look for, and when, and possibly being able to decrease body burden of these toxic chemicals if present

in elevated levels by pharmacological or other means is certainly medically desirable. Although epidemiology provides only a weak tool for dealing with relatively small numbers of persons or subtle events, it certainly may be of some usefulness in events such as this one. Certainly, as better physiological indices of exposure become available, whether urinary porphyrin patterns, fat, blood, urine or fecal chemical analysis for the chemicals, cytochrome P450 or P448 alterations, electron microscopic lesions of hepatic parenchymal cells characteristic or pathognomonic of toxic chemical exposure, patterns of elevated liver enzymes or increased serum cholesterol or triglycerides, enhance the usefulness of large scale collaborative studies and registries will come to be of markedly enhanced value. At present, relatively small numbers of patients as well as imprecise estimates of exposure constitute major problems in human studies.

9. Intense multispecialty research into all aspects of such accidents is needed. Psychiatric research to understand and prevent psychiatric illness following these environmental incidents is especially needed. Medical research considering how patients exposed should best be monitored and eventually treated is urgently indicated. Further research to explain why chemicals which seem so toxic in numerous animal species have not been demonstrated to be as toxic in man is essential to differentiate between species differences which might show man relatively impervious to these chemicals or simply to establish better studies demonstrating toxicity in humans. Better, faster, cheaper, readily performed sampling and chemical analysis techniques are certainly needed. Dioxin and furan isomer analysis frequently cost $1,000 to $2,000 each and take months to complete. These are far too costly for most parties involved and almost no organization is willing to shut down entirely for months waiting to learn whether or not a potential health hazard exists.

Legal and legislative research is needed in order to consider whether the current adversarial and legal approach to redressing wrongs and hopefully obtaining justice through law suits, now epidemic in the United States, is the most reasonable approach to justice for those injured by incidents of toxic chemical contamination. Legislative alternatives to the judicial process are possible, such as workman's compensation, or specialized approaches similar to the black lung coal mining legislative approach which supposes that working in a mine for a given number of years followed by lung diseases of certain kinds are compensable without involving a court of law are also possible. In Australia, Veterans of the Vietnam War who become ill in a fashion which might be attibuted to toxic chemical exposure are compensated unless the government can prove that the illness was not caused by Agent Orange containing 2,3,7,8, TCDD. Each of these financial and legal approaches has advantages and disadvantages, but the toxicity of these chemicals in man may remain subject to vigorous research and disagreement for many years. While scientists continue the tedious and necessary research to its ultimate but slow course justice will be sought in one way or another by those exposed to toxic chemicals at great cost to all involved.

10. Interdisciplinary communication with scientific colleagues and the general public with frequency as well as maximum clarity is essential. Meetings such as The International Dioxin Conferences with promptly published proceedings, and with maximum participation of numerous views is desirable. Hopefully future meetings will also have scientific presentations from colleagues in sociology, psychology, law, anthropology, political science and case studies from physicians and from affected persons themselves in order that we may communicate most effectively in an interdisciplinary fashion and learn from one another. Possibly even panel sessions including responsible and knowledgeable members of the press would contribute to increased understanding and better communication between those involved in past and future incidents involving these toxic chemicals.

CHEMOSPHERE (1979) 6 157-174

FORMATION OF POLYCHLORINATED DIBENZOFURANS (PCDFs) FROM THE PYROLYSIS OF INDIVIDUAL PCB ISOMERS

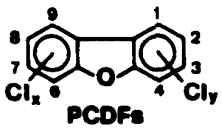
Hans Rudolf Buser
Swiss Federal Research Station
CH - 8820 Wadenswil, Switzerland

and

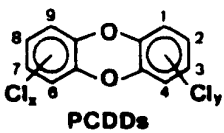
Christoffer Rappe
Department of Organic Chemistry, University of Umeå
S - 901 87 Umeå, Sweden

Introduction

The polychlorinated dibenzofurans (PCDFs, structure see below) are a series of tricyclic aromatic compounds, in chemical, biological and toxicological respects very similar to the polychlorinated dibenzo-p-dioxins (PCDDs, see below).[1]



PCDFs

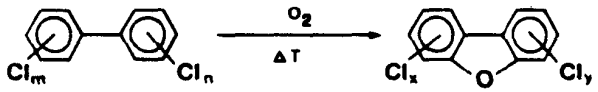


PCDDs

In all, there is a total of 135 different positional PCDF isomers, namely 4 mono-, 16 di-, 28 tri-, 38 tetra-, 28 penta-, 16 hexa-, 4 hepta- and 1 octa-CDF. The most toxic isomers appear to be the 2,3,7,8-tetra-, 1,2,3,7,8- and 2,3,4,7,8-penta-CDF, which all can be compared to the extremely toxic 2,3,7,8-tetra-CDD,[2,3] and which all have been implicated in the Yusho poisoning.[4,5]

PCDFs have been identified as undesired trace contaminants in chlor[illegible] derivatives like phenoxy acids[7] and in polychlorinated biphenyls[illegible].[8] Most recently, PCDFs have been identified in fly ash and flue gases of municipal incinerators and industrial heating facilities.[9,10] They might be ubiquitous products of combustion processes.[11,12]

PCBs are industrial chemicals of wide use and they are now known to be widely distributed in the environment. Although the thermal conversion of PCBs into PCDFs under pyrolytic conditions could be expected, experimental evidence to our knowledge was not reported prior to our previous papers.[10,13]



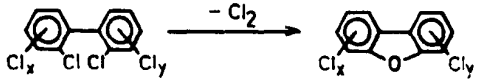
PCBs **PCDFs** $x+y \leq m+n$

However, increased levels of PCDFs (ppm-range) were observed in a PCB heated to 300° for a week in the presence of air, and in a PCB used in a heat exchange system for extended periods of time.[14,15]

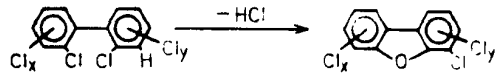
In our previous papers we have reported on the formation of PCDFs from the pyrolysis of commercial PCBs (Aroclor 1254 and 1260).[10,13] These pyrolyses were carried out in sealed quartz mini-ampoules in the presence of air at temperatures of 500-700° C. The yields of the PCDFs were in the [illegible] range. In addition to PCDFs, unreacted PCBs, chlorinated benzenes, naphthalenes and other chlorinated compounds were also observed; polychlorinated hydroxybiphenyls were found as possible intermediate products.

By using high-resolution GC and MS, we have further shown that most of the major PCDF isomers found in two fly ash samples were the same as those formed in the pyrolysis of the most common commercial PCBs, giving strong support that these PCDFs originate from the uncontrolled burning of PCBs. Using individual PCB isomers, we have also found that the cyclization processes in these pyrolyses are intramolecular and we have postulated the following three reaction routes leading to different PCDF isomers from the same PCB:[10]

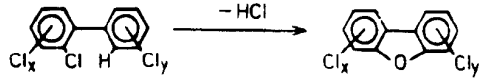
<u>reaction route 1</u>:
(loss of <u>ortho</u>-Cl_2)



reaction route 2:
(loss of HCl involving a 2,3-chlorine shift)

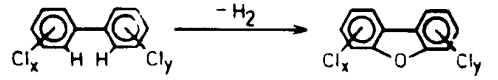


reaction route 3:
(loss of ortho-HCl)



In this paper now the occurrence of these reaction routes in the pyrolysis of individual PCBs is further documented. The formation of PCDFs was investigated in pyrolysis experiments using [illegible] biphenyl. Our experiments show the generality of the above reactions, and these can be used to predict the formation of specific PCDFs. A fourth, additional reaction route was found to occur with some PCB isomers:

reaction route 4:
(loss of ortho-H_2)



Experimental

Polychlorinated biphenyls used for pyrolysis

Eighteen PCB isomers were obtained from various sources as listed in Table I. The isomers were checked for isomeric purity and absence of PCDFs using GC-MS as previously described. Single peaks were obtained and purity was found to be generally [illegible] of the PCBs contained detectable quantities of PCDFs (<0.1%). Standard solutions were prepared at concentrations of 1-10 ng/ml in benzene.

Micropyrolysis of PCBs

Individual PCB isomers (100 µg each) were pyrolyzed at 800°C in separate quartz microampoules. The exact pyrolysis conditions were as previously described.[11] After [illegible] ml of benzene was added to each ampoule. A 2-ml aliquot was used directly for analysis.

