Chemistry of Heterocyclic Compounds, Vol. 32, No. 5, 1996

FURAN DERIVATIVES OF GROUP V ELEMENTS (REVIEW)

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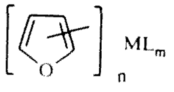
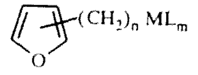
Methods of synthesis, physical properties, chemical transformations, and biological activity data for the furan derivatives of phosphorus, arsenic, and antimony are reviewed.

1. SYNTHESIS OF DERIVATIVES OF PHOSPHORUS, ARSENIC, AND ANTIMONY

Like the furan derivatives of elements of group IVB [1], the compounds of group VB can be divided into three main types, i.e., compounds with a C_{furyl}—M (I) bond and compounds in which the element is separated from the furan ring by a carbon chain (II) or a carbofunctional fragment (III). In the series of group VB elements, the compounds of phosphorus have been studied most fully.



I



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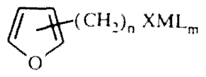
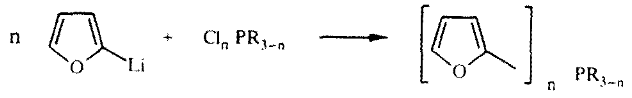


III

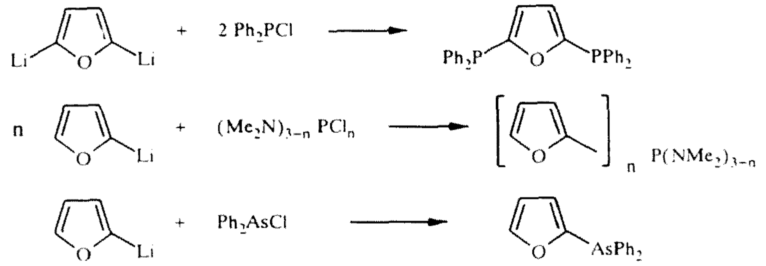
1.1. Synthesis of Compounds of Type I

As in the case of the derivatives of group IVB, the lithium synthesis is a general method for the synthesis of the furan derivatives of phosphorus and arsenic of type I. This method has been used more frequently than others for the production of furyl-containing phosphines [2-9]. The reaction of 2-furyllithium and chlorophosphines was conducted in a mixture of ether and hexane at 0 to −20°C. The yield of the furylphosphines is usually a little greater than 50%.



R = Me, *t*-Bu, Ph; n = 1...3

The lithium method was used for the synthesis of 2,5-disubstituted furylphosphine [7], furylphosphines containing a dimethylamino group in addition to the furyl substituent at the phosphorus atom [10], and diphenyl(2-furyl)arsine [11].



In addition to furylphosphines, furyl-containing phosphine oxides were obtained from 2-furyllithium and the chlorine derivatives of pentavalent phosphorus [3, 10, 12]. Thus, the reaction of phosphoryl chloride Cl_3PO and 2-furyllithium gave tri(2-furyl)phosphine oxide with a low yield, amounting to 18.4% [12]. Phosphine oxide was obtained from optically active 2,2,3,4,4-pentamethyl-1-chloro-1-oxophosphetane by the lithium method with a 65% yield [10].

Latvian Institute of Organic Synthesis, Riga. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 579-632, May, 1996. Original article submitted February 21, 1996.

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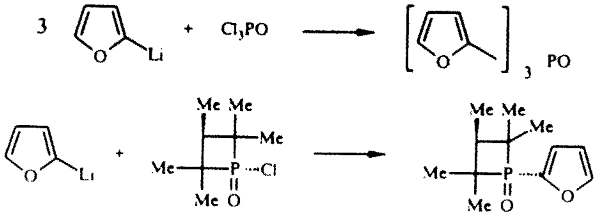
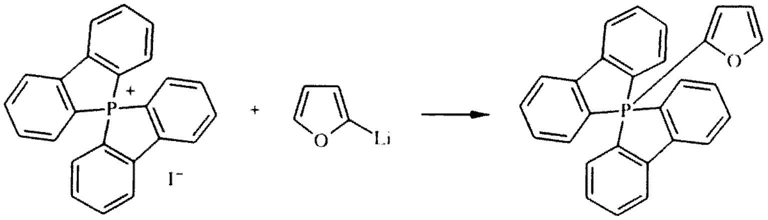
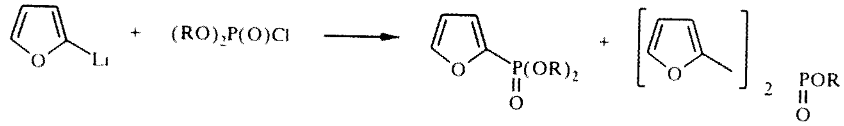


