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The Kabachnik – Fields reaction: synthetic potential and the problem of the mechanism †

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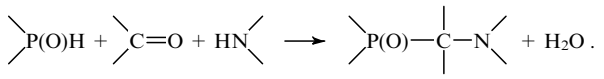
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Abstract. The published data of the last decade concerning the mechanism of the Kabachnik – Fields reaction and its significance for the chemistry of organophosphorus compounds as a method for the synthesis of α-amino phosphonates and their numerous functionally substituted derivatives and analogues, such as phosphinates and phosphine oxides, are generalised and systematised. The review discusses the classical version of the Kabachnik – Fields reaction, its modifications with the use of phosphorus chlorides, neutral esters and inorganic phosphorus acids, as well as chemical processes simulating separate steps of the reaction, *viz*., hydrophosphorylation of imines and amination of α-hydroxy phosphonates. Data on the practical application of α-amino phosphonates are presented. The bibliography includes 253 references.

I. Introduction

The Kabachnik – Fields reaction corresponds to the classical methods for the synthesis of organophosphorus compounds. It was discovered in 1952 independently by Kabachnik and Medved'[1] and Fields.[2] The reaction occurs in a three-component system consisting of a hydrophosphoryl compound, a carbonyl compound (aldehyde or ketone), and an amine and results in α-aminoalkylphosphonates commonly named as α-amino phosphonates (AP).



During the subsequent two or three decades, no intense studies in this field were carried out. However, after the discovery in the late 1960's that AP possess practically useful properties, mainly biological activity (see Ref. 3 and references cited therein), and isolation of phosphorus-containing amino acids from natural sources,[4] the areas of chemistry, biology and medicine related to the synthesis and study of the properties of AP show a real renaissance. As a confirmation it can be noted that more than 5000 studies on this topic had been published by 1993.[5] By now, this number has increased greatly. The prospects of using AP in various areas of science and engineering stimulated the development of new ways for the synthesis of AP, including polyfunctional ones. However, in our opinion, none of numerous approaches to the synthesis of AP is as general as the Kabachnik – Fields reaction.

However, no generally accepted viewpoint on the mechanism of this reaction has been developed until recently. The data concerning this matter were isolated and often contradictory. Only in recent years have kinetic and other special studies aimed at a deep study of the Kabachnik – Fields reaction and the establishment of its mechanism been carried out. As a result, the contradictions were resolved to a considerable extent; however, the reviews generalising and analysing these studies are lacking.

On the contrary, the synthetic aspects of the Kabachnik – Fields reaction have been developed rather widely and discussed in monographs[6 – 12] and reviews.[13 – 19] However, new and important results that deserve thorough consideration have also been obtained in this area during the last five years.

The purpose of the present review is to systematise, analyse and generalise the data published basically in the 1990's and related to the study of the mechanism of the Kabachnik – Fields reaction and its use for the synthesis of AP. Earlier publications will be cited only to the extent required for the understanding of the essence of the problems under discussion. In order to rank the Kabachnik – Fields reaction, estimate its significance among numerous other methods for the synthesis of AP and reveal its synthetic potential, we considered it necessary to present data on the basic methods for the synthesis of AP. Due to the abundance of data in this field, the topic is inevitably covered superficially, and we confine ourselves to the analysis of only the latest publications. Whenever necessary we have to refer the reader to the literature cited in these papers.

Chemical processes that simulate separate steps of this reaction and its versions and involve other derivatives of three-coordinate phosphorus, such as neutral esters, chlorides, inorganic acids and their silyl derivatives instead of hydrophosphoryl compounds, are discussed in more detail. We believe that the reactions of the silyl derivatives with carbonyl compounds and amines or amides in a three-component system may also be rightfully attributed to reactions of the Kabachnik – Fields reaction type. As will be shown below, reactions of P(III) derivatives often produce hydrophosphoryl compounds that react exactly in the same way as those in the 'classical' system.

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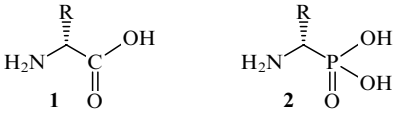
† The review is devoted to the memory of Academician M I Kabachnik (1908 – 1997).

Special attention is given to the hydrophosphorylation of imines. On the one hand, this represents one of the steps of the Kabachnik – Fields reaction and, on the other hand, a version of the Pudovik reaction, which was described in 1952[20] almost simultaneously with the pioneer research by Kabachnik and Medved' (and published in the same volume of *Doklady Chemistry*). In addition, we found it necessary to present brief information on the main areas where AP are used.

II. Application areas and principal methods for the synthesis of α-amino phosphonates

1. Application areas of α-amino phosphonates

It is believed[3] that aminomethylphosphonic acid was first mentioned in the literature in 1943.[21] Being structural analogues of α-aminocarboxylic acids **1**, α-aminoalkylphosphonic acids **2** (APA) possess diverse biological activities. For this reason, they attract steady attention of chemists, biologists, pharmacologists, physicians and other specialists who study biologically active compounds.[3, 11, 16, 18, 22, 23] Organophosphorus analogues of almost all proteinogenic amino acids have been synthesised. APA isostructural to tyrosine have been isolated from natural sources (see Ref. 24 and references cited therein).



1 **2**

APA resulting from replacement of the carboxy groups in 'normal' amino acids by the phosphonate groups inhibit the enzymes or receptors to which natural amino acids normally bind. Therefore, APA are their antagonists (see Refs 3, 25 and references cited therein). The inhibitory action of APA predetermines their physiological activity as antibacterials, neuroactive agents, antibiotics, carcinostatic, cytotoxic and other compounds of pharmacological importance.[3]

Much attention is given to the use of AP (the acids themselves, *i.e.*, APA, their mono- and diesters and some other derivatives) in peptide synthesis.[3, 26–31] Phosphonopeptides represent models of the tetrahedral transition states (activated complexes) in the hydrolysis of natural peptides.[32–34] In addition, they exhibit diverse and rather high physiological activities, such as pesticide,[35] fungicide[36] and growth-controlling[37] ones. Phosphonopeptides are inhibitors of thrombin[38] and pepsin[39] and are used as haptens of antigens affecting the production of antibodies.[40] They also manifest other kinds of physiological activities.[3]

Numerous studies have been devoted to the synthesis and study of APA possessing herbicidal properties. Of these, *N*-(phosphonomethyl)glycine, $^{-}HO_3PCH_2N^{+}H_2CH_2COOH$ is known under the trade name glyphosate and used most widely (see Ref. 41 and references cited therein). Its numerous analogues have also been obtained.[42]

A series of studies[43–45] have dealt with the development of methods for the synthesis of α-aminofluorenylphosphonates, -phosphinates and -phosphine oxides. As structural analogues of a synthetic phytohormone morfactin, they represent an interesting class of plant growth regulators and herbicides. Wide prospects of practical application of this type of AP stimulated in-depth spectroscopic studies of their structures.[45] Attempts at establishment of quantitative structure–biological activity relationships were also made.[46] It should be noted that the relation between the structure of a number of neutral AP and their antimicrobial[47] and fungicide[48] activities is well described by correlation equations.

Although the biological activity is certainly a very valuable and the most attractive property of AP, this by no means confines the prospects of their practical use. APA themselves, as well as their derivatives and analogues, correspond to polyfunctional organophosphorus compounds. They can form complexes, in which they act as mono-, bi- and polydentate ligands.[49] The electron-donating atoms of nitrogen and phosphoryl oxygen serve as coordination centres, the acid groups of APA form the corresponding salts, and the suitable functional groups specially introduced to nitrogen and phosphorus atoms and α-carbon atoms can provide additional bonding to metal ions. The same properties are used as a stereocontrolling factor in enantioselective synthesis of AP (see below).

Kabachnik was one of the first to study the complexing properties of AP,[50–52] using linear and cyclic (cyclopendant) AP as the complexones. Recently, the first X-ray characteristics of an AP metallocomplex, *viz.*, a coordination compound of Cu(II) with *O*-ethyl hydrogen α-(2-pyridyl)-*N*-isopropylaminomethylphosphonate, have been obtained.[53] Complexes of chromium with fluorenylphosphonates have been synthesised.[54] In recent years, complexes of AP with lanthanides and actinides have been proposed for diagnostics with the use of the NMR technique.[55, 56]

Extraction processes involving AP have been studied. It was shown that APA can be used in hydrometallurgy.[57] Processes for gold extraction with neutral AP and efficient separation of Au(III) from the commonly accompanying ions, Fe(III) and Cu(II),[58] as well as extraction of Pd(II) in strongly acidic media have been reported.[59] The acid – base properties of *O*,*O*-dialkyl *N*,*N*-dialkylaminoalkylphosphonates have been studied. As expected, they appeared to be weaker bases than amino acids. The pK_{BH} values (in aqueous propan-2-ol) are 9.2 – 9.7, whereas pK_{BH} of histamine is ~5. Substituents at the α-carbon atom and nitrogen do not affect essentially the AP basicity.

Due to the ability of AP to complexation, they can serve as carriers for α-hydroxy and α-amino acids through lipophilic liquid membranes,[60] which is a new promising direction for their utilisation. *N*-Bornyl-AP,[61] (*d*)-*N*-α-methylbenzyl-AP and other linear and cyclic AP,[62, 63] as well as calix[4]arenes with α-amino phosphonate fragments in the bottom and top rings were chosen for molecular recognition of substrates.[64] Generally, the latter derivatives appeared to be more efficient transport agents than their acyclic analogues. The flux of α-hydroxy acids is most strongly affected by the nature of substituents at the α-carbon atom in AP. It is remarkable that the AP studied can also be used for the separation of D- and L-forms of α-hydroxy and α-amino acids.[60]

The results of these studies are in good agreement with the data obtained in a study of the thermochemistry of AP.[65–67] Specific features of dissolution of neutral AP in solvents of various nature (hexane, CCl_4, $CHCl_3$) characterise these compounds as distinct proton acceptors. However, with respect to sufficiently strong bases, for example, pyridine, AP behave as proton donors. Calculations of the enthalpy of solvation showed the predominant effect of steric factors of the substituents on the liability to biphilic reactions of this kind.[68]

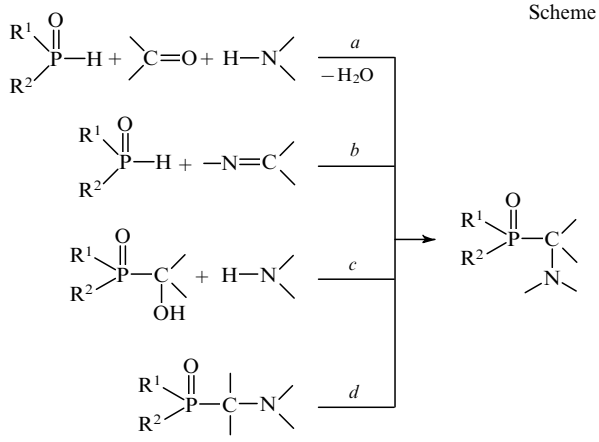
Finally, it is worthy of mentioning that analytical methods for the determination of enzyme inhibitors, including APA esters, have been developed.[69]

2. Principal methods for the synthesis of α-amino phosphonates

No simple and versatile methods for the synthesis of AP existed before the discovery of the Kabachnik – Fields reaction. Single attempts at the preparation of AP mentioned in the early studies[1–3, 70, 71] did not satisfy the researchers because of multistep syntheses and low efficiency. The credit for the intense progress in studies on the chemistry and biology of AP in the last decade should be given to the development of a series of highly efficient one-pot or two- or three-step methods for the synthesis of AP. The Kabachnik – Fields reaction occupies the leading position among these methods. It is now believed that the Kabachnik – Fields reaction and its constituting separate steps are the most convenient methods for the synthesis of AP, including homochiral ones (see Section IV).

The basic problem in the synthesis of AP is the formation of the aminoalkylphosphonate fragment, P(O) – C – N. Therefore,

Scheme 1

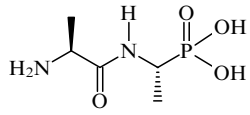


R^1, R^2 = Alk, Ar, AlkO, ArO, H, OH, $OSiR_3$;

(*a*–*d*) — see the text.

the synthetic routes shown in Scheme 1 are of prime interest. However, prior to the discussion of the synthetic versions presented in the scheme, it should be mentioned that the stereochemical aspects of these reactions are very important.

As in case of α-amino acids, the biological activity of AP is largely determined by the absolute configuration of the stereogenic α-carbon atom. Of the four possible diastereomers of the antibiotic alaphospholine **3**, the (*S*,*R*)-diastereomer manifests the greatest activity against pathogenic microorganisms. The three other stereoisomers are much inferior to this compound in activity (see Ref. 72 and references cited therein).



(4*S*,1*R*)-**3**

The first synthesis of an optically active APA was carried out in 1972.[73] The most comprehensive information on the methods for the stereoselective synthesis of AP is presented in the review by Kukhar' *et al.*[18] containing the data published before the middle of 1992. Since then, a large number of publications describing new ways for the enantioselective synthesis of AP have appeared; the main attention in the present review is given to these methods.

The strategy for the synthesis of AP that envisages the formation of the amino phosphonate framework, P(O)–C–N, is based mainly on the use of the Kabachnik – Fields reaction in a three-component system 'phosphite – carbonyl compound – amine' and its various versions [Scheme 1, pathway (*a*)]. As will be shown below, the Pudovik reaction, *i.e.*, catalysed or non-catalysed addition of hydrophosphoryl compounds to imines [pathway (*b*)], as well as nucleophilic amination of hydroxy phosphonates [pathway (*c*)], represent separate steps of the two- (or more)-step Kabachnik – Fields reaction. We shall consider these three most important methods for the synthesis of AP separately in Section III.

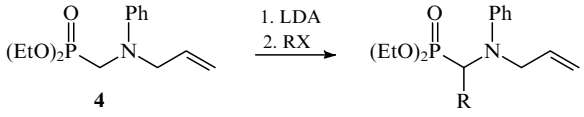
In the present section, we pay the main attention to the strategy designated as pathway (*d*) in Scheme 1 (C-, N-, P-modification). Numerous methods for the synthesis of AP based on this approach assume that a preliminarily created combination of phosphoryl, α-carbon and amine fragments is used as the key synthon. The synthesis of the target AP, including peptides, homochiral APA, *etc.* is carried out by introduction of the desired functional groups to the α-carbon atom (C-modification), to the nitrogen atom (N-modification) and to the phosphorus atom (P-modification). It should be noted that this strategy is being developed intensely in recent years. Special attention has been paid to the stereocontrolled functionalisation of AP at all the reaction centres specified above. Data published before the middle of 1992 have been systematised in a review (Ref. 18). Here we present only the studies that have not been mentioned there and in subsequent publications.

a. C-Modification

It is known that the carbon atom bonded with the phosphoryl group, which has considerable electron-withdrawing properties, possesses a pronounced anionoid character. This circumstance is widely used in organic and organometallic synthesis, for example, for functionalisation of the α-carbon centre or for olefination of carbonyl substrates by the Horner – Wittig – Emmons reaction.[74] Generation of carbanions from AP and their subsequent C-functionalisation is a popular approach for the synthesis of diverse polyfunctional AP by reactions of α-phosphoryl amino carbanions with appropriate electrophilic reagents. In these processes, the following starting compounds are used: APA or their esters containing the P(O)CH(R)N moiety with a terminal primary, secondary or tertiary amino group or imines incorporating the C=N–CH(R)P(O) fragment. The latter are usually obtained by the reaction of AP having a primary amino group with aldehydes or ketones.[75] Other procedures, *e.g.*, the reaction of α-oxo phosphonates with primary amines[76] or the reaction of dialkyl phosphites with hexahydrotriazine, have also been reported.[77]

C-Alkylation of acyclic AP [Scheme 2, pathway (*a*)] is used rather seldom, probably because of their rather low CH-acidity. The α-phosphoryl carbanion is probably insufficiently stable due to the presence of an electron-withdrawing phosphoryl group and an electron-donating amino group.

Nevertheless, easy introduction of a methyl, phenylthio, and other heteroatomic groups to the α-carbon atom of AP **4** (THF, −70 °C) by treating phosphoryl carbanions with appropriate halogen-containing reagents of the RX type has been described recently.[78]



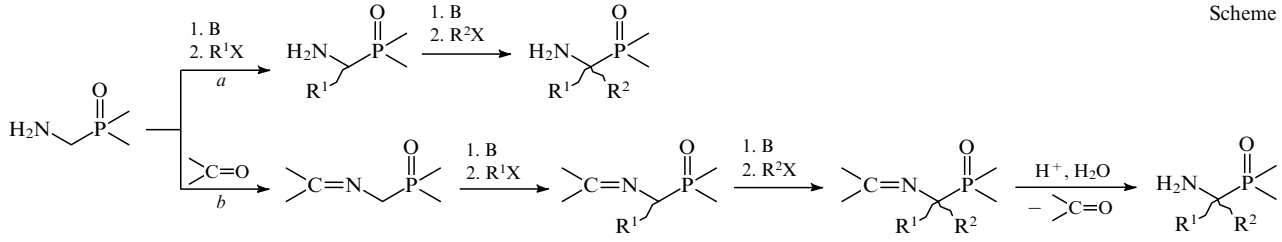
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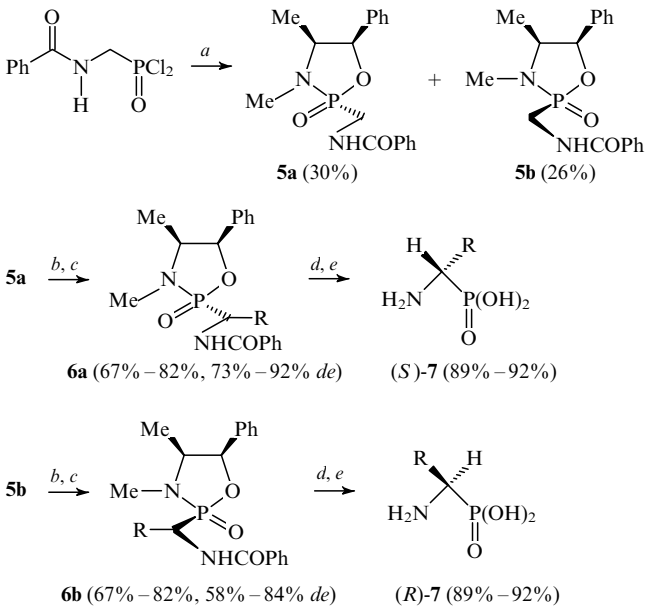
LDA = $LiNPr^i_2$;

R = $SiMe_3$ (79%), $SnBu_3$ (52%), SPh (60%), Me (70%).

However, in the series of heterophosphacyclanes containing endo- and exocyclic nitrogen atoms, the method for the synthesis of AP discussed above [Scheme 2, pathway (*a*)] is much more popular. A scheme for the synthesis of APA by alkylation of a five-membered cyclic ephedrine derivative **5** can be given as an example.[79]

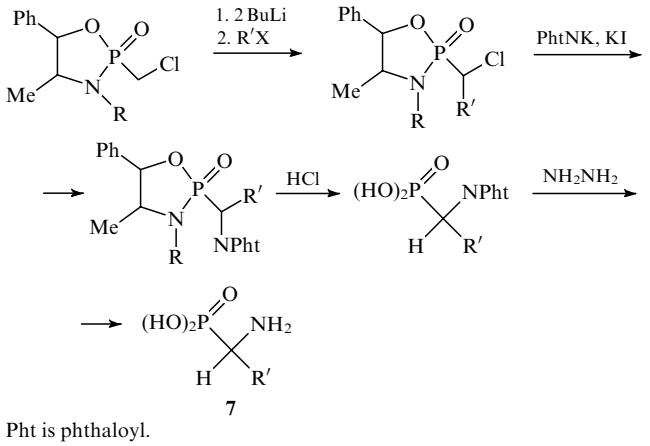
Scheme 2





(*a*) Ephedrine, NEt_3, THF; (*b*) BuLi, THF, −70 °C; (*c*) RX, −70 °C; (*d*) conc. HCl, 110 °C, 20 h; (*e*) Me–(epoxide); *de* is diastereomeric excess.

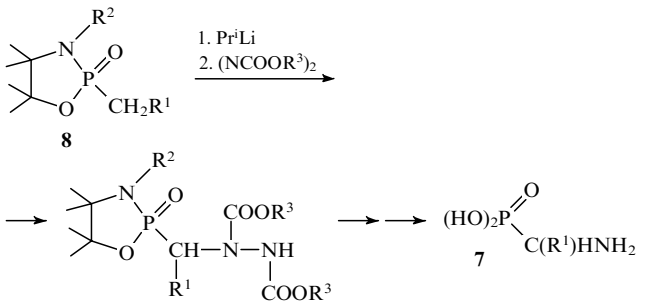
Homochiral 2-benzoylaminomethyl-3,4-dimethyl-2-oxo-5-phenyl-1,3,2-oxazaphospholanes **5a** and **5b** ('chiral phosphorus'), epimeric at position 2, were separated by column chromatography and subjected to C-alkylation under mild conditions to give enantiomers **6a** and **6b**. Subsequent hydrolysis of compounds **6a** and **6b** resulted in the APA (*S*)-**7** and (*R*)-**7**, respectively. Later,[80] this strategy was used for the synthesis of APA **7** from enantiomeric oxazaphospholanes with the exocyclic chloromethyl group.



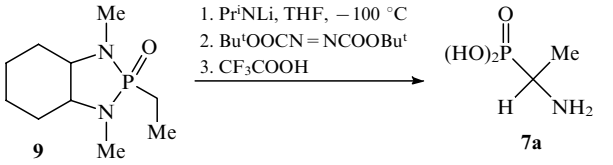
Pht is phthaloyl.

In recent years, functionalisation of methylphosphonates has been carried out according to the electrophilic amination scheme (see Ref. 72 and references cited therein). Strictly speaking, these processes do not conform to the strategy of C-alkylation of AP [Scheme 2, pathway (*a*)], as the amino group is not 'yet' present at the α-carbon atom of the starting phosphonates. However, since we are speaking of reactions of α-phosphoryl carbanions, we considered it appropriate to mention here this method for the synthesis of AP.

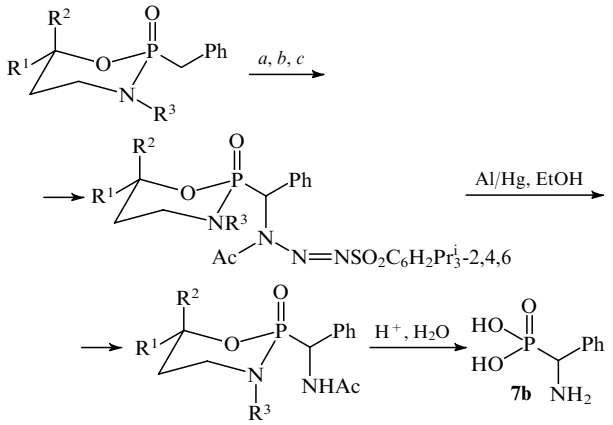
The reaction of oxazaphospholanes **8** with Pr^iLi and then with azodicarboxylate results in products of the addition to the N = N bond. Their subsequent hydrolysis gives the APA **7**.[81]



The same reaction was carried out with bicyclic phosphonamide **9**.[82]



In the reaction with oxazaphosphorinane, aryl azide serves as the aminating reagent.[83]



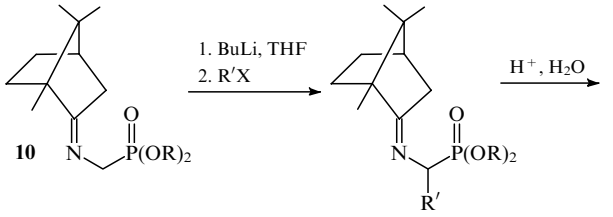
(*a*) BuLi; (*b*) 2,4,6-$Pr^i_3C_6H_2SO_2N_3$; (*c*) Ac_2O.

