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GEORGE OLAH DOCTORAL SCHOOL

THE *HIRAO* P–C COUPLING REACTION AS AN IMPORTANT TOOL FOR THE SYNTHESIS OF PHOSPHONATES, PHOSPHINATES AND TERTIARY PHOSPHINE OXIDES – ALTERNATIVE METHODS

Summary of PhD Thesis

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1. Introduction

Phosphorus-containing compounds play an essential role in vital processes of the living world. For example, adenosine triphosphate (ATP) is responsible for the intracellular energy transfer of living organisms, phosphate diesters serve as the backbone of DNA and RNA chains, and phospholipids form biological membranes. The importance of organophosphorus compounds requires the elaboration of highly efficient synthetic methods from research and development chemists. Synthetic derivatives are used in many fields, such as in agriculture (mostly as insecticides and herbicides), in the plastic industry, and medicine. Besides, they are used as catalyst ligands, as well as important building blocks of synthetic chemistry. Altogether, investigating their syntheses is a topic of current interest.

I have done my PhD research work under the supervision of *Dr. György Keglevich* at the Department of Organic Chemistry and Technology of the Budapest University of Technology and Economics. The research of the *Green Chemical and Organophosphorus Group* is focused on studying organophosphorus chemical transformations in accordance with the principles of green chemistry.

This work is aimed at studying the preparation of phosphonates, phosphinates, and tertiary phosphine oxides, which may be used for various purposes. This topic has a long tradition in our research group. Our main goal was to investigate the theoretical and practical aspects of the transition metal-catalyzed P–C cross-coupling reactions that can be performed without the addition of conventional ligands, and the esterifications, transesterifications, together with *O*-alkylations providing *P*-esters. This allows the conscious design and development of new, environmentally friendly processes.

2. Background

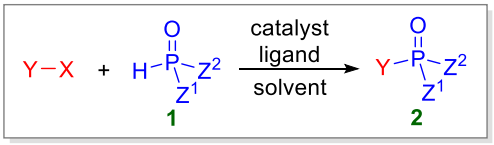
2.1. The *Hirao* P–C cross-coupling

The first P–C coupling reaction was elaborated four decades ago by *Hirao* et al., who reacted dialkyl phosphites with aryl or vinyl halides in the presence of $Pd(PPh_3)_4$.[1] Later, instead of the expensive and sensitive catalyst, the combination of Pd-, Ni- or Cu-precursors with *P*- or *N*-ligands became widespread (*Scheme 1*).[2] More recently, such modern techniques as microwave (MW) irradiation or phase transfer catalysts (PTC) were used in order to increase efficiency. In our research group, palladium- and nickel-catalyzed P–C coupling methods have

[1] Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. *Tetrahedron Lett.* **1980**, *21*, 3595.

[2] Henyecz, R.; Keglevich, G. *Curr. Org. Synth.* **2019**, *16*, 523.

been developed without the addition of conventional ligands under MW conditions. This means a major step forward as products can be prepared more economically, and with lower environmental impact.[3]



X = I, Br, Cl, OTf, $B(OH)_2$
Y = phenyl, substituted phenyl, heteroaryl, naphtyl, vinyl
Z = alkyl, aryl, alkoxy, aryloxy

catalyst: $Pd(PPh_3)_4$/Pd-, Ni- or Cu-precursor (and ligand)
Pd-precursor: $Pd(OAc)_2$, $PdCl_2$, $Pd_2(dba)_3$
Ni-precursor: $Ni(cod)_2$, $NiCl_2$, $NiBr_2$, $NiCl_2$, $Ni(OAc)_2$, $NiCl_2$, $Ni(acac)_2$
Cu-precursor: CuI, Cu_2O, $Cu(OAc)_2$, CuCl, CuBr
ligand: Ph_3P, BINAP, dppf, dppp, dppb, dcypt, 2,2'-bipyridine, TMEDA, DMEDA, 1,10-phenantroline
base: Et_3N, $^iPr_2NEt$, *N*-methylmorpholine, K_2CO_3
solvent: toluene, THF, MeCN, DMF, DMSO

Scheme 1. *The most common implementations together with the progressions of the Hirao reaction.*

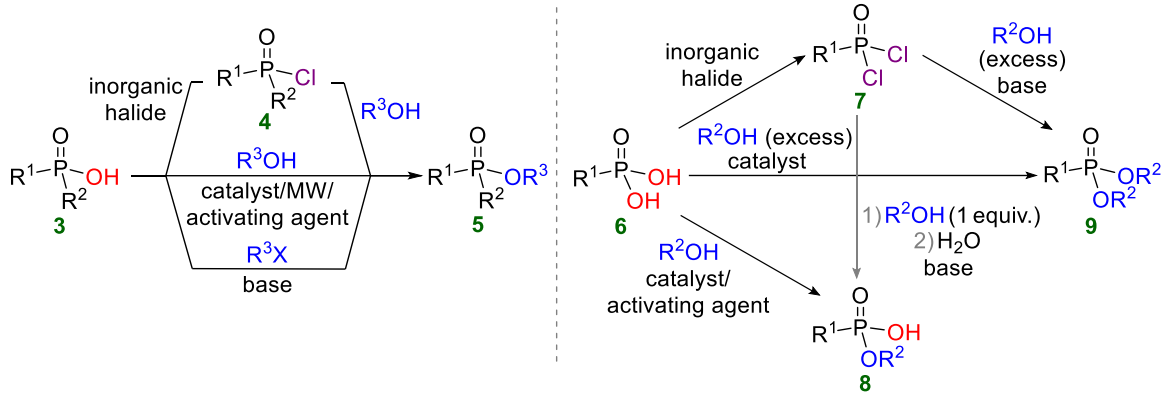
One of the our main goals was to investigate the theoretical background of the previously developed palladium- and nickel-catalyzed P–C cross-coupling reactions that can be performed without the addition of the conventional ligands. With the optimal reaction conditions in hand, we wanted to extend the method for the preparation of new derivatives.