Phosphorane with pentacoordinated phosphorus was synthesized with a 66% yield by the reaction of 2-furyllithium with dibiphenylenephosphonium iodide at −20°C [13].



The chlorine atom in dialkylphosphorochloridates [2, 9] is also substituted by a furyl group during treatment with 2-furyllithium. However, according to data in [9], the process is nonselective, and partial substitution of one alkoxy group is observed. For instance, if R = Et the yields of the monofuryl and difuryl compounds are 57 and 18% respectively.

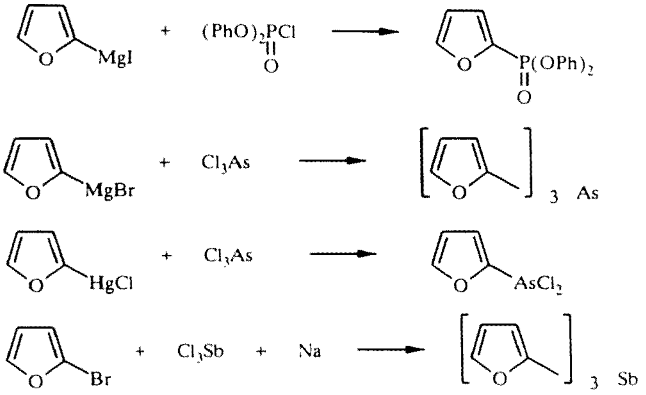


R = Me, Et

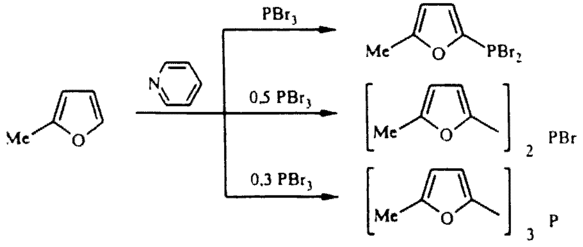
There is very little information on the introduction of various heteroorganic groups into the furan ring without the use of furyllithium.

The synthesis of diphenyl 2-furylphosphonate from diphenyl phosphorochloridate was realized with 2-furylmagnesium iodide. The yield of the reaction product was small and amounted to 27.6% [14].

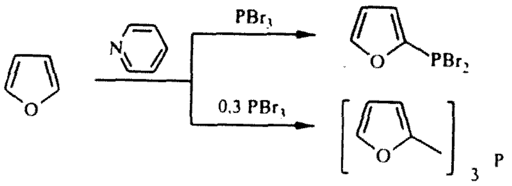
Tri(2-furyl)arsine was also obtained in the reaction of 2-furylmagnesium bromide with trichloroarsine, while 2-furyldichloroarsine was formed in the reaction of equimolar amounts of 2-furylmercuric chloride and trichloroarsine [15]. Tri(2-furyl)stibine was obtained by the condensation of 2-bromofuran with trichlorostibine in the presence of sodium [16].



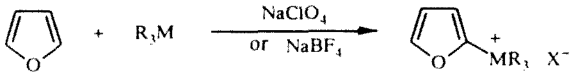
Furan and 2-methylfuran are phosphorylated by phosphorus tribromide under the influence of pyridine. 2-Methylfuran reacts even at 20°C with the almost quantitative formation of (5-methyl-2-furyl)dibromophosphine. At higher temperatures it is possible to obtain di(5-methyl-2-furyl)phosphine [17].



Unsubstituted furan hardly reacts at all at 20°C. (2-Furyl)dibromophosphine and tri(2-furyl)phosphine were obtained by heating a mixture of furan, tribromophosphine, and pyridine at 180°C. Di(2-furyl)bromophosphine is formed as impurity [17].

