Conference paper

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Opportunities and challenges for combining electro- and organometallic catalysis in C(sp²)-H phosphonation

https://doi.org/10.1515/pac-2018-0904

Abstract: The chemistry of organoelemental compounds including carbon-phosphorus derivatives is now one of the most rapidly developing fields of research, regarding both fundamental science and solution of applied problems. Extensive opportunities for the synthesis of organophosphorus compounds are opened up by the use of unconventional methods, first of all, electrochemical ones, which combine the benefits of usual homogeneous chemistry in solution and electrochemistry, where reactants are generated at the electrodes directly in the reaction system. The interest in the organic electrosynthesis is caused by several factors, including mild conditions (room temperature, atmospheric pressure), the possibility of conducting reactions in a closed system with a low concentration of the catalyst, which is readily regenerated. This mini-review generalizes the achievements in the field of development of new electrochemical, efficient and atom-economical, catalytic methods for the formation of aromatic carbon – phosphorus bonds and some historical background of these approaches.

Keywords: aromatic C–H bonds; catalysis; dialkyl H-phosphonate; diaryl phosphine oxide; electrosynthesis; ICPC-22; metal complex; phosphonation.

Organic electrosynthesis as a advanced green methodology

We live in the period of integration of different fields of science, as a result of which their mutual enrichment takes place. The methodology of classical synthetic organic chemistry is increasingly developed through new approaches and principles that use reagents in situ, new materials and technological solutions. Integration processes are also reflected in the field of electrochemistry of organic compounds, or ECOC, which, although having a noticeable history, has successfully manifested itself in practice nowadays. Here we do not present a comprehensive consideration of the principles and practical aspects of the ECOC, because another problem was posed. Now chemistry, as an advanced science, is called to ensure the sustainable development of society, using various methods and approaches that must follow the requirements of “green chemistry”. And here ECOC found its place, which explains the interest to it from researchers and practicing engineers.

Thus, organic electrochemistry is now also developing as an integrating area, including not only organic electrosynthesis, but also material chemistry, catalytic chemistry, biochemistry, medical chemistry and environmental chemistry. The principles of electrochemistry are widely used in organic synthesis. Organic electrochemistry involves the activation of organic molecules by transferring electrons from or to the electrode.

Article note: A collection of invited papers based on presentations at the 22nd International Conference on Phosphorous Chemistry (ICPC-22) held in Budapest, Hungary, 8–13 July 2018.

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surface. In the process, it is possible to obtain a variety of new products, to study the redox properties of substances and to realize a variety of transformations, where oxidation or reduction is the key stage. An important aspect of electrochemical methodology is that many electrochemical processes meet the requirements of ecological cleanness. Indeed, electrochemical reactions have a number of advantages: mild conditions of their flow, high rates, selectivity of the process, as well as convenient operational control using parameters such as current density and potential. It is easy to automate the control of electrochemical processes. Electrochemical methods can be recommended for preventive protection of the environment, since special reagents are not required.

Organic electrochemistry, in particular, organic electrosynthesis, was developed by combining with new ways of carrying out organic reactions and organic synthesis. The 21st century is sometimes called the century of ecology, and organic electrosynthesis is attractive in terms of the requirements of green chemistry within the concept of sustainable development, since it does not require any hazardous reagents and produces less waste than any other chemical synthesis.

So, in recent years, electrochemical processes have proven themselves as a way to a low-waste, low-tonnage, highly clean production of significant compounds. Their advantages are non-thermal activation and clean (minimum reagents) conditions; whereas electron, as is known, is a reagent that does not pollute the environment. The direct relationship between organic electrosynthesis and the requirements (criteria) of green chemistry is observed in the following positions [1]:

- a) the ability to perform direct, indirect or paired electrolysis can significantly improve atom-economy; it is possible to avoid waste if the reagents are generated stoichiometrically in the electrochemical cell.
- b) the use of mediators – catalysts in the reduction of energy consumption and chemical wastes;
- c) the use of renewable starting materials is fully consistent with the methodology of green chemistry;
- d) the use in the electrosynthesis of “green” solvents – ionic liquids or microemulsions;
- e) the energy gain, if the room temperature of the process, mediators-catalysts and paired electrosynthesis are used;
- f) real-time monitoring of electrolysis can easily be carried out due to using electroanalytical control methods;
- g) safety is increased and the probability of accidents is reduced due to the generation or regeneration in situ of the reaction particles or dangerous toxic reagents.

