Chemical characterisation and strategic selection of BFRs for PBT assessment

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Summary

A few brominated flame retardants (BFRs) make up the vast majority of the total production volume of BFRs. However, a far more structurally diverse set of BFRs are reported to be in use or have been used as flame retardants. This paper presents a set of BFRs with a large structural variation to be used in the assessment of their persistence, bioaccumulation potential, and toxicity (PBT). These compounds are in addition selected to facilitate the establishment of structure-activity relationships (SARs) with the aim to reach an understanding of the effects and fate in the environment of yet untested BFRs.

Introduction

Brominated flame retardants are used in many products of the modern society. Examples of products are textiles, paints, thermoplastics, and foams, where BFRs fulfil a crucial function to slow down and/or inhibit fires and thus decrease the effects and number of accidents. Flame retardants can be divided into brominated monomers, additives, and reactives depending on their mode of incorporation into the polymers.[1] Brominated styrenes and butadienes are examples of monomers, polybrominated diphenylethers (PBDEs) and hexabromocyclododecane (HBCDD) are additives, whereas tetrabromobisphenol-A (TBBP-A) is an example of a reactive flame retardant. On an environmental perspective, the additives are considered the most interesting BFRs due to possible leakage from the products. The reactives form covalent bonds with the material and should therefore only pose a risk during production, transport and if not fully bonded to the material. Despite the obvious focus on additive BFRs, reactives should not be neglected and TBBP-A is an example of a reactive BFR that has been found in the environment. TBBP-A has e.g. been detected in sewage sludge in a study by Sellström et al 1999 and in serum of computer technicians as reported by Jakobsson et al 2002.[2,3]

The aim of the present study was to give an overview of the chemical characteristics of a large share of the brominated organic compounds produced for use as flame retardants. This information was applied to search for suitable candidates for testing their PBT characteristics. The study is based on computation of chemical descriptors using semi-empirical methods in combination with multivariate statistics.

Material and Methods

In total, 63 compounds are included in this study as basically found in a list provided by the Danish EPA[4], with a few exceptions described below. The set contains two polybrominated biphenyls (PBBs), viz. 153 and 209. PBDEs were selected mainly from the study by Sjödin et al, 1998 who identified PBDEs 28, 47, 66, 85, 99, 100, 138, 153, and 154 in a commercial product, Bromkal 70-5DE.[5] In addition, PBDEs 183, 204, and 209 were included to cover the higher brominated congeners. A number of brominated monomers, such as the styrenes and butadienes, were added with different numbers of bromines and substitution pattern. Two phosphates were included, viz. bis(2,3-dibromopropyl)phosphate and tris-(tribromoneopentyl)phosphate. The three indenes in the set were brominated from a known structure with five, seven and eight bromines, respectively, as these are not yet structurally specified in CAS. The major alterations made from the list of BFRs provided by the Danish EPA were the following; polymers were included as monomers, oligomers were omitted, individual PBDEs, PBB 153, 85-22-3, 87-82-1, 84852-53-9, 3072-84-2, 19186-97-1, and 5412-25-9 were added.

In order to characterise the various BFRs included in this study, a set of 15 physico-chemical parameters was obtained. The compounds were drawn in HyperChem where the structures were initially optimised with a molecular mechanics method (MM+) followed by the semi-empirical AM1 method.[6] The calculated parameters include the energy of the highest (HOMO) and lowest molecular orbital (LUMO), the difference between HOMO and LUMO, and the heat of formation. In HyperChem also molecular volume and molecular surface area were achieved. To reflect the hydrophobicity of the compounds, logP was included as calculated using SMILES and the Kowwin software.[7] Finally, Dragon was used to get parameters, such as number of bromines, carbons, hydrogens, oxygens, and acceptor atoms for hydrogen bonds, molecular weight, and most negative and most positive partial atomic charge.[8]

The information in the 15 physico-chemical parameters was studied and decomposed into a few new latent variables using principal component analysis (PCA).[9] The calculated principal components can in addition be used as variables in statistical design to select representative compounds for certain types of structures. This strategy based on combining PCA and factorial design has earlier been applied for PCBs and PCDD/Fs.[10,11]

Results and Discussion

Three significant principal components (PCs) accounted for 84% of the variation in the 15 physico-chemical parameters of the 63 BFRs. The calculated PCs reflect the spread in chemical characteristics of the BFRs, which mainly is related to the compounds molecular size, maximum negative and positive charge, number of acceptor atoms for hydrogen bonds, number of bromines, and HOMO energy. The three calculated principal components were applied in a factorial design set on two levels to reach in total 8 design levels. The design was complemented with two centre points to cover the interior region of the chemical domain and thus 10 structurally diverse compounds could be selected.