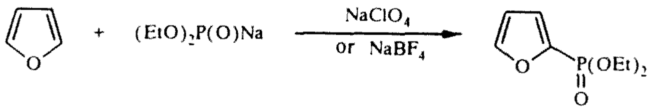


During electrochemical oxidation at a platinum [18, 20] or glassy graphite [19] electrode in a 10-30-fold excess of furan in acetonitrile in the presence of sodium perchlorate or sodium fluoroborate, trialkyl(aryl)phosphines [18, 19] and the corresponding arsines form furyl-containing phosphonium and arsonium salts.

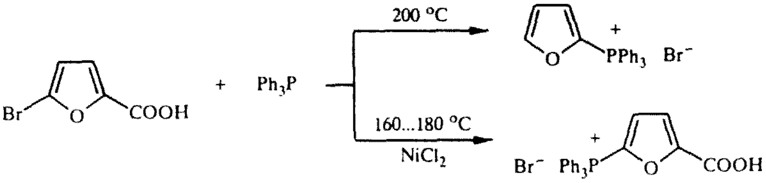


$M = P, As; X = ClO_4, BF_4$

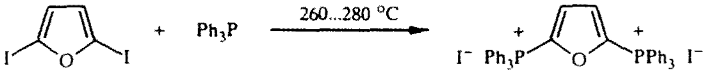
Sodium diethyl phosphite enters into an analogous reaction in a furan—phosphite ratio of 2.5-4:1 [21].



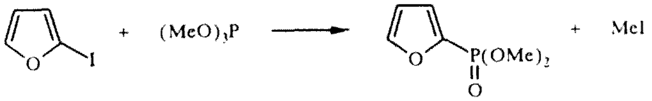
5-Bromo-2-furancarboxylic acid does not undergo any changes when heated with triphenylphosphine in nitrobenzene, dimethylformamide, p-xylene, or benzonitrile. However, simultaneous decarboxylation occurs when the reagents are heated above 200°C without a solvent, and a triphenyl(2-furyl)phosphonium salt is formed with a 50% yield. It was possible to retain the carboxyl group in the furan ring by keeping 5-bromo-2-furancarboxylic acid and triphenylphosphine at 160-180°C for 3-5 h in the presence of nickel chloride [22].



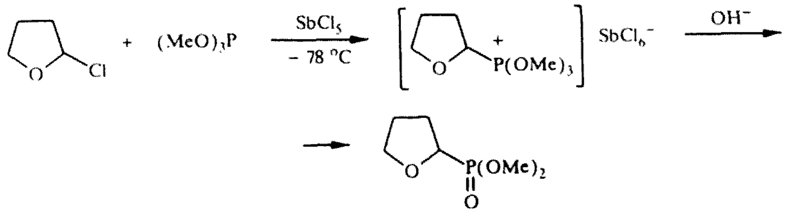
A diphosphonium salt was produced by heating a mixture of 2,5-diiodofuran and triphenylphosphine at 260-280°C [22].



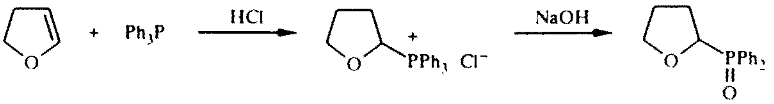
A furyl-containing phosphonate was synthesized by low-temperature UV photolysis of a mixture of 2-iodofuran with an excess of trimethyl phosphite. The low yield of the reaction product (26%) was explained [23] by the photolytic instability and also by the poor quality of the iodofuran (80% purity).



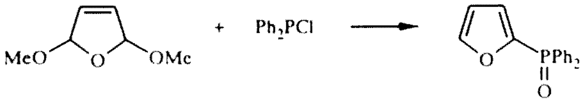
2-Chlorotetrahydrofuran reacts with trimethyl phosphite and antimony pentachloride at low temperature (−78°C) with the formation of (2-tetrahydrofuryl)trimethoxyphosphonium hexachloroantimonate, which is easily dealkylated to dimethyl 2-tetrahydrofurylphosphonate [24].