Table 1. List and sources of PCB isomers investigated

Compound	Source	Compound	Source
2,3,4,5-tetrachlorobiphenyl	a	2,4,5,2',4',5'-hexachlorobiphenyl	b
2,3,5,6-	a	2,4,6,2',4',6'-	b
2,6,2',6'-	b	2,4,5,2',4',6'-	c
		2,3,4,2',3',4'-	d
		2,3,5,2',3',5'-	d
		2,3,6,2',3',6'-	a
2,3,4,5,6-pentachlorobiphenyl	c	3,4,5,3',4',5'-	d
2,4,5,2',5'-	c	2,3,4,5,2',3',4'-heptachlorobiphenyl	e
2,4,6,3',4'-	d	2,3,4,5,2',4',5'-	e
2,4,6,2',4'-	c		
2,3,6,2',5'-	a	2,3,4,5,2',3',4',5'-octachlorobiphenyl	c

a = Dr. J. McKinney, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

b = Dr. K. Andersson, University of Umeå, Umeå, Sweden

c = RFR Corp., Hope, RI, USA, courtesy of Dr. J. McKinney

d = Dr. C.A. Wachtmeister, University of Stockholm, Stockholm, Sweden

e = Dr. Y. Masuda, Daiichi College of Pharmaceutical Sciences, Fukuoka, Japan

GC-MS Analysis

A Finnigan 4000 quadrupole GC-MS instrument with EI source and coupled to a 50 m 0.36 mm ID OV-17 glass capillary column was used. The column was interfaced to the MS via a platinum capillary interface. The operating conditions were as previously described,[10] however, the column showed somewhat higher elution temperatures for PCDFs (same order of elution) than a previous OV-17 column interfaced via a glass lined stainless steel tube.

In a first phase, complete mass spectra were recorded using the data system. In a second phase, the samples were reanalyzed with optimal isomer separation using mass specific detection (mass fragmentography) of PCDFs by monitoring molecular ions at m/z 270, 304, 338, 372, 406 and 440 for the tri- to octachloro compounds.

Standard and reference PCDF isomers

The PCDF isomers available as reference and standard compounds for the present investigation are listed in Table 2. They were the gifts of Drs. Masuda, McKinney, Morita and Poland, and of Mr. Garå and Mr. Lindahl. In Figure 1, we give mass fragmentograms of a composite sample of these compounds showing the elution of tetra-, penta- and hexa-CDFs (peak identifications given in Table 2).

In addition, we established the elution order of the 4 hepta-CDFs (1,2,3,4,6,7,8- < 1,2,3,4,6,7,9- < 1,2,3,4,6,8,9- < 1,2,3,4,7,8,9- ; all separated on OV-17, see Figure 5) from chlorination experiments ($SbCl_5$ in CCl_4, 15 min at 50°C) using 2,3,7,8-tetra-, 1,3,4,7,9-penta- and 1,2,4,6,8,9-hexa-CDF; 1,2,3,4,6,7,9-hepta-CDF was present as minor product in 2,3,4,6,7,8-hexa-CDF.

Table 2. Standard and reference PCDFs used in the present study

Compound	Peak number (see Fig. 1)	Source and remarks
2,3,8-tri-CDF	-	a
1,3,6,8-tetra-CDF	1	a,b
1,3,7,8-	2	b
2,4,6,8-	3	b,c
1,3,6,7-	4	a
1,2,4,6-	5	a
2,3,6,8-	6	a,d
2,3,7,8-	7	e
3,4,6,7-	8	a
1,2,4,6,8-penta-CDF	9	c,f
1,3,4,7,8-	10	b (contains also 1,3,4,6,8-penta-CDF)
1,2,4,7,8-	11	d,b (contains also 1,2,4,6,8-penta-CDF)
1,3,4,7,9-	12	b
1,2,3,7,8-	13	g
2,3,4,6,8-	14	c,f
1,2,3,4,8-	15	f
1,2,3,6,7-	16	d
2,3,4,8,9-	17	d
2,3,4,7,8-	18	e
1,3,4,8,9-	19	b (contains also 1,3,4,7,8-penta-CDF)
2,3,4,6,7-	20	d
1,2,4,8,9-	21	b (contains also 1,2,4,7,8-penta-CDF)
1,2,3,4,6,8-hexa-CDF	22	c,f
1,2,4,6,7,8-	23	c,f
1,2,4,6,8,9-	24	c
1,2,3,4,7,8-	25	d
1,2,3,6,7,8-	26	d
2,3,4,6,7,8-	27	c,f (contains also 1,2,3,4,6,7,8-hepta-CDF)
1,2,3,4,6,7,8-hepta-CDF	-	c,f (contains also 2,3,4,6,7,8-hexa-CDF)

a = Dr. M. Morita, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan

b = Mr. R. Lindahl, University of Umeå, Sweden; prepared through Pd(II) acetate cyclization of polychlorinated diphenylether.[16]

c = Mr. A. Garå, University of Umeå, Sweden; prepared from 2,7-dibromo-dibenzofuran by acetylation, chlorination and reduction.[17]

d = Dr. Y. Masuda, Daiichi College of Pharmaceutical Sciences, Fukuoka, Japan

e = Dr. J. McKinney, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

f = Mr. A. Garå, University of Umeå, Sweden; prepared through Pd(II) acetate cyclization of polychlorinated diphenylether.[16]

g = Dr. A. Poland, McArdle Laboratory, Madison, Wisc., USA

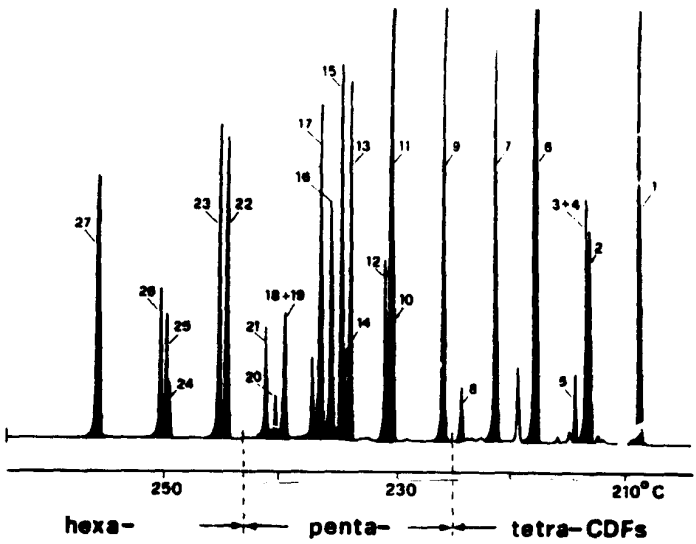


Figure 1 : Mass fragmentograms (m/e 304, 338 and 372) of a composite sample of different PCDF reference compounds showing elution of tetra-, penta- and hexa-CDFs (for peak identifications see Table 1); 50 m SE-54 glass capillary column, 100-260° at 2°/min, 260° (30 min).

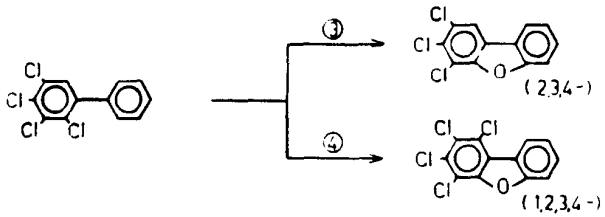
Results and Discussion

Pyrolysis of tetrachlorobiphenyls

The pyrolysis of three tetrachlorobiphenyls was studied (see Table 1). The fragmentograms of the pyrolyzed samples are given in Figure 2, from which the yields of tri- and tetra-CDFs.

The pyrolysis of 2,3,4,5-tetrachlorobiphenyl lead to the formation of a tri- and a tetra-CDF (see Figure 2a). The former is expected to be 2,3,4-tri-CDF formed via reaction route 3 (see Scheme below). The formation of a tetra-CDF from this PCB has to involve a new, previously[12] not observed reaction route with loss of ortho-Cl, cyclization route 4, Scheme below); the isomer expected is 1,2,3,4-tetra-CDF. The same tetra-CDF was also found from the pyrolysis of 2,3,4,5,6-pentachlorobiphenyl (see later) and 2,3,4,5-tetrachlorobiphenyl via reaction routes 1 and

and in fact only very minor amounts of additional isomers were observed.



