Russian Chemical Reviews **81** (3) 221 – 238 (2012) © 2012 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2012v081n03ABEH004248

The application of green chemistry methods in organophosphorus synthesis

I L Odinets, E V Matveeva

Contents

I.	Introduction	221
II.	The Wittig and Horner – Wadsworth – Emmons reactions	222
III.	The Kabachnik – Fields reaction	228
IV.	Reactions of P – C bond formation	230
V.	Reactions of phosphines with aldehydes	233
VI.	Other types of organophosphorus reactions	234
VII.	Conclusion	236

Abstract. Data concerning the synthesis of organophosphorus compounds in ionic liquids, in water and under solvent-free conditions are considered and summarized. It is shown that this strategy, which complies with the definition of green chemistry, has advantages in terms of the rate of the process and the yields of target products as compared with syntheses in common organic solvents. The Wittig, Horner – Wadsworth – Emmons, Kabachnik – Fields, Arbuzov and Michaelis reactions are considered as examples. The bibliography includes 178 references.

I. Introduction

The so-called green chemistry (or environmentally friendly chemistry) is one of the most topical trends in modern chemistry. Green chemistry relies on the development of synthetic strategies that do not affect the environment rather than on the reliability of equipment and prevention of industrial disasters. This tendency is confirmed by the increasing number of publications on this topic during the last decade. This is caused by the growth of scale and the range of chemical and pharmaceutical products, *i.e.*, by the strong necessity of the application of processes that are safe both for the humankind and the environment. Presumably, for this reason, even in fundamental research, the attention is focused on known reactions that have a high applied value.

Theoretically, it is desirable to carry out the chemical reactions without any solvents. In those cases where it is either impossible or inconvenient regarding the isolation of target products, the main alternatives to flammable and toxic organic solvents are ionic liquids (ILs),[1–7] water[8–10] and supercritical liquids.[11,12] The ability to readily dissolve organic, organometallic and inorganic compounds, the non-volatility, low toxicity and the possibility of reuse are the advantages of ionic liquids. Moreover, the interconnection between fundamental and applied studies has led to a rather wide application of the reactions in ionic liquids on an industrial scale.[13] Water is not only the cheapest but also an absolutely non-toxic solvent. Though the enzymatic processes in nature occur exactly in aqueous medium, even recently, most researchers have not considered the use of water as a solvent for organic reactions. However, nowadays this tendency is brought to the forefront and gives excellent results. Moreover, Sharpless and Fokin with co-authors[14,15] have shown that the low solubility of organic compounds in water is not an unfavourable factor but on the contrary it only facilitates the isolation of target products. Supercritical liquids also find their niche in the implementation of chemical and biotechnological processes and play an important role in material science.[16] Besides the features mentioned above, the most important feature of green solvents is their ability to promote many reactions.

Now the ionic liquids are widely used in the alkylation, Diels – Alder and Friedel – Crafts reactions, in different catalytic processes (cross-coupling, aldol condensation, hydrogenation, hydrosilylation, *etc.*), in different types of polymerization, in peptide synthesis, *etc.* Besides the pure synthetic approach, the application of ionic liquids as solvents for the processing of biomass[17] and in pharmaceutics,[18] as superhydrophobic coatings[19] and so on is worth mentioning.

The number of papers concerning the application of water as a solvent in such classical organic reactions as the Diels – Alder, Michaelis and Mannich reactions, the allylation reaction, the aldol-type reactions and many others is constantly increasing. The supercritical carbon dioxide (sCO_2) also finds wide application. Specifically, its combi-

I L Odinets, E V Matveeva A N Nesmeyanov Institute of Organoelement Conpounds, Russian Academy of Sciences, ul. Vavilova 28, 119991 Moscow, Russian Federation. Fax (7-499) 135 50 85, tel. (7-499) 135 93 56, e-mail: odinets@ineos.ac.ru (I L Odinets), matveeva@gmail.com (E V Matveeva)

Received 1 July 2011
Uspekhi Khimii **81** (3) 221 – 238 (2011); translated by P A Nikitina

nation with nano-sized catalyst attached to a solid support adds significant advantages to the catalytic process. This combination allows one to avoid the use of organic solvents and also to isolate the catalyst from the reaction mixture and to regenerate it.[20]

However, the methods and principles of green chemistry penetrate into chemistry of organophosphorus compounds rather slowly. To a large extent, this is determined by the established point of view that the synthesis of such compounds requires a protective inert atmosphere, vacuum lines and thoroughly dehydrated solvents. Therefore, even the method of phase-transfer catalysis,[21] *i.e.*, carrying out the reaction at the interface between organic and aqueous phases, has found its application in the chemistry of organophosphorus compounds much later than in general organic synthesis. Though the percentage of studies concerning the use of green chemistry principles in the whole number of papers on organophosphorus synthesis is rather small, it is thought reasonable to summarize these data and the advantages that are gained by researchers in this field. The present review deals with the recent achievements concerning the synthesis of organophosphorus compounds or the reactions with them that occur in ionic liquids, in water or in the absence of solvent. As for the supercritical liquids, to the best of our knowledge, there is a single paper[22] on enzymatic kinetic separation of racemic hydroxymethylphosphonates in sCO_2.

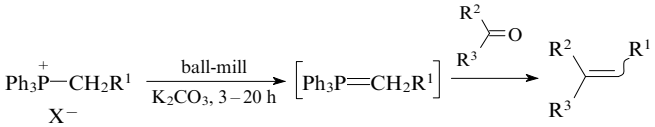
II. The Wittig and Horner – Wadsworth – Emmons reactions

The Wittig reaction the discovery of which brought the Nobel Prize in Chemistry in 1979 to Georg Wittig, and the related Horner – Wadsworth – Emmons reaction, which was described in the 1960s, are among the most convenient methods for the regioselective formation of C=C bonds (so-called P=O olefination reactions). Presumably, the strategy of synthesis of alkenes with strictly defined position of double bond based on these reactions is the most widespread example of the use of organophosphorus compounds in general organic synthesis and, specifically, in the synthesis of natural products and their analogues.

The phosphorus ylides are used as organophosphorus substrates in the Wittig reaction. The ylides may be either reactive, non-stabilized and generated *in situ* from corresponding phosphonium salts under the action of bases, or they may be stabilized. Meanwhile, in the Horner – Wadsworth – Emmons reaction, phosphonate carbanions stabilized by electron-withdrawing substituents are used most often. Phosphonate carbanions are more basic (nucleophilic) and reactive than phosphonium ylides.[23] The main advantage of P=O olefination by means of the Horner – Wadsworth – Emmons reaction is thought to be the possibility of easy removal of phosphate by-products when the reaction mixture is treated with water, in contrast to the sometimes problematic separation of alkene from phosphine oxide (using crystallization or chromatography) in the Wittig reaction. At the same time the undoubted advantages of the latter reaction include the easy structural modification of the ylide or its salt precursor and higher stereoselectivity (usually *Z*-alkenes prevail in the case of non-stabilized ylides and *E*-alkenes predominate in the case of stabilized ylides) in comparison with the reaction involving phosphonates.[24] In other words, these two methods are mutually complementary and they are almost equally used.

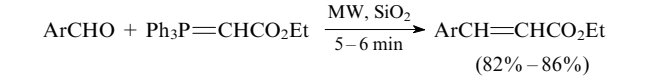
Usually the Wittig reaction is carried out in various solvents ranging from hexane to DMSO, the reaction rate in nonpolar solvents being lower than in polar ones. This reaction has practical significance; that is why, numerous attemtps at its optimization have been made. A variety of procedures are described in literature. They include the use of high temperature[25] or pressure,[26,27] auxiliary additives (lithium salts,[28,29] cyclodextrin,[30] benzoic acid[31–35]), ultrasonic,[36] light[37] or microwave[38–42] irradiation in organic solvents and also phase transfer catalysis conditions in two-phase systems water – organic solvent with *in situ* generation of the ylide.[21,43,44]

Balema *et al.*[45] have shown that it is possible to carry out the synthesis of stabilized, semistabilized or non-stabilized phosphorus ylides and the subsequent Wittig reaction in the absence of any solvent, *i.e.*, by mechanochemical reaction using a ball mill and potassium carbonate as a base. The yields of ylides are nearly quantitative (the stabilized ylides may be isolated in a pure state), while the yields of P=O olefination products are 73% – 92%. Under such conditions, the P=O olefination may be carried out as a one-pot process starting from triphenylphosphine, the corresponding halide and carbonyl compound. Rather low stereoselectivity is a drawback of this method. The ratio of the forming *E* : *Z* isomers varies from 60 : 40 to 70 : 20.



R^1 = H, Ph, Bn, CO_2Et; R^2 = H, Me;
R^3 = 1-Naph (Naph is naphthyl), 4-BrC_6H_4; X = Br, Cl.

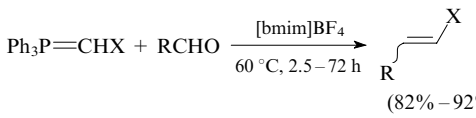
Under the conditions of solid-phase synthesis on exposure to microwave radiation (MW), both non-stabilized[46] and stabilized ylides[38] have been involved into the Wittig reaction with aromatic aldehydes. In the former case, in spite of the simplicity of the procedure and short reaction time, the yields of alkenes were only 41% – 68%, the *E* : *Z* ratio varying from 1 : 1 to 3.1 : 1. In the case of stabilized ylides (the reaction was carried out in the presence of SiO_2 as inert support for 5 – 6 minutes), the yields of products were from 82% to 96%, only the corresponding *E*-isomers being formed.



Ar = XC_6H_4 (X = H, 3-Me, 3-Br, 3-NO_2, 4-Cl, 4-Br, 4-NO_2).

As an alternative to organic solvents, Le Boulaire and Gree[47] proposed carrying out the Wittig reaction of stabilized ylides in ionic liquid, *i.e.*, [bmim]BF_4 (bmim is 1-butyl-3-methylimidazolium). Under such conditions leading to unsaturated products in 82% – 92% yield and to high *E*-selectivity (85% – 98%), it is possible to use both aromatic and aliphatic aldehydes, the nature of carbonyl reagent strongly influencing the time of the reaction (2.5 – 72 hours at 60 °C). The subsequent extraction with diethyl ether leads to a mixture of target alkene and phosphine oxide (in a 80 : 20 ratio), which may be easily

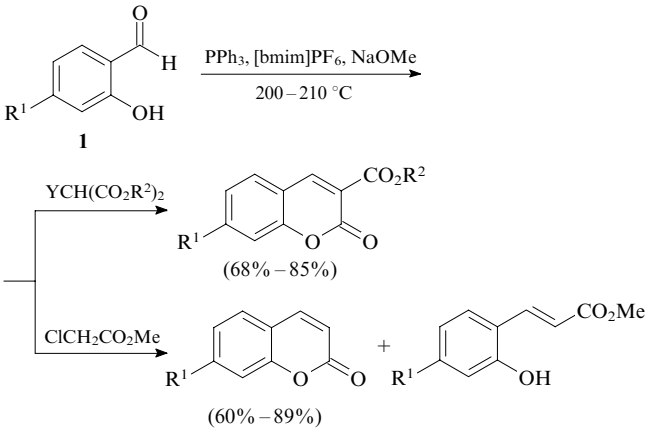
separated into individual compounds on passing through a small layer of silica gel.



X = CO_2Me, Ac, CN; R = Bu^i, n-C_5H_{11}, cyclo-C_6H_{11}, PhCH=CH, MeCH=CH, YC_6H_4 (Y = H, 4-Cl, 2-NO_2, 4-OMe, 4-Me).

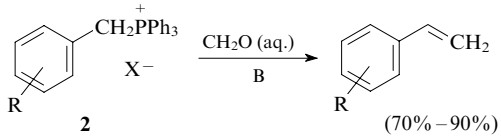
The repeated extraction of ionic liquids with toluene results in complete recovery of phosphine oxide and excess phosphorane. After two extractions (diethyl ether, then toluene), IL no longer contains organophosphorus admixtures and may be repeatedly used in the reaction without loss of activity for at least 6 times. In addition, this ionic liquid may be repeatedly used as the reaction medium in the Wittig reaction for other starting reactants, and the products of the second reaction do not contain the impurites formed in the first one.

The one-pot version of the reaction has been applied for the synthesis of 3-unsubstituted and 3-alkoxycarbonyl-substituted coumarins.[48] Triphenylphosphine (1.5 equiv.), diethyl choloromalonate, dialkyl malonate or methyl chloroacetate (1.2 equiv.) and 2-hydroxybenzaldehyde derivatives **1** were used as starting compounds, the reaction was carried out in the presence of NaOMe in the [bmim]PF_6 ionic liquid. Salts of bmim with Cl^-, Br^-, BF_4^- and $AlCl_4^-$ anions were also tested as reaction media.



R^1 = H, OH, OMe, NEt_2; R^2 = Me, Et; Y = H, Cl.

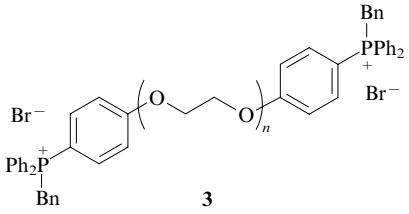
Data on the possibility of performing the Wittig reaction in water in the absence of organic co-solvent first appeared in the literature back in 1970s. Substituted styrenes have been synthesized from aqueous formaldehyde (unlike other aliphatic aldehydes, formaldehyde is not self-condensed in basic media) and the corresponding ylides, which were obtained *in situ* from phosphonium salts **2** under the action of Na_2CO_3 (Ref. 49) or 50% NaOH.[50, 51]



R = H, 2-NO_2, 4-CN, 4-Br, 4-Me, 4-OMe, 4-CO_2H; X = Cl, Br; B is base.

Surprisingly for a long time there were no further attempts to expand the scope of applicability of this method, apparently due to the whole range of prejudices associated with the low solubility of phosphonium salts and ylides in water, their susceptibility to hydrolysis and the preferences to homogeneous reactions. The interest in the possibility of carrying out the P=O olefination in water (and specifically in a number of papers[49–51]) appeared later, at the turn of the century, in connection with the growth of popularity of green chemistry methods.

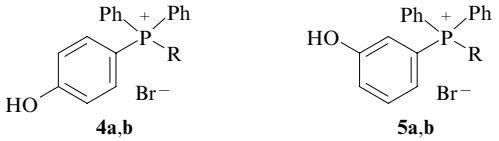
Originally it was supposed to raise the solubility of organophosphorus substrates in water by the introduction of additional functional groups. Thus, Janda and co-workers[52] have synthesized phosphonium salts based on poly(ethylene glycol) (PEG), which were water soluble at pH 7. The reactions of salt **3** with *para*-substituted benzaldehydes (4-RC_6H_4CHO) in aqueous NaOH gave the corresponding stilbenes in 49% (R = Bu^t) up to 95% (R = H) yields, the average $E:Z$ isomer ratio being close to the statistic one (with the exception of R = H and Cl, in these cases this ratio was 75 : 25).

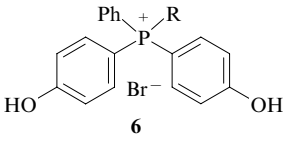


The variation of the reaction conditions, *i.e.*, the change in the concentration of NaOH (from 1 M to 2 M) and the increase in temperature up to 90 °C, had almost no effect on the yield of the products or on the stereochemical outcome of the reaction. The PEG phosphine oxide by-products can be easily reduced by lithium aluminium hydride (THF, 20 °C, 0.5 h, quantitative yield) to the corresponding phosphine, which can be alkylated to provide recycling of the starting phosphonium salt.