Moreover, most of the electrochemical processes are easily scaled, which creates prospects for their industrial implementation in low-tonnage or large-tonnage production.

The recent achievements in the field of “green” electrocatalytic methods for aromatic carbon – phosphorus bond formation and historical background of these approaches have been described in this paper.

### Background of organic electrochemistry

The concept of organic electrochemistry is relatively new, despite its having a long history. In 1800, the Italian physicist Volta invented the famous voltaic pile. The study of the relationships and the connection between chemical and electrical phenomena, the investigation of the action of a galvanic current on various substances in solutions was initiated in the work of British scientists V. Nicholson and A. Carlisle. The work of Nicholson and Carlisle aroused great interest, since it was easy to see in it a fundamentally new method for studying chemical phenomena. Therefore, very soon many scientists in various countries began to design voltaic batteries of different capacities and to study the chemical action of galvanic electricity and the reasons for its formation in the voltaic pile. In Russia, the invention of the voltaic pile became known a few months after its demonstration by Nicholson and Carlisle in England. Already in October 1800 the St. Petersburg Academy of Sciences received a letter from the Russian envoy in The Hague, D.A. Golitsyn, in which a new source of current was described in detail. In September 1801, Academician A.A. Musin-Pushkin first demonstrated the
Voltaic pile and its action before the Conference of the Academy of Sciences. In 1802, the Russian physicist-chemist V.V. Petrov constructed a battery: a horizontal pile consisting of 4200 copper and zinc circles. V.V. Petrov’s battery at one time was one of the most powerful sources of current in the entire world. V.V. Petrov described the results of his numerous experiments in 1803 in the book “News of galvanic-voltaic experiments”, published in St. Petersburg [2].

In 1803, V.V. Petrov published an article on the electrolysis of alcohols and aliphatic oils. A year later, Grotthuss from Lithuania, who proposed the ionic mechanism of electrolysis, discovered that a dilute solution of indigo-white can be easily electrochemically oxidized to indigo-blue. In 1833, Faraday discovered Faraday’s law, and a year later he discovered that hydrocarbons can be formed by electrolysis of an aqueous solution of acetic acid salt [2]. Unfortunately, he could not identify the products. In 1849, the student of Wöhler, Kolbe, discovered the electrochemical oxidation of carboxylic acid (RCOOH) to dimeric alkane (R-R) and CO₂, known as Kolbe electrolysis [3–5]. Thus, Faraday and Kolbe were pioneers in the study of organic electrochemical processes. From the late 19th century to the early 20th century, the electrochemical processes of oxidation and reduction of various compounds were intensively studied. Thus, the use of electrolysis to obtain organic compounds continued in the first half of the 20th century. A typical example is an electrochemical process of reducing nitrobenzene to aniline. It is important to note that organic electrochemistry developed along with the discovery of new electroanalytical methods, such as polarography, which was developed by J. Heyrovsky, and then by Thaci in the early 1920s [6].

However, the studies of organic electrosynthesis were completely halted during the Second World War. In 1964, M. Baizer developed a method for the electrochemical hydrodimerization of acrylonitrile, which is a very useful industrial method for the production of adiponitrile. This invention again stimulated research in the field of organic electrosynthesis by many electrochemists and organic chemists [2].

Since then, the development of organic electrochemistry, in particular, organic electrosynthesis, has been marked by the inclusion of new types of organic reactions and modern organic syntheses. In addition, reactions with various aprotic polar organic solvents were developed, which made it possible to detect electrogenerated unstable intermediates. In addition, cyclic voltammetry and related electroanalytical methods helped to understand the kinetics and mechanisms of many organic electrode processes.

