PHOSPHORYLATED PYRIDINES AND THEIR BENZO-HOMOLOGS (REVIEW)

A. A. Tolmachev and É. S. Kozlov

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Methods are discussed for the phosphorylation of pyridines and their benzo-homologs to give compounds containing P—Het or P—CH_2Het bonds. The chemical properties of these compounds are considered.

The chemistry of heterocyclic compounds containing phosphorus substituents has developed extremely rapidly in recent times, as a result of their increasing preparative and practical importance. Many of these compounds possess biological activity, complexing properties, corrosion-inhibitory properties, etc. The 1971 review of Redmore [1] included virtually all the information on phosphorylated heterocycles. Since that time, however, the amount of work carried out has been so great that reviews have appeared which are devoted to the phosphorylation of single systems, such as benzimidazole [2] and indole [3], and the need has arisen for similar reviews for pyridine and its benzo-homologs, since existing reviews are fragmentary [4, 5] or obsolete [1, 6].

The amount of literature on compounds containing phosphorus and pyridine moieties is extremely large [7]. We have therefore, in this review, considered only those compounds with phosphorus—carbon bonds of the types P—Het and P—CH_2Het, the properties of which show most clearly the mutual effects of the heterocyclic and phosphorus-containing residues. The review covers literature up to July 1985. Complexes derived from phosphorylated nitrogen heterocycles have not been considered in view of the volume of this literature, which could form the subject of a separate review.

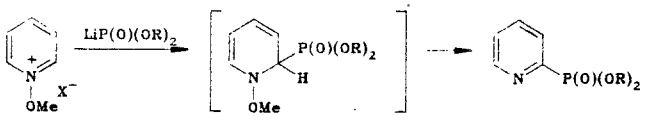
1. HETEROCYCLES CONTAINING A TETRACOORDINATED PHOSPHORUS ATOM

1.1. Compounds Phosphorylated in the ortho- OR para-Position to the Nitrogen Atom

The phosphorylated nitrogen heterocycles considered in this section are the most readily accessible and interesting from the preparative point of view. Methods for their preparation are for the most part based on the phosphorylation of heterocyclic cations or halogenated heterocycles, and their properties have been the subject of numerous studies.

Methods of Preparation. The method most frequently employed, namely phosphorylation of heterocyclic cations with trialkyl phosphites or dialkyl phosphite salts, was discovered independently by Redmore [8] and Soviet workers [9].

By reacting various N-methoxypyridinium, -quinolinium, and -isoquinolinium cations with lithium or sodium dialkyl phosphites, Redmore obtained a wide variety of phosphorylated heterocycles [10-14]. The reaction between lithium dialkyl phosphites and the unsubstituted N-methoxypyridinium cation gave exclusively 2-phosphorylated pyridines, as shown by their PMR spectra [11].



When sodium dialkyl phosphites were used, the 4-phosphorylated pyridines were present as impurities, and the overall yields of phosphorylated products fell [10-14].

Unsubstituted N-methoxyquinolinium cations also give principally the 2-phosphorylated heterocycles [12, 13], but when a substituent ortho- to the heterocyclic nitrogen is present,

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660.
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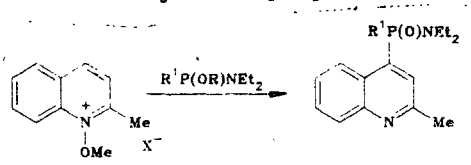
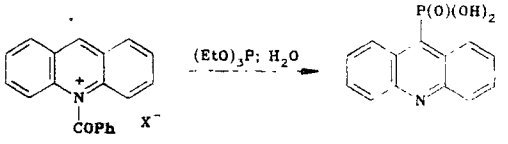
the 4-substituted quinolines are obtained in substantially lower yields [10, 15].

It is interesting that the presence of substituents in the 3-position of the pyridine ring (CH_3, C_6H_5, F, Cl [10, 12, 13]) results in the preferential formation of 2- rather than 6-phosphorylated pyridines despite the steric factors operating, perhaps as a result of the stabilization of an intermediate. The accumulation of this latter compound in the reaction mixture explains the considerable increases in yield obtained when the reaction is carried out at reduced temperatures [16].

N-Methoxyquinaldinium cations are also phosphorylated by the Arbuzov reaction by ester amides of phosphorous acid, but in lower yields [15].

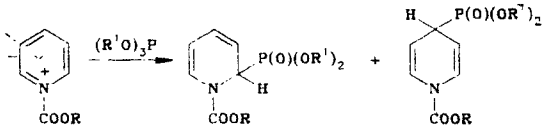


Sheinkman et al. have phosphorylated N-acylpyridinium, -quinolinium, and -acridinium cations with triethyl phosphite under severe conditions [9, 17-19]. Following hydrolysis of the reaction mixture, the corresponding phosphonic acids were obtained.



