Predictive methods for determining the thermal decomposition properties of hazardous substances

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Due to the fast development and availability of computers, predictive approaches are increasingly used in the evaluation process of hazardous substances complementary to experiments. Their use was recommended as alternative to experimental testing by the REACH regulation to complete the lack of knowledge on properties for existing substances that must be registered before 2018 (upon quantities). Among the proposed predictive approaches, Quantitative Structure Property Relationships (QSPR) are powerful methods to predict macroscopic properties from the only molecular structure of substances.
In that context, the HAZPRED project (2015-2018, founded by the SAF€RA consortium) aims to develop theoretical models (e.g. QSPR) and small-scale tests to predict complex physico-chemical properties (e.g. thermal stability, explosivity) of hazardous substances to complete the lack of knowledge on these hazardous substances quickly or to understand their decomposition behaviour better.
In particular, this contribution will present the work done in this project on the physical hazards of organic peroxides and self-reactive substances: gathering of existing experimental data, new experimental campaigns, review of existing models and proposition of new estimation methods.

1. Introduction

Up to now, experimental characterization is used by laboratories to gather data on physico-chemical hazardous properties of energetic substances. Due to the fact that these tests are complex, costly and require a large amount of substances (more than 1 kg for hazardous properties such as explosivity) and dedicated facilities (both small and large scale), alternative or predictive methods are more and more encouraged. In particular, the development and use of QSPR models are recommended by the REACH regulation. Moreover, QSPR or small-scale tests (requiring lower quantities of materials) present a real interest for screening purposes in R&D development phases (even when chemicals are not yet synthesized) or when they are very expensive or dangerous for the users (e.g. toxic). These estimation methods can be used to replace huge experimental characterization and avoid important time and costs on potential late-stage failures.
In this context, the HAZPRED project addresses the development and use of predictive methods, in particular QSPR and small-scale tests, for investigating hazardous properties of chemical substances in a regulatory or risk assessment context. Two families of hazardous substances were particularly targeted, organic peroxides and self-reactive substances, that are both thermally instable substances.
For each system, after a collection of existing data on physical hazards (from literature and new experiments) and a review of existing prediction methods, works were initiated towards predictive approaches for the estimation of these properties.

2. Organic Peroxides and Self-Reactive Substances

Organic Peroxides (OP) and Self-Reactive Substances (SRS) are two classes of thermally unstable substances that can undergo self-accelerating decomposition, burn rapidly and even, in some cases, be explosive under the effect of various types of stimuli (e.g. impact, friction). They can also react dangerously with other substances. For this reason, these compounds are classified under specific classes in chemical safety regulations like the UN Recommendations for the Transport of Dangerous Goods (UN, 2017) or the European Regulation related to the Classification, Labelling and Packing of substances (CLP) (EC, 2006).
Organic peroxides are defined by their molecular structure, as organic substances (liquid or solid) that contain O-O bonds in their structure (as shown in Figure 1). They are classified in class 5.2 in the TDG recommendations.
Self-reactive substances are defined as thermally unstable substances liable to undergo a strongly exothermic decomposition without participation of oxygen (air) and classified in class 4.1. In this class of compounds are found different types of nitrogenated compounds as presented in Figure 1.