A publication of A.M. Butlerov in 1870 on the electrolysis of a solution of valerian acid [7] can be considered as a starting point in the history of organic electrochemistry in Russia. This emphasizes the role of Kazan, where this outstanding scientist worked, in the formation of a new field of science. The main achievements of Kazan researchers in the field of organic electrochemistry are connected with the identification of the role of individual stages in the mechanism of electrode reactions in various media, including chemical reactions, the stages of elimination and protonation, catalytic processes, mediator processes with the use of electron carriers. In the methods of studying, the use of the EPR method discovered in Kazan by Ye. Zavoisky in the difficult years of the Second World War (1944) was successful, which made it possible to detect the intermediate formation of particles of a radical nature in electrochemical reactions [2, 8, 9].

The synthetic aspect of organic electrochemistry is an important component of this field and its successes: we note the results of research on the nitration of aromatics, the electrosynthesis of organophosphorus compounds [2, 10–21]. In the past 20 years, new efficient methods for synthesizing organophosphorus compounds in electrocatalytic conditions have been developed, and a new scientific direction has been developed – the study of the processes of electrochemical activation and transformation of elemental phosphorus under the action of organic and organometallic compounds, the scientific foundations have been created of highly efficient, resource-saving and ecologically safe technology of electrosynthesis of the most important classes of organophosphorus compounds: trialkyl-, triaryl, triamide and dialkyl phosphates, tertiary phosphines and phosphonium salts from white phosphorus under conditions of metal complex catalysis, electrocatalytic processes involving transition metals have been developed, their regularities have been clarified, the factors determining the reactivity of catalysts have been identified, new effective methods for the synthesis of various compounds with P–E bonds (E = C, O, N, Si) have been discovered, new approaches
have been developed to the study of the mechanism of the release of tetrahedra of white phosphorus in the conditions of metal complex catalysis, detection of the intermediates and prediction of the choice of the most effective reagents by electrochemical methods [10–21].

The rich potentialities of the intensively developed direction of the electrochemistry of elemental phosphorus and the advantages of electrochemical methods for the synthesis of organophosphorus compounds, which are either unavailable, or experimentally difficult, or have ecological limitations, are demonstrated. As a result of the carried out researches, the foundation is laid for the realization of the developed processes for obtaining organophosphorus compounds from elemental phosphorus at the technological level. Phosphorylation of arenes is a new stage in the development of the electrochemistry of organic organophosphorus compounds.

**C(sp²-H) phosphonation**

It can be considered that organic chemistry is currently targeted at developing ideal transformations aimed at the synthesis of complex molecules that are efficient, economical and environmentally friendly [1, 22]. The reactions of functionalizing the carbon-hydrogen bonds catalyzed by transition metals, which convert the widely distributed, but usually inert, C–H bonds directly to the carbon-carbon (C–C) and carbon-heteroatom bonds (for example, C–O, C–N or C–Hal) are very promising in this respect.

The transition-metal-catalyzed reactions are among the most valuable transformations in organic synthesis and are generally based on catalytic cycle involving transition metal complexes at various oxidation states. In this context, electrochemistry provides advantageous methods both for synthetic purposes and for mechanistic investigation [1, 2, 11]. Electrosynthesis is useful in transition metal catalysis to generate the active catalyst form without specially added reducing or oxidizing agents. Performed in mild conditions, it offers more environmentally non-polluting alternatives to traditional organic synthesis. Electrochemical methods should be used in combination with spectroscopy techniques to provide a detailed characterization of the intermediate species. We propose a “green” one-step catalytic method for introduction of phosphorus-containing functional groups to different compounds with C(sp²)-H bonds assisted by electrochemical reduction or oxidation of metal complexes under mild conditions. The catalytically active form of metal complexes (NiIII/IV or Pd III/IV, Fe II/III, Ag I/II etc.) is generated and regenerated on the electrode without specially added reducing agents (or oxidants). Key organometallic intermediates are isolated and characterized. Advantages of directed metal-induced aromatic C–H-phosphorylation are demonstrated for manifold compounds in this mini-review.