2.2. Synthesis of phosphonates and phosphinates by nucleophilic substitution

The most common, rapid and efficient way for the synthesis of phosphinates (**5**) and phosphonates (**8** and **9**) is to react the corresponding *P*-chlorides (**4** or **7**) with alcohols (*Scheme 2*). However, the rather expensive starting materials are often prepared *in situ* from phosphinic or phosphonic acids (**3** or **6**), and hydrogen chloride is formed in the reaction, which reduces atom efficiency. Therefore, it may be more convenient to synthetize the esters from the corresponding *P*-acids.[4] The esterification of phosphinic acids (**3**) may be carried out in the presence of special catalysts, activating agents (DCC or T3P® reagent) or directly under MW conditions. Additionally, the desired phosphinates (**5**) may be obtained by *O*-alkylation. The reaction of phosphonic acids (**6**) and alcohols – depending on the reaction conditions applied – leads to mono- and diesters (**8** and **9**).

[3] Jablonkai, E.; Keglevich, G. *Tetrahedron Lett.* **2013**, *54*, 4185.; Keglevich, G.; Jablonkai, E.; Balázs, L. B. *RSC Adv.* **2014**, *4*, 22808.

[4] Kiss, N.; Keglevich, G. *2. Methods for the preparation of phosphinates and phosphonates with a focus on recent advances.* In *Organophosphorus Chemistry* (Ed. G. Keglevich); De Gruyter, **2018**; 35.



R = H, alkyl, aryl
inorganic halide: $SOCl_2$, $(COCl)_2$
catalyst: Zn, CaO, Bu_2Sn, $PhSO_2OH$, 4-$MeC_6H_4SO_2OH$, β-naphtolsulfonic acid, $PhAsO_3H_2$
activating agent: DCC or T3P® reagent
DCC = *N*,*N*′-dicyclohexylcarbodiimide
T3P® = cyclic tri-*n*-propylphosphonic anhydride

Scheme 2. *Preparation of phosphinates (**5**) and phosphonates (**7**, **8**, **10**, **11**) from the corresponding P-chlorides (**4** or **6**) or acids (**3** or **9**).*

In this field, we wished to evaluate the existing synthetic methods from a practical point of view. Then, based on our conclusions, our aim was to develop new processes, and to prepare particularly valuable esters using modern chemical techniques.

3. Experimental methods

The MW-assisted reactions were carried out in a CEM® Discover (Model SP) microwave reactor. The continuous-flow MW reactions were performed in a system comprising an HPLC pump, a CEM Flow Cell Accessory®, a CEM Discover® (300 W) MW reactor, a cooler, and a backpressure regulator (17.2 bar). Under conventional heating, the experiments were accomplished in an oil bath.

Conversion values were determined by ^{31}P NMR analyses of the crude products after filtration through a thin (2-3 cm) layer of silica gel. Purification of the products was carried out by flash column chromatography using silica gel. The yields were calculated from isolated masses. The products were characterized by ^{31}P, ^{13}C, and ^{1}H NMR, as well as HRMS spectroscopic methods, and melting point measurements of the crystalline compounds. In some cases, HPLC-MS analyzes were also realized to identify the products or by-products.

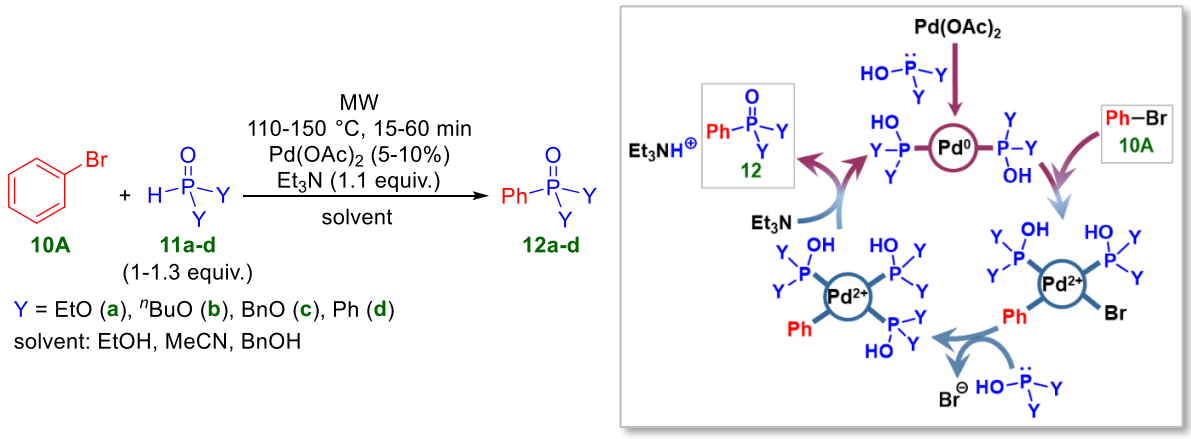
Quantum chemical calculations were performed using the Gaussian09 program package and the B3LYP method, or by the Gaussian16 software with M06-2X function.