As shown in Figure 3a, the pyrolysis of 2,3,3',4-tetrachlorobiphenyl leads to the formation of a tri-CDF. The product expected is 1,2,4-tri-CDF formed via route ③ in Fig. 3. The formation of di-, tri- and tetra-CDFs from this PCB via reaction routes ①, ② and ④ is not possible and in fact no additional PCDFs were observed.

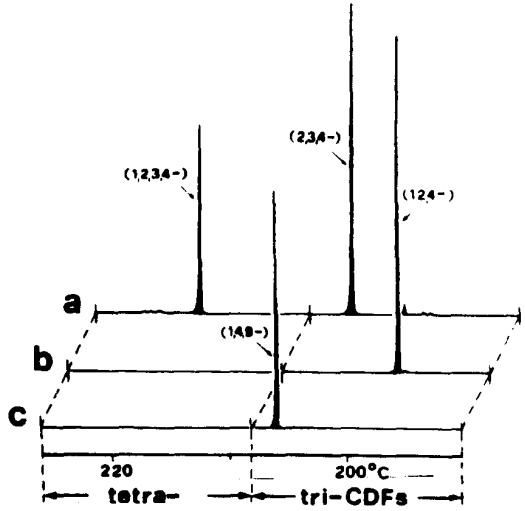
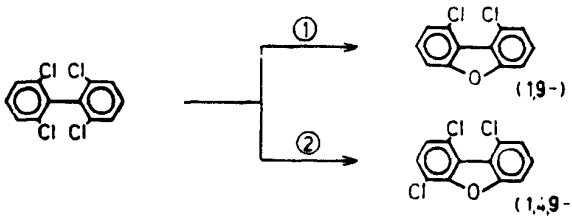


Figure 2 : Mass fragmentograms (m/e 270 and 304) of pyrolyzed tetrachlorobiphenyls showing elution of tri- and tetra-CDFs from (a) 2,3,3',4,5-, (b) 2,3,5,6-and (c) 2,3',4',5,6'-tetrachlorobiphenyl. Column conditions as in Figure 1. Retention times of CDFs identified are given in parenthesis.

As previously reported,[10] the pyrolysis of 2,6,2',6'-tetrachlorobiphenyl yielded a di- and a tri-CDF (elution of tri-CDF shown in Figure 2a). The expected di-CDF is the 1,9- substituted isomer formed via reaction route 1. The formation of a tri-CDF from this tetrachlorobiphenyl has to involve a rearrangement reaction; the isomer expected is 1,4,9-tri-CDF (reaction route 2). This PCB cannot form tri- and tetra-CDFs via reaction routes 3 and 4, and again no additional PCDFs were observed.

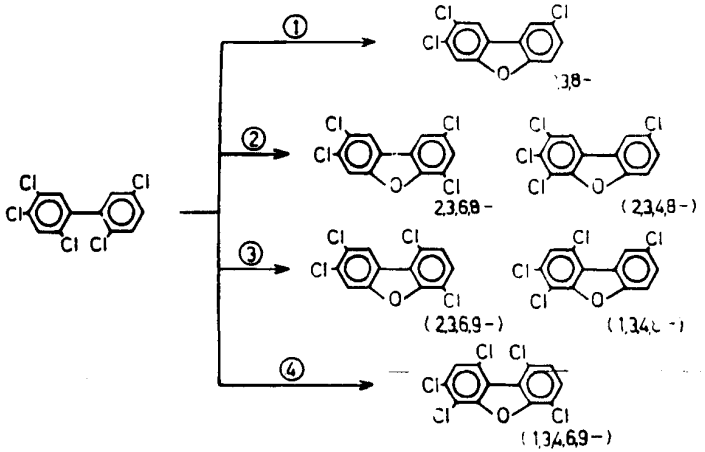


Pyrolysis of pentachlorobiphenyls

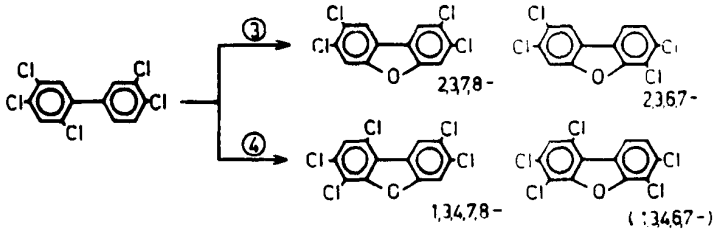
The pyrolysis of five pentachlorobiphenyls was investigated (see Table 1). Mass fragmentograms showing the elution of tri-, tetra- and penta-CDFs are given in Figure 3.

The pyrolysis of 2,3,4,5,6-pentachlorobiphenyl lead to the formation of a tetra-CDF as the major product and smaller amount of four tri-CDFs (see Figure 3a). The tetra-CDF expected is the 1,2,3,4-substituted isomer formed via reaction route 1; the same isomer was also observed from the pyrolysis of 2,3,4,5-tetrachlorobiphenyl. The formation of PCDFs via reaction routes 1, 2 and 4 is not possible from this PCB. The finding of small amounts of tri-CDFs could mean that these PCDFs are formed in a non-specific dechlorination process of 1,2,3,4-tetra-CDF or of pentachlorobiphenyl prior to cyclization. In either case, the expected PCDFs contain Cl-substituents exclusively in one of the two carbon rings of the dibenzofuran nucleus (4 possible isomers). Two of these tri-CDFs were tentatively identified as 1,2,4- and 2,3,4-tri-CDFs, pyrolysis products of 2,3,4,5- and 2,3,5,6-tetrachlorobiphenyl (see Figure 2a and b).

As shown in Figure 3b, 2,4,5,2',5'-pentachlorobiphenyl formed a major tri-CDF and smaller amounts of 4 tetra-CDFs and a penta-CDF. This number of PCDFs can be expected from the pyrolysis of this PCB via reaction routes 1, 2, 3 and 4 (see Scheme below). PCDFs identified by co-chromatography with reference compounds (see Table 2) were 2,3,8-tri- and 2,3,6,8-tetra-CDF formed via reaction routes 1 and 2, respectively. So far, no attempts have been made to assign the remaining tetra-CDFs. A small amount of a penta-CDF was observed; the expected compound is 1,3,4,6,9-penta-CDF formed via reaction route 1.



The pyrolysis of 2,4,5,3',4'-pentachlorobiphenyl lead to the formation of two tetra- and a penta-CDF (see Figure 3c). No tri-CDFs can be expected from this PCB via reaction route 1. The two tetra-CDFs were identified by co-chromatography with reference compounds (see Table 2) as the 2,3,7,8- and 2,3,6,7- substituted isomers, formed via reaction route 3. This PCB cannot form tetra-CDFs via reaction route 2 and in fact no additional tetra-CDFs were observed. Pyrolysis of this PCB is expected to form two penta-CDFs via reaction route 4, namely 1,3,4,7,8- and 1,3,4,6,7-penta- (see Scheme below). However, only the formation of 1,3,4,7,8-penta-CDF could be confirmed.