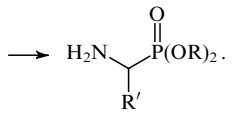
In all cases, high diastereoselectivity of amination and high chemical yield of APA **7** were achieved (see also Ref. 18).

Successful use of carbanions stabilised by 1,3,2-diheterophosphacyclane substituents in the C-modification is, probably, largely caused by the rather high CH-acidity and, accordingly, high stability of these systems. It is known that incorporation of a four-coordinate phosphorus atom in a ring increases its electron-withdrawing properties.[74] This is particularly pronounced in the chemical behaviour of 1,3,2-diheterophospholanes.[84]

A similar effect is achieved in the case of iminomethylphosphonates [Scheme 2, pathway (*b*)]. Charge delocalisation by two acceptor substituents, *viz*., the imino and phosphoryl groups, lowers the energy of a carbanion.

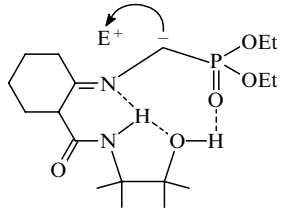
Enantioselective syntheses of AP by C-modification, *i.e*., alkylation of an α-imino carbanion with alkyl halides, carbonyl compounds and unsaturated electrophilic reagents, have been performed successfully with camphor derivatives **10** and a number of similar structures.





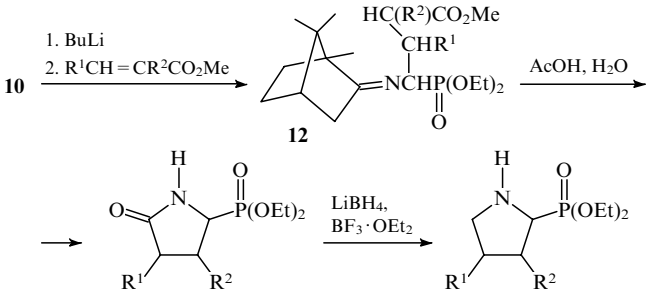
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It was shown recently that high diastereomeric excess (*de*) in C-modification can be achieved due to the chelation effect[85] provided by the introduction of suitable functional groups capable of forming intramolecular hydrogen bonds, as, *e.g.*, in structure **11**.

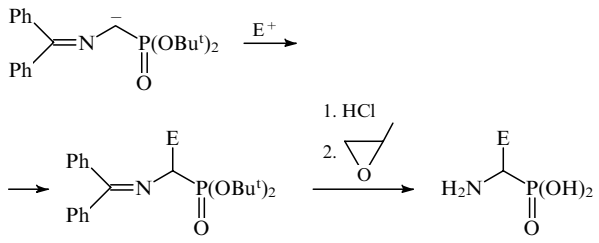


11

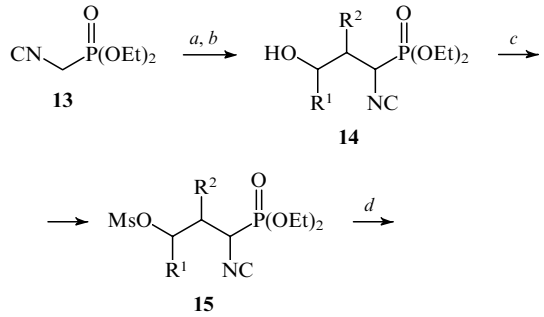
The carbanions generated from phosphorus-containing Schiff's bases **10** (R = Et) enter into the Michael reaction.[86] Adducts **12** undergo cyclisation in acidic medium to 5-oxo-2-pyrrolidinylphosphonate subsequent reduction of which results in diethyl 2-pyrrolidinylphosphonate.



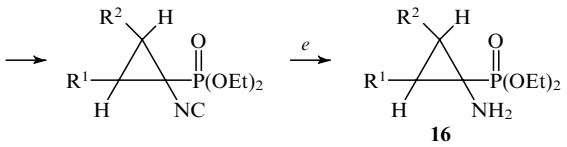
Secondary processes occurring after the electrophilic step of C-modification of AP expand the synthetic potential of phosphorylated imines. More often, however, the alkylation product is subjected to acid hydrolysis in order to obtain APA.[87]



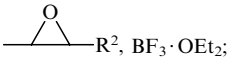
It has to be noted that the carbonyl compounds from which imine synthons are obtained can be regenerated by acid hydrolysis of phosphorylimines.[18] This strategy for the synthesis of AP has been expanded[88] for isocyanomethylphosphonate **13**.



15



16

(*a*) BuLi or Bu^tCH_2OK; (*b*) , $BF_3 \cdot OEt_2$;

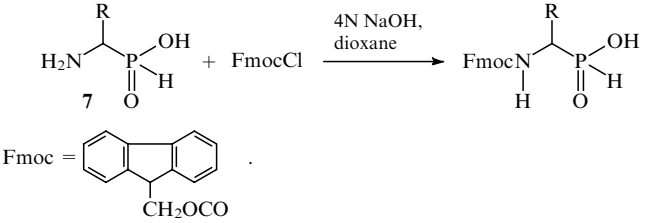
(*c*) MsCl, Et_3N; (*d*) Bu^tCH_2OK; (*e*) HCl, MeOH.

(1-Aminocyclopropyl)phosphonates **16** were obtained by alkylation of the phosphonate **13**-derived carbanion with epoxides to give the hydroxy phosphonate **14**. The mesylate **15** obtained from the latter undergoes cyclisation in the presence of bases to give a cyclopropane intermediate subsequent methanolysis of which in acidic medium results in the target product **16**. Other examples of similar reactions are described in Ref. 18.

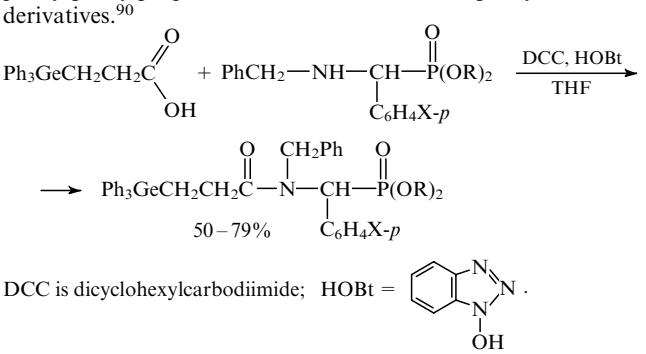
b. N-Modification

This type of AP reactions is responsible for their inhibitory effect with respect to enzymes and enables the involvement of APA and their esters in peptide synthesis. These processes were analysed in the reviews cited above,[3, 16, 34, 38, 39] and their examination is beyond the scope of our review; we shall describe only some of the results obtained in this field lately.

Fluorenylmethyl chloroformate was used as an acylating agent in the synthesis of α-(9-fluorenylmethoxycarbonylamino)alkylphosphinates.[89]

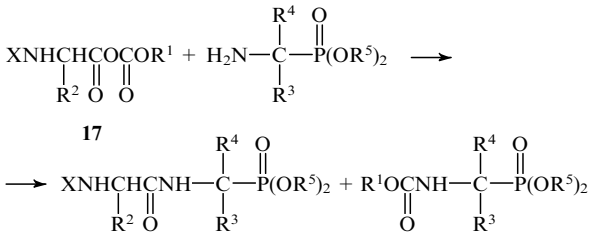


α-Aryl-(*N*-benzyl)aminomethylphosphonates react with β-triphenylgermylpropionic acid to afford germylated AP derivatives.[90]

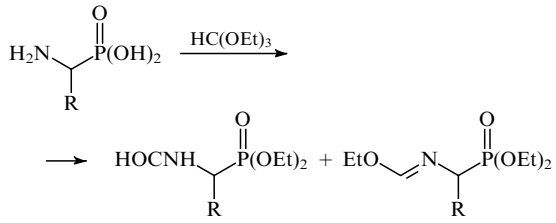


Germylated AP manifest high antitumour activity that surpasses the efficiency of nongermylated AP derivatives in assays with sarcoma-180.[90]

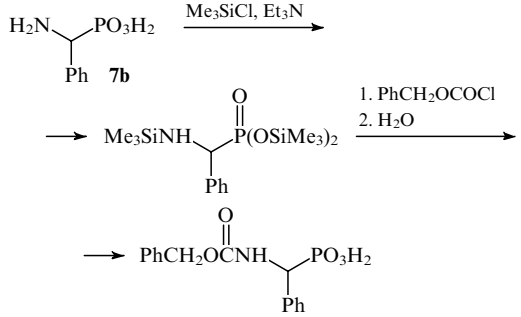
Acylation of AP containing a primary amino group with asymmetrical anhydride **17** results in a mixture of both possible *N*-acylated products.[91]



The readily occurring reaction of APA with ethyl orthoformate [92] results in a mixture of (*N*-formyl)amino- and (*N*-ethoxymethylene)imino derivatives of alkylphosphonates.

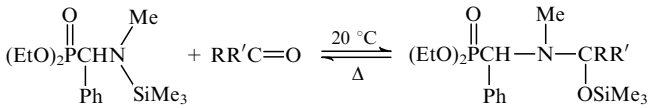


The well-known method to increase the nucleophilicity of the nitrogen atom by introduction of a trialkylsilyl group ('silyl activation') was successfully used in peptide synthesis in the *N*-acylation of APA **7b** with benzyl chloroformate.[93]



It should be noted that this synthetic technique has also been used in the synthesis of phosphorus analogues of glycine containing the dimethylphosphine oxide group.[94]

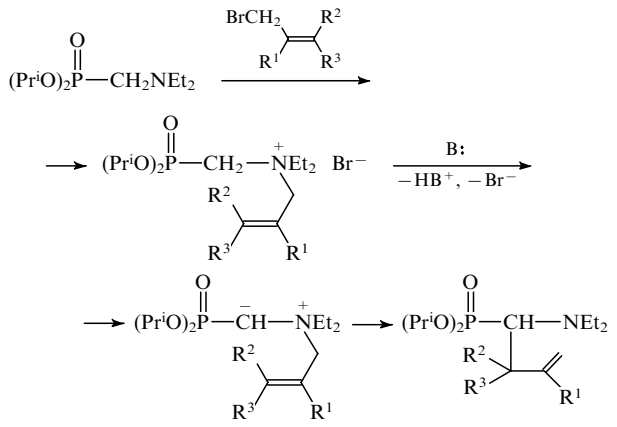
N-Silylated AP add to acetone, benzaldehyde and *p*-bromobenzaldehyde at room temperature.[95]



Distillation of (*N*-methyl-*N*-silyloxyalkyl)phenylmethylphosphonates results in their dissociation to the original AP and carbonyl compounds.

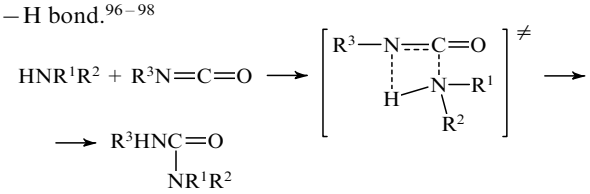
Nucleophilic reactions involving the nitrogen atom of AP are not limited to the substitution processes. Other reactions characteristic of primary, secondary and tertiary amines are also typical of AP. Among these, reactions of quaternisation and especially reactions of addition to unsaturated compounds are well studied.

An unusual sigmatropic [2.3]-rearrangement of *N*-allylammoniomethyl phosphonates occurs in the presence of bases.[78]



In this case, quaternisation of the tertiary amine centre is followed by the Cope rearrangement into the corresponding C-substituted AP, *viz*., 1-aminobut-3-enylphosphonate.

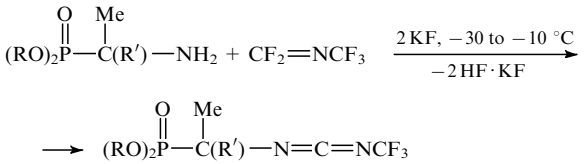
Of addition reactions, those of AP with aryl isocyanates have been studied in detail.[96–100] Comparative study of the kinetics of addition of amines and their α-phosphorylated analogues, *i.e*., AP, to phenyl isocyanate revealed similarity of the addition mechanisms. In both cases, a concerted mechanism of addition is postulated with a four-centred transition state in which the C–N bond is formed in the activated complex somewhat earlier than the N–H bond.[96–98]



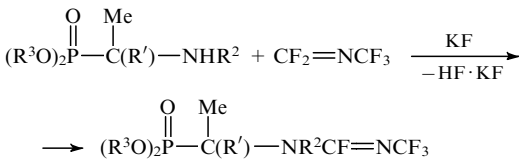
R^1 = Alk, Ar; R^2 = H, Alk, Ar, $CH_2P(O)(OR^4)_2$; R^3 = Ar.

The small activation enthalpies and the high negative activation entropies are in good agreement with this conclusion. As was to be expected, AP are appreciably less active in this reaction than their aliphatic analogues, *i.e*., dialkylamines. This is due to a decrease in the nucleophilicity of the amino group in the AP molecule due to the electron-withdrawing effect of the phosphoryl group. In a series of phosphorylated nucleophiles, good agreement between their reactivities and steric effects of the substituents at the phosphorus atom is observed, as follows from high correlation factors of the corresponding equations.[96]

Reactions of AP with perfluoro-*N*-methylformimine probably occur according to the addition–elimination scheme.[101] The synthetic result of this reaction, which occurs under very mild conditions, depends on the degree of substitution at the α-amino group. Primary α-phosphorylalkylamines are transformed to the corresponding α-(*N*′-trifluoromethylcarbodiimido)alkylphosphonates.



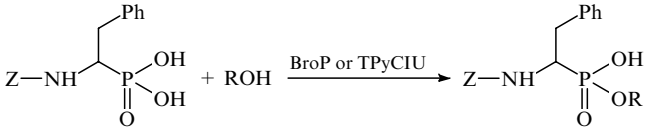
Secondary amines react with the elimination of one molecule of hydrogen fluoride and form α-(perfluoro-*N*-methylformamidino)alkylphosphonates under the same conditions.



c. P-Modification

In the chemistry of AP, this type of reactions is normally represented by saponification and esterification of phosphorus acid derivatives. Though these reactions play an important role in the synthesis of APA and their esters, they are of no special interest in the context of this review. Of recent studies, we shall mention only Ref. 102.

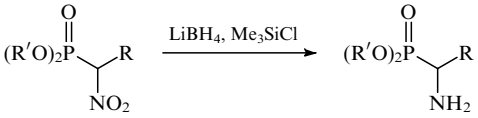
Selective mono-esterification of APA occurs with sterically hindered alcohols in the presence of bromo[tris(dimethyl-amino)]-phosphonium hexafluorophosphate (BroP) or *N*,*N*,*N*′,*N*′-bis(tetramethylene)chloronium tetrafluoroborate (TPyCIU).



d. Other methods

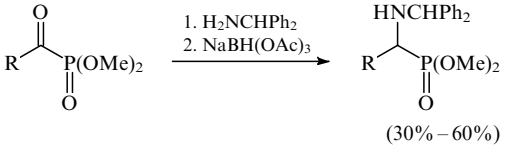
The simplest and rather common method for the synthesis of AP is reduction of nitrogen-containing organophosphorus compounds that already have a phosphonate framework with the α-nitrogen atom under the action of various hydrogenating agents.

For example, α-nitro phosphonates can easily be transformed to AP even at room temperature in almost quantitative yields.[103]



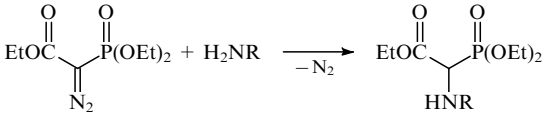
Reduction of hydroxyiminophosphonate with sodium borohydride occurs in the presence of MoO_3 or $NiCl_2$ (see Ref. 104).

Reductive amination of α-oxo phosphonates in the presence of triacetoxyborohydride gives the corresponding AP in moderate yields.[76]



This reaction occurs in two steps: Schiff's bases are formed in the first step and reduced in the second step.

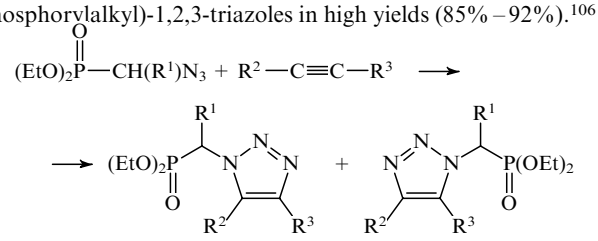
Other reactions of unsaturated organophosphorus compounds containing, or devoid of, a potential amino group were used in the synthesis of AP. Ethyl (diethoxyphosphoryl)diazoacetate is obviously inserted as a carbene into the N – H bond of amines and amides.[105]



R = Alk, Ar, Ac, $COOBu^t$ *etc.*

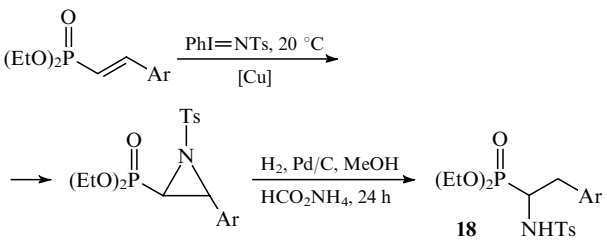
The reaction takes place under drastic conditions, *viz.*, refluxing in toluene in the presence of palladium salts.

Diethyl azidoalkylphosphonate undergoes 1,3-dipolar cycloaddition with alkynes to give 4,5-disubstituted 1-(1-diethoxyphosphorylalkyl)-1,2,3-triazoles in high yields (85% – 92%).[106]



Reactions of unsaturated organophosphorus compounds with nitrogen-containing 1,3-dipoles are well studied and are discussed in a review.[107]

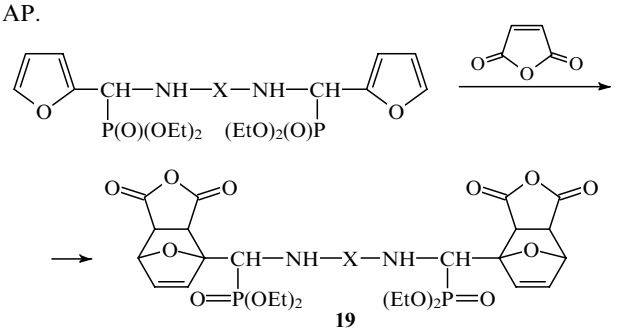
Vinylphosphonates are attractive synthons when choosing a strategy for the synthesis of AP. Recently,[108] a convenient method to involve them in the reaction with *N*-tosyliminophenyl-λ^3-iodane in the presence of Cu(II) or Cu(I) triflate has been described.



18

Catalytic hydrogenation of the aziridine intermediate occurs regiospecifically to give the AP **18**. The solvent used in this reaction affects essentially the rate of the process. For example, a 70% – 80% yield of compound **18** is reached in 10 min in acetonitrile, in 1 – 3 h in CH_2Cl_2, and in 76 – 90 h in benzene. Enantioselective synthesis of AP from vinyl-phosphonates and -phosphinates was also carried out with the use of nickel complexes of natural amino acids. As a result, the latter undergo condensation at the terminal carbon atom of the phosphorus reagent.[18, 109]

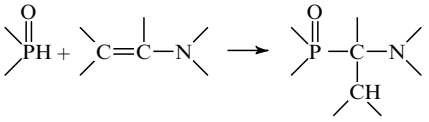
Polyfunctional AP can be obtained by functionalisation involving other unsaturated fragments as well. For example, bisphosphonates **19** were synthesised[110] which represent the Diels – Alder adducts of maleic anhydride with furan derivatives of AP.



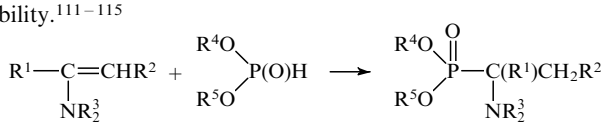
19

Yet another promising strategy for the synthesis of AP has found quite a limited use so far. This is phosphorylation of unsaturated compounds containing the nitrogen atom at the α-position to the double bond, for example, enamines and similar compounds.

The so-called electrophilic version of the Pudovik reaction makes an exception.



It is known[10] that hydrophosphorylation of enamines under classical conditions of the Pudovik reaction, which is base-catalysed addition, could not be carried out until the late 1980's. A simple one-step method for the synthesis of AP was created only after the discovery of the electrophilic version of the Pudovik reaction, which occurs with vinyl ethers, enamines and other electron-excess alkenes and five-membered cyclic alkylenephosphorous acids characterised by an increased proton-donor ability.[111 – 115]



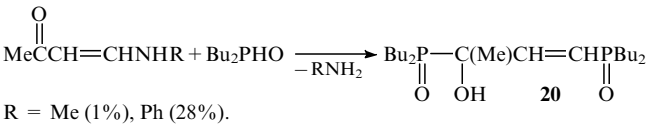
R^1 = Alk, Ar; R^2 = H, COOEt, COMe *etc.*;

R_2^3 = $(CH_2)_5$, $CH_2CH_2OCH_2CH_2$, Me_2;

R^4, R^5 = CH(Me)CH(Me), $CH(Me)CH_2$, CMe_2CMe_2, $CH_2CMe_2CH_2$, *o*-C_6H_4; $R^4 = R^5$ = $CHF_2CF_2CH_2$, $ClCH_2CH_2$.

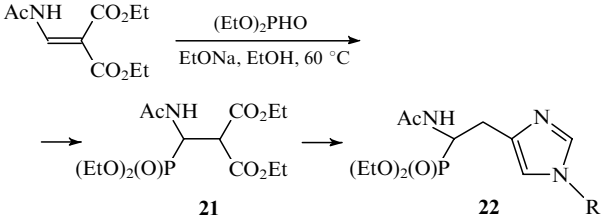
Synthetic, kinetic and thermochemical studies[8, 111 – 115] of this reaction together made it possible to establish its mechanism. It consists of pre-equilibrium transfer of a proton from the phosphorous acid to the enamine and addition of the cyclophosphite anion to the α-carbon atom. As is frequently observed in electrophilic addition of proton-containing reagents, the addition occurs according to the Markovnikov rule. However, this method was found to be unsuitable for the hydrophosphorylation of aminobutenones.[116] Enamino ketones with *N*-methyl and *N*-phenyl groups react without participation of the carbon – carbon double bond. Dibutylphosphine oxide adds to the ketone carbonyl group,

and the second phosphine oxide molecule replaces the amino group to give the diphosphorylated unsaturated alcohol **20**.



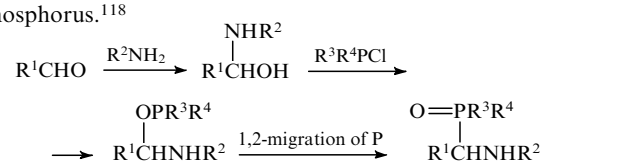
R = Me (1%), Ph (28%).

It is rarely possible to employ the classical nucleophilic Pudovik reaction for the synthesis of AP.[117] For example, the addition of diethyl phosphite to *N*-acetylaminomethylidenemalonic ester gave the AP **21**, which served as the starting reagent in the synthesis of phosphonohistidine **22**.



This reaction was successful due to the presence of three strongly electron-withdrawing substituents in the unsaturated electrophilic reagent, *viz*., two ethoxycarbonyl groups and an acylamino group.

