PHOSPHORYLATED 1,3-DIAZOLES (REVIEW)

G. L. Matevosyan and P. M. Zavlin

UDC 547.26'118

The principal methods for obtaining and converting phosphorylated 1,3-diazoles, including ^{32}P-labeled compounds and compounds that contain spin labels, and their use in organic synthesis, molecular biology, bioorganic chemistry, medicine, and agriculture are examined.

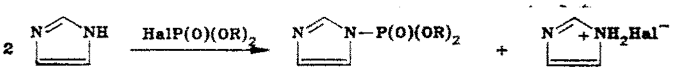
In the last decades phosphorylated azoles have attracted the attention of organic chemists and biochemists in connection with the outstanding advances in the synthesis of physiologically active substances, the study of nucleic acids, and the biosynthesis of proteins and with the development of research on bioenergetics, the structure of complex phospholipids, phosphoproteins, etc. [1-10]. Numerous derivatives of phosphorylated imidazoles, benzimidazoles, and imidazolines and systems condensed with them have already found application as pesticides [8-13], plant-growth regulators [9-24], and medicinal preparations [25-28].

The present review correlates the principal methods for obtaining phosphorylated 1,3-diazoles that are used as synthones, phosphorylating and protecting reagents, and physiologically active substances and encompasses studies published from 1953 to 1987.

N-Phosphorylated 1,3-Diazoles

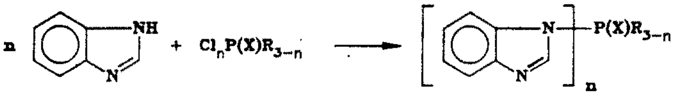
The most widely used method for obtaining N-phosphorylated azoles is the direct phosphorylation of the corresponding heterocycles with the halides, esters, amides, amido esters, isocyanates, and thiocyanates of phosphorus-containing acids. Carbodiimidazoles and trimethylsilyl and metal derivatives of 1,3-diazoles are widely used to stimulate the introduction of the phosphoryl group.

The formation of N-phosphorylated imidazoles was noted for the first time in the 1950s during a study of model reactions involving the inactivation of chymotrypsin with diisopropyl fluorophosphate [29]. It was later found that N-phosphorylated imidazoles could be synthesized [29, 30].



Hal=F, Cl; R=Alk, Ar

Mono-, di-, and tri(1-benzimidazolido)phosphites, -phosphates, and -thiophosphates are formed smoothly in the reaction of benzimidazole with the chlorides of phosphorus-containing acids in the presence of triethylamine under mild conditions [9, 14, 31-33].

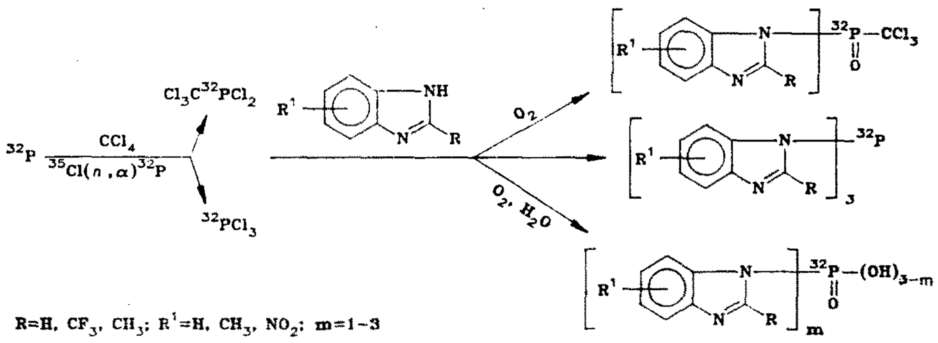


n=1-3; X=O, S; R=ArNH, ArO

Only disubstituted benzimidazolidophosphites, -phosphates, and -thiophosphates [32-34] were obtained in the phosphorylation of 5(6)-substituted benzimidazoles with phosphorus trichloride.

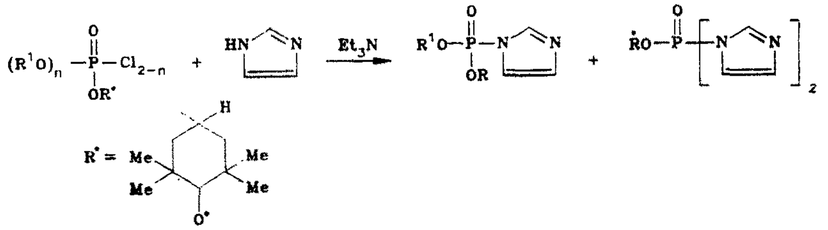
Leningrad Agricultural Institute, Leningrad–Pushkin 189620. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 723-740, June, 1990. Original article submitted May 6, 1987; revision submitted January 8, 1989.

^{32}P-Labeled compounds were obtained to study the distribution, transport, metabolism, and mechanism of the action of physiologically active phosphorylated benzimidazoles [9-26, 35-37] by irradiation of saturated solutions of phosphorus and the corresponding benzimidazole in CCl_4 with fast neutrons [38-40]

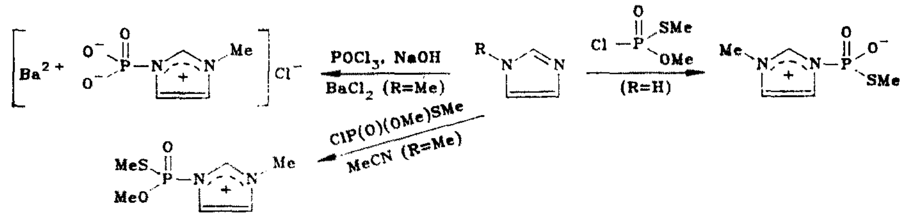


The corresponding 1-benzimidazolido-^{32}P-phosphites were isolated and identified under similar conditions in the case of thorough isolation of the target from oxygen [39, 40].

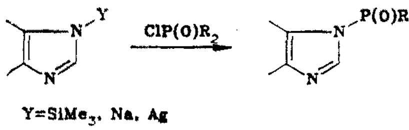
Spin-stable imidazolidophosphates were obtained as spin probes [41-43]:



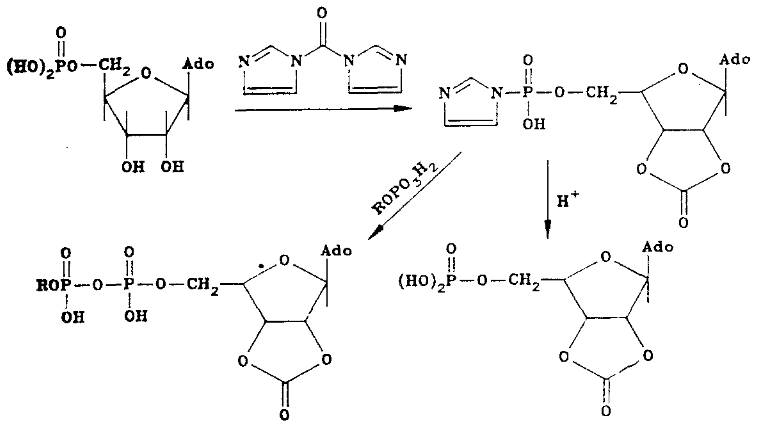
It has been proposed that 1-methylimidazolido(thio)phosphates, obtained via the following scheme, be used for the selective phosphorylation of amino acids [44] and oligonucleotide synthesis [45-47]:



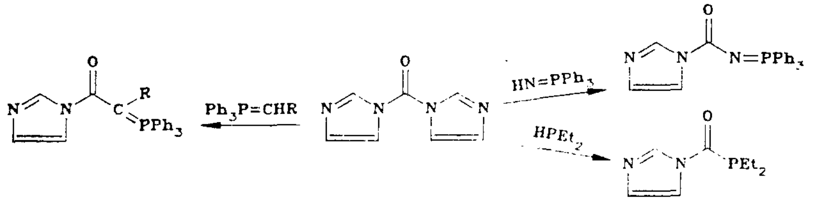
N-Trimethylsilyl [48, 49] and metal derivatives of imidazole [50-52] are readily phosphorylated by chlorides of phosphorus acids:



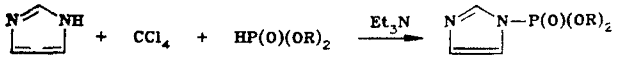
The carbodiimidazole method of phosphorylation, which consists in the reaction of carbodiimidazole with chlorides and esters of phosphorus-containing acids, has become widely used for the synthesis of nucleotides [53-61], including ^{32}P-labeled nucleotides [62-64]. 2',3'-Substituted derivatives of adenosine mono-, di-, and tri-5'-phosphates were obtained by the action of carbodiimidazole on the nucleoside 5'-phosphate [65]:



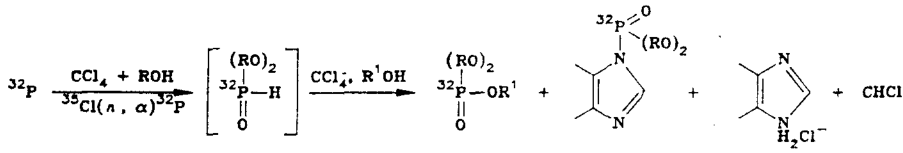
Diverse phosphorus-containing derivatives of imidazole could be obtained by using carbonyldiimidazole [66]:



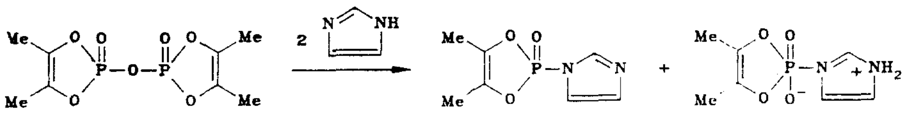
The possibility of obtaining imidazolidophosphates via the Atherton–Todd reaction has been demonstrated [67]:



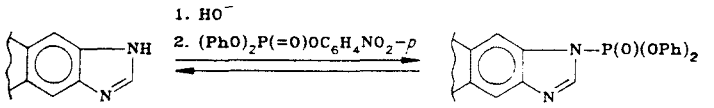
The specific catalytic function of azoles in processes involving the phosphorylation of alcohols with hot ^{32}P atoms, which is due to the intermediate formation of azolido-^{32}P-phosphates, was observed in realizing the Atherton–Todd reaction under conditions of nuclear-chemical synthesis with stabilization of the ^{32}P recoil atoms in a CCl_4–alkanol–azole system [68-70]:



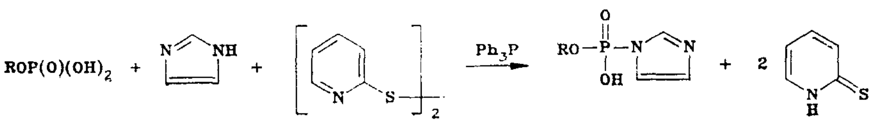
It was found that 1,2-dimethylethylenedioxyphosphorylimidazole could be obtained via the scheme [71-73]



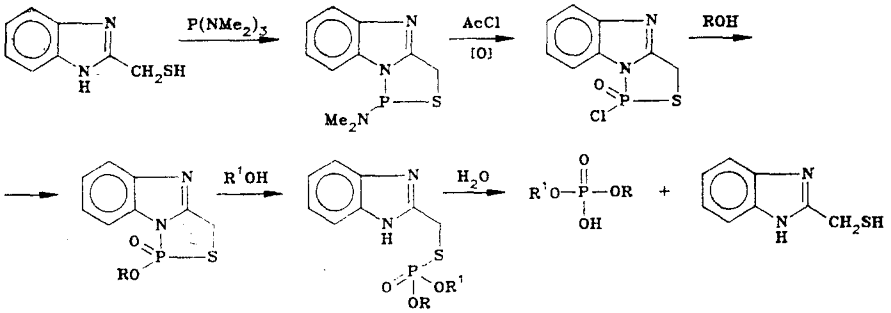
Benzimidazole and naphth-2,3-imidazole are phosphorylated smoothly by p-nitrophenyl diphenyl phosphate [74]:



Redox phosphorylation has been proposed for obtaining phosphorylated imidazoles. Thus, the corresponding imidazolidophosphates were obtained by the reaction of a monoalkyl phosphate, imidazole, triphenylphosphine, and di(2-pyridyl) disulfide [75]:

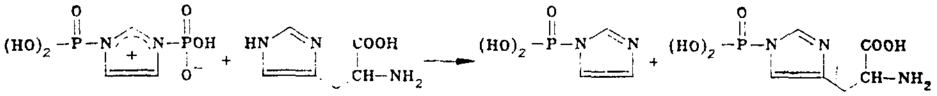


The cyclophosphorylation of 2-methylmercaptobenzimidazole was recently accomplished in order to obtain an effective phosphorylating and protective reagent for oligonucleotide synthesis [76]:



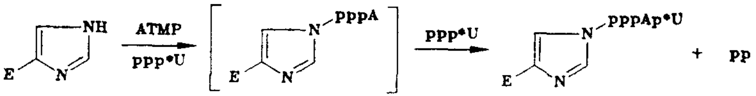
R и R¹ — nucleosides

The possibility of the phosphorylation of the imidazole fragment of histidine with imidazolidophosphates has been previously demonstrated [77-79]:



It was found that the transphosphorylation of serine [80] and tryptophan [81] could be accomplished by means of imidazolidophosphates.

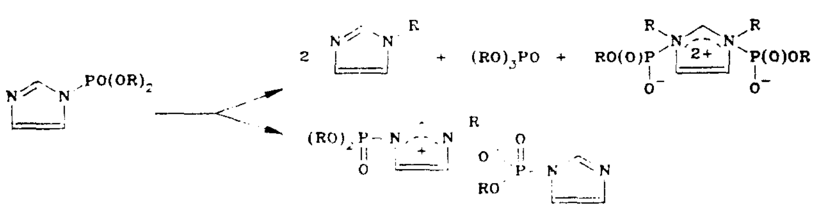
The possibility of the selective phosphorylation of the imidazole residue of histidine by the reaction of the enzyme with adenosine 5-trimetaphosphate (ATMP) and uridine triphosphate (PPP*U) labeled in the α-position of the triphosphate residue [82] was demonstrated during a search for effective reagents for the affine modification of enzymes [4]:



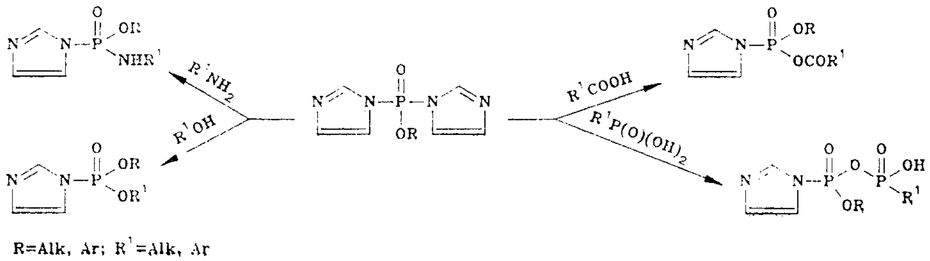
E — enzyme with a histidine residue

In the chemical modeling of photophosphorylation [5] it was established that the oxidation of diimidazolylferrihemochrome with oxygen in the presence of AMP or ADP and an inorganic phosphate leads to ADP and ATP with the intermediate formation of a phosphoimidazole [83].

Upon heating imidazolidophosphates undergo a number of transformations, at the foundation of which lie processes involving intermolecular alkylation [84]:

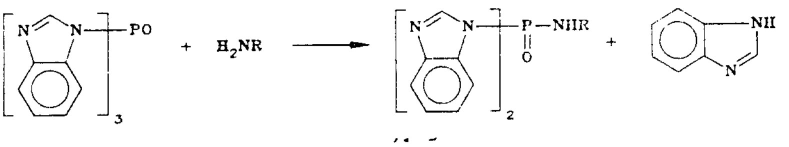


Imidazolidophosphites are distinguished by high reactivities with respect to different types of nucleophiles [53-61]; this expands the possibilities of their production and application [41-43]:

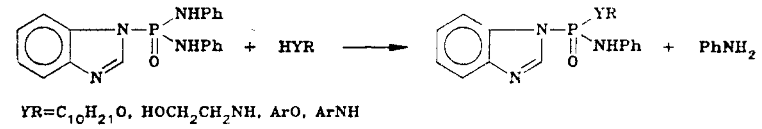


A study of the principles of nucleophilic substitution at the tetracoordinated phosphorus atom made it possible to develop original and accessible methods for obtaining unsymmetrical N-phosphorylated azoles from the corresponding phosphorylated nitrogen heterocycles via transesterification and transamidation with alcohols, phenols, amines, amino alcohols, and aminophenols [9, 33].

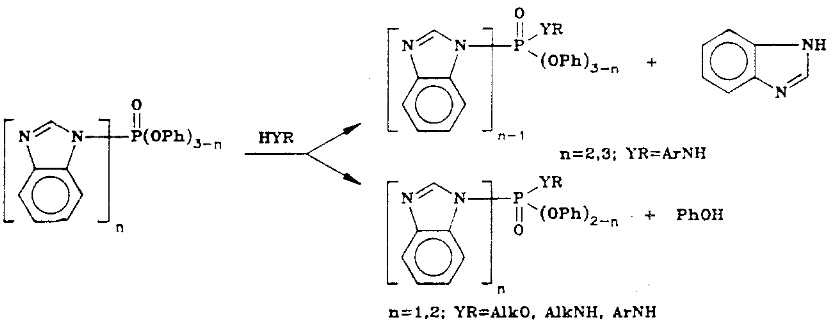
Tri(1-benzimidazolido)phosphate smoothly phosphorylates aniline, ethanolamine, and p-aminophenol [85]:



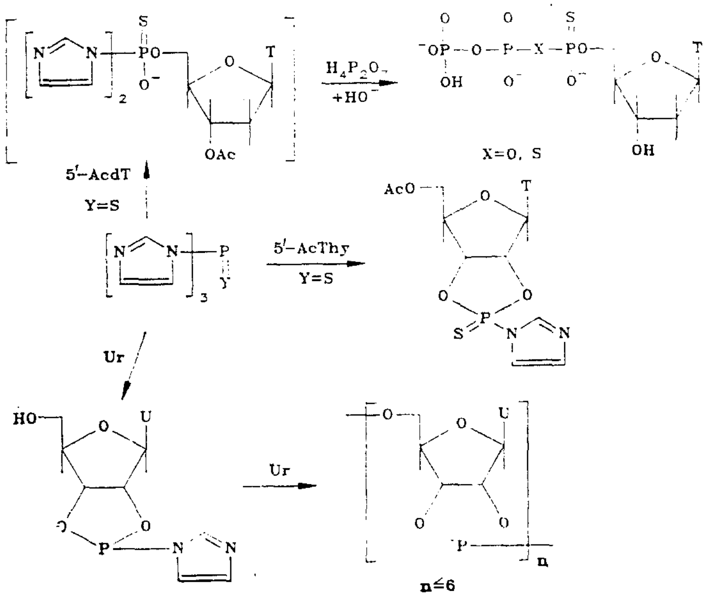
Exclusively the phenylamino group undergoes substitution in the reaction of (1-benzimidazolido)phosphate dianilide with nucleophilic reagents [86]:



In the case of O-phenyl(1-benzimidazolido)phosphates the reactions proceed via two pathways, depending on the nature of the nucleophile [87]:



In the case of 1-benzimidazolidophosphates, reactions involving nucleophilic substitution at the phosphorus atom are described by a general scheme of bimolecular nucleophilic substitution of the $S_N2(P)$ type, and their reactivities are described by the Hammett equation [88, 89].