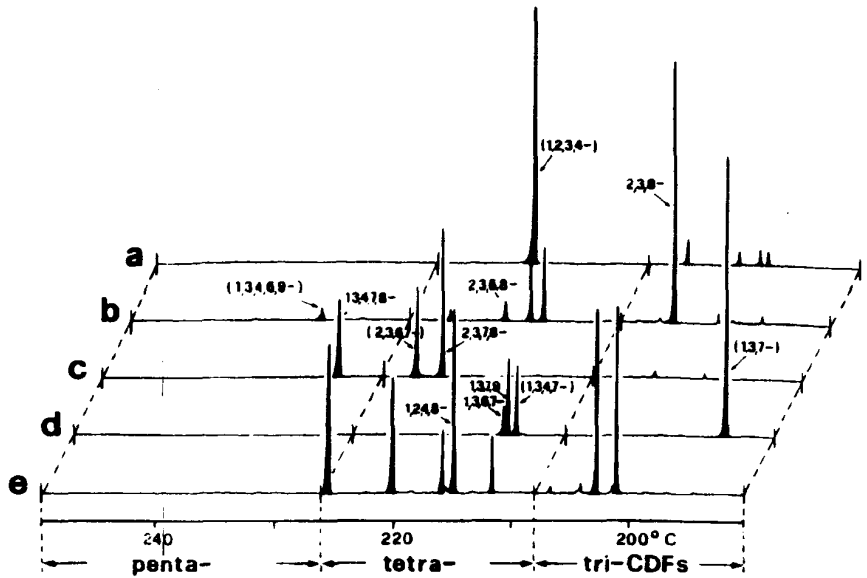
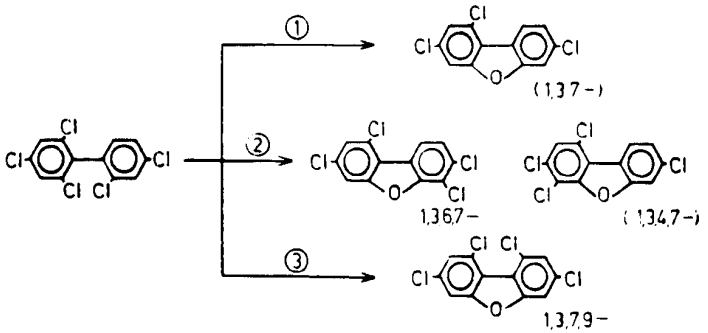
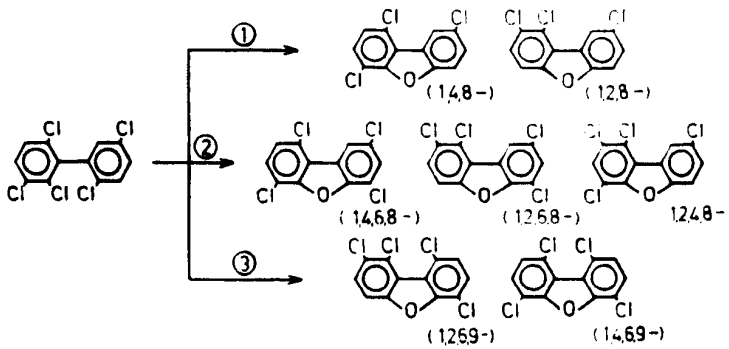


Figure 1 Mass fragmentograms showing elution of tri-, tetra- and penta-CDFs from [illegible] of pyrolyzed pentachlorobiphenyl, showing elution of 1,3,7-, 1,3,8-, (1,3,4,6,9-), 1,3,4,7,8-, (2,3,6,7-), 2,3,7,8-, (1,3,4,7-), 1,2,4,8-, (1,2,3,4-), 2,3,8- and 1,3,6,7,8- pentachlorobiphenyl. [illegible]

Pyrolysis of 2,4,6,2',4'-pentachlorobiphenyl gave a [illegible] and three tetra-[illegible] as shown in Figure 3d. This number of isomers can be expected from this [illegible] via routes 1, 2 and 3 (see Scheme below). The formation of a [illegible] is not possible and in fact no penta-CDF was observed. [illegible] 1,3,7- substituted isomer. Two of the tetra-CDFs were confirmed as 1,3,6,7- and 1,3,7,9-tetra-CDF formed via reaction routes 2 and 3, [illegible] the third [illegible] eluting) is expected to be 1,3,4,7-tetra-CDF, an additional isomer formed via reaction route 2.



The pyrolysis of 2,3,5,2',5'-pentachlorobiphenyl [illegible] and five tetra-CDFs (see Figure 3e) is explained from the [illegible] and 3 (see Scheme below). Again, the [illegible] not possible and in fact no penta-CDF [illegible]



One of the main products was tentatively identified as 1,2,4,8-tetra-CDF. Pyrolysis product of 2,4,5,4'-tetrachlorodiphenylether.[18] Two of the tetra- [illegible]1,2,6,9- and 1,4,6,9-) are also expected pyrolysis products of 2,3,6,2',3',6'-hexachlorobiphenyl (see later).

Pyrolysis of hexachlorobiphenyls

The pyrolysis of seven hexachlorobiphenyls was investigated (see Table 1). Mass fragmentograms of pyrolyzed samples are given in Figure 4. They show the elution of tetra-, penta- and hexa-CDFs.

The results of the pyrolysis of 2,4,5,2',4',5'- and 2,4,6,2',4',6'-hexachlorobiphenyl were previously reported.[10,13] However, the identity of some of the resulting PCDFs was tentative and could not be confirmed at the time for lack of reference compounds. Additional standards available now made it possible to confirm these tentative identifications. In case of 2,4,5,2',4',5'-hexachlorobiphenyl, the formation of a tetra- and two penta-CDFs was observed (see Figure 4a). These PCDFs were identified as 2,3,7,8-tetra-, 2,3,4,7,8- and 1,3,4,7,8-penta-CDF formed via reaction routes 1, 2 and 3, respectively. In case of 2,4,6,2',4',6'-hexachlorobiphenyl, a tetra- and a penta-CDF were found (see Figure 4b) and identified as 1,3,7,9-tetra- and 1,3,4,7,9-penta-CDF formed via reaction routes 1 and 2. The formation of a penta-CDF via reaction route 3 is not possible with this PCB and in fact no additional penta-CDF was observed. None of the two hexachlorobiphenyls showed the formation of significant amounts of hexa-CDFs.

From the pyrolysis of 2,4,5,2',4',5'-hexachlorobiphenyl, the formation of a major tetra- and some minor penta-CDFs was observed (see Figure 4c). The tetra-CDF expected is the 1,3,7,8- substituted isomer formed via reaction route 1; the expected penta-CDFs are 2,3,4,7,9- and 1,3,4,7,8-penta-CDF (reaction route 2), and 1,3,4,7,9-penta-CDF (reaction route 3). However, only the formation of 1,3,4,7,8- and 1,3,4,7,9-penta-CDF could be confirmed, the formation of 2,3,4,7,9-penta-CDF remained unclear.

The pyrolysis of 2,3,4,2',3',4'-hexachlorobiphenyl lead to the formation of one tetra- and a penta-CDF (see Figure 4d). They were identified as 3,4,6,9-tetra- and 2,3,4,7,9-penta-CDF, the isomers expected from the pyrolysis of this PCB via reaction routes 1 and 3, respectively. The formation of a penta-CDF via reaction route 2 is not possible with this hexachlorobiphenyl. The formation of a hexa-CDF could not be confirmed.

The pyrolysis of 2,3,5,2',3',5'-hexachlorobiphenyl gave a major and a minor tetra-CDF and a major penta-CDF (see Figure 4e). The major PCDFs were identified as 2,4,6,8-tetra- and 1,2,4,6,8-penta-CDF, the expected products from the pyrolysis of this PCB via reaction routes 1 and 3, respectively. Again, the formation of a penta-CDF via reaction route 2 is not possible with this PCB, and in fact no additional isomer was observed. The identity and source of the additional, minor tetra-CDF remained unclear.

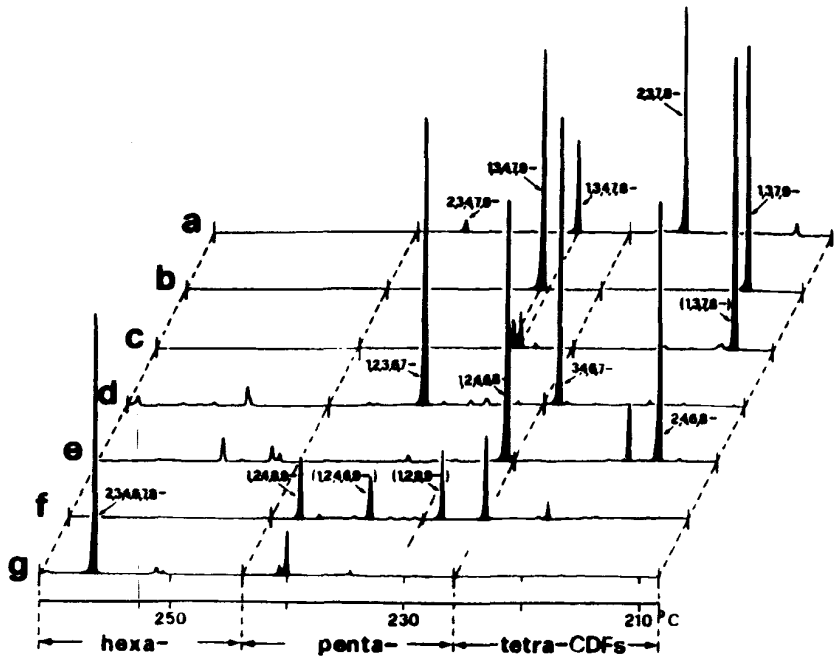
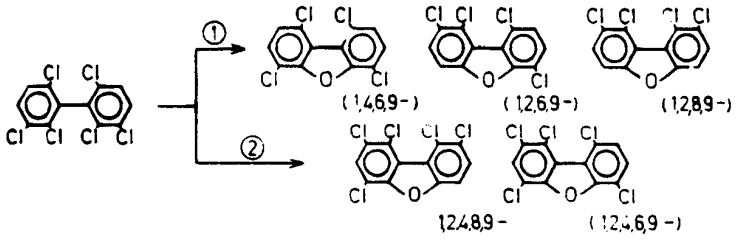
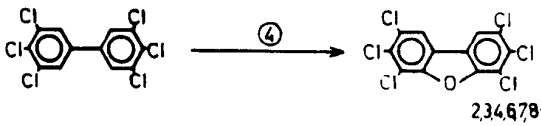


