Polish Journal of Environmental Studies Vol. 10, No. 4 (2001), 217-235

Thermodynamic and Physico-Chemical Descriptors of Chloronaphthalenes: An Attempt to Select Features Explaining Environmental Behaviour and Specific Toxic Effects of These Compounds

J. Falandysz[1], T. Puzyn[1], B. Szymanowska[1], M. Kawano[2], M. Markuszewski[3], R. Kaliszan[3], P. Skurski[4], J. Błażejowski[4], T. Wakimoto[2]

[1] Department of Environmental Chemistry & Ecotoxicology, University of Gdansk, 18 Sobieskiego Str., PL 80-952 Gdansk, Poland [2] Department of Environment Conservation, Ehime University, 3-5-7 Tarumi, Matsuyama 790-8566, Japan [3] Department of Biopharmaceutics and Pharmacodynamics, Medical University of Gdansk, 107 Gen. J. Hallera Str., PL 80-416 Gdansk, Poland
[4] Department of Physical Chemistry, University of Gdansk, 18 Sobieskiego Str., PL 80-952 Gdansk, Poland

Received: December 4, 2000
Accepted: February 22, 2001

Abstract

35 physico-chemical descriptors were used to characterize all 75 congeners of chloronaphthalene in terms of their environmental stability and specific dioxin-like toxicity. A prepared basic thermodynamic and physico-chemical property data matrix of PCNs was interpreted using Principal Component Analysis (PCA). The PCA of the thermodynamic and physico-chemical data matrix created a four-dimensional model that explained 76% (58% + 9% + 5% + 4%) of the total variance. The loading plot shows that the first PC is influenced by variables describing degree of chlorination, molecular weight, polarizability and lipophilicity. The best positively correlated descriptors are: retention time, standard molar entropy, heat capacity, a first-order molecular connectivity index, logarithm of octanol-water partition coefficient, the Wiener Index, specific polarizability, a third order shape index for molecules, the sum of absolute of the charges on each atom of the molecule, molecular weight, polarizability, refractivity, solvent-accessible surface, van der Waals surface, solvent-accessible volume, van der Waals volume. Negatively correlated descriptors are: standard enthalpy of formation and energy of HOMO. The second PC is strongly influenced by energy of LUMO, while substitution pattern parameters, number of chlorine atoms at α-positions and vicinal (adjacent) carbon atoms substitution pattern are less important parameters. The third PC depends on dipole moment and the largest negative charge, and on substitution at position 2 of naphthalene nuclei, while the symmetry group parameter is determined by PC4. There are small groups consisting of compounds which have similar values of LUMO energy and substitution pattern. The congeners of CN substituted with chlorine at positions 1, 2, 3, 6 and 7 (Fv/Fv PCN congeners), and next those substituted at positions 1, 2, 3

Correspondence to: Prof, dr hab. J. Falandysz

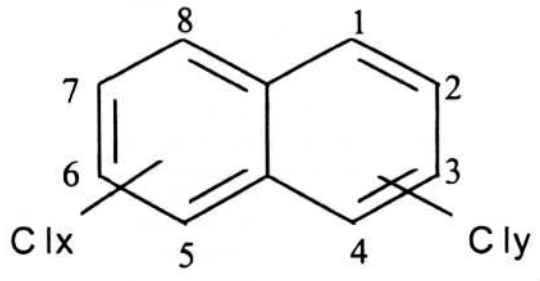
and 6 or 7 (Fr/Fv PCB congeners) are considered to be most potent in terms of dioxin-like toxicity, and followed by those substituted at four positions (Fr/Fv), at three positions (Tr/Fv) and so on. The thermodynamic stability of the congeners of CN depends on the number of attached chlorine and structure of the molecule. Among the 75 congeners of CN only a few, like PCN nos. 42, 52/60, 61, 66/67, are relatively resistant to biodegradation and biomagnify in animals occupying a higher position in the marine food web, and with a particular homologue group they are characterised by the lowest absolute values of energy of LUMO.

Keywords: polychlorinated naphthalenes, PCNs, chloronaphthalenes, CNs, pollution, contaminants, physico-chemical properties, toxicity, multivariate analysis.

Introduction

Polychlorinated naphthalenes (PCNs) are an important group of persistent organic pollutants (POPs) exhibiting significant toxicity [1, 5, 6, 34, 35, 57, 65, 77, 78] and widespread occurrence in the environment [7-10, 13-26, 32, 37, 39, 40, 50, 56, 62]. These substances are an example of the first group of dioxin-like compounds synthesised in the past in large quantity and to which human beings and wildlife were exposed. Many congeners of chloronaphthalene were recently identified and quantified in biota from the Baltic Sea and the Great Lakes of North America, and also their presence in ambient air and sediment in the northern hemisphere [3, 13-26, 44, 47-51, 53-54, 59]). Differences in persistency under environmental conditions, bioaccumulation and biomagnification potential of PCN congeners has also been indicated [10, 14, 16, 18, 49, 75]. Chloronaphthalenes are nearly planar compounds and can contribute to aryl hydrocarbon (Ah) receptor-mediated toxicity similar to that of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (Table 1), and therefore are of concern on their environmental sources of pollution and effects.

Technical PCN formulations were produced as Halowaxes in the past by the Koppers Co. Inc., Pittsburg, PA, USA [30, 76]. Melted naphthalene and chlorine in the presence of a catalyst ($FeCl_3$ or $SbCl_5$) are substrates involved in the synthesis of PCNs on a technical scale. Seventy-five congeners of chloronaphthalene are theoretically possible (Appendix). The chlorination pathways upon Halowax preparation involve an electrophilic aromatic substitution with chlorine, which leads to the generation of characteristic pattern of chloronaphthalene homologue group. Naphthalene undergoes electrophilic and nucleophilic substitution predominantly at the apical α-positions (1, 4, 5, 8 - positions) of the molecule (Scheme 1), and the entering chlorine will be directed to *para* (or *ortho)* position relative to a chlorine already present in the aromatic system [46]).



Scheme 1. Structure and ring numbering system of PCNs. Positions 1, 4, 5, and 8 are called apical α-positions, and positions 2, 3, 6, and 7 are lateral /3-positions or *peri* positions.

There are seven known basic technical Halowax mixtures, *i.e.* Halowax 1031, 1000, 1001, 1099 (also 1099b), 1013, 1014 and 1051 [7, 30, 46]. Halowax formulations differ from each other with regard to their physical appearance, melting points (from mobile liquids to waxes with melting point at 185°C), various chlorine content, and abundance of chloronaphthalene homologue groups and individual congeners [7, 30]. The batch-to-batch difference of chloronaphthalene homologue group content (%) was reported for Halowax 1014 [37, 38, 41]).

Apart from the Halowax formulations from the Koppers Company, there were many other PCN mixtures and manufacturers known. In Europe, PCN formulations such as Nibren Wax (Bayer AG, formerly Farbenindustrie, Germany), Perna Wax (Chemische Fabrik Greisheim, Germany), Basileum (Desowag-Bayer, Germany), (Electron, Germany), Seekay Wax (ICI Runcorn, Great Britain), Clonacire Wax (Prodelec, Paris, France) and Cerifal Materials (Caffaro, Italy), and in the USA: N-Oil and N-Wax (Halochem and Chemisphere Company) were produced and used [7, 46].

Polychlorinated naphthalenes are hydrophobic, possess high chemical and thermal stability, good weather resistance, and electrical insulating properties, low flammability and are compatible with other materials and chemically inert. These substances were introduced as industrial chemicals shortly before World War I. The physical and chemical properties and applications of PCNs are largely similar to that of polychlorinated biphenyls (PCBs), which are known much better both as hazardous industrial chemicals and environmental pollutants, and which become a substitute to PCNs [11].

Since PCNs are persistent under environmental conditions, when released at sites of formation, manufacture, use or disposal they will simply cause pollution problems. Groundwater samples collected during 1995-1996 from the aquifer of the Llobregat River near Barcelona (NE Spain) contained PCNs in concentrations from <0.5 ng/dm^3 to 79 μ/dm^3 due to petrol pollution, and tetrachloronaphthalenes were present as a dominating CN homologue group [62]. A recent study has shown that chlor-alkali plants contribute to sources of PCNs in the environment. Toxic equivalents of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD TEQs) estimated for PCN

Table 1. Comparison of relative dioxin-like potencies reported for individual chloronaphthalene congeners expressed relative to a 2,3,7,8-TCDD standard. Values reported were calculated as a quotient of EC-50 (EC-SO$_{TCDD}$/ EC-50$_{PCN}$), [5, 6, 35, 36, 77] and [78], respectively.

PCN congener	IUPAC No.	H4II-EROD	H4II-EROD	H4II-luc	H4II-luc
2-CN	2	<0.00000022			
1,4-DiCN	5	0.0000000051*			0.0000002*
2,4-OH-CN	–	0.000000033			
2,7-DiCN	12	<0.00000042			<0.00000069
1,2,7-TriCN	17	<0.00000084			
1,2,4,7-TetraCN	34	<0.00000042			<0.00000069
1,2,6,8-TetraCN	40				0.000016*
1,3,5,7-TetraCN	42	<0.0000042			<0.0000069
2,3,6,7-TetraCN	48				
12,3,5,7-PeCN	52	0.0000042			
1,2,3,6,7-PeCN	54	0.000092		<0.00069	0.00017
1,2,3,7,8-PeCN	56	0.000024		0.00049	
1,2,4,5,6-PeCN	57	0.0000017		0.0000037	
1,2,4,6,7-PeCN	60	<0.00000042			<0.000028
1,2,4,6,8-PeCN	61	<0.00000042			
1,2,3,4,5,6-HxCN	63		0.002		
1,2,3,4,5,7-HxCN	64		0.00002		
1,2,3,4,6,7-HxCN	66	0.00061		0.0024	0.0039
1,2,3,5,6,7-HxCN	67	0.00028	0.002		0.001
1,2,3,5,6,8-HxCN	68		0.002		0.00015
1,2,3,5,7,8-HxCN	69		0.002		
1,2,3,6,7,8-HxCN	70	0.002		0.0095	0.00059
1,2,4,5,(6,7),8-HxCN	71/72		0.000007*		
1,2,3,4,5,6,7-HpCN	73	0.00040	0.003	0.0006	0.001

* Roughly

congeners found in sediments collected at the chlor-alkali facilities were greater than those estimated for PCBs, PCDDs and PCDFs [53]. Biota from the Baltic Sea accounted for up to 10% of the sum of TCDD TEQs for those compounds [29].

Chloracne and liver disease and necrosis in humans, X-disease in cattle, 7-ethoxyresorufin-*O*-deethylase (EROD) induction and early life stage toxicity in fish has been linked to exposure to chloronaphthalenes [1, 57, 65]. Although the use of PCNs has declined in the past few decades, they are not prohibited in most countries [46]. Polychlorinated naphthalenes also occur as technical impurities in PCB formulations and so can be found in many PCB applications including transformers, capacitors and insulating oils [9, 64]. In addition to their industrial synthesis, chloronaphthalenes are by-products of a number of thermal processes, such as copper ore smelting, aluminium smelting, municipal solid waste incineration, pyrolysis of chlorinated solvents such as polyvinyldiene chloride and tetrachloroethylene, and some of polycyclic aromatic hydrocarbons (PAHs) [2, 10, 43, 63, 71, 72, 79, 81]. Environmental exposure of humans to PCNs may be a cause for concern. Human milk in Europe and human adipose tissue in Japan has been found recently to contain PCNs [55, 61]. There is a lack of exact and chronological data on production volume of PCNs or their time-trends and amounts possibly released into the environment. The amount of PCNs potentially available from technical PCN and PCB formulations are around 150,000 and 200 metric tonnes, respectively, and due to formation in thermal processes in the 20th century about 1-10 metric tones [10]. In an attempt to reconstruct the historical inputs of PCNs in Europe the dated core from the profundal sediments of Esthwaite Water in England

Table 2. Symmetry and physico-chemical properties of PCNs (for explanation of the symbols/parameters see Table 3).