Finally, we shall note the unusual synthesis of AP through 1,2-phosphorylotropic migration in a series of *N*-acylated derivatives of α-aminoalkyl compounds of three-coordinate phosphorus.[118]



R^1 = CCl_3, $H(CF_2)_4$, $H(CF_2)_6$; R^2 = PhCO, $P(O)(OEt)_2$, $P(O)Ph_2$;
R^3 = R^4 = AlkO, Alk_2N, Ar.

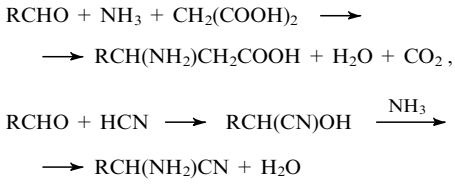
The α-amino alcohol formed in the first step of the reaction esterifies the P(III) halide to give the P(III) alkoxy derivative, which then undergoes isomerisation to the corresponding AP.

The material presented in this section shows that essential progress in the creation of new types of AP has been achieved during the search for practically useful compounds. The ever-increasing complication of the AP structures demands a wider use of diverse approaches for the functionalisation of the starting substances. However, the analysis of the results obtained shows that the main problem in AP chemistry, *viz*., the formation of the α-alkylaminophosphinyl fragment P(O)–CR_2–N, can be best solved using the Kabachnik – Fields reaction. This explains, first of all, the keen interest of researchers in the studies of various aspects of the Kabachnik – Fields reaction in the last decade. This primarily corresponds to the investigations into the reaction mechanism, as the desired synthetic result can only be achieved on the basis of in-depth understanding of the factors governing this complex process.

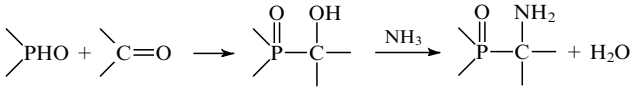
III. The mechanism of the Kabachnik – Fields reaction

As noted above, the Kabachnik – Fields reaction, *i.e*., a three-component reaction of hydrophosphoryl compounds with ammonia, amines or other NH-compounds and aldehydes or ketones, is a unique method for the formation of the AP framework [N–C–P(O)]. However, a common viewpoint on the mechanism of this reaction has not been worked out until recently, as the conclusions were based mainly on synthetic studies. Spectral and kinetic data were obtained later.

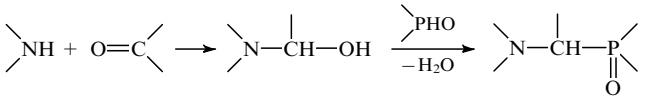
The main problem in the understanding of the mechanism of the Kabachnik – Fields reaction is the determination of the sequence of separate steps of this process. In their early studies, Kabachnik and Medved' believed that it was similar to the Rodionov reaction employed for the synthesis of β-amino acids or the Zelinsky reaction, *i.e*., the formation of amino nitriles upon treatment of aldehydes with ammonium cyanide (see Refs 1, 119 – 121 and references cited therein).



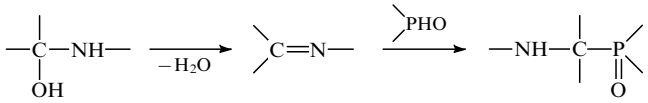
Studies of the reaction of hydrophosphoryl compounds with aldehydes[1] and ketones[119] made it possible to suggest a scheme of aminoalkylation of hydrogen phosphites and phosphonites,[120, 121] which involves the addition of a hydrophosphoryl compound to the C=O bond with subsequent replacement of the hydroxy group of the α-hydroxy phosphonate by the amino group.



Fields[2] used primary and secondary amines instead of ammonia in a three-component mixture containing dialkyl phosphites and carbonyl compounds. For example, exothermic reaction of diethyl phosphite with diethylamine and formaldehyde gives *N*,*N*-diethylaminomethylphosphonate in 94% yield. Fields[2] believed that the reaction occurred as the Mannich reaction, *viz*., the reaction of an amine with an aldehyde first produces an α-amino alcohol, which reacts with a hydrophosphoryl compound to give finally an AP.

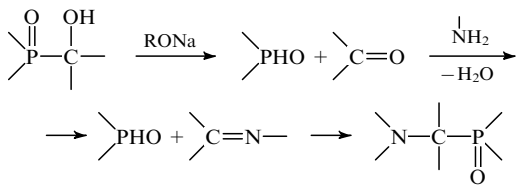


In the opinion of Fields,[2] the reaction with primary amines might also occur through intermediate imines. An imine formed in the first step, *i.e*., the product of dehydration of an α-amino alcohol, readily added a hydrophosphoryl compound.



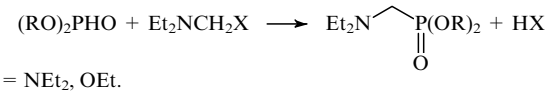
Thus, in the studies of the Kabachnik – Fields reaction,[2] the important assumption has been made that aminoalkylation of hydrophosphoryl compounds could occur through a step of formation of an imine and its subsequent involvement in the Pudovik reaction.

The experimental fact that the methoxy group in methoxymethylphosphonate is not exchanged for the amino group on heating with ammonia provides evidence in support of the 'imine' pathway of the Kabachnik – Fields reaction.[122] In addition, hydroxy phosphonates, *i.e*., addition products of dialkyl phosphites to carbonyl compounds, do not react with ammonia under the mild reaction conditions used by Fields.[2] The hydroxy group can be replaced by the amino group only in the presence of sodium alkoxide. It is believed to cause the decomposition of a hydroxy phosphonate into the original compounds, *viz*., hydrogen phosphite and a carbonyl compound.[122] The process subsequently goes through a step of formation of an imine, which adds a hydrophosphoryl compound according to the Pudovik reaction scheme.



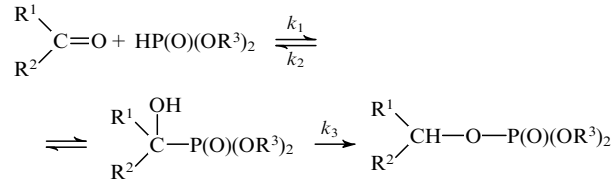
The reversibility of the formation of hydroxy phosphonates received a convincing experimental confirmation in the studies by Gancarz *et al.*[5, 123–125] It was found that hydroxy phosphonates obtained from aliphatic and aromatic aldehydes and ketones decompose into the original hydrophosphoryl and carbonyl compounds under certain conditions in the presence of primary or tertiary amines (butylamine, triethylamine), as well as amines in the presence or in the absence of proton donors (ethanol). Hence, the formation of hydroxy phosphonates under conditions of the Kabachnik – Fields reaction does not necessarily imply that the formation of the ultimate AP should definitely occur according to the 'hydroxy phosphonate' pathway. As shown above, the phosphite and carbonyl compound formed upon decomposition of hydroxy phosphonates can give the final AP according to the 'imine' pathway, *viz.*, through condensation of a carbonyl compound and an amine into an imine and its subsequent hydrophosphorylation.

At first glance, this viewpoint does not explain the participation of secondary amines in the Kabachnik – Fields reaction. However, according to the data obtained by Petrov *et al.*,[122] in this case either the addition of hydrophosphoryl compounds to iminium salts or the Mannich reaction occur. The possibility of the latter pathway is confirmed by the formation of AP in the reaction of dialkyl phosphites with *N*,*N*,*N*′,*N*′-tetraethylmethylenediamine or with ethoxymethyldiethylamine.



X = NEt_2, OEt.

On the other hand, it was found[123–125] that hydroxy phosphonates are not only formed reversibly from aromatic ketones under conditions of the Kabachnik – Fields reaction but also are irreversibly converted to phosphates according to the well-known phosphonate – phosphate rearrangement scheme.



R^1, R^2 = Ar;

Relative reaction rate constants: $k_1 = 100$, $k_2 = 1$, $k_3 = 6$.

The fastest step of the reaction is the formation of a hydroxy phosphonate. Its rearrangement to a phosphate occurs six times faster than the decomposition to the original compounds.

It is necessary to emphasise that both Kabachnik with Medved' and Fields have made their conclusions on the sequence of the reaction steps without carrying out special mechanistic studies. Therefore, they did not contrast the two possible routes of the aminoalkylation of hydrophosphoryl compounds, *viz.*, the 'hydroxy phosphonate' and 'imine' pathways. The experimental data reported in their and other studies cited above[2, 119–121] as well as in some later publications[122, 126, 127] allow one to assume that, depending on the nature of the reactants (hydrophosphoryl and carbonyl compounds and amines), the reaction mechanism and the sequence of steps can vary.

An assumption was made[128–130] that the formation of AP *via* hydroxy phosphonates occurs with amines whose basicity is sufficiently high ($pK_a > 6$). Otherwise ($pK_a < 6$), the 'imine' mechanism operates. This conclusion is based on the shift of signals in the ^{31}P NMR spectrum of diethyl phosphite in its mixtures with amines. The δ ^{31}P value is the higher the more basic the amine. Furthermore, it was considered[129, 130] that the increase in the yield of AP in the Kabachnik – Fields reaction with weakly basic amines upon addition of crown ethers confirmed the scheme discussed above.

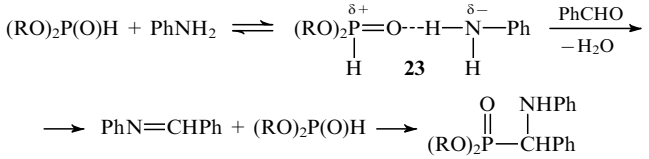
The idea that the mechanism of the Kabachnik – Fields reaction displays certain dualism seems quite reasonable. However, not all of the statements given in Ref. 129 appear to be convincing, and some of the postulates seem unlikely. Thus the suggestion that weakly basic amines can protonate the phosphoryl oxygen atom of a phosphite and the amide anion thus formed adds to a carbonyl compound to form methylolamine and/or imine[129] is wrong, in our opinion, as the amines are too weak acids to protonate the weakly basic oxygen atom of the P=O group.

A confirmation that the Kabachnik – Fields reaction can follow both of the pathways discussed here, *viz.*, 'hydroxy phosphonate' and 'imine', was obtained[131–139] by the authors of the present review in a complex study including kinetic, spectroscopic and preparative methods.

We studied three-component systems containing a hydrophosphoryl compound, a carbonyl compound, and an amine, in which the nature of each reagent and the reaction conditions (solvent, additives of various types) were varied widely. We also studied the possibilities of bimolecular processes in the following pairs: hydrophosphoryl compound – carbonyl compound, hydrophosphoryl compound – amine, hydroxy phosphonate – amine, and hydrophosphoryl compound – imine. It was found that each of the reaction partners affects somewhat the reaction efficiency and its pathway.

A kinetic study of the reaction in the system dialkyl(methyl or pentyl) phosphite – benzaldehyde – aniline and reactions in the pairs $PhNH_2$ + PhCHO, dipentyl phosphite + PhCHO, and dipentyl phosphite + PhN=CHPh has made it possible to establish that the 'imine' mechanism operates in this case.[131] UV spectroscopic study of the reaction kinetics permitted detection of an increase in the optical density of the mixture due to the formation of an imine chromophore in the beginning of the process. The formation of an imine is the fastest reaction of all reactions possible in this system. It is catalysed by a dialkyl phosphite. The reaction of phosphites with benzaldehyde in the absence of acidic additives (formic acid or aniline hydrochloride) does not occur at all. Pyridine, whose basicity is equal to that of aniline, but which cannot serve as a proton donor and does not participate in the reaction, does not catalyse it. Hence, the basicity of aniline is insufficient to catalyse the addition of dialkyl phosphites to benzaldehyde. This rules out the intermediate formation of hydroxy phosphonates.

Thus, due to low basicity, aniline manifests proton-donor properties and forms a pre-reaction complex of the type **23** with the phosphite. The reaction of the complex **23** with benzaldehyde results in an imine hydrophosphorylation of which gives the target AP.

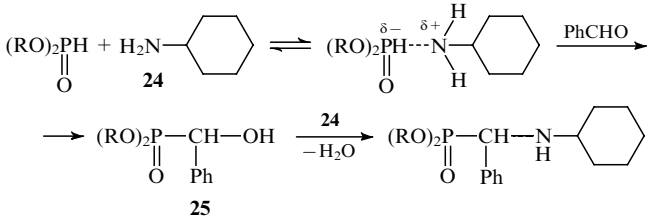


A study of this system in solvents of different nature, *viz.*, in benzene (neutral medium) or propan-2-ol (a potential proton donor), in the presence and in the absence of acidic admixtures made it possible to reveal the effect of acid catalysis on the rate of each step of this reaction. The use of a strong proton donor, such as HCOOH, always accelerates the reaction by the general acid catalysis mechanism. This effect is most pronounced in a polar solvent, *viz.*, propan-2-ol. Propan-2-ol itself is inefficient as a

proton donor. It manifests only solvation effects, slowing down the reaction in some cases due to the formation of H-complexes with basic reagents.

Different kinetics were observed if the relatively weak base, aniline, was replaced by the appreciably more basic cyclohexylamine **24**.[136] It was found that the reaction of amine **24** with benzaldehyde is very slow and results in benzylidenecyclohexylamine, which is practically insoluble both in the selected media and in the majority of organic solvents. Attempts of addition of dialkyl phosphites to *N*-cyclohexylbenzylideneamine even in the presence of strong acids and bases failed.

These data indicate that in the system 'hydrophosphoryl compound – amine **24** – benzaldehyde', the 'hydroxy phosphonate' mechanism operates. According to this pathway, the reaction starts with the addition of a phosphite to benzaldehyde catalysed by the amine **24** (the Abramov reaction), followed by the replacement of the hydroxy group by the cyclohexylamino group.

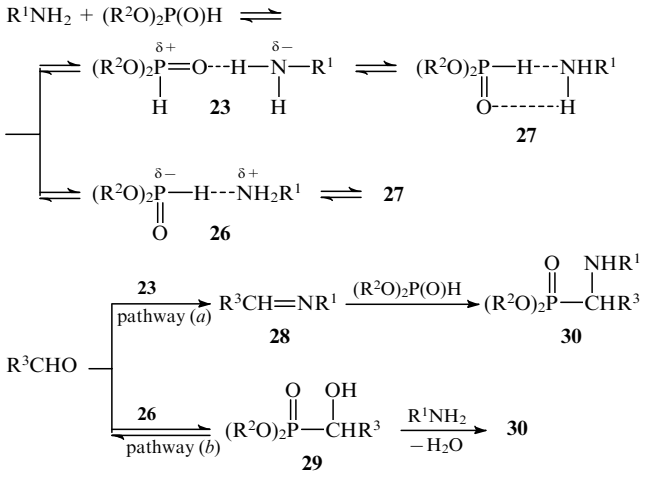


A special ^{31}P NMR study made it possible to detect the formation of the hydroxy phosphonate **25** in all cases. If a catalytic amount of the amine **24** is used, the phosphonate **25** is the sole reaction product. As the amine concentration increases, the signal intensity for the final product (AP) increases, while that for the phosphonate **25** decreases. In the system with aniline discussed above, the formation of the hydroxy phosphonate was never detected.

The results of these studies lead to the conclusion on the decisive role of the amine basicity. Variation of the nature of the amine enables 'switching' of the reaction from one pathway to the other.

To estimate the effect of the carbonyl component on the reaction pathway, the same complex of studies was carried out in the system 'dialkyl phosphite – aniline – substituted benzaldehyde'. Electron-donating *p*-methoxy and *p*-dimethylamino groups and electron-withdrawing *p*-bromo and *m*-nitro groups were used as the substituents. It was found that in all cases the 'imine' reaction pathway (Scheme 3) was realised and its general laws were obeyed. However, on switching from electron-donating substituents to electron-withdrawing ones, the rate of imine formation increases both in the carbonyl compound – amine pair and in the three-component system.

Scheme 3



On the other hand, unlike benzaldehyde, its derivatives with both electron-donating and electron-withdrawing substituents undergo the Abramov reaction with phosphites to produce the corresponding hydroxy phosphonates. Moreover, simultaneous formation of both an imine and a hydroxy phosphonate was reported. The rate of the Abramov reaction for the aldehydes with electron-donating substituents exceeds the rate of imine formation by almost an order of magnitude. However, this does not suggest that the 'hydroxy phosphonate' mechanism is preferable kinetically, since, first, the Abramov reaction is reversible, and, second, the ability of transformation of hydroxy phosphonates to AP depends on the basicity of the amine. Weakly basic amines cannot replace the hydroxy group in a hydroxy phosphonate molecule. Thus, even if the formation of the latter is preferable kinetically, thermodynamic control directs the reaction with weakly basic amines to the 'imine' pathway.

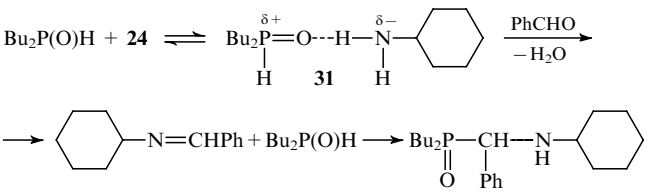
In some cases, *e.g.*, for anisaldehyde, the ratio of rates of all pairwise reactions possible under the Kabachnik – Fields reaction conditions allows both reaction pathways. However, even in this case, the reaction follows mainly the 'imine' pathway, while the 'hydroxy phosphonate' pathway is minor if aniline is used as the amino component.[137]

In the general case, the basicity of the amine is the crucial factor that determines the reaction pathway, in particular, the possibility of formation of pre-reaction complexes **23** or **26** (Scheme 3). Weakly basic amines, which can act with hydrophosphoryl compounds as H-donors, direct the reaction to the 'imine' pathway [pathway (*a*)].

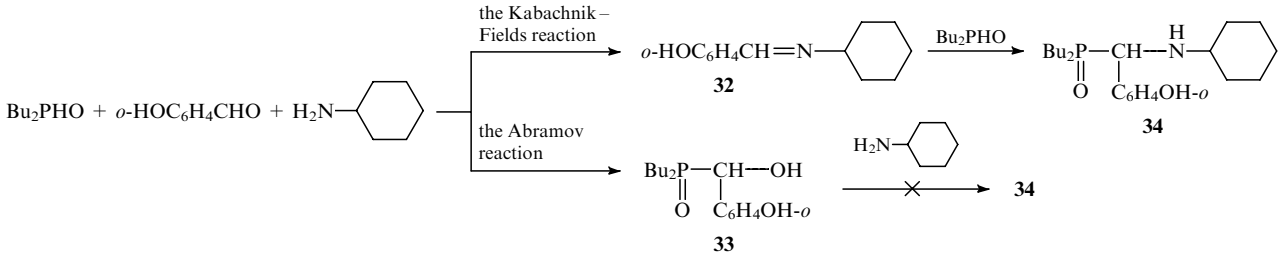
Strong bases enable nucleophilic interaction of the pre-reaction complex **26** with carbonyl compounds and thus favour the 'hydroxy phosphonate' direction. An important role belongs to the reactivity of reactants, which affects the ratio of rates of decomposition of the hydroxy phosphonate and replacement of the hydroxy group in it by the amino group according to the pathway **29** → **30**. An intermediate case is possible as well: a biphilic reaction of a hydrophosphoryl compound with an amine with the formation of the complex **27**. This version assumes the probability of parallel reactions through both pathways.

The importance of consideration of all factors in the determination of the reaction pathway is clearly seen where salicylaldehyde is used in the reaction.[138] Irrespective of the amine basicity, the reaction with salicylaldehyde occurs exclusively according to the 'imine' pathway. The reason for this is the thermodynamic instability of the hydroxy phosphonate obtained from this aldehyde in the Abramov reaction.

The nature of the hydrophosphoryl compound is also of significant importance.[139] As will be shown below (Section IV) and as follows from Scheme 3, the acid – base interaction of a hydrophosphoryl compound with an amine is the crucial factor that determines the direction of the reaction. Replacement of the alkoxy groups by alkyls in a hydrophosphoryl compound, *i.e.*, going from dialkyl phosphites to dialkyl phosphinites and especially to phosphinous acids, alters the ability of a hydrophosphoryl compound to form a pre-reaction complex with an amine. High basicity of the phosphoryl oxygen atom in dibutylphosphinous acid and the decrease in PH-acidity of the hydrophosphoryl compound due to the replacement of electron-withdrawing alkoxy substituents at the phosphorus atom by electron-donating alkyl groups is the reason for the 'switch' of the reaction pathway from the 'hydroxy phosphonate' pathway, which is typical of dialkyl phosphites, to the 'imine' one if cyclohexylamine **24** is used as the amine component.



Scheme 4



Although phosphinous acids undergo smooth addition to carbonyl compounds, even in the absence of catalysts, the effect of the pre-equilibrium step, which involves the formation of the complex **31** and the addition of cyclohexylamine **24** to benzaldehyde catalysed by dibutylphosphinous acid, is more essential. An alternative mechanism involving nucleophilic attack of the dibutylphosphinite anion on the carbonyl carbon atom is noncompetitive in this case.

In a three-component system 'dibutylphosphinous acid – salicylaldehyde – cyclohexylamine', the hydrophosphoryl compound can enter into nucleophilic reactions both with an amine, which determines the 'imine' mechanism of the Kabachnik – Fields reaction, and with salicylaldehyde. However, in the latter case, the product of the Abramov reaction, *viz*., compound **33**, does not react with cyclohexylamine, and the product of the Kabachnik – Fields reaction, *viz*., aminomethylphosphine oxide **34**, is not formed (Scheme 4).

High stability of the hydroxy phosphonate **33** precludes its decomposition into the original components. Both addition processes resulting in the imine **32** and hydroxy phosphonate **33** are competitive, and compound **33** is the side reaction product. This result confirms once again the general scheme of the Kabachnik – Fields reaction (Scheme 3) and explains numerous experimental observations that the purity and yield of the reaction product increase if the reaction is carried out not in a three-component system but rather in a stepwise manner, for example, with isolation of the imine.[140, 141] It is difficult to interpret unequivocally the competitive reactions of two nucleophiles in a system 'hydrophosphoryl compound – carbonyl compound – amine', *viz*., the phosphite (the Abramov reaction, the 'hydroxy phosphonate' pathway) and the amine (the 'imine' pathway), in terms of electrophilicity of the carbonyl carbon atom.[142, 143] It was not possible to reveal the relationship between the preference of attack by a particular nucleophile (amine or phosphite) and the steric requirements for the formation of adducts.[142] It is believed [142, 143] that the experimental results obtained from kinetic data and density functional[143] calculations are best explained from the HSAB standpoint. According to this concept, hard acids (aliphatic aldehydes and ketones) react faster with the hard bases (amines). Soft bases, *i.e*., phosphites, preferably react with soft acids, such as aromatic carbonyl compounds. Similar opinions have also been expressed earlier.[144] We believe than these observations are only estimates that cannot rationalise the diversity of factors that determine the reaction pathway (for example, its changes on varying the substituents at the phosphorus atom in a hydrophosphoryl compound[139]).

The general mechanism of the Kabachnik – Fields reaction presented in this section (Scheme 3) has much larger interpretative and predictive power.

IV. Synthetic potential of the Kabachnik – Fields reaction

The ample synthetic potential of the Kabachnik – Fields reaction has allowed it to occupy a deserved position in the arsenal of preparative chemistry of organophosphorus compounds. The possibility of variation of the functional groups in the carbonyl and amine components, the involvement of various types of derivatives of trivalent (three-coordinate) phosphorus in the reaction, the rather mild reaction conditions and the possibility of further one-pot modification of the resulting AP, all these attractive aspects of the three-component method for the synthesis of AP by the Kabachnik – Fields reaction stimulated the search of newer substrates for this reaction. Here we make an attempt to classify the versions of the Kabachnik – Fields reaction according to the starting P(III) compound.