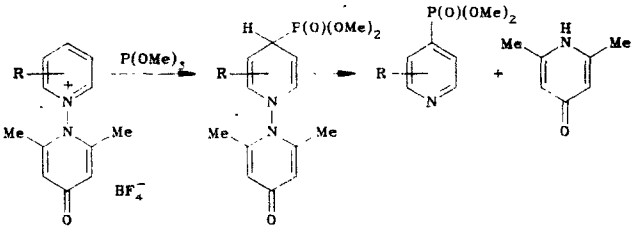
The pyridine- and quinolinephosphonic acids obtained by these workers were regarded as the 2-phosphono-derivatives without any proof whatsoever. In the case of pyridine, this conclusion appears to be erroneous (see below).

Subsequently, phosphorylation with trialkyl phosphites was used to obtain dihydropyridines, dihydroquinolines, and dihydroisoquinolines, under very mild conditions and in high yields [20-24]. This reaction has recently been extended to a broad range of related nitrogen heterocycles [25-29].



The bulk of the radical R^1 influences the product ratio in pyridines. When trimethyl phosphite is used, the ratio is approximately unity, but with triethyl and triisopropyl phosphites 4-addition occurred almost exclusively [21].

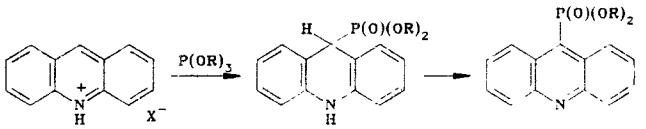
It is interesting that pyridinium and quinolinium salts, despite their differing structures, are phosphorylated by trimethyl phosphite in the 4-position only [30].



In contrast to pyridinium salts, N-acylquinolinium cations give solely the 2-phosphorylated products [23]. Isoquinolinium salts are invariably phosphorylated in the 1-position [22, 24, 30].

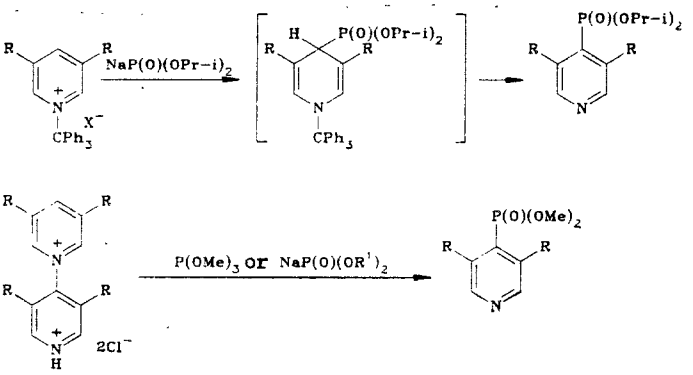
Attempts to utilize dialkyl phosphite salts instead of trialkyl phosphites either gave lower yields [20], or were unsuccessful [30].

Simple salts of heterocyclic cations could be phosphorylated with trialkyl phosphites or dialkyl phosphite salts only in the cases of acridine and 9-methylacridine [8, 31-33]. Phosphorylated dihydroacridines are readily dehydrogenated by chloranil [8].

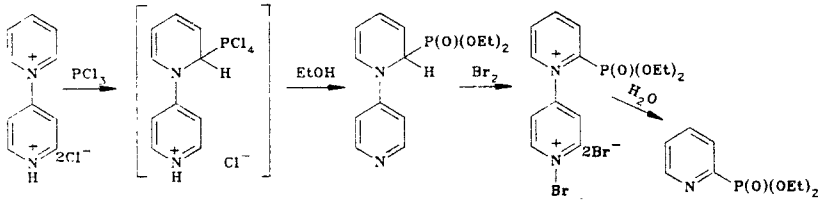


N-Alkylated acridinium and -isoquinolinium cations are readily phosphorylated [8, 31-33]. When pyridine or quinoline methiodides are reacted with sodium diethyl phosphite, mixtures of the 2- and 4-phosphorylated dihydropyridines and dihydroquinolines were obtained [33], but according to other workers the N-methylpyridinium cation is phosphorylated in the 4-position only [34]. Trimethyl phosphite reacts with quinoline methiodide also in this position [25].

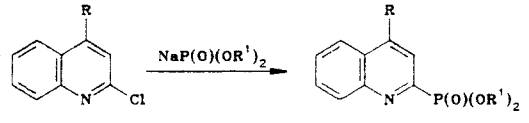
Pyridinium cations carrying more complex alkyl or aryl substituents on the nitrogen have been used successfully for the preparation of 4-phosphorylated pyridines [35, 36].



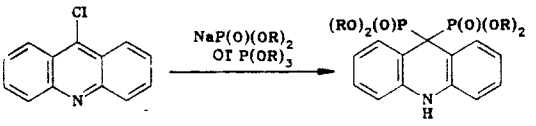
The readily accessible pyridine-pyridinium dichloride, which is used extensively in the synthesis of substituted pyridines, is also phosphorylated by dialkyl phosphites or by phosphorous acid [37, 38] to give substantial amounts of 4-hydroxypyridines. The use of pyridine-pyridinium dichloride has also been proposed for the preparation of pyridine-2-phosphonic acids [39].