Unlike traditional methods used to form these bonds, the direct C–H substitution eliminates the need for preliminary functionalization (e.g. halogenation or boronization) of the initial substrate, which reduces the number of stages and reduces the amount of unwanted waste in multi-stage processes. Thus, atom-saving and shortest synthesis paths can be achieved with a smaller number of stages [23, 24]. For this reason, the functionalization of C–H bonds catalyzed by transition metals has attracted enormous attention in recent decades [25–28].

One of the main problems of the new synthesis processes involving high oxidation palladium catalysts is that co-oxidants are required, mainly in stoichiometric or larger quantities, for example, transition metal salts or organic oxidants such as silver salts, organic peroxydes and electrophilic fluorine reagents, which are often expensive or difficult to separate from reaction mixtures [26–32]. In addition, every time a new ligand or substrate, or reaction conditions are used, a broad screening is required to select the optimal oxidant (Scheme 1). The problems of choosing oxidants from the electrochemical point of view are described in detail in a recent review [32].

Electrolysis at a controlled potential under mild conditions is a real alternative to classical methods, as demonstrated, for example, by a work of Kakiuchi et al. [33], describing the effective electrochemical ortho-halogenation of arylpyridine derivatives in the presence of palladium salts.
We proposed to develop a cheaper, “green”, and more manageable electrochemical alternative to these C–H substitution reactions and to use mild electrosynthesis conditions with a controlled anode potential to achieve the formulated goals.

All possible ways of oxidative C–H-functionalization proposed in the literature necessarily include the oxidation stage: one or more. We assumed that the oxidation of Pd (II) complexes can be carried out effectively on the electrode, replacing the chemical oxidant by electrochemical oxidation. This would make it possible to obtain the proposed bimetallic complex Pd (III) and/or Pd (IV) preparatively under electrosynthesis conditions and use it as a model intermediate for studying the ways of catalytic C–H substitution. One of the tasks was to realize the entire process of C–H functionalization electrochemically, under conditions of generation of an oxidized form of a palladium catalyst on an electrode, which had not previously been realized by anyone. We also tried to develop new examples of catalytic C–H-functionalization reactions on more accessible, common metals such as nickel, manganese, cobalt, since such examples are much less common than with palladium.

Although to the present time, various reactions of direct functionalization of C–H bonds, including those catalyzed by transition metals, have been successfully carried out, the examples of the formation of carbon-phosphorus bonds are very limited, apparently because of the strong coordinating properties of phosphorus reagents [34]. Electrochemical methods of substituting a hydrogen atom with phosphorus-containing groups are very few; mainly the last successful examples are described only for the functionalization of nitroaromatic substrates [17, 35]. The formation of the carbon-phosphorus bond under the conditions of catalytic action of transition metals is regarded as an important methodology for obtaining various kinds of phosphorus compounds, such as phosphonates, phosphinates, phosphine oxides, phosphines, etc. However, the first catalytic methods of introducing phosphorus groups into various structures, the importance of which is particularly significant in connection with the requirements of “green chemistry”, have been developed quite recently [36–39].

Common problems in the implementation of the C–H-substitution reaction described above are also present in the processes involving P-nucleophiles. In the latter case, an oxidizing agent is also necessary; whereas for each pair of substrates one has to carry out preliminary experiments taking into account the ability of the reagents to oxidize, primarily the nucleophile, which cannot but influence the result of the reaction. The known co-oxidants used are expensive (for example, salts of the metals of the platinum and silver group), whereas organic high-molecular-weight oxidants are difficult to separate from the reaction mixture. Moreover, they are often not sufficiently selective [26–32].