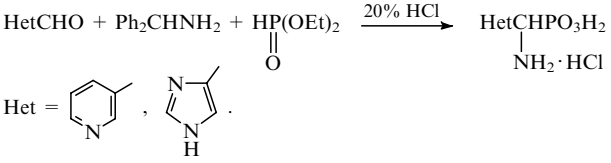
1. The classical version

a. Reactions of hydrophosphoryl compounds

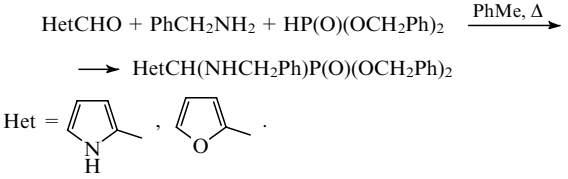
The scope of the Kabachnik – Fields reaction and its applicability to various types of hydrophosphoryl compounds, aldehydes and ketones, and secondary amines and ammonia outlined in the early studies satisfied to a certain extent the needs for the synthesis of AP with rather simple structures. The results of these studies are covered in reviews.[6, 12] The scope of compounds that are being used in this reaction has now expanded appreciably.

First, this refers to the synthesis of AP containing heterocyclic substituents at the C- and N-centres.

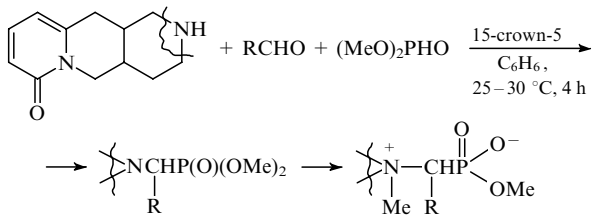
Pyridine, pyrrole and imidazole derivatives were synthesised by a one-pot procedure using diethyl phosphite and benzhydrylamine.[140] In the presence of hydrochloric acid, the benzhydryl protective group is removed and the process goes through condensation and hydrolysis to give the corresponding α-aminohetarylmethylphosphonic acids.



The reaction of heterocyclic aldehydes with benzylamine and dibenzyl phosphite occurs at elevated temperature and results in *O*,*O*,*N*-tribenzyl phosphonates. Consecutive addition of the amine and the phosphite to the aromatic aldehyde assumes the initial formation of a Schiff's base.[140]



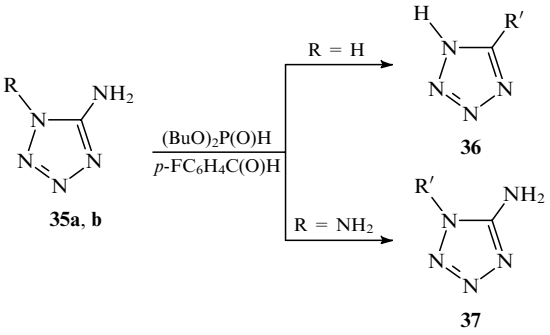
The alkaloid cytisine reacts with aliphatic and aromatic aldehydes and dimethyl phosphite under mild conditions in the presence of catalytic amounts of crown ethers to give the corresponding AP.[145] On refluxing in benzene, amino phosphonate derivatives of cytisine form internal salts.



R	Pr^i	Ph	4-$MeOC_6H_4$
Yield (%)	78	80	90

It should be noted that dealkylation involving the dimethoxyphosphoryl group can complicate the Kabachnik–Fields reaction, especially if weakly reactive aromatic aldehydes, that are most susceptible to this process, are used.[146]

Phosphorylmethyl derivatives of aminotetrazoles are readily formed in the reaction with dibutyl phosphite and *p*-fluorobenzaldehyde.



R = H (**a**), NH_2 (**b**); R′ = $(BuO)_2P(O)CH(C_6H_4F\text{-}p)NH$.

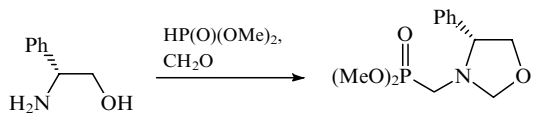
5-Aminotetrazole (**35a**) reacts with dibutyl phosphite on the amino group at position 5 to give compound **36**, whereas in 1,5-diaminotetrazole (**35b**) it is the amino group at the nitrogen atom that undergoes phosphorylalkylation. Taking into account the tendency of 1,5-diaminotetrazole (**35b**) to form Schiff's bases, the 'imine' pathway of the reaction resulting in the AP **37** seems to be preferential.[147]

In a search for biologically active AP, aminomethyldiphenylphosphine oxides[148] as well as bisphosphonate derivatives of tetrahydropyran, its thio and seleno analogues[149] have been synthesised recently.

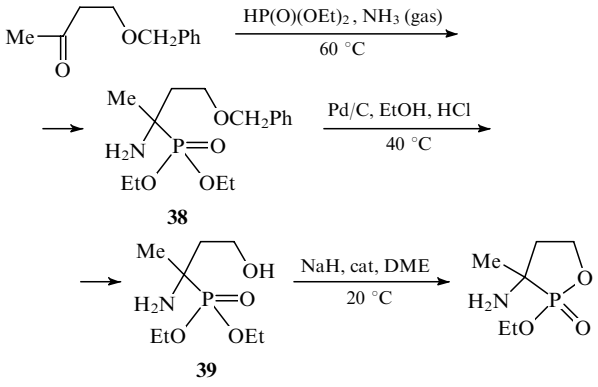


R^1 = H: R^2 = CH_2Ph, $(CH_2)_2Ph$, 2-pyridyl; R^1 = R^2 = CH_2Ph.

The use of appropriate bifunctional amines in the Kabachnik–Fields reaction allows the synthesis of heterocyclic compounds. For example, chiral phosphorylated oxazolidine is formed in a one-pot procedure from (*R*)-(−)-phenylglycinol, formaldehyde and dimethyl phosphite in boiling methanol.[150]

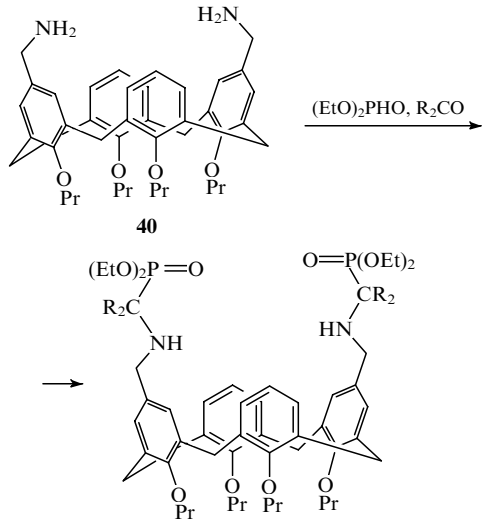


Heterocyclisation was successfully used in the synthesis of 3-amino-2-oxo-1,2-oxaphosphacyclanes.[151] A one-pot synthesis of AP **38** from 4-benzyloxy-2-butanone, ammonia and diethyl phosphite followed by its hydrogenolysis results in alkanol **39**. Intramolecular transesterification of the latter gives the 1,2-oxaphospholane.



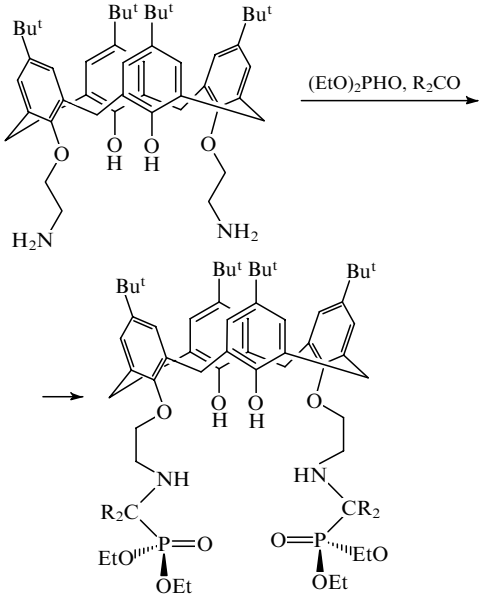
AP used in membrane extraction were obtained recently from calix[4]arene. Modified calix[4]arene platforms with (phosphorylalkyl)aminoalkyl fragments in the top and bottom rings were prepared from dialkyl phosphites and the appropriate carbonyl compounds.[60, 64]

Regiospecific amination of calix[4]arene gave compound **40**, and in the 'top' rim of its platform two phosphorylalkyl groups were introduced.

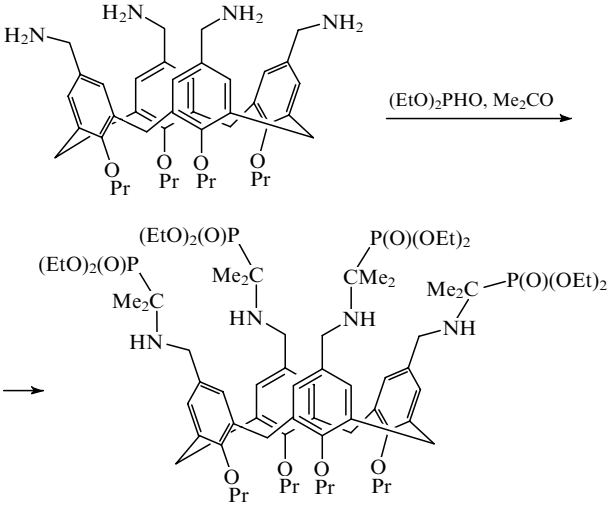


R_2 = Me_2, $(CH_2)_5$.

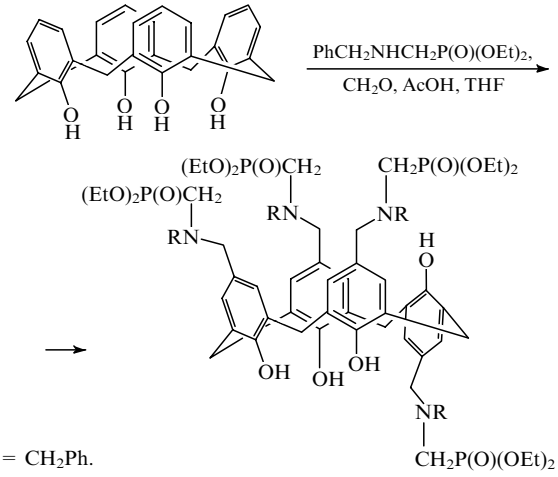
The amino phosphonate fragments in the 'bottom' rim were obtained using a calix[4]arene platform carrying β-aminoethoxy groups.



Four amino phosphonate groups were introduced in a similar way using a tetrakis(aminomethyl) derivative of calix[4]arene. As a result of the reaction, all phosphorus-containing fragments were located in the 'top' rim.



Modification of calix[4]arene with diethyl *N*-benzylaminomethylphosphonate gave a tetrasubstitution product in the 'partial cone' conformation.



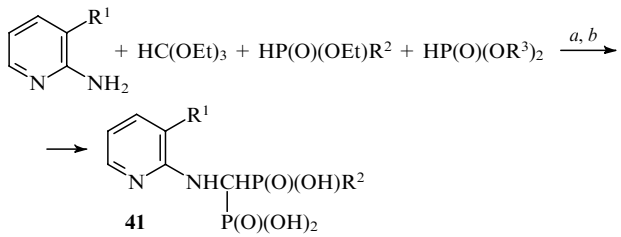
R = CH_2Ph.

Orthoformate was successfully used instead of carbonyl compounds in the classical version of the Kabachnik – Fields reaction. In this case, two phosphoryl groups rather than one can be attached to the carbon atom. Condensation of dibenzylamine and diethyl phosphite with orthoformate (1 : 3 : 1.2, refluxing for 24 h) gives dibenzylaminomethylenediphosphonate (yield 58%).[152]

$$(PhCH_2)_2NH + 2\,(EtO)_2PHO + HC(OEt)_3 \longrightarrow$$
$$\longrightarrow (PhCH_2)_2NCH[P(O)(OEt)_2]_2 + 3\,EtOH$$

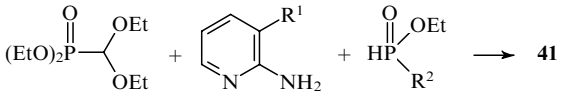
The reaction of benzylamine with one equivalent of $HC(OEt)_3$ and four equivalents of diethyl phosphite at 160 °C with subsequent acidification of the reaction mixture gave diaminomethylphosphonate $(PhCH_2NH)_2CHP(O)(OEt)_2$ in 34% yield.[152]

This version of the reaction makes it possible to introduce organophosphorus groups of different structures into an AP during one chemical process. For example, a phosphite and a phosphonite participate in a one-pot synthesis of phosphonatophosphinate **41**.[153]



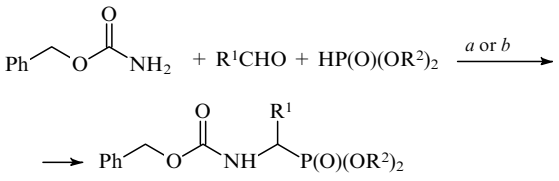
(*a*) Δ (−EtOH); (*b*) H_2O, Δ (−R^3OH); R^1 = H, Me; R^2 = Me, Bu; R^3 = Et, Pr^i.

The drawback of this method is that it gives, along with asymmetrical phosphonatophosphinates, a small amount of symmetrical bisphosphonates and bisphosphinates. This can be avoided if phosphorus-containing groups are introduced successively. For example, α-phosphonoacetal, alkylphosphonite and aminopyridines react under these conditions to give compound **41** exclusively.



The scope of the classical version of the Kabachnik – Fields reaction is expanded if carbamates, amides of carboxylic and phosphorus acids and some other compounds are used as the amine component.

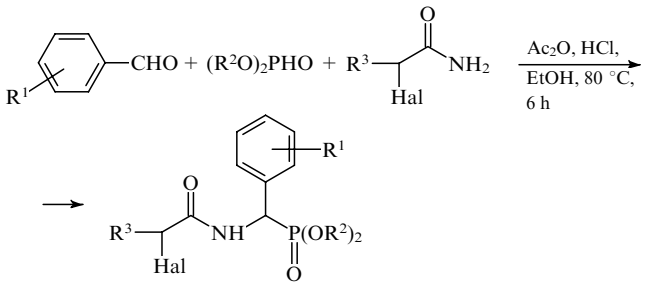
Benzyl carbamate, an aliphatic or aromatic aldehyde and diethyl phosphite react at room temperature in the presence of a mixture of acetic acid and thionyl chloride [method (*a*)] or acetyl chloride [method (*b*)] to give moderate to high yields of AP containing an *N*-benzyloxycarbonyl group, which can easily be removed if necessary.[154]



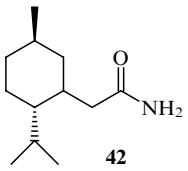
(*a*) AcOH, $SOCl_2$, 20 °C, 20 min, Δ, 2 – 12 h;

(*b*) AcCl, 0 – 5 ⟶ 20 °C (43% – 98%).

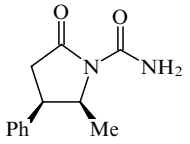
A modification of this method was suggested for the Kabachnik – Fields reaction with α-halocarboxamides.[155] Their condensation with aromatic aldehydes and hydrophosphoryl compounds occurs in the presence of an alcoholic solution of HCl or *p*-toluenesulfonic acid in acetic anhydride.



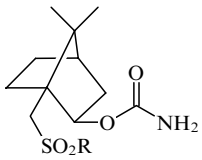
The diastereoselectivity of condensation of chiral cyclic carbamates and ureas according to the scheme of the Kabachnik – Fields reaction depends largely on the nature of the cyclic compound. The highest diastereomeric excess (*de*) in the one-pot synthesis of AP from diethyl phosphite, benzaldehyde and compounds **42** – **44a** – **c** containing an amino group is reached for derivatives of camphorsulfonic acid **44a** – **c**.[156]



42

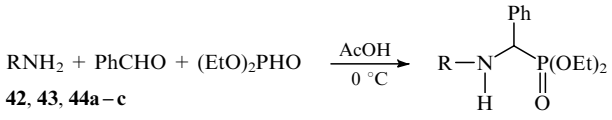


43



44a–c

R = N(cyclo-C_6H_{11})$_2$ (**a**), NPr^i_2 (**b**), C_6H_4OMe-4 (**c**).

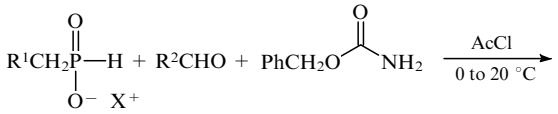


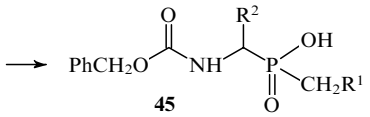
42, **43**, **44a–c**

Starting compound	**42**	**43**	**44a**	**44b**	**44c**
Yield of AP (%)	71	84	75	73	77
de (%)	14.4	34.1	99	96.4	96.2

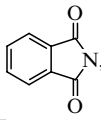
If benzaldehyde is replaced by other aldehydes (anisaldehyde, α-naphthaldehyde or *p*-tolualdehyde) in the reaction with carbamates **44**, the *de* remains at about 99%. The *de* is small (56%) only in the case of cyclohexanecarbaldehyde.

It is noteworthy that both hydrophosphoryl compounds and their salts can participate in this condensation.[157]



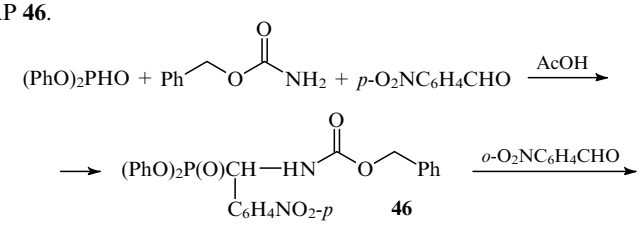


45

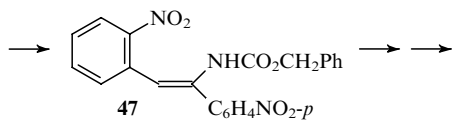
X = H,  ; R^1 = H, Pr, , EtOOCCH$_2$;

R^2 = H, Me, Et, Bu^i, Ph, *p*-$MeOC_6H_4$.

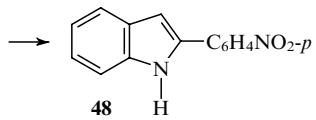
The AP **45** obtained this way were used as synthons in the development of a new approach to the synthesis of functionalised indoles.[158] The reaction between diphenyl phosphite, benzyl carbamate and *p*-nitrobenzaldehyde in acetic acid results in the AP **46**.



46

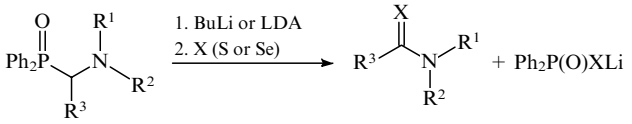


47



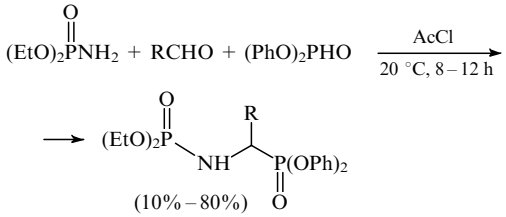
48

Dephosphonylation of amino phosphonate **46** by the Horner–Wittig–Emmons reaction with *o*-nitrobenzaldehyde gives the enamine **47**, which is converted in two steps to the C-substituted indole **48**. The use of α-aminophosphine oxide provides a convenient method for the synthesis of thio- and selenoamides.[159] In this reaction, generation of a carbanion is followed by cleavage of the P–C bond under the action of two equivalents of sulfur or selenium.



R^1, R^2 = Me, Ph, $(CH_2)_2O(CH_2)_2$; R^3 = H, Alk, alkenyl; X = S, Se.

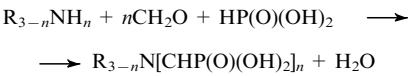
The use of acetyl chloride as the condensation agent makes it possible to introduce an organophosphorus radical to the amine centre of AP if *O*,*O*′-diethyl phosphoramidite is used as the amine component.[160]



R = Pr, Pr^i, Ph, *p*-MeC_6H_4, *p*-$MeOC_6H_4$, *p*-$Me_2NC_6H_4$.

b. Reaction of inorganic phosphorus acids

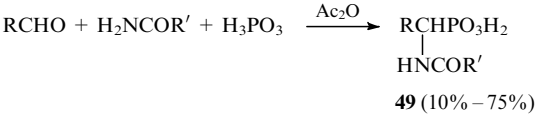
This version of the Kabachnik–Fields reaction is also named[161] the Moedritzer–Irani reaction in the name of the researchers who were the first to use inorganic phosphorus acids of the lowest oxidation state for the synthesis of APA in a three-component system 'hydrophosphoryl compound–carbonyl compound–amine'.[71]



Reaction of orthophosphorous acid with formaldehyde is known to occur almost quantitatively. Since both primary and secondary amines can be involved, the Mannich reaction mechanism is considered most probable for these reactions,[71] although other mechanisms are not ruled out either.

Attempts at expanding this version of the Kabachnik–Fields reaction to aliphatic aldehydes and ketones failed.[162] The 'imine' version of the reaction is preferable for these compounds (see below).

Acylamides readily undergo condensation with aldehydes and phosphorous acid under the action of acetic anhydride.[163]



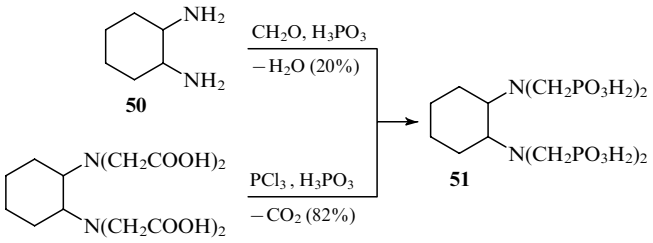
49 (10%–75%)

R = Me, Pr^i, Ph, 3-$NO_2C_6H_4$, 4-ClC_6H_4, 4-MeC_6H_4;

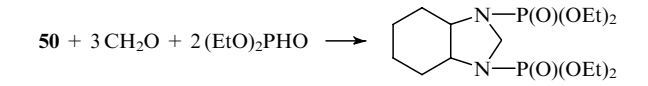
R′ = PhCOO, PhCO, Ac.

Presumably, the condensation of an aldehyde with an amide is followed by decomposition of the condensation product to APA **49**.[163]

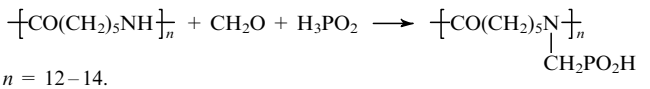
The reaction of 1,2-cyclohexanediamine **50** with formaldehyde and phosphorous acid occurs in a low yield.[161] The yield of tetraphosphonate **51** increases considerably if 1,2-cyclohexanediaminotetraacetic acid is phosphorylated with a mixture of H_3PO_4 and PCl_3.