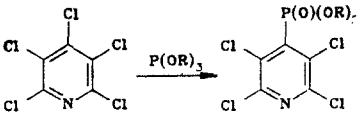
Attempts to carry out the Michaelis–Bekker and Arbuzov reactions with monohalopyridines by many workers have been unsuccessful [40, 41]. The use of catalysts enabled phosphorylation products to be isolated in yields of around 1% [10]. Michaelis–Bekker phosphorylation was relatively successful only in the case of 2-chloroquinolines [40]



In these reactions, 9-chloroacridine gives not the monophosphorylated acridine, as erroneously believed earlier [42], but the diphosphorylation product [8].

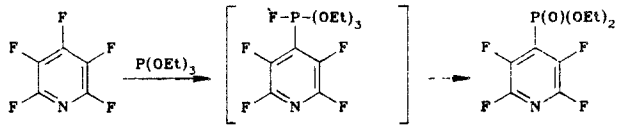


The presence of acceptor substituents in nitrogen heterocycles facilitates phosphorylation. It was shown in 1969 that perchlorpyridine undergoes the Arbuzov reaction to give the 4-phosphorylated products [43]. Subsequently, an extensive range of phosphites were used in this reaction [44-46].



The reaction between the 4-phosphorylated perchloropyridine and triethyl phosphite in the presence of copper salts gave a 2,4-diphosphorylated pyridine, the first compound to contain two atoms of phosphorus attached to the pyridine ring [47].

Perfluoropyridine also undergoes Arbuzov phosphorylation [48, 49]. The effects of Lewis acids on this reaction have been studied, leading to the conclusion that a fluorophosphorane is formed as an intermediate [49].

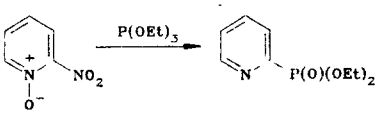


This postulated fluorophosphorane was later identified by its NMR spectra [41], but it was not possible to detect the analogous chlorophosphorane in the reaction with perchloropyridine. The best yields in these reactions were obtained with triisopropyl phosphite, which is usually of low reactivity [46]. The much more reactive dialkyl phosphonites phosphorylate perchloro-pyridine in very low yields [45, 46], and in the case of perfluoropyridine none of the required products could be isolated [46]. These anomalous results were explained as being due to the increased rates of side reactions with reactive phosphites.

Halo-3,5-dinitropyridines and halo-3-nitroquinolines undergo the Arbuzov reaction in addition to perhalopyridines [50, 51]. According to Kato et al. [51], when 4-chloro-3-nitroquinoline reacts with trimethyl phosphate, in addition to phosphorylation, reduction of the nitro group occurs, but in the cases of 2- and 4-chloro-3,5-dinitropyridines phosphorylation takes place so rapidly that the nitro-group remains unaffected.

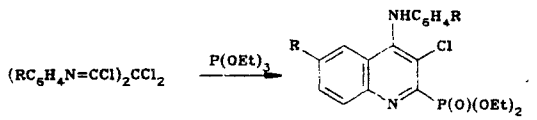
Analogs of halonitropyridines (halopyrimidines and halo-sym-triazines) also undergo Arbuzov phosphorylation [1, 52].

It is interesting that 2-nitropyridine N-oxide is one of the few aromatic compounds in which the nitro-group is replaced by the phosphoryl group [53].

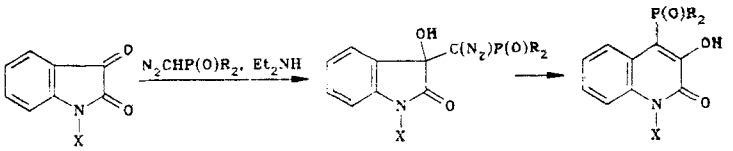


On heating halogenated pyridines, dipyridyl, and quinolines with triphenylphosphine and triethylphosphine, the phosphonium salts are formed [54, 55]. We have found that 2-bromopyridine and 2-bromoquinoline give the phosphonium salts even on heating with hexamethyltriamidophosphite. The successful outcome of these reactions is made possible by the thermal stability of the salts formed, and the high nucleophilicity of the phosphorus atom in these reagents. Pyridyltriphenylphosphonium salts had previously been obtained by reacting 2-pyridinemagnesium halides with triphenylphosphine in the presence of cobalt salts, or by the electrochemical oxidation of triphenyl-phosphine in the presence of pyridine [56, 57].

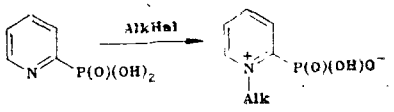
Some phosphorylated quinolines have been obtained by cyclization. For example, the reaction of dichloromalonic acid bisimidoylchloride with an excess of triethyl phosphite gives 2-phosphorylated quinolines [58]. The structures of the compounds obtained were established by x-ray diffraction [59].



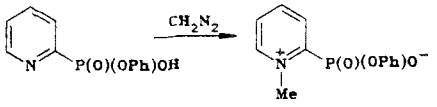
Treatment of N-substituted isatins with phosphorylated diazomethanes in the presence of diethylamine, followed by further reactions, gave the phosphorylated quinolines [60].