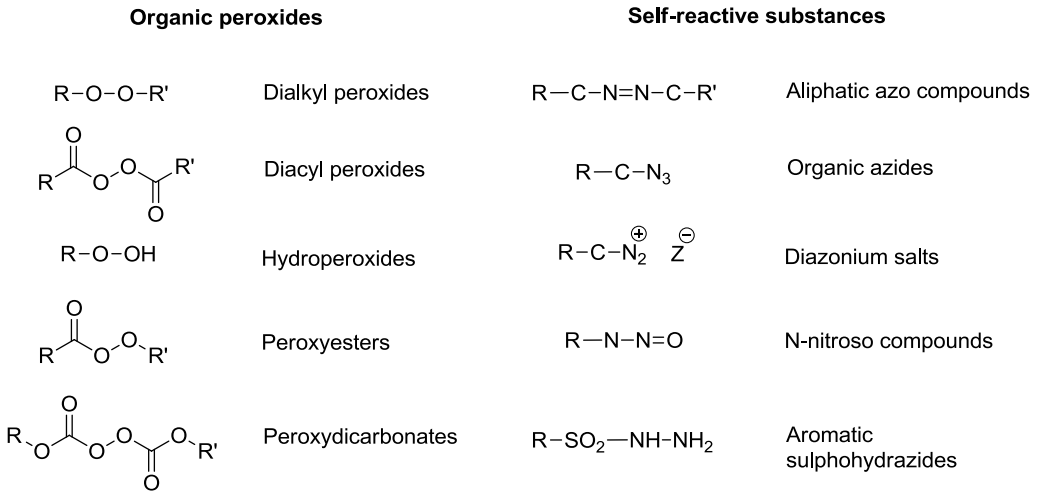

Figure 1: Different families of organic peroxides and self-reactive substances (list is not exhaustive)

3. Collection and evaluation of existing experimental data and predictive models on organic peroxides

3.1 Collection of existing experimental data on organic peroxides

Resources of reliable data are rare in the open literature, where comprehensibility of results is partly a weak point. One credible source, open to members of the International Group of Experts on the Explosion Risks of Unstable Substances (IGUS), is a so called “Datatop”, collected by TNO (2013), The Netherlands. It is a compilation of organic peroxide classification data and is published multi-annual. Another source is the data collection of BAM owns measurements. From both sources, results of tests and classification of new pure organic peroxides and mixtures of organic peroxides are incorporated in the Recommendations on the Transport of Dangerous Goods (Model Regulations) (UN 2017).
Datatop and BAM collections combine nearly 400 entries for organic peroxides, whereby e.g. for one substance more than one entry can exist. One reason is e.g. the different final classifications of diluted peroxides depending on varying concentration, and/or on varying diluent. The properties used for classification purposes are listed in these databases. Several tests are mandatory to classify a sample according to the Recommendations on the Transport of Dangerous Goods (Manual of Tests and Criteria) (UN 2015). Included are laboratory tests and tests of the sample as packaged for transport concerning specific properties like a possible propagation of a detonation or of a deflagration. To address another important parameter for transport, the self-accelerating decomposition temperature (SADT) must be determined. Seemingly a huge data collection is available for developing predictive models. But it must be remembered, that the characterization of a property isn’t done with a singular test. Different tests for the same substance property are combined in a test series. So, the characterization of a property is not necessarily connected to a single measured value and therefore difficult to describe in a model.
Also, the effects of varying concentrations, different diluents or additives (mostly stabilizers) on estimated properties are manifold and for a systematic approach not sufficiently to describe. For the development and test

of predictive models at best homogeneous data are needed. Excluding e.g. dilution effects the data are reduced to entries for technical pure substances, namely with concentrations higher than 90 % w/w.
One property which is estimated for all samples and in advance of all other tests, is the screening of the thermal stability with Differential Scanning Calorimetry (DSC). It is a common standard test in safety labs and provide amongst others the released decomposition energy, which is a valuable characteristic of the sample. A combination of this characteristic, of the peroxide structure and other measurable test data seems to be a promising projection for a descriptive model.

3.2 Simple correlation between DSC data and SADT

Thermal analysis methods like DSC offer the possibility to determine kinetic parameters of a reaction, including activation energy, pre-exponential factor and reaction model. With the knowledge of the kinetics, of the parameters of the packaging like size, heat transfer properties and physical properties of packaged substance, which influence the heat transfer, the SADT can be calculated.
For a first assessment of SADT, at least for a hint, if SADT will be lower than 75 °C (a limit for specific transport requirements), a faster approach would be desirable. A simple diagram, like the one published by Yoshida (1987) for the correlation of SADT and DSC-Onset temperature for thermal instable substances, would be of interest. Desirable would be a linear dependence for organic peroxides too and relatively good correlation was found for 23 pure organic peroxides, as evidenced in Figure 1a.
Malow and Wehrstedt (2005) developed an approach to predict SADT for pure liquid organic peroxides, from dynamic DSC runs. The transfer equation, based on the standard theory of explosion by Semenov and already used for the evaluation of DTA runs (Steinbach and Klais, 1997) was adopted for DSC. Calculated and measured SADT (UN H.4 test, UN 2015) values were in good agreement for the 10 studied organic peroxides. In the context of the HAZPRED project this dataset has been successfully extended by measurements of additional pure 13 peroxides (see Figure 1b), 6 of them not in the liquid but solid state at ambient conditions. Only Di(2-ethylhexyl)peroxydicarbonate presents a significant deviation (calc. 23 °C vs. exp. 10°C). Origin of this deviation is under study. It also may be noticed that this approach might be inefficient for diluted peroxides.