Figure 4 : Mass fragmentogra[illegible] 338 and 322) of pyrolyzed hexachlorobiphenyls showing elution of tetra-, penta- a hexa-CDFs from [illegible]-2,3,4',5'-, (b) [illegible]-2,4,6,2',4',6'-, (c) 2,4,5,2',4',6'-, (d) 2,3,4,5',3',4'-, (e) 2,3,4,5',3',5'-, (f) 2,3,4,2',3',6'-[illegible] (g) 2,3,4,5,3',4',5'-hexachlorobiphenyl. Column conditions as in Table 1

Pyrolysis of 2,3,6,2',3',6'-hexachlorobiphenyl yielded three tetra- and two penta-CDFs (see Figure 4f), the number of isomers expected via reaction route 1 and 2 (reaction route 3 and 4 not possible for this PCB). In case of the tetra-CDFs, the expected isomers are 1,4,6,9-, 1,2,6,9- and 1,2,3,9-tetra-CDF. The first two eluting isomers were also observed from the pyrolysis of 2,3,6,2',5'-pentachlorobiphenyl (see earlier). Therefore, the last eluting tetra-CDF was tentatively identified as the 1,2,8,9-substituted isomer. In case of the penta-CDFs, the expected isomers are 1,2,4,8,9- and 1,2,4,6,9-penta-CDF. The formation of 1,2,4,8,9-penta-CDF could be confirmed by co-chromatography with a reference sample (see Table 2); the identification of 1,2,4,6,9-penta-CDF as the first eluting isomer remains tentative.



The major pyrolysis product of 3,4,5,3',4',5'-hexachlorobiphenyl was identified as 2,3,4,6,7,8-hexa-CDF (see Figure 4g). This PCDF is formed [illegible] formation of tetra- and penta-CDFs via reaction routes 1, [illegible] this PCB isomer. Nevertheless, small amounts of penta-CDFs were [illegible] identity and source of these compounds remained unclear.

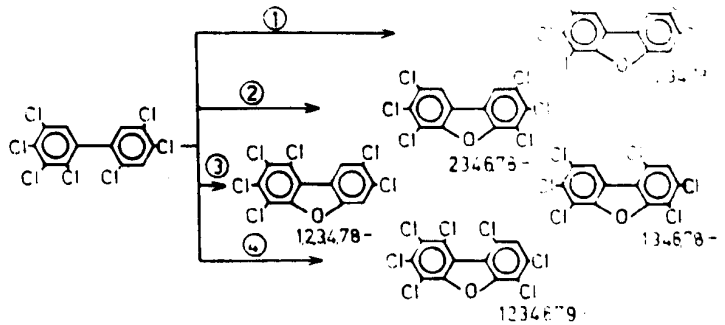


...lysis of hepta- and octachlorobiphenyls

The pyr...ysis of two hepta- and one octachlorobiphenyl wa... All three isomers are main components ... pentachloro-...grams of pyrolyzed samples are ...

The pyrolysis of 2,3,4,5,2',3',4'-heptachlorobiphenyl ... and hepta-CDFs ... Figure 3). A ... 2,3,4,5,2'-penta-CDF, the expected product from the ... route 1. In case of the hexa-CDFs, the formation of ... products originated from each of the expected ... 2,3,4,5,2'- via reaction route 2). The ... chart of a reference sample (see Table ... isomer spectra. The identity was confirmed ... not expected via reaction route 2, however, ... 2,3,4,6,2'-hepta-CDF were also found. ... known but was not the main component ...

The pyrolysis of 2,3,4,5,2',3',4'-... octa-, hexa- and hepta-CDFs ... 2,3,4,5,2'- substituted ... formation of two hexa- and a ... assigned as 1,2,3,4,7,8-hexa-CDF, ... formed via reaction routes 3 and 4, respectively. ... hexa-CDF is expected to be 1,2,3,4,7,9-hexa-... route 3. The mass fragmentogram also ... attributed to 1,2,3,4,6,7-hepta-... route 3. However, smaller amounts of ...



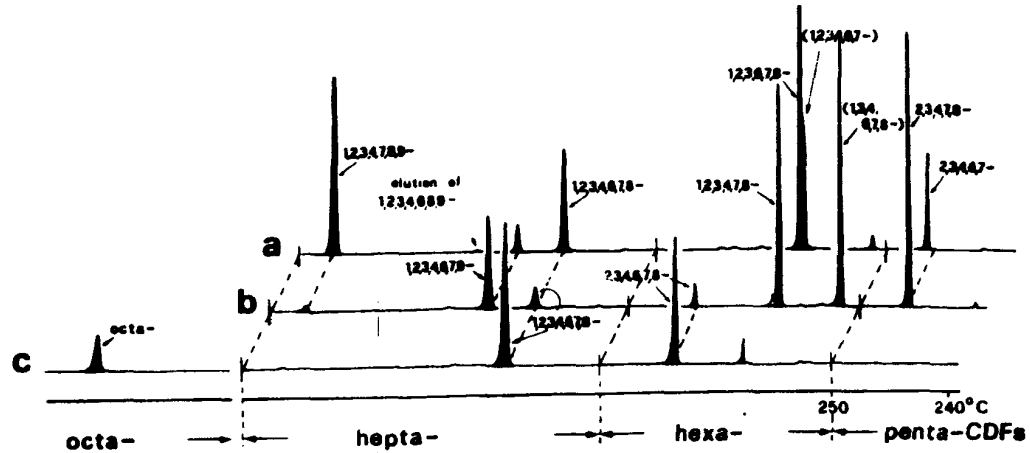


Figure 5 : Mass fragmentograms (m/z 406 and 440) of pyrolyzed hepta- and octachlorobiphenyls showing elution of penta-, hexa-, hepta- and octa-CDF from (a) 2,3,4,5,2',3',4'-, (b) 2,3,4,5,2',4',5'-hepta- and (c) 2,3,4,5,6,2',3',4',5'-octachlorobiphenyl. Column conditions as in Figure 1.

The pyrolysis of 2,3,4,5,2',3',4',5'-octachlorobiphenyl yielded hexa-, hepta- and octa-CDFs (see Figure 5c). The main hexa-CDF was confirmed as the 2,3,4,6,7-substituted isomer formed via reaction route 1. In addition, a minor hexa-CDF was also observed, the identity and source of which remained unclear. The hepta-CDF was confirmed as the 1,2,3,4,6,7,8- substituted isomer, the expected product formed via reaction route 3. The mass fragmentogram also shows the elution of octa-CDF, the pyrolysis product formed via reaction route 4.

Conclusions

The pyrolysis of 18 individual PCBs was studied and shown to result in the formation of PCDFs via intramolecular cyclizations. The yields of PCDFs were estimated to be in the range of 0.1% up to several %. Again the application of high-resolution GC and MS is documented as a necessity for the separation and identification of the PCDFs formed. Pyrolysis of individual PCBs has proven to be useful for the preparation of individual PCDFs in situations where only minute amounts of isomers are required for reference purposes, mainly in GC-MS analyses.

The formation of the PCDFs was found to follow four general reaction routes involving the loss of Cl_2, H_2, and HCl with or without a 2,3-chlorine migration (see Introduction). Due to the observed generality, it is possible to predict the structure of the resulting PCDFs.