4. New scientific results

4.1. *Hirao* reaction without the addition of conventional ligands

4.1.1. Theoretical background of the palladium-catalyzed P—C coupling reactions

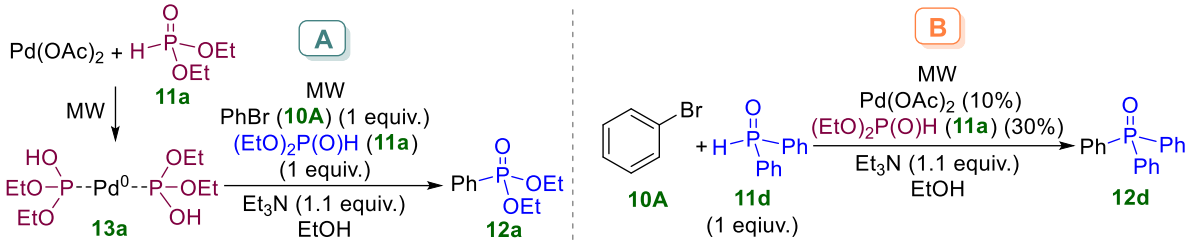
At first, the background of the previously developed palladium-catalyzed *Hirao* reaction under MW conditions in the absence of traditional *P*-ligands was investigated. Bromobenzene (**10A**) was reacted with dialkyl phosphites (**11a-c**) or diphenylphosphine oxide (**11d**) measured in with different molar ratios in the presence of $Pd(OAc)_2$ (*Scheme 3*). It was found that the *P*-reagents (**11a-d**) should be used in excess to the bromobenzene (**10A**) to ensure the catalytic cycle. The presence of 5/10% of palladium acetate requires the addition of 1,15/1,3 equivalents of the >P(O)H reagent: 1 equivalent is the reactant of the *Hirao* reaction, 5/10% provide the reduction of Pd^{II} to Pd^0, and the remaining 10/20% serve as the *P*-ligand of the Pd-catalyst. According to quantum chemical calculations, after the formation of the Pd^0 catalyst, the cycle follows the usual order of oxidative addition, ligand exchange, deprotonation, and reductive elimination.



Scheme 3. *The P–C coupling of bromobenzene (**10A**) and >P(O)H compounds (**11a-d**) in the presence of $Pd(OAc)_2$.*

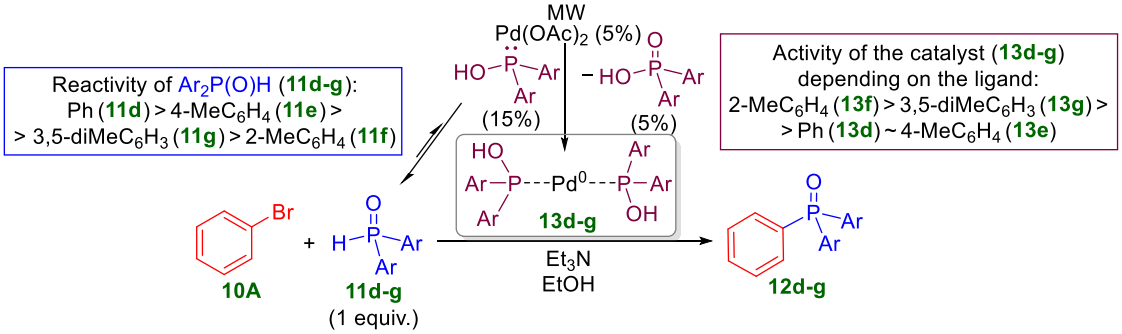
4.1.2. Formation of the Pd-catalyst in the Hirao reaction

To study the formation of the catalyst in detail, the complex (**13a**) formed from the reaction of $Pd(OAc)_2$ and diethyl phosphite (**11a**) was isolated and utilized in the P–C coupling reaction (*Scheme 4*, route "**A**"). We took the advantage that different >P(O)H compounds form catalysts of distinct activity, and in the reaction of bromobenzene (**10A**) and diphenylphosphine oxide (**11d**) the excess of the *P*-reagent could be replaced by the cheaper and less sensitive diethyl phosphite (**11a**) (*Scheme 4*, route "**B**").



Scheme 4. *Exploitation of the catalyst formed from palladium acetate and diethyl phosphite (**11a**).*

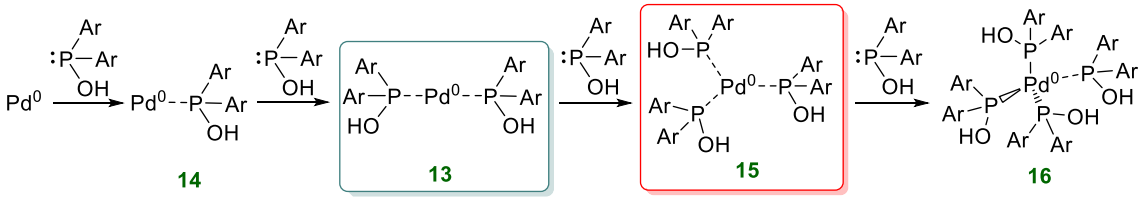
During the P–C coupling of bromobenzene (**10A**) and diarylphosphine oxides (**11d-g**) we found that the phosphinoylation with bis(2-methylphenyl)phosphine oxide (**11f**) and bis(3,5-dimethylphenyl)phosphine oxide (**11g**) was significantly faster than with diphenylphosphine oxide (**11d**) or bis(4-methylphenyl)phosphine oxide (**11e**). The former >P(O)H reagents (**11f** and **11g**) could be used as selective *P*-ligands in the *Hirao* reaction of diphenylphosphine oxide (**11d**). Further experiments showed that the time course of the transformation was influenced by two factors: the reactivity of phosphine oxides applied (**11d-g**), and the activity of the catalyst (**13d-g**) formed (*Scheme 5*). The activity of the catalyst (**13**) has a greater effect than the reactivity, so the reaction of bis(2-methylphenyl)phosphine oxide (**11f**) is the fastest, despite being the least reactive of the diarylphosphine oxides tested.