Despite the success of some researchers, first of all, Murakami et al. [40] and Yu et al. [41] in the ligand-directed C–H-phosphonation of aromatic substrates, many complicating factors, namely, high process temperatures, reaction time, the need to use an excess of expensive silver oxidizer AgOAc, an additional base, as well as reagents to facilitate the stage of restorative elimination, not always satisfactory yields, suggest that the search for new simpler and more effective solutions is an important and perspective direction.
The first attempts of electrochemical C–H phosphorylation date back to the late 1970s. The possibility of obtaining arylphosphonates with the yield of up to 59% by electrochemical oxidation of tri- or dialkylphosphites in the presence of benzene or its derivatives was first described by Masui et al. [42] in 1979 and a little later was repeated by Kargin et al. [43] at the benzene: diethylphosphate ratio of 5:1 in acetonitrile in the presence of the NaClO4, background salt (Scheme 2).

In this approach, the authors assumed that the primary product of the synthesis is the phosphonium salt ArP(OEt)3+, which is converted to arylphosphonate under the influence of sodium alcoholate or Na3PO4, whereas the acidification of the electrolyte greatly reduces the yield. Gallardo et al. proposed the electrochemical phosphonation of nitroderivatives of benzene by phosphorus (III) compounds, including diethylphosphite, under oxidative conditions [35], however for unsubstituted benzene his approach does not work, since the key stage of the process is the nucleophilic addition of the H-phosphonate to the aromatic ring (SNAr mechanism), which is followed by oxidation of σ-H adducts (Scheme 3).

The synthesis of arylphosphonates by direct phosphorylation of the C–H bond of aromatic substrates remains one of the most important approaches, since it corresponds to the principles of green chemistry, namely atom-saving, one-stage, low-waste, etc. The search for catalytic conditions in this regard is particularly attractive, given the fact that catalytic reactions of phosphorylation of aromatic compounds are few.

A new idea has appeared to use the possibilities of organic electrosynthesis using metal complex catalysts to solve these problems.

The accumulated experience of electrochemical C–H acetoxylation and perfluoroalkylation [44–47] was used to develop the C–H phosphonation method of 2-phenylpyridine under electrochemical oxidation conditions involving the Pd(OAc)2 catalyst and diethylphosphite as an accessible phosphor precursor under mild conditions [48, 49]. The use of the electrochemical method allowed to carry out the reaction without a specially added oxidizer (AgOAc or other) at a controlled potential under milder conditions at room temperature, and also to analyze the individual reaction stages.

So, we developed the ligand-directed CH-phosphorylation by electrochemical oxidation involving catalyst Pd(OAc), and diethyl H-phosphonate as an accessible phosphorus precursor. Electrochemical method allows to conduct the reaction under mild conditions without a specially added oxidant (silver salts or other) with a controlled potential at room temperature and to analyze particular reaction steps.

The joint electrochemical oxidation of 2-phenylpyridine, phosphite dropwise added during the electrolysis, and palladium acetate as catalyst gives the product of ortho-phosphorylation of 2-phenylpyridine in good yield (Scheme 4).

We have demonstrated that the key intermediates of ligand-directed C–H phosphorylation are the acetate-bridged dipalladacycle and dipalladacycle with two phosphorus ligands formed therefrom by reaction with a phosphorylating agent (diethyl phosphite) (Scheme 5) [47, 49, 50].

\[
\begin{align*}
(RO)_2P & - \epsilon^- \\
(RO)_2P^+ + ArH & \rightarrow (RO)_2PAr + H^+ \\
(RO)_2PAr - \epsilon^- & \rightarrow (RO)_2PAr^+ \\
Na_3PO_4 + H^+ & \rightarrow Na_2HPO_4 + Na^+ \\
(RO)_2PAr + RONa & \rightarrow ArP(O)(OR)_2 + ROR + Na^+
\end{align*}
\]

Scheme 2: Metal-free arene phosphorylation.

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{NO}_2 \\
\text{NO}_2 & \quad \text{H}_2\text{CO}_2\text{OCH}_3 \\
\text{t-ButOK} & \rightarrow \text{P(O)(OCH}_3)_2 \\
\text{t-ButOK} & \rightarrow -2 \epsilon^- - \text{H}^+
\end{align*}
\]

Scheme 3: Gallardo reaction [35].
Interestingly, the geometry of bridged binuclear Pd complexes depends on the nature of the bridging ligands and directly affects their redox reactivity. For example, while the diphosphonate-bridged palladacycles 2 are essentially planar and exhibits no metal-metal interactions, the acetato-bridged complexes 1 adopt an open “clamshell” geometry with two Pd centers in close proximity (Scheme 5) [47, 49, 50].