No	C1	C2	C3	C4	C5	C6	C7	C8	SYM	VC	AC	RT	PL	H	S	CP	HOMO	LUMO	X1	LogP	WienI	Sp.Pol	Dipole	MaxQ+	Ka3	AbsQ	MaxQ-	Mass	POLAR	REF	Log P	SAsurf	VdWsurf	SASvol	VdWvol
1	1	0	0	0	0	0	0	0	Cs	NVC	1	0.528	5.588	34.5353	89.959	34.769	-0.62	-8.803	5.377	3.99771	140	0.139939	0.383414	0.116684	1.09923	1.65464	-0.11077	162.62	19.6	47.3	3.57	331.65	169.9	488.2	144.48
2	0	1	0	0	0	0	0	0	Cs	NVC	0	0.667	2.526	33.7853	86.554	32.861	-0.605	-8.897	5.3602	3.98044	144	0.139717	0.539477	0.119108	1.218047	1.65598	-0.12279	162.62	19.6	47.3	3.57	336.22	171.9	493.1	144.71
3	1	1	0	0	0	0	0	0	Cs	HVC	1	1.089	0.301	28.8778	93.013	36.526	-0.779	-8.816	5.7877	4.37716	178	0.140438	0.535431	0.118481	1.31571	1.70326	-0.13577	197.06	21.6	52.1	4.08	348.08	181	517.7	155.76
4	1	0	1	0	0	0	0	0	Cs	PVC	1	1.058	0.347	28.0394	93.375	36.577	-0.802	-8.878	5.7709	4.36565	179	0.140267	0.634856	0.13011	1.436468	1.67104	-0.11716	197.06	21.6	52.1	4.08	347.29	180.5	515.7	154.35
5	1	0	0	1	0	0	0	0	C2v	D/QVC	2	1.055	0.352	28.688	93.156	36.519	-0.826	-8.77	5.7877	4.39026	176	0.140445	0.406645	0.119537	1.31571	1.66567	-0.11272	197.06	21.6	52.1	4.08	332.53	172.1	495	148.9
6	1	0	0	0	1	0	0	0	C2h	DTVC	2	1.055	0.352	28.6746	92.584	36.504	-0.816	-8.803	5.7877	4.43923	176	0.140267	0.000189	0.117786	1.31571	1.65792	-0.11379	197.06	21.6	52.1	4.08	338.63	175.8	505	152.39
7	1	0	0	0	0	1	0	0	Cs	D/QVC	1	1.055	0.352	27.8996	93.097	36.538	-0.801	-8.89	5.7709	4.41044	181	0.140162	0.258226	0.120422	1.436468	1.66205	-0.12029	197.06	21.6	52.1	4.08	347.48	180.4	516.1	154.57
8	1	0	0	0	0	0	1	0	Cs	PVC	1	1.055	0.352	27.9059	93.073	36.536	-0.799	-8.861	5.7709	4.37874	180	0.140205	0.526365	0.129293	1.436468	1.66502	-0.11879	197.06	21.6	52.1	4.08	344.86	179.3	512.7	153.6
9	1	0	0	0	0	0	0	1	C2v	HVC	2	1.181	0.198	31.32	92.049	36.465	-0.809	-8.719	5.7877	4.37963	175	0.140971	0.450924	0.118336	1.31571	1.66808	-0.11043	197.06	21.6	52.1	4.08	336	174.1	501.1	151.79
10	0	1	1	0	0	0	0	0	C2v	HVC	0	1.067	0.333	28.3198	93.325	36.573	-0.757	-8.969	5.7709	4.36774	182	0.140259	0.629029	0.120366	1.436468	1.69668	-0.13423	197.06	21.6	52.1	4.08	341.53	176.4	506.4	151.24
11	0	1	0	0	0	1	0	0	C2h	DTVC	0	1.06	0.344	27.1327	92.858	36.586	-0.791	-8.91	5.754	4.44296	186	0.139939	0.000092	0.120141	1.574646	1.66349	-0.12297	197.06	21.6	52.1	4.08	331.23	170	490.4	145.83
12	0	1	0	0	0	0	1	0	C2v	D/QVC	0	1.06	0.344	27.1454	93.35	36.609	-0.784	-9.003	5.754	4.39596	185	0.13996	0.401343	0.12094	1.574646	1.66441	-0.12046	197.06	21.6	52.1	4.08	339.39	175.2	502.2	149.52
13	1	1	1	0	0	0	0	0	Cs	PVC	1	1.389	0.079	23.5194	96.122	38.299	-0.922	-8.888	6.1984	4.73117	220	0.140748	0.582227	0.121825	1.500977	1.75525	-0.14799	231.51	23.5	56.9	4.6	346.37	181.4	519.3	157.99
14	1	1	0	1	0	0	0	0	Cs	QVC	2	1.371	0.088	23.2523	99.56	40.239	-0.971	-8.796	6.1984	4.72844	218	0.140582	0.612622	0.131568	1.500977	1.72994	-0.1302	231.51	23.5	56.9	4.6	340.02	177.8	510	155.38
15	1	1	0	0	1	0	0	0	Cs	D/TVC	2	1.371	0.088	23.1136	95.643	38.243	-0.961	-8.835	6.1984	4.76804	220	0.140536	0.238039	0.120128	1.500977	1.71653	-0.13343	231.51	23.5	56.9	4.6	343.6	180	516.3	157.54
16	1	1	0	0	0	1	0	0	Cs	D/TVC	1	1.366	0.09	22.3232	95.892	38.299	-0.951	-8.868	6.1815	4.79241	226	0.140416	0.019575	0.121126	1.620674	1.71931	-0.13612	231.51	23.5	56.9	4.6	344.39	180.1	516.2	156.52
17	1	1	0	0	0	0	1	0	Cs	QVC	1	1.366	0.09	22.3338	99.571	40.245	-0.943	-8.901	6.1815	4.75491	224	0.14045	0.372914	0.13001	1.620674	1.72238	-0.13323	231.51	23.5	56.9	4.6	354.14	186.2	530.7	160.62
18	1	1	0	0	0	0	0	1	Cs	PVC	2	1.436	0.068	25.7309	94.924	38.207	-0.954	-8.74	6.1984	4.74136	218	0.141387	0.41105	0.120115	1.500977	1.72294	-0.14057	231.51	23.5	56.9	4.6	338.45	176.4	508.3	155.13
19	1	0	1	0	1	0	0	0	Cs	TVC	2	1.315	0.111	22.3052	99.461	40.251	-0.982	-8.865	6.1815	4.74841	220	0.140349	0.428829	0.131177	1.620674	1.68791	-0.11685	231.51	23.5	56.9	4.6	344.92	180.4	516.5	157.15
20	1	0	1	0	0	1	0	0	Cs	DDVC	1	1.31	0.114	21.5166	96.541	38.359	-0.969	-8.982	6.1647	4.77114	226	0.14024	0.225544	0.131091	1.755282	1.68928	-0.1178	231.51	23.5	56.9	4.6	352.27	184.8	527	159.42
21	1	0	1	0	0	0	1	0	Cs	TVC	1	1.31	0.114	21.5121	99.651	40.306	-0.971	-8.9	6.1647	4.76497	226	0.140295	0.278907	0.130949	1.755282	1.69021	-0.11895	231.51	23.5	56.9	4.6	353.6	185.5	528.3	159.73
22	1	0	1	0	0	0	0	1	Cs	QVC	2	1.379	0.085	24.9501	98.881	40.214	-0.977	-8.81	6.1815	4.74157	220	0.141133	0.420877	0.131538	1.620674	1.69457	-0.11305	231.51	23.5	56.9	4.6	342.8	179.1	514.4	156.6
23	1	0	0	1	1	0	0	0	Cs	D/TVC	3	1.384	0.084	25.7541	94.956	38.199	-1.002	-8.872	6.1984	4.76132	216	0.141148	0.230056	0.121149	1.500977	1.68643	-0.11874	231.51	23.5	56.9	4.6	336.88	176.1	506.8	155.19
24	1	0	0	1	0	1	0	0	Cs	DDVC	2	1.315	0.111	22.1869	96.25	38.295	-0.99	-8.841	6.1815	4.77684	222	0.140302	0.164124	0.130458	1.620674	1.68598	-0.1164	231.51	23.5	56.9	4.6	348.48	182.7	522.1	158.7
25	1	0	0	0	0	1	1	0	Cs	QVC	1	1.342	0.1	22.5298	99.526	40.261	-0.939	-8.934	6.1815	4.74912	224	0.140453	0.423488	0.130531	1.620674	1.71393	-0.1316	231.51	23.5	56.9	4.6	349.84	183.8	525	159.49
26	0	1	1	0	0	1	0	0	Cs	D/TVC	0	1.393	0.081	21.7626	96.129	38.336	-0.929	-9.005	6.1647	4.77009	230	0.140424	0.228324	0.122205	1.755282	1.71378	-0.13438	231.51	23.5	56.9	4.6	365.24	192.9	548.1	165.66

Cont. Table 2

No	C1	C2	C3	C4	C5	C6	C7	C8	SYM	VC	AC	RT	PL	H	S	CP	HOMO	LUMO	X1	LogP	WienI	Sp.Pol	Dipole	MaxQ+	Ka3	AbsQ	MaxQ-	Mass	POLAR	REF	Log P	SAsurf	VdWsurf	SASvol	VdWvol
27	1	1	1	1	0	0	0	0	C2v	QVC	2	1.82	0.016	18.8035	102.272	41.967	-1.082	-8.816	6.1647	4.77009	230	0.140424	0.228324	0.122205	1.755282	1.71378	-0.13438	231.51	23.5	56.9	4.6	365.24	192.9	548.1	165.66
28	1	1	1	0	1	0	0	0	Cs	TVC	2	1.754	0.021	17.8434	102.181	41.991	-1.091	-8.886	6.6091	5.06392	267	0.140993	0.391369	0.132009	1.713245	1.77934	-0.14543	265.95	25.4	61.7	5.12	368.82	197.6	561.9	174.04
29	1	1	1	0	0	1	0	0	Cs	DDVC	1	1.754	0.021	17.0508	99.144	40.083	-1.083	-8.953	6.5922	5.08028	274	0.140872	0.230116	0.123609	1.83403	1.78006	-0.14848	265.95	25.4	61.7	5.12	373.24	199.3	565.9	174.2
30	1	1	1	0	0	0	1	0	Cs	TVC	1	1.754	0.021	17.0473	102.36	42.029	-1.079	-8.939	6.5922	5.0845	273	0.140917	0.181631	0.130393	1.83403	1.78227	-0.14537	265.95	25.4	61.7	5.12	369.46	196.9	559.7	172.32
31	1	1	1	0	0	0	0	1	Cs	QVC	2	1.941	0.011	20.4682	101.498	41.944	-1.086	-8.813	6.6091	5.06508	266	0.141672	0.312628	0.123244	1.713245	1.78332	-0.15317	265.95	25.4	61.7	5.12	361.18	192.3	549.6	170.06
32	1	1	0	1	1	0	0	0	Cs	TVC	3	1.824	0.016	20.4013	101.316	41.926	-1.134	-8.759	6.6091	5.05781	264	0.141542	0.391451	0.132997	1.713245	1.75848	-0.13262	265.95	25.4	61.7	5.12	356.95	189.1	542	168.28
33	1	1	0	1	0	1	0	0	Cs	DVC	2	1.637	0.031	16.8106	102.381	42.009	-1.128	-8.846	6.5922	5.0765	271	0.140703	0.277596	0.132293	1.83403	1.75773	-0.13043	265.95	25.4	61.7	5.12	364.2	193.3	551.4	170.02
34	1	1	0	1	0	0	1	0	Cs	DVC	2	1.637	0.031	16.8132	102.499	42.011	-1.123	-8.88	6.5922	5.08156	270	0.140752	0.219311	0.132387	1.83403	1.75868	-0.12976	265.95	25.4	61.7	5.12	364.38	193.2	550.9	169.92
35	1	1	0	1	0	0	0	1	Cs	TVC	3	1.824	0.016	20.3726	101.246	41.916	-1.134	-8.741	6.6091	5.06023	263	0.141543	0.364546	0.133031	1.713245	1.75578	-0.1354	265.95	25.4	61.7	5.12	356.97	189	541.3	167.89
36	1	1	0	0	1	1	0	0	C2h	DDVC	2	1.711	0.024	17.6117	102.129	41.967	-1.099	-8.847	6.6091	5.10156	271	0.140898	0.000138	0.120748	1.713245	1.78036	-0.13435	265.95	25.4	61.7	5.12	360.15	190.9	545.7	168.76
37	1	1	0	0	1	0	1	0	Cs	DVC	2	1.637	0.313	16.8176	102.335	42.011	-1.114	-8.912	6.5922	5.08429	270	0.140743	0.189019	0.131718	1.83403	1.75385	-0.13097	265.95	25.4	61.7	5.12	359.71	190.4	543.3	167.6
38	1	1	0	0	1	0	0	1	Cs	DDVC	3	1.824	0.016	20.2557	97.869	39.946	-1.134	-8.748	6.6091	5.09111	265	0.141545	0.033981	0.121992	1.713245	1.74988	-0.13847	301.41	27.7	67.9	5.76	413.42	223.1	626.6	189.16
39	1	1	0	0	0	1	1	0	Cs	TVC	1	1.754	0.021	17.0144	102.071	42.008	-1.077	-8.938	6.5922	5.08557	275	0.140835	0.176695	0.131126	1.83403	1.77824	-0.13387	265.95	25.4	61.7	5.12	364.44	193.6	551.6	169.65
40	1	1	0	0	0	1	0	1	Cs	TVC	2	1.832	0.016	19.435	101.379	41.945	-1.114	-8.807	6.5922	5.07878	270	0.141467	0.176062	0.132104	1.83403	1.75685	-0.14118	265.95	25.4	61.7	5.12	356.16	188.8	540.1	166.57
41	1	1	0	0	0	0	1	1	C2v	QVC	2	1.907	0.012	20.2043	101.197	41.897	-1.086	-8.78	6.6091	5.07357	267	0.141761	0.214608	0.120891	1.713245	1.78548	-0.13826	265.95	25.4	61.7	5.12	354.77	187.8	538.4	166.49
42	1	0	1	0	1	0	1	0	C2h	NVC	2	1.562	0.042	16.0205	106.085	44.026	-1.139	-8.899	6.5754	5.10236	271	0.14058	0.000037	0.131732	1.968054	1.72558	-0.11308	265.95	25.4	61.7	5.12	362.65	192.8	548.9	168.84
43	1	0	1	0	1	0	0	1	Cs	DVC	3	1.749	0.021	19.4923	101.718	41.952	-1.154	-8.79	6.5922	5.07996	266	0.14131	0.165178	0.132952	1.83403	1.72492	-0.12196	265.95	25.4	61.7	5.12	354.33	188	538.8	166.65
44	1	0	1	0	0	1	1	0	Cs	DVC	1	1.679	0.027	16.2179	102.454	42.058	-1.1	-8.985	6.5754	5.09481	276	0.14066	0.082676	0.131684	1.968054	1.74854	-0.1304	265.95	25.4	61.7	5.12	385.97	209.4	587.2	179
45	1	0	1	0	0	1	0	1	C2v	DVC	2	1.758	0.02	18.6817	102.029	42.023	-1.131	-8.907	6.5754	5.09186	271	0.141224	0.049747	0.132442	1.968054	1.73096	-0.11194	265.95	25.4	61.7	5.12	366.53	195	555.2	170.79
46	1	0	0	1	1	0	0	1	D2h	DDVC	4	1.936	0.011	23.6317	96.996	39.875	-1.18	-8.653	6.6091	5.0875	261	0.142127	0.000067	0.122813	1.713245	1.71665	-0.11881	265.95	25.4	61.7	5.12	354.47	188.5	540.7	169.11
47	1	0	0	1	0	1	1	0	C2v	DVC	2	1.67	0.028	16.8954	102.473	42.003	-1.118	-8.895	6.5922	5.0946	271	0.140722	0.077635	0.131601	1.83403	1.74625	-0.1274	265.95	25.4	61.7	5.12	368.49	196.9	559.1	172.53
48	0	1	1	0	0	1	1	0	D2h	DDVC	2	1.796	0.018	16.448	102.296	42.041	-1.062	-9.076	6.5754	5.10165	281	0.140844	0.000446	0.122829	1.968054	1.7705	-0.13215	265.95	25.4	61.7	5.12	376.2	202.2	571.8	175
49	1	1	1	1	1	0	0	0	Cs	TVC	3	2.352	0.003	15.9927	103.957	43.65	-1.236	-8.77	7.0366	5.33647	314	0.14213	0.270274	0.127821	1.791132	1.85526	-0.14719	300.4	27.3	66.5	5.64	370.25	200.4	571.6	180.33