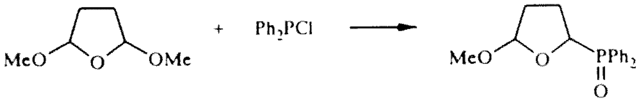
The phosphonium salt of tetrahydrofuran is easily formed during the treatment of a benzene solution of 2,3-dihydrofuran with gaseous hydrogen chloride for 5-10 h at room temperature. The salt was then converted into the corresponding 2-tetrahydrofurylphosphine oxide by reaction with a 3N solution of sodium hydroxide at boiling point [25].



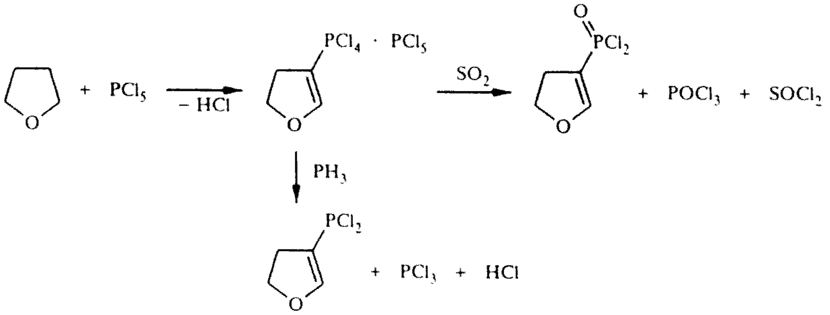
Without mention of the details of the synthesis or the yield of diphenyl(2-furyl)phosphine, it was stated in [26] that this compound was the only product of the reaction of diphenylchlorophosphine and 2,5-dimethoxy-2,5-dihydrofuran.



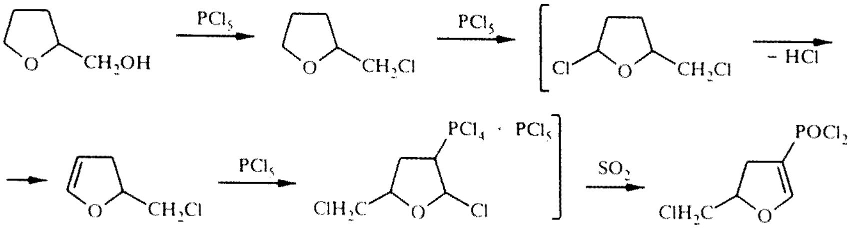
Diphenyl[2-(5-methoxy)tetrahydrofuryl]phosphine oxide was obtained with a 90% yield in the reaction of 2,5-dimethoxytetrahydrofuran with diphenylchlorophosphine in dichloromethane at 0°C [26].



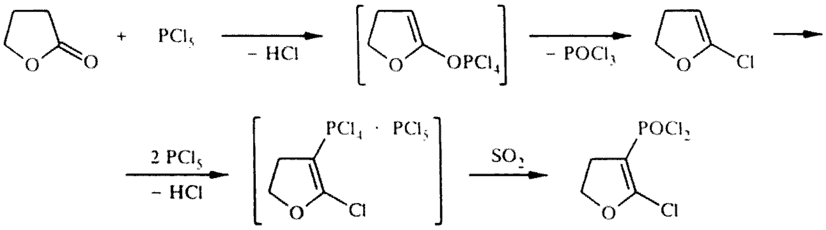
An extremely interesting and quite widely studied method for the synthesis of various derivatives of 2,3-dihydrofuran with a phosphorus atom at position 4 of the ring is the reaction of tetrahydrofuran compounds with phosphorus pentachloride [27-31]. Thus, the reaction of tetrahydrofuran with phosphorus pentachloride in absolute benzene is exothermic and therefore requires cooling to 5-10°C. The initially formed complex is decomposed by sulfur dioxide with the formation of 2,3-dihydro-4-furylphosphonic dichloride [27] or is reduced by phosphine to 2,3-dihydro-4-furyldichlorophosphine [32].