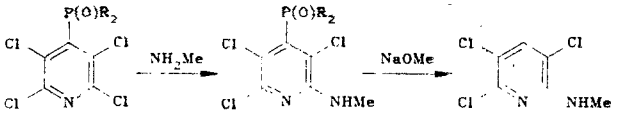
Chemical Properties. Most of these heterocyclic phosphonates are hydrolyzed to the corresponding phosphonic acids, the properties of which are well known. 2-Pyridyl- and tetrachloro-4-pyridylphosphonic acids react with phosphorus pentachloride to give the acid chlorides [16, 61], from which thioanhydrides, esters, amides, and other derivatives are obtained in the usual ways [15, 16, 47, 61]. 2-Pyridylphosphonic acid undergoes alkylation at nitrogen to give the betaine [12, 13].



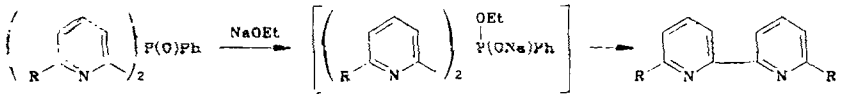
A similar betaine is obtained on reacting the monophenyl ester of this acid with diazomethane [62].



A characteristic property of some of these compounds is the lability of the C–P bond. For example, 3,5-dinitro-2-(or 4)-diethoxyphosphonylpyridine loses its phosphorus grouping even on heating with hydrochloric acid [50]. 4-Phosphorylated tetrachloropyridines are stable to hydrochloric acid, but are dephosphorylated by sodium hydroxide, sodium diethyl phosphite, or sodium methoxide [44, 47]. The introduction of a methylamino group into these compounds strengthens the C–P bond, which is then cleaved only by sodium methoxide [47].



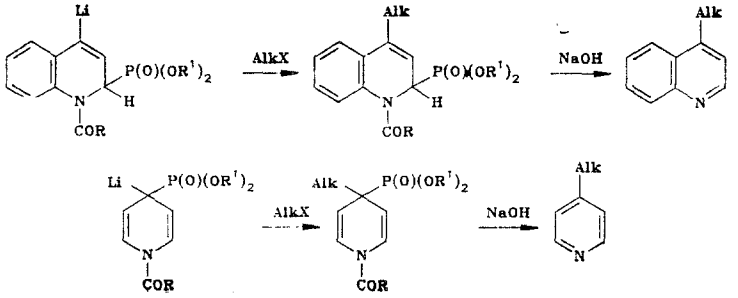
Also worthy of note is the reaction of alkoxides with di-(2-pyridyl)phenylphosphine oxide, which is converted into dipyridyls [63]. The C–C bond is formed intramolecularly, as shown by the preparation of unsymmetrical dipyridyls with different radicals R. The reaction is assumed to take place via intermediate phosphoranes, the presence of which is also postulated in the dephosphorylation of tetrachloropyridines [47, 63].



Pyridine- and quinolinephosphonium salts also show enhanced sensitivity to nucleophiles, being cleaved instantaneously by dilute ammonia solution, but with sodium p-nitrophenoxide a reaction occurs which is rare for phosphonium salts, namely nucleophilic replacement of the phosphorus group [54]. Similar lability in phosphonium salts is seen when other acceptor groups are attached to the phosphorus [64].

The properties of phosphorylated dihydro-derivatives of nitrogen heterocycles have been examined closely. Phosphorylated N-alkyl- and NH-dihydroacridines, and N-acyldihydroisoquinolines can be metallated, and undergo the Horner–Wittig reaction with aldehydes [8, 22, 32] and ketones [32]. A number of these metallated derivatives are alkylated by alkyl halides. It is interesting to note that the dihydroquinoline anion is alkylated only in the free position, whereas the dihydropyridine anion undergoes reaction at the carbon atom bonded to phosphorus.

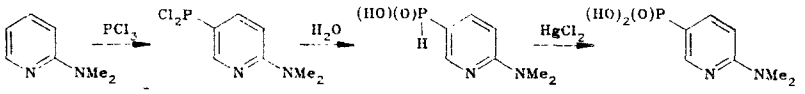
Such reactions have been used in the synthesis of alkaloids [65]. The proton of the $CHP(O)(OR)_2$ group is replaceable by an alkyl group and by direct reaction with orthoformic ester [8].



1.2. 3(5)-Phosphorylated Pyridines and 3-Phosphorylated Quinolines

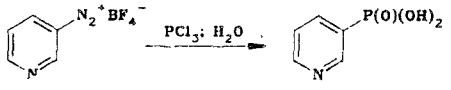
Methods for the preparation of 2- and 4-phosphorylated pyridines are, generally speaking, unsuitable for the synthesis of the 3- and 5-substituted analogs, which are therefore frequently obtained by different methods.

A 5-phosphorylated pyridine was first obtained by reacting 2-dimethylaminopyridine with phosphorus trichloride [66].

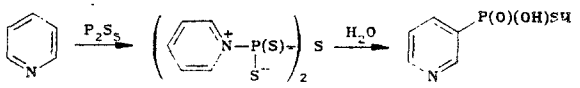


The dichlorophosphine was not isolated, and the position of phosphorylation was not proved. We have repeated this work, and established the structure of the product by elemental analysis and its ^{1}H and ^{31}P NMR spectra.