Cont. Table 2

No	C1	C2	C3	C4	C5	C6	C7	C8	SYM	VC	AC	RT	PL	H	S	CP	HOMO	LUMO	X1	LogP	WienI	Sp.Pol	Dipole	MaxQ+	Ka3	AbsQ	MaxQ-	Mass	POLAR	REF	Log P	SAsurf	VdWsurf	SASvol	VdWvol
50	1	1	1	1	0	1	0	0	Cs	DVC	2	2.151	0.006	12.4106	105.168	43.75	-1.229	-8.879	7.0197	5.3513	322	0.14129	0.178675	0.1312	1.900824	1.85698	-0.14176	300.4	27.3	66.5	5.64	377.31	204.3	579.7	181.55
51	1	1	1	0	1	1	0	0	Cs	DVC	2	2.151	0.006	12.3928	104.924	43.733	-1.219	-8.911	7.0197	5.35125	324	0.141248	0.180476	0.132594	1.900824	1.84971	-0.14643	299.39	26.9	66.5	5.45	379.48	204.4	581	181.41
52	1	1	1	0	1	0	1	0	Cs	NVC	2	2.033	0.008	11.6053	108.671	45.745	-1.239	-8.938	7.0029	5.35667	324	0.141131	0.114814	0.132516	2.02091	1.82352	-0.143	300.4	27.3	66.5	5.64	390.11	212.3	598.7	186.48
53	1	1	1	0	1	0	0	1	Cs	DVC	3	2.234	0.004	15.0657	104.211	43.671	-1.253	-8.805	7.0197	5.34682	318	0.141884	0.154172	0.133792	1.900824	1.81992	-0.15102	300.4	27.3	66.5	5.64	376.76	204.4	579.6	182.16
54	1	1	1	0	0	1	1	0	Cs	DVC	1	2.119	0.005	11.7885	105.048	43.776	-1.205	-9	7.0029	5.36105	330	0.141221	0.061294	0.131439	2.02091	1.84488	-0.1461	300.4	27.3	66.5	5.64	384.25	208.6	589.5	183.6
55	1	1	1	0	0	1	0	1	Cs	DVC	2	2.267	0.004	14.2461	104.459	43.742	-1.235	-8.885	7.0029	5.34733	324	0.141768	0.162492	0.1328	2.02091	1.82507	-0.15387	300.4	27.3	66.5	5.64	377.77	204.4	580.3	181.43
56	1	1	1	0	0	0	1	1	Cs	TVC	2	2.385	0.003	15.125	118.101	43.677	-1.213	-8.832	7.0197	5.35319	322	0.142048	0.073642	0.125121	1.900824	1.85122	-0.15071	300.4	27.3	66.5	5.64	387.91	212.2	598.2	186.95
57	1	1	0	1	1	1	0	0	Cs	DVC	3	2.219	0.004	14.955	103.982	43.661	-1.25	-8.777	7.0197	5.34597	320	0.141841	0.172255	0.133511	1.900824	1.82684	-0.13958	300.4	27.3	66.5	5.64	377.72	203.7	579.2	181.88
58	1	1	0	1	1	0	1	0	Cs	NVC	3	2.101	0.006	14.201	107.932	45.67	-1.276	-8.839	7.0029	5.35952	320	0.14165	0.018521	0.133805	2.02091	1.80824	-0.1363	300.4	27.3	66.5	5.64	379.85	205.1	581.7	181.95
59	1	1	0	1	1	0	0	1	Cs	DVC	4	2.302	0.004	18.3454	103.227	43.595	-1.301	-8.692	7.0197	5.34176	314	0.142473	0.14843	0.13462	1.900824	1.80678	-0.13199	300.4	27.3	66.5	5.64	367.99	197.9	565.7	178.47
60	1	1	0	1	0	1	1	0	Cs	NVC	2	2.033	0.008	11.5683	105.102	43.767	-1.244	-8.91	7.0029	5.35597	326	0.141071	0.129695	0.132889	2.02091	1.82373	-0.12951	300.4	27.3	66.5	5.64	382.62	207	585.8	182.75
61	1	1	0	1	0	1	0	1	Cs	NVC	3	2.101	0.006	14.1714	107.765	45.665	-1.28	-8.798	7.0029	5.34973	320	0.141632	0.136268	0.133711	2.02091	1.80045	-0.13577	299.39	26.9	66.5	5.45	376.66	202.2	576.1	180.77
62	1	1	0	1	0	0	1	1	Cs	DVC	3	2.219	0.004	14.928	103.959	43.657	-1.255	-8.785	7.0197	5.34578	318	0.141938	0.170709	0.13379	1.900824	1.84077	-0.13622	300.4	27.3	66.5	5.64	380.44	206.6	584.9	183.92
63	1	1	1	1	1	1	0	0	Cs	DVC	3	2.809	9E-04	10.5814	106.592	45.394	-1.353	-8.801	7.4473	5.57934	376	0.142331	0.051919	0.130406	1.999226	1.93556	-0.14437	334.84	29.3	71.3	6.16	391.73	214.9	609.5	194.4
64	1	1	1	1	1	0	1	0	Cs	NVC	3	2.647	0.001	9.8325	110.479	47.41	-1.373	-8.835	7.4304	5.57438	377	0.142153	0.127285	0.133621	2.110459	1.90571	-0.1477	334.84	29.3	71.3	6.16	387.44	211.9	601.4	191.19
65	1	1	1	1	1	0	0	1	C2v	DVC	4	2.861	8E-04	14.0125	105.756	45.323	-1.393	-8.714	7.4473	5.57693	370	0.142961	0.005931	0.131175	1.999226	1.90866	-0.14391	334.84	29.3	71.3	6.16	386.07	211.7	602.8	193.16
66	1	1	1	1	0	1	1	0	C2v	NVC	2	2.589	0.002	7.1966	107.805	45.51	-1.343	-8.927	7.4304	5.58632	384	0.1416	0.027863	0.132225	2.110459	1.9274	-0.13939	334.84	29.3	71.3	6.16	400.28	220.1	620.1	195.64
67	1	1	1	0	1	1	1	0	C2h	NVC	2	2.589	0.002	7.2124	111.203	47.462	-1.336	-8.957	7.4304	5.58839	384	0.14157	0.000107	0.132879	2.110459	1.92427	-0.14429	334.84	29.3	71.3	6.16	398.83	218.8	617.2	194.96
68	1	1	1	0	1	1	0	1	Cs	NVC	3	2.647	0.001	9.8067	110.312	47.386	-1.372	-8.839	7.4304	5.57278	379	0.142077	0.156803	0.13435	2.110459	1.90288	-0.15224	334.84	29.3	71.3	6.16	391.05	213.4	606.2	192.59
69	1	1	1	0	1	0	1	1	Cs	NVC	3	2.647	0.001	9.7779	110.19	47.38	-1.371	-8.825	7.4304	5.56417	378	0.142233	0.263566	0.134294	2.110459	1.90796	-0.14865	334.84	29.3	71.3	6.16	391.94	215	608.5	193.23
70	1	1	1	0	0	1	1	1	C2v	DVC	2	2.886	7E-04	9.8349	106.865	45.455	-1.331	-8.893	7.4304	5.56683	383	0.142288	0.227928	0.127443	2.110459	1.9239	-0.15156	334.84	29.3	71.3	6.16	401.85	221.4	624.2	197.35
71	1	1	0	1	1	1	0	1	C2h	NVC	4	2.705	0.001	13.1069	109.203	47.314	-1.416	-8.72	7.4304	5.57866	374	0.142695	0.000157	0.135023	2.110459	1.88798	-0.13295	334.84	29.3	71.3	6.16	376.59	205	584.5	185.97
72	1	1	0	1	1	0	1	1	C2v	NVC	4	2.705	0.001	13.106	109.323	47.313	-1.412	-8.736	7.4304	5.56855	373	0.142771	0.144862	0.135314	2.110459	1.90938	-0.13518	334.84	29.3	71.3	6.16	382.17	209	594.2	189.3
73	1	1	1	1	1	1	1	0	Cs	NVC	3	3.31	3E-04	5.4588	112.809	49.113	-1.461	-8.85	7.8579	5.75684	442	0.142638	0.165514	0.134488	2.188128	2.0081	-0.15004	369.29	31.2	76.1	6.67	394.31	218.1	617.8	198.17
74	1	1	1	1	1	1	0	1	Cs	NVC	4	3.368	2E-04	8.804	111.758	49.043	-1.501	-8.749	7.8579	5.75333	436	0.143206	0.16045	0.135593	2.188128	2.0068	-0.14508	369.29	31.2	76.1	6.67	385.95	212.6	606.1	195.27
75	1	1	1	1	1	1	1	1	D2h	NVC	4	4.03	7E-05	4.5203	114.201	50.775	-1.583	-8.769	8.2855	5.91231	505	0.143598	0.000141	0.135076	2.289658	2.12636	-0.14287	403.73	33.1	81	7.19	394.85	220	626.4	203.82

was investigated. It has been revealed that the PCN peak in the late 1950s to mid-1960s predates the PCBs peak by around 20 years [32].