Oxidation potentials of key intermediates show that the phosphonated complex is oxidized harder than acetate, which can lead to unwanted side reaction of ortho-acetoxylation of substrate (Fig. 1). To obtain the desired product in good yield, it is necessary to provide the conditions for the preferential oxidation of phosphonate complex (Scheme 6) [50].

The preparative oxidation of phosphonate complexes has been studied and is presented here on the example of the benzoquinoline complex 4 (Scheme 7, Fig. 1). It is found that the amount of electricity required for the complete conversion of 4 into the product diethyl aryl phosphonate is 2e per each atom of palladium, so, PdII/PdIV pair runs [51]. It should also be noted that mononuclear arylphosphonate palladium complex [51] was detected as a reaction intermediate.

So, other diphosphonate-bridged dipalladacycles have been oxidized irreversibly and quantitatively afford corresponding arylphosphonates in preparative oxidations carried out under mild conditions without

![Scheme 4: Ligand-directed 2-phenylpyridine ortho-phosphonation.](image)

![Scheme 5: Dipalladacycle intermediates.](image)

**Fig. 1:** Cyclic voltammograms of phosphonated and acetated dipalladacycles.
any added oxidants (Scheme 8). Therefore, this oxidation way may be applied in synthesis of new arylphosphonates from different arenes in ligand-directed aromatic C–H phosphorylation reactions.

The advantages of the method are mild conditions (room temperature), and absence of specially added chemical oxidants.

To obtain the target product in good yield, it is necessary to provide conditions for the predominant oxidation of the phosphorus complex, i.e. to perform electrolysis at the oxidation potential of phosphonate-bridged Pd complex. Supposed catalytic cycle, involving the steps of cyclometallation, oxidation, reductive elimination, and taking into account the possible side acetoxylation reaction is presented in the Scheme 9 [50].

Dialkyl aryl phosphonates are important as intermediates in the synthesis of pesticides and bioactive compounds [52–61]. The preparation of aryl phosphonate through the direct phosphorylation of C–H bond of aromatic substrates remains one of the most important approaches because it corresponds to the
principles of green chemistry, namely, because this approach is atom-saving, single-step, low in waste, etc. The desired catalytic conditions are particularly attractive, given the fact that the catalytic reactions of phosphorylation aromatic compounds are limited. Perhaps, in this respect, benzene is one of the most challenging substrates, given that its structure has no favorable C–H substitution factors, i.e., functional groups, activating bonds or directing functionalization. Typically, if it is possible to select conditions for the phosphorylation of benzene, its derivatives give even higher yields. Coumarin 3-phosphonate is interesting due to its biological activity, cytotoxicity toward cancer cells of leukemia [53–55]. It is usually obtained through Arbuzov or Knoevenagel reactions. Generally these methods give byproducts and often based on the multi-stage consecutive reactions that do not conform to atom-saving principles, and hence have a low efficiency [62].

We chose metal complexes in the (II) oxidation state which could be easily electrochemically oxidized to M(III): Mn(II)bpy and Ni(II)bpy as catalytic systems for the electrochemical phosphorylation of arenes [63–65]. A new approach to the phosphorylation of benzenes bearing both electron withdrawing and electron donating substituents on the ring and some coumarins (coumarin, 6-methylcoumarin, 7-methylcoumarin) under the action of dialkyl H-phosphonates was proposed. Joint catalytic oxidation of arene and H-phosphonate (1:1) in electrochemical mild conditions (room temperature, normal pressure) using new bimetallic MnII/NiIII catalytic system was performed yielding to dialkyl aryl phosphonate with high yield (up to 70%) and full conversion of H-phosphonate. One percent of bimetal catalyst exhibits good catalytic activity (Scheme 10). The success was achieved through a fast catalytic cycle and rapid regeneration on the electrode.