The results support our earlier conclusion that pyrolysis of PCBs is resulting in the formation of highly toxic compounds. Consequently, the uncontrolled burning of PCBs is a threat to the environment and should be avoided.

Acknowledgements

We thank Mr. A. Garå and Mr. R. Lindahl, Drs. K. Anderson, Y. Masuda, M. Morita, A. Poland and C.A. Wachtmeister for making available the [illegible] reference compounds used in the present investigation.

References

1. C. Rappe, H.R. Buser and H.-P. Bosshardt, Ann. New York Acad. Sci., in press.
2. A. Poland, E. Glover and A.S. Kende, J. Biol. Chem., Vol. [illegible]
3. J.A. Moore, E.E. McConnell, D.W. Dalgard and M.A. Harris, Ann. New York Acad. Sci., in press.
4. H. Kuroki and Y. Masuda, Chemosphere, 7, 771 (1978).
5. H.R. Buser, C. Rappe and A. Garå, Chemosphere, 7, 439 (1978).
6. C. Rappe, A. Garå and H.R. Buser, Chemosphere, in press.
7. C. Rappe, H.R. Buser and H.-P. Bosshardt, Chemosphere, 7, 431 (1978).
8. J.G. Vos, J.H. Koeman, H.L. van der Maas, M.C. ten Noever de Brauw and R. de Vos, Food Cosmet. Toxicol., 8, 625 (1970).
9. K. Olie, P.L. Vermeulen and O. Hutzinger, Chemosphere, 6, 455 (1977).
10. H.R. Buser, H.-P. Bosshardt, C. Rappe and R. Lindahl, Chemosphere, 7, 419 (1978).
11. Dow Chemical Company, The Dow Chemistries of [illegible], August, November, 1970.
12. R.J. Smith, Science, 202, 1165 (1978).
13. H.R. Buser, H.-P. Bosshardt and C. Rappe, Chemosphere, 7, 439 (1978).
14. M. Morita, J. Nakagawa, K. Akiyama, S. Mizuno and Y. [illegible], Bull. Environ. Contam. Toxicol., 18, 67 (1977).
15. M. Morita, J. Nakagawa and C. Rappe, Bull. Environ. [illegible] (1978).
16. Å. Norstrom, K. Andersson and C. Rappe, [illegible]
17. A.S. Kende, J.J. Wade, M. DeCamp, D. Ridge and S. J. Nagel, [illegible] of the American Chemical Society, Los Angeles, [illegible]
18. H.R. Buser, Dissertation, University of Umeå, Sweden, 1978.
19. M. Zell, H.J. Neu and K. Ballschmiter, Chemosphere, 7, 69 (1978).

(Received in UK 8 February 1979)

LÄKARTIDNINGEN

ARSE

Christoffer Rappe*: Dioxins and dibenzofurans--Focus on two groups of substances [Dioxiner och dibensofuraner--twa substansgrupper i blickpunkten].
Läkardningen, 76 (1-2), 1979, p. 21-23.

* PhD, is Professor of Organic Chemistry at the University of Umeå.

Translated from Swedish by the Ralph McElroy Co., Custom Division, 2102 Rio Grande, Austin, Texas 78705 USA

Code: 239-2451

DIOXINS AND DIBENZOFURANS -- FOCUS ON TWO GROUPS OF SUBSTANCES

Summary

The toxicological effects of dioxins and dibenzofurans are discussed with special emphasis on possible carcinogenic effects. The presence of these pollutants in various products is disclosed as well as the possibility of new formation, especially from chlorophenols and PCB, particularly during combustion reactions. In the article the possibility is discussed of exposing people at work and in the environment.

Dioxins are a group of substances which recently have attracted great interest among researchers as well as the general public. The disaster in the chemical factory near Seveso in northern Italy in July, 1976, was caused by a discharge of the exceedingly toxic 2,3,7,8-tetrachloride-dioxin (TCDD). The quantity has been estimated at 2.5 kg. Fear of the same toxic substance was one of the reasons for the great commotion at BT-Kemi in Teckomatorp. Fortunately, these apprehensions have proved to be considerably exaggerated.

In recent years, there has been intensive discussion in this journal of certain effects of both phenoxyacids and hexachlorophene (Axelson, 1977; Axelson, Sundell, 1977; Byström et al., 1977; Halling, 1977; Hardell, 1977; Johansson, Wahlberg, 1977; Westerholm, 1977; Hardell, Sandström, 1978; Källén, 1978). Since these substances have a direct association with dioxins and dioxin-like combinations, it may be relevant here to present an overview of the present state of knowledge.

The polychlorinated dioxins (PCDDs) are a series of tricyclic aromatics. The number of ~~carbon~~ chlorine atoms may vary between 1 and 8, and there is a total of 75 different position isomers. The polychlorinated dibenzofurans (PCDFs) are very similar to the dioxins, both with regard to chemistry and to biology. The number of PCDF isomers is 135 (Figure 1).

From a chemical point of view, both the PCDDs and the PCDFs are quite stable molecules. The photochemical (light) decomposition appears to be the most important reaction; however, investigations in the United States and in Italy have established that in and on the ground the half-life is one year (Young et al., 1976). Under artificial conditions, a considerably quicker decomposition has been observed (Crosby, Wong, 1977), but it is uncertain how frequently these conditions may be found in nature. Like many other environmental poisons, for example DDT and PCB, the PCDDs and the PCDFs have the ability to accumulate in the food chain. This applies to aquatic as well as to terrestrial organisms (Firestone, 1978; Isensee, 1978). The substances concentrate particularly in fatty tissues and in the liver (Nagayama et al., 1977).

The reason for the great interest in PCDDs and PCDFs is that certain isomers of these substances have proved to be exceedingly toxic, especially 2,3,7,8-tetra-CDD and some others with 4 to 6 chlorine atoms (Figure 2).

All of these have an LD_{50} value of 1 to 100 µg/kg for the most sensitive animals species. A good correlation has also been found between toxicity and induction of certain liver enzymes. Moreover, noteworthy distinctions have been found in biological activity between the various isomers. A factor of 1,000 to 10,000 has been reported for isomers as closely related as 2,3,7,8- and 1,2,3,4-tetra-CDD (Poland et al., 1976; McConnell et al., 1978). This shows that it is quite necessary to define carefully which isomer or isomers of these potentially dangerous substances are found in various preparations and environments.

Biological effects

As far as sublethal and chronic effects of PCDDs and PCDFs are concerned, only 2,3,7,8-tetra-CDD has been investigated to any large extent. The typical effects in animal experiments are damage

to the liver and thymus gland which, in turn, have caused effects upon enzyme activation and immunity defense. This may be the explanation of why the joint exposure to phenoxyacid 2,4,5-T and 2,3,7,8-tetra-CDD has been proved to produce vigorous synergistic effects in animal experiments (Allred, Strange, 1977). TCDD has also proved to be a very potent teratogen.

Recently, several good summaries have been published regarding the most important biological investigations of PCDDs and PCDFs (IARC, 1977, 1978a, b; Moore, 1978; Poland, Glover, 1978; Vos, 1978).

The possible carcinogenic effects of these substances are of special interest. In the course of the evaluation, which was made at IARC in Lyon approximately one year ago, it was found to be difficult to establish any actual evaluation because data were lacking (IARC, 1977). Since that time, a number of animal experiments have been concluded and published. All of these demonstrate that TCDD in small doses can produce tumors (Allen et al., 1977; Allen, Norback, 1977; Di Giovanni et al., 1977; Van Miller et al., 1977; Kociba et al., 1978; Toth et al., 1978).

Low general organ specificity has been observed in these experiments which may be interpreted to mean that TCDD has a general promotional effect. This is in good agreement with the results which were recently published by Kouri and Nebert (1977). Moreover, it may be noted that a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexa-CDD proved to be capable of producing tumors in animal experiments (Holmes et al., 1978).