Bennett et al. [67] obtained pyridine-2-phosphonic acid by the Friedman–Dok reaction, but in low yields. This is the sole example of the use of this reaction for heterocyclic compounds.

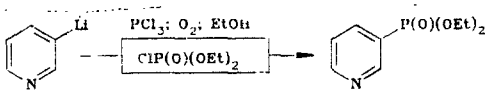


The analogous monothiophosphonic acid was synthesized from pyridine and phosphorus pentasulfide, following hydrolysis of the intermediate betaine [68].

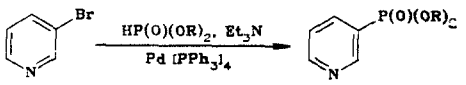


Similar migrations of groups of any type from the nitrogen of the pyridine ring have not been reported (other than in the Ladenburg reaction [69]).

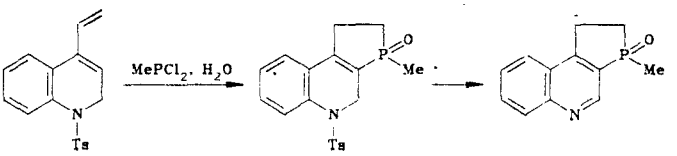
3-Phosphorylated pyridines may also be obtained from 3-lithiopyridine and phosphoryl chlorides [70].



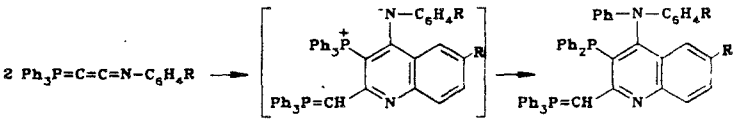
Much higher yields are obtained in the reaction between 3-bromopyridine and a mixture of diethyl phosphite and triethylamine in the presence of a palladium catalyst [71]. Attempts to use other catalysts for the phosphorylation of the pyridine ring have not met with success.



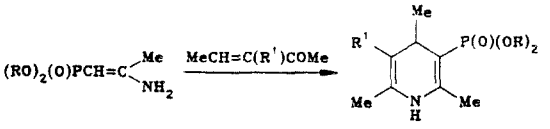
The first 3-phosphorylated quinoline was synthesized by the MacCormack reaction [72, 73].



An unusual cyclization of phosphorus ylids with cumulative double bonds has given a quinoline containing a 3-diphenylphosphino-group, the structure of which was established by x-ray diffraction and its chemical behavior [74].

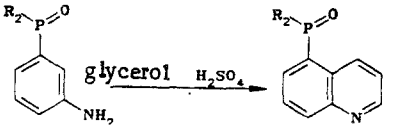


A number of 3-phosphorylated dihydropyridines have also been obtained by cyclization of phosphorylated anamines with α,β-unsaturated aldehydes and ketones [75, 76].

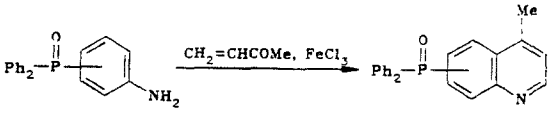


1.3. Quinolines Phosphorylated in the Benzene Ring

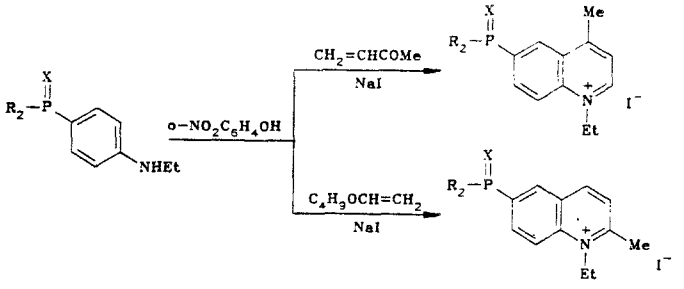
The principal method for the preparation of these compounds is by cyclization of phosphorylated anilines, as in the Skraup reaction. m-Phosphorylated anilines give the 5- rather than the 7-substituted quinolines, as shown by their NMR spectra [77].



The cyclization of thio-oxides under these conditions results in simultaneous oxidation to the oxides [77]. When m-(diphenylphosphonyl)aniline is cyclized in lepidine, the 5-phosphoryl derivative only is formed in low yield, but the p-substituted analog cyclizes quite readily [78].



We have recently developed a simple method of synthesis of p-phosphorylated N-ethylanilines, and have used it to obtain some quinaldinium and lepidinium salts [79, 80]. The cyclization conditions are such that both sulfur and selenium attached to phosphorus are retained.



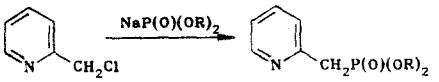
Skraup cyclization was used to obtain quinoline-6-phosphonic and 6-quinolylmethanephosphonic acids [81], and (6-quinolylmethyl)triphenylphosphonium salt [82]. 6-Triphenylphosphonioquinaldines can be obtained by heating 6-iodoquinaldine with triphenylphosphine at 230-240°C [79]. This reaction has been used to obtain a wide variety of phosphonium salts [83].

Cyanine dyes have been obtained from phosphorylated quinaldine and lepidine salts, and the effects of the phosphorus groups on their spectral properties have been examined [84, 85].