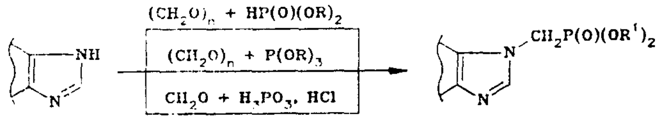
In bioorganic chemistry the imidazole method is widely used to create a phosphodiester bond in the phospholipid series [2, 90] and an internucleotide phosphotriester bond [90, 91], as well as for the abiogenic synthesis of a peptide bond [3]. For example, tri(1-imidazolido)thiophosphate is used for the synthesis of polynucleotide thiophosphates of thymidine [92, 93], while tri(1-imidazolido)phosphite is used for the synthesis of an oligonucleotide phosphite of uridine [94, 95].

The phosphorylation of uridine with tri(1-imidazolido)phosphite [85] proceeds selectively at the 2',3'-hydroxy groups with the formation of 2',3'-cyclophosphoimidazole, which then undergoes oligomerization.

N-Phosphonalkylated 1,3-Diazoles

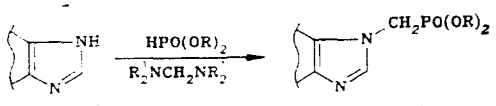
New variants of reactions involving Kabachkin–Fields phosphonmethylation [96] with the participation of formylbenzimidazole, aminals, and nitroso compounds and phosphonethylation [9] using bis(2-chloroethyl) vinylphosphonate as the phosphorylating reagent have been developed for obtaining N-phosphonalkylated azoles; it was established that the introduction of electron-donor substituents into various positions of the heteroring facilitates phosphonmethylation and phosphonethylation processes, whereas the introduction of electron-acceptor substituents hinders them [9, 97].

N-Phosphonmethylated imidazoles and benzimidazoles were obtained for the first time via the Kabachkin–Fields reaction [98, 99] by the reaction of azoles with paraformaldehyde or formalin with alkyl phosphites or phosphorous acid in the presence of HCl [97-103]:



R=Alk; R'=H, Alk

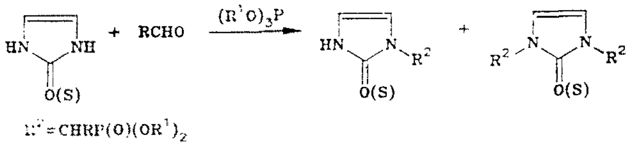
The nature of the aldehyde component also affects the course of the phosphonmethylation reaction. Thus, the phosphonmethylation of benzimidazole with diethyl phosphite and benzaldehyde under similar conditions proceeds in quantitative yield [97, 102]. One should particularly note the expediency of using aminals in obtaining N-phosphonmethylated azoles [104]:



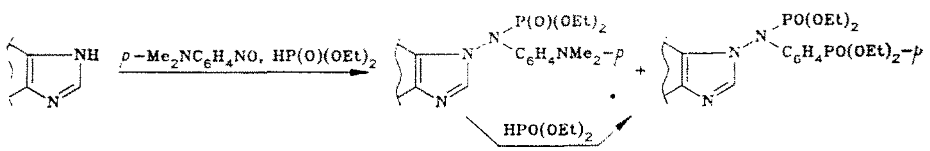
R=Alk; R'=Me, Et, Pr, Bu, i-Bu, –N(CH$_2$CH$_2$)$_2$O

The rate-determining step in this process is the reaction of the dialkyl phosphites with the aminals [104]. Mono- and diphosphonmethylated derivatives were obtained by the phosphonmethylation of benzimidazolin-2-one or benzimidazoline-2-thione using aminals. A phosphonmethylated 2-mercaptobenzimidazole is formed in the case of 1,3-benzimidazoline-2-thione at a reagent ratio of 1:1:1.

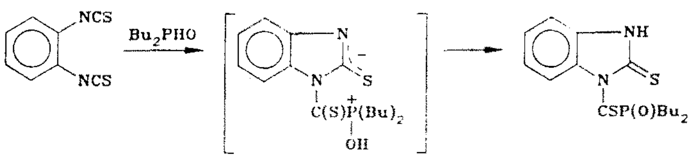
The phosphonmethylation of imidazolin-2-one and imidazoline-2-thione with trialkyl or (better) triaryl phosphites in the presence of aldehydes has been reported [105].



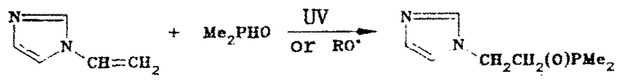
Aromatic nitroso compounds [106, 107] also undergo the Kabachnik–Fields reaction [97, 99] with the participation of imidazole and benzimidazole; products of replacement of the dimethylamino group by a diethylphosphonato group are also formed from p-nitroso-N,N-dimethylaniline [107]:



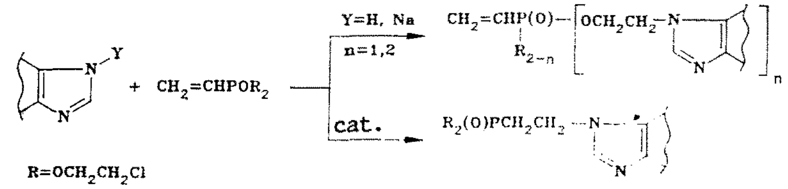
N-(Dibutylphosphinoxidothiocarbonyl)benzimidazole-2-thione was recently obtained by the reaction of o-phenylene diisocyanate with dibutylphosphonous acid [108]:



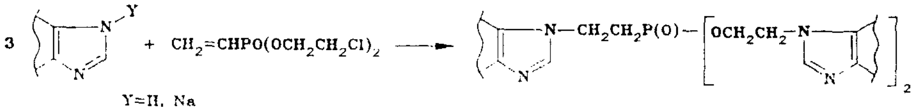
A phosphonethylated imidazole was obtained under the conditions of radical addition of dimethyl phosphite to N-vinylimidazole [109]:



Phosphonethylated imidazoles and benzimidazoles are formed in the reaction of 1,3-diazoles with bis(2-chloroethyl) vinylphosphonate (vinifos) [9, 103, 110-112]:



In the absence of a catalyst (KOH, MeONa, $AlCl_3$) a mixture of mono- and disubstituted products is formed as a result of nucleophilic attack on imidazole at the β-carbon atom of the 2-chloroethoxy group of vinifos [103]. Sodium benzimidazolate undergoes this reaction involving nucleophilic substitution at the 2-chloroethoxy group [111]. Since nucleophilic addition to the double bond of vinifos can be stimulated by both activation of the nucleophile and by an increase in the electrophilicity of the double bond, reactions of imidazole and benzimidazole with bis(2-chloroethyl) vinylphosphonate were accomplished under conditions of basic and acidic catalysis [111, 112]. Substituted benzimidazoles that contain electron-acceptor substituents in the 5 or 6 positions do not undergo phosphonethylation under acid-catalysis conditions [112]. The introduction of electron-donor substituents into the 2 position of the benzimidazole ring facilitates phosphonethylation, whereas the introduction of electron-acceptor substituents hinders it [89, 111, 112]. The conditions found for nucleophilic addition and nucleophilic substitution made it possible to realize the successive participation of three molecules of imidazole or benzimidazole in these reactions [103, 112, 113]:

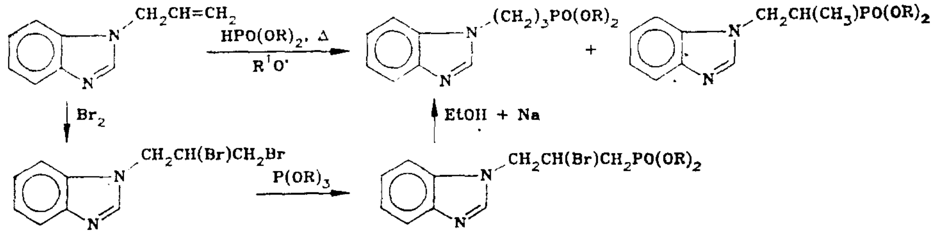


Phosphonethylated azoles that retain a vinyl grouping in their compositions are readily brominated or hydrobrominated (in the presence of traces of tert-butyl hydroperoxide). The bromo derivatives obtained can be used in the synthesis of phosphorylated azoles with different types of fusion of the heterorings [103].

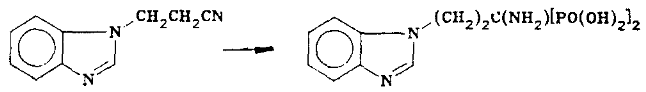
The corresponding labeled phosphonethylated 1,3-diazoles [116, 117] were synthesized by the reaction of imidazole, benzimidazole, or 2-benzylbenzimidazole with bis(2-chloroethyl) vinyl-^{32}P-phosphonate [114, 115].

