# MULTIVARIATE PHYSICO-CHEMICAL CHARACTERISATION OF POLYBROMINATED DIPHENYL ETHERS (PBDE)

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## Introduction

Polybrominated diphenyl ethers (PBDEs) have been extensively used as flame-retardants in different polymers, in e.g. electronic equipment such as computers and television sets [1]. Mainly two technical mixtures have been used, viz. the Deca-BDE and Bromkal70-5DE.

PBDEs was first discovered in 1981 in samples of pike, eel, and sea trout [2] and has from this point been found in a variety of environmental samples, e.g. in Atlantic pilot whale (*Globicephala melas*) where as many as 19 PBDEs has been identified [3]. However, in environmental samples such as soil a large number of not yet characterised PBDEs are found.

The technical PBDE mixture Bromkal70-5DE and a set of synthesised congeners has been analysed and identified by GC-MS. Relative retention times (RRT) of 31 PBDEs has been analysed on four capillary columns, ranging from non-polar to polar columns [4].

Increasing levels of PBDEs in the environment may cause a long-term environmental problem. Hence, a systematic approach for assessment of fate and risks of the PBDEs includes the development of a model describing the chemical variation within the large number of possible congeners.

The aim of this project is to achieve a systematic overview of the physico-chemical variation in the group of PBDEs and to select an appropriate sub-set of PBDEs for use in future studies of the chemical and biological behaviour of these compounds. Further, a quantitative structure-property model was calculated and used for prediction of relative retention times.

## Materials and methods

All physico-chemical properties were generated by the Windows based molecular modelling software HyperChem® and the ChemPlus™ Module [5]. Molecular geometry optimisation (using the Polak-Ribiere algorithm) was made for all the 209 PBDEs with the semi-empirical AM1 Hamiltonian [6], and additional properties often used in quantitative structure-activity relationships (QSARs) were calculated. All calculations were performed on a standard personal computer fitted with a 350 MHz processor and 256 MB of internal memory.

The physico-chemical properties generated were e.g. a diverse set of molecular energies, heat of formation, atomcharges, (x, y, z) moments of inertia, frontier orbital energies, and total dipole moments. Also some empirically generated QSAR properties as the $\log_{10}$ octanol-water partition coefficients, molar refractivity, polarizability, mass, Van der Waals and solvent accessible volumes and surface areas, see **Table 1**.

Principal component analysis (PCA) and partial least square (PLS) models were calculated using the Simca-P® software [7].

**Table 1.** Calculated semiempirical and QSAR parameters with abbreviations included in the PCA model.

| Electronic and other molecular properties | Abbreviation | Unit |
|---|---|---|
| Atom Energy | AE | kcal/mol |
| Binding Energy | BE | kcal/mol |
| Core Energy | CE | kcal/mol |
| Electronic Energy | EE | kcal/mol |
| Heat of formation | dH | kcal/mol |
| Atom Charges on the phenyl carbons and Oxygen | C1-6, C8-13, Oxy | eV |
| Moments of Inertia | Mom(X, Y, Z) | |
| Energy of the Highest Occupied Molecular Orbital | HOMO | eV |
| Energy of the Lowest Unoccupied Molecular Orbital | LUMO | eV |
| HOMO-LUMO Energy Gap | dE | eV |
| Total Dipole Moment | Dp | Debye |
| $\mathrm{Log}_{10}$ Octanol-Water Partition Coefficients | Log P | |
| Molar Refractivity | MR | $Å^3$ |
| Polarisability | Pol | $Å^3$ |
| Molecular Mass | Mw | g/mol |
| Van der Waals Area | VdWA | $Å^2$ |
| Solvent Accessible Area | Area | $Å^2$ |
| Van der Waals Volume | VdWV | $Å^3$ |
| Solvent Accessible Volume | Vol | $Å^3$ |

## Results and Discussion

In this study 33 physico-chemical parameters were used. PCA gave 7 principal components (PC) which explained 94% of the variation in the data set. The first four PCs explained 84% of the variation, divided into 53%, 14%, 11%, and 6%, respectively. Variables influencing PC1 were related to size/bulk, e.g. EE, dH, Log P, Mw, Volume and Area components. In PC2 and PC3 variables related to structure/symmetric properties given by Atom charges and HOMO, LUMO, dE were of high importance, and in PC4 the dipole momentum (Dp) and Mom(X,Y,Z) made a high contribution.

A quantitative structure-property relationship (QSPR) for the RRTs determined for 31 PBDE congeners [4] using the partial least square (PLS) method [8] was calculated. The 31 congeners cover the di- to hepta-BDEs, and the structures are mainly *ortho* and *para* substituted. A model with predictive capability can give prediction of RRTs for “unknown” PBDEs in environmental samples. The PLS model predicted 95 %, 94%, 89%, and 84 % in two components of the variation in the RRTs for the four columns CPSil-8, HP-1701, SP-2380, and SB-Smectic [4]. A plot of the predicted versus observed RRTs, for the CPSil-8 column, is shown in **Figure 1**. The model was applied to a test-set consisting of the remaining PBDE congeners and allowed predictions of RRT for a large number of congeners. However, many PBDE outliers were found, e.g. 87 PBDEs were classified as outliers for the CPSil-8 column. This indicates that the 31 PBDEs that has been syntesised and characterised do not cover certain variations in the physico-chemical properties for all congeners [4].