Scheme 5. *Factors influencing the Hirao reaction of bromobenzene (**10A**) and diarylphosphine oxides (**11d-g**).*

The detailed mechanism of catalyst formation was evaluated by quantum chemical calculations, which showed a similar energetic profile for all diarylphosphine oxides (**11d**,**f**,**g**) studied, so we did not get an appropriate explanation for the significant difference in the activity of the catalysts experienced above.

Finally, investigations on the complexation of Pd^0 with $Ar_2P(OH)$ ligands revealed that while with $(2\text{-MeC}_6H_4)P(OH)$ and $(3,5\text{-diMeC}_6H_3)P(OH)$ ligands the formation of the bis-ligated Pd-complex (**13**) (*i.e.* the active catalyst in the *Hirao* reaction) is exothermic, the tris-ligation is unfavorable. At the same time, with $Ph_2P(OH)$, the formation of the inactive tris-complex (**15**) does not have a significant energy barrier (*Scheme 6*). Thus, the steric hindrance of the methyl groups in the aromatic ring determines the ligation along with the effect of the catalyst.



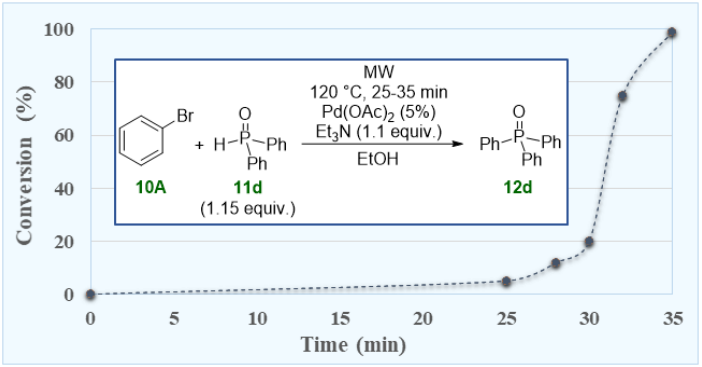
Ligand [$Ar_2P(OH)$]	ΔH (kJ/mol)			
	14	**13**	**15**	**16**
$Ph_2P(OH)$	–106,2	**–39,1**	**4,8**	79,1*
$(2\text{-}MeC_6H_4)_2P(OH)$	–90,6	**–27,7**	**51,3**	174,6*
$(3,5\text{-}diMeC_6H_3)_2P(OH)$	–97,2	**–31,2**	**18,1**	83,0*

* Estimated values.

Scheme 6. *Complexation of Pd^0 with the trivalent tautomeric form of diarylphosphine oxides.*

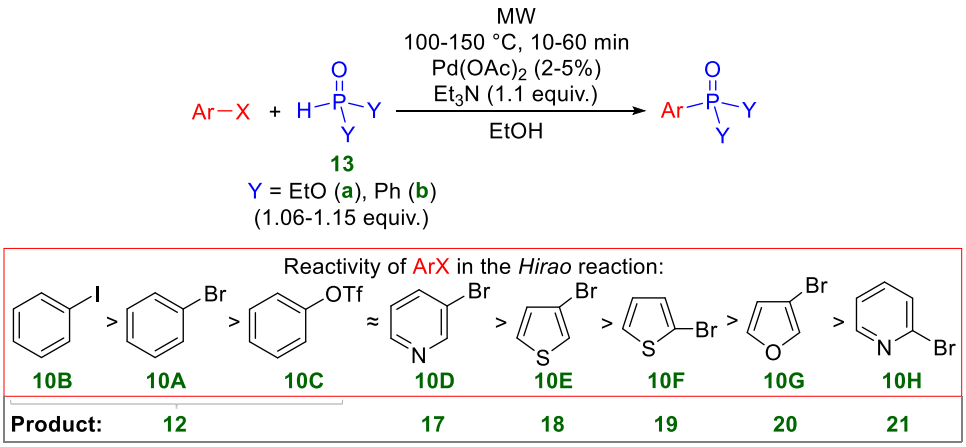
4.1.3. A survey on the reactivity of aromatic substrates and extensions of the Pd-catalyzed cross-coupling

The P–C coupling of bromobenzene (**10A**) with diphenylphosphine oxide (**11d**) at 120 °C took place *via* an induction period, during which the active catalyst (**13**) might be formed from the Pd^{II} salt and the >P(O)H species (*Scheme 7*).



Scheme 7. *Time course of the Hirao reaction of bromobenzene (**10A**) and diphenylphosphine oxide (**11d**).*

Studying the relative reactivity and a practical comparison of aromatic substrates with different leaving groups [*i.e.* bromobenzene (**10A**), iodobenzene (**10B**), or phenyl trifluoromethanesulfonate (**10C**)] showed that the most suitable substrates of the P–C coupling reactions are the bromoarenes. After that, the Pd-catalyzed *Hirao* reaction was extended to the synthesis of various heteroaryl (pyridyl-, thienyl-, or furyl-) phosphonates and phosphine oxides (**17**-**21**) (*Scheme 8*).



