One for all and all for one? To what extent can phosphorus-based flame retardants be treated as groups?

Peter Fisk, June 28, 2022

peter.fisk@greenchemicaldesign.com

BACKGROUND

- Peter Fisk has been asked by pinfa to review independently whether organophosphorus flame retardants can be considered for regulatory purposes in one or more groups.

- Or should each substance be considered individually?

METHODS

The stepwise methodology used was:

- Collect physicochemical, environmental and health data from REACH registration sources or reliable published sources where necessary;
- Examine the possibility of any coherent grouping in structure-based groups possible; those groups should be consistent with the hazard-related registration data.

WEIGHT OF EVIDENCE

- The OPFRs subject to this study are data-rich in respect of the key requirements of the REACH Regulation and most weight of evidence should be given to such data, not to non-standard (and non-guideline) studies.
    - Due to the data rich nature of the dossiers, read-across was hardly used in REACH dossiers for OPFRs
- There is no immediate or major need for collection of further data due to the large amount of reliable Klimisch 1 and 2 OECD or comparable guideline studies from the REACH dossiers.

CONCLUSION ABOUT A SINGLE GROUP

OPFRs cannot be grouped together in one single group as this cannot be justified by conclusive scientific means following the basic rules for grouping:

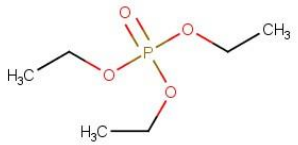
- different chemical structures;
- different physical-chemical properties
- different toxicological properties (no extensive patterns can be seen)
- different eco-toxicological properties, although the trend with log K_{ow} are normal
- different environmental fate properties, although certain features gave rise to ready biodegradation

ARE THERE ANY STRUCTURAL GROUPS? 1

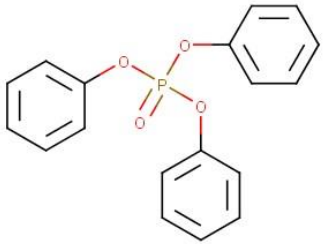
There are potential structural groups of OPFRs based on structural features and physicochemical properties. These structural groups are:

- Trialkylphosphates
- Triarylphosphates
- Monoalkyldiarylphosphates
- Chloroalkylphosphates
- Bisarylphosphates
- Phosphonates

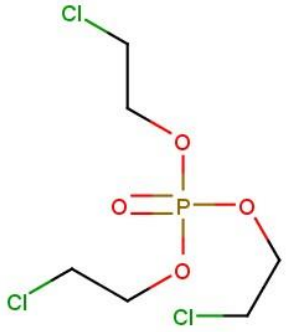
Examples



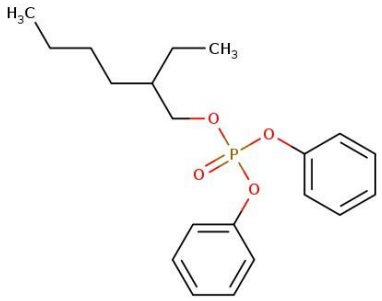
trialkyl phosphate



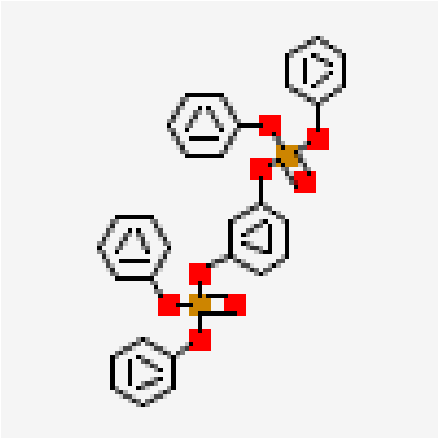
triaryl phosphate



chloroalkyl phosphate



diaryl alkyl phosphate



aryl bisphosphate

phosphonate

ARE THERE ANY STRUCTURAL GROUPS? 2

- The origin of the differences between these groups lies at least in part in the types and energies of fundamental intermolecular forces; these differences are shown well by examination of Hansen Solubility Parameters (HSP).

- The HSP values were calculated and it was observed that the dispersion (δD) and polarity (δP) properties varied widely, but the hydrogen bonding energy (δH) varied very little so that was not used further.

- HSP values relate directly to fundamental molecular properties in respect of absolute intermolecular energies.