The reaction of 1,2-cyclohexanediamine **50** with formaldehyde and diethyl phosphite results in a bicyclic bisphosphonate.[161]

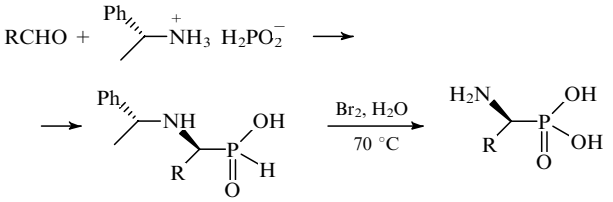


Hypophosphorous acid in a mixture with formaldehyde undergoes polymer-analogous Kabachnik – Fields reaction with polycaprolactam. This method has been used for the synthesis of materials with low flammability.[164]



$n = 12-14$.

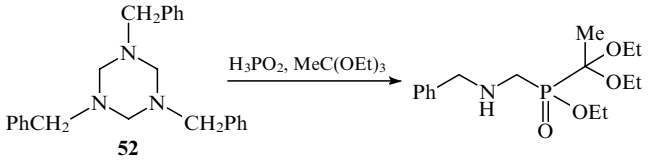
Salts of hypophosphorous acid with (*R*)-(+)- or (*S*)-(−)-1-phenylethylamine react with aldehydes in boiling ethanol to form homochiral APA.[165] The protective group at the nitrogen atom is easily removed by a standard method, and the intermediate phosphonous acid is converted into the APA.



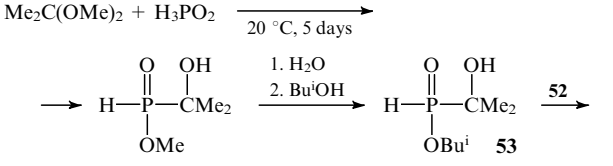
R = Pr^i, Bu^i, cyclo-C_6H_{11}, Ph, $PhCH_2$.

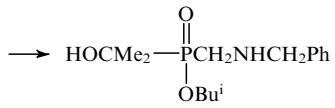
Recently, an efficient method for the synthesis of AP has been developed in which 80% – 90% aqueous solutions of hypophosphorous acid is used as the hydrophosphoryl compound. In this case, orthoesters and acetals were used instead of carbonyl compounds, and 1,3,5-tribenzylhexahydro-1,3,5-triazine **52** was chosen as the amine component.

The reaction of triazine **52** with triethyl orthoacetate and H_2PO_3 gives an amino phosphinate under very mild conditions and in high yield.[166]



A three-step synthesis of a phosphinate containing both an α-hydroxy and an α-amino group in different *P*-alkyl substituents simultaneously[167] involves the initial formation of a phosphonite from 2,2-dimethoxypropane and hypophosphorous acid, its subsequent transesterification to the more hydrolytically stable isobutyl phosphonite **53** and the reaction of the latter with triazine **52** to give the AP.

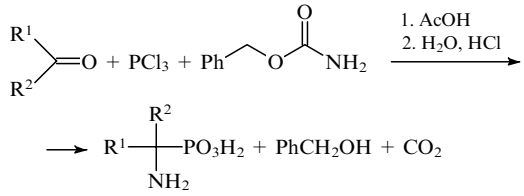




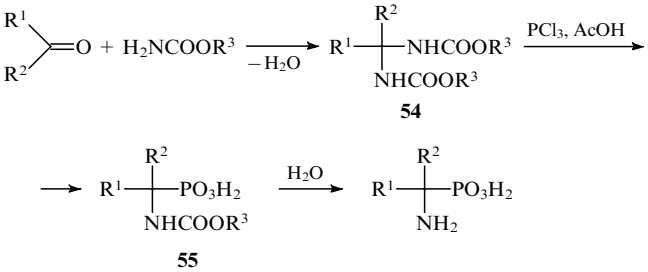
In these cases, commercial 50% hypophosphorous acid can be used following its concentration *in vacuo*. The efficiency of this approach in comparison with the methods based on the use of anhydrous H_3PO_2 is noteworthy (see Ref. 166 and references cited therein).

2. Reactions of trivalent phosphorus chlorides

This version of the Kabachnik – Fields reaction based on phosphorus trichloride was used in the synthesis of APA in 1978.[168]

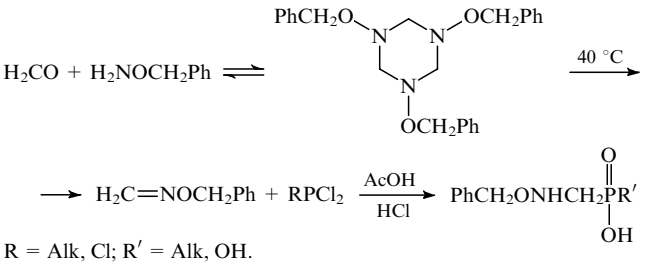


The method is equally applicable to alkyl(aryl)dichloro- and dialkyl(aryl)chloro-phosphines.[169,170] It is considered[170] that the process starts with condensation of an amide with a carbonyl compound. The alkylidenebisamide **54** thus formed is phosphorylated to AP **55**, hydrolysis of which results in an APA.



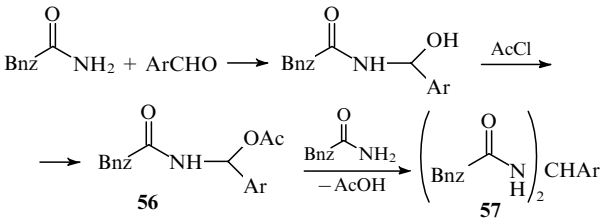
The method was expanded to a wide set of amides, carbonyl compounds and P(III) chlorides (see Ref. 171 and references cited therein). Another interpretation of aminomethylation of P(III) chlorides is considered in detail in Ref. 171.

The method based on the use of PCl_3 was applied successfully to the synthesis of α-aminoarylalkylphosphonic acid[36] and its monoesters,[172] as well as a large number of APA containing fluorinated aryl substituents.[173] Aminomethylol synthons[174] or hexahydrotriazine derivatives were also used as aminoalkylating agents.[174,175] The latter compounds have repeatedly been used in the synthesis of AP. *N*,*N*,*N*-Tribenzyloxyhexahydrotriazine is reversibly formed in the condensation of formaldehyde with *O*-benzylhydroxylamine and undergoes conversion to *O*-benzylformaldoxime on gentle heating, which reacts with P(III) chlorides in acidic medium to give the corresponding APA.[175]

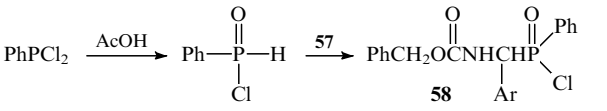


R = Alk, Cl; R′ = Alk, OH.

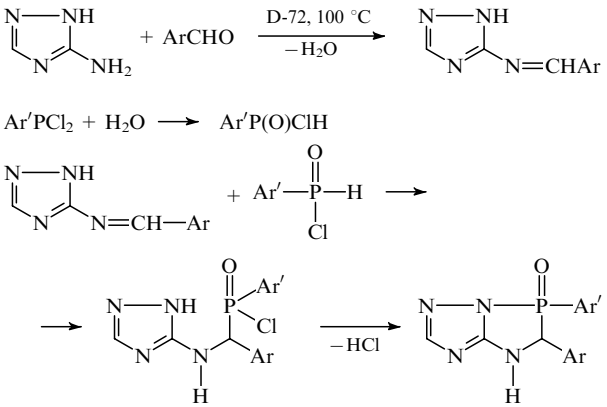
The mechanism of aminomethylation of P(III) chlorides is rather complex. It can be different in each particular case. For instance, in the system 'benzyl carbamate – aromatic aldehyde – phenyldichlorophosphine – acyl chloride',[176] the addition of the amide to the aldehyde occurs first, and then acylation of the resulting acylaminoalkanol produces compound **56**.



The reaction of the acylated carbamate **56** with the starting amide gives the diamide **57**. The acetic acid evolved converts phenyldichlorophosphine into phenylphosphinic chloride. The latter cleaves the N–C bond in diamide **57** and converts it into the final amidomethylphosphinic chloride **58**.



A similar reaction of aryldichlorophosphines, aromatic aldehydes and 5-amino-1,2,4-triazole occurs in the presence of cation-exchange resins (D-72, Amberlyst-15) and results in 6-phospha-4,5,6-trihydroimidazo[2,3-*e*]-1,2,4-triazole. It is believed[177] that the Schiff's base is formed first and then adds arylphosphinic chloride.



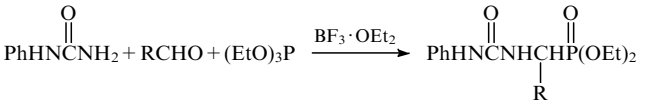
Intramolecular dehydrochlorination of the addition product results in the final bicycloamidophosphinate.

3. Reactions of neutral phosphites and their analogues

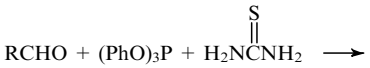
Reactions of natural α-amino acids with trialkyl and triaryl phosphites have long and successfully been used in peptide synthesis. As a rule, the non-classical Arbuzov reaction occurs in this case (see, *e.g.*, Ref. 178).

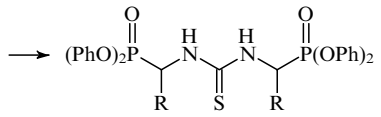
A three-component system 'phosphite–carbonyl compound–amine' was successfully used in a number of syntheses of AP derivatives of urea and thiourea.

Triethyl phosphite undergoes condensation with an aldehyde and phenylurea in the presence of boron trifluoride etherate on refluxing in toluene to give the corresponding AP.[179]

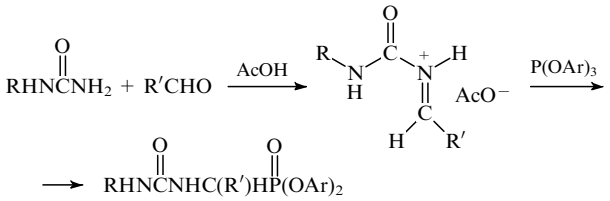


A similar reaction of a thiourea[180] and *N*-substituted thioureas[181] occurs with triphenyl phosphite in the presence of glacial acetic acid. Under certain conditions, both amino groups of thiourea can be involved in this reaction.



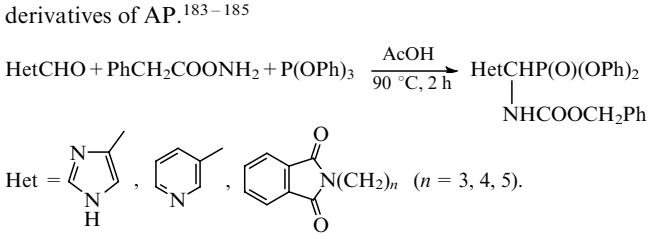


The stereochemistry of condensation of chiral carbamates and thioureas with benzaldehyde or aliphatic aldehydes and triaryl phosphites in the presence of acetic acid depends on the chirality of the starting amine: (+)-AP are obtained from chiral (+)-carbamates and ureas; accordingly, (−)-AP are formed from (−)-amides.[182] The reaction occurs *via* an immonium salt with subsequent *syn*- or *anti*-attack of the phosphite on the iminium carbon atom.

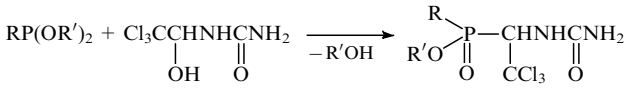


Ar = Ph, 2-MeC$_6$H$_4$.

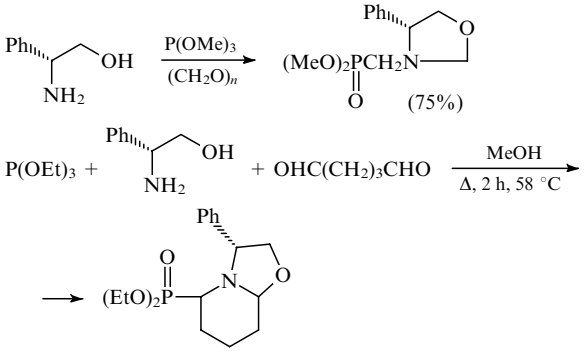
The 'triphenyl phosphite' version of the Kabachnik–Fields reaction was successfully used for the synthesis of *C*-hetaryl derivatives of AP.[183–185]



The mechanism of these reactions has not been discussed in detail. However, in this case the reaction begins most probably with the interaction of the aldehyde with the amino component. The smooth reaction of phosphinites and phosphonites with chloralurea[186] can probably serve as a model of the second step of the 'trialkyl phosphite' version of the Kabachnik–Fields reaction.

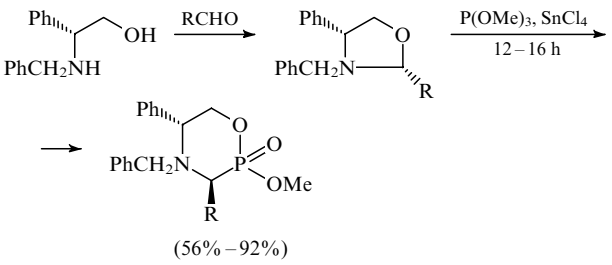


As in the classical version of the Kabachnik–Fields reaction, in this case it is possible under certain conditions to carry out cyclisation by the one-pot technique, for example, in the N-phosphonoalkylation of (*R*)-(−)-phenylglycinol;[187,188] in the latter case glutaraldehyde replaces formaldehyde in a three-component mixture.[188]

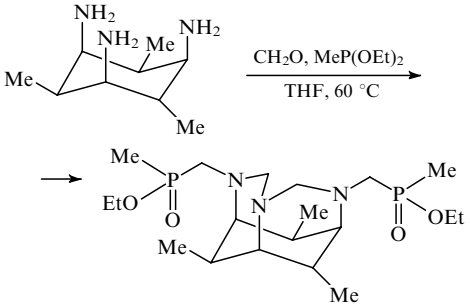


The reaction can also be carried out stepwise.[187] For example, *N*-benzylphenylglycinol reacts with an aldehyde to form oxazolidine with high diastereomeric excess. The latter reacts with

trimethyl phosphite in the presence of $SnCl_4$ to give an oxazaphosphorinane.



Polydentate ligands, *viz*., bisphosphinate triaminocyclohexanes, were obtained by the 'phosphonite' version of the Kabachnik – Fields reaction with diethyl methylphosphonite and paraform.[189]



It is possible to introduce two phosphorylmethylene groups into a 1,3,5-triamino-2,4,6-trimethylcyclohexane molecule due to the fact that all of its methyl groups occupy the equatorial positions, while all amino groups occupy the axial ones.

4. Reactions in two-component systems

As discussed above, reactions in two-component systems resulting in APA and their esters and involving interactions in the pairs hydrophosphoryl compound – imine and hydroxy phosphonate – amine are, in essence, separate steps of the Kabachnik – Fields reaction. It is often impossible to distinguish between three- and two-component systems. This can depend on the order of mixing the reactants.

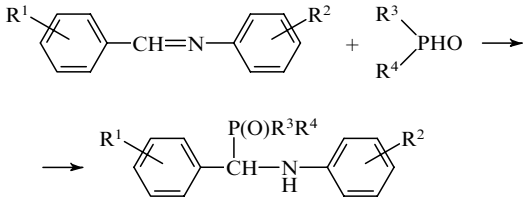
On the other hand, it has repeatedly been noted that it is often preferable to carry the reaction out in a stepwise way rather than to use a one-pot three-component process: the chemical yield and *de* of the AP are generally higher in two-component processes. The methods that have been developed most extensively recently include enantioselective addition of hydrophosphoryl compounds to imines and replacement of the hydroxy group in hydroxy phosphonates by the amino group under the Mitsunobu reaction conditions.[190] We shall give these processes the most attention in our review.

a. Addition of hydrophosphoryl compounds to imines

The addition of hydrophosphoryl compounds to imines, discovered simultaneously with the Kabachnik – Fields reaction, corresponds to the Pudovik reaction type[20] and has been covered rather comprehensively in reviews.[6,10] Some examples of asymmetric synthesis of AP in the 'imine' version are discussed in another review.[18] However, many new studies have been published in recent years which are to some extent relevant to the problem under discussion. Important data on the mechanism of the 'imine' method and the catalytic effects observed have been obtained.

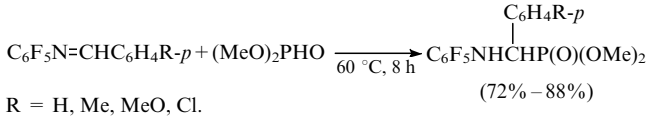
The 'imine' method should be preferred when choosing the strategy for the synthesis of AP if it is necessary, first, to reach the maximum diversity of functional groups at the N and C atoms in the target AP and, second, to enable conditions for the maximum stereoselectivity of addition of hydrophosphoryl compounds to the C = N bond.

The reaction of hydrophosphoryl compounds with the Schiff's bases studied in detail by Pudovik[20] continues to draw the attention of researchers due to the simplicity of the procedure and useful properties of the AP obtained in this way.



The reaction occurs in a condensed phase or in a solution in the presence of acidic and basic catalysts or without them at all, sometimes upon simple mixing of the reagents.[191,192]

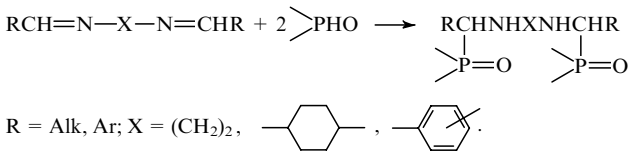
The reaction of hydrophosphoryl compounds with the Schiff's bases containing fluorine atoms in the *N*- and/or *C*-aryl fragments (Ar = 2-, 3-, 4-FC_6H_4; 2-, 3-, 4-$F_3CC_6H_4$; 2-, 4-$F_3CCOC_6H_4$; 3,4-$F_2C_6H_3$ and others)[193–195] allows one to obtain biologically active fluorinated AP. The reaction occurs on heating of the starting reagents to 90 – 110 °C without a catalyst. *N*-Pentafluorophenylaldimines add dimethyl phosphite even more readily.[196]



R = H, Me, MeO, Cl.

Aryl-substituted AP are formed as a mixture of diastereomers (chiral α-carbon atom). The presence of each of the stereomers is confirmed by analysis of ^1H and ^{13}C NMR spectra. In some cases, these diastereomers could be separated by column chromatography.

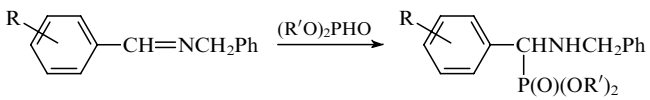
Bisamino phosphonates of various structures were synthesised by addition of hydrophosphoryl compounds to bisimines.[192–195]



R = Alk, Ar; X = $(CH_2)_2$, .

The NMR and mass spectroscopic, as well as other characteristics of bisamino phosphonates have been studied.[197–199]

Numerous *N*-substituted AP derivatives, mainly *N*-benzyl ones, were obtained for use in peptide synthesis. The addition of hydrophosphoryl compounds to *N*-benzylbenzylideneimines occurs very readily. Lower dialkyl phosphites react at room temperature to give the corresponding AP in very high yields.[36,200,201]

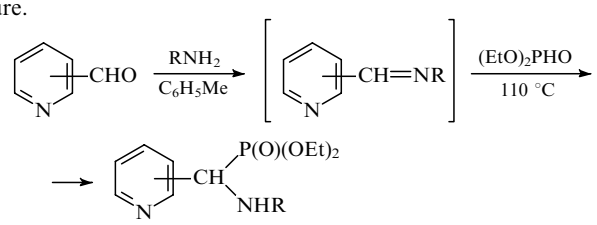


Longer reaction time and higher temperature are needed with the lengthening of the alkyl chain in the hydrophosphoryl compound (R′). For example, at R = n-C_5H_{11}, the reaction at 80 °C takes 8 h or longer. A similar effect is caused by replacement of the C-aryl group by C_6F_5 (however, there are exceptions: see Ref. 196).

N-Protected alkylideneimines,[202] perfluoroisopropylidene-*N*-acylimine,[203] *N*-tritylmethyleneimine,[75] and many other compounds (see the review[18] and references cited therein) also add hydrophosphoryl compounds rather easily, usually on heating in the absence of catalysts, giving AP in high yields.

The 'imine' method is widely used in the synthesis of hetaryl derivatives of AP. In this case, the structures of heterocyclic

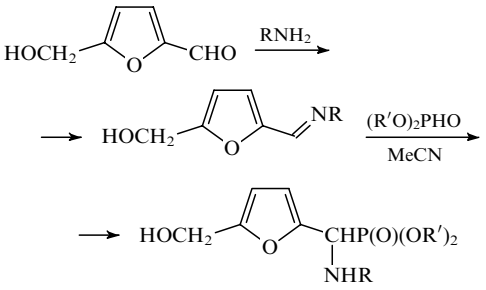
fragments can be varied widely. An array of *C*-pyridine derivatives have been obtained by addition of diethyl phosphite *in situ* to the appropriate Schiff's bases.[204] 1-, 2- and 3-formylpyridines readily react with amines in a toluene solution, forming the corresponding aldimines, which are hydrophosphorylated in a one-pot procedure.



R = Bu, Ph, CH_2Ph, $CHPh_2$.

One-step syntheses of 1-(2-aminoethyl)pyridyl-1-arylmethylphosphonates[205] and analogous APA monoesters were carried out in a similar way.[206] It is noteworthy that the addition of dialkyl phosphites to the Schiff's bases containing a pyridine fragment under mild conditions (at room temperature, in the absence of catalysts) has been reported.[207]

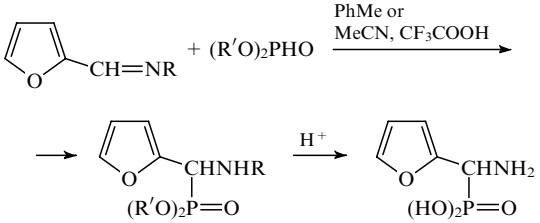
The results obtained in a study of the reaction of hydrophosphoryl compounds with imines containing furan and thiophene rings are also worth noting. 5-Hydroxymethylfurfural readily reacts with ethyl- and benzylamines to give the corresponding aldimines.



R = CH_2Ph, CH_2–furyl, Bu^t, (*R*)- and (*S*)-CHMePh; R′ = Et, CH_2Ph.

Subsequent addition of diethyl phosphite gives (in the case of chiral amines) a diastereomeric mixture of AP in 2 : 1 ratio.[208] When pure enantiomeric amines are used, the resulting imines react with dibenzyl phosphite to give a mixture of AP, from which individual stereoisomers can be isolated by chromatography.

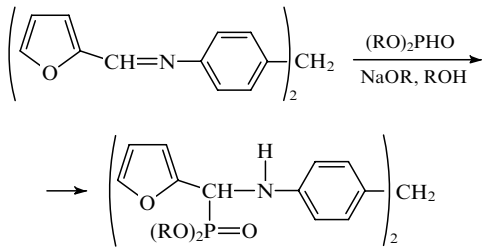
The same scheme was used for the synthesis of (2-furyl)aminomethylphosphonic acid.[209]



R = CH_2Ph, CPh_3; R′ = Et, CH_2Ph.