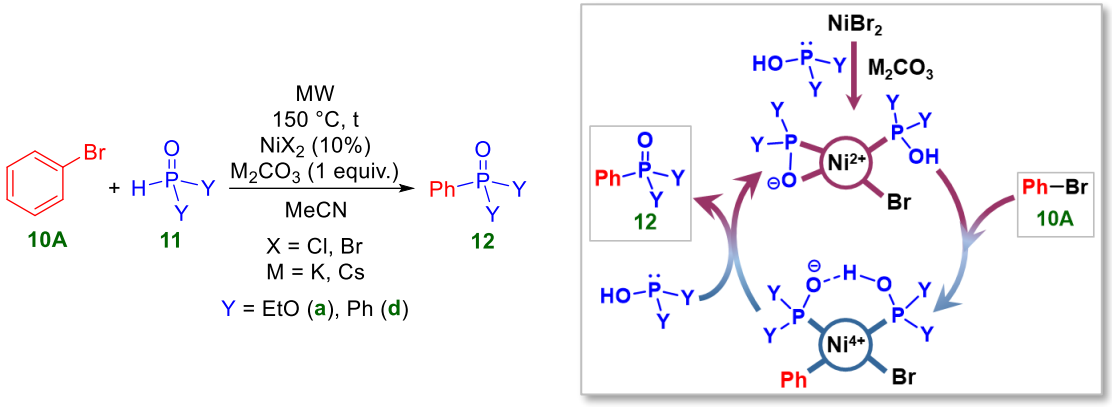
Scheme 8. *Extensions of the Pd-catalyzed P–C coupling reaction without the addition of conventional ligands.*

4.1.4. Theoretical background of the nickel-catalyzed Hirao reaction

4.1.4.1. P–C coupling reactions using $NiCl_2$ precursor without adding reducing agents or conventional ligands

The theoretical background of nickel-catalyzed P–C coupling reactions was evaluated as well, since they can also be realized without the addition of conventional ligands.

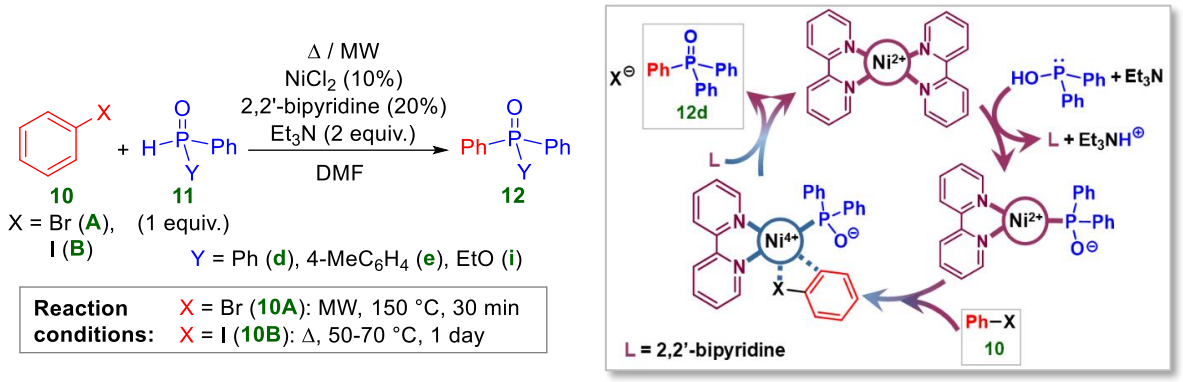
In the phosphorylation of bromobenzene (**10A**) using 10% of Ni^{II} salt, the optimal amount of the >P(O)H reagent (**11a** or **11d**) was 1.2 equivalents, suggesting that the >P(O)H compound acts only as a *P*-ligand, and the "NiX_2-catalyzed" *Hirao* reaction proceeds without reduction of Ni^{II}. According to quantum chemical studies, the catalyst is a Ni^{II} complex containing >P(OH) ligands, and the catalytic cycle takes place *via* Ni^{II}→Ni^{IV} oxidation, and not through the previously considered probable Ni^{0}→Ni^{II} transition (*Scheme 9*).



Scheme 9. *Theoretical aspects of the P–C couplings in the presence of Ni^{II}-salts and in the absence of reducing agents or ligands.*

4.1.4.2. A study on the P–C coupling reaction in the presence of $NiCl_2$ as the precursor, Zn as the reducing agent and 2,2'-bipiridine as the *N*-ligand

Our next goal was to compare the developed P–C coupling method with the "reductive" type *Hirao* reaction applying $NiCl_2$ as the catalyst precursor, 2,2'-bipyridine as the *N*-ligand and Zn as the reducing agent. We found that there was no need for the addition of the previously used Zn to reduce Ni^{II}. The reaction of the more reactive iodobenzene (**10B**) took place under mild conditions, while MW irradiation and higher temperature of 150 °C was required for the conversion of the less active bromobenzene (**10A**) (*Scheme 10*).