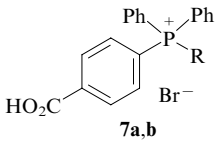
A similar idea, *i.e.*, the use of hydroxy- or carboxy-substituted phosphonium salts **4**–**7**, which would certainly be soluble in alkaline medium (unlike the alkenes that are formed during their reaction with aldehydes), was proposed by Russel and Warren.[53]

For the hydroxy-substituted salts **4**–**6**, both the positions and the number of hydroxy groups in the benzene ring have a significant effect on the yield of desired stilbenes. Thus, whereas the presence of one hydroxy group is necessary for salt solubility, the presence of two hydroxy-substituted phenyl groups significantly decreases the reactivity of the conjugated ylide (salt **6** reacts only with benzaldehyde). The highest yields of the products, 70%–100% (20 °C, 12 h, $E:Z$ = 7 : 3), were obtained for salt **5a** with the OH group in *meta*-position. However, the attempts to extend these conditions to other aldehydes (formaldehyde, 3- and 4-hydroxybenzaldehydes, butanal, chloral) failed. In all cases, the starting compounds were recovered unchanged.





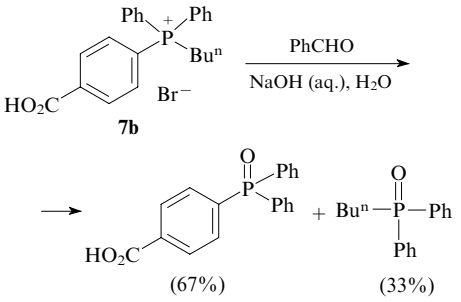
6



7a,**b**

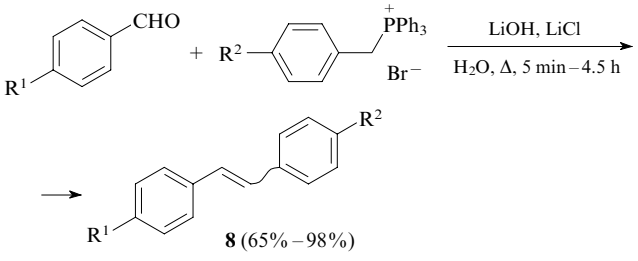
R = Bn (**a**), Bu^n (**b**).

The substituent R also has a significant impact on the result of the reaction: alkyl derivatives **4b** and **5b** do not undergo the Wittig reaction. Carboxy-substituted salt **7a** also posesses reduced reactivity, and butyl derivative **7b** is hydrolyzed in alkaline medium.



Thus, the principle of modification of phosphonium salts (as the precursors of ylides in the Wittig reaction) for increasing their solubility in water turned out to be a poor solution for carrying out this reaction in aqueous medium. First of all, only some salts give alkenes in good yields. Second, the stereochemical outcome of the reaction is far from being perfect. Finally, all the examples described are limited to aromatic aldehydes.

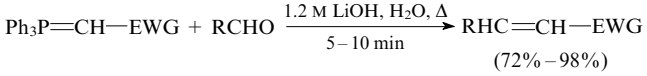
In view of the rather low efficiency of application of phosphonium salts, Wu and co-workers [54] proposed using lithium chloride as an auxiliary reagent. In water, this compound promotes the Wittig reaction of aromatic aldehydes with semistabilized ylides that are generated *in situ* from the corresponding phosphonium salts under the action of 1.5 equiv. MOH (M = Li, Na). The authors emphasized that in water, the Wittig reaction proceeds at a significantly higher rate than in organic solvents (from 5 to 240 minutes in boiling water), and the yield of stilbenes **8** is 65% – 98%. The function of LiCl is not only to accelerate the reaction but also to inhibit the hydrolysis of ylide and its salt precursor. LiCl has no effect on the stereochemical outcome of the process. In this case, the *E*/*Z*-selectivity of the reaction depends both on the substituents in the benzene rings of the ylide (or phosphonium salt) and in aromatic aldehyde and on the nature of the alkali metal.



8 (65% – 98%)

R^1, R^2 = H, Cl, NO$_2$, OMe.

Similarly, LiCl was used to carry out the Wittig reaction in water with stabilized ylides.[55] In this case, too, the presence of the salt had no effect on the ratio of isomers: the reaction occured non-stereoselectively for aliphatic aldehydes. For aromatic aldehydes, the *E*-isomer predominated, the selectivity decreasing for less sterically hindered cyano-substituted ylide (EWG = CN, EWG is Electron Withdrawing Group).

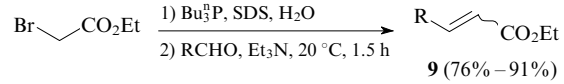


EWG = CO$_2$Et, Ac, CN; R = Ph, 4-O$_2$NC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-HOC$_6$H$_4$, n-C$_7$H$_{15}$, 2-Fu (Fu is furyl).

The LiCl – LiOH system was also effective for the one-pot reaction in water. The starting compounds used included Ph$_3$P, α-bromoacetate or α-bromoacetonitrile and aromatic aldehydes.[56]

A kinetic study of the effects of 'salting-out' additives (LiCl and NaCl) and anti-hydrophobic ('in-salting') additives (guanidinium chloride, GnCl) on the Wittig reaction of aromatic or aliphatic aldehydes with stabilized carbethoxy-substituted ylide in water was performed.[57] The results demonstrated the dependence of the effeciency of such additives on temperature. At 25 °C, the relative reaction rate in the presence of 1 M solutions of LiCl and NaCl was lower than in pure water, whereas at 55 °C, it was higher (reaction rate constant k_{rel} = 1.1 – 1.2). An inverse relationship was observed for guanidinium chloride: at 25 °C, k_{rel} was 0.99, and at 55 °C, k_{rel} was 0.55. Besides, at room temperature an increase in the salt concentration resulted in a sharp decrease in the reaction rate. This unusual influence of temperature on the salt effects implies that the addition of salting-out or in-salting additives has an impact on the hydrophobicity of the surface of solid particles of the insoluble ylide in the heterogeneous process, the salt effect being changed in the case of aqueuos homogeneous reactions.

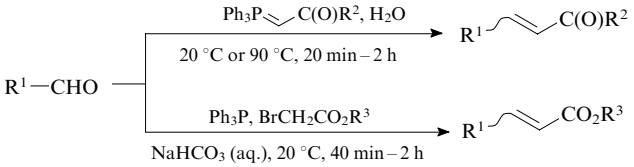
As an alternative, Orsini *et al.*[58] proposed performing the Wittig reaction in water at room temperature in the presence of sodium dodecyl sulfate (SDS) as a micelle forming agent. In the three-component one-pot reaction in which the ylides are formed *in situ* from tributylphosphine and ethyl bromide, it is possible to use aromatic, heterocyclic and aliphatic aldehydes. The yield of alkenes **9** is 70% – 90%, the *E*-isomer being the predominant product (the *E* : *Z* ratio is on averages 75 : 25). In all of the studied reactions, the micellar system was on average 10% more effective than the system with LiCl.



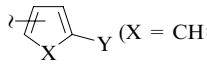
R = n-C$_7$H$_{15}$, 4-O$_2$NC$_6$H$_4$, 4-MeOC$_6$H$_4$, PhCH$_2$CH$_2$, PhCH=CH, 2-Fu.

Also, it has been shown that the Wittig reaction with stabilized ylides can be carried out in water (at room temperature or with heating) without any auxiliary additives.[59, 60] Particularly, the reaction rates in the presence and in the absence of SDS (30 mol.%) were comparable, though the addition of DMSO (5 mol.%), PhCO$_2$H (10 mol.%) or LiCl (10 mol.%) accelerated the reaction at room temperature. Moreover, the reaction rate in water (or on water)

was considerably higher than in organic solvents (ranging from CCl_4 to methanol), the yields of the products being 80% – 98%, and the *E*-selectivity being 99%. In the case of aliphatic aldehydes, benzaldehyde and aromatic aldehydes activated by electron-withdrawing groups, the reaction proceeds at room temperature; aldehydes or ketones insoluble in water give products in high yileds as the temperature is increased to 90 °C. Furthermore, the reaction may be carried out as a three-component one-pot process in a saturated aqueous solution of sodium hydrogencarbonate (20 °C, 40 min to 3 h) starting with triphenylphosphine, alkyl bromoacetate and aromatic aldehyde ArCHO (Ar is substituted phenyl, C_6F_5, 2-naphthyl, substituted pyridyl or thienyl).



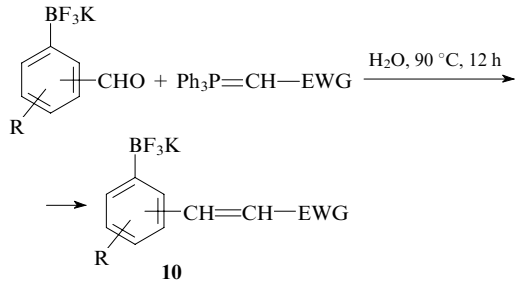
R^1 = Ph, 4-$O_2NC_6H_4$, 4-NCC_6H_4, 4-BrC_6H_4, 4-HOC_6H_4, 2-$O_2NC_6H_4$, 2,5-$Me_2C_6H_3$, Bu^n, Bu^s, n-C_5H_{11}, n-C_8H_{17}, CO_2H, PhCH=CH,



(X = CH=N, S; Y = H, Br, Me, NO_2), *etc.*;

R^2 = OMe, OPh, Bu^t, CH_2CCl_3; R^3 = Et, Bn, Bu^t.

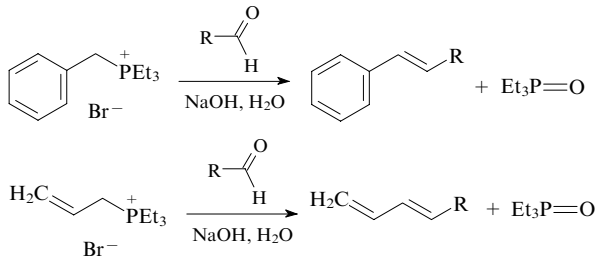
The Wittig reaction between stabilized ylides and trifluoroborate-substituted aldehydes was carried out under similar conditions (H_2O, 90 °C). Target alkenes **10** formed in 60% – 90% yields, the *E*:*Z* isomer ratio varying from 51:49 to the exclusive formation of *E*-form.[61]



10

R = F, MeO; EWG = CO_2Me, Ac, $C(O)NMe_2$, CN.

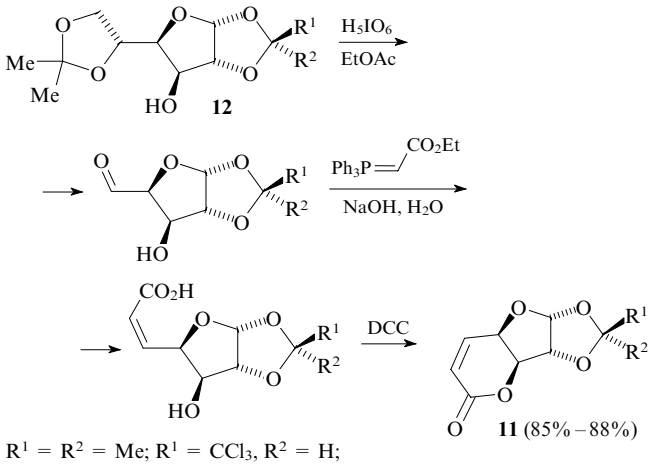
McNulty and Das carried out the Wittig reaction in the absence of any additives between semistabilized ylides generated *in situ* from trialkylallylphosphonium[62] or trialkylbenzylphosphonium[63] salts in aqueous sodium hydroxide (4 equiv.) and a wide range of aromatic, aliphatic and unsaturated aldehydes. The ylide is formed exclusively due to the deprotonation of the allyl or benzyl position, the target organic product being easily separated from trialkylphosphine oxides, which are soluble in water (unlike triphenylphosphine oxide). It is the ease of separation of the secondary product that is the main advantage of this approach. The reaction is highly stereoselective and gives the corresponding *E*-alkenes in good yields. This method was used for the preparative-scale synthesis of antitumour agents of the *trans*-stilbene series such as resveratrol and *trans*-3,4,5,4′-tetramethoxystilbene (DMU-212) without the use of organic solvents at any stage.



R is substituted phenyl, pyrrol-2-yl, indol-3-yl.

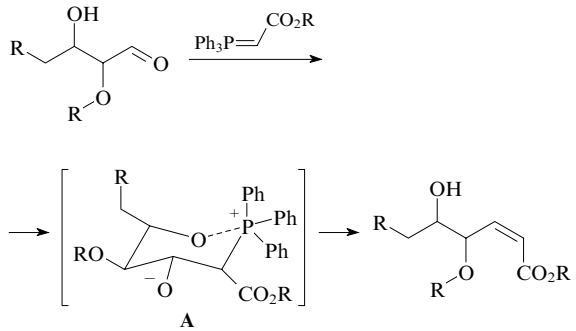
In elaboration of this method, the authors proposed[64] generating phosphonium salts directly from trialkylphosphine hydrobromides and allyl or benzyl alcohol under solvent-free conditions and using microwave irradiation at the stage of the Wittig reaction. This allowed them to proceed to weak bases such as potassium carbonate, to reduce the reaction time to 0.5 h (75 – 100 °C), and also to introduce ketones as the carbonyl components.

A highly selective (giving only *Z*-isomers) version of the Wittig reaction in water was used for fast preparation of unsaturated derivatives of 7,3-lactone-α-D-xylofuranose **11** from D-glucose derivatives **12** (the total yield over three stages was 85% – 88%).[65]



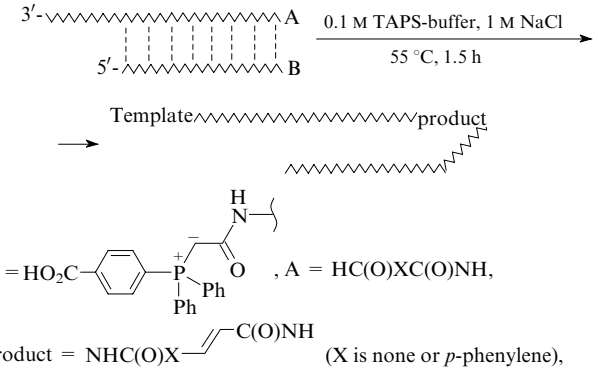
R^1 = R^2 = Me; R^1 = CCl_3, R^2 = H;
DCC is *N*,*N*′-dicyclohexylcarbodiimide.

Theoretical *ab initio* calculations for the model reaction confirm the hypothesis of stabilization of intermediate *anti*-betaine **A** due to the solvation effect of the solvent (water) as the main factor determining the *Z*-selectivity of the process.[65]



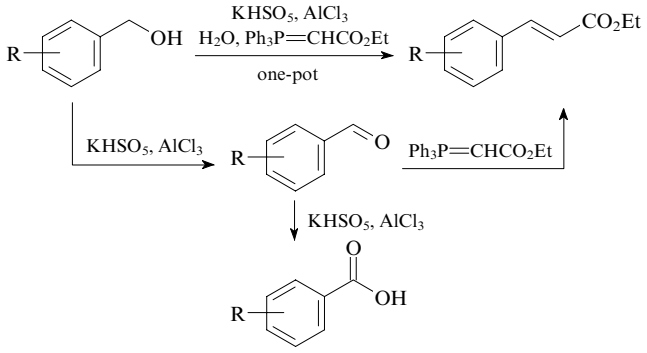
Carrying out the Wittig reaction in water also found application in DNA-templated synthesis. The corresponding alkenes were obtained in 93% – 97% yields from DNA-

bound stabilized ylides and 3′-matrices modified by aldehyde moieties in water at room temperature at pH 6.0 – 8.0.[66]



The authors suppose that such transformations, along with other DNA-templated reactions, provide an opportunity for sequence-specific translation of DNA libraries into the libraries of structurally and functionally diverse synthetic products.