Methods for obtaining physiologically active oligomeric phosphorylated benzimidazoles with prolonged action via the homopolycondensation of bis(2-chloroethyl) 2-(1-benzimidazolyl)ethylphosphonate or the heteropolycondensation of bis[2-(1-benzimidazolyl)ethyl] vinylphosphonate with ethylene glycol, ethanolamine, and diethanolamine have been developed on the basis of phosphonethylated benzimidazoles [112, 118, 119].

Phosphonalkylated benzimidazoles were obtained from allylbenzimidazole by both the addition of diethyl phosphite to it in the presence of tert-butyl hydroperoxide and by the successive bromination of N-allylbenzimidazole, introduction of the resulting bromo derivative into the Arbuzov rearrangement, and hydrogenation [119, 120]:



A bis(phosphonpropylated) benzimidazole was obtained by the reaction of N-(cyanoethyl)benzimidazole with phosphorus tribromide [120]:

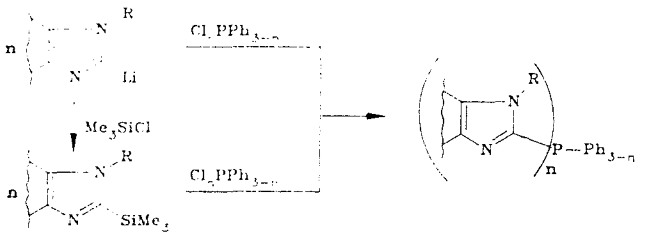


2-Phosphorylated 1,3-Diazoles

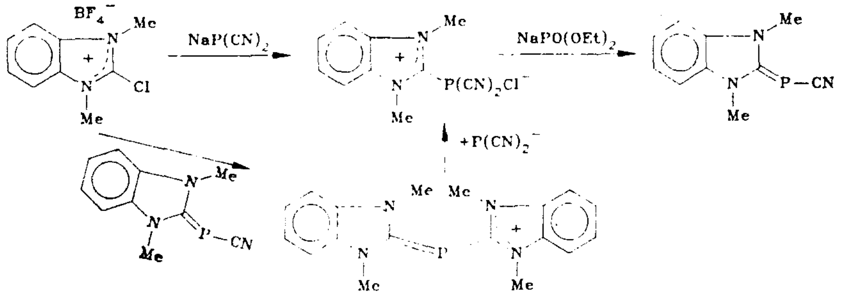
2-Phosphorylated 1,3-diazoles are readily obtained by phosphorylation of lithium and trimethylsilyl derivatives of azoles with chlorides of phosphorus-containing acids or by cyclophosphorylation of o-phenylenediamine via the Phillips–Ladenburg method [96] using phosphorus-containing acetals, imido esters, chloroacetylenes, dichloromethylenamides, and 1-(oximino)-2-alkanones.

The specific synthesis of arazole phosphacyanines was accomplished as a result of the synthesis and study of the structures [121, 122] and reactivities of 2-phosphorylated azoles [121], and various physiologically active substances such as nucleotide analogs of 8,5'-cycloadenosine 5'-monophosphate [123] or (5-diazoniabenzimidazol-2-yl)alkyl P^2-(5'-adenosyl)diphosphate – an effective inhibitor of hydrogenase [6] – were also created.

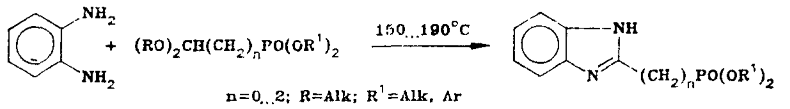
2-Phosphorylated imidazoles [124, 125] and benzimidazoles [126] were obtained through lithium or trimethylsilyl derivatives:



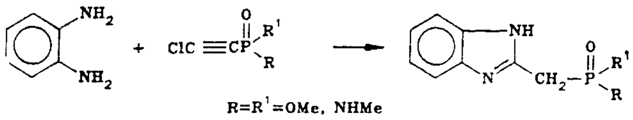
The phosphorylation of derivatives of 1,3-dimethylbenzimidazoline with the sodium salt of dicyanophosphine in the presence of [18]-crown-6 has been proposed [122]:



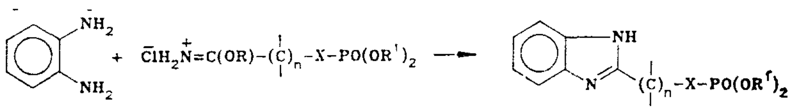
2-Phosphorylated and 2-phosphonalkylated benzimidazoles were obtained [127, 128] by the reaction of phosphorylated acetals with o-phenylenediamine. Removal of the acetal grouping from the phosphoryl grouping facilitates cleavage of the C–O–C bond and increases the yields of the desired products.



2-Phosphonmethylated benzimidazoles are readily formed in the reaction of o-phenylenediamine with chloroethynylphosphonates [129]:

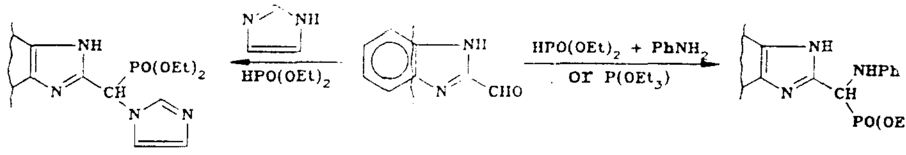


Diverse organophosphorus derivatives of 2-alkylbenzimidazole were obtained by the reaction of dialkylphosphoncarboxylic acid imido ester hydrochlorides with o-phenylenediamine [130-132]:

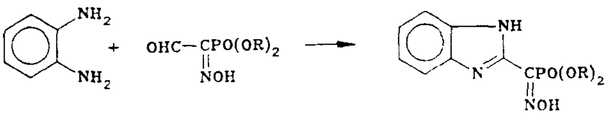


$n=1$, 2; X=O or is absent   R=R^1=Alk

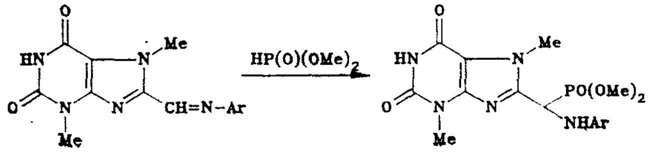
2-Formylbenzimidazole was used as the aldehyde component in the phosphonmethylation reaction to obtain 2-phosphorylated benzimidazoles [133].



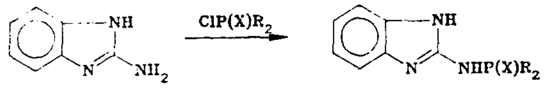
2-Phosphonmethylated benzimidazoles containing a nitroxyl grouping were obtained by the reaction of o-phenylenediamine with 1-oximino-1-dialkoxyphosphorylglyoxal [134]:



2-Phosphonmethylated purines were obtained via the scheme [135]



It is interesting to note that 2-amino diazoles are phosphorylated at the exocyclic nitrogen atom [10, 136]:



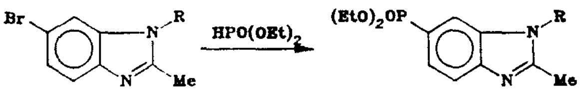
X = O, S

Mono- and Bicyclic 1,3-Diazoles That Are Phosphorylated in Other Positions

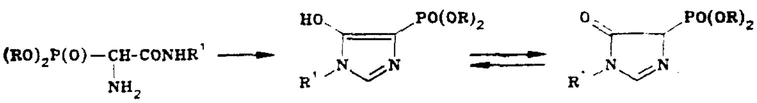
It has been proposed that azoles that are phosphorylated in the 4(5) positions be obtained via schemes that stipulate the use of the corresponding phosphorus-containing o-phenylenediamine derivatives in the Phillips–Ladenburg reaction [96], as well as by phosphorylation of bromobenzimidazoles with dialkyl phosphites or by the reaction of aminophosphonacetamides, acylvinylphosphonates, and acylaminovinylphosphonium salts with ortho esters, amines, amidines, and α-amino heterocycles.

The first example of obtaining a 5(6)-phosphorylated benzimidazole was described in [137].