1.4. Pyridines and Quinolines Phosphorylated in the α-Position of the Side Chain

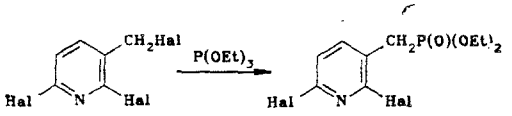
These compounds have found extensive application in the Horner–Wittig and Wittig reactions, and their complexing abilities have also been closely examined.

Methods of Preparation. The principal method for the preparation of these compounds is the Michaelis–Bekker reaction of halomethylpyridines and -quinolines, the first example of which was carried out with 2-chloromethylpyridine in 1956 [86].

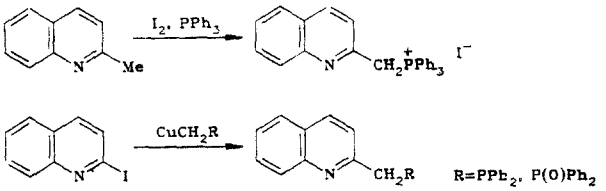


2-Chloromethylpyridine N-oxide reacts similarly [87]. This reaction has been used to obtain side-chain phosphorylated 3- and 4-methylpyridines [87-90] and 2-, 6-, and 8-methyl quinolines [91-93]. The sodium salts of thiophosphorous [94] and phosphonous acids [88] have also been used in this reaction.

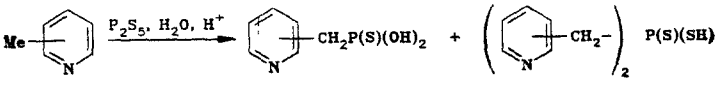
When the Arbuzov reaction is carried out in place of the Michaelis–Bekker reaction, the yields are lower [86], or the reaction fails completely [93], probably as a result of side reactions involving alkylation of pyridine by the alkyl halides [95]. However, 2,6-dihalo-3-(halomethyl)pyridines have been phosphorylated by the Arbuzov reaction in high yields [96].



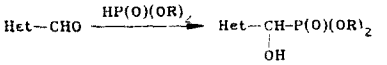
Halomethyl derivatives of pyridine and quinoline react readily with phosphines to give phosphonium or bisphosphonium salts [97-102], but in many instances they are accessible with difficulty, or are of low stability. Alternative methods of phosphorylation are therefore of importance, for example reactions similar to the Otolev–King [103], or the use of phosphorylated derivatives of methylcopper [104].

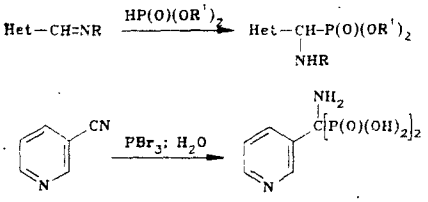


The direct phosphorylation of picolines, quinaldines, or their salts has not been described, in contrast to acylation [105, 106]. Only one example is known of the direct replacment of the hydrogen of the methyl groups in α- and γ-picolines [68].

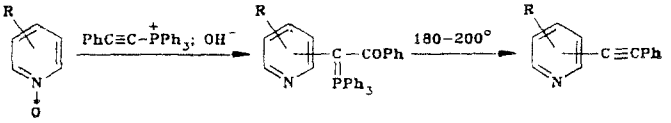


The addition of phosphorus reagents to functional groups in pyridine and quinoline has been reported, namely to the aldehyde [3, 7, 107, 108], azomethine [109, 110], and nitril groups [111]. The heterocyclic moiety has no significant effect on the course of these reactions.



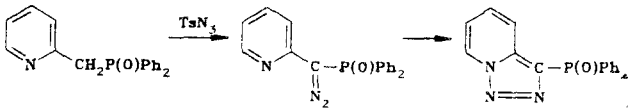


The reaction of pyridine N-oxides with a phosphonium salt containing the phenylacetylene group is most unusual [112]. The phosphorus ylids formed in this reaction undergo thermal decomposition to give difficulty-accessible substituted pyridines.



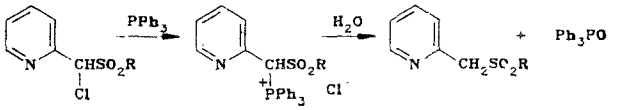
Chemical Properties. Side chain-phosphorylated methylpyridines and methylquinolines readily undergo the Horner–Wittig and Wittig reactions with aldehydes and ketones [86-88, 96-98, 113]. These methods have been used to obtain compounds of highly complex structure, such as polyenes [98, 113] and cycloalkaloids [97]. The techniques for carrying out these reactions are constantly being improved. For example, good results are obtained when phase-transfer catalysis is employed [114, 115].

Many reactions of these compounds involve the reactive methylene group situated between the heterocycle and the phosphorus atom. This group readily adds two molecules of acrylonitrile [90], and the sodio-derivatives can be peralkylated [86]. 2-(Diphenylphosphonylmethyl)pyridine, like the corresponding (carbonylmethyl)pyridines [116], gives a bicyclic compound with tosyl azide [117].