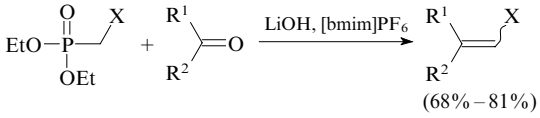
The combination of aqueous version of the Wittig reaction and the synthesis of carbonyl compounds by oxidation of alcohols using the $KHSO_5 - AlCl_3$ system of reagents (domino reaction) was found to be convenient. Though the yield of alkene in the one-stage version is moderate (> 52%), the advantages of the method are the simplicity of the synthesis, the conditions fitting with the green chemistry criteria, *i.e.*, the absence of heavy metals and chlorinating solvents and high stereochemical purity of the products (> 99% of *E*-isomer).[67]



R = H, 4-Cl, 4-NO_2, 4-NH_2, 4-OH, 4-OMe, 4-Me, 2-Me.

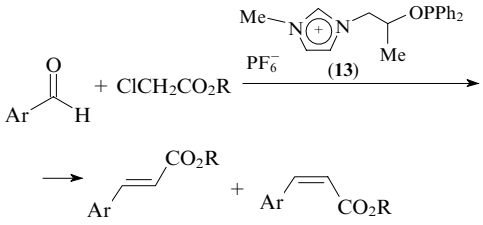
Thus, obviously, the limited solubility of organophosphorus substrates is not a factor preventing performing of the Wittig reaction in water with stabilized and semistabilized ylides, these processes being faster and more effective than those in organic solvents.

The Horner – Wadsworth – Emmons P=O olefination related to the Wittig reaction may also be carried out in the absence of organic solvent, *i.e.*, in ionic liquids or in water. In particular, *E*-isomers of β-substituted acrylic esters were obtained by the reaction of diethyl phosphonoacetate and aldehydes in $[bmim]PF_6$ in the presence of lithium hydroxide.[68] It should be noted that the bases commonly used as deprotonating agents in polar solvents, *i.e.*, K_2CO_3 and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), turned out to be inactive in $[bmim]PF_6$, and the use of stronger bases (NaOH, KOH) resulted only in the hydrolysis of ester groups at the phosphorus atom. The authors attributed this difference in the behaviours of lithium hydroxide and other alkali metal hydroxides to the strong ion – dipole interaction of Li^+ ions with water being formed in the reaction. As a result, water is withdrawn from the reaction sphere, and thus the hydrolysis is inhibited. After the removal of LiOH by filtration, washing with water and subsequent drying *in vacuo*, the ionic liquid may be used in other reactions, including the reactions with other reactants.



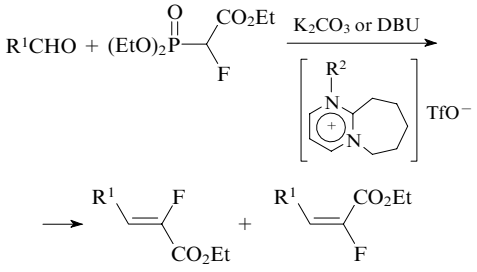
X = CO_2Et, $C(O)R^3$ (R^3 = Me, Et, Pr^n);
R^1 = H: R^2 = cyclo-C_3H_5, Bu^i, Ph, PhCH=CH, 2-Py (Py is pyridyl);
$R^1 - R^2 = (CH_2)_5$.

Valizadeh and Shockravi[69] proposed using phosphinite-functionalized imidazolium ionic liquid **13** as both the solvent and a reactant in the one-pot version of this reaction. Its reaction with aromatic aldehydes and chloroacetates in the presence of sodium methoxide gave products in up to 74% – 87% yields (the *E*:*Z* isomer ratio varied from 73:27 to 88:12). The reaction time was 10 – 12 h under the conditions of thermal induction or 8 – 12 min under microwave irradiation.



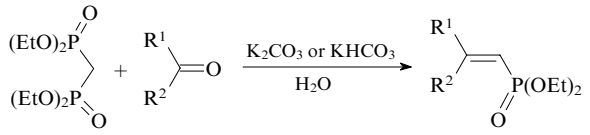
Ar = Ph, 4-NCC_6H_4, 4-MeC_6H_4, 4-AcC_6H_4; R = Me, Et.

In the case of monofluorinated phosphonoacetates, the corresponding alkenes were obtained in good yields (77% – 88%) only if the reaction was carried out in 8-substituted 1,8-diazabicyclo[5.4.0]undec-7-ene trifluoromethanesulfonate (triflate, TfO). The yield dramaticaly decreased if $[emim]BF_4$ and $[emim]PF_6$ (emim is 1-ethyl-3-methylimidazolium) were used.[70] The ratio of *E*:*Z* isomers depended on the base used, being ~70:30 (K_2CO_3) and 30:70 (DBU).



R^1 = Ph, PhCHMe, n-C_6H_{13}, 2-Py; R^2 = Me, Et.

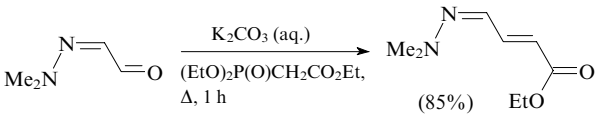
The possibility of carrying out such transformation in water as a liquid–liquid heterogeneous reaction in the presence of a concentrated aqueous solution of potassium carbonate or hydrogencarbonate (6–10 mol litre^{-1}) in the absence of organic co-solvent or phase-transfer catalysts was described back in the 1980s.[71,72] The reaction of methylenebisphosphonates used as the phosphorus component with aldehydes in water (100 °C) in the presence of 2 equiv. of potassium carbonate gave phosphorylated *E*-alkenes **14** in high yields.[73]



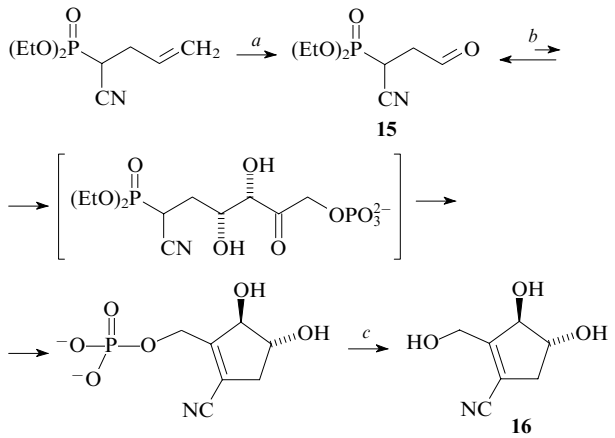
14 (60%–97%)

R^1 = H: R^2 = cyclo-C_3H_5, Bu^i, Ph, PhCH=CH, 2-Py;
R^1–R^2 = $(CH_2)_5$.

It is possible to use aldehydes with acid- or base-labile groups under similar conditions. This was demonstrated by the example of β-dimethylhydrazonoacetaldehyde.[74]

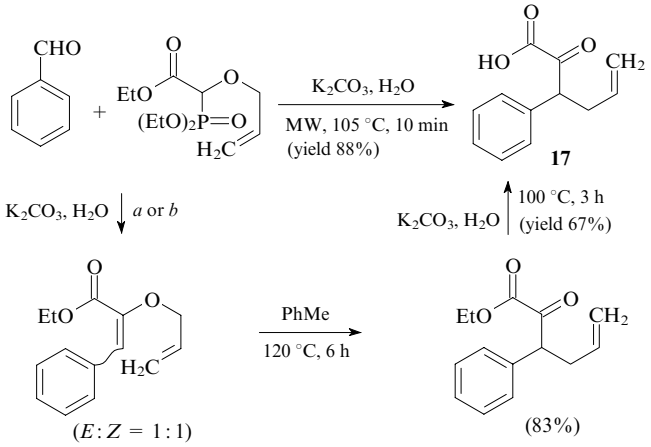


The 'aqueous' version of the Horner–Wadsworth–Emmons reaction proved to be convenient for carrying out tandem processes. In particular, the combination of enzymatic aldol condensation of phosphorylacetonitrile-substituted aldehyde **15** and dihydroxyacetone phosphate (DHAP) catalyzed by fructose 1,6-diphosphate aldolase (FDP-aldolase, EC 4.1.2.13) and the intramolecular Wittig reaction was found to be a convenient method of preparation of a polyhydroxylated cyclopentene **16**, cyclitol.[75]



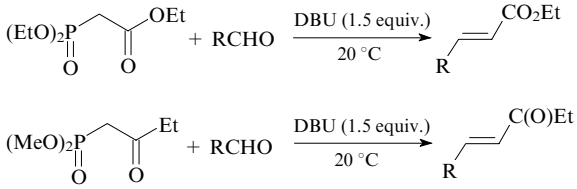
(*a*) 1) O_3, −78 °C; 2) Me_2S, −78 → 0°C; (*b*) DHAP, FDP aldolase, pH 1–6.8, 23 °C, 20 h; (*c*) phosphatase, pH 4.8, 1.5 h.

In another example, the consecutive Horner–Emmons reaction, Claisen rearrangement and hydrolysis in water under microwave irradiation provided an easy transformation of aldehydes to β-substituted 2-oxohex-5-enoic acids **17**. The yield of the product is obviously higher in comparison with the stepwise synthesis.[76]



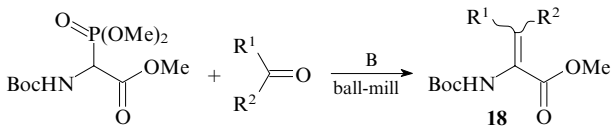
(*a*) 25 °C, 3 h (yield 96%); (*b*) 55 °C, 30 min (yield 100%).

However, perhaps the highest efficiency is observed in the case of the Horner–Wadsworth–Emmons reaction carried out under solvent-free conditions using tertiary amines as bases (DBU is the optimum).[77] The process time being on average 0.5–4 h (depending on the aldehyde used), the target products are obtained in 90%–98% yields and with a 97%–99% *E*-selectivity. The high *E*-selectivity is maintained if 1-alkyl-substituted esters of phosphorylacetic acids and phosphorylated ketones are used as starting phosphorus substrates.



R = Bu^t, cyclo-C_6H_{11}, n-C_7H_{15}, 2-EtC_5H_{10}, Ph, 4-ClC_6H_4, 4-MeC_6H_4, PhCH=CH, 2-Fu, BnOCHMe.

Meanwhile, the solid-phase Horner–Wadsworth–Emmons reaction of amino-substituted phosphonoacetates in a ball-mill in the presence of DBU affords products **18** in lower yields than in the presence of solid potassium or caesium carbonate.[78] Unsaturated amino esters are formed as single *Z*-isomers, which also predominate if the reaction is carried out in water. This is the distinction from the Wittig reaction for which the stereochemical outcomes in ball-mill and in solution were exactly the opposite.[45]



R^1 = H: R^2 = Pr^n, Bu^i, Bu^t, Bn, Ph, 2-BrC_6H_4, 3,5-$(MeO)_2C_6H_3$, 2-Py, 2-Fu, 1-Naph; R^1 = R^2 = Ph; R^1 = Me, R^2 = Et;
Boc is *tert*-butyloxycarbonyl.

Thus, the Wittig and the Horner–Wadsworth–Emmons reactions can be effectively and stereoselectively carried out in ionic liquids or water as alternative reactive medium, and also as solvent-free synthesis. From the practical point of view, regarding the cost of the solvent, the reaction rate, the yields of products and the possibility

of preservation of acidic or basic labile groups and stereochemical outcome, it seems reasonable to consider carrying out such syntheses in water.

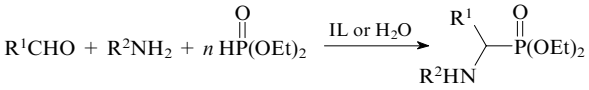
III. The Kabachnik – Fields reaction

The Kabachnik – Fields reaction (discovered independently by Kabachnik and Fields in 1952) involving three components, namely, amine, carbonyl compound (aldehyde or ketone) and hydrophosphoryl compound, still remains the most convenient method of preparation of α-aminophosphonates. Being structural analogues of α-amino acids, these compounds possess a wide range of biological activities.[79,80] They are applied as antibiotics,[81] enzyme inhibitors,[82] antitumour agents,[83,84] insecticides and herbicides.[85] Furthermore, α-aminophosphonates are interesting ligands for homogeneous[86,87] or organic[88] catalysis and as α-hydroxy- and α-amino acid carriers through lipophilic membranes.[89]

Under the classical conditions, the Kabachnik – Fields reaction occurs at 80 – 120 °C in the presence of NaOEt in polar solvents (*e.g.*, alcohols). Lewis acids such as $SnCl_2$,[90] $BF_3 \cdot Et_2O$,[91,92] $MgBr_2$,[93] rare-earth triflates[94] may be also used as catalysts. The reaction is carried out in nonpolar solvents such as dichloromethane, dichloroethane or diethyl ether.

Lee *et al.*[95] have shown that the interaction of an aromatic aldehyde, aniline and diethyl phosphite catalyzed by Yb, Sc, Dy, Sm and La triflates in the imidazolium ionic liquid at room temperature proceeds more efficiently than in a traditional solvent, *i.e.*, dichloromethane. At the same time, anhydrous $Sm(OTf)_3$ (10 mol.%) proved to be the optimal catalyst, the activity of ionic liquids decreasing in the order $[bmim]PF_6 > [bmim]OTf > [bmim]SbF_6 \gg [bmim]BF_4$ (Scheme 1).

Scheme 1



R^1 = $R^3C_6H_4$, 2-Naph, Pr^i, Bu^n, n-C_9H_{19}, MeCH=CH, PhCH=CH, 2-Fu, 2-Th (Th is thienyl); R^2 = $R^3C_6H_4$ (R^3 = H, 4-F, 4-Cl, 3-NO_2, 4-Me, 4-CF_3, 4-OMe), Bn, cyclo-C_6H_{11}.

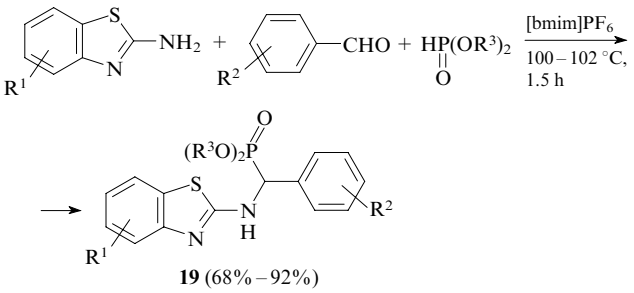
n	Reaction conditions	Yield (%)	Ref.
4	$[bmim]PF_6$, $Sm(OTf)_3$ (10 mol.%), 20 °C, 27 h	99	95
1.2	$[bmim]BF_4$, $Yb(OTf)_3$ (10 mol.%), MW, 2 min	99	96
1	$[bmim]BF_4$, 20 °C, 4.5 – 9 h	81 – 93	97
1	[bmim]Cl, MW, 90 °C, 30 – 40 min	55 – 74	98
1	H_2O, $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ (0.16 mol.%),[a] 80 °C, 0.5 – 2 h	90 – 98	99
1.5	H_2O, β-CD (10 mol.%),[b] 100 °C, 24 h	45 – 82	100

[a] 3,4-tmtppa is tetrakis(*N*-methyl-3,4-pyridinium)porphyrazinate (see below), [b] β-CD is β-cyclodextrin.