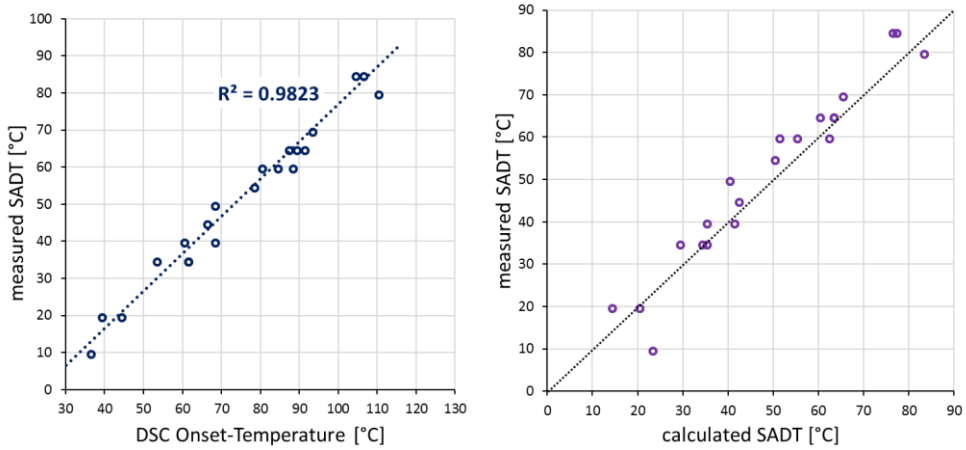

Figure 1: Measured SADT vs. experimental DSC Onset-Temperatures (a) and calculated SADT (b).

3.3 Existing QSPR models for organic peroxides

Few QSPR models dedicated to organic peroxides were found in literature in the last decade. Lu et al. (2011) proposed preliminary models for the decomposition energy and onset temperature of OP. Developed from a database of only 16 organic peroxides, the authors were not able to perform any external validation. So, if observed correlations revealed promising with R^2 of 0.92 and 0.96 for the decomposition energy and onset temperature of decomposition, respectively, their real predictive powers are unknown.
More recently, within the French PREDIMOL project, INERIS used a larger set of 38 data issued from a dedicated experimental campaign, allowing an external validation of new predictive models. New QSPR models (Prana, 2014) were developed for the decomposition energy and onset temperature by using, notably, descriptors related to the properties of the peroxy bond and applying a complete validation process, according to the OECD validation principle for regulatory purpose (OECD, 2007). The performances of the models in external validation were good with R^2_{ext} of 0.81 and 0.83 pour the decomposition energy and the onset temperature, respectively. Nevertheless, as shown in Eq. 1 (for the heat of decomposition), the application of these models requires quantum chemical calculations.

$$\Delta H/C = 54\ {}^{1}\kappa - 990 n_{OO} + 1293 d_{OO} + 2631 Q_{OO} - 19371 \quad (1)$$

with C the concentration in organic peroxide, $^{1}\kappa$ the Kier shape index (order 1), n_{OO} the number of peroxy bonds, d_{OO} the distance of the peroxy bonds and Q_{OO} the Mulliken mean atomic charge on the O atoms of the peroxy bonds.

To access easier prediction, new models (Prana, 2017) were developed for the heat of decomposition focusing on the constitutional descriptors. If their performances were slightly lower than the quantum chemical one, they allow first estimation of the heat of decomposition based on the only knowledge of the 2D structure of OPs. These data were also used by Zohari (2016) to develop prediction models also based on simple constitutional descriptors with good predictive performances in prediction (R^2_{ext}=0.92), even if their validation may be enforced considering the relatively large numbers of structural features encountered into the descriptors included into these models compared to the numbers of compounds used to develop them.