On each design level four to fourteen compounds were positioned and from these levels three candidates were selected (Table 1). The first option (called optimal) was selected purely on its position in the chemical domain and the candidate was picked to represent as well as possible that region in all three dimensions. By this strategy the most extreme compounds was avoided. Two additional candidates per design level were selected to reach sets that are reasonably well distributed in the chemical domain, but have in addition properties that facilitate chemical analysis and experimental handling. Accordingly volatile and reactive compounds were avoided in these sets. Another factor taken into consideration in the practical set was environmental relevance and so the most widely used BFRs were added to this set. The third set of BFRs (called alternative) could as well be used as representatives of BFRs, but includes less known compounds.

Table 1. The selected candidates presented with their CAS numbers from each design level (DL) and the two centre points (CP) of the factorial design (FD).

DL	Optimal	Practical	Alternative
1	446255-54-5	207122-16-5	68631-49-2
2	6607-46-1	87-82-1	3278-89-5
3	20566-35-2	79-94-7	39635-79-5
4	3234-02-4	118-79-6	608-33-3
5	61262-53-1	84852-53-9	13654-09-6
6	34994-48-4	103-64-0	98-81-7
7	52434-59-0	4162-45-2	19186-97-1
8	1522-92-5	3322-93-8	3194-57-8
CP1	41318-75-6	41318-75-6	41318-75-6
CP2	3194-55-6	3194-55-6	3194-55-6

The compounds of the practical set shows a wide span in chemical characteristics, e.g. the number of bromines span from 1 to 10, molecular weights from 183 to 943, log P values ranges from 3 to 12, and the number of acceptor atoms of hydrogen bonds from none to 4. The selected BFRs include a tri- and a hepta-brominated diphenylether, the well-known TBBP-A and HBCDD, but also the less studied beta-bromostyrene, TBBP-A bis (2-hydroxyethyl) ether, and a brominated cyclohexane derivative (Figure 1). By applying these 10 compounds in future testing protocols of various PBT characteristics, a better understanding of the behaviour in the environment of brominated organic compounds could be reached. In addition, this approach enables development of SAR models for prediction of crucial properties of other non-tested BFRs. We have recently proposed a set of PBDEs, which could well be used as a complement in order to both reach a general assessment of BFRs and to perform more detailed studies on one specific group of compounds.[12]

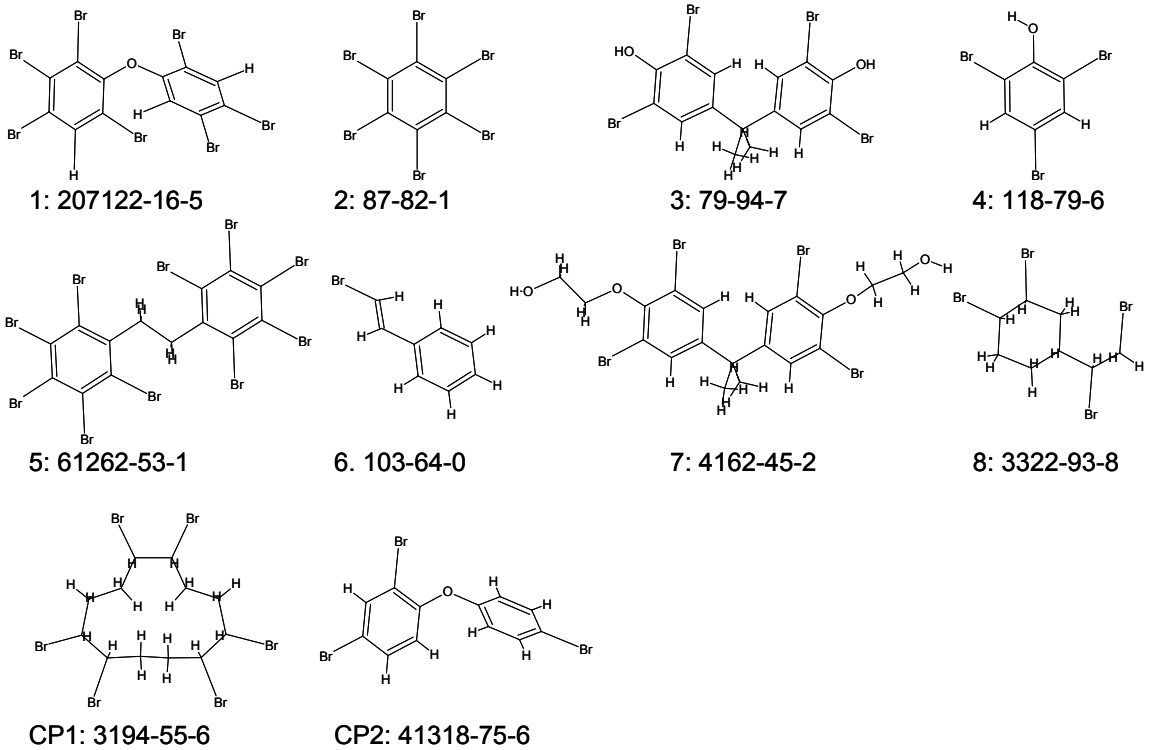

Figure 1. Molecular structures and corresponding CAS numbers of the practical set.

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