Additional microwave irradiation (850 W) of the reaction mixture results in completion of the triflate-catalyzed condensation of benzaldehyde, aniline and diethyl phosphite in ionic liquids in 2 min. All catalysts display high activity both in $[bmim]BF_4$ and in $[bmim]PF_6$.[96] Experiments on the regeneration of the catalytic system showed that the $[bmim]BF_4 - Yb(OTf)_3$ system (10 mol.%) is the best one. It may be used up to five times without the loss of activity (average yield of products > 99%).

At the same time, it has been reported[97] that the Kabachnik – Fields reaction of aromatic or aliphatic aldehydes, aniline derivatives and diethyl phosphite may be successfully carried out in ionic liquid at room temperature in the absence of both the catalyst and the additional irradiation. Unlike the mentioned above metal triflate catalysis, the starting reactants were used in stoichiometric quantities, the highest yields (81% – 93%) were obtained in $[bmim]BF_4$ in 4.5 – 9 h, and evacuation of the ionic liquid at 80 °C after each cycle allowed its repeated use without any loss of activity. The reaction rate considerably decreases in going to bulkier 4-phenoxyquinazoline derivatives of aniline. Additional thermal (90 °C) or microwave (40 W) activation in [bmim]Cl results in the products being formed in 55% – 74% yield over a short period of time (30 min).[98]

Heterocyclic amines may also be involved in the Kabachnik – Fields reaction in ionic liquids without a catalyst.[101] In the case of 2-aminobenzothiazolines, the best yields of compounds **19** were obtained in $[bmim]PF_6$ at elevated temperature (100 – 102 °C). It is of interest that in $[bmim]HSO_4$, the product yields dramatically decrease due to the protonation of the starting amine. It is worth noting that some of α-aminophosphonates **19** containing benzothiazole moiety and fluoro-substituted phenyl group exhibited high anticancer activity *in vitro* against PC3, A431, A375 and Bcap cell lines.[101]



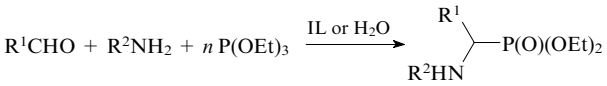
19 (68% – 92%)

R^1 = 4-Me, 6-OMe; R^2 = 2-F, 4-F, 4-CF_3; R^3 = Me, Et, Pr^n, Pr^i, Bu^n.

It should be noted that the use of hydrates of rare-earth metal salts [*e.g.*, $Yb(OTf)_3H_2O$] or the repeated use of a water-containing system IL – catalyst in a triflate-catalyzed three-component reaction[95] results in considerable decrease in the yields of the target products (to 60% – 70%). In this context, it was hypothesized that the use of triethyl phosphite instead of diethyl phosphite in the Kabachnik – Fields reaction may turn this drawback into an advantage because of the fact that the phosphorus substrate would be hydrolyzed to give diethyl phosphite and ethanol under the action of water formed during the reaction (Scheme 2). Indeed, by means of this modification, the reaction time was considerably reduced (from 27 to 2 h) and the catalytic system based on scandium triflate could be reused several times without any loss of activity.

Some ionic liquids can serve as not only as reaction media but also as efficient catalysts of the Kabachnik – Fields reaction. Thus, in the case of substituted aldehydes, anilines and triethyl phosphite in the absence of any additional solvent, the use of 50 mol.% 1-benzyl-3-methylimidazolium with acidic anion affords the desired α-aminophosphonates in high yields within 10 – 30 min at room temperature.[102]

Scheme 2

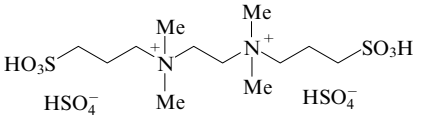


R^1 = $R^3C_6H_4$ (R^3 = H, 4-F, 4-Cl, 4-CF_3, 4-Me, 4-OMe, 3-NO_2), Bu^i, $PhCH_2CH_2$, PhCH=CH, 1-Naph, 2-Fu;
R^2 = Ph, Bn, Ph_2CH, PhMeCH, 2-$MeOC_6H_4$.

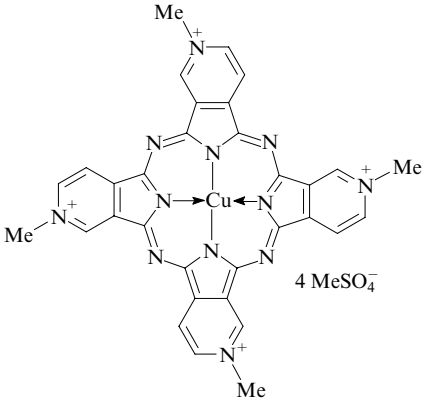
n	Reaction conditions	Yield (%)	Ref.
4	[bmim]PF_6, $Sc(OTf)_3$ (1 mol.%), 20 °C, 2 h	90–99	95
1.2	[bnmim]HSO_4 (50 mol.%),[a] 20 °C, 10–30 min	80–96	102
1	H_2O, [bsmim]HSO_4 (10 mol.%),[b] 20–60 min	80–96	103
2.5	H_2O, $Sc(O_3SOC_{12}H_{25}\text{-n})_3$ (10 mol.%), 30 °C, 20–120 min	78–95	104

[a] bnmim is 1-benzyl-3-mehtylimidazolium, [b] bsmim is 1-(4-sulfobutyl)-3-methylimidazolium.

After the introduction of the sulfonic acid residue into the imidazolium cation, such ionic liquids as [bsmim]HSO_4 (Ref. 103) and [bsmim]OTf (Ref. 105) catalyze the reaction only in the presence of water. In comparison with water-free version, the reaction rate does not decrease in this case, the activities of diethyl phosphite and triethyl phosphite are approximately equal and in the case of trimethyl phosphite, it is possible to obtain the product of its reaction with aniline and 4-methoxyacetophenone (60 min, yield 90%). It is worth noting that on going from the imidazolium cation to the diammonium salt of propanesulfonic acid ([tmedaps]HSO_4), it is no longer necessary to add water, 5 mol.% of this ionic liquid is enough to obtain high product yields.[106]



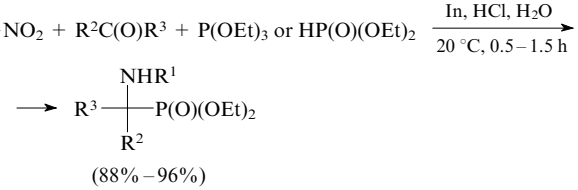
[tmedaps]HSO_4



[Cu(3,4-tmtppa)]$(MeSO_4)_4$

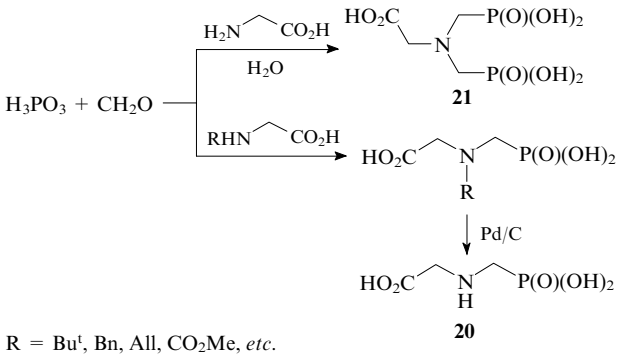
Not only ionic liquids find their application as catalysts in the synthesis of α-aminophosphonates in water (see Scheme 2). In particular, the Lewis acid $Sc(O_3SOC_{12}H_{25}\text{-n})_3$ consisting of scandium(III) cation and amphiphilic dodecyl sulfate anions catalyzes the reaction of triethyl phosphite (4 equiv.), aliphatic and aromatic aldehydes and amines at room temperature with the formation of various α-aminophosphonates in high yields.[104] Sobhani *et al.*[99] have proposed the use of minor amounts of pyridinoporphyrazine copper salt [Cu(3,4-tmtppa)]$(MeSO_4)_4$ (0.16 mol.%) as a stable water-soluble catalyst of this reaction. This gave the target products in 90%–98% yields within 0.5–2 h both in the case of triethyl and diethyl phosphite (see Scheme 1).

Das *et al.*[107] have obtained α-aminophosphonates from substituted nitrobenzenes, aromatic or aliphatic carbonyl compounds and di(tri)ethyl phosphite using one-pot reaction in water. Indium chosen as the reducing agent for the nitro group transforms to $InCl_3$ in the presence of hydrochloric acid, and this product catalyzes the second step.



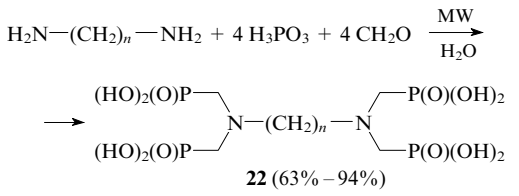
R^1 = Ar; R^2 = H: R^3 = Ar, 1-Naph, PhCH=CH, 2-Th, 2-Fu, Pr^i;
R^2 = Me: R^3 = 4-ClC_6H_4, Bu^i; R^2–R^3 = $(CH_2)_5$.

When speaking about the Kabachnik–Fields reaction, one cannot help mentioning its application for production of one of the most well-known herbicides, *i.e.*, phosphonomethylglycine (**20**). The direct interaction of aqueous solution of glycine, formaldehyde and phosphorus trichloride or phosphorous acid usually gives the product of bisphosphonomethylation,[108] glyphosine (**21**), which possesses weak herbicidal properies and has been proposed as a plant growth regulator.[109] It is possible to avoid the formation of this by-product using N-protected glycine (*tert*-butyl, benzyl, 1-phenylethyl, trityl, allyl, β-hydroxyethyl, cyanomethyl, chloromethyl, *etc.*, groups may be used for protection). The subsequent deprotection was accomplished in the presence of palladium-on-carbon, by refluxing with hydrohalic acids or by electrochemical method.[110]



R = Bu^t, Bn, All, CO_2Me, *etc.*

The same version of the Kabachnik–Fields reaction called the Moedritzer–Irani reaction, *viz.*, the reaction of alkylenediamines or polyethylenimines, phosphorous acid and formaldehyde, in water may be activated by microwave irradiation. Corresponding poly(α-aminophosphonic) acids **22** are obtained in high yields over short periods of time (1–15 min).[111]

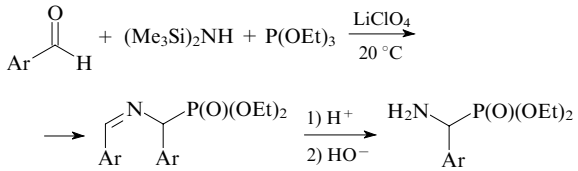


22 (63% – 94%)

n = 1 – 10.

There are many recent publications devoted to the Kabachnik – Fields reaction catalyzed by Lewis or Brønsted acids performed in solvent-free conditions.† In this case, it is possible to involve a wide range of amines and not only aldehydes but also ketones in the reaction (Table 1). Among the works presented in Table 1, special mention should be made of the use of nanoparticles of mixed iron(II, III) oxide [123] and iron(III) oxide [124] as catalysts, which can be easily removed from the reaction mixture using a magnet and reused without any loss of activity for at least ten cycles.

α-Aminophosphonates with a free amino group have also been synthesized by the solvent-free Kabachnik – Fields reaction using hexamethyldisilazane as the amino component. Target products **23** are formed in high yields at room temperature within 15 – 45 minutes with a twofold excess of lithium perchlorate and triethyl phosphite as the starting phosphorus substrate.[127]



23 (80% – 92%)

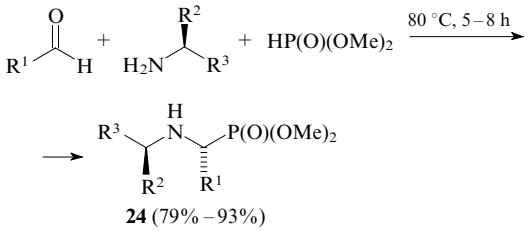
Ar = XC_6H_4 (X = H, 4-Me, 4-Cl, 3-NO_2, 2-OMe).

If one uses diethyl phosphite and $Al(OTf)_3$ (10 mol.%) as the catalyst, the time of a similar reaction varies from 15 to 120 min at 80 °C.[128]

In the absence of a solvent, the three-component reaction of amine, aldehyde or ketone and diethyl phosphite proceeds considerably faster (1 – 10 min) under the action of microwave radiation on an inert solid surface, *e.g.*, silica gel,[129] montmorillonite KSF,[130] Amberlite-IR 120 [131] or acidic aluminium oxide.[132] The use of the latter provides the preparation of products with a free amino group from ammonium formate.

It should be noted that in the absence of a catalyst or a solid phase, the corresponding α-amino(2-alkoxyethyl)-phosphonates [133] and derivatives of formic acid, phenyl- or benzylamine and diethyl phosphite or diphenylphosphinous acid [134] were also synthesized in good yields at a stoichiometric reactant ratio under microwave radiation. The microwave irradiation of reaction mixtures at the amine : diethyl phosphite : carbonyl compound ratio of 1 : 3 : 1 allows one to introduce various ketones including natural porphyrins into the Kabachnik – Fields reaction with amine and diethyl phosphite.[135] The two-component version of this transformation (the Pudovik reaction) in which the Shiff bases synthesized from natural amino acids are used instead of amine and carbonyl compound requires the addition of CdI_2 (5 mol.%) as the catalyst.[136] Xia and Lu [137] initiated this process by ultrasound; however, the fact that the above two reactions are carried out in excess diethyl phosphite as a solvent precludes assigning them to green chemistry processes to the full extent.

The Kabachnik – Fields reaction can also proceed with high yields in the absence of any solvents or catalysts. In the case of triethyl phosphite, aniline and aldehydes, the reaction is completed at room temperature in 8 – 60 min,[138] and the reaction of aldehydes, optically active alkylphenylamines and dimethyl phosphite performed at 80 °C for 5 – 8 h gives a mixture of diastereoisomers **24** in a ~75 : 25 ratio.[139]



24 (79% – 93%)

R^1 = Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$, Pr^i, Bu^i, Bu^t; R^2 = Me, Et; R^3 = Bu^t, Ph, 1-Naph.

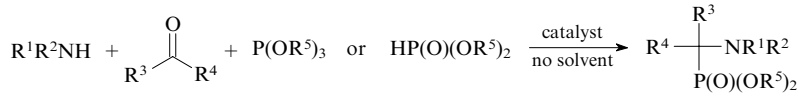
Thus, in order to obtain racemic α-aminophosphonates, it is possible to apply with almost equal efficiency the reactions in ionic liquids or in water in the presence or in the absence of catalysts depending on the reactants used, and also it is possible to carry out the process under solvent-free conditions under the action of acidic catalysts. No data can be found in the literature concerning the possibility of asymmetric synthesis of most demanded optically active derivatives under such conditions.

