Benign Organophosphate Flame Retardants in the Circular Economy

Synthetic chemicals are inherent to the modern society we live in, contributing to health, safety, and comfort. The production and use of chemicals are rising at an ever-growing pace.[1] An important class of these chemicals are organophosphates, which are frequently used as flame retardants. Organophosphate compounds are connected to two big environmental challenges formulated in the planetary boundaries concept:[2,3] the global phosphorus cycle and chemical pollution. Strikingly, the planetary boundary of the global phosphorus cycle is already surpassed to a critical level.[2,3] Massively exploited fossil resources of phosphorus are depleting and, at the same time, the linear use of phosphorus leads to accumulation in the environment, where the excess causes eutrophication of waterbodies.[4,5]

Organophosphate chemicals are currently produced from mined phosphate rock, via a wasteful and inherently energy intensive synthetic route with excessive redox cycling (grey arrows, Figure 1). Phosphate rock (P^{V}) is first converted to white phosphorus, P_4 (P^0), chlorinated to phosphorus trichloride, PCl_3 (P^{III}), and then functionalized to organophosphate esters (P^{V}). Phosphorus is thus reduced from oxidation state +5 to 0 in its elemental form and then oxidized back to oxidation state +5 in the phosphate ester product. This successive reduction and re-oxidation require large amounts of energy. Furthermore, the use of chlorinated intermediates leads to the formation of unwanted chlorinated byproducts.

During their use and end-of-life stage organophosphate chemicals enter the environment. This is hard to prevent completely, as they are mostly used as additives on, e.g., clothes; during washing of textiles containing flame retardants, these chemicals leach into the wastewater. As a result, organophosphates are now widespread in the environment, being regularly detected in European water bodies, in biota across the world and even in environments without regular human activity such as pristine mountain lakes.[6–9] Furthermore, adverse effects on human and environmental health have been found for some compounds of this class.[10] Addressing the challenges outlined above, I explore and implement a systems approach to create safe and sustainable organophosphate flame retardants fit for the circular economy, adhering to the Circular Chemistry principles.[11]

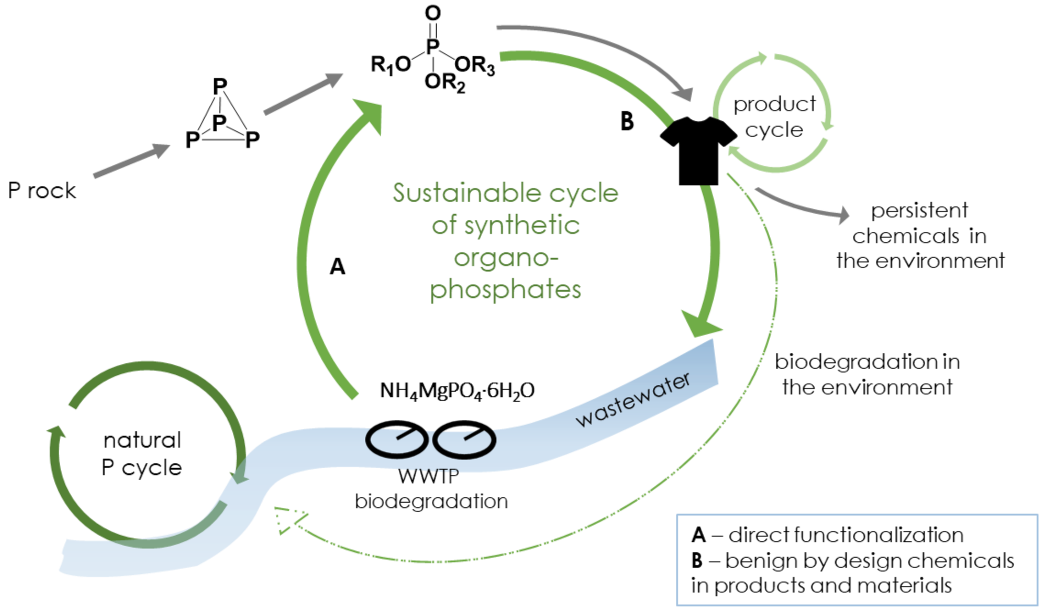

Figure 1: Traditionally, organophosphates are made from phosphate rock and white phosphorus (P_4) in an energy intensive and wasteful manner and persist in the environment (grey arrows). We design safe and biodegradable organophosphates (B), synthesized from struvite ($NH_4MgPO_4·6H_2O$) as a renewable resource by direct functionalization (A; green arrows).