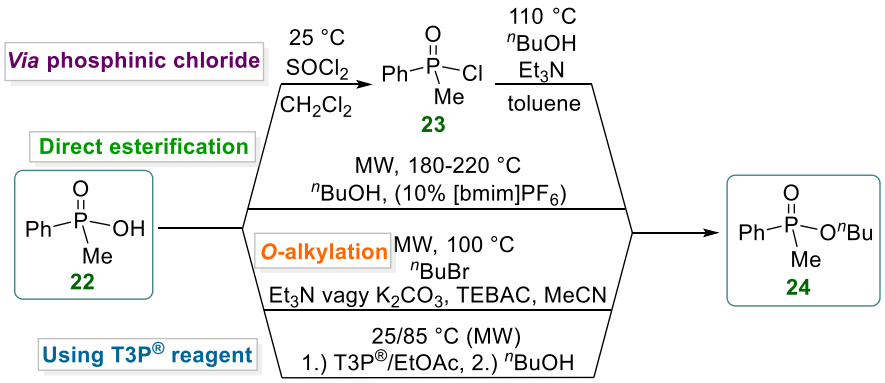
Scheme 10. *The „Ni^{II}-2,2'-bipyridine-catalyzed" Hirao reaction.*

It became clear that the "reductive" type cross-coupling does not follow the $Ni^0 \rightarrow Ni^{II}$ mechanism proposed previously. Our experiments and theoretical calculations confirmed that the P–C coupling reaction in the presence of 2,2'-bipyridine ligand took place *via* the $Ni^{II} \rightarrow Ni^{IV} \rightarrow Ni^{II}$ protocol. This can be considered as a brand new observation, since so far the $Ni^0 \rightarrow Ni^{II} \rightarrow Ni^0$ way was assumed in all cases. Considering that the "Ni^{II}/>P(OH)-catalyzed" *Hirao* reaction also occurs similarly, such catalysis may be of general value.

4.2. Synthesis of phosphinates and phosphonates

4.2.1. Preparation of butyl methyl-phenylphosphinate: a case study

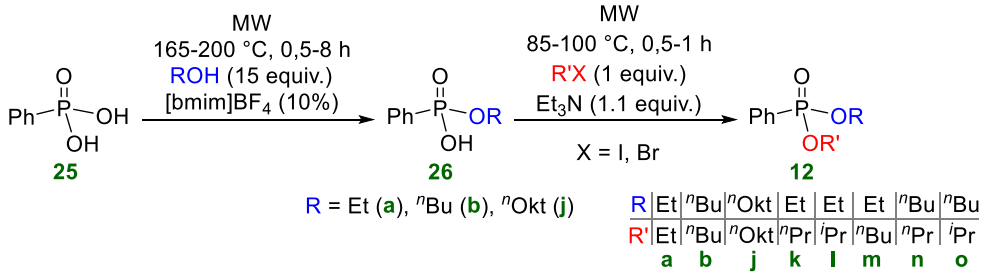
Four methods providing phosphinic esters were compared *via* a case study of the preparation of the butyl methyl-phenylphosphinate (**24**) (*Scheme 11*). Critical evaluation of the advantages and disadvantages of each method showed that in small (0.5-1 g) scale the MW-assisted transformations of the corresponding *P*-acid (**22**) were appropriate. Larger scale realization justified the utilization of the classical method starting from the phosphinic chloride (**23**) due to the scaling up problems of the MW technology and the high cost of T3P® reagent.



Scheme 11. *Synthesis of butyl methyl-phenylphosphinate (**24**) in several ways.*

4.2.2. Synthesis of the mono- and diesters of phenylphosphonic acid

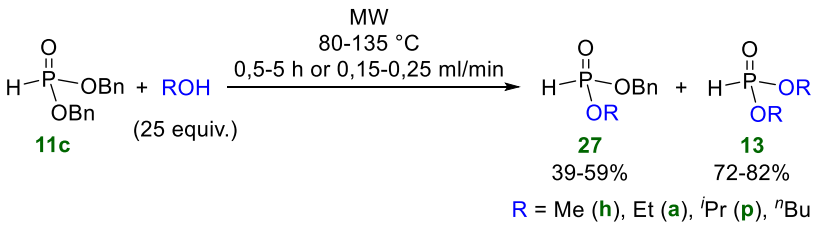
A new stepwise protocol for the synthesis of dialkyl phosphonates was developed including the MW-assisted direct esterification of phenylphosphonic acid (**25**) in the first step, and *O*-alkylation of the resulting monoesters (**26**) in the second step (*Scheme 12*). Phosphonates (**12a**,**b**,**j**,**k-o**) with both identical and different alkyl groups could be prepared by this two-step process.



Scheme 12. *Esterification of phenylphosphonic acid (**25**) and the O-alkylation of the resulting monoesters (**26**).*

4.2.3. Alcoholysis of dibenzyl phosphite

The alcoholysis of dibenzyl phosphite (**11c**) was also studied to synthesize *P*-esters containing different alkoxy groups. Depending on the reaction conditions applied, beside the "double-transesterified" dialkyl phosphites (**11a**,**b**,**h**,**p**), particularly valuable alkyl benzyl-*H*-phosphonates (**27**) could be obtained in acceptable yields (*Scheme 13*). The alcoholysis was also carried out on larger scale in a continuous flow MW reactor.