IV. Reactions of P – C bond formation

Ionic liquids have also been used as the reaction media for the Arbuzov reaction, which is essential for organophosphorus chemistry. In the case of haloalkanes activated with an electronegative group, the application of imidazolium ionic liquids [Rmim]X [Rmim = bmim or hmim (1-hexyl-3-methylimidazolium); X = Br, BF_4, PF_6, NTf_2] as the only reaction medium or as the two-phase IL – co-solvent system considerably reduces the reaction time, the nature of anion of ionic liquid having a critical influence on the yield of the target product.[140] In the case of triethyl phosphite, the most suitable ionic liquid is [bmim]NTf_2 (the reaction time at 100 °C is 5 – 20 min). For a more nucleophilic ethyl diphenylphosphinite at elevated temperature, the activity of ionic liquids varies in the following order: [bmim]Br ⩽ [bmim]PF_6 < [bmim]BF_4 < [bmim]NTf_2. However, the reaction can also proceed at room temperature approximately over the same period of time. Under these conditions, [hmim]Br was the most active ionic liquid. After the reaction, the ionic liquid may be reused without the loss of activity at least in 5 subsequent cycles. It should be noted that if *m*-xylylene dibromide is used in the reaction mentioned, then the corresponding diphosphorylated products are formed. In the presence of phosphonium ionic liquids,

† It should be noted that in a paper [112] dealing with catalysis by zirconium(IV) compounds, it has been shown that under these conditions, the interaction with dialkyl phosphites (diethyl and dimethyl phosphites) is faster than with trialkyl phosphites (triethyl and trimethyl phosphites).

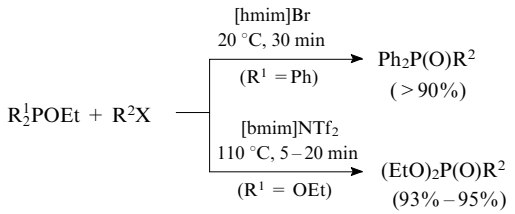
Table 1. The influence of the catalyst on the rate of the Kabachnik – Fields reaction under solvent-free conditions.



Amine	Carbonyl compound	Phosphite	Catalyst (quantity, mol.%)	Reaction conditions	Yield (%)	Ref.
R^1 = H, R^2 = 4-$MeOC_6H_4$	R^3 = H: R^4 = Ar, PhCH=CH, 2-Fu, 2-Th, Bu^t	DEP	CF_3CO_2H (25)	20 °C, 24 h	81 – 99	113
R^1 = H: R^2 = Ar, Bn, Bu^n; R^1 = R^2 = Et [a]	R^3 = H: R^4 = Ar, PhCH=CH, Pr^i	DEP	NH_2SO_3H (20)	20 °C, 1 – 4 h	76 – 94	114
R^1 = H: R^2 = Ar, Bu^t	R^3 = H: R^4 = Ar, PhCH=CH, 1-Naph, 2-Fu, 3-Ind; $R^3 – R^4 = (CH_2)_5$; R^3 = Me, R^4 = 4-ClC_6H_4	DEP	$Al(OTf)_3$ or $Cu(OTf)_2$ (10)	80 °C, 5 min – 4.5 h	70 – 98	115
R^1 = H: R^2 = Ar, Bn	R^3 = H: R^4 = Ar, PhCH=CH	DEP	$BiNO_3 \cdot 5H_2O$ (10)	20 °C, 5 – 10 h MW, 1 – 4 min	80 – 95 88 – 98	116
R^1 = H: R^2 = Ar, 2-Py, 1-Ad, Bn, cyclo-C_6H_{11}; $R^1 – R^2 = (CH_2)_5$, $O(CH_2CH_2)_2$	R^3 = H: R^4 = Ar, 1-Naph, 2-Py, 2-Fu, 2-Th, Pr^i; R^3 = Me, R^4 = Ph; $R^3 – R^4 = (CH_2)_5$ (see [b])	DMP, DEP	$Mg(ClO_4)_2$ (5)	20 °C, 2 min – 6 h (for ketones, 80 °C, 0.5 – 6 h)	80 – 98	117
			$ZrOCl_2 \cdot 8H_2O$ (10)	20 °C, 5 min – 4 h (for ketones 80 °C, 1 – 4 h)	75 – 96	112
R^1 = H: R^2 = Ar, Bn	R^3 = H: R^4 = Ar, PhCH=CH; $R^3 – R^4 = (CH_2)_4$, $(CH_2)_5$	DMP, DEP	KF/NP [c]	20 °C, 14 h	61 – 87	118
R^1 = H: R^2 = Ar, Bn, Pr^n, $(CH_2)_3OH$; $R^1 – R^2 = (CH_2)_5$, $O(CH_2CH_2)_2$	R^3 = H: R^4 = Ar, PhCH=CH, 3-Th, Bu^i, $PhCH(CO_2H)$; $R^3 – R^4 = (CH_2)_5$; R^3 = Me: R^4 = Ph, Bu^t	DEP	TiO_2 (20)	50 °C, 1 – 6 h	76 – 98	119
R^1 = H, R^2 = Ar	R^3 = H: R^4 = Ar, 2-Cl-3-Qui, PhCH=CH, 2-Fu, 2-Th, Pr^i ; $R^3 – R^4 = (CH_2)_5$; R^3 = Me, R^4 = Ph	TEP	$KAl(SO_4)_2 \cdot 12H_2O$ (alum) (20)	20 °C, 5 – 90 min (for ketones 80 °C, 1 h)	82 – 97	120
R^1 = H: R^2 = Ar, Bn	R^3 = H: R^4 = Ar, Pr^n	TMP, TEP	$Al(H_2PO_4)_3$	100 °C, 15 – 30 min	75 – 95	121
R^1 = H, R^2 = Ar	R^3 = H, R^4 = Ar	TMP, TEP	$HClO_4/SiO_2$ (3)	80 °C, 40 – 120 min	71 – 98	122
R^1 = H: R^2 = Ar, 2-Py; $R^1 – R^2 = (CH_2)_5$, $O(CH_2CH_2)_2$	R^3 = H: R^4 = n-C_5H_{11}, Ar, PhCH=CH, 2-Py; $R^3 – R^4 = (CH_2)_5$	DEP	Fe_3O_4 nanoparticles (5)	50 °C, 20 – 55 min	79 – 94	123
R^1 = H, R^2 = Ph; $R^1 – R^2 = O(CH_2CH_2)_2$	R^3 = H: R^4 = Ar, PhCH=CH, 2-Fu, Bu^t, cyclo-C_6H_{11}	DMP	γ-Fe_2O_3-@HAp-$Si(CH_2)_3$. .$NHSO_3H$ (0.7) [d]	20 °C, 1.5 – 3.5 h	94 – 97	124
See [e]		DEP	$Na_2CaP_2O_3$	20 °C, 12 – 24 h	76 – 91	125
See [f]		DEP	MoO_2Cl_2 (5)	80 °C, 5 – 60 min	80 – 95	126

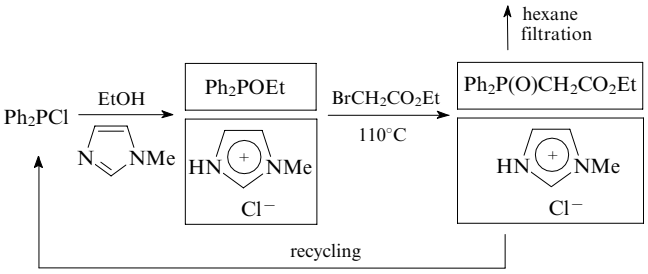
Note. The following notation is used: Ar is substituted phenyl group, Ind is indolyl, Ad is adamantyl, Qui is quinolinyl. DEP is diethyl phosphite, DMP is dimethyl phosphite, TEP is triethyl phosphite, TMP is trimethyl phosphite. [a] The reaction of Et_2NH, ArCHO and $HP(O)(OEt)_2$ in the presence of 20 mol.% of sulfamic acid at 20 °C gives the corresponding α-hydroxyphosphonate (yield >85%) in 15 min. [b] Indan-1-one was also used as a ketone. [c] Natural phosphate preliminarily stored in an aqueous solution of KF and then dried. [d] Nanoparticles of hydroxyapatite-encapsulated γ-Fe_2O_3, whose surface is modified by covalently bonded sulfamide groups. [e] Aldimine ArCH=NAr was introduced into the reaction instead of aldehyde and amine. [f] Aldimine ArCH=NR (R = Ar, n-C_6H_{13}) was used.

the reaction pathway changes. Only the hydrolysis of ester groups at the P^{III} atom in the starting substrate takes place.



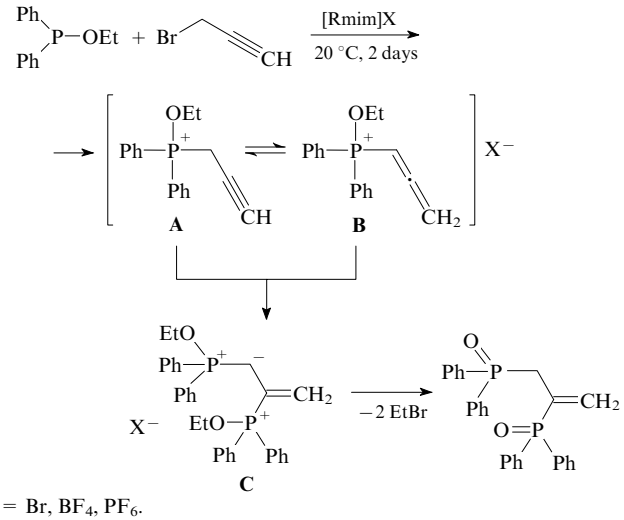
R^2 = Bn, CH_2CN, CH_2CO_2Et; X = Cl, Br.

The procedure of the Arbuzov reaction with activated alkyl halides in ionic liquids can be combined with the so-called BASIL™-process [141], *i.e.*, the commercial synthesis of the esters of trivalent phosphorus. In this process, 1-methylimidazole is used as the acceptor of hydrochloric acid, resulting in the formation of 1-methylimidazolium chloride ([mim]Cl), which is an ionic liquid with a melting temperature of 76 °C. If alkyl halide is added to the obtained reaction mixture, then this ionic liquid also serves as an activating medium. This furnishes the target products in high yields directly from phosphorus acid chlorides in one-pot synthesis (the frames mean the presence of reactants in different phases).[140]



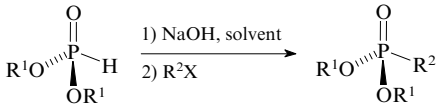
In the case of other types of alkyl halides, the application of ionic liquid as a solvent may result in the domination of competitive reactions or in abnormal transformation pathway. Thus, if n-butyl bromide is used as electrophilic component, the formation of the corresponding hydrophosphoryl compounds (*i.e.*, diethyl phosphite and diphenylphosphinous acid) becomes the dominating pathway. In the case of diphenylphosphinite, the oxidation of the forming diphenylphosphinous acid and the formation of tetraphenyldiphosphine 1-oxide proceed simultaneously at elevated temperature.[142]

The reaction of diphenylphosphinite with propargyl bromide in ionic liquids yields 2,3-bis(diphenylphosphoryl)-prop-1-ene instead of the expected products of the Arbuzov reaction regardless of the ratio of the starting reactants.[142, 143] It has been shown that unlike common organic solvents, ionic liquids promote the addition of the second nucleophile molecule to the intermediate quasiphosphonium salt **A** (or to the product of its acetylene – allene rearrangement **B**), which is formed according to the traditional mechanism of the Arbuzov reaction. The formation of bis-phosphonium intermediate **C** has been proved by spectroscopy in ionic liquids with non-coordinating anions (X = BF_4).



X = Br, BF_4, PF_6.

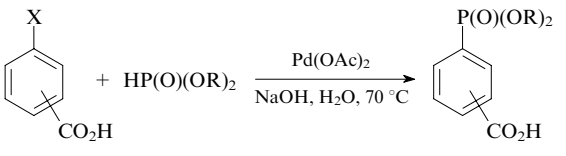
The Michaelis – Becker reaction, which is similar to the Arbuzov reaction, is also successfully carried out in the medium of [bmim]BF_4 either in the presence of sodium hydroxide as a base or starting with sodium phosphites. It is worth noting that unlike the imidazolium ionic liquids, the phosphonium ones are hydrolyzed with the subsequent destruction into the corresponding phosphine oxide and alkane under the reaction conditions.[144]



R^1 = Me, Et, Bu^n; R^2 = Me, Bn.

Due to the low reactivity of aryl halides in the Arbuzov and the Michaelis – Becker reactions, arylphosphonates are formed in low yields. As it is generally known, the reaction of aryl halides with dialkyl phosphites catalyzed by palladium complexes (the Hirao reaction) is the optimal method of their preparation.[145 – 147] The mechanism of this transformation is similar to other processes of cross-coupling that include oxidative addition, transmetallation and reductive elimination. In common organic solvents, such reaction goes under continuous heating (120 °C, 2.5 – 18 h), but the use of microwave radiation results in shorter reaction times.[148, 149] The yields of the products usually vary in the range of 74% – 90%, except for β-aryl-substituted steroids obtained by this method (yields 19% – 52%).

At the same time, the application of aqueous medium (*e.g.*, a 1 : 1 MeCN – H_2O mixture) [150] or just water as an only solvent (in the presence of water-soluble phosphine 3-$NaSO_3C_6H_4PPh_2$ or in the ligand-free variant) [151] makes it possible to considerably reduce the temperature and the reaction time, giving target products **25** in almost quantitative yields.

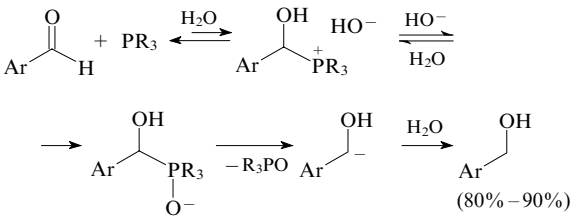


25 (95% – 97%)

X = I, Br; R = Me, Et.

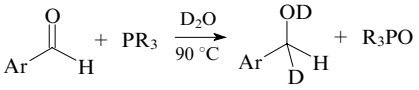
V. Reactions of phosphines with aldehydes

Moiseev and co-workers[152] have shown that the use of water as a solvent results in the change of the pathway of the reaction of phosphines with aldehydes. Thus, water-soluble tris(3-hydroxypropyl)phosphine (THPP) promotes base-catalyzed self-condensation of aliphatic aldehydes. At the same time the redox reaction of THPP and aromatic aldehydes containing such substituents as Hal, OMe, Me and OH at 90 °C under argon yields the corresponding benzyl alcohols and the phosphine oxidation product, *i.e.*, phosphine oxide.[152]

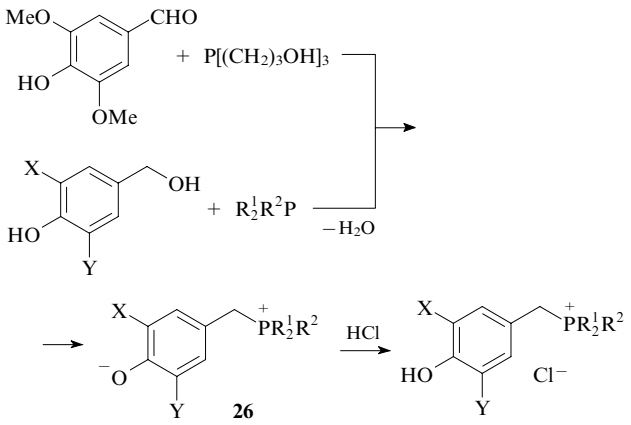


R = $(CH_2)_3OH$; Ar = Ph, 3,4-$(MeO)_2C_6H_3$, 3-HOC_6H_4, 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-$HalC_6H_4$ (Hal = Cl, Br, I), 2-MeC_6H_4.