Direct functionalization of phosphates obtained from waste streams (Figure 1A) circumvents the reduction to- and subsequent oxidation of elemental phosphorus, reducing energy demand and increasing atom economy substantially. Interestingly, the question of how inorganic phosphorus sources, such as struvite, can be functionalized to organic phosphorus compounds is a prime subject of the discipline of prebiotic chemistry, which investigates the chemical basis for the origin of life. Inspired by this research, I search for redox-efficient synthetic pathways to organophosphates, starting from renewable phosphate resources obtained from urban mines: the local wastewater treatment plants (WWTPs). To prevent emission to the environment that prevents eutrophication of water bodies, phosphates present in wastewater are increasingly precipitated as struvite ($NH_4MgPO_4 \cdot 6H_2O$). I aim to directly convert struvite to benign organophosphates.

While the synthesis is the start of a chemical's life cycle, this phase is short compared to the use and end-of-life phases. To zoom in on the challenge, I focus in particular on one organophosphate flame retardant, tri-*iso*-butyl phosphate (TiBP). 1.000 – 10.000 tonnes of TiBP are used in the EU annually, amongst other applications, as an additive flame retardant for textiles, such as in fire fighter clothes.[12] As such, this compound has been detected in water bodies and was thus added to a list of compounds which could be of environmental concern.[13] If the textiles containing TiBP are re-used and recycled, TiBP continues to leach into the environment. The presence of this chemical additive is thus hindering a circular material flow. Design for recycling or degradability in the case of additives which are hard to recover, is a core principle of Circular Chemistry. By designing less hazardous and less persistent alternatives, the sustainability of a chemical across the entire life cycle beyond production is addressed.

I developed a framework for the systematic, computer-aided redesign of industrial organophosphates for improved environmental properties. The use of cheminformatics tools is inspired by drug discovery processes and opens new possibilities to guide the design. For my case study, numerous alternative organophosphate structures to TiBP were generated *in silico* and screened with QSAR (Quantitative Structure Activity Relationships) tools for enhanced biodegradability. Designing additives like TiBP for biodegradability (Figure 1B) is a major handle to prevent pollution: if the chemicals do not persist in the environment, the risk of long-range transport accumulation in biota and thus exceedance of chronic effect levels is reduced. Instead, the chemical is degraded and enters the natural phosphorus cycle. I have used QSAR tools, such as contained in the software EpiSuite from the US EPA, to fill data gaps in chemicals assessments in regulatory contexts to reduce cost and avoid animal testing. Screening the ca. 8.2 million molecules I generated yielded a virtual library of about 46.000 organophosphate structures which were classified as readily biodegradable. For these molecules, several environmentally relevant properties were predicted with further QSAR models: atmospheric half-lives, soil adsorption coefficient, log K_{ow}, aqueous solubility, vapor pressure, atmospheric half-lives, bioconcentration factor and genotoxicity. The alternative chemical structures were ranked according to their predicted properties. Importantly, an alternative chemical to TiBP with less-hazardous environmental properties enables the safe re-use and recycling of the textiles it is applied to. From the compounds that were ranked highest according to their predicted properties, I selected the best candidates, by looking at synthesizability, availability of possible starting materials and chemical stability. To be able to verify its performance, I successfully synthesized the alternative compound di-*n*-butyl ethanol phosphate, of which the experimental testing of physio-chemical properties and properties related to environmental hazards is currently ongoing.

The redesign of the compound chosen for this case study demonstrates how an integrated approach and life cycle thinking allows for the design of safe and sustainable chemicals. This study will serve to remove barriers associated with chemical additives and help pave the way towards a safe circular economy.

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