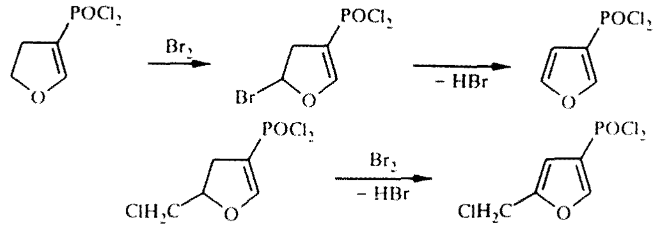
The reaction of phosphorus pentachloride with tetrahydrofuryl alcohol [28] probably takes place according to the following scheme:



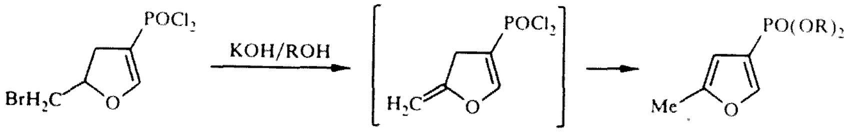
The product in the reaction of phosphorus pentachloride with γ-butyrolactone in a ratio of 3:1 is 5-chloro-2,3-dihydro-4-furylphosphonic dichloride [29].



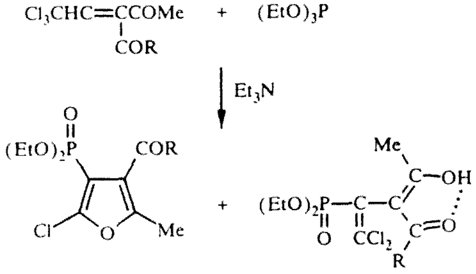
2,3-Dihydro-4-furylphosphonic dichloride and some of its 2-substituted derivatives were used successfully in the synthesis of 3-furylphosphonic compounds [28, 33]. It was found, for example, that the acid dichloride is easily brominated at position 2 with bromine in carbon tetrachloride and also with bromosuccinimide. In turn, the obtained product is dehydrobrominated during distillation, and 3-furylphosphonic dichloride is formed with a yield of 45% [33]. A similar reaction was carried out with 2-chloromethyl-2,3-dihydro-4-furylphosphonic dichloride [28].



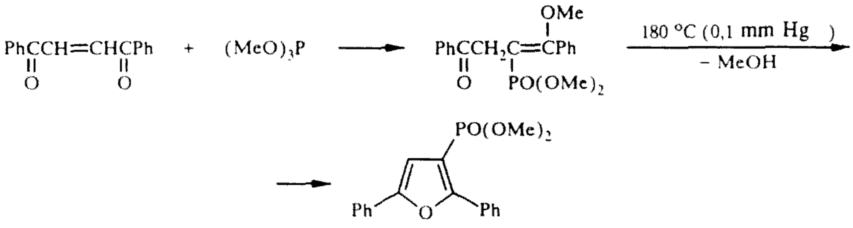
The dehydrobromination of 2-bromomethyl-2,3-dihydro-4-furylphosphonic dichloride was also realized [28] with an alcohol solution of potassium hydroxide. The reaction takes place according to the following scheme:



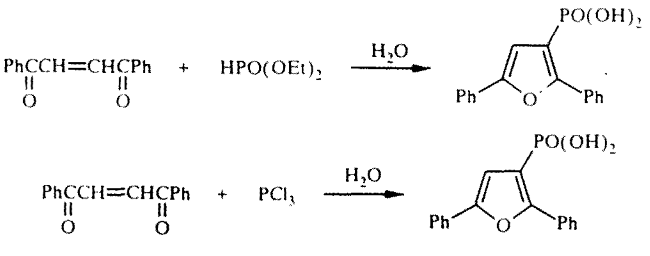
In a number of cases, cyclization has been used for the synthesis of 3-substituted furylphosphonates. Thus, the reaction of 1,1-diacyl-3,3,3-trichloropropenes with triethyl phosphite in the presence of triethylamine led to the formation of 3-furylphosphonates with yields of 60% or more. In addition to the phosphorylated furan, the formation of a noncyclic phosphonate with yields of up to 25% was also observed [34].



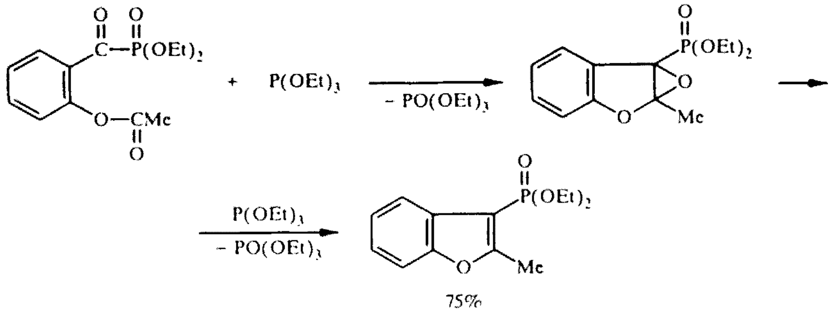
Trimethyl phosphite reacts with dibenzoylethylene in methylene chloride at room temperature [35]. A noncyclic phosphonate is formed initially. When heated under vacuum it undergoes cyclization with the elimination of methanol.