Against the background of uncommonly vigorous biological effects for the PCDDs and PCDFs, it is surprising that it has not yet been possible to identify metabolites of these substances in any animal. The toxic effects are considerably retarded since the animals used in experiments only die after three to four weeks in spite of very massive doses. It has been found that the dioxins are excreted slowly just as they are, and the half-life is approximately one month for small rodents (IARC, 1977; Poland, Glover, 1978; Vos,

1978). For larger mammals, the half-life is considerably longer (D. Jensen, Dow Chemicals, Midland, USA, personal communication). Furthermore, it appears that for the more highly chlorinated combinations the half-life generally is longer than for the lower combinations (Nagayama et al., 1977), but great distinctions are found between isomers with the same degree of chlorination (C. Rappe, Y. Masuda, H. R. Buser, unpublished data).

Occurrence of PCDDs and PCDFs

Neither dioxins nor dibenzofurans have had any technical application; however, they do occur as pollutants in a great many technical products. The phenoxyacid 2,4,5-T (now totally prohibited in Sweden) contains the dangerous dioxin TCDD. Use of this phenoxyacid started towards the end of the 1940's, and during the 50s and 60s it was generally used in Sweden for foliage control in the lumber industry.

The greatest quantities and the products most likely containing the most dioxin were used in the war in Southeast Asia towards the end of the 60s (the defoliant Agent Orange). Analyses of civilian and military preparations from this time have shown that in singular instances TCDD contents of approximately 50 mg/kg (IARC, 1977) could be measured; a median value is considered to be 1-2 mg/kg. During the 1970s, the contents have been lowered as a result of the fact that the authorities in a number of countries have introduced restrictions (maximum 0.1 mg/kg) and most preparations now satisfy this rule.

The chlorinated phenols have a comprehensive technical application, for example in saw mills, as a discoloring agent, in pressure impregnation of wood products, in tanning of leather and as a bactericide in the paper industry. In Sweden, the greatest quantity of chlorophenols was used as a discoloring agent in saw mills; however, this use has, in principle, been prohibited since January 1, 1978.

The technical preparations are very impure (Nilsson et al., 1978), and the contents of PCDDs and PCDFs are in the vicinity of 100-1,000 mg/kg.

The biological and toxicological picture is complicated by a great variety of various isomers. The principal preparations on the Swedish market contained approximately 20 different PCDF isomers (Rappe et al., 1978). The majority of these pollutants has not been identified or toxicologically tested. Imported pentachlorophenol has been proved to contain 1,2,3,6,7,8-hexa-CDD.

A similar pollution situation is found for the polychlorinated biphenyls as well (PCB). Previously, these preparations were used i in a variety of different combinations, such as in transformers, condensers, hydraulic liquids, heat transfer liquids, paints, plastics, foundry sand and paper for automatic copying (IARC, 1978a). In Sweden, they are now only permitted as dielectrics in condensers, but even here they will be exchanged for other products. However, this applies only to newly built condensers; all of those which are in operation continue to contain PCB--an estimated 100,000 units with a combined 2,500 tons of PCB. Even if condensers are completely closed systems, all of them sooner or later will have to be opened, which poses occupational and environmental risks.

The PCB preparations themselves are a mixture of some 50 similar combinations; however, the technical products contain as much as 1-10 mg/kg of a mixture of PCDFs (IARC, 1978a), but the discrete components have not been identified. On the other hand, it has been established that the toxic activity of the preparations is parallel to the content of PCDFs (Vos et al., 1970).

The bactericide hexachlorophene is manufactured from the same initial material as the phenoxyacid 2,4,5-T, and it may therefore contain the same quantities of the dioxin TCDD; by further purification, the TCDD content has been lowered to 0.03 mg/kg or less in this product. On the other hand, hexachlorophene contains approximately 100 mg/kg of chlorinated xanthenes, the possible

toxic qualities of which are entirely untested (Göthe, Wachtmeister, 1972; Baughman, 1974).

Formation of PCDDs and PCDFs

By analysis of so-called fly ash from municipal refuse combustion plants and industrial central heating operations in Holland and Switzerland, it has recently been established that this ash contains both PCDDs and PCDFs (Olie et al., 1977). The quantity varied but was on the order of magnitude of 0.5-1 mg/kg (Buser, Bosshardt, 1978). Corresponding analysis of the ash from the municipal central heating plant in Umeå showed no occurrence of these pollutants.

The number of components in the fly ash is very great, 30-40 isomers of either PCDDs and PCDFs. Together with two Swiss colleagues we have identified the most common components; we did so in order to be able to make a dependable risk calculation. We found that the most dangerous PCDDs were only lesser components; however, the most dangerous PCDFs were the dominating ones (Buser et al., 1978a, b).

The occurrence of PCDDs and PCDFs in fly ash demonstrates that these disagreeable substances can be reconstituted in the case of pyrolosis or combustion. We now also know that they are formed by incomplete combustion of chlorophenols (PCDDs) and PCB (PCDFs), and the small quantities in the fly ash have been formed by unintentional combustion. If this risk is to be eliminated, control of what is combusted or burned must be improved.

Combustion of foliage or cutter shavings impregnated with chlorophenols has resulted in noteworthy quantities of dioxins, 100-1,000 µg/g chlorophenol. In spite of the fact that the relatively harmless PCDDs dominate in the smoke gases, it has appeared that when impure technical preparations are used during the combustion occasionally more than 10 µg/g chlorophenol is more formed of the truly highly toxic 2,3,7,8-tetra- and 1,2,3,7,8-penta-CDD (Rappe et al., 1978).

In the case of heating of PCB to 500-700°C, large quantities of PCDFs are formed, up to 3-25%. Precisely as in the case of the fly ahs the most disagreeable PCDF components dominated (2,3,7,8-tetra-CDF) (Buser et al., 1978c). This uncontrolled combustion of PCB is a very serious risk which must be taken into account in the handling and above all the destruction of the great quantities of PCB found in condensers both here and abroad.

Groups exposed

The most serious exposure of workers has happened in connection with accidents in the manufacture of 2,4,5-trichlorophenol or other chlorophenols. Up to the present, 14 accidents of this nature are known, and the one near Seveso was the most recent to occur. In this instance, even the civilian population was exposed.

BT-Kemi has been the only manufacturer of chlorophenols in Sweden, but it has never produced 2,4,5-trichlorophenol--only 2,4-di- and 2,4,6-trichlorophenol.

The number of workers exposed in these accidents is 500 to 1000. The most common symptoms are chloracne, liver damage, and heart and vascular diseases; however, a great variety of other symptoms have also been described (IARC, 1978b).

The group of workers that has been studied most intensively is the 75 who were hurt in connection with an explosion at the BASF factory in Ludwigshafen in 1953. Of the 17 persons now dead, six died from various tumor illnesses (expected number: 3). The number of stomach tumors was 4, compared to the expected 1 to 2 (IARC, 1978b).

As a result of the comprehensive use of chlorophenols, large groups have been exposed to these preparations and to the pollutants found in them. Among the groups most exposed may be mentioned workers at sawmills, in the paper industry, and in tanneries. At many sawmills here in Sweden, previously shavings and other products were burned

which had been treated with chlorophenol, but it is difficult, retrospectively, to quantify these potential risks (chlorophenols are now prohibited in sawmills).

As far as PCB is concerned, special attention must be given to the exposure which has occurred in the manufacture and repair of condensers, but also in connection with work with hydraulic oils and paint for ship bottoms.

In December, 1977, a transformer burned in central Toronto. The firefighters and workers who fought the fire did not take any special protective measures. PCB is erroneously considered to be very resistant to fire. Subsequently, several workers have had various complaints. A testing of soot has indicated considerably increased contents of both PCB and PCDFs (the Toronto Globe and Mail, 1977-12-17 and Newsrelease Ontario, Ministry of the Environment, 1978-02-13).

The most serious poisoning with PCB and PCDFs occurred in 1968, in southwest Japan. Because of a leak in a heat exchanger, a quantity of rice oil for domestic purposes was polluted with PCB, the so-called Yusho disaster. More than 1,200 persons have been classified as victims of this poisoning, all of them with serious cloracne. The content of PCB in the rice oil was approximately 1 mg/g; however, the content of PCDFs was approximately 500 times higher than normal (Nagayama et al., 1977); Rappe et al., 1977; Buser et al., 1978d).

In an epidemiological case-control study, it has been demonstrated that personnel exposed to phenoxyacids and chlorophenols as well have a clearly increased risk of being killed by malignant mesenchymal tumors of the soft parts (Hardell, Sandström, 1978). These results may be interpreted to mean that either both phenoxyacids and chlorophenols are carcinogenic or, on the other hand, that these effects occur due to those PCDDs and PCDFs which are found as pollutants in these preparations. The phenoxyacid 2,4,5-T contains 2,3,7,8-tetra-CDD and pentachlorophenol 1,2,3,6,7,8-hexa-CDD, both of which have caused tumors in animal experiments (see above).