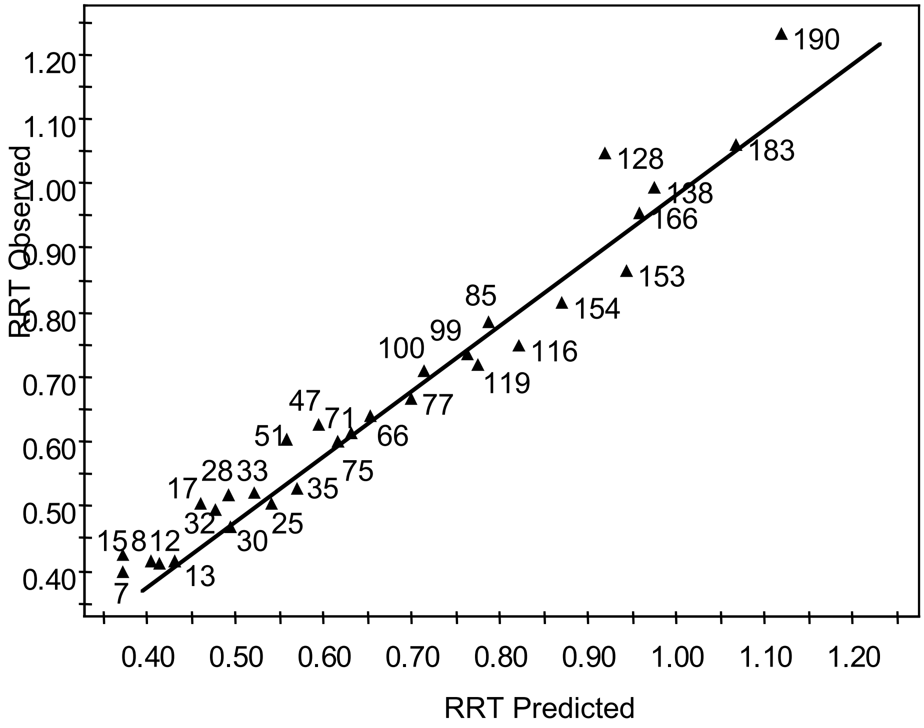

**Figure 1.** Relative Retention Times (RRTs) of PBDE congeners for Observed RRTs [4] (non-polar CPSil-8 column) versus Predicted RRTs.

Principal component analysis condenses the initial descriptors to a few, orthogonal PCs summarising the major variation pattern in the data (here: variation in chemical structure). The derived PCs may then conveniently be used as design variables in a statistical experimental design, such as a factorial design (FD) [9]. A FD generates a set of representative compounds by introducing systematic variation into a set of congeners to be tested.

Using the first four PCs from the PCA as design variables, a $2^4$-factorial design [9] was built, see **Table 2**. The PC scores were used to classify the 209 PBDEs depending on the sign and value on each PC. After this sub-grouping 16 PBDEs can be selected, one for each design level, to be used for future experimental testing. In addition, centre-points (i.e. congeners) can be selected to represent the interior part of the design. Some PBDE congeners can be selected based on commercial availability and other congeners has to be syntesised.

A systematic approach in the fate and risk assessment of PBDEs is needed. An optimised test protocol can be achieved by introduction of maximum chemical variation within selected test compounds. By selecting representative sets of test compounds and using multivariate chemical data, stable models can be obtained which are valid for a large number of untested compounds. Finally, this new strategy for assessment of the PBDEs in combination with QSARs/QSPRs is suggested to be used in the screening of the environmental behaviour of PBDEs.

**Table 2.** A $2^4$ FD showing the distribution of the 209 PBDEs over 16 design levels based on the first four PCs. In addition eight center-poins[a] are selected. IUPAC numbering according to [10].

| Design levels | | | | PBDE-congeners (IUPAC) |
|---|---|---|---|---|
| + | + | + | + | 113,129,130,135,164,165,172,173,174,175,198,199,202,208 |
| – | + | + | + | 6,8,12,35,38,40,44,58,59,72,73,76,78,92,122,124 |
| + | – | + | + | 84,88,98,104,131,132,136,142,144,145,176,186,200,201 |
| – | – | + | + | 10,16,19,27,33,41,48,51,53,54,71,82,87,102 |
| + | + | – | + | 111,112,134,146,151,163,178,179,185,193 |
| – | + | – | + | 2,5,11,14,20,23,34,36,43,56,57,65,80,83 |
| + | – | – | + | 90,91,93,96,140,142,147,148,149,150,152,177,182,187,188 |
| – | – | – | + | 1,13,22,24,32,42,45,46,64 |
| + | + | + | – | 108,120,121,133,157,159,161,167,180,191,192,194,205,206,209 |
| – | + | + | – | 25,52,55,67,68,79,107,127 |
| + | – | + | – | 119,128,138,153,154,155,158,168,171,196,197 |
| – | – | + | – | 3,4,7,17,29,30,47,49,50,62,66,69,75,77,85,101,103 |
| + | + | – | – | 89,94,114,141,156,162,169,170,189,190,195 |
| – | + | – | – | 9,26,39,61,63,70,81,106,109,118,126 |
| + | – | – | – | 99,100,115,117,137,139,160,166,181,183,184,203,204,207 |
| – | – | – | – | 15,18,21,28,31,37,60,74 |
| 0 | 0 | 0 | 0[a] | 86,95,97,105,110,116,123,125 |

## Acknowledgement

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