In the first step, the reaction goes through the formation of phosphonium derivatives. That was proved by the isolation of a product containing the deuterium atom at the benzyl carbon atom in a model experiment in D_2O.

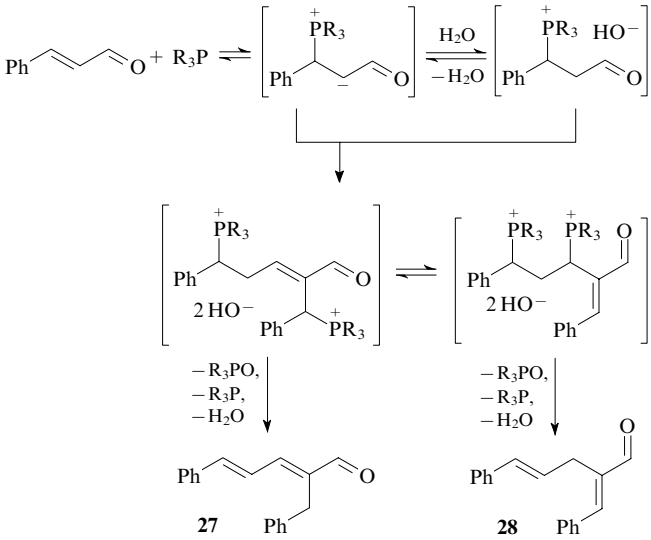


If a hydroxy group is present in the *para*-position of the starting aldehyde, then its reduction product, benzyl alcohol, reacts with phosphine more actively than the aldehyde, resulting in the formation of zwitter-ionic phosphobetaine **26**.[153] The interaction of equimolar amounts of phosphines with 4-hydroxybenzyl alcohols in water also yields phosphobetaines **26**. The latter transform under the action of dilute HCl into the corresponding phosphonium chlorides in high yields.[153] 2-Hydroxybenzyl alcohols also undergo similar reaction.



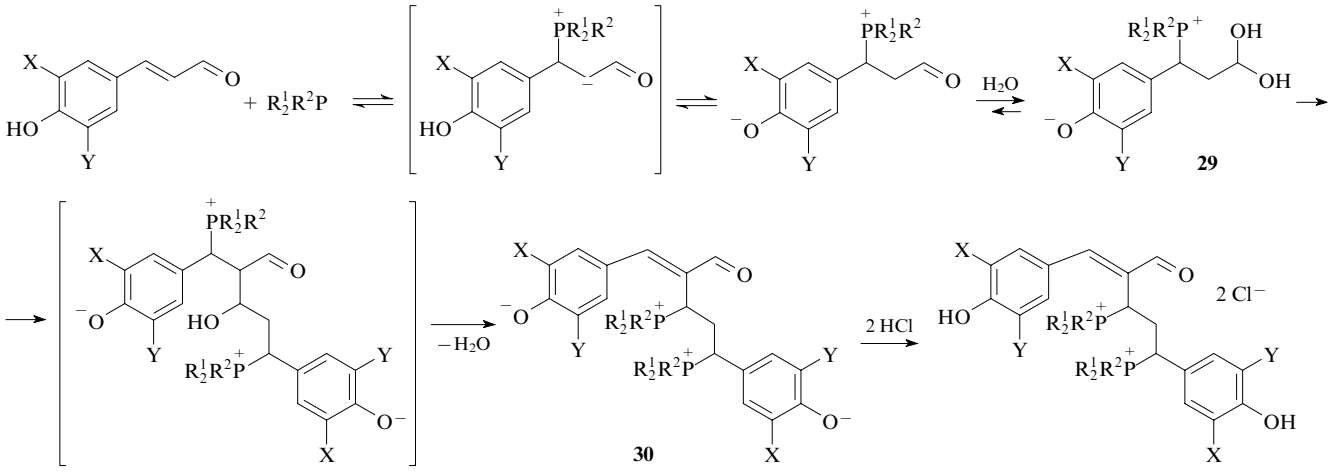
X, Y = H, OMe; R^1 = R^2 = Me, Et, Pr^n, Pr^i, $(CH_2)_3OH$; R^1 = Me, R^2 = Ph; R^1 = Ph, R^2 = Me.

The reaction of tris(3-hydroxypropyl)phosphine with cinnamaldehyde in water at room temperature also involves the formation of intermediate phosphonium salts. As a result, the formation of two isomeric products is observed, namely, 2-benzyl-5-phenylpenta-2,4-dienal (**27**) and 5-phenyl-2-(phenylmethylene)-4-pentenal (**28**). The formation of



R = $(CH_2)_3OH$.

Scheme 3



X, Y = H, OMe; R^1 = R^2 = Me, Et, Pr^n, Pr^i, cyclo-C_6H_{11}, $(CH_2)_3OH$, $(CH_2)_2CN$; R^1 = Me, R^2 = Ph; R^1 = Ph: R^2 = Me, 3-$NaSO_3C_6H_4$.

unstable intermediate salts has been confirmed by their stabilization with DCl.[154]

The reaction mechanism is general. A wide range of phosphines $R^1_2R^2P$ [$R^1 = R^2$ = Me, Et, Pr^i, cyclo-C_6H_{11}, $(CH_2)_3OH$, $(CH_2)_2CN$; R^2 = Ph: R^1 = Me, Et; R^1 = Ph: R^2 = Me, 3-$NaSO_3C_6H_4$] react with α,β-unsaturated hydroxy-substituted aromatic aldehydes in water at room temperature giving zwitter-ionic monophosphonium species **29**. In some cases [for $R^1 = R^2$ = Me, Et, $(CH_2)_3OH$; R^2 = Ph: R^1 = Me, Et], the zwitter-ions undergo self-condensation resulting in bisphosphonium derivatives **30**, which transfrom into the corresponding racemic dichloride salts under the action of HCl (Scheme 3).[155]

VI. Other types of organophosphorus reactions

Most of the other types of organophosphorus reactions for which ionic liquids or water may be used as activating media belong to the nucleophilic substitution or addition type. Often they proceed with the participation of peripheral functional groups of organophosphorus reagents.

In particular, ionic liquids have acquired the reputation of convenient media for the esterification of various acids including phosphonic and phosphinic ones, with trialkyl orthoacetates.[156] Among the tested ionic liquids, [bmim]PF_6 proved to be most active. In this medium, the target methyl and ethyl esters of carboxylic acids including sterically hindered and Cbz-substituted amino acids (Cbz is benzyloxycarbonyl), and also ethyl esters of sulfinic acids, phenols and thiols are obtained in high yields of 90% – 98% (80 °C, 1.5 – 5 h).

$$R^1CO_2H \xrightarrow[[bmim]PF_6,\ 80\ ^\circ C]{MeC(OR^2)_3} R^1CO_2R^2 \quad (90\% - 98\%)$$

R^1 = BnNHCH$_2$, Cbz-Trp, n-$C_8H_{17}CH{=}CH(CH_2)_7$, 1,3-ClC_6H_3, 2,4,6-$Me_3C_6H_2$, 3,4,5-$(MeO)_3C_6H_2$, 2-Naph, *etc.*;
R^2 = Me, Et; Trp is tryptophan.

In the case of phosphorus-based acids, the use of trimethyl orthoacetate provides the target methyl esters within 1 – 2 h in high yields (79% – 98%). When triethyl orthoacetate is used, the yields of corresponding esters go down.

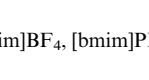
$$R^1{-}P(O)(OH){-}R^2 \xrightarrow[[bmim]PF_6,\ 80\ ^\circ C]{MeC(OMe)_3} R^1{-}P(O)(OMe){-}R^2 \quad (79\% - 98\%)$$

R^1 = Ph: R^2 = Bn, C(O)Bu^t, $(CH_2)_3CO_2Me$, OH; $R^1 = R^2$ = Bu^{n}O.

Direct amidation of phosphorylacetic acids easily takes place in imidazolium and phosphonium ionic liquids in the presence of triphenyl phosphite as an activating agent. This transformation provides the possibilities of synthesizing various carbamoylmethylphosphine oxides **31** from one organophosphorus substrate. The oxides **31** are efficient extractants of transplutonium elements.[157] It is supposed that the reaction goes through the formation of an intermediate phenyl phosphorylacetate, which contains a good leaving (phenoxy) group and transforms into the amide moiety under the action of N-nucleophile. Since all the phosphite bonds are reactive, 0.35 mole of $(PhO)_3P$ is enough for carrying out this reaction. In terms of the reaction rate, the ease of isolation of the target products and the cost of IL, the reaction media of choice are [bmim]Br and [$P(C_6H_{13}$-n$)_3(C_{14}H_{29}$-n)]Cl. It is possible to carry out the reaction both in ionic liquid as a single solvent and in two-phase system IL – dibutyl ether. The yields of target products do not decrease, and after the separation of the product with the ether layer, IL may be reused without loss of activity for at least 5 times.

$$R^1{-}P(O)(OH){-}R^2 \xrightarrow[110\ ^\circ C,\ 0.5-1\ h]{R^3R^4NH,\ (PhO)_3P,\ IL} R^1{-}P(O)(NR^3R^4){-}R^2$$

31

R^1, R^2 = AlkO, Alk, Ph; R^3, R^4 = H, Alk, Ar, $ArCH_2$; IL = [bmim]Br, [bmim]BF_4, [bmim]PF_6, [bmmim]BF_4 (bmmim = ), [(n-$C_8H_{17})_4P$]Br, [(n-$C_6H_{13})_3$(n-$C_{14}H_{29}$)P]Cl, [(n-$C_6H_{13})_3$(n-$C_{14}H_{29}$)P]BF_4.

The substitution of an amine group for the methoxy group in 2-methoxyethyltriphenylphosphonium bromide also easily occurs in aqueous solution, leading to 2-aminoethyl derivatives **32** in quantitative yields.[158] These compounds are used as intermediates for the synthesis of different pharmaceuticals such as acrivastine, pyrrobutamine, triprolidine and zimelidine. The presence of hydroxy groups in the starting amine has no influence on the reaction pathway or on the yields of the products. However, nucleophiles that are insoluble in water (*e.g.*, thiols and anilines) and α-amino acid esters do not enter into this reaction under these conditions.

$$MeO(CH_2)_3PPh_3^+\ Br^- + R^1R^2NH \xrightarrow[60\ ^\circ C,\ 2\ h]{H_2O} R^1R^2N(CH_2)_3PPh_3^+\ Br^-$$

32 (89% – 97%)

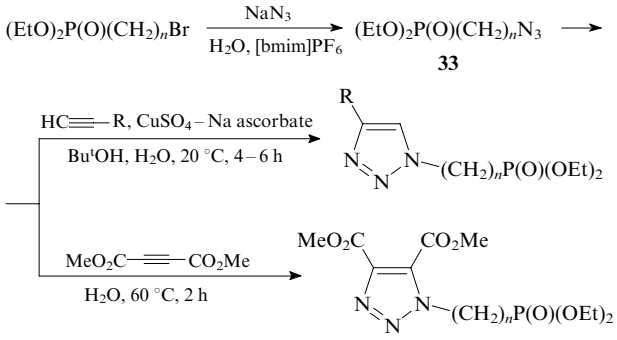
$R^1 = R^2$ = Me, Et, Pr^i, $(CH_2)_2OH$;
$R^1 - R^2$ = $(CH_2)_4$, $(CH_2)_2O(CH_2)_2$, $(CH_2)_5$.

A two-phase system based on hydrophobic ionic liquid [bmim]PF_6 and water proved to be an effective medium for the nucleophilic substitution of an azido group for the bromine in alkyl bromophosphonates.[159] The reaction proceeds at 20 °C or at higher temperature yielding 95% – 98% of target products **33** (purity > 95%). The ionic liquid may be used in the subsequent reactions for at least 5 times without loss of activity (Scheme 4).

The obtained ω-azidophosphonates **33** were used in the Cu^{I}-catalyzed 1,3-dipolar cycloaddition with both terminal[159] and internal[143] alkynes (so-called 'click' or CuAAC reaction[160 – 163]). In the former case, a mixture of *tert*-butyl alcohol with water proved to be the optimal reaction medium for generation of copper(I) *in situ* from a Cu^{II} compound; with dimethylacetylene dicarboxylate, the reaction proceeds at high rate in water in the absence of any co-solvents or catalysts.

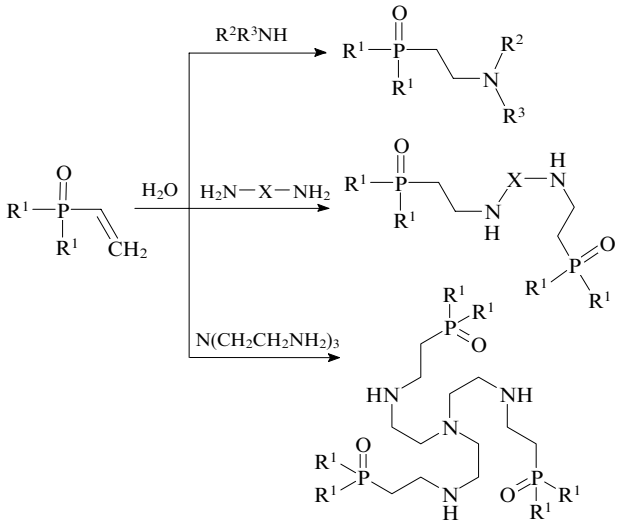
Water as a solvent also promotes significantly the addition of amines to vinylphosphoryl substrates leading to β-aminophosphoryl compounds. The latter may be of interest as biologically active compounds with wide range of activity,[79, 80] chelating agents[164, 165] or precursors of aminophosphine ligands.[166] This transformation proceeds under

Scheme 4



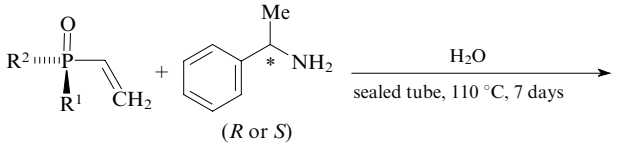
n = 2–4; R = Ph, Bu^n, CH_2NMe_2, $CH_2C(CO_2Me)(XH)CF_3$ (X = O, CbzN, $PhSO_2N$).

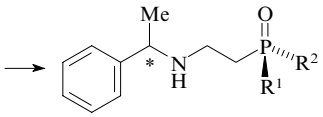
classical conditions on heating over a long period of time if the excess of amine or basic catalysts (metal Na, NaOH, *etc.*) is used. At the same time, in water equimolar amounts of reactants interact both in the case of water-soluble diethyl vinylphosphonate [167] and in the case of water-insoluble diphenylvinylphosphine oxide,[168] forming the corresponding derivatives of primary and secondary amines, including polyamines, in high yields.



R^1 = EtO, Ph; R^2 = H: R^3 = Bu^n, Bu^t, n-C_6H_{13}, n-C_8H_{17}, Bn, CHPhMe; R^2 = R^3 = Et, n-C_8H_{17}; R^2–R^3 = $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$, $(CH_2)_2C(O)(CH_2)_2$; X = $(CH_2)_2$, 4-$CH_2C_6H_4CH_2$.