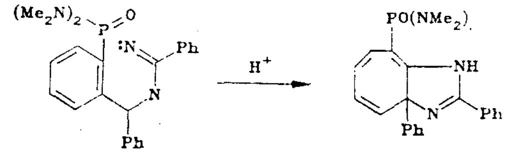
The possibility of the phosphorylation of bromobenzimidazoles with diethyl phosphite in the presence of catalytic amounts of tetrakis(triphenylphosphine)palladium was recently demonstrated [138]:



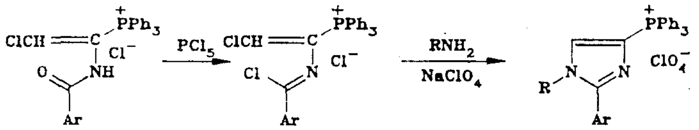
1-Alkyl-4-phosphonylimidazol-5-ones were obtained in the reaction of aminophosphonacetamides with ethyl orthoformate [139]:



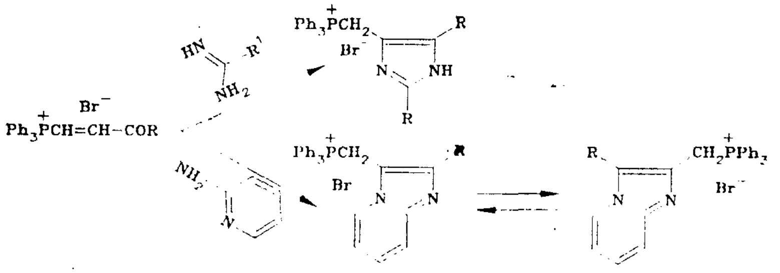
The synthesis of 8-bis(dimethylamino)phosphonyl-2,3*a*-diphenyl-1,3*a*-dihydrocyclohepta[d]imidazole was presented in [140]:



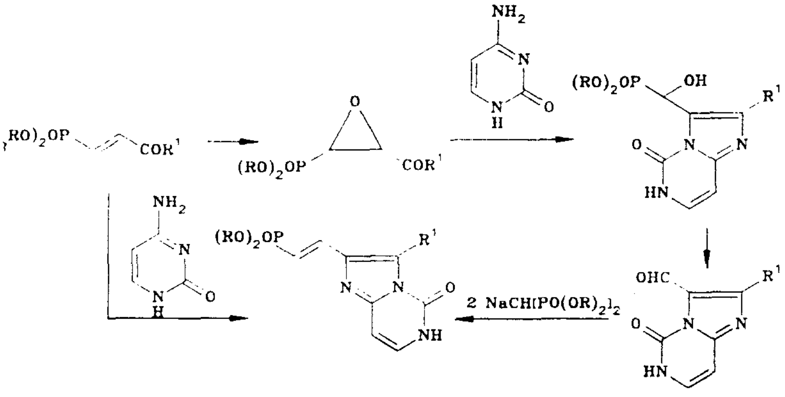
$C_{(4)}$-Phosphonium derivatives of imidazole were obtained on the basis of 2-chloro-1-acylaminovinyltriphenylphosphonium chlorides [141]:



Methods for obtaining 4(5)-phosphorylated imidazoles and condensed (with imidazole) heteroaromatic systems by the reaction of β-acylvinylphosphonium salts with guanidine [142], aminopyridine, aminopyrimidine [143, 144], adenine [145], and other bases [144, 145] have been developed.

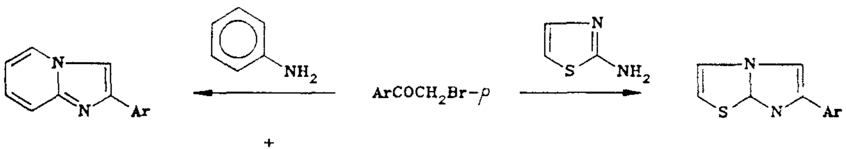


It was found that similar compounds could also be obtained via the scheme [146]

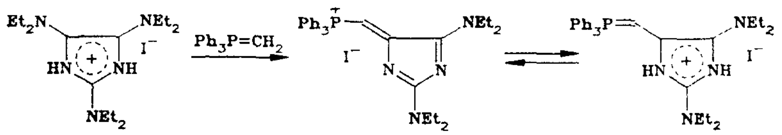


2-Aminopyridine and 2-aminopyrimidine undergo the same reaction [146].

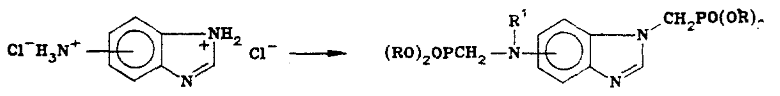
A convenient method for the synthesis of phosphorylated imidazo[1,2-*a*]pyridines and imidazo[2,1-b]thiazoles has been proposed [147]:



Yet another method for the $C_{(4)}$-phosphorylation of imidazole by means of a phosphorus-containing ylid was demonstrated in [148]:



Bis(phosphonmethylated) derivatives of 5(6)-aminobenzimidazole were obtained via the scheme [97, 149, 150]



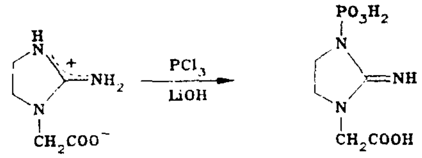
R=Alk, R^1=H; R=H, R^1=$CH_2PO_3H_2$

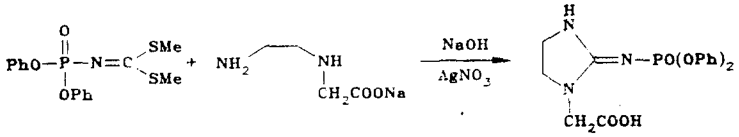
When dialkyl phosphites and paraformaldehyde are used, 1- and 5(6)-bis(phosphonmethylation) occurs, whereas bis- and tris(phosphonmethylation) products are formed in the case of phosphorous acid and formalin in the presence of HCl [97].

Phosphorylated Imidazolines and Imidazolidines

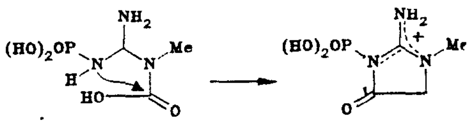
The principal methods for the synthesis of phosphorus-containing imidazolines and imidazolidines and their derivatives are, first of all, phosphorylation of cyclocreatine or imidazolidines with chlorides of phosphorus-containing acids, alkyl phosphites, and diazophosphonates; second, cyclophosphorylation of phosphocreatine and its structural analogs – carboxyalkyl-N-phosphorylguanidine and carbethoxymethylimidourea; third, condensation of β-hydroxyalkylamino acids with cyanoamidophosphates, phosphorus-containing imido esters with ethylenediamine, 2-hydroxyphosphonylethanols with urea, and phosphoryl-2-oximinoacetates with isocyanates.

The catalytic action of 1-carboxymethyl-2-iminoimidazolidine (cyclocreatine) – a substrate of creatinekinase, which plays a role in the accumulation and transfer of energy in transphosphorylation with the formation of phosphocreatine – was observed in a study of biological phosphorylation [151, 152]. In this connection, various derivatives of phosphocyclocreatine that have high physiological activity were synthesized [152-154]:

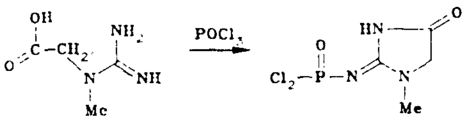




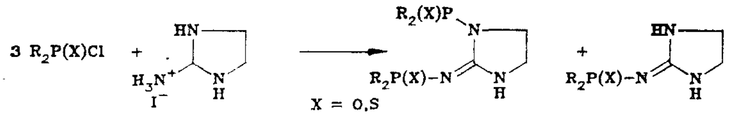
Cyclophosphocreatinone was obtained via the scheme [155]



It should be noted that creatine is readily phosphorylated by refluxing in excess phosphorus oxychloride with the formation of dichlorophosphorylcreatinone [156]:



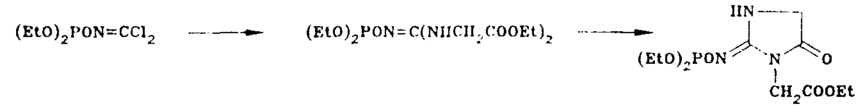
Products of diphosphorylation of 2-iminoimidazolidine were isolated in the reaction of equimolar amounts of 2-aminoimidazoline hydriodide with thiophosphonic acid chlorides. The reaction of 3 moles of the chloride with 1 mole of 2-aminoimidazoline hydriodide leads to the formation of a mixture of di- and monophosphorylation products [157]:



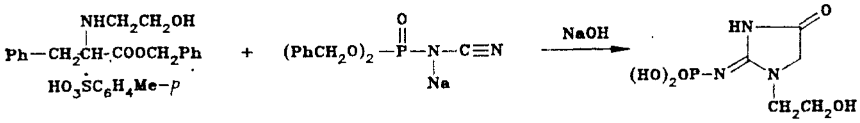
Under similar conditions, 2-aminoimidazoline forms only a monophosphorylimidazoline [157].

Another method for the synthesis of phosphorylated imidazolidines consists in the cyclization of N-α-carboxyalkyl-N'-phosphorylguanidine derivatives [158-160]:

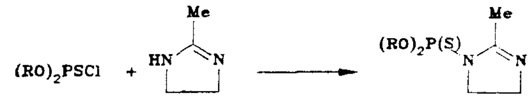
The reaction of a dichloromethyleneamidophosphate with glycine ethyl ester gives the corresponding substituted guanidine, which upon fractionation splits out a molecule of alcohol and is converted to a phosphoryliminoimidazolidine derivative [161]:



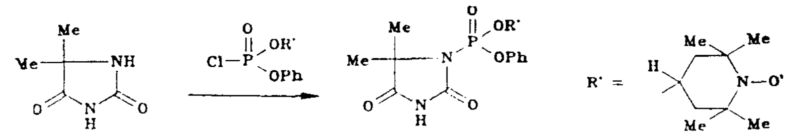
1-(2-Hydroxyethyl)-2-phosphoryliminoimidazolidin-4-ones are also formed in the condensation of N-β-hydroxyalkylamino acid ester tosylates with salts of phosphorylated cyanoamides with subsequent hydrolysis [162]:



The direct phosphorylation of 2-methylimidazoline has also been described [163]:

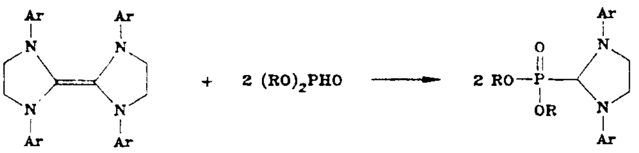


A method for the direct phosphorylation of 3,5-dimethylimidazolidine-2,4-dione with chlorides of phosphorus-containing acids with a spin-stable label has been proposed [43]:

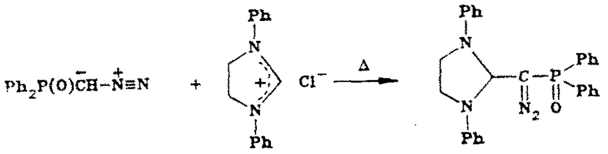


Phosphorylated 3-(3,5-dihalophenyl)imidazolidine-2,4-diones have been patented as pesticides [164].