A series of models (Pan, 2014; Gao, 2015; Wang 2016) were also proposed to predict the self-accelerating decomposition temperature (SADT) of organic peroxides using the QSPR approach without any experimental measurement. The best predictive performances were proposed by Wang et al. (2016) with a prediction error of 6.4°C calculated on test set of 10 compounds. If the obtained performances are already promising, further experimental data with more details on the tested samples and experimental protocols may be required. Indeed, some details on the tested samples and protocols are critical for the reliability and the homogeneity of the data in the perspective of development and validation of predictive models. Indeed, some commercial OP are mixtures, some are strongly diluted in solvent and different protocols can be used to determine the SADT.

4. Production of new dataset and first predictive models for self-reactive substances

4.1 Collection of existing experimental data on self-reactive substances

If data availability for organic peroxides could be regarded as good (but difficult to use in detail), the data availability for self-reactive substances and its use revealed quite more challenging.

According to the test methods, they behave very similarly to organic peroxides and are described in the same chapter in the UN Recommendations (UN 2015). No data collection like to the one built for organic peroxides exist. Nevertheless, some reliable data can be accessed from the UN database, Model Regulations (UN 2017), and from BAM own ones.

As already mentioned for organic peroxides, also for an individual self-reactive substance several entries can exist due to varying concentration or addition of supplementary components. An arrangement in groups is more difficult, even if typical structural patterns like azo- imidazole- or other groups are identified. Often more than one characteristic group can be found in the structure. Several compounds are salts, whereby the cation is identical, but the anion is different.

With restriction to technical pure substances about 100 data were collected, a mapping to a specific functional group gave about 60 entries for diazonium salts. Unfortunately, there are only fragmentary data for an individual entry. Often, measured values are given as “higher than” or “lower than”, which is difficult to implement in a model. Additionally, basic data from DSC are frequently missing. So, these data revealed not sufficient to access predictive methods

4.2 New experimental campaigns on potential self-reactive substances

In this situation, the measurement of 50 technical pure, potential self-reactive substances, supplied by Bayer AG, gave at least a reliable dataset for DSC and BAM Fallhammer Test (UN test 3a (ii)/A14; UN 2015) results. Most compounds (29) are characterized by one functional nitro group, whereby 6 of them also contain a pyrazole group. Five other substances have two nitro-groups each. Other functional groups are e.g. nitroso, trazine and azo, partly combined in a structure with another functional group. The basic structure of all, except of one compound is a five- or six-membered ring, mostly aromatic, several times with a hetero atom like N, S or O. Rings are substituted differently. A systematic assignment to defined substance groups is not possible, due to the presence of multiple functional groups in their structures. All compounds are solids, but not for all a melting peak in the thermogram could be detected.

The decomposition energy of all samples covered a range from about -3400 $J.g^{-1}$ to -312 $J.g^{-1}$, whereby a positive test result in the Fallhammer Test did not depend on the height of the decomposition energy. In the Fallhammer Test, the individual sample was exposed firstly to an impact energy of 25 J. As shown in Table 1, only one substance showed a positive result. In a second run, the samples were stressed with 40 J. Finally, three samples more showed a positive result. A simple correlation between Onset Temperature and Fallhammer Test result could not be found too.

Table 1: Substances with positive results "+" at 25 J and 40 J, respectively according to BAM Fallhammer Test

Name	25 J	40 J
1,3-Bis-(3,4-dichlorophenyl)-2-λ-4-diazathia-1,2-diene		+
4-Chloro-3-(dimethylnitroryl)benzoic acid		+
2,6-Dimethyl-3-nitro-1-(2,4,6-trichloro-3-nitrophenyl)-pyridin-4(1H)-one	+	+
6-Hydroxy-5-nitropyrimidin-4(3H)-one		+

4.3 Structure-Property analysis

No QSPR model dedicated to self-reactive substances was found in literature, probably due to the small number of complete and fully documented experimental data, limited to few compounds (like 2,2'-azobisisobutyronitrile (AIBN) or 2,2'-azobis-(2-methylbutyronitrile (AMBN)) in available literature. Taking advantage of the new experiments performed within the HAZPRED project, a structure-property analysis was initiated on thermal stability properties (onset and maximum temperatures, heat of decomposition). It may be noticed that, for sake of homogeneity on molecular structure description, salts and hydrated structures were excluded. Thus, the investigated database contained 45 potential self-reactive substances.