This study expands the characterisation of all 75 chloronaphthalene congeners by computing some of their basic thermodynamic and physical-chemical property data, which are useful descriptors for further Quantitative Structure Activity Relationship (QSAR) analysis and modelling.

The aim of this study is to extract from the collection of physico-chemical descriptors an information describing in the best way differences/similarities existing between 75 congeners of chloronaphthalene.

Materials and Methods

This paper is divided into two parts. In the first part, a matrix of physico-chemical descriptors was prepared. In the second part, the matrix was analysed using the statistical method of PCA (principal component analysis) and information about similarities between several chloronaphtalene congeners was extracted. For better understanding the information gathered, the electrostatic potential surfaces were drawn for all 75 congeners using SPARTAN 4.0 programme package [4, 36, 42, 45, 52, 58, 74].

Matrices of Physicochemical Descriptors

In the first step, 35 physico-chemical descriptors for all congeners were computed or taken from the literature [12, 28, 60] (Tables 2 and 3). Geometry optimization was carried out using the semiempirical PM3 method [67-69] implemented in MOPAC 93 [70], and HyperChem™ programme package [42]. The QSAR analysis was carried out employing the SciQSAR™ programme package [66].

Table 3. Physico-chemical data of all 75 congeners of chloronaphthalene used in the study.

Descriptor no.	Parameter	Reference
1-8	Substitution pattern	73, 74
9	Symmetry of the molecule	12
10	Vicinal carbon atoms substitution pattern	10, 16
11	Number of chlorine atoms at αpositions	60
12	Retention time	60
13	Vapour pressure	60
14	Standard entalphy of formation	12
15	Standard molar enthropy	12
16	Heat capacity	12
17	Energy of HOMO	12
18	Energy of LUMO	12
19	X1 (a first-order molecular connectivity index)	58, 68, 70
20	Log K_{ow}	58, 68, 70
21	WienI (the Wiener Index)	68, 80
22	Specific polarizability of a molecule	68
23	Dipole moment of the molecule	68
24	Maxq+ (the largest positive charge over the atoms in a molecule)	68
25	Ka3 (Kappa Alpha 3; a third order shape index for molecules)	33, 58, 68
26	Absq (the sum of absolute values of the charges on each atom of the molecule, in electrons)	33, 68
27	Maxq- (the largest negative charge over the atoms in a molecule)	68
28	Molecular weight of a molecule	68
29	Molecular polarizability	42
30	Molecular refractivity	42
31	Log P (hydrophobicity)	42
32	Sasurf (solvent-accessible surface area)	42
33	Vdwsurf (Van der Waals surface area)	42
34	Sasvol (solvent-accessible volume)	42
35	Vdwvol (Van der Waals volume)	42

Variables 1-8 describe naphthalene nuclei chlorination patterns. They were obtained by giving the eight positions open for chlorine substitution in the naphthalene molecule an indicator variable "1" or "0" depending on the presence or absence of chlorine atoms [58, 74].

The symmetry of each molecule (variable 9) was described by one of four possible point groups: C2v (one C2 rotation axis - rotation by 180° and two vertical symmetry planes), C2h (one C2 rotation axis and one horizontal plane), D2h (three C2 rotation axis and one horizontal plane) and Cs (only one plane). The values were extracted directly from MOPAC 93 data files [70].

The vicinal carbon atoms substitution pattern on one or two rings of naphthalne nuclei (variable 10) was reported elsewhere [12, 20]. Depending on a number of vicinal carbon atoms unsubstituted with chlorine at one or two rings, there are a possible eleven different configurations: NVC-C1 PCNs (congeners with no vicinal carbon atoms unsubstituted with chlorine or vicinal hydrogen atoms), DVC-C1 PCNs (congeners which have two vicinal carbon atoms unsubstituted with chlorine/two vicinal hydrogen atoms), DDVC-C1 PCNs (congeners which have two pairs of vicinal carbon atoms unsubstituted with chlorine/two pairs of vicinal hydrogen atoms), TVC-C1 PCNs (having three vicinal carbon atoms unsubstituted with chlorine/three vicinal hydrogen atoms), DTVC-C1 PCNs (congeners which have two and three vicinal carbon atoms unsubstituted with chlorine/two and three vicinal hydrogen atoms), QVC-C1 PCNs (congeners which have four vicinal carbon atoms unsubstituted with chlorine/four vicinal hydrogen atoms), D/TVC-C1 PCNs (congeners which have two and three vicinal carbon atoms unsubstituted with chlorine/two and three vicinal hydrogen atoms), D/QVC-C1 PCNs (congeners which have two and four vicinal carbon atoms unsubstituted with chlorine/two and four vicinal hydrogen atoms), PVC-C1 PCNs (congeners which have five vicinal carbon atoms unsubstituted with chlorine/five vicinal hydrogen atoms), HxVC-Cl PCNs (congeners which have six vicinal carbon atoms unsubstituted with chlorine/six vicinal hydrogen atoms), and HpVC-Cl PCNs (congeners which have seven vicinal carbon atoms unsubstituted with chlorine/seven vicinal hydrogen atoms) (Table 4).

The number of chlorine atoms at α-positions (variable no 11), GC retention times (variable no 12) and supercooled liquid vapour pressure (variable no 13) were taken from the reference (60). The basic thermodynamic properties such as standard enthalpy of formation, standard free enthalpy of formation, molar entropies, heat capacities, energies of HOMO and LUMO (variables 14-18) were extracted from MOPAC 93 data files.

Variables 19-28 were computed using the SciQSAR™ programme package [66]). There are useful QSAR properties such as: a first-order molecular connectivity index (computed over all single bonds of hydrogen-suppresed graphs of the molecules - no hydrogen atoms present); logarithm of the n-octanol-water partition coefficient (logarithm - base 10 - of the ratio of the value of concentrations of a solute distributed between the water-immiscibile solvent, *i.e.* n-octanol - water); the Wiener Index (defined as the sum of the distance between any two carbon atoms in the molecule, in terms of carbon-carbon bonds); specific polarizability of the molecule (defined as a molecular polarizability/molecular volume); dipole moment of the molecule (calculated by the Gasteiger-Marsili method); the largest positive charge over the atoms in a molecule; a third order shape index for molecules - Kappa Alpha 3 (encodes identity of atoms involved in assessing the shape of a molecule and discerns isomers of the same molecule; the sum of absolute values of the relative charges on each atom of the molecule; the largest negative charge over the atoms in a molecule and molecular weight [33, 58, 66, 80].

Variables 29-35 were calculated by using the HyperChem programme package [42]. These are: molecular polarizability (calculated by the atom-based method; refractivity (calculated by the atom-based fragment method developed by Ghose and Crippen); logarithm of the octanol-water partition coefficient (calculated by the atom fragment method); solvent-accessible surface area; Van der Waals surface area; solvent-accessible molecular volume; and Van der Waals molecular volume [31, 36, 42, 58].

Principal Component Analysis of the Data Matrix

In the second step, the collection of physico-chemical data was analyzed using the Principal Component Analysis (PCA) method. PCA is a multivariate projection method summarizing the systematic information in the data matrix. Mathematically, it is the matrix decomposition into means x_k^{mean} scores t_{ia}, loading p_{ak} and residuals e_{ik}, according to the equation (i):

$$x_{ik} = x_k^{mean} + \sum_{a=1}^{A} t_{ia} p_{ak} + e_{ik} \qquad \text{(i)}$$

where x_{ik} are the physico-chemical descriptors compiled in the multivariate characterization. Index i is used for the compounds (i = 1,2,3,...,75), while index k for the descriptors (k = 1,2,3,...,35). Each score 4, describes the location of the i-th compound along α-th principal component (PC) at the score plot. The absolute value of a loading p_{ak} informs how much the descriptor (variable k) contributes to α-th PC. The sign of a loading shows whether the variable is positively or negatively correlated to the PC. The first calculated principal component explains the main variation in the data, the second represents the next largest variance, *etc.* [45, 52, 73-74].

Results and Discussion

The computed basic thermodynamic and physico-chemical descriptors for chloronaphthalenes together with some data taken from literature are presented in Table 2. All congeners of chloronaphthalene are thermodynamically unstable. Nevertheless, the absolute values of standard enthalpy of formation (ΔfH°) and free enthalpy of formation (ΔfG°) decrease with increasing numbers of attached chlorine atoms. This means that less chlorinated congeners are more susceptible to degradation than those which are more chlorinated. Thus, in descending order, octa-, hepta-, hexa- and penta-CNs are

more stable than tetra-, tri-, di- or mono-CNs, respectively. The thermodynamic stability of the congeners of chloronaphthalene depends not only on the number of attached chlorine atoms but also on their structure. For example, 1,3,5,7-TeCN (no. 42), l,2,3,5,7-/l,2,4,6,7-PeCN (nos. 52/60), 1,2,4,6,8-PeCN (no. 61) and 1,2,3,4,6,7-/1,2,3,5,6,7-hexaCN (nos. 66/67) all posses one of the lowest absolute values of standard enthalpy of formation and free enthalpy of formation within a given chloronaphthalene homologue group (Table 2). These congeners indicated above were identified recently as most abundant in tissues of top marine predators such as the adult white-tailed sea eagle [23]. They are also characterised by the greatest values of biomagnification factor when calculated for white-tailed sea eagle, black and fish in relation to their food [9,13,14]. Another characteristic feature of these relatively persistent congeners of chloronaphthalene is a specific structure - no one has vicinal (adjacent) carbon atoms unsubstituted with chlorine on one or both rings (Table 4). In other words they have no vicinal hydrogen atoms [16].

HOMO energies of chloronaphthalenes differ only slightly and changes of these do not correlate with a degree of chlorination. The negative energies of HOMO and LUMO approximate, according to Koopman's theory, the first ionization potential and electron affinity of molecules, respectively. The dipole moments are more dependent on the constitution and less on degree of chlorination of molecules. Hence, the congeners of chloronaphthalene with chlorine atoms distributed symmetrically exhibit minimal values of dipole moments and those with chlorine atoms distributed non-symmetrically - the highest values of this quantity. Higher chlorinated congeners will more easily attract an electron than less chlorinated ones. However, all congeners of chloronaphthalene should form thermodynamically stable negative ions.

35 physico-chemical descriptors for each congener (Table 3) were taken for analysis by Principal Component (PCA) method. The PCA of the physico-chemical data matrix gave a four-dimensional model that explained 76% (58% + 9% + 5% + 4%) of the total variance. The loading plot shows that the first PC is influenced by variables describing degree of chlorination, molecular weight, polarizability and lipophilicity (Fig. 1).

The best positively correlated descriptors are: retention time, standard molar entropy, heat capacity, a first-order molecular connectivity index, logarithm of octanol-water partition coefficient, the Wiener Index, specific polarizability, a third order shape index for molecules, the sum of absolute values of charges on each atom of the molecule, molecular weight, polarizability,

Table 4. Selection of chloronaphthalene congeners according to the pattern of substitution of vicinal carbon atoms on one or two rings with chlorine.