N-Benzylated imines add hydrogen phosphites in toluene without catalyst or in acetonitrile with a catalytic amount of CF_3COOH. *N*-Tritylated imines give an AP just upon mixing the reagents. It was reported that an attempt at detritylation of an AP resulted in destruction of the AP with cleavage of the P–C bond. Similar fragmentation of AP has also been observed in other cases.[203, 204, 210]

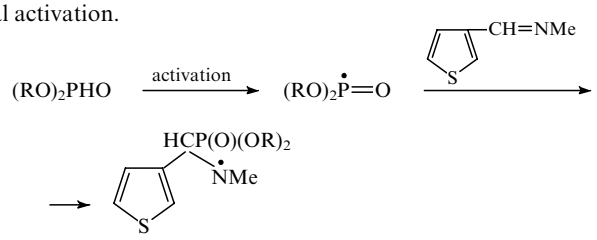
Bis(amino phosphonates) containing terminal 2-furyl groups were obtained and used as monomers for the synthesis of polymeric materials with low flammability.[211, 212]



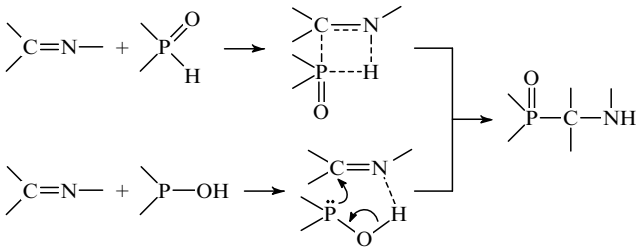
The addition of the hydrophosphoryl compound occurs at room temperature in the presence of catalytic amounts of sodium alkoxide.

Important observations related to the activation of addition of dialkyl phosphites to hetarylimines with an *N*-thiophene or *N*-pyrrole fragment were obtained.[213, 214] The addition of a hydrophosphoryl compound can occur on prolonged heating (72–96 h) of a mixture of the reactants at 60 °C. The process is accompanied by formation of side products. Attempts to optimise conditions of the synthesis of AP by carrying out the reaction in various solvents failed in general: this only increased the time of conversion.

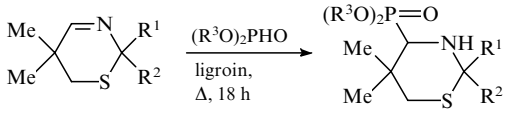
On the other hand, sonochemical (ultrasonic) activation of the addition reaction was found to be rather efficient. Both in a condensed phase and in a solution, even short sonication increases abruptly the temperature of the reaction mixture, hence the yield of AP increases and the reaction time is decreased to 5–120 min. This phenomenon was explained[213] using EPR spectroscopy with a spin trap: phosphinyl radicals were detected during sonochemical activation.



The uninitiated reaction occurs by a concerted mechanism with a four- or five-centred transition state. This mechanism agrees with the stereochemical result of addition to furfuraldimine.[208]

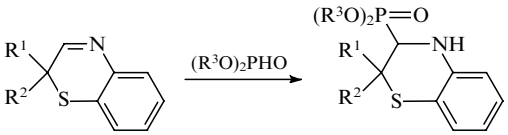


A method for the introduction of heterocyclic fragments into an AP molecule by addition of a hydrophosphoryl compound to the endocyclic C=N bond in unsaturated five- and six-membered cyclic imines was developed. In these cases, the amino phosphonate fragment C–N is included in the heterocycle. Chiral 2*H*-5,6-dihydro-1,3-thiazines react with dialkyl phosphites to give diastereomeric AP in a ratio from 52 : 48 to 88 : 12, depending on the substituents in the imine and in the phosphite.[215]

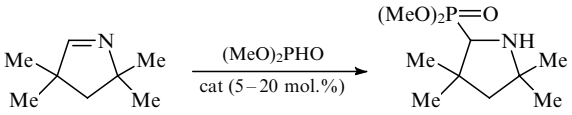


R^1 = H, Me, Et; R^2 = Me, Et, Bu^t, CMe_2CH_2Cl; R^1, R^2 = $(CH_2)_4$, $(CH_2)_5$; R^3 = Me, Et.

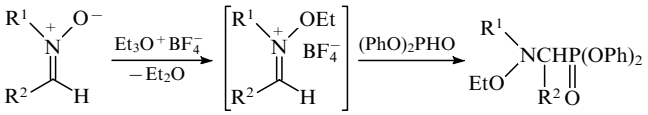
The addition of hydrophosphoryl compounds to 2*H*-1,4-benzothiazines and 2*H*-1,3-oxazolidines occurs under the same conditions.[100]



Hydrophosphorylation of cyclic imines catalysed by chiral lanthanide catalysts results in a high *de* (up to 98%).[216] In the presence of chiral titanium catalyst, the reaction is nonstereospecific. The mechanism of asymmetric induction of cyclic imines has not been discussed.

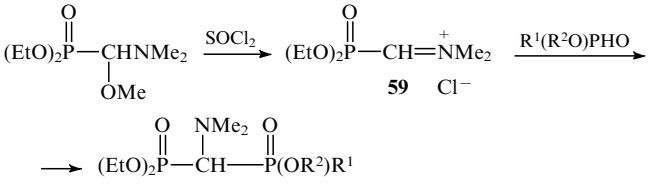


Hydrophosphorylation of oximinium salts, which is a version of the 'imine' method for AP synthesis, has been performed in only a few cases. In our opinion, this is rather a promising method. The addition of diphenyl phosphite to the $C=N^+$ bond of a nitrone is carried out in the presence of an alkylating agent, *viz*., triethyloxonium tetrafluoroborate, at room temperature in 3 h.[217] The processes is nonstereospecific; however, rather high enantioselectivity is observed for chiral nitrones [R^1 = CH(Me)Ph].



R^1 = Me, CH(Me)Ph; R^2 = Ph, $MeOC_6H_4$; R^1, R^2 = $(CH_2)_3$.

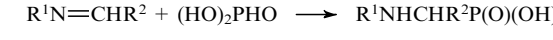
The addition of alkyl phosphinites to phosphonyliminium salt **59** also occurs nonstereospecifically.[218] In this case, two chiral centres are induced in the AP, *viz*., the α-carbon atom and the phosphinate phosphorus atom.



R^1 = Me, Ph; R^2 = Et, Bu.

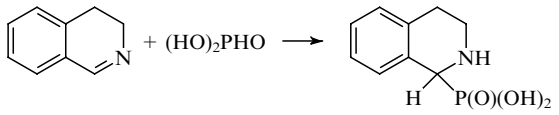
Broad diversity of possibilities for the synthesis of AP by the 'imine' pathway is due to the variability of the substituents not only in the imine but also in the phosphorus-containing addend. Inorganic phosphorus acids and various silylated organophosphorus compounds have been used for the synthesis of APA.

It has already been noted[162] that attempts to use phosphorous acid in the classical three-component version of the Kabachnik – Fields reaction was not always successful. The 'imine' method turned out to be more efficient.[162]

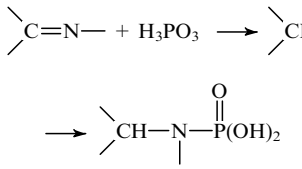


R^1 = Me, Et, Bu^t, $PhCH_2$; R^2 = Pr^i, Ph, 4-ClC_6H_4, 2-HOC_6H_4.

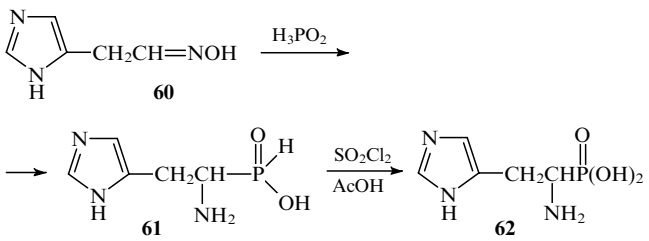
The addition to the intracyclic bond of 3,4-dihydroisoquinoline, resulting in 1,2,3,4-tetrahydroisoquinoline-1-phosphonic acid, occurs successfully.[162] It is believed that the reaction occurs in an autocatalytic mode with preliminary protonation of the nitrogen atom.



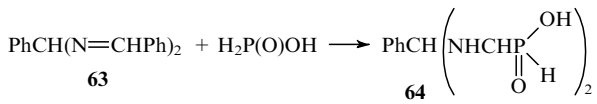
Under certain conditions, phosphorous acid can be a reducing agent with respect to an imine. In this case, it is not the AP that is formed as the final product but rather an isomeric amido phosphate, which is believed[162] to result from the reaction of the intermediate amine with metaphosphoric acid.



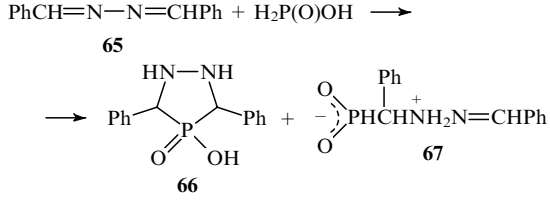
The phosphorus analogue of histidine **62** was obtained by the addition of hypophosphorous acid to the oxime **60**. The phosphinic acid **61** obtained in 19% yield was transformed in an almost quantitative yield into the target product **62** by oxidation with sulfuryl chloride in glacial acetic acid.[219]



The addition of inorganic phosphorus acids to both C=N bonds of bisimines was carried out. The reaction of geminal diimine **63** with hypophosphorous acid[220] gives, contrary to expectations, bisphosphinic acid **64** rather than a cyclic phosphonic acid.

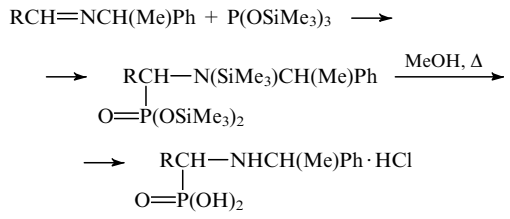


A similar reaction of diimine **65**, which is carried out by prolonged storage of the reaction mixture (20 °C, 20 – 25 days), gives a five-membered cyclic phosphinic acid **66**[221] and a linear product **67** formed due to addition to one of the C=N bonds.



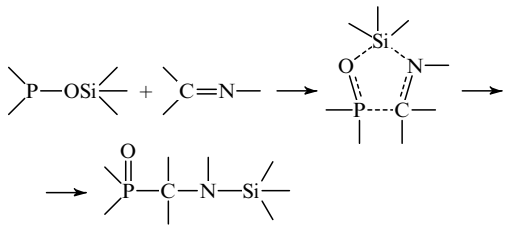
It is of note that the ratio of products **66** : **67** in a crystalline state is 1 : 4, whereas their ratio is 1 : 1 in dioxane solution, according to ^{31}P NMR data.[221] The possibility of mutual transformation of compounds **66** and **67** during dissolution and isolation from the solution cannot be ruled out.

Silyl ethers of phosphorus acids of low oxidation states behave in reactions with imines similarly to phosphorous acid, its esters and other hydrophosphoryl compounds. For example, tris(silyl) phosphite in the presence of Lewis acids ($ZnCl_2$, $BF_3 \cdot OEt_2$) or strong protic acids (CF_3COOH, *p*-$MeC_6H_4SO_3H$) forms a product of phosphonosilylation of imines.[222] On refluxing in methanol, desilylation of the adduct occurs, resulting in the corresponding APA isolated as a hydrochloride.

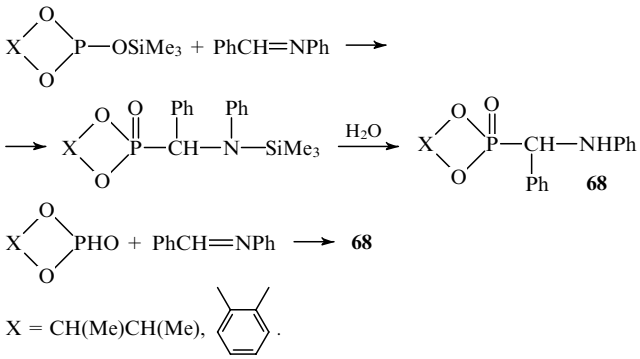


R = Me, Pr^i, Ph.

This strategy has been widely used later in the synthesis of AP. For example, dialkylsilyl phosphites can be easily added to imines. It is believed[223] that this involves concerted 1,2-addition with formation of a five-centred activated complex.[224]

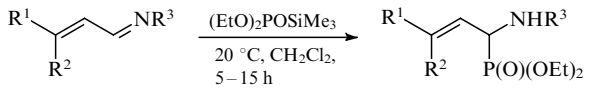


The easily hydrolysable adducts obtained by addition of cyclic silyl phosphites to benzylideneaniline (80 °C, 2 h, benzene) could not be isolated in the pure state. Their hydrolysis products **68** are identical with the AP synthesised from an imine and cyclic hydrogen phosphites.[225]



X = CH(Me)CH(Me), .

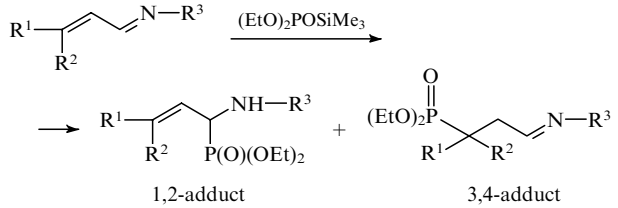
Enimines containing aromatic substituents at the C and N atoms react with silyl phosphites to give 1,2-adducts, *i.e.*, products of addition to the C = N bond (see Ref. 226).



R^1, R^2 = Ph, Me;

R^3 = Pr^i, Bu^n, Bu^t, Ph, 4-MeOC$_6$H$_4$, 4-O$_2$NC$_6$H$_4$, 2,4,6-Me$_3$C$_6$H$_2$.

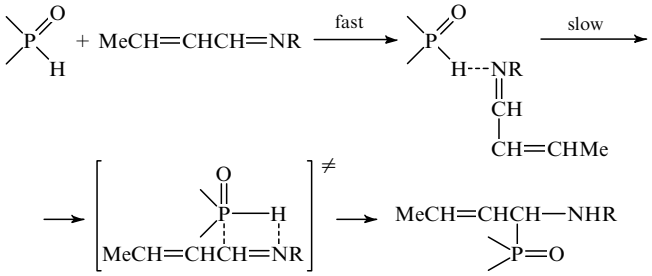
The addition of silyl phosphites to aliphatic enimines under the same conditions gives a mixture of products of 1,2-addition to the C = N bond and 3,4-addition to the C = C bond containing no silyl groups, obviously due to hydrolysis.



1,2-adduct 3,4-adduct

For imines with R^1, R^2 = Me and R^3 = Bu^n or Pr^i, the isomer ratio is 95 : 5 in favour of the 1,2-adduct. In the case of a sterically hindered enimine (R^3 = Bu^t), the 3,4-adduct predominates in the reaction products (ratio 35 : 66).

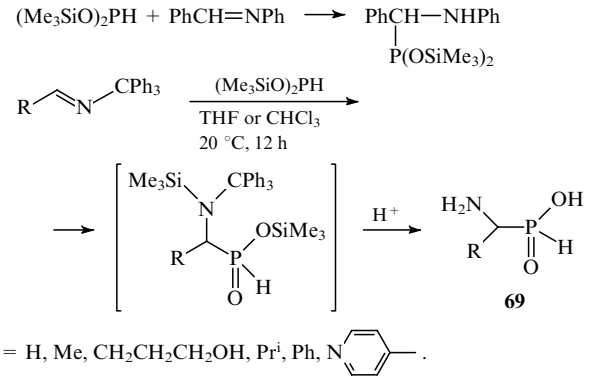
A detailed study of the reaction of enimines with hydrophosphoryl compounds showed that it always involves the imine fragment of the enimine. Kinetic[227,228] and thermochemical[65] studies made it possible to establish the hydrophosphorylation mechanism.



R = cyclo-C$_6$H$_{11}$.

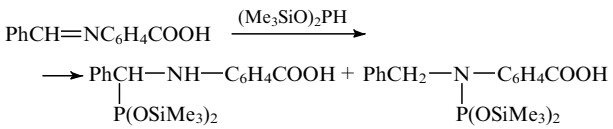
The fast formation of the pre-reaction H-complex is followed by the slow step of addition of the hydrophosphoryl compound *via* a four-centred transition state.

Bis(trimethylsilyl) hypophosphite almost instantly adds to imines even at 0 °C, giving adducts which easily undergo hydrolysis and oxidation in air. Based on spectral studies, the NH-phosphonite structure with three-coordinate phosphorus is assigned to the adduct formed.[207,229] The reaction of bis(trimethylsilyl)hypophosphite with *N*-tritylimines is believed to occur[230] with cleavage of the Si–O bond to give phosphinate **69**. In this case, the structure of the adduct was not studied.



R = H, Me, CH$_2$CH$_2$CH$_2$OH, Pr^i, Ph, N .

It is remarkable that the reaction of weakly basic bis(trimethylsilyl) hypophosphite with *N*-benzylideneaminobenzoic acid can involve the attack by the P(III) atom both on the carbon and nitrogen centres of the imine.[231]



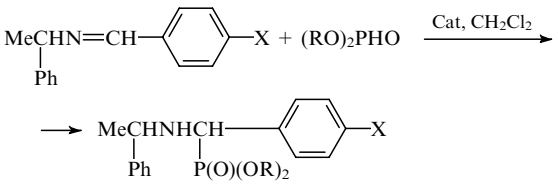
It has repeatedly been noted that the possibility to carry out a stereocontrolled reaction is of great importance when one selects the strategy for the synthesis of APA and their derivatives. Obviously, the 'imine' method, which assumes the formation of a concerted cyclic transition state, is the method of choice.

Sometimes a high *de* is reached in other methods as well.[18] Catalytic methods to control the stereochemical result of the hydrophosphorylation of imines have been suggested in recent years.

The effect of electronic, steric and external (catalyst, medium) reaction conditions on the stereoselectivity of hydrophosphorylation of imines have been revealed using molecular mechanics methods[232] and by analysis of structural and other factors.[233]

For example, the substituents in the benzene ring weakly affect both the chemical yield and the *de* in the reaction of imines obtained from 1-phenylethylamine and *para*-substituted benzaldehydes with dialkyl phosphites[234] (Scheme 5).

Scheme 5



70

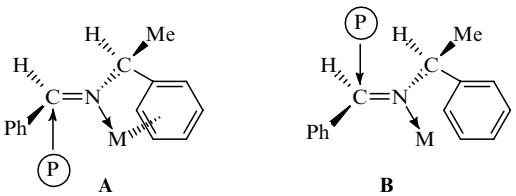
X	H	Me	OMe	Cl	Br	F
Yield of **70** (%)	80	84	72	79	77	80
de (%)	61	54	60	56	54	56

R	Me	Et	Pr^i	Bu^n	Bu^i	Ph
Yield of **70** (%)	85	85	61	74	72	78
de (%)	43	61	83	68	71	80

Catalyst	$AlCl_3$	$BF_3 \cdot OEt_2$	$ZnCl_2$	TsOH	–
Yield of **70** (%)	77	80	75	72	65
de (%)	70	61	−30	−50	−16

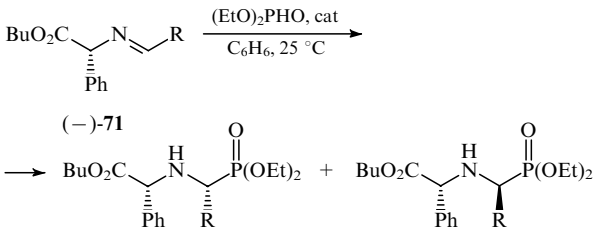
The increase in the volume of substituents at the phosphorus atom decreases the chemical yield but increases the *de* The yield and *de* are considerably affected by catalysts used for this purpose, such as Lewis acids. A negative *de* upon changing the catalyst means the predominance of the other enantiomer, *i.e.*, the change in the direction of stereoinduction.

In the general case, a pronounced effect of catalysis is observed: the degree of conversion increases in comparison with non-catalysed addition. However, a catalyst basically affects the ease of the reaction. A catalysed process occurs at room temperature, while a non-catalysed one requires heating of the reaction mixture to 140 °C. The different effect of $AlCl_3$ and BF_3 on *de*, on the one hand, and $ZnCl_2$ and TsOH, on the other, is explained[234] by the different character of the donor-acceptor interaction between the imine and the catalyst. Whereas Lewis acids form **A**-type chelate complexes due to the transfer of *n*- and π-electron density to the vacant orbitals of the central atom with *s-cis*-arrangement of the C=N fragment and aryl substituent, $ZnCl_2$ and TsOH interact only with the imine nitrogen atom, causing a P-nucleophile to attack an imine in conformation **B**.



A **B**

The effect of catalysts[72] and of the way of the phosphite anion generation[235] on the stereochemistry of the hydrophosphorylation of imines containing a complementary functional group that can provide chelation has been studied in detail. The imine **71** adds diethyl phosphite without a catalyst in 120 h. In the presence of Lewis acids or CF_3COOH, the reaction occurs faster. In all cases, a mixture of diastereomers **72a** and **72b** with low *de* is formed.

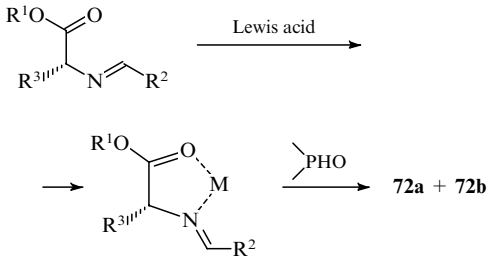


(+)-**72a** (major product) (−)-**72b** (minor product)

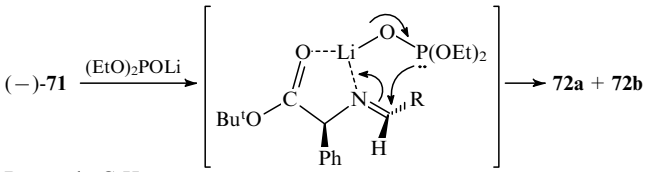
R = cyclo-C_6H_{11}.

Catalyst	Time /h	Yield (%)	*de* (%)
–	>120	87	38
$ZnCl_2$	7	84	48
$MgCl_2$	>48	40	38
CF_3COOH	>48	48	14

It is believed that the stereocontrolling role of Lewis acids consists in the formation of chelates. However, this effect appears to be insufficient to ensure high diastereoselectivity of the hydrophosphorylation step.



At the same time, high diastereoselectivity is reached if lithium diethyl phosphite is used.

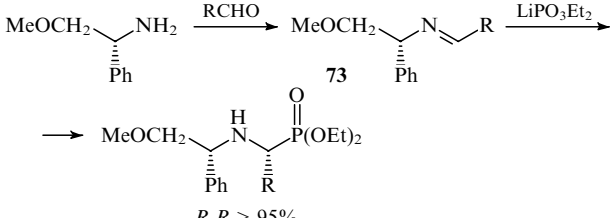


R = cyclo-C_6H_{11}.

Conditions	Yield (%)	*de* (%)
$(EtO)_2PHO$, Bu^tOLi, CH_2Cl_2, −70 to 25 °C	38	94
$(EtO)_2PHO$, BuLi, THF, −78 to 25 °C	75–80	94–96

The chelate structure of the intermediate with *trans*-arrangement of the nucleophile and the stereo-controlling phenyl group is responsible for this impressive stereochemical result. The yield of the adduct depends on the reaction conditions and the method of generation of the phosphite anion. The best result was achieved using butyllithium as the base.