The structure of each compound was encoded into a SMILE code. These structures were loaded into Dragon software (Kode, 2016) and 3792 molecular descriptors were calculated. Three properties were analysed: the heat of decomposition, the onset temperature, the maximum decomposition temperature.

A partial least square (PLS) analysis was performed using SIMCA P+ software (Umetrics, 2009). This projection method allowed a mapping of the samples in the chemical space of the database (represented by the calculated molecular descriptors) considering the correlation of the descriptors with target properties. After data curation (to eliminate descriptors with no (or almost no) variance in the dataset), a first PLS analysis was performed on the 45 samples characterized by 1909 molecular descriptors and considering the three investigated properties. Among these three properties, the heat of decomposition was found to present the best correlation with the molecular structures of the investigated compounds with R^2_Y = 0.65 compared to 0.22 and 0.24 for the onset and maximum decomposition temperatures, respectively.

To improve the structure-property analysis for this property, a new PLS analysis was fitted by focusing on the heat of decomposition. The score scattering plot of the obtained PLS (in Figure 2) illustrates the dispersion of the molecules in the chemical space and the correlation of this chemical space with the properties (from blue for the lowest ΔH to red for the highest ones). The final PLS model estimates the heat of decomposition with a correlation R^2 of 0.80.

Considering these preliminary results, further works are in progress to develop new QSPR models for this property using a full validation process including an external validation to estimate their predictive capabilities.

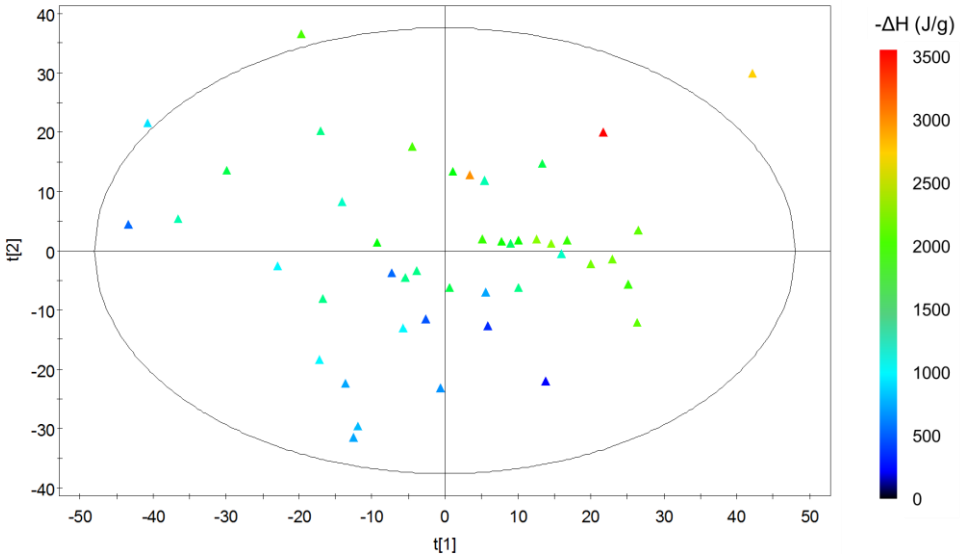

Figure 2: Representation of the potential self-reactive substances in the PLS model obtained for the heat of decomposition

5. Conclusions

The in-depth review of available data on organic peroxides and self-reactive substances illustrated well the importance of data curation when looking at the hazardous properties of reactive substances and, in particular, in the perspective of prediction methods.

If first QSPR models were already proposed in literature for organic peroxides, the HAZPRED project encouraged the follow up of these research by improving data curation to improve the development and validation of models and by extending the availability of robust and homogeneous data.

In this perspective, new experimental data were generated on the thermal stability and impact sensitivity of a series of potential self-reactive substances. The ongoing work towards structure-property trends on the thermal stability already provided promising results. Validated QSPR models are now expected, in particular for the heat of decomposition from the new data obtained from the new experimental campaigns conducted in this project using homogeneous protocols and with complete documentation on the tested samples.

Acknowledgments

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