Code/pattern of unsubstitution of vicinal carbon atoms with chlorine	Total number of congeners	Homologue group	Total number of isomers	PCN no.
NVC-Cl PCNs	15	Tetra-	1	42
		Penta-	4	52, 58, 60, 61
		Hexa-	7	64, 66, 67, 68. 69, 71, 72
		Hepta-	2	73, 74
		Octa-	1	75
DVC-Cl PCNs	18	Tetra-	7	33, 34, 37, 43, 44, 45, 47
		Penta-	8	50, 51, 53, 54, 55, 57, 59, 62
		Hexa-	3	63, 65, 70
DDVC-Cl PCNs	7	Tri-	2	20, 24
		Tetra-	5	29, 36, 38, 46, 48
TVC-Cl PCNs	10	Tri-	2	19, 21
		Tetra-	6	28, 30, 32, 35, 39, 40
		Penta-	2	49, 56
DTVC-Cl PCNs	2	Di-	2	6, 11
QVC-Cl PCNs	7	Tri-	4	14, 17, 22, 25
		Tetra-	3	27, 31, 41
D/TVC-Cl PCNs	4	Tri-	4	15, 16, 23, 26
D/QVC-Cl PCNs	3	Di-	3	5, 7, 12
PVC-Cl PCNs	4	Di-	2	4, 8
		Tri-	2	13, 18
HxVC-Cl PCNs	3	Di-	3	3, 9, 10
HpVC-Cl PCNs	2	Mono-	2	1, 2

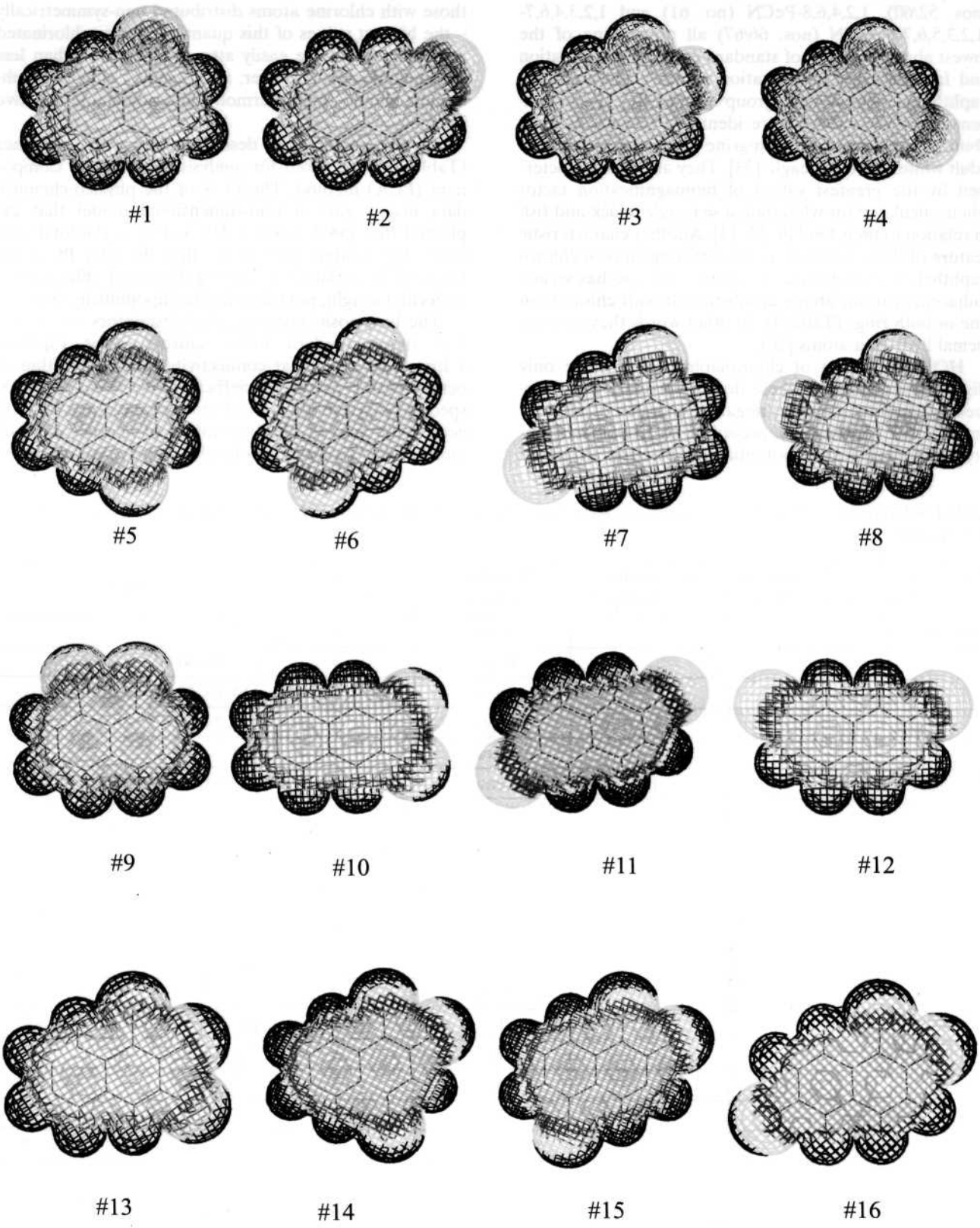


Fig. 1. The electrostatic potential surfaces of mono-, di- and tri-CNs.

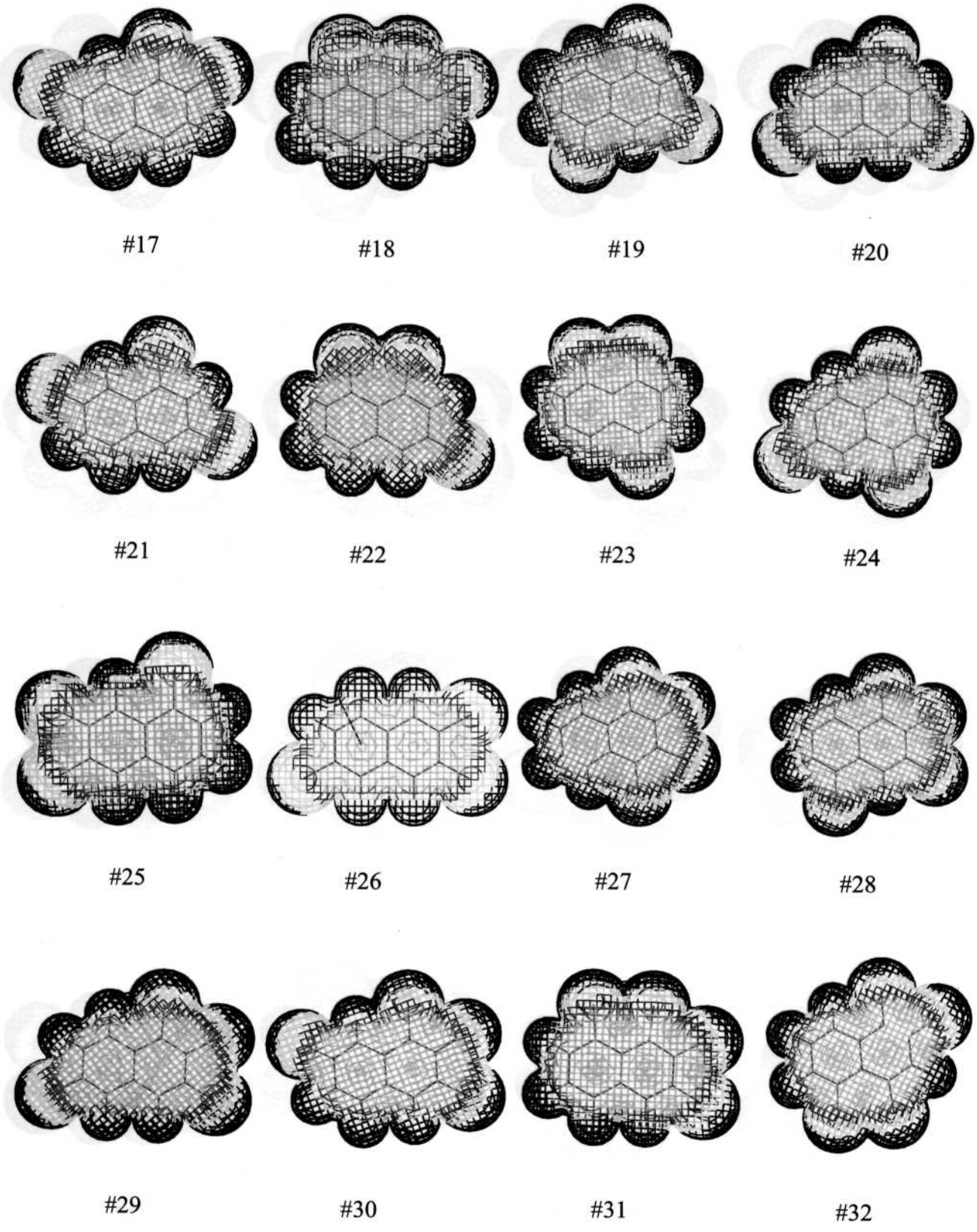


Fig. 2. The electrostatic potential surfaces of tri-, and tetra-CNs.

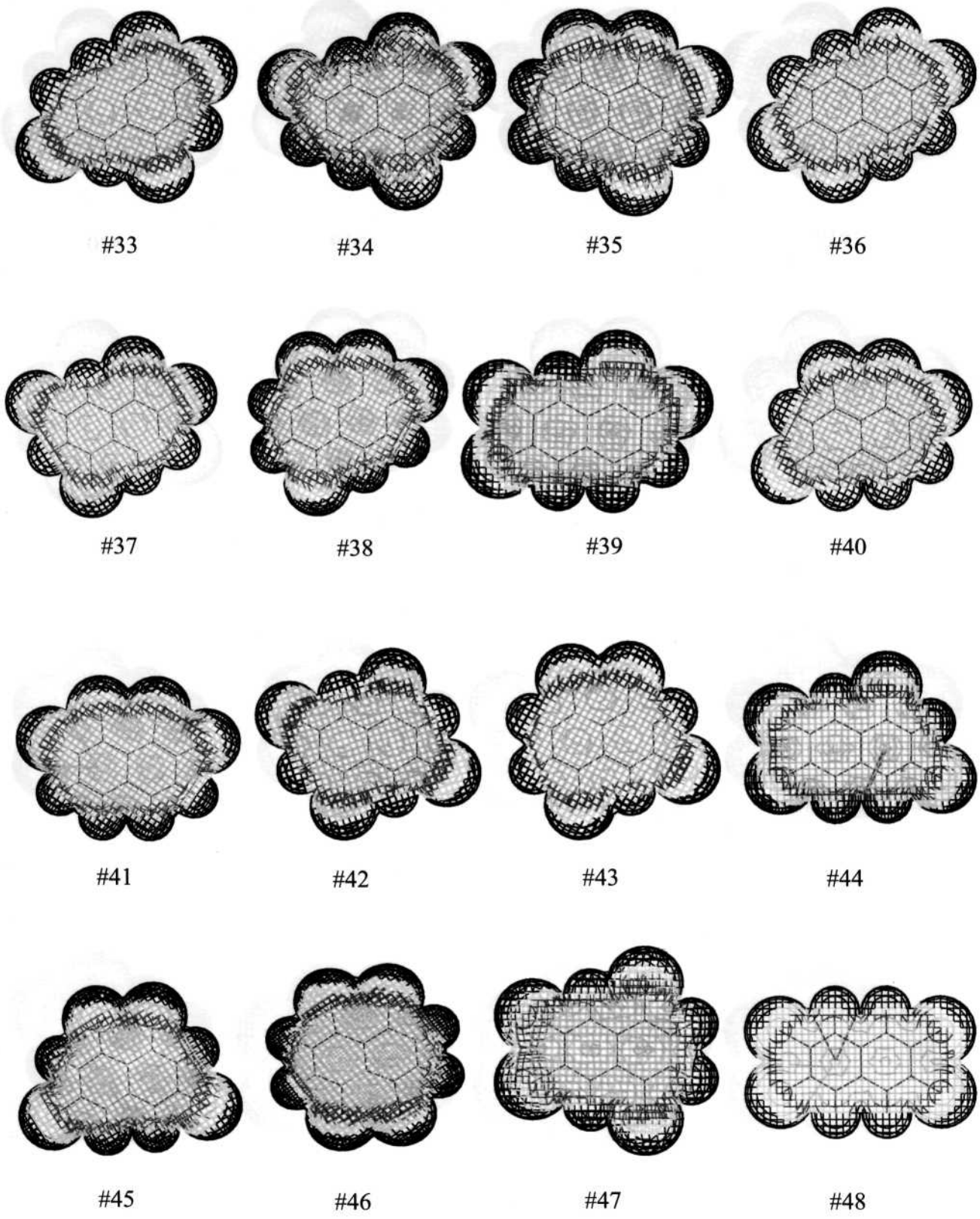


Fig. 3. The electrostatic potential surfaces of tetra-CNs.