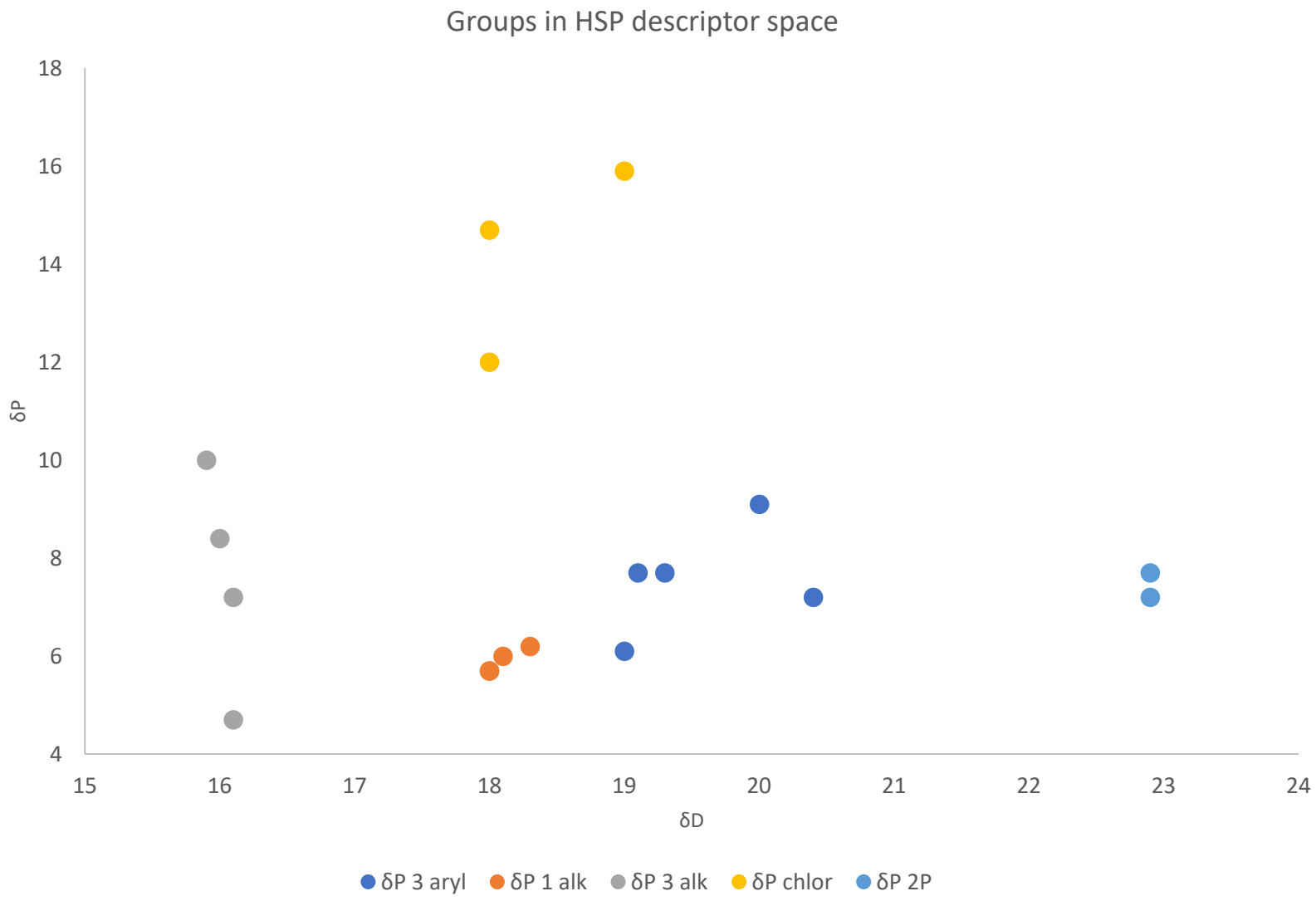
ARE THERE ANY STRUCTURAL GROUPS? 3

The figure following shows how the groups are formed in HSP property space.

δP values for various structural types are plotted against δD; the structural groups identified were substances with various attachments to the P=O group:

- Three aryl rings - δP 3 aryl in the graph
- Two aryl rings, one alkyl chain - δP 1 alk
- Three alkyl chains - δP 3 alk
- Three chloroalkyl chains - δP chlor
- Two P atoms, various - δP 2P

GROUPING OF PHOSPHATE ESTERS FROM STRUCTURE AND HSP VALUES



ARE THERE ANY STRUCTURAL GROUPS? 4

- The five structural groups separated well in HSP descriptor space with each structural groups' members well clustered together.