The enhanced acidity of the methylene protons is also clearly apparent in studies of prototropic equilibria of the ylid shown below, which is almost completely shifted to the less acid form, in contrast to the equilibrium of the ylid in which the pyridine ring is replaced by the benzene ring [99, 100].

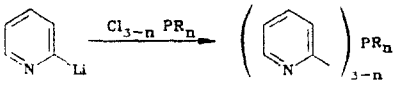
If a hydrogen of the methylene group is replaced by an acceptor group, the C–P bond is readily cleaved. This property has been utilized for the replacement of chlorine by hydrogen [101].



In the side chain-phosphorylated methylpyridines, studies have been carried out on alkylation at nitrogen [103], the preparation of N-oxides [87], partial and complete hydrolysis of the phosphorus ester groups [86, 92], and conformational equilibria using vibrational spectra [92].

2. HETEROCYCLES WITH TRI- AND TETRACOORDINATED PHOSPHORUS

Methods of Preparation. The reaction between 2-magnesio- and 2-lithiopyridines and tervalent phosphorus acid chlorides gives 2-pyridylphosphines [118-126]. The use of lithium derivatives is preferred, since substantially better yields of pyridylphosphines are obtained [125].



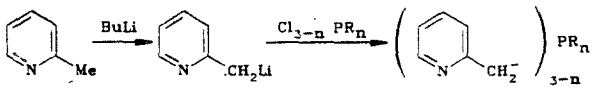
n = 0-3

3-Pyridylphosphines are formed only to a small extent in these reactions, and do not appear to have been isolated in the pure state [118, 125].

4-Lithiopyridine reacts with diphenylchlorophosphine to give 4-pyridyldiphenylphosphine, but tris-(4-pyridyl)phosphine could not be obtained [102, 125]. Attempts to replace the acid chlorides in these reactions by tervalent phosphorus esters were unsucccessful [125]. Perchlorinated analogs were obtained in relatively high yields both from lithio- and magnesio derivatives [126].

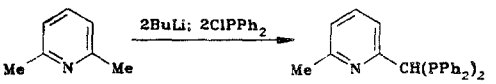
This method was also used to prepare 8-phosphorylated quinolines, including some with dimethylamido groups at phosphorus, these being the first examples of tervalent phosphorus acids with a phosphorus–heterocycle bond [127].

This method is particularly convenient for the preparation of side chain-phosphorylated α-picolines and quinaldines, in view of the relative ease of obtaining the appropriate lithiu compounds [128-132].



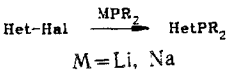
n = 0-3

When 2,6-lutidine is reacted with two equivalents of the appropriate reagents, the same carbon atom is bisphosphorylated [125-129].



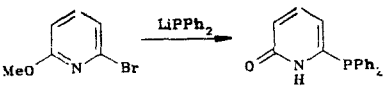
These methods have also been used for the preparation of (2-pyridylmethyl)arsines [119] and (2-pyridylmethyl)stibines [133].

In many instances a more convenient method of phosphorylation than that described above is the reaction of alkali metal phosphides with halo- or dihalopyridines and their benzo-homologs [63, 124, 134-138].



M=Li, Na

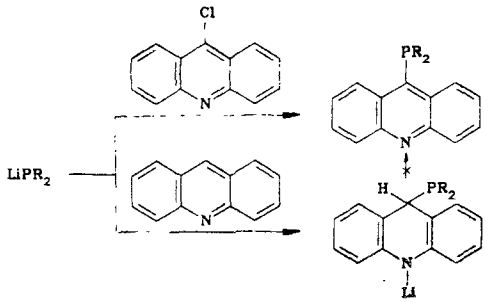
In addition to monosubstituted 2- and 4-halopyridines, this reaction has also been carried out with 2,6-dibromopyridine and 6,6'-dibromodipyridyl [135]. 2-Bromo-6-methoxy-pyridine in this reaction gives a phosphorylated pyridone [135].



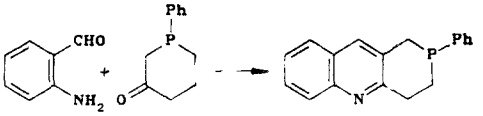
This method has been used with success to obtain 2-(methylphosphino)pyridines [128], 8-phosphinoquinolines [127, 137, 138[, and 9-phosphinoacridines [134]. Sodium diphenylphos-phide has been used also to obtain 2-diphenylphosphinoquinolines [139], but in this instance the 2-haloquinoline was not used, but rather the radical generated therefrom.

Metal phosphides also react with unsubstituted acridine as with the diene system, to give dihydro-derivatives which, however, could not be oxidized [134].

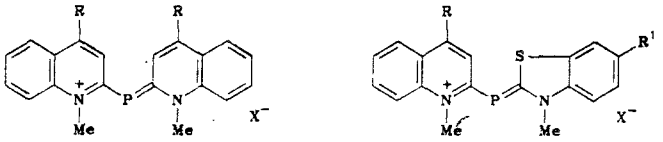
Sodium phosphides usually give better results than lithium phosphides [124, 136]. This method has also been used to obtain 2- and 4-pyridyl- and 8-quinolyl-substituted arsines and stibines [136, 140].