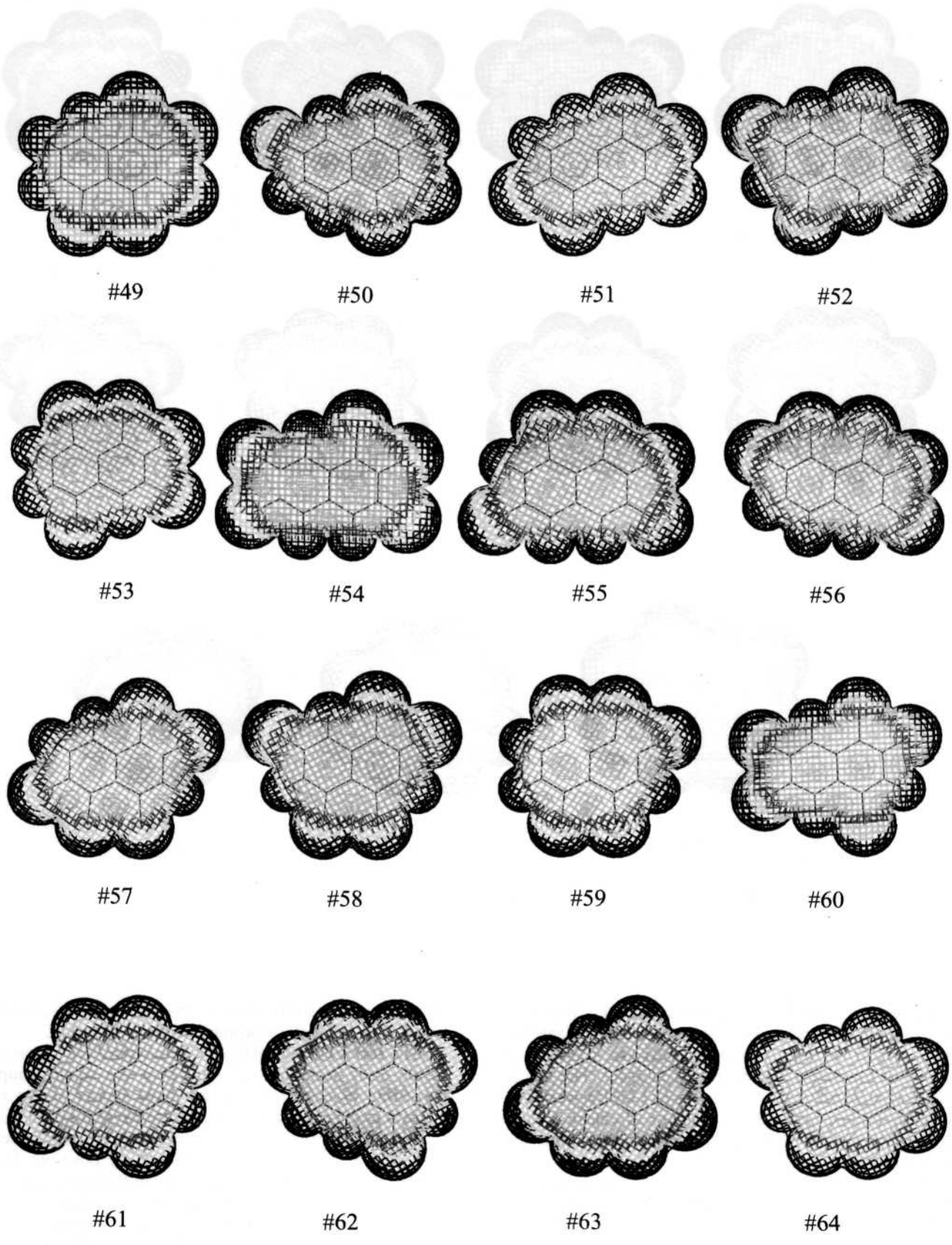


Fig. 4. The electrostatic potential surfaces of penta- and hexa-CNs.

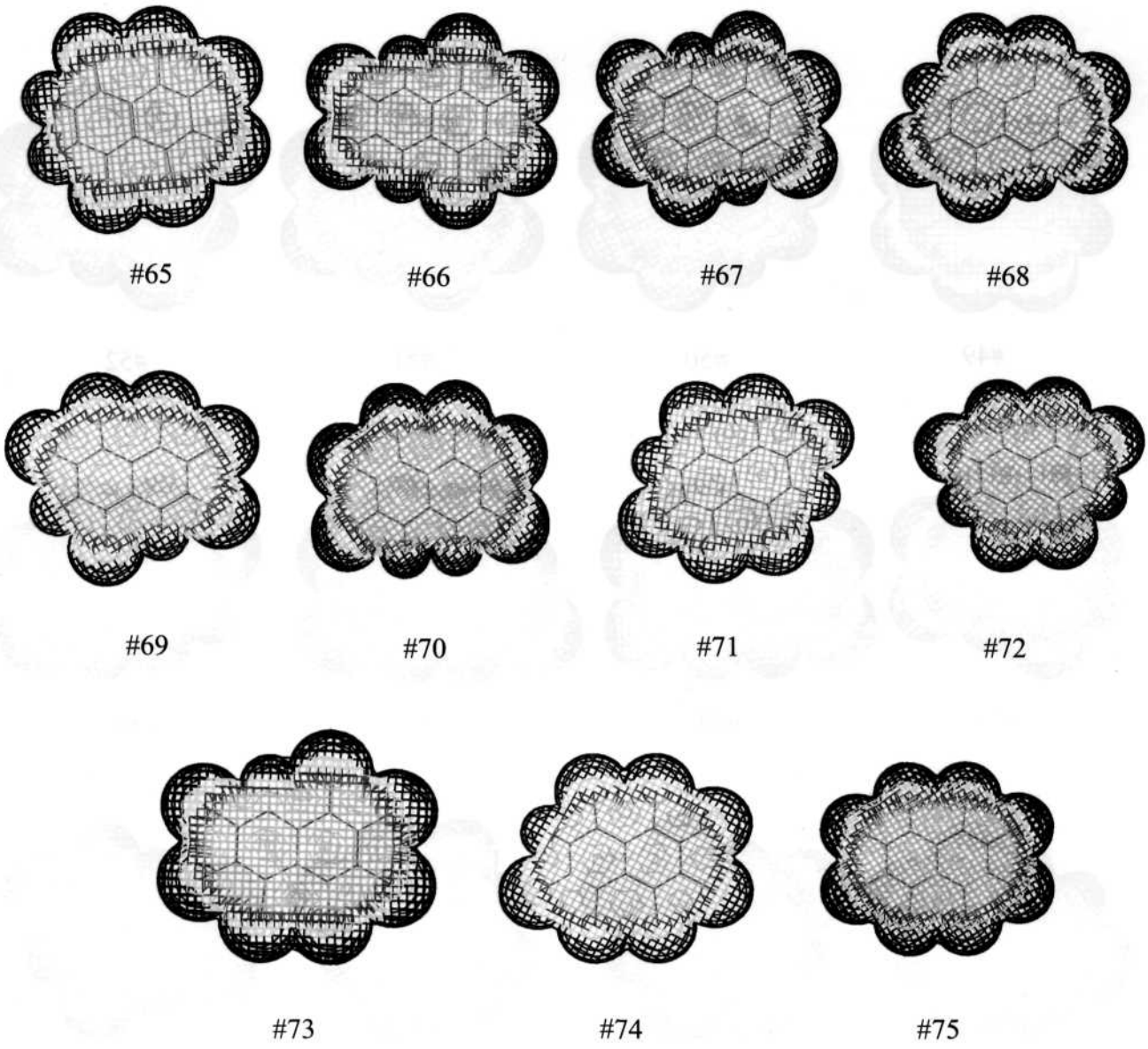


Fig. 5. The electrostatic potential surfaces of hexa-, hepta- and octa-CNs.

refractivity, solvent-accessible surface, van der Waals surface, solvent-accessible volume and van der Waals volume. Negatively correlated descriptors are: standard enthalpy of formation and energy of HOMO. The second PC is strongly influenced by energy of LUMO, while substitution pattern parameters, number of chlorine atoms at α-positions and vicinal (adjacent) carbon atoms substitution pattern are less important.

The third PC (Fig. 2) is depended on dipole moment, the largest negative charge, and on substitution at position 2 of naphthalene nuclei, while symmetry group parameter is determined by PC4. The resulting score plot is shown in Figure 3. The congeners are distributed in eight prominent groups, monochloronaphtalenes to the left, and then successively, the di-, tri-, tetra-, penta-, hexa-, hepta-CNs and octachloronaphtalene to the right.

The second Principal Component separates congeners inside each prominent group. There are small groups consisting of compounds which have similar values of LUMO energy and substitution patterns. It is interesting that chloronaphthalene congeners which are substituted with chlorine at all five (1,2,3,6 and 7) positions (indicated by Fv/Fv) are located always in the upper part of each prominent group. The next clusters, which can be found in lower parts of the scatter plot, consist of the chloronaphthalene congeners, which are substituted with chlorine only at four (Fr/Fv), three (Tr/Fv) and so on positions (Table 5).

Table 5. Polychlorinated naphthalene subgroups separated by the second PC.

Subgroup	PCNs No.
Pentachloronaphtalenes	
Fv/Fv	54
Fr/Fv	50, 51, 52, 55, 56, 60
Tr/Fv	49, 53, 57, 58, 61, 62
Tw/Fv	59
Hexachloronaphtalenes	
Fv/Fv	66, 67, 70
Fr/Fv	63, 64, 68, 69
Tr/Fv	65, 71, 72
Heptachloronaphtalenes	
Fv/Fv	73
Fr/Fv	74
Octachloronaphtalenes	
Fv/Fv	75

Compared to this extracted structure information describing similarities in physico-chemical properties of CN congeners to data from dioxin-like activity in *in vitro* bioassays, it can be observed that chloronaphtalenes substituted with chlorine at positions 1, 2, 3, 6 and 7 (Fv/Fv PCN congeners), and next those substituted at positions 1, 2, 3 and 6 or 7 (Fr/Fv PCB congeners) are considered to be most potent in terms of dioxin-like toxicity. It seems to be possible to estimate the values of TCDD TEFs (or relative toxic potency, RTP) of the chloronaphthalene congeners, which until now were not tested experimentally and/or those for which no standards are available [27].

The surfaces of an electrostatic potential surrounding for all 75 chloronaphthalene congeners are given in Figures 4-8. The electrostatic potential surrounding molecules reflects their ability to interact with nucleophilic or electrophilic reagents. Blue colour indicates negative and red positive values of the electrostatic potential. The deeper the colour, the more distinctive the ability to interact. The regions of highly positive potential are susceptible to nucleophilic substitution and negative potential to electrophilic substitution. As these reactions should indicate on chemical degradation of chloronaphthalenes, a thorough analysis of electrostatic potential around molecules enables preliminary insight into reactivity, possibilities of interaction and their derivatives.

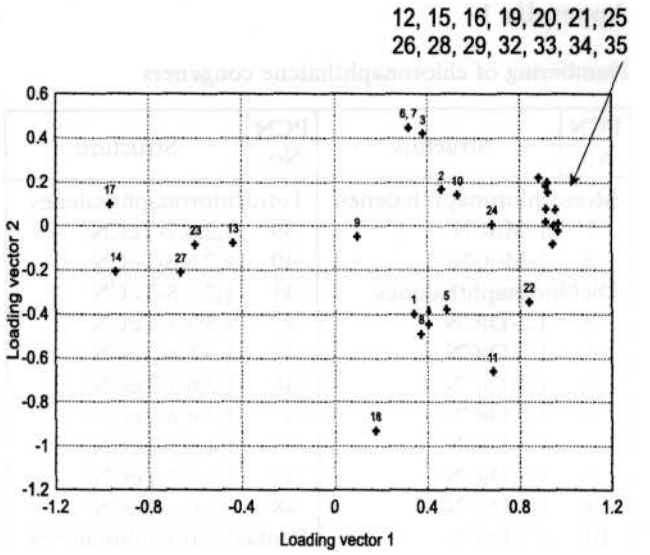


Fig. 6. Loading plot. Loading vector 2 versus Loading vector 1 (the number of variables are given in Table 3 and explained in **text).**

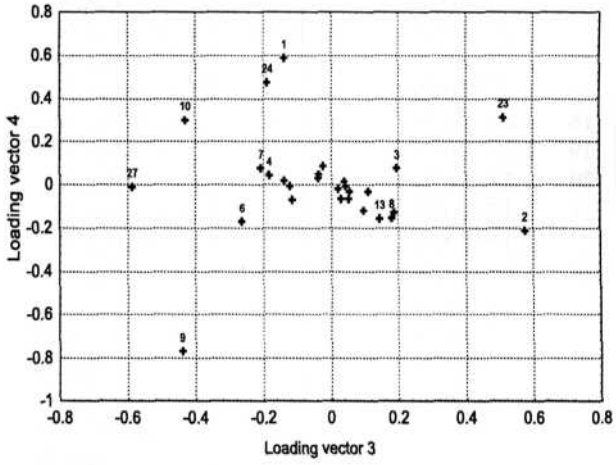


Fig. 7. Loading plot. Loading vector 4 versus Loading vector 3 (the number of variables are given in Table 3 and explained in **text).**

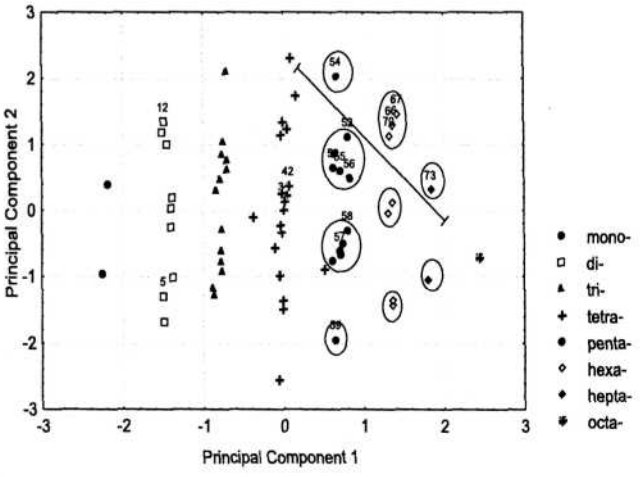


Fig. 8. Score plot of Principal Component 2 versus Principal Component 1.