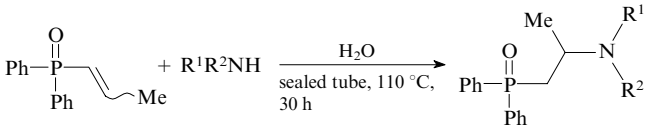
The reaction can be carried out at room temperature or on heating. The latter does not lead to any by-products and has no effect on the stereochemical outcome of the reaction if optically active amines are used; optically or diastereomerically pure phosphine oxides are formed in almost quantitative yields.[166]





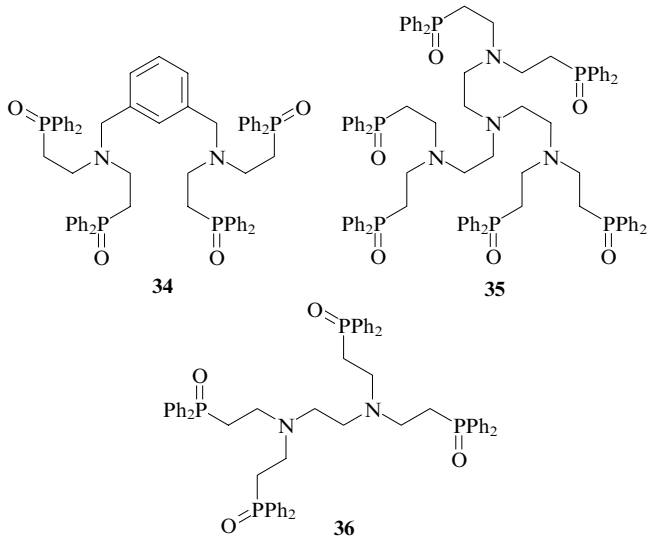
R^1 = Ph: R^2 = Ph, Bu^t; R^1 = Bu^t, R^2 = Ph.

Similarly, the addition of secondary amines to diphenylprop-1-enylphosphine oxide was performed in water at elevated temperature in a sealed tube.[169] The use of an excess of amine considerably complicates the procedure of purification of the final products.

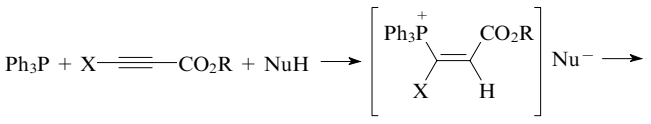


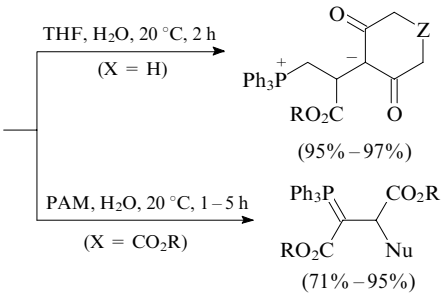
R^1 = R^2 = Me, Et; R^1–R^2 = $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$.

It should be noted that unlike the classical conditions, the use of water allows easy double phosphonoethylation of primary amines, thus opening the opportunities for the synthesis of oligodentate NP(O)-ligands of intricate structures, *e.g.*, compounds **34**–**36**.[167, 168]

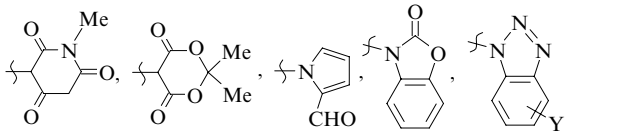


The conditions corresponding to the green chemistry principles have found application in the three-component reaction of triphenylphosphine, dialkyl acetylenedicarboxylates and various nucleophiles, which is an effective and well-proven method of preparation of functional stabilized phosphorus ylides.[170] In particular, the synthesis of P-ylides (more specifically, the corresponding zwitter-ionic salts) in the reaction with C-, N- and O-nucleophiles has been described. Such processes are carried out either in water as a single solvent in the presence of polyacrylamide (PAM),[171] β-cyclodextrin [172] or sodium dodecyl sulfate [173] (10 mol.%) as a catalyst or in a mixture of water and THF (1 : 1).[174, 175]



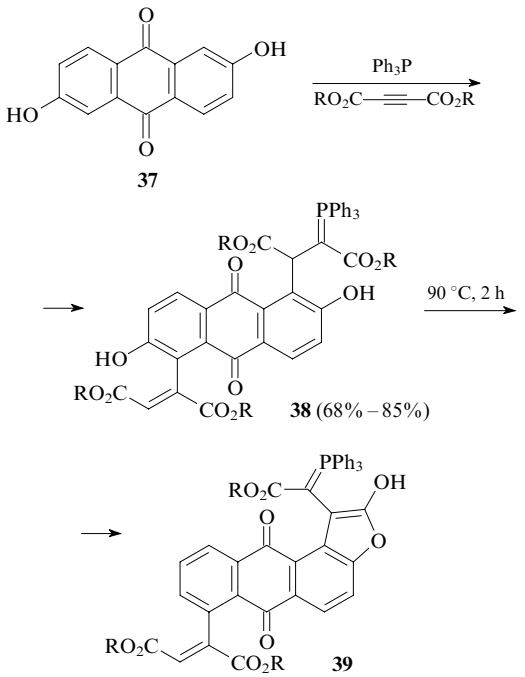


R = Me, Et, Pr^i, Bu^t; Z = CH_2, CMe_2;[174] Nu = $CH(CO_2Et)_2$, $CHAc_2$,



(Y = H, Cl, Me).[172]

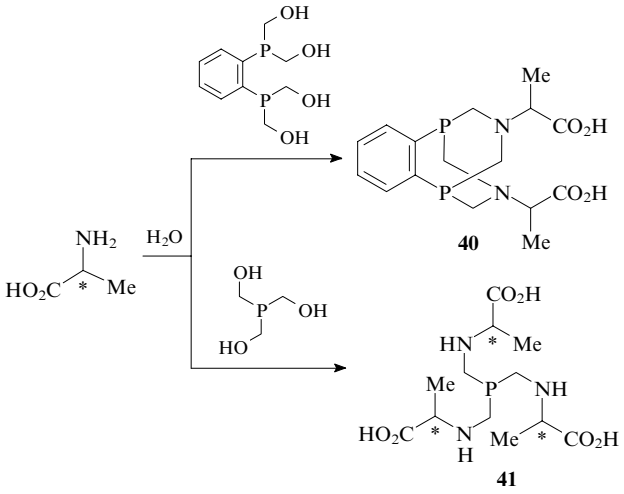
The reaction can also be carried out under solvent-free conditions.[176] Thus, in the case of di(OH)-nucleophile, *i.e.*, 2,6-dihydroxyanthraquinone (**37**), asymmetric phosphanylidene anthracenyl derivatives **38** were obtained in high yields at room temperature in the absence of solvent.



R = Me, Et, Pr^i, Bu^t.

Evidently, these products are formed upon elimination of triphenylphosphine from the precursory symmetric intermediate. In the absence of a solvent, compounds **38** also transform at 90 °C into phosphanylidene anthra[2,1-b]furans **39** due to the intramolecular attack of the phenol hydroxy group next to the phosphanylidene moiety.

An uncommon result in the synthesis of unnatural amino acids has been obtained *via* the interaction of bis- and tris(hydroxymethyl)phosphines with alanine (5 – 6-fold excess) in water (the Mannich reaction). In these transformations, peptide-like functionalized phosphines with cyclic (**40**)[177] and acyclic (**41**)[178] structures, respectively, are formed in high yields (> 90%).



VII. Conclusion

In spite of rather limited amount of literature data, the prospects of carrying out the reaction with the involvement of organophosphorus substrates or in the synthesis of organophosphorus compounds with practically valuable properties, using ionic liquids, water or in the absence of a solvent, are unquestionable for many transformations described above. Though in most cases the mechanism of promoting of most processes is only hypothetical it is obvious that the use of water (equally in the cases of reactions in water or 'on water') provides the previously unachievable result in terms of stereoselectivity of the processes and the yields of target products of the Wittig – Horner P=O olefination, for the preparation of β-aminophosphorus compounds and arylphosphonates, for the cycloaddition reactions of organophosphorus substrates. Besides high reaction rates and almost quantitative yields of products, note the low cost of this solvent in the combination with surprising simplicity and environmental safety of isolation procedures. In the preparation of α-aminophosphonates *via* the Kabachnik – Fields reaction when it is possible to use all of the above approaches, the synthesis under solvent-free conditions, in particular, with the use of γ-Fe_2O_3 nanoparticles encapsulated in hydroxyapatite, should be given special attention. Performing the reactions of nucleophilic substitution of peripheral functional groups in organophosphorus substrates in two-phase systems IL – water with possible recycling of more expensive IL also leads to a wide variety of possibilities. And, undoubtedly, it seemed important for us to attract researchers' attention to the opportunities of using green chemistry methods in the field of organophosphorus synthesis.

The review has been prepared with the financial support of the Council for Grants of the President of the Russian Federation for Support of Young Russian Scientists (Project MK-425.2010.3).

References

1. *Ionic Liquids: Industrial Applications for Green Chemistry (ACS Symp. Ser.)* Vol. 818 (Eds R D Rogers, K R Seddon) (Washington, DC: American Chemical Society, 2002)
2. N F Matsatsinis, R D Rogers, K R Seddon *Green Industrial Applications of Ionic Liquids* (Amsterdam: Springer, 2003)

3. *Ionic Liquids as Green Solvents: Progress and Prospects (ACS Symp. Ser.)* Vol. 856 (Eds R D Rogers, K R Seddon) (Washington, DC: American Chemical Society, 2003)
4. P Wasserscheid, T Welton *Ionic Liquids in Synthesis* (Weinheim: Wiley-VHC, 2003)
5. L A Aslanov, M A Zakharov, N L Abramycheva *Ionnye Zhidkosti v Ryadu Rastvoritelei* (Ionic Liquids in Solvent Rows) (Moscow: Moscow State University, 2005)
6. G Keglevich, Z Baan, Z Finta, I Hermecz, T Novak, I L Odinets *Curr. Org. Chem.* **11** 107 (2007)
7. J P Hallett, T Welton *Chem. Rev.* **111** 3508 (2011)
8. P A Grieco *Organic Synthesis in Water* (London: Blackie Academic, 1998)
9. C-J Li, T-H Chan *Comprehensive Organic Reactions in Aqueous Media* (New York: Wiley, 2007)
10. C-J Li *Chem. Rev.* **105** 3095 (2005)
11. J M Desimone, W Tumas *Green Chemistry Using Liquid and Supercritical Carbon Dioxide* (New York: McGraw Hill, 2003)
12. F M Kerton *Alternative Solvents for Green Chemistry* (Cambridge: Royal Society of Chemistry, 2009)
13. N V Plechkova, K R Seddon *Chem. Soc. Rev.* **37** 123 (2008)
14. S Narayan, J Muldoon, M G Finn, V V Fokin, H C Kolb, K B Sharpless *Angew. Chem., Int. Ed.* **44** 3275 (2005)
15. A Chanda, V V Fokin *Chem. Rev.* **109** 725 (2009)
16. C Aymonier, A Loppinet-Serani, H Reveron, Y Garrabos, F Cancell *J. Supercrit. Fluids* **38** 242 (2006)
17. H Olivier-Boubigou, L Magna, D Morvan *Appl. Catal., A* **373** 1 (2010)
18. H Mizuuchi, V Jaitely, S Murdan, A T Florence *Eur. J. Pharm. Sci.* **33** 326 (2008)
19. J J Tindale, P J Ragogna *Chem. Commun.* 1831 (2009)
20. D A Lemenovskii, G P Brusova, V V Timofeev, S A Yurin, V N Bagratashvili, V K Popov *Priroda* (6) 42 (2006)
21. M I Kabachnik, T A Mastryukova *Mezhfaznyi Kataliz v Fosfororganicheskoi Khimii* (Phase Transfer Catalysis in Organophosphorus Chemistry) (Moscow: URSS, 2002)
22. M Albrycht, P Kielbasinski, J Drabowich, M Mikolajczyk, T Marsuda, T Harada, K Nakamura *Tetrahedron: Asymmetry* **16** 2015 (2005)
23. R Appel, R Loos, H Mayr *J. Am. Chem. Soc.* **131** 704 (2009)
24. Y Kiyotsuka, Y Katayama, H P Acharya, T Hyodo, Y Kobayashi *J. Org. Chem.* **74** 1939 (2009).
25. G Fodor, I Tomoskozi *Tetrahedron Lett.* **2** 579 (1961)
26. A Nonnenmacher, R Mayer, H Plieninger *Liebigs Ann. Chem.* 2135 (1983)
27. N S Isaacs, G N El-Din *Tetrahedron Lett.* **28** 2191 (1987)
28. H O House, V K Jones, G A Frank *J. Org. Chem.* **29** 3327 (1964)
29. D L Hooper, S Garagan, M M Kayser *J. Org. Chem.* **59** 1126 (1994)
30. G Westman, O Wennerström, I Raston *Tetrahedron* **49** 483 (1993)
31. S Fliszar, R F Hudson, G Salvadori *Helv. Chim. Acta* **47** 159 (1964)
32. C Ruchardt, P Panse, S Eichler *Chem. Ber.* **100** 1144 (1967)
33. E J Corey, D A Clark, G Goto, A Marfat, C Mioskowski, B Samuelsson, S Hammarstrom *J. Am. Chem. Soc.* **102** 1436 (1980)
34. D P Marriott, J R Bantick *Tetrahedron Lett.* **22** 3657 (1981)
35. T Thiemann, C Thiemann, S Sasaki, V Vill, S Mataka, M Tashiro *J. Chem. Res., Synop.* 248 (1997)
36. C C Silveira, G Perin, A L Braga *J. Chem. Res., Synop.* 92 (1994)
37. J K Matikainen, S Kaltia, T Hase *Synlett* 817 (1994)
38. C Xu, G Chen, C Fu, X Huang *Synth. Commun.* **25** 2229 (1995)
39. A Spinella, T Fortunati, A Soriente *Synlett* 93 (1997)
40. J Wesman *Org. Lett.* **3** 3745 (2001)
41. J Wu, H Wu, S Wei, W-M Dai *Tetrahedron Lett.* **45** 4401 (2004)
42. J Wu, L Sun, W-M Dai *Tetrahedron* **62** 8360 (2006)
43. J A Stafford, J E McMurry *Tetrahedron Lett.* **29** 2531 (1988)
44. J-J Hwang, R-L Lin, R-L Shieh, J-J Jwo *J. Mol. Catal. A* **142** 125 (1999)
45. V P Balema, J W Wiench, M Pruski, V K Pecharsky *J. Am. Chem. Soc.* **124** 6244 (2002)
46. Z E Martin, C Kellen-Yuen *J. Chem. Educ.* **84** 2004 (2007)
47. V Le Boulaire, R Gree *Chem. Commun.* 2195 (2000)
48. H Valizadeh, S Vaghefi *Synth. Commun.* **39** 1666 (2009)
49. M Butcher, R J Mathews, S Middleton *Aust. J. Chem.* **26** 2067 (1973)
50. R Broos, M Anteunis *Synth. Commun.* **6** 53 (1976)
51. R Broos, D Tavernier, M Anteunis *J. Chem. Educ.* **55** 813 (1978)
52. F Sieber, P Wentworth Jr, J D Toker, A D Wentworth, W A Metz, N N Reed, K D Janda *J. Org. Chem.* **64** 5188 (1999)
53. M G Russel, S Warren *J. Chem. Soc., Perkin Trans. 1* 505 (2000)
54. J Wu, D Li, D Zhang *Synth. Commun.* **35** 2543 (2005)
55. J Wu, D Zhang, S Wei *Synth. Commun.* **35** 1213 (2005)
56. J Wu, C Yue *Synth. Commun.* **36** 2939 (2006)
57. S Tiwari, A Kumar *Chem. Commun.* 4445 (2008)
58. F Orsini, G Sello, T Fumagatti *Synlett* 1717 (2006)
59. J Dambacher, W Zhao, A El-Batta, R Anness, C Jiang, M Bergdahl *Tetrahedron Lett.* **46** 4473 (2005)
60. A El-Batta, C Jiang, W Zhao, R Anness, A L Cooksy, M Bergdahl *J. Org. Chem.* **72** 5244 (2007)
61. G A Molander, R A Oliveira *Tetrahedron Lett.* **49** 1266 (2008)
62. J McNulty, P Das *Tetrahedron Lett.* **50** 5737 (2009)
63. J McNulty, P Das *Eur. J. Org. Chem.* 4031 (2009)
64. J McNulty, P Das, D McLeod *Chem. – Eur. J.* **16** 6756 (2010)
65. E Ramirez, M Sanchez, R L Meza-León, L Quintero, F Sartillo-Piscil *Tetrahedron Lett.* **51** 2178 (2010)
66. Z J Gartner, M W Kanan, D R Liu *Angew. Chem., Int. Ed.* **41** 1796 (2002)
67. S Wu, H Ma, Z Lei *Tetrahedron* **66** 8641 (2010)
68. G V Kryshtal, G M Zhdankina, S G Zlotin *Mendeleev Commun.* 176 (2002)
69. H Valizadeh, A Shockravi *Synth. Commun.* **39** 4341 (2009)
70. T Kitazume, G J Tanaka *J. Fluorine Chem.* **106** 211 (2000)
71. J Villeras, M Rambaud *Synthesis* 300 (1983)
72. J Villeras, M Rambaud, M Graff *Tetrahedron Lett.* **26** 53 (1985)
73. M Rambaud, A del Vecchio, J Villeras *Synth. Commun.* **14** 833 (1984)
74. M Schimtt, J J Bourguignon, C G Wermuth *Tetrahedron Lett.* **31** 2145 (1990)
75. H J M Gijsen, C-H Wong *Tetrahedron Lett.* **36** 7057 (1995)
76. E Quesada, R J K Taylor *Synthesis* 3193 (2005)
77. K Ando, K Yamada *Tetrahedron Lett.* **51** 3297 (2010)
78. A Baron, J Martinez, F Lamaty *Tetrahedron Lett.* **51** 6246 (2010)
79. V P Kukhar, H R Hudson *Aminophosphonic and Aminophosphinic Acids* (Chichester: Wiley, 2000)
80. B Lejczak, P Kafarski, in *Phosphorus Heterocycles I (Topics in Heterocyclic Chemistry)* (Ed. R K Bansal) (Berlin, Heidelberg: Springer, 2009) Vol. 20, p. 31
81. F R Atherton, C H Hassal, R W Lambert *J. Med. Chem.* **29** 29 (1986)
82. S De Lombaert, L Blanchard, T Tan, Y Sakane, C Berry, R D Ghai Bioorg *Med. Chem. Lett.* **5** 145 (1995)
83. P Kafarski, B Lejczak *Curr. Med. Chem.* **1** 301 (2001)
84. WO 2007045496 (2007); *Chem. Abstr.* **136** 35625 (2007)
85. J Emsley, D Hall *The Chemistry of Phosphorus* (London: Harper and Row, 1976)
86. Edg Alonso, Edu Alonso, A Solis, C del Pozo *Synlett* 698 (2000)
87. J M Vila, M Gayoso, M Lopes Torres, J Fernandez, A Fernandez, J M Ortigueira, N A Bailey, H Adams *J. Organomet. Chem.* **511** 129 (1996)
88. P Diner, M Amedjkouh *Org. Biomol. Chem.* **4** 2091 (2006)
89. R A Cherkasov, V I Galkin *Russ. Chem. Rev.* **67** 857 (1998); [*Usp. Khim.* **67** 940 (1998)]
90. S Laschat, H Kunz *Synthesis* 90 (1992)
91. I L Odinets, O I Artyushin, N Shevchenko, P V Petrovskii, V G Nenajdenko, G-V Roschenthaler *Synthesis* 577 (2009)
92. I L Odinets, O I Artyushin, N Shevchenko, P V Petrovskii, V G Nenajdenko, G-V Roschenthaler *J. Fluorine Chem.* **130** 662 (2009)
93. J Zon *Pol. J. Chem.* **55** 643 (1981)
94. C Qian, T Huang *J. Org. Chem.* **63** 4125 (1998)
95. S-g Lee, J H Park, J Kang, J K Lee *Chem. Commun.* 1698 (2001)