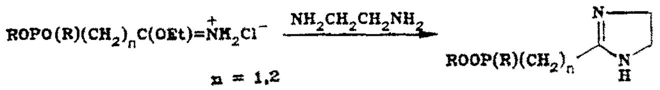
The possibility of obtaining 2-imidazolidinylphosphonates from ethylenetetramines and dialkyl phosphites has been demonstrated [165]:



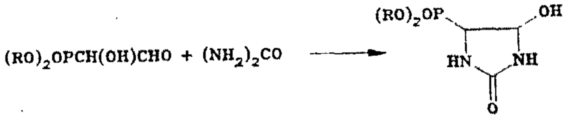
A $C_{(2)}$-phosphorylated imidazolidine was obtained from α-diazophenylphosphonate and 1,3-diphenylimidazolidinium chloride [166]:



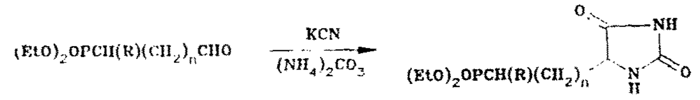
Various $C_{(2)}$-phosphonalkylated imidazolines have been described [167]:



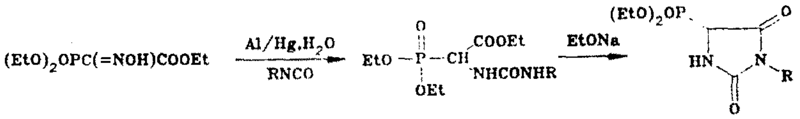
4-Hydroxy-5-phosphonyl-2-imidazolidinones were obtained by the reaction of 2-hydroxy-2-phosphonylethanal with urea [168]:



$C_{(4)}$-Phosphorylated imidazolidine-2,4-diones were synthesized via the scheme [169]



The synthesis of 5H-5-phosphorylated hydantoins based on hydroxyiminophosphonacetic acid esters has been described [170]:



In conclusion, it should be noted that direct phosphorylation and cyclophosphorylation of azoles are the simplest and most accessible methods. In addition to this, new variants of the classical Arbuzov, Atherton–Todd, Phillips–Ladenburg, Mannich, Kabachnik–Fields, and other reactions are widely used for the synthesis of various phosphorylated azoles.

LITERATURE CITED

1. A. F. Pozharskii, A. D. Granovskii, and A. M. Simonov, *Usp. Khim.* 35, 261 (1966).
2. M. N. Preobrazhenskaya, *Usp. Khim.* 41, 9 (1972).
3. L. N. Moiseeva, R. F. Zaitsev, and T. E. Pavlovskaya, *Izv. Akad. Nauk SSSR, Ser. Biol.*, No. 1, 26 (1982).
4. D. G. Knorre and V. V. Vlasov, *Usp. Khim.* 54, 1420 (1985).
5. A. A. Yasnikov, *Zh. Vses. Khim. Obshch.* 31, 556 (1986).
6. A. Burkhard, A. Dworsky, R. Jeck, M. Peelffer, S. Pundak, and C. Woenckhaus, *Z. Physiol. Chem.* 362, 1079 (1981).
7. D. Ranganathan, F. Farooqui, D. Bhattacharyya, J. Metrotra, and K. Kegavan, *Tetrahedron* 42, 4481 (1986).
8. M. Eto, *Organophosphorus Pesticides. Organic and Biological Chemistry* (1976), p. 67.
9. G. L. Matevosyan and P. M. Zavlin, *Zh. Obshch. Khim.* 52, 1441 (1982).
10. L. V. Razvodovskaya, A. F. Grapov, and N. N. Mel'nikov, *Usp. Khim.* 51, 239 (1982).

11. Yu. N. Fadeev and K. V. Novozhilov (eds.), *Scientific Foundations of Plant Protection* [in Russian], Kolos, Moscow (1984), p. 138.
12. M. S. Yakubchik and G. L. Matevosyan, in: *Proceedings of the All-Union Institute for the Protection of Plants* [in Russian], Leningrad (1981), p. 98.
13. G. L. Matevosyan and P. M. Zavlin, in: Summaries of Papers Presented at the All-Union Conference on Chemical Agents for the Protection of Plants, Ufa (1982), p. 162.
14. G. L. Matevosyan and P. M. Zavlin, USSR Authors' Certificate, No. 732,272; *Byull. Izobret.*, No. 17, 12 (1980).
15. G. L. Matevosyan, P. M. Zavlin, and V. E. Sovetkina, "Regulators of the growth and development of plants," in: Summaries of Papers Presented at the 1st All-Union Conference, Nauka, Moscow (1981), p. 200.
16. V. E. Sovetkina, A. D. Shishov, G. L. Matevosyan, and P. M. Zavlin, USSR Authors' Certificate No. 959,724; *Byull. Izobret.*, No. 35, 45 (1982).
17. V. E. Sovetkina, A. D. Shishov, G. L. Matevosyan, and P. M. Zavlin, *Khim. Sel'sk. Khoz.*, No. 12, 23 (1982).
18. V. P. Kotov and G. L. Matevosyan, *Khim. Sel'sk. Khoz*, No. 2, 43 (1984).
19. S. L. Tyuterev, V. V. Meloyan, and G. L. Matevosyan, *Khim. Sel'sk. Khoz*, No. 8, 28 (1984).
20. G. L. Matevosyan and A. I. Drizhachenko, Materials from the 3rd Symposium with Foreign Participation on Problems of Seeds, Vol. 2, Halle (East Germany) (1984), p. 370.
21. G. L. Matevosyan, A. A. Asmagulyan, and S. M. Agadzhanyan, *The Utilization of Growth Regulators and Polymeric Materials in Vegetable Growing*: Collection of Scientific Proceedings of the Leningrad Agricultural Institute [in Russian], Leningrad (1984), p. 6.
22. K. L. Nazaretyan, A. A. Asmagulyan, S. M. Agadzhanyan, P. M. Zavlin, G. L. Matevosyan, and V. E. Sovetkina, *Organophosphorus and Organosilicon Compounds* [in Russian], Leningrad (1985), p. 145.
23. A. A. Meloyan, G. L. Matevosyan, and G. R. Dolbaya, *Agrokhimiya*, No. 3, 113 (1986).
24. G. L. Matevosyan, *The Utilization of Growth Regulators and Polymeric Materials in Vegetable Growing*: Collection of Scientific Proceedings of the Leningrad Agricultural Institute [in Russian], Leningrad (1986), p. 4.
25. V. V. Volkov, P. M. Zavlin, M. M. Dronov, G. L. Matevosyan, and I. B. Maksimov, in: Material from the Symposium on Urgent Problems of Ophthalmopathohistology, Moscow (1982), p. 24.
26. G. L. Matevosyan, A. M. Makarov, M. M. Dronov, V. V. Volkov, and P. M. Zavlin, Summaries of Papers Presented at the 7th All-Union Conference on the Chemistry of Organophosphorus Compounds, Leningrad (1982), p. 242.
27. J. P. Declerq, A. Dubourg, G. Etemad-Aoghadam, A. Klaebe, and J. J. Perie, *Phosph. Sulf.* **21**, 31 (1984).
28. E. B. Brosalina and S. A. Grachev, *Bioorg. Khim.* **12**, 248 (1986).
29. T. Wagner-Jaurregg and B. E. Hackley, *J. Am. Chem. Soc.* **75**, 2125 (1953).
30. J. Baddiley, J. G. Buchanan, and R. Letters, *J. Chem. Soc.*, No. 11, 2812 (1956).
31. P. M. Zavlin and G. L. Matevosyan, *Zh. Obshch. Khim.* **47**, 483 (1977).
32. G. L. Matevosyan, P. M. Zavlin, and R. M. Matyushicheva, *The Chemistry and Practical Application of Organosilicon and Organophosphorus Compounds* [in Russian], Leningrad (1977), p. 36.
33. G. L. Matevosyan, "The production and study of the phosphorylating ability of (1-benzimidazolido)phosphates," Master's Disseration, Institute of Chemistry, Academy of Sciences of the Estonian SSR, Tallinn (1978).
34. P. I. Zavlin, G. L. Matevosyan, and R. M. Matyushicheva, *Zh. Obshch. Khim.* **47**, 484 (1977).
35. G. L. Matevosyan, A. M. Makarov, and P. M. Zavlin, *Scientific Proceedings of the Leningrad Agricultural Institute* [in Russian], Vol. 414 (1981), p. 22.
36. G. L. Matevosyan, A. M. Makarov, P. M. Zavlin, and V. E. Sovetkina, *Agrokhimiya*, No. 9, 100 (1984).
37. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, in: Abstracts of the 12th International Hot-Atom Chemistry Symposium, Balatonfured (Hungary) (1984), p. 42.
38. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, *Zh. Obshch. Khim.* **52**, 2363 (1982).
39. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, *Zh. Obshch. Khim.* **53**, 505 (1983).
40. A. M. Makarov, Abstract of Master's Dissertation, Moscow (1983), p. 16.
41. G. Sosnovsky and M. Z. Konieczny, *Naturforschung.* **32**, 1182 (1977).
42. M. Konieczny and G. Sosnovsky, *Naturforschung.* **33**, 1033 (1978).
43. M. Konieczny and G. Sosnovsky, *Synthesis*, No. 9, 682 (1981).
44. E. Jampel, M. Wokselman, and M. Vilkas, *Tetrahedron Lett.* **9**, 3533 (1968).
45. U. Asselline and N. T. Thuong, *Tetrahedron Lett.* **22**, 847 (1981).
46. V. A. Efimov and S. V. Reverdatto, *Tetrahedron Lett.* **23**, 961 (1982).