Appendix 1

Numbering of chloronaphthalene congeners

PCN No.	Structure	PCN No.	Structure
Monochloronaphthalenes		Tetrachloronaphthalenes	
1	1-MoCN	39	1,2,6,7-TeCN
2	2-MoCN	40	1,2,6,8-TeCN
Dichloronaphthalenes		41	1,2,7,8-TeCN
3	1,2-DiCN	42	1,3,5,7-TeCN
4	1,3-DiCN	43	1,3,5,8-TeCN
5	1,4-DiCN	44	1,3,6,7-TeCN
6	1,5-DiCN	45	1,3,6,8-TeCN
7	1,6-DiCN	46	1,4,5,8-TeCN
8	1,7-DiCN	47	1,4,6,7-TeCN
9	1,8-DiCN	48	2,3,6,7-TeCN
10	2,3-DiCN	Pentachloronaphthalenes	
11	2,6-DiCN	49	1,2,3,4,5-PeCN
12	2,7-DiCN	50	1,2,3,4,6-PeCN
Trichloronaphthalenes		51	1,2,3,5,6-PeCN
13	1,2,3-TrCN	52	1,2,3,5,7-PeCN
14	1,2,4-TrCN	53	1,2,3,5,8-PeCN
15	1,2,5-TrCN	54	1,2,3,6,7-PeCN
16	1,2,6-TrCN	55	1,2,3,6,8-PeCN
17	1,2,7-TrCN	56	1,2,3,7,8-PeCN
18	1,2,8-TrCN	57	1,2,4,5,6-PeCN
19	1,3,5-TrCN	58	1,2,4,5,7-PeCN
20	1,3,6-TrCN	59	1,2,4,5,8-PeCN
21	1,3,7-TrCN	60	1,2,4,6,7-PeCN
22	1,3,8-TrCN	61	1,2,4,6,8-PeCN
23	1,4,5-TrCN	62	1,2,4,7,8-PeCN
24	1,4,6-TrCN	Hexachloronaphthalenes	
25	1,6,7-TrCN	63	1,2,3,4,5,6-HxCN
26	2,3,6-TrCN	64	1,2,3,4,5,7-HxCN
Tetrachloronaphthalenes		65	1,2,3,4,5,8-HxCN
27	1,2,3,4-TeCN	66	1,2,3,4,6,7-HxCN
28	1,2,3,5-TeCN	67	1,2,3,5,6,7-HxCN
29	1,2,3,6-TeCN	68	1,2,3,5,6,8-HxCN
30	1,2,3,7-TeCN	69	1,2,3,5,7,8-HxCN
31	1,2,3,8-TeCN	70	1,2,3,6,7,8-HxCN
32	1,2,4,5-TeCN	71	1,2,4,5,6,8-HxCN
33	1,2,4,6-TeCN	72	1,2,4,5,7,8-HxCN
34	1,2,4,7-TeCN	Heptachloronaphthalenes	
35	1,2,4,8-TeCN	73	1,2,3,4,5,6,7-HpCN
36	1,2,5,6-TeCN	74	1,2,3,4,5,6,8-HpCN
37	1,2,5,7-TeCN	Octachloronaphthalenes	
38	1,2,5,8-TeCN	75	1,2,3,4,5,6,7,8-OCN

Acknowledgements

Thus study was supported by the Japan Society for the Promotion of Science (JSPS) under a Senior Short-Term Invitation Fellowship Program for Research in Japan awarded to prof. J. Falandysz, and partly by the Polish State Committee of Scientific Research (KBN) under the Scientific and Technological Cooperation Joint Project between Poland and Japan for 1999-2000 (R-92) and 2001-2003, and grant DS/8250-4-0092-01.

References

1. AKERBLOM N., OLSSON K., BERG A. H., ANDERSSON P. L., TYSKLIND M., FORLIN L., NORRGREN L. Impact of polychlorinated naphthalenes (PCNs) in juvenile Baltic salmon, *Salmo salar*. Evaluation of estrogenic effects, development, and CYP1A induction. Archives of Environ mental Contamination and Toxicology, **38,** 225, **2000.**
2. AITTOLA J-P, PAASIVIRTA J, VATTULAINEN A, SINKKONEN S, KOISTINEN J, TARHANEN J. Formation of chloroaromatics at a metal reclamation plant and efficiency of stack filter in their removal from emission. Organohalogen Compounds, **19,** 321, **1994.**
3. ASPLUND L. Development and application of methods for determination of polychlorinated organic pollutants in biota. Ph. D. Thesis, Stockholm University, **1994.** ISBN 91-7152-272-2.
4. BAKER J. An algotithm for the location of transition states. Journal of Computational Chemistry, **7,** 385, **1986.**
5. BLANKENSHIP A., KANNAN K., VILLALOBOS S., VILLENEUVE D., FALANDYSZ J., IMAGAWA T., JAKOBSSON E., GIESY J. Relative potencies of Halowax mixtures and individual polychlorinated naphthalenes (PCNs) to in duce Ah receptor-mediated responses in the rat hepatoma H4IIE-luc cell bioassay. *Dioxin'99, 19th Symposium on Halogenated Environmental Organic Pollutants*, September 12-17, 1999, Venice, Italy. Organohalogen Compounds, **42, 217, 1999.**
6. BLANKENSHIP A., KANNAN K, VILLALOBOS S., VILLENEUVE D., FALANDYSZ J., IMAGAWA T., JAKOBSSON E., GIESY J. Relative potencies of Halowax mixtures and individual polychlorinated naphthalenes (PCNs) to in duce Ah receptor-mediated responses in the rat hepatoma H4IIE-Luc cell bioassay. Environmental Science and Tech nology, 34, 3153, **2000.**
7. BRINKMAN U. A. T. H, REYMER H. G. M. Poly chlorinated naphthalenes. Journal of Chromatography, **127,** 203, **1976.**
8. ELJARRAT E., CAIXACH J, JIMENEZ B., GONZALEZ M. J., RIVERA J. Polychlorinated naphthalenes in sedi ments from the Venice and Orbetello Lagoons, Italy. Chemosphere, 38 (8), 1901, **1999.**
9. FALANDYSZ J. Polichlorowane naftaleny w srodowisku. Farmacja Polska, **37 (3)** 125, **1981.**
10. FALANDYSZ J. Polychlorinated naphthalenes: an environ mental update. Environmental Pollution, **101 (1),** 77, **1998.**
11. FALANDYSZ J. Polychlorinated biphenyls (PCBs) in the environment: chemistry, analysis, toxicity, concentrations and risk assessment (in Polish). Fundacja Rozwoju Uniwersytetu Gdanskiego. ISBN-83-86230-52-5. Gdansk, **1999.**
12. FALANDYSZ J., RACINIEWSKA M., BLAZEJOWSKI J, GOLASZEWSKA I., SKURSKI P. Thermodynamic and physicochemical properties *vis.* some ecotoxicological fea tures of polychlorinated naphthalenes. *Dioxin'98, 18th Sym posium on Halogenated Organic Pollutants*, Stockholm, Au gust 17-21,1998. Organohalogen Compounds, **36,** 471,**1998.**
13. FALANDYSZ J., STRANDBERG L., BERGQVIST P-A, STRANDBERG B., RAPPE C. Spatial distribution and bioaccumulation of polychlorinated naphthalenes (PCNs) in mussel and fishes from the Gulf of Gdansk, Baltic Sea. The Science of the Total Environment, **203 (2)** 93, **1997.**
14. FALANDYSZ J., STRANDBERG B., STRANDBERG L., BERGQVIST P-A., RAPPE C. Concentrations and biomagnification of polychlorinated naphthalenes in black cormor-

ants *Phalacrocorax carbo sinensis* from the Gulf of Gdansk, Baltic Sea. The Science of the Total Environment, **204 (2)** 97, **1997.**

15. FALANDYSZ J., RAPPE C: Specific pattern of tetrachloronaphthalenes in black cormorant. Chemosphere, 35 (8) 1737, **1997.**
16. FALANDYSZ J. Bioaccumulation and biomagnification features of polychlorinated naphthalenes. *Dioxin'97, 17th Symposium on Chlorinated Dioxins and Related Compounds,* Indianapolis, August 24-29, 1997. Organohalogen Compounds, **32,** 374, **1997.**
17. FALANDYSZ J., STRANDBERG L., STRANDBERG B., RAPPE C. Polichlorowane naftaleny (PCNs) w omutku *Mytilus trosulus* i storni *Platychthis flesus* z Zatoki Gdaiiskiej. Bromatologia i Chemia Toksykologiczna, **30 (2),** 183, **1997.**
18. FALANDYSZ J., RAPPE C. Spatial distribution in plankton and bioaccumulation features of polychlorinated naphthalenes in a pelagic food chain in southern part of the Baltic proper. Environmental Science and Technology, 30 (11), 3362, **1996.**
19. FALANDYSZ J., STRANDBERG L, BERGQVIST P-A., KULP S. E., STRANDBERG B., RAPPE C. Polychlorinated naphthalenes in sediment and biota from the Gdansk Basin, Baltic Sea. Environmental Science and Technology, 30 (11), 3266, **1996.**
20. FALANDYSZ J., STRANDBERG B, KULP S. E., STRANDBERG L., BERGQVIST P-A., RAPPE C. Kongenero-specyficzna analiza chloronaftalenow w ciernikach *Gasterosteus aculleatus* z roznych miejsc w Zatoce GdaAskiej. Bromatologia i Chemia Toksykologiczna, **26 (4),** 393, **1996.**
21. FALANDYSZ J., KULP S. E., STRANDBERG L., STRANDBERG B., BERGQVIST P-A., RAPPE C. Polichlorowane naftaleny w morswinach *Phocoena phocoena.* Roczniki Panstwowego Zaktadu Higieny, **47 (3),** 265, **1996.**
22. FALANDYSZ J., STRANDBERG L., KULP S. E., STRANDBERG B., BERGQVIST P-A., RAPPE C. Polichlorowane naftaleny w niektorych gatunkach ryb z Zatoki Gdafiskiej. Bromatologia i Chemia Toksykologiczna, **29 (3),** 253, **1996.**
23. FALANDYSZ J, STRANDBERG L., KULP S.E., STRANDBERG B., BERGQVIST P-A., RAPPE C. Congener-specific analysis of chloronaphthalenes in white-tailed sea eagles *Haliaeetus albicilla* breeding in Poland. Chemosphere, **33 (1),** 51, **1996.**
24. FALANDYSZ J., STRANDBERG B., STRANDBERG L., BERGQVIST P-A., KULP S. E., RAPPE C. Badania rozmieszczenia przestrzennego chloronaftalenow w storni *Platychthis flesus* z Zatoki Gdanskiej. Roczniki Panstwowego Zaktadu Higieny, **47 (3),** 257, **1996.**
25. FALANDYSZ J, STRANDBERG L., BERGQVIST P-A., STRANDBERG B., RAPPE C. Analysis of the spatial distribution of chloronaphthalene congeners in stickleback *Gasterosteus aculeatus* from the Gulf of Gdansk, Baltic Sea. *Dioxin'96, 16th Symposium on Chlorinated Dioxins and Related Compounds,* Amsterdam, August 12-16, 1996. Organohalogen Compounds, **28,** 446, **1996.**
26. FALANDYSZ J., STRANDBERG B., STRANDBERG L., RAPPE C. Polychlorinated naphthalenes in three-spined stickleback *Gasterosteus aculeatus* from the Gulf of Gdansk. Chemosphere, 37 (9-12), 2473, **1998.**
27. FALANDYSZ J., PUZYN T. Relationships between energy of LUMO and dioxin-like activity of PCNs in the luciferase test. *Dioxin 2000, 20th Symposium on Halogenated Environmental Organic Pollutants,* August 14-17, 2000, Monterey, California. Organohalogen Compounds, **47,** 163, **2000.**
28. FLANDYSZ J., PUZYN T., MARKUSZEWSKI M., KALISZAN R. Multivariate physico-chemical characterisation of polychlorinated naphthalenes (PCNs). *Dioxin 2000, 2Oh Symposium on Halogenated Environmental Organic Pollutants,* August 14-17, 2000, Monterey, California. Organohalogen Compounds, **47,** 147, **2000.**
29. FALANDYSZ J., KANNAN K, KAWANO M., RAPPE C. Relative contribution of chlorinated naphthalenes, -biphenyls, -dibenzofurans and -dibenzo-p-dioxins to toxic equivalents in biota from the south coast of the Baltic Sea. *Dioxin 2000, 2ffh Symposium on Halogenated Environmental Organic Pollutants,* August 14-17, 2000, Monterey, California. Organohalogen Compounds, **47,** 9, **2000.**
30. FALANDYSZ J., KAWANO M., UEDA M., MATSUDA M., KANNAN K., GIESY J. P., WAKIMOTO T. Composition of chloronaphthalene congeners in technical chloronaphthalene formulations of the Halowax series. Journal of Environmental Sciences and Health, 35A **(3),** 111, **2000.**
31. GASTEIGER J., MARSILI M. Iterative partial equalization of orbital electronegativity - a rapid access to atomic charges. Tethrahedron, 36, 3219, **1980.**
32. GEVAO **B.,** HARNER T, JONES K. C. Sedimentary record of polychlorinated naphthalene concentrations and deposition fluxes in a dated lake core. Environmental Science and Technology, **34 (1),** 33, **2000.**
33. HALL L., KIER B. The molecular connectivity chi indexes and kappa shape indexes in structure-property modeling. Reviews in Computational Chemistry, **2,** 367, **1991.**
34. HANBERG A, STAHLBERG M., GEORGELLIS A., DE WIT C, AHLBORG U. G. Swedish dioxin survey: evaluation of the H-4-II E bioassay for screening environmental samples for dioxin-like enzyme induction. Pharmacology and Toxicology, **69,** 442, **1991.**
35. HANBERG A., WAERN F, ASPLUND L, HAGLUND E., SAFE S. Swedish dioxin survey - determination of 2,3,7,8-TCDD toxic equivalent factors for some polychlorinated biphenyls and naphthalenes using biological tests. Chemosphere, **20,** 2261, **1990.**
36. HANSCH C, LEO A. Exploring QSAR. Fundamentals and applications in chemistry and biology. American Chemical Society. ISBN 0-8412-2993-7. Washington, DC **1995.**
37. HARNER T., BIDLEMAN T. F. Polychlorinated naphthalenes in urban air. Atmospheric Environment, 31 (23) 4009, **1997.**
38. HARNER T., BIDLEMAN T. F. Measurement of octanol-air partition coefficients for polycyclic aromatic hydrocarbons and polychlorinated naphthalenes. Journal of Chemical Engineering Data, 43 (1) 40, **1998.**
39. HARNER T., LEE R.T.M., JONES K.C. Polychlorinated naphthalenes in the atmosphere of the United Kingdom. Environmental Science and Technology, in press, **2000.**
40. HARNER T., KYLIN H., BIDLEMAN T. F., HALSALL C, STRACHAN W. M. J., BARRIE L. A, FELLIN P. H. Polychlorinated naphthalenes and coplanar polychlorinated biphenyls in Arctic air. Environmental Science and Technology, 32 (21), 3257, **1998.**
41. HELM PA., JANTUNEN L.M.M., BIDLEMAN T.F., DORMAN F.L. Complete separation of isomeric penta- and hexachloronaphthelenes by capillary gas chromatography. Journal of High Resolution Chromatography, **22 (11)** 639, **1999.**