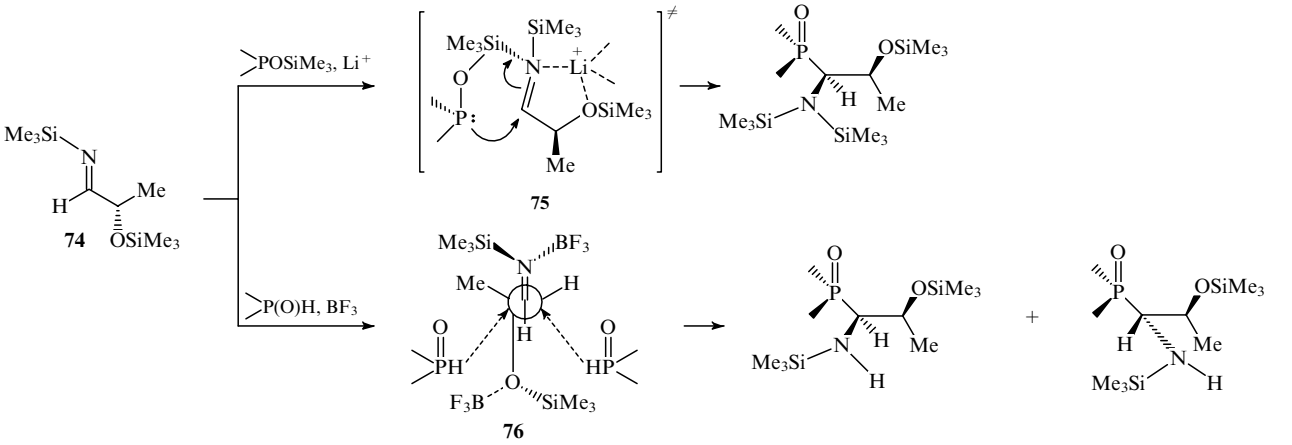
The stereochemically individual imine **73** obtained by the condensation of the appropriate amine with cyclohexanecarbaldehyde adds lithium diethyl phosphite to give the *R,R*-isomer of an *N*-protected AP with *de* > 95%.[236]



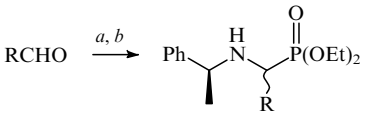
R,R > 95%

R = cyclo-C_6H_{11}.

Scheme 6



The reaction of the same aldehyde with diethyl phosphite and (*S*)-α-phenylethylamine is less stereospecific: a mixture of diastereomeric AP (ratio *S*,*R* : *S*,*S* = 5 : 1) is formed (see Ref. 236).

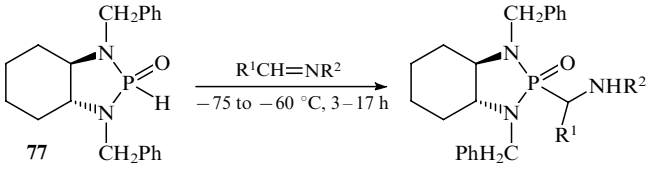


R = cyclo-C_6H_{11};

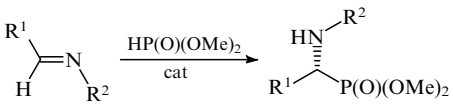
(*a*) (*S*)-PhCH(Me)NH_2, MeOH; (*b*) 3 HP(O)$(OEt)_2$, 3 days, 25 °C.

High stereospecificity of reactions was achieved by addition of phosphites to bis-silylated imine **74** in the presence of lithium ions (Scheme 6).[237] Enantiofacial preference of attack on the imine carbon by the P(III) atom is due to the formation of a highly-organised cyclic transition state **75** due to chelation by a Li^+ ion. The addition of dialkyl phosphites to the imine **74** catalysed by BF_3 is not accompanied by formation of a cyclic transition state and/or intermediate. In this case, the attack by a phosphite in acyclic complex **76** can occur on the two sides with equal probability. This causes the formation of a diastereomeric mixture of products.

The absence of stereoselectivity was also noted in the case of boron trifluoride-catalysed addition of chiral cyclic diamidophosphite **77** to imines.[238] The reaction occurs under very mild conditions; it is also possible to use $TiCl_4$ as the catalyst, while $SnCl_4$ chlorinates the cyclophosphite to the corresponding chlorophosphate.



Catalytic asymmetric synthesis of AP with the use of a wide range of imines and dimethyl phosphite was carried out in the presence of an asymmetric lanthanide-based catalyst.[33]

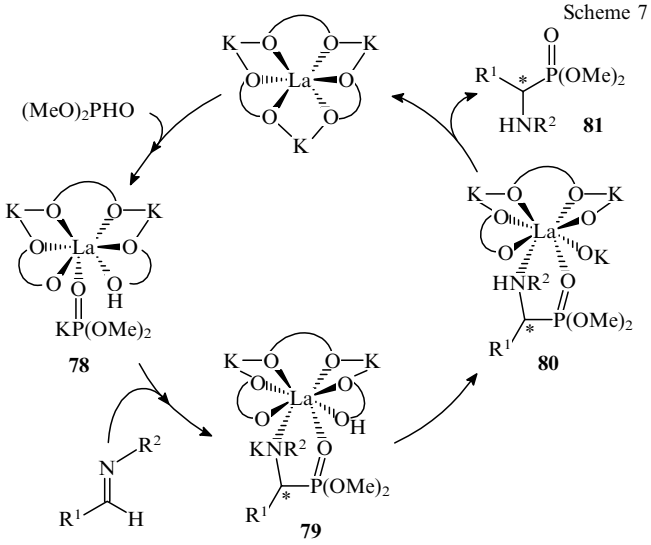


R^1 = Me, Et, Pr^i, PhCHMe, n-C_5H_{11}, cyclo-C_6H_{11};

R^2 = Tr, $CHPh_2$, 4-$MeOC_6H_4$.

The reaction occurs with excess of a hydrophosphoryl compound in THF at room temperature or on gentle heating (50–60 °C). A chelate heterobimetallic complex involving a lanthanide, the chelating ligand BINOL[33] and potassium ions (potassium carbonate) is used as the catalyst. The catalytic cycle is presented in Scheme 7.

Scheme 7



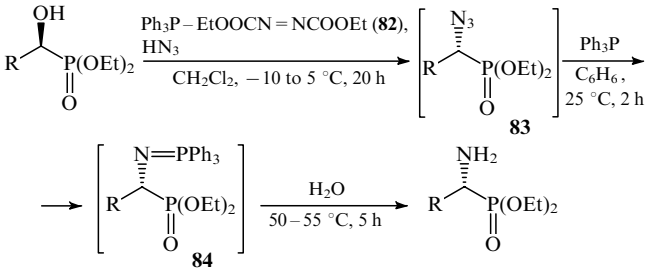
The first step of the process is deprotonation of the phosphite and generation of potassium dimethyl phosphite, which is coordinated by the lanthanide with formation of the complex **78**; the latter reacts with the imine to give the optically active K salt of AP **79**. Replacement of the K^+ ion by a proton at the amine centre results in the complex **80**. In the final step, the product of catalytic asymmetric synthesis **81** is liberated from the coordination sphere. In this process, the lanthanum complex acts as a polyfunctional asymmetric catalyst of AP synthesis with high *de* (96%). A drawback of the method is the rather small number of catalytic cycles. This is probably due to the too high acceptor ability of the lanthanum complex with respect to AP.

b. Reaction of hydroxy phosphonates with amines

As noted above, the reaction of hydroxy phosphonates with amines is a model of the 'hydroxy phosphonate' pathway of the Kabachnik – Fields reaction. It has been studied in much more detail than the alternative 'imine' route, *i.e.*, hydrophosphorylation of imines. Relatively little convincing evidence has been obtained that the Kabachnik – Fields reaction occurs through the step of formation of α-hydroxyalkylphosphoryl intermediates. Moreover, as already mentioned, in certain cases the formation of hydroxy phosphonates is undesired for successful use of the Kabachnik – Fields reaction for preparative purposes.

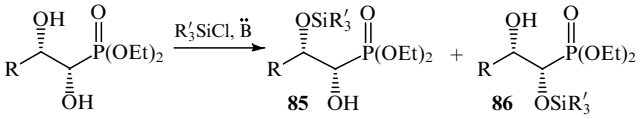
Nevertheless, there are many examples of transformation of hydroxyalkylphosphoryl synthons to the corresponding aminoalkylphosphoryl products by the reaction of hydroxy phosphonates with amines (see Refs 13 and 122 and references cited therein). In recent years, conditions for carrying out this process in a preparative and stereocontrolled way have been found.

The condensation under the action of the azodicarboxylate–triorganylphosphine system (the Mitsunobu reaction[190]) has found use for replacement of the hydroxy group by the amino group in a one-pot procedure.[239–242] Hydroxy phosphonates and phosphine oxides obtained by the Abramov reaction from the appropriate hydrophosphoryl and carbonyl compounds by treatment with the Mitsunobu reagent **82** and HN_3 are converted with inversion of the configuration to α-azido phosphonate **83**. The reaction of triphenylphosphine with phosphonate **83** by the Staudinger reaction results in phosphimide intermediate **84**. The latter is hydrolysed to the target AP.

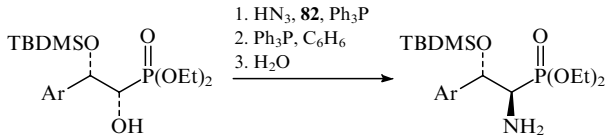


In the one-pot procedure, the intermediate azide and phosphimine are not isolated. Since the Mitsunobu reaction with secondary alcohols, including the above hydroxy phosphonates, occurs stereospecifically by the S_N2 mechanism, the formation of the azido phosphate involves inversion of configuration of the α-carbon atom. Subsequent phosphimination and hydrolysis do not involve this centre.

The Mitsunobu reaction described here, which enables conversion of hydroxy phosphonates to the corresponding azides, has been used[243] for the stereoselective conversion of monosilylated α,β-dihydroxy phosphonates. Optically active silyloxy phosphonates result from the reaction of *threo*-α,β-dihydroxy phosphonates with chlorosilane in the presence of bases.

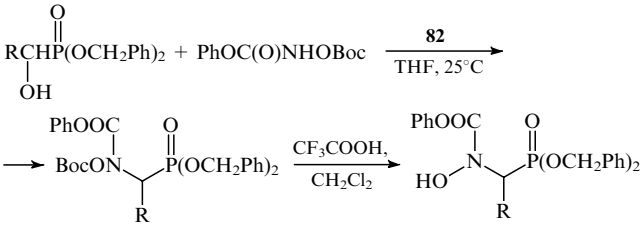


Depending on the nature of the substituents R and R′ and the base used, the ratio of β- and α-silylated products **85**:**86** is from 1:1 to 99:1. Most often, the regioisomer **85** predominates (>90%). Its amination[239] involves exclusively the carbon atom carrying the hydroxy rather than the silyloxy group and is accompanied by inversion of configuration.



Ar = 4-$MeOC_6H_4$, TBDMS = Bu^tMe_2Si.

The Mitsunobu reaction is used in the synthesis of potential haptens, *viz*., *N*-hydroxy-α-amino phosphonates, for the condensation of hydroxy phosphonates with *N*-phenoxycarbonyl-*O*-*tert*-butoxycarbonylhydroxylamine.[244]



As a rule, the reaction goes only in one direction, *viz*., with the formation of AP (40%–75%). α-Hydroxy-2-phenylethylphosphonate is an exception, it undergoes intramolecular (rather than intermolecular) dehydration to give 62% of styrylphosphonate $PhCH=CHP(O)(OCH_2Ph)_2$.

V. Conclusion

Despite the impressive progress in the synthesis and studies of properties of AP, not all the problems have been solved. The problem of stereocontrol in the 'imine' method for the synthesis of AP is still urgent, to say nothing about the enantioselective synthesis using a three-component system in the one-pot version. It is easy to predict that the basic efforts in studying the AP chemistry will be concentrated in this direction, and the Kabachnik – Fields reaction is promising for solving these problems.

The prospects of chemical modification of AP with introduction of new, more and more complex groups, including those with definite configurations, to C-, N- and especially P-centres are far from exhausted.

This aspect of AP chemistry is closely related to the problem of the effect of phosphorus-containing groups on the adjacent reaction centre.[96,97] The attention to α-functionalised organophosphorus compounds has increased abruptly in recent years. This is evident, for example, from recent publications on the chemistry of α-phosphorylated alcohols (α-hydroxy phosphonates),[97,245] α-halogeno phosphonates,[246] α-oxo phosphonates,[247] and α-phosphonoalkyl phosphites.[248] Reactions that occur at the α-carbon centre and formally do not involve the phosphorus atom are still largely controlled by the phosphorus-containing fragment. It not only determines the type and rate of the reaction but also, in some cases, changes the reaction rate by a few orders (see, for example, Ref. 249) and even changes the reaction mechanism.[97] A large number of studies deal with the problem of the quantitative estimation of the effect of phosphorus-containing groups (see Refs 250–252 and references cited therein). This problem still remains the focus of attention of experts in quantitative organic and organometallic chemistry.[253] The quantitative estimation of the dependence of the reaction pathway both of AP and components of the Kabachnik – Fields reaction on the structure is an important problem which is waiting for solution.

One may believe that the area of the application of AP will be much expanded. In addition to the search for new biologically active compounds of high efficiency among APA, their derivatives and analogues, an abrupt growth of interest should be expected to the prospects of practical application related to their complex-forming properties. These applications may primarily include the use of AP as recognising agents (synthetic receptors) and chiral ligands in metal complexes, as well as selective highly-efficient complexones, extraction agents and analytical reagents.

Analysis of the data presented above allows one to consider the discussed area of chemistry as not only rather topical but also having wide prospects in the future.

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References

1. M I Kabachnik, T Ya Medved' *Dokl. Akad. Nauk SSSR* **83** 689 (1952) [a]
2. E K Fields *J. Am. Chem. Soc.* **74** 1528 (1952)
3. P Kafarski, B Lejczak *Phosphorus Sulfur Silicon Relat. Elem.* **63** 193 (1991)
4. M Horiguchi, M Kandatsu *Nature* (*London*) **184** 901 (1959)
5. R Gancarz, I Gansarz *Tetrahedron Lett.* **34** 145 (1993)
6. A N Pudovik, I V Gur'yanova, E A Ishmaeva, in *Reaktsii i Metody Issledovaniya Organicheskikh Soedinenii* (Reactions and Methods of Investigation of Organic Compounds) (Moscow: Khimiya, 1968) Vol. 19
7. D Redmore, in *Topics in Phosphorus Chemistry* Vol. 8 (Eds M Grayson, E J Griffith) (New York: Willey-Interscience, 1976) p. 515
8. R L Hildebrand, J Curley-Joseph, H J Lubansky, T O Henderson, in *Topics in Phosphorus Chemistry* Vol. 11 (Eds M Grayson, E J Griffith) (New York: Willey-Interscience, 1983) p. 297

9. R M Williams, in *Synthesis of Optically Active α-Amino Acids (Organic Chemistry Series)* Vol. 7 (Oxford: Pergamon Press, 1989)
10. I V Konovalova, L A Burnaeva *Reaktsiya Pudovika* (Pudovik Reaction) (Kazan: Kazan State University, 1991)
11. P Mastalerz, in *Handbook of Organophosphorus Chemistry* Ch. 7 (Ed. R Engel) (New York: Marcel Dekker, 1992)
12. F Heaney, in *Comprehensive Organic Functional Group Transformations* Vol. 4 (Ed. G W Kirby) (Cambridge: Cambridge University Press, 1995)
13. K A Petrov, V A Chauzov, T E Erokhina *Usp. Khim.* **43** 2045 (1974) [*Russ. Chem. Rev.* **43** 984 (1974)]
14. E E Nifant'ev *Usp. Khim.* **47** 1565 (1978) [*Russ. Chem. Rev.* **47** 835 (1978)]
15. V P Kukhar', V A Solodenko *Usp. Khim.* **54** 1504 (1984) [*Russ. Chem. Rev.* **56** 859 (1987)]
16. P Kafarski, P Mastalerz *Beitr. Wirk. Forsch.* **H21** 1 (1984)
17. B Drawan, D Redmore *Phosphorus Sulfur Relat. Elem.* **32** 119 (1987)
18. V P Kukhar', N Yu Svistunova, V A Solodenko, V A Soloshonok *Usp. Khim.* **62** 284 (1993) [*Russ. Chem. Rev.* **62** 261 (1993)]
19. L Maier, P J Diel *Phosphorus Sulfur Silicon Relat. Elem.* **90** 259 (1994)
20. A N Pudovik *Dokl. Akad. Nauk SSSR* **83** 865 (1952) [a]
21. US P. 2 328 358 (1943); *Chem. Abstr.* **38** 4587 (1943)
22. R Engel, in *Handbook of Organophosphorus Chemistry* Ch. 11 (Ed. R Engel) (New York: Marcel Dekker, 1992) p. 559
23. D E C Corbridge *Phosphorus — An Outline of its Chemistry, Biochemistry and Uses* Ch. 3 (New York: Elsevier, 1993)
24. E K Baylis, C D Cambell, J G Dingwall *J. Chem. Soc., Perkin Trans. 1* 2845 (1984)
25. Y Song, D Niederer, P M Lane-Bell, L K P Lam, S Crawley, M M Palcic, M A Pickard, D L Pruess, J C Vederas *J. Org. Chem.* **59** 5784 (1994)
26. R.L.Hildebrand (Ed.) *The Role of Phosphonates in Living Systems* (Boca Raton, FL: CRC Press, 1983)
27. P Hermon, I Lukas, B Maca, M Bodesinsky *Phosphorus Sulfur Silicon Relat. Elem.* **79** 43 (1993)
28. P Kafarski, B Lejczak, P Mastalerz *Beitr. Wirk. Forsch.* **H25** 1 (1985)
29. V A Solodenko, T NKasheva, V P Kukhar' *Zh. Obshch. Khim.* **59** 2786 (1989) [b]
30. D G Cameron, H R Hudson, M Pianka, J F Volekman *Phosphorus Sulfur Silicon Relat. Elem.* **88** 15 (1994)
31. H R Hudson, M Pianka, J F Volekman , C S Creaser *Phosphorus Sulfur Silicon Relat. Elem.* **92** 171 (1994)
32. N F Jakobson, P A Bartlett *J. Am. Chem. Soc.* **103** 654 (1981)
33. H Sasai, S Arai, J Takara, M Shibasaki *J. Org. Chem.* **60** 6656 (1995)
34. S Ikeda, J A Ashley, P Wirsching, K D Jauda *J. Am. Chem. Soc.* **114** 7601 (1992)
35. C Fest, K J Schmidt *Organophosphorus Pesticides* (Berlin: Springer, 1982)
36. L Maier, P J Diel *Phosphorus Sulfur Silicon Relat. Elem.* **57** 57 (1991)
37. B Lejczak, P Kafarski, R Gancarz *Pestic. Sci.* **22** 263 (1988)
38. L Cheng, A Goodwin, M Scully, V V Kakkar, G Cleason *Tetrahedron Lett.* **32** 7333 (1991)
39. P A Bartlett, J E Hanson, P P Giannousis *J. Org. Chem.* **55** 6268 (1992)
40. R Hirschman, A B Smith, C M Taylor, P A Benkovich, S D Taylor, K M Yager, P A Sprengler, S J Kenkovich *Science* **265** 234 (1994)
41. K H Krawczyk, T J Bartczak *Phosphorus Sulfur Silicon Relat. Elem.* **82** 117 (1993)
42. G Forlani, P Kafarski, B Lejczak, B Boduszek, R Gancarz, C Torreilees, J Solodenko, H Wojtasek, J Hafner, J Koft, P Wieczorek *Phosphorus Sulfur Silicon Relat. Elem.* **109**/**110** 353 (1996)
43. P Kafarski, B Lejcrak, R Gancarz, E Jaskulska, P Mastalerz, S Wieczorek, I Zbyryl *Pestic. Sci.* **16** 239 (1985)
44. H Wojtasek, P Wieczorek, B Lejczak, B Boduszek, R Gancarz, P Kafarski *Pestic. Sci.* **32** 245 (1991)
45. S Wieczorek, B Boduszek, W A Wlkopolski, R Gancarz, E Jaskulska *J. Prakt. Chem.* **329** 165 (1987)
46. R Gancarz, M Dudek *Phosphorus Sulfur Silicon Relat. Elem.* **144** 135 (1996)
47. V I Krutikov, A N Lavrent'ev *Zh. Obshch. Khim.* **63** 102 (1993) [b]
48. V I Krutikov, E V Sukhanovskaya, T D Chermenskaya *Zh. Obshch. Khim.* **63** 1270 (1993) [b]
49. N M Dyatlova, V Ya Temkina, K I Popov *Kompleksony i Kompleksonaty Metallov* (Complexones and Metal Complexonates) (Moscow: Khimiya,1988)
50. M I Kabachnik, T Ya Medved', N M Dyatlova, O G Arkhipova *Usp. Khim.* **37** 1161 (1968) [*Russ. Chem. Rev.* **37** 503 (1968)]
51. M I Kabachnik, T Ya Medved', N M Dyatlova, M V Rudomino *Usp. Khim.* **43** 1554 (1974) [*Russ. Chem. Rev.* **43** 733 (1974)]
52. M I Kabachnik, in *Khimiya i Primenenie Fosfororganicheskikh Soedinenii (Tr. VII Vsesoyuz. Konf. po Khimii Fosfororganicheskikh Soedinenii)* [The Chemistry and Application of Organophosphorus Compounds (The Proceedings of the VIIth All-Union Conference on the Chemistry of Organophosphorus Compounds)] (Moscow: Nauka, 1987) p. 279
53. S W A Bligh, N Choi, S Failla, P Finocchiaro, A Il'yassov, M Libertini, C M McGrath, M McPartlin, T Woodroffe *J. Chem. Soc., Dalton. Trans.* 3833 (1994)
54. A Bartecki, B Bachmatink, M Cieslak-Golonka, R Gancarz *Monats. Chem.* **111** 851 (1980)
55. R Engel *Chem. Rev.* **77** 349 (1977)
56. S W A Bligh, N Choi, D S C Green, H R Hudson, C M McGrath, M M Pianka *Polyhedron* **12** 2887 (1993)
57. S V Jagodic, M J Herak *J. Inorg. Nucl. Chem.* **32** 1323 (1970)
58. A R Garifzyanov, E Yu Mikryukova, V F Toropova *Zh. Obshch. Khim.* **61** 1346 (1991) [b]
59. A R Garifzyanov, E Yu Mikryukova, V F Toropova *Zh. Obshch. Khim.* **61** 1342 (1991) [b]
60. I I Stoikov, Candidate Thesis in Chemical Sciences, Kazan State University, Kazan, 1997
61. I S Antipin, I I Stoikov, A R Garifzyanov, A I Konovalov *Dokl. Akad. Nauk* **347** 626 (1996) [a]
62. I S Antipin, I I Stoikov, A R Garifzyanov, A I Konovalov *Phosphorus Sulfur Silicon Relat. Elem.* **111** 117 (1996)
63. I S Antipin, I I Stoikov, A R Garifzyanov, A I Konovalov *Zh. Obshch. Khim.* **66** 402 (1996) [b]
64. I S Antipin, I I Stoikov, E M Pinkhassik, N A Fitseva, I Stibov, A I Konovalov *Tetrahedron Lett.* **38** 5865 (1997)
65. V V Ovchinnikov, A A Sobanov, A N Pudovik *Dokl. Akad. Nauk SSSR* **333** 48 (1993) [a]
66. V V Ovchinnikov, V V Brus'ko, A A Sobanov *Termochim. Acta* **233** 153 (1994)
67. V V Ovchinnikov *Zh. Obshch. Khim.* **66** 463 (1996) [b]
68. V V Ovchinnikov, E V Sagdeev, I I Stoikov, Yu G Safina, V F Sopin *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
69. E E Stoikova, Candidate Thesis in Chemical Sciences, Kazan State University, Kazan, 1997
70. M E Chalmers, G M Kosolapoff *J. Am. Chem. Soc.* **75** 5278 (1953)
71. K Moedritzer, R R Irani *J. Org. Chem.* **31** 1603 (1966)
72. A B Smith III, K M Yager, C M Taylor *J. Am. Chem. Soc.* **117** 10 879 (1995)
73. W F Gilmore, H A McBride *J. Am. Chem. Soc.* **94** 4361 (1972)
74. R A Cherkasov, A N Pudovik *Usp. Khim.* **63** 1087 (1994) [*Russ. Chem. Rev.* **63** 1019 (1994)]
75. P P McCleery, B Tuck *J. Chem. Soc., Perkin Trans 1* 1319 (1989)
76. A Ryglowski, P Kafarski *Tetrahedron* **32** 10 685 (1976)
77. L Maier *Phosphorus Sulfur Silicon Relat. Elem.* **53** 43 (1990)
78. M Gulca-Purcaresu, E About-Jaudet, N Colliguon, M Saquet, E Masson *Tetrahedron* **52** 2075 (1996)
79. M Sting, W Steglich *Synthesis* 132 (1990)
80. R Jacquier, M L Hassani, C Petrus, F Petrus *Phosphorus Sulfur Silicon Relat. Elem.* **81** 83 (1993)
81. G Jommi, G Miglierini, R Pagliarin, G Sello, M Sisti *Tetrahedron* **48** 7275 (1992)
82. S Hannesian, Y Bennani *Synthesis* 1272 (1994)
83. S E Denmark, N Chatani, S V Pansare *Tetrahedron* **48** 2191 (1992)
84. R A Cherkasov, V V Ovchinnikov, A N Pudovik, M A Pudovik *Usp. Khim.* **51** 1305 (1982) [*Russ. Chem. Rev.* **51** 746 (1982)]
85. G Cabella, G Jommi, R Pagliarin, G Sello, M Sisti *Tetrahedron* **51** 1817 (1995)
86. U Groth, L Richter, U Schollkopf *Liebigs Ann. Chem.* 903 (1992)
87. J P Genet, J Uzicel, U Port, A M Touzin, S Roland, S Thorimbert, S Tanier *Tetrahedron Lett.* **33** 77 (1992)
88. U Groth, L Lehmann, L Richter, U Schollkopf *Liebigs Ann. Chem.* 427 (1993)