For the future evaluation of the suitability of the phenoxyacids as herbicides in agriculture and forestry, it is obviously absolutely necessary to establish what caused this increased tumor frequency. As far as the chlorophenols are concerned, it may be noted that they continue to be used as bactericides in liquids for cutting, refrigeration, and grinding.

It has also been discussed in various contexts to what extent the general public may have been exposed to phenoxyacids and TCDD, for example, during the war in Vietnam, and in north Värmland (Torsby). From Vietnam, there are reports of a considerable increase in abortions as well as instances of primary liver cancer among the population that has come into direct contact with the sprayings (Ton That Tung, 1977). As far as perinatal mortality in north Värmland is concerned, it has been the subject of a special investigation (Council on Social Affairs, 1977). Without entering into any detailed analysis, I do want to point to the fact that the word dioxin is not mentioned in this investigation. This is especially noteworthy against the background of:

1. 2,4,5-T being used in foliage control;
2. 2,4,5-T contained approximately 1 µg TCDD/kg (or more) at this time;
3. TCDD is considered the most powerful teratogen known and is fetotoxic as well (IARC, 1978b); and
4. TCDD may concentrate in the fatty tissues of animals (for example, elk, reindeer) eating sprayed vegetation.

If any connections were found to exist between prenatal death, malformations, and sprayings, then the most likely avenue of exposure is by way of consumption of meat containing dioxin. This exposure was not discussed by the investigators.

The increased interest in dioxins and benzofurans during recent years has resulted in much new material coming out concerning groups which previously had been occupationally exposed to these substances. Any total risk evaluation, especially for the long-range effects, is

not as yet possible; however, IARC/NIEHS has a special program for these substances with planned meetings every other year, and within WHO work is proceeding with a "Health Criteria Document". Recent accomplishments within analytical organic chemistry have demonstrated that these disagreeable substances appear more generally than previously assumed. An increased level of knowledge concerning these substances is necessary in order that the risks may be minimized.

References

ALLEN J R, BARSOTTI D A, van MILLER J P, ABRAHAMSSON L J, LALICH J J: Morphological changes in monkeys consuming a diet containing low levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Food Cosmet Toxicol 15: 401–410 1977

–, NOLBACK D M: Carcinogenic potential of the polychlorinated biphenyls. Origins of Human Cancer. Cold Spring Harbor Laboratory 171–186 1977

ALLRED P M, STRANGE J R: The effects of 2,4,5-Trichlorophenoxyacetic acid and 2,3,7,8-tetrachlorodibenzo-p-dioxin on developing chicken embryos. Arch Environ Contam Toxicol 6: 483–489 1977

AXELSON O: Hexachlorophene and the teratogenic effect. Läkartidningen 74: 1911–1912, 1977.

BUNCELL L: Phenoxyacids and cancer. Läkartidningen 74: 2887–2888, 1977.

BAUGHMAN R W: Tetrachlorodibenzo-p-dioxin in the environment. High resolution mass spectrometry at the picogram level. Thesis, Harvard University 1974. Appendices C and D

BUSER H R, BOSSHARDT H-P: Polychlorierte Dibenzo-p-dioxine, Dibenzofurane und Benzole in der Asche kommunaler und industrieller Verbrennungsanlagen. Mitt Gebiete Lebensm Hyg 69: 104–112 1978

–, RAPPE C: Identification of polychlorinated dibenzo-p-dioxin isomers found in fly ash. Chemosphere 7: 165–172 1978 a

–, RAPPE C, LINDAHL R: Identification of polychlorinated dibenzofuran isomers in fly ash and PCB pyrolyses. Chemosphere 7: 419–429 1978 b

–, RAPPE C: Formation of polychlorinated dibenzofurans (PCDFs) from the pyrolysis of PCBs. Chemosphere 7: 109–119 1978 c

–, RAPPE C, OARA A: Polychlorinated dibenzofurans (PCDFs) found in Yusho oil and used Japanese PCB. Chemosphere 7: 419–427 1978 d

BYSTROM G., LUNDGREN M., MEYERLIE A., PALMBORG M: A study of causes of birth malformation and prenatal mortality in Värmland. Läkartidningen 74: 2167–2169, 1977.

CROSBY D G, WONG A S: Environmental degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Science 195: 1337–1338 1977

DI GIOVANNI J, VIAJE A, BERRY D L, SLAGA T J, JUCHAU M R: Tumor-initiating ability of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and Aroclor 1254 in the two stage system of mouse skin carcinogenesis. Bull Environ Contam Toxicol 18: 352–357 1977

FIRESTONE D: The 2,3,7,8-tetrachlorodibenzo-para-dioxin problem: a review. Ecol Bull (Stockholm) 27: 41–54 1978

GÖTHE R, WACHTMEISTER C A: Synthesis of 1,2,4,5,7,8-hexachloroxanthene. Acta Chem Scand 26: 2523 1972

HALLING H: Suspected association between Hexachlorophenol exposure and birth malformation, Läkartidningen 74: 842–846, 1977.

HARDELL L: Malignant mesenchymal tumors and exposure to phenoxyacids–a clinical observation, Läkartidningen 74: 2783–2784, 1977.

HARDELL L, SANDSTRÖM A.: Malignant mesenchymal tumors of the soft parts and exposure to phenoxyacids or chlorophenols, Läkartidningen 75: 3535–3536, 1978.

HOLMES P A, RUST J H, RICHTER W R, SHEFFNER A M: Long term effects of TCDD and HCDD in mice and rats. Abstract 26 New York Acad Sci, Science Week June 21–June 30, 1978

ISENSEE A R: Bioaccumulation of TCDD. Ecol Bull (Stockholm) 27: 253–262 1978

JOHANSSON G., WAHLBERG J.E.: Eczema and chemicals, Läkartidningen 74: 3183–1877.

KOCIBA R J, KEYES D G, BEYER J E, CARLSON R S, DERINGER P J: Long-term toxicologic studies of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in laboratory animals. Abstract 25 New York Acad Sci, Science Week June 21–June 30, 1978

KOURI R, NEBERT D W: Genetic regulation of susceptibility to polycyclic hydrocarbon-induced tumors in the mouse. Origins of Human Cancer. Cold Spring Harbor Laboratory 811–836 1977

KALLÉN B: Delivery results among hospital employees, Läkartidningen 75: 3569–3570, 1978.

McCONNELL E, MOORE J, HASEMAN J, HARRIS M: The comparative toxicity of chlorinated dibenzo-p-dioxin isomers in mice and guinea pigs. Toxicol Appl Pharmacol 44: 335–355 1978

MOORE J A: The dioxin problem – overview. Ecol Bull (Stockholm) 27: 134–144 1978

NAGAYAMA J, MASUDA Y, KURATSUNE M: Determination of polychlorinated dibenzofurans in tissues of patients with «Yusho». Food Cosmet Toxicol 15: 195–198 1977

NILSSON C-A, NORSTRÖM Å, ANDERSSON K, RAPPE C: Impurities in commercial products related to pentachlorophenol. Environ Sci Res Ser 11: 313–323 1978

OLIE K, VERMEULEN P L, HUTZINGER O: Chlorodibenzo-p-dioxins and chlorodibenzofurans are trace components of fly ash

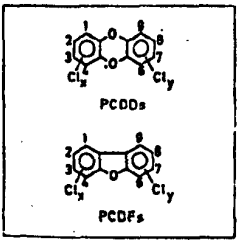


Figure 1. The chemical structure of PCDDs and PCDFs.

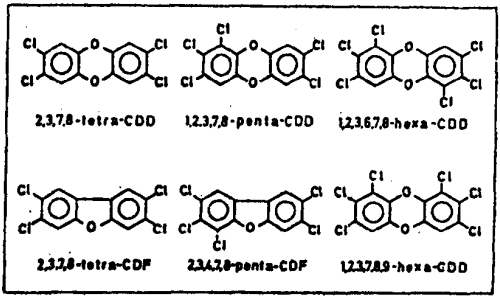


Figure 2. Isomers of PCDDs and PCDFs.