96. S-g Lee, J K Lee, C E Song, D-C Kim *Bull. Korean Chem. Soc*. **23** 667 (2002)
97. J S Yadav, B V S Reddy, P Sreedhar *Green Chem*. **4** 436 (2002)
98. S Bai, B Song, P S Bhadury, S Yang, D Hu, W Xue *Chin. J. Chem*. **29** 109 (2011)
99. S Sobhani, E Safaei, M Asadi, F Jalili *J. Organomet. Chem*. **693** 3313 (2008)
100. B Kaboudin, M Sorbiun *Tetrahedron Lett*. **48** 9015 (2007)
101. L Jin, B Song, G Zhang, R Xu, S Zhang, X Gao, D Hu, S Yang *Bioorg. Med. Chem. Lett*. **16** 1537 (2006)
102. S A Sadaphal, S S Sonar, A H Kategaonkar, M S Shingare *Bull. Korean Chem. Soc*. **30** 1054 (2009)
103. D Fang, C Jiao, C Ni *Heteroat. Chem*. **21** 546 (2010)
104. K Manabe, S Kobayashi *Chem. Commun*. 669 (2000)
105. J Akbari, A Heydari *Tetrahedron Lett*. **50** 4236 (2009)
106. D Fang, J Yang, C Ni *Heteroat. Chem*. **22** 5 (2011)
107. B Das, G Satyalakshmi, K Suneel, K Damodar *J. Org. Chem*. **74** 8400 (2009)
108. K Moedritzer, R R Irani *J. Org. Chem*. **31** 1603 (1966)
109. P Wareing *Agric. Prog*. **55** 5 (1980)
110. L Maier *Phosphorus, Sulfur, Silicon Relat. Elem*. **61** 69 (1991)
111. D Villemin, B Moreau, A Elbilali, M-A Didi, M Kaid, P-A Jaffres *Phosphorus, Sulfur, Silicon Relat. Elem*. **185** 2511 (2010)
112. S Bhagat, A K Chakraborti *J. Org. Chem*. **73** 6029 (2008)
113. T Akiyama, M Sanada, K Fuchibe *Synlett* 1463 (2003)
114. S D Mitragotri, D M Pore, U V Desai, P P Wadgaonkar *Catal. Commun*. **9** 1822 (2008)
115. H Firiuzabadi, N Iranpoor, S Sobhani *Synthesis* 2692 (2004)
116. A K Bhattacharya, T Kaur *Synlett* 745 (2007)
117. S Bhagat, A K Chakraborti *J. Org. Chem*. **72** 1263 (2007)
118. M Zahouily, A Elmakssoudi, A Mezdar, A Rayadh, S Sebti *Catal. Commun*. **8** 225 (2007)
119. M Hosseini-Sarvari *Tetrahedron* **64** 5459 (2008)
120. S S Sonar, K F Shelke, G K Kakade, B B Shingate, M S Shingare *Chin. Chem. Lett*. **20** 1042 (2009)
121. M T Maghsoodlou, S M Habibi-Khorassani, R Heydari, N Hazeri, S S Sajadikhah, M Rostamizadeh *Chin. J. Chem*. **28** 285 (2010)
122. M T Maghsoodlou, S M Habibi-Khorassani, R Heydari, N Hazeri, S S Sajadikhan, M Rostamizadeh *Arab. J. Chem*. **4** 481 (2011)
123. B V S Reddy, A S Krishna, A V Ganesh, G G K S N Kumar *Tetrahedron Lett*. **52** 1359 (2011)
124. M Sheykhan, L Ma'mani, A Ebrahimi, A Heydari *J. Mol. Catal. A* **335** 253 (2011)
125. A Elmakssoudi, M Zahouily, A Mezdar, A Rayadh, S Sebti *C. R. Chimie* **8** 1954 (2005)
126. R G Noronha, C C Romao, A C Fernandes *Catal. Commun*. **12** 337 (2011)
127. N Azizi, F Rajabi, M R Saidi *Tetrahedron Lett*. **45** 9233 (2004)
128. S Sobhani, Z Tasrifi *Heteroat. Chem*. **20** 109 (2009)
129. Z-P Zhan, R-F Yang, J-P Li *Chem. Lett*. **34** 1042 (2005)
130. L S Yadav, B V Subba Reddy, C Madan *Synlett* 1131 (2001)
131. A Bhattacharya, K C Rana *Tetrahedron Lett*. **49** 2598 (2008)
132. B Kaboudin, R Nazari *Tetrahedron Lett*. **42** 8211 (2001)
133. Y Xu, K Yan, B Song, G Xu, S Yang, W Xue, D Hu, P Lu, G Ouyang, L Jin, Z Chen *Molecules* **11** 666 (2006)
134. G Keglevich, A Szekrenyi *Lett. Org. Chem*. **5** 616 (2008)
135. M M Kabachnik, E V Zobnina, I P Beletskaya *Synlett* 1393 (2005)
136. M M Kabachnik, E V Villemson, I P Beletskaya *Zh. Org. Khim*. **44** 1605 (2008) [a]
137. M Xia, Y-D Lu *Ultrason. Sonochem*. **14** 235 (2007)
138. S Chandrasekhar, C Narsihmulu, S S Sultana, B Saritha, J S Prakash *Synlett* 505 (2003)
139. G D Tibhe, S Lagunas-Rivera, E Vargas-Diaz, O Garcia-Barradas, M Ordonez *Eur. J. Org. Chem*. 6573 (2010)
140. E V Matveeva, I L Odinets, V A Kozlov, A S Shaplov, T A Mastryukova *Tetrahedron Lett*. **47** 7645 (2006)
141. WO 2003062251 (2003); *Chem. Abstr*. **139** 149757 (2003)
142. E V Matveeva, V A Kozlov, I L Odinets *Mendeleev Commun*. **20** 145 (2010)
143. I L Odinets, E V Matveeva, E V Sharova, O I Artyushin, V A Kozlov, D V Vorob'eva, S N Osipov, T A Mastryukova, G-V Roschenthaler *Phosphorus, Sulfur, Silicon Relat. Elem*. **183** 383 (2008)
144. A P Vu, E A Shaffer, L K B Congiardo, D A Knight *Phosphorus, Sulfur, Silicon Relat. Elem*. **185** 1845 (2010)
145. T Hirao, T Masunaga, Y Ohshiro, T Agawa *Tetrahedron Lett*. **21** 3595 (1980)
146. T Hirao, T Masunaga, N Yamada, Y Ohshiro, T Agawa *Bull. Chem. Soc. Jpn*. **55** 909 (1982)
147. T Hirao, T Masunaga, Y Ohshiro, T Agawa *Synthesis* 56 (1981)
148. M Kalek, A Ziadi, J Stawinski *Org. Lett*. **10** 4637 (2008)
149. W Jiang, G Allan, J J Fiordeliso, O Linton, P Tannenbaum, J Xu, P Zhu, J Gunnet, K Demarest, S Lundeen, Z Sui *Bioorg. Med. Chem*. **14** 6726 (2006)
150. A Casalnuoro, J Calabrese *J. Am. Chem. Soc*. **112** 4324 (1990)
151. I P Beletskaya, M M Kabachnik, M D Solntseva *Zh. Org. Khim*. **35** 79 (1999) [a]
152. D V Moiseev, B R James, T Q Hu *Inorg. Chem*. **45** 10338 (2006)
153. D V Moiseev, B O Patric, B R James *Inorg. Chem*. **48** 239 (2009)
154. D V Moiseev, B R James, T Q Hu *Inorg. Chem*. **46** 4704 (2007)
155. D V Moiseev, B O Patric, B R James, T Q Hu *Inorg. Chem*. **46** 9389 (2007)
156. T Yoshino, S Imori, H Togo *Tetrahedron* **62** 1309 (2006)
157. E V Sharova, O I Artyushin, A S Shaplov, G V Myasoedova, I L Odinets *Tetrahedron Lett*. **49** 1641 (2008)
158. G V Rao, G C Reddy *Tetrahedron Lett*. **49** 824 (2008)
159. O I Artyushin, D V Vorob'eva, T P Vasil'eva, S N Osipov, G-V Roschenthaler, I L Odinets *Heteroat. Chem*. **19** 293 (2008)
160. M Meldal, C W Tornoe *Chem. Rev*. **108** 2952 (2008)
161. G C Tron, T Pirali, R A Billington, P L Canonico, G Sorba, A A Genazzani *Med. Res. Rev*. **28** 278 (2008)
162. C Mamat *Mini-Rev. Org. Chem*. **6** 21 (2009)
163. H Struthers, T L Mindt, R Schibli *Dalton Trans*. **39** 675 (2010)
164. F Palacios, C Alonso, J M de los Santos *Chem. Rev*. **105** 899 (2005)
165. E Gumienna-Kontecka, J Galezowska, M Drag, R Latajka, P Kafarski, H Kozlowski *Inorg. Chim. Acta* **357** 1632 (2004)
166. A M Maj, K M Pietrusiewich, I Suisse, F Agbossou, A Morteux *Tetrahedron: Asymmetry* **10** 831 (1999)
167. E V Matveeva, P V Petrovskii, I L Odinets *Tetrahedron Lett*. **49** 6129 (2008)
168. E V Matveeva, P V Petrovskii, Z S Klemenkova, N A Bondarenko, I L Odinets *C. R. Chimie* **13** 864 (2010)
169. D J Collins, S-A Mollard, N Rose, J M Swan *Aust. J. Chem*. **27** 2365 (1974)
170. A Ramazani, A R Kazemizadeh, E Ahmadi, N Noshiranzadeh, A Souldozi *Curr. Org. Chem*. **12** 59 (2008)
171. R Heydari, M T Maghsoodlou, R N Yami *Phosphorus, Sulfur, Silicon Relat. Elem*. **183** 2578 (2008)
172. M R Islami, I Yavari, A M Tikdari, L Ebrahimi, S Razee, H R Bijanzadeh *Izv. Akad. Nauk, Ser. Khim*. 2084 (2002) [b]
173. R Heydari, M T Maghsoodlou, S M Habibi-khorassani, N Hazeri, F Barahuie, M Rostamizadeh *Arab. J. Chem*. **3** 229 (2010)
174. F Nasiri, M Bidar *Phosphorus, Sulfur, Silicon Relat. Elem*. **183** 1344 (2008)
175. M R Islami, Z Hassani, H Sheibani *Phosphorus, Sulfur, Silicon Relat. Elem*. **177** 2547 (2002)
176. F Nourmohammadian, M D Gholami *Phosphorus, Sulfur, Silicon Relat. Elem*. **185** 340 (2010)
177. D E Berning, K V Katti, C L Barnes, W A Volkert *J. Am. Chem. Soc*. **121** 1658 (1999)
178. K V Katti, R Kannan, K K Katti, N Pillarsetty, C L Barnesb *Phosphorus, Sulfur, Silicon Relat. Elem*. **177** 1587 (2002)

[a] — *Russ. J. Org. Chem. (Engl. Transl.)*
[b] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*