A high yield was obtained only with the participation of two metals and due to their synergetic action. The initial stage of the cycle can involve the formation of the metal phosphonate, oxidized at low anodic

Scheme 9: Catalytic cycle of arene phosphonation.
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potentials with elimination of phosphonate radical, the stages of arene phosphorylation, followed by regeneration of Mn$^{II}$ at Ni$^{II}$ [63]. The mechanism of the process requires further research.

The advantages of the electrochemical aromatic phosphonation, such as atom-economy, low costs and availability of reagents, cobalt-catalysis conditions, ethanol-water green solvent and high yields, are used to develop new greener synthetic routes to substituted aromatic organophosphorus compounds [66]. Joint electrolysis of arenes (benzene or coumarine derivatives) and dialkyl-H-phosphonate (EtO)$_2$P(O)H in the presence of bpyCoCl$_2$ catalyst (5%) in an ethanol-aqueous solution in reductive conditions allows obtaining the desired products in one step (Scheme 11).

Radical mechanism of catalytic reactions was proved by ESR experiments (Scheme 12) [66].

Phosphorus heterocycles have aroused great interest for synthetic chemists over the last few years because of their wide applications in organic synthesis, medicinal chemistry and materials science. Among them, benzo[b]phosphole derivatives, phosphorus-containing π-conjugated compounds, have attracted significant attention as promising organic optoelectronic materials due to their unique physical and photoelectric properties. A silver-mediated C–H/P–H functionalization reaction of arylphosphine oxides with internal alkynes was described for the direct preparation of benzo[b]phosphole oxides with a high yield (Scheme 13) [67]. We proposed more convenient and simple way carried out in mild conditions (room temperature) and

(1 %) [MnCl$_2$(bpy)/Ni(BF$_4$)$_2$(bpy)]

$\text{Ar}^{-}+\text{H-PO(OAlk)$_2$} \rightarrow 2e, 25 °C \rightarrow \text{Ar-PO(OAlk)$_2$}$

$\text{Alk} = \text{Et, i-Pr, n-Bu}$

$\text{Ar} = \text{benzene, coumarine, 7-methylcoumarine, 6-methylcoumarine,}$

$\text{benzonitrile, N,N-dimethylaniline, nitrobenzene}$

Products:

\[
\begin{align*}
\text{PO(OEt)$_2$} & \quad \text{PO(Oi-Pr)$_2$} & \quad \text{PO(O-nBu)$_2$} \\
\text{PO(O-nBu)$_2$} & \quad \text{PO(Oi-Pr)$_2$} & \quad \text{PO(OEt)$_2$}
\end{align*}
\]

$\text{R} = \text{m-CN, p-CN, m-NMe$_2$, p-NMe$_2$, m-NO$_2$, p-NO$_2$}$

Scheme 10: Mn/Ni-catalyzed arene phosphonation in oxidative conditions.

(5%) [CoCl$_2$(bpy)]

$\text{Ar}^{-}+\text{H-PO(OEt)$_2$} \rightarrow 2e, 25 °C \rightarrow \text{Ar-PO(OEt)$_2$}$

$\text{Ar} = \text{benzene, coumarine, 7-methylcoumarine, 6-methylcoumarine,}$

$\text{benzonitrile, N,N-dimethylaniline, nitrobenzene}$

\[
\begin{align*}
\text{PO(OEt)$_2$} & \quad \text{PO(OEt)$_2$} & \quad \text{PO(OEt)$_2$} \\
\text{R} = \text{H, m-CN, p-CN, m-NMe$_2$, p-NMe$_2$, m-NO$_2$, p-NO$_2$}
\end{align*}
\]

Yields of,

- in CH$_3$CN 53–80 %,
- in [EtOH:water] (7:3) 50–70 %,
- in water 7–12 %

Scheme 11: Cobalt-catalyzed reductive phosphonation.
low silver catalyst loading. Our approach excludes traditional excess of silver oxidant and high temperature, palladium or other expensive catalysts, which is more efficient relative to the procedures known in the literature.