Scheme 13. *The reaction of dibenzyl phosphite (**11c**) with C_1-C_4 alcohols under MW conditions.*

5. Theses

I. We have proved by experiments that in the P–C coupling reaction of bromobenzene under MW irradiation, without the addition of the conventional *P*-ligands, in the presence of 5% of $Pd(OAc)_2$ the >P(O)H compounds should be measured in 1.15 equivalents: 1 equivalent is the *P*-reagent, 5% serve as reducing agent, and the remaining 10% are involved as *P*-ligands of the Pd-catalyst. [2]

II. We have shown that the difference in reaction times required for the P–C coupling of diarylphosphine oxides with bromobenzene is influenced by two main factors: the reactivity of the diarylphosphine oxides and the activity of the catalyst they form. The latter of the two has greater effect as a consequence of steric hindrance affecting ligation. The Pd-catalyzed *Hirao* reaction was extended for the preparation of heteroaryl derivatives. [3] [4]

III. We were the first who observed that the *Hirao* reaction of bromobenzene and diphenylphosphine oxide applying $Pd(OAc)_2$ and Et_3N under MW conditions begins with an initial, so-called induction period that is even longer than the reaction time itself. [8]

IV. We have proved that in the reaction of bromobenzene with >P(O)H compounds using $NiCl_2$ without the addition of ligands or reducing agents, surprisingly, the active catalyst is a Ni^{II}-complex containing >P(OH) ligands. Hence, no reduction of Ni^{II} occurred, but a $Ni^{II} \rightarrow Ni^{IV} \rightarrow Ni^{II}$ catalytic cycle was observed. [9]

V. We have confirmed that the P–C coupling in the presence of $NiCl_2$, 2,2'-bipyridine as the ligand, and Zn as the reducing agent also takes place *via* the $Ni^{II} \rightarrow Ni^{IV}$ oxidation instead of the previously assumed $Ni^{0} \rightarrow Ni^{II}$ catalysis. Thus, there is no need to add a reducing agent to perform the *Hirao* reaction. [10]

VI. Analogously to the environmentally friendly preparation of phenylphosphinates, a two-step MW-assisted protocol was developed for the synthesis of phosphonates by the direct esterification of phenylphosphonic acid followed by the *O*-alkylation of the resulting monoesters. We have also prepared valuable phosphonates with a chirality center; continuous implementation seemed advantageous. [1] [5] [7]

6. Possibilities for the application

In the field of the *Hirao* cross-couplings, we have proved that by exploring the theoretical background of the coupling reactions, the catalyst systems could be simplified. The decisive parameter is the quality of the transition metal applied, which should be selected based on the planned reagents and conditions. Since the palladium- and nickel-catalyzed cross-couplings may be realized more economically, and without the loss of efficiency in the absence of conventional ligands, this direction is worth to follow. In addition, the new Ni^{II}-catalyzed mechanism explored opens up further perspectives. Overall, a deeper understanding of the reactions under discussion allows a more conscious design and development of later transformations.

During the preparation of phosphonates and phosphinates by substitution (esterification, transesterification and *O*-alkylation) methods, we have showed that a well-thought-out evaluation of existing synthetic methods helps to plan and implement subsequent syntheses according to the principles of green chemistry.

In the vast majority of the investigated reactions, the positive effect of the MW technique was demonstrated, and in accordance with the modern chemical trends, we confirmed that the use of continuous flow reactors increases the efficiency.

In addition, the synthetic importance of the compounds prepared must not be forgotten either. They may be valuable starting materials for further transformations.

7. Publications

7.1. Full scientific publications related to the PhD Thesis

[1] Kiss, N. Z.; Henyecz, R.; Jablonkai, E.; Keglevich, G.: Synthesis of *n*-butyl ester and *n*-butylamide of methyl-phenylphosphinic acid – Two case studies. *Synth. Commun*. **2016**, *46* (9), 766–774, doi: 10.1080/00397911.2016.1171361. [IF: 1,134, C: 2, HR: 100%]

[2] Keglevich, G.; Henyecz, R.; Mucsi, Z.; Kiss, N. Z.: The palladium acetate-catalyzed microwave-assisted Hirao reaction without an added phosphorus ligand as a “green” protocol: A quantum chemical study on the mechanism. *Adv. Synth. Catal*. **2017**, *359* (24), 4322–4331, doi: 10.1002/adsc.201700895. [IF: 5,123, C: 5, HR: 100%]

[3] Henyecz, R.; Mucsi, Z.; Keglevich, G.: Palladium-catalyzed microwave-assisted Hirao reaction utilizing the excess of the diarylphosphine oxide reagent as the *P*-ligand; A study on the activity and formation of the "PdP_2" catalyst. *Pure Appl. Chem*., **2019**, *91* (1), 121–134, doi: 10.1515/pac-2018-1004. [IF: 1,919, C: 2, HR: 100%]

[4] Henyecz, R.; Oroszy, R.; Keglevich, G.: Microwave-assisted Hirao reaction of heteroaryl bromides and >P(O)H reagents using $Pd(OAc)_2$ as the catalyst precursor in the absence of added *P*-ligands. *Curr. Org. Chem.*, **2019**, *23* (10), 1151–1157, doi: 10.2174/1385272823666190621114915. [IF: 1,933, C: 2, HR: 80%]

[5] Henyecz, R.; Kiss, A.; Mórocz, V.; Kiss, N. Z.; Keglevich, G.: Synthesis of phosphonates from phenylphosphonic acid and its monoesters. *Synth. Commun.*, **2019**, *49* (20), 2642–2650, doi: 10.1080/00397911.2019.1637894. [IF: 1,796, HR: 60%]