42. HyperChem™. Release 5.0 for Windows, Reference Man ual. Hypercube, Inc., Publication HC50-00-01-00, **1996.**
43. IMAGAWA T., YAMASHITA N. Estimation of emission sources of polychlorinated naphthalenes using finger-print method for isomer composition (in Japanese). Journal of Environmental Chemistry, **6 (4),** 495, **1996.**
44. ISHAQ R., KARLSON K., NAF C. Tissue distribution of polychlorinated naphthalenes (PCNs) and *non-ortho* chlor inated biphenyls *(non-ortho* PCBs) in harbour porpoises *(Phocoena phocoena)* from Swedish waters. Chemosphere, in press, **2000.**
45. JACKSON J.E. A user's guide to principal components. J. Wiley Sons, New York, USA, **1991.**
46. JAKOBSSON E. Synthesis and analysis of polychlorinated naphthalenes. Biological and environmental implications. Ph. D. Thesis, Stockholm University, **1994.** ISBN 91 7153 241 2.
47. JANSSON B., ANDERSSON R., ASPLUND L., BE RGMAN A., LITZEN K., NYLUND K., REUTHER-GARDH L., SELLSTROM U., UVEMO U-B., WAH-LBERG C, WIDEQUIST U. Multiresidue method for **the** gas-chromatographic analysis of some polychlorinated and polybrominated pollutants in biological samples. Fresenius' Journal of Analytical Chemistry, **340,** 439, **1991.**
48. JARNBERG U. Analytical methods for studying poly chlorinated naphthalene congener profiles and levels in the environment. Ph. D. Thesis, Stockholm University, **1997.** ISBN 91-7153-6582.
49. JARNBERG U., ASPLUND L., DE WITT C, EGEBACK A-L. WIDEQUIST U., JAKOBSSON E. Distribution of polychlorinated naphthalene congeners in environmental and source-related samples. Archives of Environmental Contamination and Toxicology, **32,** 232, **1997.**
50. JARNBERG U., ASPLUND L., EGEBACK A-L. JAN SSON B., UNGER M., WIDEQUIST U. Polychlorinated naphthalene congener profiles in background sediments compared to a degraded Halowax 1014 technical mixture. Environmental Science and Technology, **33 (1),** 232, **1999.**
51. JARNBERG U., ASPLUND C, DE WIT C, GRAF-STROM A-K., HAGLUND P., JANSSON B, LEXEN K., STRANDELL M., OLSSON M., JONSSON B. Poly chlorinated biphenyls and polychlorinated naphthalenes in Swedish sediment and biota: Levels, patterns, and time trends. Environmental Science and Technology, **27** (7), 1364, **1993.**
52. JOLLIFFE T. Principal component analysis. Springer-Ver-lag, New York, USA, **1986.**
53. KANNAN, K., IMAGAWA T, BLANKENSHIP A. L, GIESY J. P. Isomer-specific analysis and toxic evaluation of polychlorinated naphthalenes in soil, sediment, and biota collected near the site of a former chlor-alkali plant. Envi ronmental Science and Technology, **32** (17), 2507, **1998.**
54. KANNAN K., YAMASHITA N., IMAGAWA T., DE-COEN W, KHIM J. S., DAY R. M., SUMMER C. L., GIESY J. P. Polychlorinated naphthalenes and poly chlorinated biphenyls in fishes from waters including the Great Lakes. Environmental Science and Technology, **34** (4), 566, **2000.**
55. KAWANO M, UEDA M., FALANDYSZ J., MATSUDA M. Polychlorinated naphthalenes (PCNs) in human adipose tissue in Japan. *Dioxin 2000, 2O^{h} Symposium on Halogenated Environmental Organic Pollutants,* August 14-17, 2000, Mon terey, California. Organohalogen Compounds, **47,** 159, **2000.**
56. KAWANO M., UEDA M., MATSUI M., KASHIMA Y., MATSUDA M., WAKIMOTO T. Extractable organic halo gens (EOX: CI, Br and I), polychlorinated naphthalenes and polychlorinated dibenzo-p-dioxins and dibenzofurans in ashes from incinerators located in Japan. Organohalogen Compounds, **36,** 221, **1998.**
57. KOVER F. Environmental Hazard Assessment Report: Chlorinated Naphthalenes; EPA 560/8-75-001; USA. Envi ronmental Protection Agency, Washington DC, USA.
58. KUBINYI H. QSAR: Hansch analysis and related ap proaches. VCH. ISBN 1-56081-768-2. Weinheim (Ger many), **1993.**
59. LEE R. G. M., BURNETT V., HARNER T., JONES K. C. Short-term temperature-dependent air-surface exchange and atmospheric concentrations of polychlorinated naphtha lenes and organochlorine pesticides. Environmental Science and Technology, **34 (3),** 393, **2000.**
60. **LEI** Y. D, WANIA F., SHIU W. Y. Vapour pressures of the polychlorinated naphthalenes. Journal of Chemical and En gineering Data, **44** (3), 5777, **1999.**
61. LUNDEN A, NOREN K. Polychlorinated naphthalenes and other organochlorine contaminants in Swedish human milk, 1972-1992. Archives of Environmental Contamination and Toxicology, **34,** 414, **1998.**
62. MARTI **I.,** VENTURA F. Polychlorinated naphthalenes in ground water samples from the Llobregat aquifer (Spain). Journal of Chromatography A, **786,** 135, **1997.**
63. NAKANO T., FUJIMORI K., TAKAISHI Y., UMEDA H. Isomer specific analysis of polychloronaphthalenes *(in Ja panese).* Reports of Hyogo Prefectural Institute of Environ mental Sciences, **25,** 33, **1993.**
64. YAMASHITA N, KANNAN K, IMAGAWA T, MIYAZAKI A, GIESY J.P. Concentrations and profiles of polychlorinated naphthalene congeners in eighteen technical polychlorinated biphenyl preparations. Environmental Science and Technology, **34,** 4236, **2000.**
65. POPP W., NORPOTH K., VAHRENHOLZ C, HAMM S., BALFANZ E., THEISEN J. Polychlorinated naphthalene exposures and liver function changes. American Journal of Industrial Medicine, 32, 413, 1997.
66. SciQSAR™. User Guide.
67. STEWART J. J. P. Optimalization of parameters for semiempirical methods. I Method. Journal of Computa tional Chemistry, **10,** 209, **1989.**
68. STEWART J. J. P. Optimalization of parameters for semiempirical methods. II Applications. Journal of Com putational Chemistry, **10,** 221, **1989.**
69. STEWART J. J. P. Semiempirical molecular orbital methods. Reviews in Computational Chemistry, **1,** 45, **1990.**
70. STEWART J. J. P. Mopac 93. Copyright Fujitsu, Tokyo, **1993.**
71. THEISEN J., MAULSHAGEN A., FUCHS J. Organic and inorganic substances in the copper slag "Kieselrot". Chemo sphere, **26,** 881, **1993.**
72. TIERY D. A., TAYLOR P. H, KASNER J., DELLINGER B. Gas phase formation of chlorinated aromatic compounds from the pyrolysis of tetrachloroethylene. Combustion Science and Technology, **74,** 137, **1992.**
73. TYSKLIND M., ELG K, ANDERSSON P. L., VAN BAVEL B. HAGLUND P. The use of multivariate experi mental design in the selection of polychlorinated naphtha lenes for screening of biochemical and toxicological effects. Organohalogen Compounds, **28,** 545, **1986.**

74. TYSKLIND M, LUNDGREN K., RAPPE C, ERIKSSON L., JONSSON J., SJOSTROM M., AHLBORG U. G. Multivariate characterization and modeling of polychlorinated dibenzo-p-dioxins and dibenzofurans. Environmental Science and Technology, 26, 1023, **1992.**
75. TYSKLIND M, NYSTROM M., AKERBLOM N., *AN*-DERSSON P. L, VAN BAVEL B., NORRGREN L. Determination and modelling of biomagnification factors for polychlorinated naphthalenes (PCNs) in salmon *(Salmo salar).* Organohalogen Compounds, **39,** 13, **1998.**
76. USEPA. Category of substances known as chlorinated naphthalenes proposed determination of significant new uses. Federal Register, **48,** 20668, **1983.**
77. VILLALOBOS S. A, PAPOULIAS D. M., MEADOWS J, BLANKENSHIP A. L., PASTVA S. D., KANNAN K., HINTON D. E., TILLIT D. E., GIESY J. P. Toxic responses of medaka, d-rR strain, to polychlorinated naphthalene mixtures after embryonic exposure by in ovo nanoinjection: a partial life-cycle assessment. Environmental Toxicology and Chemistry, **19 (2),** 432, **2000.**
78. VILLENEUVE D. L, KHIM J. S., KANNAN K., FALANDYSZ J., BLANKENSHIP A. L., NIKIFOROV V., GIESY J.P. Relative potencies of individual polychlorinated naphthalenes to induce dioxin-like responses in fish and mammalian in vitro bioassays. Archives of Environmental Contamination and Toxicology, **39,** 273, **2000.**
79. WIEDMANN T., BALLSCHMITER K. Halogenated naphthalenes as precursors and products in flame chemistry. Organohalogen Compounds, **9,** 331, **1992.**
80. WIENNER H. Structural determination of paraffin boiling points. Journal of the American Chemical Society, **69,** 17, **1947.**
81. YASUHARA A, MORITA M. Formation of chlorinated aromatic hydrocarbons by thermal decomposition of vinylidene chloride polymer. Environmental Science and Technology, **22,** 646, **1988.**