Redox properties of key intermediate of catalytic cycle have been investigated by cyclic voltammetry and EPR spectroscopy. The silver diphenylphosphine oxide-intermediate oxidizes easier (+0.5 V vs. Ag/AgCl) than all reaction precursors to form phosphinoyl radical Ph₂P(O)˙ fixed as a spin-adduct by ESR (Scheme 14). Thus radical mechanism going through Ag⁺/Ag⁰ couple was developed for electrocatalytic conditions [67].

A convenient external oxidant-free method of phosphorylation of azole derivatives by dialkyl-H-phosphonates through catalytic oxidation of their mixture under electrochemical mild conditions (room temperature) in the presence of silver salts or oxide (1 %) was proposed (Scheme 15) [68, 69]. This method allows obtaining the desired azole dialkylphosphonates with good yield (up to 75 %).

The transformations of silver and phosphorous precursors and intermediates were investigated using cyclic voltammetry, ESR, NMR spectroscopy, and a radical process mechanism was proposed. It has been found that the key intermediated AgP(O)(OEt)₂ is oxidized earlier than other components of the reaction mixture with elimination of a radical. ESR spectrum of this radical's adduct was obtained in the presence of radical trap PBN, alpha-phenyl N-tert-butyl nitrone (Scheme 16) [69].

Summarizing, we can state that aromatic C–H phosphonation may be realized both in reductive and oxidative conditions electrochemically by radical pathway of metal-mediated transformations.
Scheme 14: Catalytic cycle for silver-mediated C–H/P–H functionalization reaction.

Scheme 15: Phosphorylation of azole derivatives.

Scheme 16: Catalytic cycle for azole phosphorylation.
Ferrocene derivatives with phosphorus-containing substituents (phosphines, phosphonic acid moieties, etc.) gave rise to a new class of organophosphorus compounds, which are very powerful ligands that have unique features in metal-catalyzed organic reactions. We proposed new approach for ferrocene phosphorylation using α-hydroxylalkylphosphonate as “masked” phosphorylating agent, by electrochemical reduction of ferrocene and hydroxylalkylphosphonate mixture at −50 °C (Scheme 17) [70].

The method makes it possible to obtain the product of diethyl ferrocenyl phosphonate with a high yield (87–89 %) and full conversion of the initial dialkylphosphite in one stage. It is evidenced that ferrocene reduction is carried out with preservation of the iron charge in the ferrocene fragment and with the formation of a cyclopentadienyl ligand radical anion at −3.3 V and −50 °C. In fact, in the reaction conditions we simultaneously generated dialkyl H-phosphonate from hydroxylalkylphosphonate by a known reaction, as well as ferrocene radical anions, which react with each other, ultimately producing a phosphorylated ferrocene with good yield in a single stage. Interestingly, in the proposed low-temperature conditions phosphorous acid H3PO3 can also serve as a phosphorylating reagent using a lead cathode because it does not reduce in the available area of potentials with Pb at −50 °C. The yield for Fc-P(O)(OH)2 was 36 % only [70]. This reaction is somewhat analogous to the Hirao C–P coupling [71, 72].

**Conclusion**

Recently, the ever increasing key role of organophosphorus compounds in various fields of science and practice has stimulated new researchers to dig into this line of research. However, the success can be achieved only with the search for novel approaches to compounds having phosphorus -carbon bonds to avoid considerable amounts of by-products, first of all, catalytic processes. The direct C–H-bond phosphorylation is among such processes. Summing up, we can say that electrosynthesis of organophosphorus compounds with P–C bonds has shown a high potential as a powerful method, yielding a variety of different products. These novel approaches allow avoiding considerable amounts of by-products, based on the atom-economic, environmentally friendly, easy-to-perform catalytic processes. It can be assumed that future advanced developments in organic electrochemistry will be achieved through integration with other fields of science, as mentioned above [73]. Many recently proposed and described in this review new approaches and techniques constitute an important practical path of synthesis of valuable phosphorylated products that are potentially important in the pharmaceutical, agrochemical and related industries.

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