89. P Dumy, R Escal, J P Girard, J Parello, J P Vidal *Synthesis* 1226 (1992)
90. Li-Y Mao, R-Y Chen *Phosphorus Sulfur Silicon Relat. Elem.* **111** 166 (1996)
91. P Kafarski, B Lejczak *Tetrahedron* **45** 7387 (1989)
92. E Zymanczyk-Duda, B Lejczak, P Kafarski *Phosphorus Sulfur Silicon Relat. Elem.* **112** 47 (1996)
93. A Mucho, P Kafarski, F Plenat, H J Cristan *Phosphorus Sulfur Silicon Relat. Elem.* **105** 187 (1995)
94. T Kankorat, I Neda, P G Jones, R Schmutzler *Phosphorus Sulfur Silicon Relat. Elem.* **112** 247 (1996)
95. A N Pudovik, G M Saakyan, V K Khairullin, M A Pudovik *Zh. Obshch. Khim.* **67** 1991 (1997) [b]
96. R D Sayakhov, A V Mironov, V I Galkin, G A Kutyrev, R A Cherkasov *Zh. Obshch. Khim.* **63** 2476 (1993) [b]
97. R A Cherkasov, V I Galkin, R D Sayakhov, A V Mironov, G A Kutyrev *Zh. Obshch. Khim.* **64** 57 (1994) [b]
98. R A Cherkasov, V I Galkin, R D Sayakhov *Phosphorus Sulfur Silicon Relat. Elem.* **111** 98 (1996)
99. S Failla, P Finocchiro, G La Rosa *Phosphorus Sulfur Silicon Relat. Elem.* **113** 225 (1996)
100. M Hatani, J R Goerlich, R Schmutzler, H Groger, J Martens *Synth. Commun.* **26** 3685 (1996)
101. I V Martynov, A Yu Aksinenko, V B Sokolov, A N Chekhlov, A N Pushin, O V Korenchenko *Phosphorus Sulfur Silicon Relat. Elem.* **49**/**50** 222 (1966)
102. N Galleotti, J Coste, P Bedos, P Jouin *Tetrahedron Lett.* **37** 3997 (1996)
103. D Green, S Elgendy, G Patel, J A Baban, E Skordalakes, N Husman, V V Kakkar, J Deadman *Phosphorus Sulfur Silicon Relat. Elem.* **113** 303 (1996)
104. A E Demir, S O Tanyeli, S Demic, O O Evin *Tetrahedron Lett.* **37** 407 (1996)
105. L Ferris, D Haigh, Ch J Moody *J. Chem. Soc., Perkin Trans. 1* 2885 (1996)
106. F Palacios, A M Ochoa de Retana, J Paglday *Heterocycles* **38** 95 (1994)
107. N G Khusainova, A N Pudovik *Usp. Khim.* **47** 1507 (1978) [*Russ. Chem. Rev.* **47** 803 (1978)]
108. D Y Kim, D Y Rhie *Tetrahedron* **53** 13 603 (1997)
109. V Kukhar, V Solodenko, V Soloshonok, T Kashtva *Phosphorus Sulfur Silicon Relat. Elem.* **109**/**110** 529 (1996)
110. I Kraicheva, R Stevanova, G Borisov *Phosphorus Sulfur Silicon Relat. Elem.* **79** 107 (1993)
111. V V Ovchinnikov, S V Cherezov, R A Cherkasov, A N Pudovik *Zh. Obshch. Khim.* **55** 1244 (1985) [b]
112. Yu G Safina, G M Malkova, R A Cherkasov, V V Ovchinnikov *Zh. Obshch. Khim.* **60** 221 (1990) [b]
113. Yu G Safina, G M Malkova, R A Cherkasov, A N Pudovik *Dokl. Akad. Nauk SSSR* **316** 1474 (1990) [a]
114. Yu G Safina, R A Cherkasov *Zh. Obshch. Khim.* **62** 945 (1992) [a]
115. Yu G Safina, G M Malkova, R A Cherkasov *Zh. Obshch. Khim.* **62** 945 (1992) [b]
116. A A Sobanov, R A Cherkasov *Zh. Obshch. Khim.* **64** 1219 (1994) [b]
117. J H Merret, W C Spurden, W A Thomas, B P Tong, W A Whitcombe *J. Chem. Soc., Perkin Trans. 1* 61 (1988)
118. T V Kim, E I Kiseleva, P P Onys'ko, A D Sinitsa *Phosphorus Sulfur Silicon Relat. Elem.* **109**/**110** 397 (1996)
119. T Ya Medved', M I Kabachnik *Dokl. Akad. Nauk SSSR* **84** 717 (1952) [a]
120. M I Kabachnik, T Ya Medved' *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 868 (1953) [c]
121. M I Kabachnik, T Ya Medved' *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 1024 (1954) [c]
122. A Petrov, V A Chauzov, T S Erokhina *Zh. Obshch. Khim.* **45** 737 (1975) [b]
123. R Gancarz *Phosphorus Sulfur Silicon Relat. Elem.* **83** 59 (1993)
124. R Gancarz, I Gancarz, U Walkowjak *Phosphorus Sulfur Silicon Relat. Elem.* **104** 45 (1995)
125. R Gancarz *Kabachnik – Fields Reaction. Synthesis of Biologically Active Compounds (Scientific Papers of the Institute of Organic Chemistry Biochemistry and Biotechnology of the Wrotslav University of Technology), Wrotslav, 1997* p. 77
126. M Soroka, J Zygmunt *Synthesis* 370 (1988)
127. B I Kotovich *Zh. Obshch. Khim.* **57** 1416 (1987) [b]
128. V I Krutikov, A N Lavrent'ev, E V Sukhanovskaya *Zh. Obshch. Khim.* **61** 1321 (1991) [b]
129. V I Krutikov, E V Sukhanovskaya, I L Tsar'kova *Zh. Obshch. Khim.* **62** 2708 (1992) [b]
130. V I Krutikov, E V Sukhanovskaya, T D Chermenskaya, V M Adanin *Zh. Obshch. Khim.* **63** 1776 (1993) [b]
131. V I Galkin, E R Zvereva, A A Sobanov, I V Galkina, R A Cherkasov *Zh. Obshch. Khim.* **63** 2225 (1993) [b]
132. V I Galkin, E R Zvereva, A A Sobanov, I V Galkina, R A Cherkasov *Phosphorus Sulfur Silicon Relat. Elem.* **111** 142 (1996)
133. V I Galkin, E R Zvereva, A A Sobanov, I V Galkina, R A Cherkasov, in *The IXth International Symposium on Phosphorus Chemistry (Abstracts of Reports), St.-Petersburg, 1993* p. 54
134. I V Galkina, E R Zvereva, G M Saakyan, V I Galkin, A A Sobanov, R A Cherkasov, in *The IXth International Symposium on Phosphorus Chemistry (Abstracts of Reports), St.-Petersburg, 1993* p. 116
135. R A Cherkasov, V I Galkin, E R Zvereva, A A Sobanov, I V Galkina, in *The XIth International Conference on Chemistry of Phosphorus Compounds (Abstracts of Reports), Kazan, 1996* p. 198
136. V I Galkin, A A Sobanov, I V Galkina, R A Cherkasov *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
137. I V Galkina, E R Zvereva, V I Galkin, R A Cherkasov *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
138. I V Galkina, A A Sobanov, V I Galkin, R A Cherkasov *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
139. I V Galkina, V I Galkin, R A Cherkasov *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
140. B Boduszek *Phosphorus Sulfur Silicon Relat. Elem.* **111** 209 (1996)
141. J S Weczorek, B Boduszek, R Gancarz *J. Prakt. Chem.* **326** 349 (1984)
142. R Gancarz *Tetrahedron* **51** 10 627 (1995)
143. R Gancarz, I Gancarz, A Masiowska *Phosphorus Sulfur Silicon Relat. Elem.* **111** 195 (1996)
144. L V Nesterov *Dokl. Akad. Nauk SSSR* **304** 53 (1989) [a]
145. S D Fazylov, L M Gazaliev, L M Vlasova, R Z Kiselev, V K Byistro *Zh. Obshch. Khim.* **66** 238 (1996) [b]
146. R Gancarz *Phosphorus Sulfur Silicon Relat. Elem.* **92** 193 (1994)
147. V I Krutikov, A L Kovalenko, E V Sukhanovskaya *Zh. Obshch. Khim.* **61** 257 (1991) [b]
148. V A Frolovskii, Yu N Studnev, G G Rozantsev *Zh. Obshch. Khim.* **66** 692 (1996) [b]
149. S K Tukanova, B Zh Dzhiembaev, S F Khalilova, B M Butin *Zh. Obshch. Khim.* **63** 938 (1993) [b]
150. G Mury, J Royer, H-A Husson *Tetrahedron Lett.* **33** 6127 (1992)
151. J-P Finet, C Prejavile, R Lauricella, F Le Maigue, P Stipa, P Tordo *Phosphorus Sulfur Silicon Relat. Elem.* **81** 17 (1993)
152. D Kanoci, J K Danike, W J Wechter *Synth. Commun.* **26** 2037 (1996)
153. F H Ebetino, L A Jameson *Phosphorus Sulfur Silicon Relat. Elem.* **51**/**52** 23 (1990)
154. C Yuan, G Wang, S Chen *Synthesis* 522 (1990)
155. C Yuan, S Chen *Synthesis* 1124 (1992)
156. S-K Chung, D-H Kang *Tetrahedron: Asymmetry* **7** 21 (1996)
157. S Chen, J K Coward *Tetrahedron Lett.* **37** 4335 (1996)
158. H Zimmer, D W Burkhouse *Phosphorus Sulfur Silicon Relat. Elem.* **80** 135 (1993)
159. P A Ottew, A Van der Gen *Phosphorus Sulfur Silicon Relat. Elem.* **111** 191 (1996)
160. C Yuan, S Chen, G Wang *Synthesis* 490 (1991)
161. T Bailly, R Burgada *Phosphorus Sulfur Silicon Relat. Elem.* **101** 131 (1995)
162. D Redmore *J. Org. Chem.* **43** 992 (1978)
163. J Oleksyszyn, E Gruszecka *Tetrahedron Lett.* **22** 3537 (1981)
164. G Borisov, I Devedjev, V Ganev *Phosphorus Sulfur Silicon Relat. Elem.* **49**/**50** 227 (1990)
165. R Hamilton, B Walker, B J Walker *Tetrahedron Lett.* **36** 4451 (1995)
166. E K Baylis *Tetrahedron Lett.* **36** 9385 (1995)
167. E K Baylis *Tetrahedron Lett.* **36** 9389 (1995)
168. J Oleksyszyn, R Tyka, R Mastalerz *Synthesis* 429 (1978)
169. J Oleksyszyn *Synthesis* 444 (1981)
170. J Oleksyszyn *Synthesis* 722 (1980)
171. M Soroka *Liebigs Ann. Chem.* 331 (1990)
172. C Yuan, G Wang *Synthesis* 256 (1990)

173. D Green, U Gruss, G Hagele, H R Hudson, L Lindblum, M Pianka *Phosphorus Sulfur Silicon Relat. Elem.* **113** 179 (1996)
174. M Soroka *Synthesis* 547 (1989)
175. R Jacquier, C Petrus *Phosphorus Sulfur Silicon Relat. Elem.* **78** 71 (1993)
176. Q Dai, R Chen *Synthesis* 415 (1997)
177. R Lu, H Yang, Z Shang *Phosphorus Sulfur Silicon Relat. Elem.* **108** 197 (1996)
178. D Subach, R Charczuk, C Gerber, P Renaud *Helv. Chim. Acta* **72** 401 (1989)
179. J W Huber, M Middlebrooks *Synthesis* 883 (1977)
180. J Oleksyszyn, R Tyka, P Mastalerz *Synthesis* 571 (1977)
181. Z H Kudzin, W J Stec *Synthesis* 468 (1978)
182. T Oshikawa, M Yamashita *Bull. Chem. Soc. Jpn.* **62** 3177 (1989)
183. B Boduszek *Phosphorus Sulfur Silicon Relat. Elem.* **113** 209 (1996)
184. C-L J Wang, T L Taylor, A J Mical, S Spitz, T M Reilly *Tetrahedron Lett.* **33** 7667 (1992)
185. R Hamilton, B J Walker, B Walker *Tetrahedron Lett.* **34** 2847 (1993)
186. V I Krutikov, I V Ofrina, E A Kalaverdova *Zh. Obshch. Khim.* **61** 840 (1991) [b]
187. C Maury, T Charbaoui, J Royer, H -P Husson *J. Org. Chem.* **61** 3687 (1996)
188. C Maury, Q Wang, T Charbaoui, M Chiadmi, A Tomas, J Royer, H-P Husson *Tetrahedron* **53** 3627 (1997)
189. S De Angelis, A Batsanon, T Y Norman, D Parker, K Senanayake, J Vepsdainen *J. Chem. Soc., Chem. Commun.* 2361 (1995)
190. O Mitsunobu *Synthesis* 1 (1981)
191. A N Pudovik, R R Shagidullin, V K Khairullin, I I Vandyukova, A V Chernova, M A Pudovik *Izv. Akad Nauk, Ser. Khim.* 1301 (1996) [c]
192. P Finocchiaro, S Failla *Phosphorus Sulfur Silicon Relat. Elem.* **109**/**110** 189 (1996)
193. N P Osthaus, G Hagele *Phosphorus Sulfur Silicon Relat. Elem.* **111** 160 (1996)
194. U Gruss, G Hagele *Phosphorus Sulfur Silicon Relat. Elem.* **111** 159 (1996)
195. U Gruss, G Hagele *Phosphorus Sulfur Silicon Relat. Elem.* **97** 209 (1994)
196. S-Z Zhu, B Xu, J Shang, Ch Qui *Phosphorus Sulfur Silicon Relat. Elem.* **112** 219 (1996)
197. S Failla, P Finocchiaro, G Hagele, R Rapisardi *Phosphorus Sulfur Silicon Relat. Elem.* **82** 79 (1993)
198. S Failla, P Finocchiaro, V K Belsky, V F Savodnik, A N Sobolev *Phosphorus Sulfur Silicon Relat. Elem.* **80** 75 (1993)
199. S Failla, P Finocchiaro *Phosphorus Sulfur Silicon Relat. Elem.* **85** 65 (1993)
200. R-J Chen, L-Y Mao *Phosphorus Sulfur Silicon Relat. Elem.* **89** 97 (1994)
201. D Green, S Elgendy, G Patel, E Skordalakes, W Husman, V V Kakkar, J Deadman *Phosphorus Sulfur Silicon Relat. Elem.* **118** 271 (1996)
202. A C van der Laan, R Stromberg, J H van Boom, E Kuyl-Yehekiely, V A Efimov, O G Chakhmakhcheva *Tetrahedron Lett.* **37** 7857 (1996)
203. A Yu Aksinenko, A N Pushin, V B Sokolov *Phosphorus Sulfur Silicon Relat. Elem.* **84** 249 (1993)
204. B Boduszek *Tetrahedron* **52** 12483 (1996)
205. S Failla, P Finocchiaro *Phosphorus Sulfur Silicon Relat. Elem.* **114** 83 (1996)
206. S W A Bligh, C M Mc Grath, S Failla, P Finocchiaro *Phosphorus Sulfur Silicon Relat. Elem.* **118** 189 (1996)
207. V K Khairullin, A N Pudovik *Zh. Obshch. Khim.* **64** 745 (1994) [b]
208. L Cottier, G Descotes, J Lewkowski, R Skowronski *Phosphorus Sulfur Silicon Relat. Elem.* **116** 93 (1996)
209. L Cottier, G Descotes, G Conera, G Grabowski, J Lewkowski, R Skowronski *Phosphorus Sulfur Silicon Relat. Elem.* **118** 181 (1996)
210. B Boduszek, A Halama, J Zon *Tetrahedron* **53** 113999 (1997)
211. I Kraicheva *Phosphorus Sulfur Silicon Relat. Elem.* **118** 21 (1996)
212. G Borisov *Eur. Polym. J.* **28** 795 (1992)
213. C Hubert, A Munoz *J. Org. Chem.* **60** 1488 (1995)
214. C Hubert, B Oussaid, G Etemad-Mughadam, M Koelning, B Garrigues *Synthesis* 51 (1994)
215. H Groger, J Manikowski, J Martens *Phosphorus Sulfur Silicon Relat. Elem.* **116** 123 (1996)
216. H Groger, Y Saida, S Arai, J Martens, H Sasai, M Shibasaki *Tetrahedron Lett.* **37** 9291 (1996)
217. S Shatzmiller, M-Z Dolitzki, R Meirovich, R Neidlein, Ch Weik *Liebigs Ann. Chem.* 161 (1991)
218. B Costisella, I Keital, S Ozegowski *Phosphorus Sulfur Silicon Relat. Elem.* **83** 115 (1993)
219. A R Khomutov *Bioorg. Khim.* **16** 1290 (1990) [d]
220. A N Pudovik, R R Shagidullin, V K Khairullin *Izv. Akad. Nauk, Ser. Khim.* 1303 (1996) [c]
221. V K Khairullin, M A Pudovik, R R Shagidullin, R M Mukhamadeeva, I Kh Shakirov, M A Pudovik *Zh. Obshch. Khim.* **64** 613 (1994) [b]
222. J Zon *Pol. J. Chem.* **55** 643 (1981)
223. K Afarinkia, J I G Cadogan, C W Rees *Tetrahedron* **46** 7175 (1990)
224. K Afarinkia, J I G Cadogan, C W Rees *Synlett* 124 (1992)
225. Yu G Safina, V V Ovchinnikov, R A Cherkasov *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
226. K Afarinkia, J I G Cadogan, C W Rees *Synlett* 123 (1992)
227. V I Galkin, I V Bakhtiyarova, A A Sobanov, R A Cherkasov, A N Pudovik *Dokl. Akad. Nauk SSSR* **258** 634 (1985) [a]
228. A A Sobanov, I V Bakhtiyarova, E K Badeeva, M G Zimin, A N Pudovik *Zh. Obshch. Khim.* **55** 27 (1985) [b]
229. A N Pudovik, V K Khairullin, G M Saakyan, R R Shagidullin, M A Pudovik, I I Vandyukova, R Z Musin *Zh. Obshch. Khim.* **68** (9) (1998) [b] (in the press)
230. X-Y Jiao, Ch Verbruggen, M Borloo, W Bollart, A D Groot, P Dommisse, A Halmers *Synthesis* 23 (1994)
231. V K Khairullin, A N Pudovik *Zh. Obshch. Khim.* **64** 743 (1994) [b]
232. Sh Li, G-Q Wang, Ch Yuan *Chin. J. Chem.* **51** 713 (1993)
233. Ch Yuan, Sh Li, G-Q Wang, Y Mo *Phosphorus Sulfur Silicon Relat. Elem.* **81** 27 (1993)
234. Ch Yuan, Sh Cui *Phosphorus Sulfur Silicon Relat. Elem.* **55** 159 (1991)
235. K M Yager, C M Taylor, A B Smith *J. Am. Chem. Soc.* **116** 9377 (1994)
236. A B Smith, C M Taylor, S J Benkovic, R Hirschman *Tetrahedron Lett.* **35** 6835 (1994)
237. A Bongini, R Camerini, S Hofman, M Panunzio *Tetrahedron Lett.* **35** 8045 (1994)
238. K J Koeller, N P Rath, C D Spilling *Phosphorus Sulfur Silicon Relat. Elem.* **103** 171 (1995)
239. T Gaida, M Matusaiak *Synth. Commun.* **22** 2193 (1992)
240. T Gaida, M Matusaiak *Phosphorus Sulfur Silicon Relat. Elem.* **77** 192 (1993)
241. T Gaida *Phosphorus Sulfur Silicon Relat. Elem.* **85** 59 (1993)
242. T Gaida *Tetrahedron: Asymmetry* **5** 1965 (1994)
243. T Yokomatsu, K Suemune, P Yamagishi, S Shibuya *Synlett* 847 (1995)
244. V Youvereur, M-N Lalloz *Tetrahedron Lett.* **37** 6331 (1996)
245. V J Blazis, K J Koeller, C D Spieling *J. Org. Chem.* **60** 931 (1995)
246. R Waschenbusch, J Carran, A Marinetti, P Savignac *Synthesis* 727 (1997)
247. C Meier, W H G Laux *Tetrahedron* **52** 589 (1996)
248. E N Ofitserov, V F Mironov, I V Konovalova *Zh. Obshch. Khim.* **63** 2687 (1993) [b]
249. S E Tkachenko, A N Yarkevich, E N Tsvetkov, V I Galkin, R D Sayakhov, R A Cherkasov, A N Pudovik *Dokl. Akad. Nauk SSSR* **315** 628 (1990) [a]
250. T A Mastryukova, M I Kabachnik *Usp. Khim.* **38** 1751 (1969) [*Russ. Chem. Rev.* **38** 795 (1969)]
251. B I Istomin, V A Baranskii *Usp. Khim.* **51** 394 (1982) [*Russ. Chem. Rev.* **51** 223 (1982)]
252. V I Galkin, R D Sayakhov, R A Cherkasov *Usp. Khim.* **60** 1617 (1991) [*Russ. Chem. Rev.* **60** 815 (1991)]
253. A R Cherkasov, V I Galkin, R A Cherkasov *Usp. Khim.* **65** 695 (1996) [*Russ. Chem. Rev.* **65** 641 (1996)]

[a] — *Dokl. Chem. Technol., Dokl. Chem. (Engl. Transl.)*
[b] — *Russ. J. Gen. Chem. (Engl. Transl.)*
[c] — *Russ. Chem. Bull. (Engl. Transl.)*
[d] — *Russ. J. Bioorg. Chem. (Engl. Transl.)*