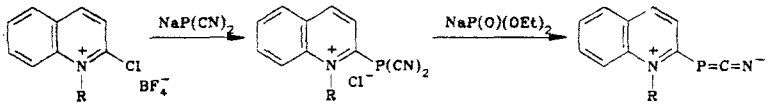
Quinolines with a phosphorus atom in the ring may be obtained by the Friedlander reaction [141, 142].



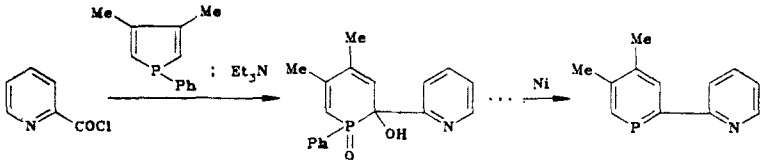
Among the first compounds of dicoordinated phosphorus obtained by Dimroth were symmetrical and unsymmetrical quino(2)phosphamethinecyanines [143, 144]. The methods of preparation, structures, and properties of these compounds were reviewed in detail by him [145].



There has been a recent report of the synthesis of a 2-phosphorylated quinoline with a dicoordinated phosphorus atom [146]. The polar structure of this compound was shown by x-ray diffraction examination and its UV spectrum (λ_{max} 485 nm).



Also noteworthy is the preparation of a compound with a pyridine and phosphabenzene ring in the same molecule [147].



Chemical Properties. The properties of the pyridylphosphines have received the closest attention. They are converted in the usual ways into oxides and thioxides [63, 118, 119]. In some instances, oxidation followed by reduction with trichlorosilane has been employed to separate and purify pyridylphosphines [63, 135]. Alkylation invariably takes placed first at phosphorus [119, 134], unlike the corresponding arsines, which are initially alkylated at nitrogen.

Some pyridylphosphonium salts have been converted into the corresponding phosphorus ylids [123, 124]. Bifunctional dipyridylphosphines have been used to prepare crown ethers [135].

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ALKYLATION OF β-DICARBONYL COMPOUNDS BY 1,2,3-TRIHALOPROPANES AS A METHOD FOR THE PREPARATION OF β-SUBSTITUTED FURANS

Sh. T. Akhmedov, N. S. Sadykhov, V. M. Ismailov, M. A. Akhundova, N. K. Sadovaya, F. N. Karimov, and N. S. Zefirov

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Alkylation of β-dicarbonyl compounds by 1,2,3-trihalides leads to a readily separable mixture of mono- and dialkylation products, and under more rigorous conditions, to 3-substituted 2,4-dimethylfurans. A similar reaction with propargyl bromide leads to furans with a "normal" structure, namely, 2,5-dimethylfurans.

The synthesis of β-substituted furans is of considerable interest, since derivatives of this type are natural compounds [1, 2]. For the synthesis of β-substituted furans, β-dicarbonyl compounds are widely used, the alkylation or condensation of which leads to structural units required for cyclization, such as 1,4-diketones, 1,4-unsaturated ketones, and their derivatives [3, 4]. Hence, a requirement for successful synthesis of β-substituted furans are convenient preparative processes for a synthesis of intermediate compounds. We have already made a detailed study of the synthetic aspects of the alkylation of compounds having an active methylene group (including β-dicarbonyl compounds) by α,ω-dihalides, and found that the use of potassium carbonate in DMSO as a condensing agent ensures high yields of the desired end products, and can be regarded as a convenient preparative method of cycloalkylation [5].

In the present work, we studied the alkylation of certain β-dicarbonyl compounds by 1,2,3-trihalopropanes. It was found that under previously proposed conditions (K_2CO_3 in DMSO) [5, 6], the reaction proceeds, depending on temperature, by two routes, and by selecting the proper conditions, it is possible to ensure a fair selectivity of its occurrence by each of these routes. Thus, alkylation of acetylacetone (I) by 1,2,3-tribromopropane (II) at 25°C gives 2-bromo-4-acetyl-1-hexen-5-one (III) as the main product. According to PMR data (see Experimental), this diketone is in equilibrium with an enol form, with the latter predominating. A small amount of a dialkylation product was obtained as a by-product, to which the structure of 2,6-dibromo-4,4-diacetyl-1,6-heptadiene (IV) can be ascribed. Compounds III and IV are readily separated by distillation. To confirm the structure of III, this compound was prepared by alkylation of acetylacetone by 2,3-dibromo-1-propene under the same conditions. The identity of the alkylation products obtained by different routes was confirmed by complete coincidence of physical constants and PMR spectral data.

In the study of the behavior of 1,2,3-tribromopropane under alkylation conditions, it was found that after 12 h of treatment of tribromopropane of K_2CO_3 in DMSO at 20°C, it converts to the extent of 43% into 2,3-dibromo-1-propene. Thus, the formation of the alkylation product of the β-dicarbonyl compound can occur by two parallel routes, including the alkylation and dehydrobromination stages, proceeding in different sequence.

M. V. Lomonosov Moscow State University, Moscow 117234. S. M. Kirov Azerbaidzhan State University, Baku 370073. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1602-1606, December, 1986. Original article submitted April 23, 1985.

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