47. N. T. Thuong, C. Barbier, and U. Asselline, *Phosph. Sulf.* **14**, 357 (1983).
48. L. Borkofer, W. Gilgenberg, and A. Ritter, *Angew. Chem.* **73**, 143 (1961).
49. H. Dorn, H. Graubaum, D. Zeigan, and R. Radeglia, *Z. Chem.* **15**, 485 (1975).
50. B. G. van den Bos, C. J. Schoot, M. J. Koopmans, and J. Meltzer, *Rec. Trav. Chim.* **80**, 1040 (1961).
51. B. A. Arbuzov, V. M. Zoroastrova, and R. Kh. Sagitova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 3, 661 (1964).
52. R. Blakely, F. Kerst, and F. H. Westheimer, *J. Am. Chem. Soc.* **88**, 112 (1966).
53. H. A. Staab, H. Schaller, and F. Cramer, *Angew. Chem.* **71**, 736 (1959).
54. F. Cramer, H. Schaller, and H. A. Staab, *Chem. Ber.* **94**, 1612 (1961).
55. H. Schaller, H. A. Staab, and F. Cramer, *Chem. Ber.* **94**, 1621 (1961).
56. F. Cramer and H. Schaller, *Chem. Ber.* **94**, 1634 (1961).
57. F. Cramer, H. Neunhoeffer, K. H. Scheit, G. Schneider, and J. Tennigkeit, *Angew. Chem.* **74**, 378 (1962).
58. F. Cramer, *Angew. Chem.* **74**, 434 (1962).
59. H. A. Staab, *Angew. Chem.* **74**, 407 (1962).
60. L. Goldam, J. W. Marsieo, and G. W. Anderson, *J. Am. Chem. Soc.* **82**, 2969 (1960).
61. D. E. Hoard and D. G. Ott, *J. Am. Chem. Soc.* **87**, 1785 (1965).
62. R. H. Symons, *Biochim. Biophys. Acta* **190**, 548 (1969).
63. R. H. Symons, *Biochim. Biophys. Acta* **209**, 296 (1970).
64. S. M. Hect and J. W. Kazarich, *Biochim. Biophys. Acta* **331**, 307 (1973).
65. M. Maeda, A. D. Patel, and A. Hampton, *Nucleic Acids Res.* **4**, 2843 (1977).
66. G. I. Derkach, I. N. Zhmurova, A. V. Kirsanov, V. I. Shevchenko, and A. S. Shtepanek, *Phosphazo Compounds* [in Russian], Naukova Dumka, Kiev (1965), p. 103.
67. L. N. Nikolenko and E. V. Degtyarev, *Zh. Obshch. Khim.* **37**, 1350 (1967).
68. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, *Zh. Obshch. Khim.* **55**, 937 (1985).
69. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, *Zh. Obshch. Khim.* **56**, 69 (1986).
70. A. M. Makarov, G. L. Matevosyan, A. S. Rodygin, and P. M. Zavlin, in: Summaries of Papers Presented at the 8th All-Union Conference on the Chemistry of Organophosphorus Compounds (1985), p. 123.
71. F. Ramirez, H. Okazaki, and J. F. Marececk, *Synthesis*, No. 9, 637 (1975).
72. F. Ramirez, H. Okazaki, and J. F. Marececk, *Tetrahedron Lett.* **18**, 2927 (1977).
73. F. Ramirez, J. S. Ricci, H. O. Kazaki, J. F. Marececk, and M. Lewy, *Phosph. Sulf.* **20**, 279 (1984).
74. C. A. Buton, *J. Am. Chem. Soc.* **103**, 5788 (1981).
75. T. Mukaiyama and M. Hashimoto, *Bull. Chem. Soc. Jpn.* **44**, 2284 (1971).
76. I. Ugi, J. Bauer, E. Fontain, N. Balgobin, J. Chattopadhyaya, T. Pathak, and X. X. Zhou, *Chem. Scripta* **26**, 205 (1986).
77. T. Rathlev and T. Rosenberg, *Arch. Biochem. Biophys.* **65**, 319 (1956).
78. D. E. Hulquist, R. W. Moyer, and P. D. Boyer, *Biochemistry* **5**, 322 (1966).
79. D. E. Hulquist, *Biochim. Biophys. Acta* **153**, 329 (1968).
80. D. Theodoropoulos, J. Gazapolus, and I. Siuchleris, *J. Chem. Soc.*, No. 21, 5257 (1960).
81. H. Hellman, F. Lingens, and H. J. Burkhardt, *Chem. Ber.* **91**, 2290 (1958).
82. A. A. Grachev and A. A. Mustaev, *FEBS Lett.* **137**, 89 (1982).
83. H. Wang, *Science* **167**, 25 (1970).
84. D. Ranganathan and W. S. Brinigar, *J. Org. Chem.* **43**, 4853 (1978).
85. G. L. Matevosyan, R. M. Matyushicheva, and P. M. Zavlin, *Zh. Obshch. Khim.* **48**, 928 (1978).
86. G. L. Matevosyan, R. M. Matyushicheva, and P. M. Zavlin, *Zh. Obshch. Khim.* **48**, 941 (1978).
87. G. L. Matevosyan, P. M. Zavlin, and R. M. Matyushicheva, *Zh. Obshch. Khim.* **48**, 2433 (1978).
88. G. L. Matevosyan and P. M. Zavlin, *Zh. Obshch. Khim.* **49**, 1252 (1979).
89. G. L. Matevosyan, P. M. Zavlin, and R. M. Matyushicheva, *The Chemistry and Practical Application of Organosilicon and Organophosphorus Compounds* [in Russian], Leningrad (1979), p. 98.
90. V. A. Sukahnov, V. A. Basharuli, A. P. Kaplun, and V. I. Shvets, *Zh. Obshch. Khim.* **49**, 235 (1979).
91. V. A. Efimov, S. V. Reverdato, and O. G. Chakhmacheva, *Bioorg. Khim.* **8**, 231 (1982).
92. F. Eckstein and H. Gindl, *Biochim. Biophys. Acta* **149**, 35 (1967).
93. F. Eckstein and H. Gindl, *Chem. Ber.* **101**, 1670 (1968).
94. T. Shimidzu, K. Yamana, A. Murakami, and K. Nakamichi, *Tetrahedron Lett.* **21**, 2717 (1980).
95. T. Shimidzu, K. Yamana, K. Nakamichi, and A. Nurakami, *J. Chem. Soc., Perkin* 2, No. 8, 2294 (1981).