[6] Henyecz, R.; Keglevich, G.: New developments on the Hirao reactions, especially from "green" point of view. *Curr. Org. Synth.*, **2019**, *16* (4), 523–545, doi: 10.2174/1570179416666190415110834. [IF: 1,983, C: 2, HR: 100%]

[7] Kiss, N. Zs.; Henyecz, R.; Keglevich, G.: Continuous flow esterification of a *H*-phosphinic acid, and transesterification of *H*-phosphinates and *H*-phosphonates under MW conditions. *Molecules*, **2020**, *25* (3), 719, doi: 10.3390/molecules25030719. [IF (2019): 3,267, HR: 100%]

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7.2. Short publications, proceedings, and book chapters related to the PhD Thesis

[11] Keglevich, G.; Kiss, N. Z.; Bálint, E.; Bagi, P.; Grün, A.; Kovács, T.; Henyecz, R.; Ábrányi-Balogh P.: Milestones in microwave-assisted organophosphorus chemistry. *Phosphorus, Sulfur Silicon Relat. Elem.*, **2016,** *191* (11-12), 1416–1420, doi: 10.1080/10426507.2016.1211657. [IF: 0,809, C: 6, HR: 25%]

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[14] Keglevich, G.; Kiss, N. Z.; Henyecz, R.; Mucsi, Z.: Microwave irradiation and catalysis in organophosphorus reactions. *Pure Appl. Chem.*, **2019**, *91* (1), 145–159, doi: 10.1515/pac-2018-0501. [IF: 1,919, HR: 100%]

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[17] Keglevich, G.; Henyecz, R.; Mucsi, Z.: Focusing on the catalysts of the Pd- and Ni-catalyzed Hirao reactions. *Molecules*, **2020**, *25* (17), 3897, doi: 10.3390/molecules25173897. [IF (2019): 3,267, HR: 100%]

7.3. Other publications related to the PhD Thesis

[18] Jablonkai, E.; Henyecz, R.; Milen, M.; Kóti, J.; Keglevich, G.: T3P®-assisted esterification and amidation of phosphinic acids. *Tetrahedron*, **2014**, *70* (44), 8280–8285, doi: 10.1016/j.tet.2014.09.021. [IF: 2,641, C: 9, HR: 30%]

[19] Ábrányi-Balogh, P.; Jablonkai, E.; Henyecz, R.; Milen, M.; Keglevich, G.: Theoretical calculations on the mechanism of the T3P®-promoted esterification and amidation of phosphinic acids. *Curr. Org. Chem.* **2016**, *20* (10), 1135–1142, doi: 10.2174/1385272820666151218204848. [IF: 1,924, HR: 100%]

7.4. Oral presentations

1. Henyecz, R.: A foszfor-szén kötés kialakítására alkalmas kapcsolási reakciók szubsztrát-függésének vizsgálata. *Új Nemzeti Kiválósági Program Konferencia,* Budapest, **2018**.
2. Henyecz, R.; Huszár, B.; Mórocz, V.; Oroszy, R.; Kiss, N. Z.; Keglevich, G.: MW-assisted synthesis of phosphonic and phosphinic esters, as well as phosphine oxides. *22nd International Conference on Phosphorus Chemistry,* Budapest, **2018**.
3. Henyecz, R.; Kiss, N. Z.; Keglevich, G.: Foszfinátok, foszfonátok és tercier foszfin-oxidok előállítása a mikrohullámú technika felhasználásával. *Kisfaludy Lajos Alapítvány tudományos előadóülése*, Budapest, **2018**.
4. Henyecz, R.: A P–C kapcsolási reakciók szubsztrátumfüggésének vizsgálata. *Oláh György Doktoráns Konferencia*, Budapest, **2019**.
5. Henyecz, R.: Microwave-assisted Hirao reaction in the absence of added P-ligands. *International Conference on Catalysis, Advanced Chemical Engineering and Technology,* Valencia, **2019**.
6. Henyecz, R.: Rézkatalizált foszfor-szén keresztkapcsolási reakciók tanulmányozása. *Új Nemzeti Kiválósági Program Konferencia*, Budapest, **2020**.

7.5. Poster presentations

1. Henyecz, R.; Kiss, N. Z.; Jablonkai, E.; Keglevich, G.: Foszfinátok előállítása észteresítési reakciókkal. *Vegyészkonferencia 2017*, Hajdúszoboszló, **2017**.
2. Henyecz, R.; Huszár, B.; Bezdán, S.; Kiss, N. Z.; Mucsi, Z.; Keglevich, G.: P–C kapcsolási reakciók optimalizálása. *Vegyészkonferencia 2017*, Hajdúszoboszló, **2017**.
3. Henyecz, R.; Jablonkai, E.; Ábrányi-Balogh, P.; Kiss, N. Z.; Keglevich, G.: T3P®-promoted esterification and amidation of phosphinic acids. *17th Blue Danube Symposium on Heterocyclic Chemistry*, Linz, **2017**.
4. Henyecz, R.; Mucsi, Z.; Kiss, N. Z.; Keglevich, G.: "P-ligand-free" palladium acetate-catalyzed P–C coupling reactions under microwave conditions. *18th European Workshop on Phosphorus Chemistry*, Uppsala, **2018**.
5. Henyecz, R.; Grenitzer, V.; Kiss, N. Z.; Mucsi, Z.; Keglevich, G.: The P–C coupling of aryl derivatives and dialkyl phosphites or diaryl phosphine oxides without the addition of conventional P-ligands. *International Conference on Phosphorus, Boron and Silicon*, Barcelona, **2018**.