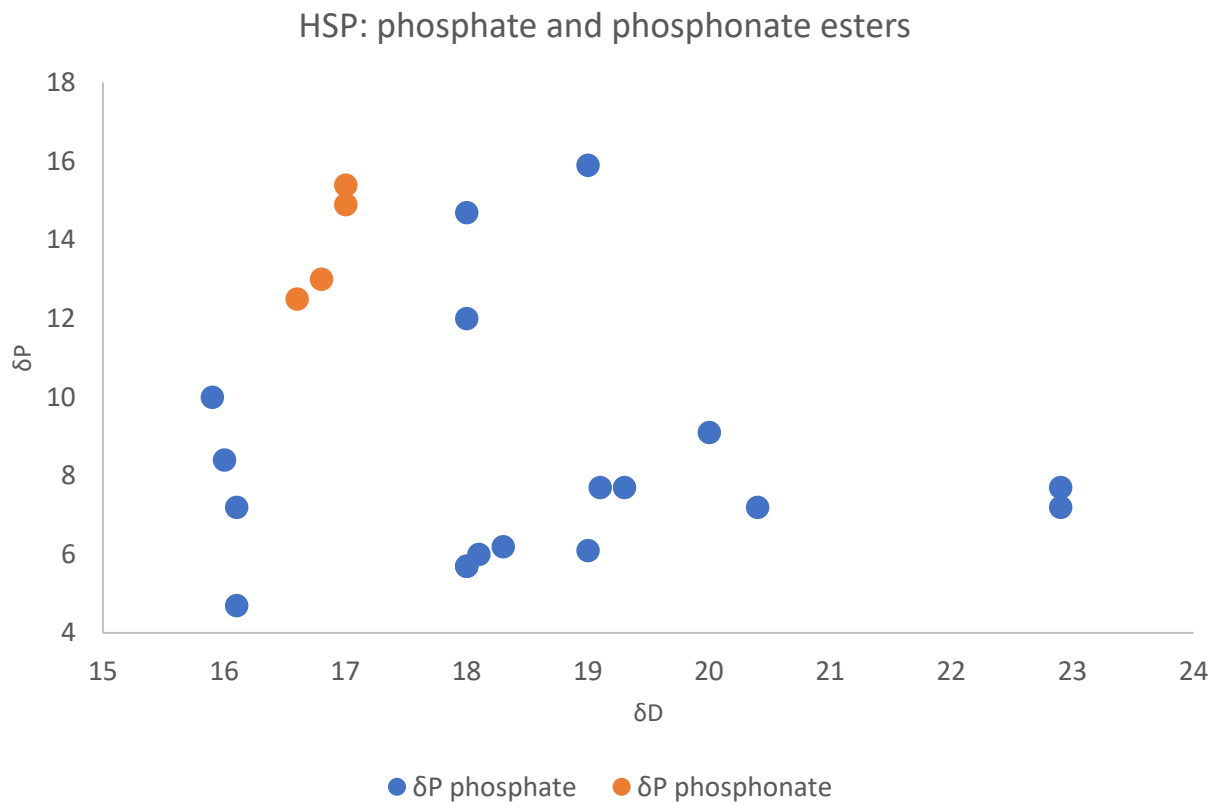
- This analysis confirms that the concept of dividing the substances based on the structural features present is a sound method,

- The range of δD and δP values is wide – therefore these are energetically-significant separations in terms of intermolecular forces.

- The usual physicochemical properties would not produce such a useful grouping.

GROUPING OF PHOSPHATE ESTERS AND PHOSPHONATE ESTERS FROM HSP VALUES

Phosphonate esters form another group, in structure, hazard properties and HSP.



CONCLUSIONS ABOUT GROUPING

- One large group for OPFRs is not sound science
- The structural groups in most cases have consistent toxicological hazard profiles; one notable exception is trialkylphosphate esters, where one substance out of four is a classified carcinogen.
- Extrapolation from one group to another is neither feasible nor can it be justified by scientific means when comparing data available on the same endpoints on the substances of the other structural groups.
- A case could be made to work one substance at a time or with the structural groups singly.