Redox-Neutral Conversion of Ubiquitous P^V Sources to a Versatile PO_2^+ Phosphorylation Reagent

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Phosphorus plays a pivotal role in organic and biological chemistry; furthermore, it is an essential element in a number of vitally important biological molecules, such as the nucleotides forming DNA and RNA biopolymers. In addition, phosphorus-containing molecules are endowed of countless applications, such as flame retardants, pharmaceuticals, food additives, pesticides, catalysts and many more. The production of most phosphorus-containing fine chemicals relies on the use of white phosphorus (P_4) derived from natural phosphate deposits (e.g. phosphate ores, like apatite), which causes their progressive depletion. In particular, industrial production of phosphorus compounds generally makes use of white phosphorus (P_4) – which is in turn obtained by reduction of phosphate ores in an arc furnace – that is (oxy)chlorinated to environmentally hazardous bulk chemicals such as PCl_3, PCl_5 and $OPCl_3$. It is therefore important to find novel, more sustainable methods for the synthesis of phosphorus-containing organic compounds, especially on a large scale.

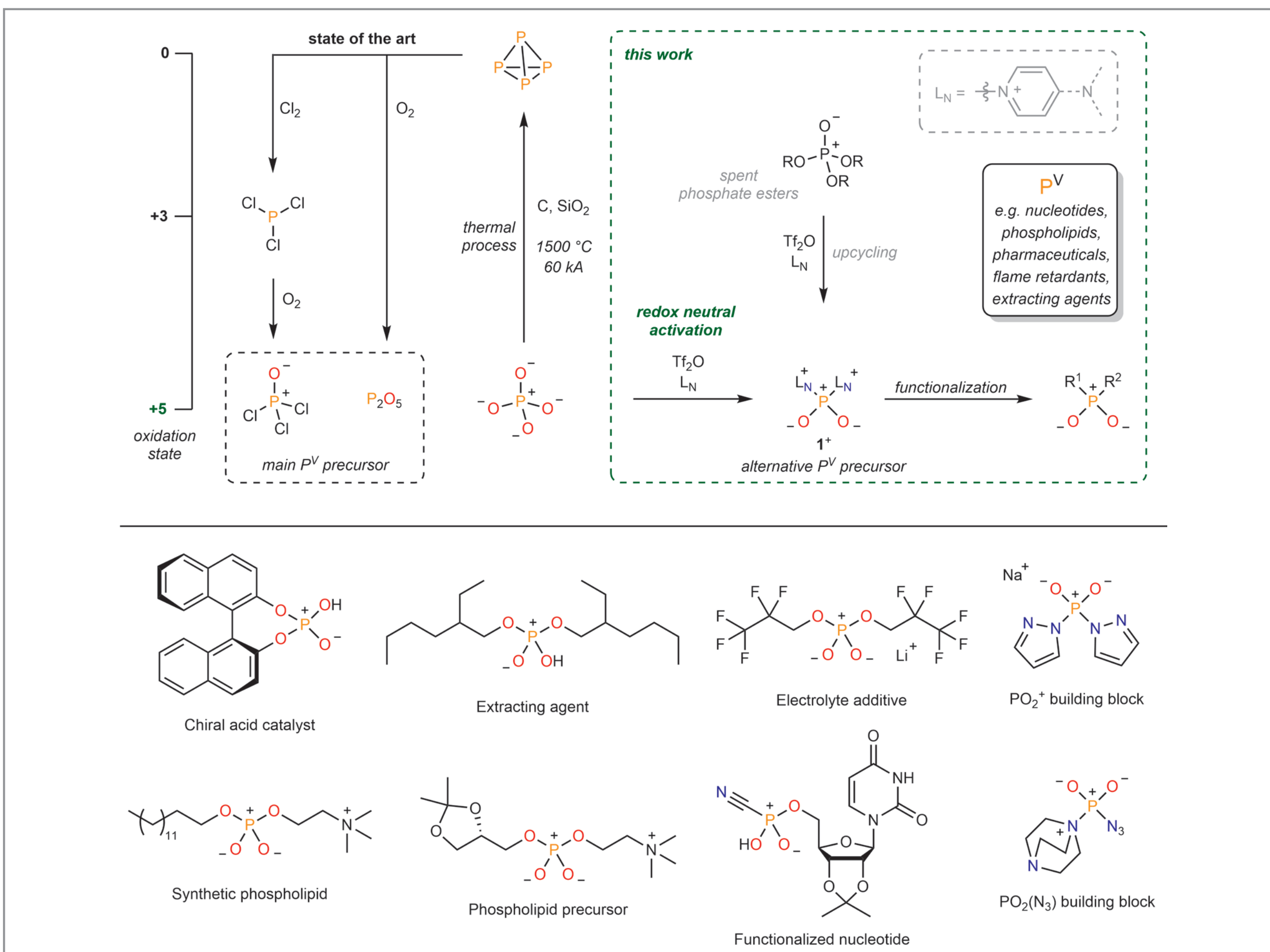

Figure 1 Redox-neutral activation of phosphate sources facilitates synthesis of a broad range of value-added P^V fine chemicals