96. K. V. Vatsuro and G. L. Mishchenko, *Name Reactions in Organic Chemistry* [in Russian], Moscow (1976).
97. G. L. Matevosyan, P. M. Zavlin, R. M. Matyushicheva, S. N. Vodavatova, A. A. Meloyan, A. D. Shishov, and B. Kh. Khalmirzaev, *The Chemistry and Practical Application of Organosilicon and Organophosphorus Compounds* [in Russian], Leningrad (1981), p. 164.
98. M. I. Kabachnik and T. Ya. Medved', *Dokl. Akad. Nauk SSSR* **82**, 164 (1952).
99. E. K. Fields, *J. Am. Chem. Soc.* **74**, 1528 (1952).
100. K. Moedritzer and R. Irany, *J. Org. Chem.* **31**, 1603 (1966).
101. G. L. Matevosyan, A. V. Zhuravlev, R. M. Matyushicheva, and P. M. Zavlin, *Zh. Obshch. Khim.* **50**, 1198 (1980).
102. G. L. Matevosyan, A. V. Zhuravlev, R. M. Matyushicheva, and P. M. Zavlin, *Zh. Obshch. Khim.* **50**, 1506 (1980).
103. G. L. Matevosyan and P. M. Zavlin, *Zh. Obshch. Khim.* **53**, 1729 (1983).
104. G. L. Matevosyan, I. G. Chezlov, I. Yu. Matyushichev, and P. M. Zavlin, *Zh. Obshch. Khim.* **56**, 1426 (1986).
105. J. A. Mikroyannidis, *Phosph. Sulf.* **12**, 249 (1982).
106. G. L. Matevosyan, A. V. Zhuravlev, and P. M. Zavlin, in: Summaries of Papers Presented at the 7th All-Union Conference on the Chemistry of Organophosphorus Compounds, Leningrad (1982), p. 230.
107. G. L. Matevosyan, A. V. Zhuravlev, and P. M. Zavlin, *Zh. Obshch. Khim.* **53**, 2401 (1983).
108. M. G. Zimin, A. V. Mironov, R. A. Cherkasov, and A. N. Pudovik, *Zh. Obshch. Khim.* **55**, 452 (1985).
109. H. J. Kleiner, *Annalen*, No. 5, 751 (1974).
110. G. L. Matevosyan, P. M. Zavlin, R. M. Matyushicheva, and S. P. Rabinovich, USSR Authors' Certificate No. 740,789; *Byull. Izobret.*, No. 22, 22 (1980).
111. G. L. Matevosyan, R. M. Matyushicheva, S. P. Rudnik, and P. M. Zavlin, *Zh. Obshch. Khim.* **50**, 64 (1980).
112. G. L. Matevosyan, P. M. Zavlin, R. M. Matyushicheva, V. E. Sovetkina, A. D. Shishov, S. L. Tyuterev, and M. S. Yakubchik, *The Chemistry and Practical Application of Organosilicon and Organophosphorus Compounds* [in Russian], Leningrad (1980), p. 101.
113. G. L. Matevosyan, P. M. Zavlin, R. M. Matyushicheva, and S. P. Rabinovich, USSR Authors' Certificate No. 742,433; *Byull. Izobret.*, No. 23, 138 (1980).
114. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, *Zh. Obshch. Khim.* **55**, 1977 (1985).
115. A. M. Makarov, G. L. Matevosyan, and P. M. Zavlin, Summaries of Papers Presented at the Conference on the Prospects for the Utilization of Physicochemical Analysis for the Development of Technological Processes and Methods for the Analytical Monitoring of Chemical and Pharmaceutical Manufacturing, Perm (1985), p. 38.
116. G. L. Matevosyan, A. M. Makarov, P. M. Zavlin, A. N. Dyumin, and V. A. Smolin, *Zh. Obshch. Khim.* **56**, 592 (1986).
117. G. L. Matevosyan, A. M. Makarov, A. N. Dyumin, V. A. Smolin, and Z. A. Stepanova, Summaries of Papers Presented at the 2nd All-Union Conference on Applied Radiobiology, Vol. 2, Kiev (1985), p. 40.
118. G. L. Matevosyan, R. M. Matyushicheva, and P. M. Zavlin, *Zh. Obshch. Khim.* **49**, 2766 (1979).
119. G. L. Matevosyan, P. M. Zavlin, A. G. Kutyumin, L. S. Nechaeva, and A. A. Meloyan, Summaries of Papers Presented at the All-Union Conference on Polymeric Materials in the Agricultural Industry, Kishinev (1985), p. 67.
120. G. L. Matevosyan, I. Yu. Matyushichev, and P. M. Zavlin, *Zh. Obshch. Khim.* **57**, 654 (1987).
121. H. Oehling, F. Baer, and K. Kimroth, *Tetrahedron Lett.* **17**, 1329 (1976).
122. A. Schmidpeter, W. Gebler, F. Zwaschka, and W. S. Sheldrick, *Angew. Chem.* **92**, 767 (1980).
123. J. A. Raleigh and R. Whitehouse, *Chem. Commun.*, No. 9, 305 (1975).
124. N. J. Curtis and R. S. Brown, *J. Org. Chem.* **45**, 4038 (1980).
125. K. Camman, *Topics in Current Chemistry. Biominetic, Biomenetic, and Bioorganic Chemistry*, Vol. 28, F. L. Boschke (ed.), Springer-Verlag, Berlin (1985), p. 143.
126. S. S. Moore and G. M. Whitesides, *J. Org. Chem.* **47**, 1489 (1982).
127. A. I. Razumov, USSR Author's Certificate No. 184,485; *Byull. Izobret.*, No. 6, 22 (1966).
128. A. I. Razumov, P. A. Gurevich, B. G. Liorber, and T. V. Borisova, *Zh. Obshch. Khim.* **39**, 392 (1969).
129. V. A. Garibina, A. V. Dogadina, B. I. Ionin, and A. A. Petrov, USSR Authors' Certificate No. 761,475; *Byull. Izobret.*, No. 33, 122 (1980).
130. S. N. Elfimova, V. E. Shishkin, and B. I. No, USSR Authors' Certificate No. 494,386; *Byull. Izobret.*, No. 45, 66 (1975).
131. V. E. Shishkin, Yu. M. Yukhno, and B. I. No, in: The Chemistry and Application of Organophosphorous Compounds: Proceedings of the 6th Conference, Naukova Dumka, Kiev (1981), p. 292.
132. S. N. Elfimova, V. E. Shishkin, and B. I. No, *Zh. Obshch. Khim.* **55**, 1630 (1985).

133. G. L. Matevosyan, R. M. Matyushicheva, S. N. Vodovatova, and P. M. Zavlin, *Zh. Obshch. Khim.* **51**, 775 (1981).
134. M. P. Sokolov, T. A. Zyablikova, Z. M. Khammatova, I. É. Ismaev, V. A. Pavlov, B. G. Liorber, and A. V. Il'yasov, *Zh. Obshch. Khim.* **55**, 1302 (1985).
135. B. P. Lugovkin, *Khim. Geterotsikl. Soedin.*, No. 5, 900 (1969).
136. A. F. Grapov, Abstract, Doctoral Dissertation, All-Union Scientific-Research Institute of Chemical Agents for the Protection of Plants, Moscow (1976).
137. R. W. Bost and L. D. Quin, *J. Org. Chem.* **18**, 358 (1953).
138. A. A. Tolmachev, É. S. Kozlov, and A. M. Pinchuk, *Zh. Obshch. Khim.* **56**, 2503 (1986).
139. P. S. Khokhlov, B. A. Kashemirov, A. D. Mikityuk, A. L. Chimishkyan, and Yu. A. Strepikheev, *Zh. Obshch. Khim.* **54**, 2701 (1984).
140. L. Dashan and S. Trippett, *Tetrahedron Lett.* **24**, 2039 (1983).
141. V. S. Brovarets, O. P. Lobanov, T. K. Vinogradova, and B. S. Drach, *Zh. Obshch. Khim.* **54**, 286 (1984).
142. R. L. Webb and J. Lewis, *J. Heterocycl. Chem.* **18**, 1301 (1981).
143. C. Ivancsics and E. Zbiral, *Annalen.*, No. 10, 1934 (1975).
144. E. Zbiral and E. Hugl, *Tetrahedron Lett.* **13**, 439 (1972).
145. E. Hugl, G. Schulz, and E. Zbiral, *Annalen.*, No. 2, 278 (1973).
146. E. Öhler, E. Zbiral, and M. El-Badawi, *Tetrahedron Lett.* **24**, 5599 (1983).
147. P. I. Yagodinets, I. N. Chernyuk, and M. I. Shevchuk, *Zh. Obshch. Khim.* **54**, 2779 (1984).
148. R. Compper and K. P. Bichlmayer, *Tetrahedron Lett.* **21**, 2879 (1980).
149. G. L. Matevosyan, A. I. Zhuravlev, and P. M. Zavlin, in: Summaries of Papers Presented at the A. E. Arbuzov All-Union Colloquium on the Synthesis, Structures, and Reactivities of Some Heteroorganic Compounds, Kazan (1981), p. 41.
150. G. L. Matevosyan and P. M. Zavlin, in: Summaries of Papers Presented at the 8th All-Union Conference on the Chemistry of Organophosphorus Compounds Devoted to the 80th Anniversary of the A. E. Arbuzov Reaction, Vol. 1, Kazan (1985), p. 32.
151. G. L. Rowley, A. L. Greenleaf, and G. L. Kenyon, *J. Am. Chem. Soc.* **93**, 5542 (1971).
152. G. R. Griffits and J. B. Walker, *Biol. Chem.* **251**, 2049 (1976).
153. G. E. Struve, C. Gazzola, and G. L. Kenyon, *J. Org. Chem.* **42**, 4035 (1977).
154. G. N. Phillips, J. W. Thomas, T. M. Annesley, and F. A. Quiocho, *J. Am. Chem. Soc.* **101**, 7120 (1979).
155. G. Lillocci and C. A. Vernon, *Gazz. Chim. Ital.* **111**, 23 (1981).
156. K. Zeilt and H. Meger, *Z. Physiol. Chem.* **252**, 101 (1938).
157. L. V. Razvodovskaya, A. F. Grapov, S. I. Orlov, É. Sh. Khasan'yanov, and N. N. Mel'nikov, *Zh. Obshch. Khim.* **50**, 329 (1980).
158. A. Jesus, German Patent No. 1,260,472; *Chem. Abstr.* **69**, 36,128 (1968).
159. A. Jesus, German Patent No. 1,260,473; *Chem. Abstr.* **69**, 36,129 (1968).
160. M. P. Alimov and P. I. Alimov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 11, 2611 (1968).
161. M. P. Alimov and P. I. Alimov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 1, 119 (1969).
162. A. Jesus, French Patent No. 2,038,713; *Chem. Abstr.* **75**, 64,275 (1971).
163. A. F. Prokof'ev, N. N. Mel'nikov, and I. L. Vladimirova, *Zh. Obshch. Khim.* **47**, 1242 (1977).
164. German Patent No. 2,925,303; *Byull. Izobret.*, No. 2, 26 (1980).
165. J. Hocker and R. Merten, *Annalen.*, No. 1, 16 (1978).
166. M. Regitz, A. Heydt, and B. Weber, *Angew. Chem., Int. Ed.* **18**, 531 (1979).
167. V. E. Shishkin, Yu. L. Zotov, and B. I. No, *Zh. Obshch. Khim.* **47**, 1270 (1977).
168. J. A. Mikroyannidis, A. K. Tsolis, and D. J. Gourghiotis, *Phosph. Sulf.* **13**, 279 (1982).
169. J. M. Varled, G. Fabre, F. Sauveur, and N. Collingnon, *Tetrahedron* **37**, 1377 (1981).
170. P. S. Khokhlov, B. A. Kashemirov, A. D. Mikityuk, and Yu. A. Strepikheev, *Zh. Obshch. Khim.* **53**, 2146 (1983).