This paper describes the efforts of Professor Jan Weigand at the Technische Universität Dresden (Germany) and coworkers in rethinking traditional synthetic schemes for the production of phosphorus-containing chemicals. "Most compounds with direct applications, such as pharmaceuticals, flame retardants, or battery electrolytes, bear phosphorus in its most stable and naturally occurring oxidation state +5," said Professor Weigand. He continued: "However, their synthesis primarily relies on P_4 as an intermediate. Even simple esters of phosphoric acid are produced via this redox detour, despite the immense energy input required to break all the stable P–O bonds in mined phosphate minerals. The scientific community has recently questioned this approach (*ACS Cent. Sci.* **2020**, *6*, 848–860), and our work serves as a viable proof-of-concept for an alternative."

The group's approach originates from a previous contribution targeting the direct functionalization of white phosphorus. "We obtained one of the key reagents involved by deoxygenation of triphenylarsine oxide with triflic anhydride (Tf_2O), stabilizing the resulting highly reactive product with 4-dimethylaminopyridine (DMAP) as an *N*-donor base (*Nat. Chem.* **2022**, *14*, 384–391)," explained Professor Weigand. He went on: "This raised the question for us whether the same combination of reagents could activate phosphate by deliberate cleavage of P–O bonds. In our initial experiments, we aimed at the complete deoxygenation of phosphate $(PO_4)^{3-}$ and quickly realized that the thermodynamically preferred outcome of our approach is the P^V precursor 1^+ (Figure 1). We then used different phosphate sources and optimized the reaction conditions accordingly. This project turned out to be very much straightforward."

The versatility and simplicity of this approach stands out. With only pyridine and triflic anhydride required, the reagents are standard laboratory chemicals accessible to the majority of the scientific community. Professor Weigand remarked: "The range of usable phosphate sources is broad, enabling the use of both primary sources like phosphoric acid or phosphorus pentoxide, and secondary sources such as certain spent phosphate esters. Furthermore, the scope of possible target compounds is immense, spanning diverse applications, whose synthesis is simplified from five or six steps with state-of-the-art methods to just two (patent applications: EP4183742A1 and DE102022120599.1)."

Professor Weigand concluded: "We are currently further developing the synthetic application of **1**[OTf] as a universal building block in phosphorus chemistry, the full potential of which has yet to be discovered."

About the authors

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Tobias Schneider received his B.Sc. in chemistry from the TU Dresden (Germany) in 2017. After interim research periods at the Hanoi University of Science and Technology (Vietnam) and Osaka University (Japan), he completed his M.Sc. degree in Dresden in 2020. He is currently working on his PhD thesis under the supervision of Prof. Jan J. Weigand, focusing on the development of alternative synthetic procedures for the production of phosphorus-containing fine chemicals.

Dr. K. Schwedtmann

Kai Schwedtmann received his diploma degree from the WWU Münster (Germany) in 2012 and started his PhD studies under the supervision of Prof. Jan J. Weigand. In 2013, he moved to TU Dresden (Germany) where he received his Dr.rer.nat. in 2016. During his PhD, he was a visiting researcher in the group of Prof. Neil Burford in 2014 at the University of Victoria (Canada). Today, he is senior researcher at TU Dresden with focus on reactive phosphorus compounds and sustainable phosphorus chemistry.

Prof. J. J. Weigand

Jan J. Weigand obtained his diploma in chemistry in 2002 and his Dr. rer. nat. in 2005 from the LMU in Munich (Germany). Awarded with the Bavarian Culture Prize in 2005, he obtained a Lynen Scholarship from the AvH Foundation for postdoctoral research at Dalhousie University in Halifax (Canada). He returned to Germany with a Lynen Return Fellowship and started his habilitation at WWU Münster in 2007 under Prof. Hahn's supervision. Shortly after, he was awarded the Liebig scholarship of the FCI, allowing him to start his independent career in 2008. In April 2010, he became a fellow of the prestigious Emmy Noether research program awarded by the DFG and received the Wöhler Research Award for Young Scientists. In July 2012, he obtained an ERC Starting Grant from the European Commission. Since January 1, 2013, he has been a Professor at TU Dresden (Germany). His research activities focus on molecular inorganic and phosphorus chemistry, the development of sustainable methods in extraction, technical applications, and novel recycling strategies. This includes innovative catalyst systems for application in the petrochemical industry and resource change to biogenic and fossil residues. In 2023, he received a Reinhardt Koselleck funding from the DFG for the project "Blueprint for a Modern Sustainable Phosphorus Chemistry".