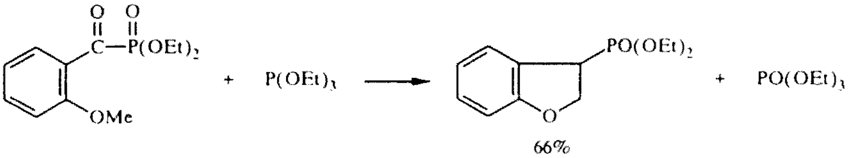


3-(2,5-Diphenylfuryl)phosphonic acid can also be obtained by the action of diethyl phosphonate in the presence of dibenzoyl peroxide at 90-95°C or of phosphorus trichloride in acetic anhydride at 33-38°C on dibenzoylethylene, followed by hydrolysis [36, 37].

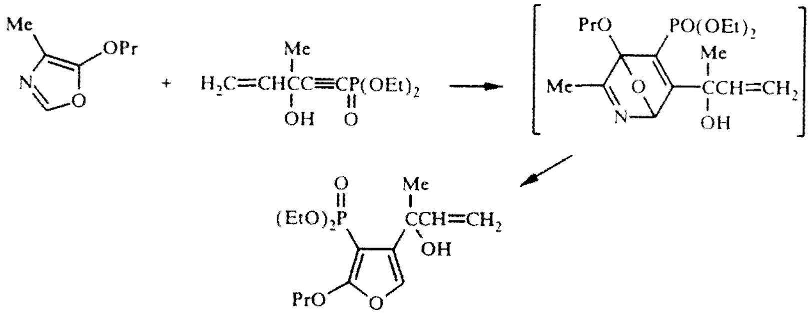


A method for the formation of the furan and dihydrofuran rings of benzofurylphosphonates was based on the cyclization of *o*-substituted aroylphosphonic diesters with trialkyl phosphites [38].

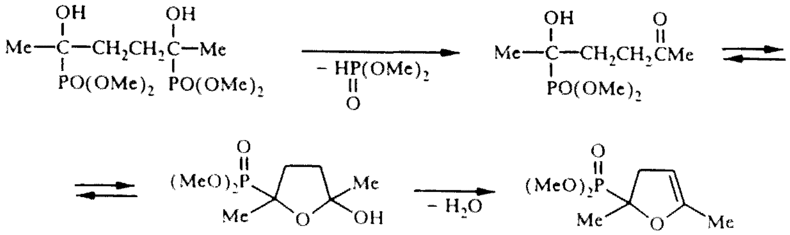




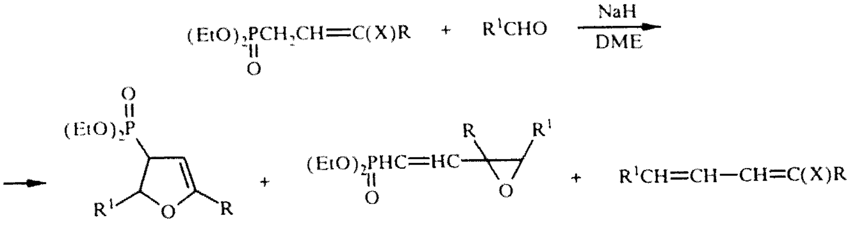
A furan ring with a phosphonate group was obtained by a retrodiene synthesis during the condensation of 4-methyl-5-propoxyoxazole with diethyl 3-methyl-3-hydroxy-4-penten-1-ynylphosphonate at 100°C in an atmosphere of nitrogen for 64 h [39].



A phosphorylated dihydrofuran was obtained by heating 2,5-bis(dimethylphosphino)hexane-2,5-diol in the presence of catalytic amounts of sodium methoxide or diethylamine or without a catalyst. At the first stage the diol undergoes dissociation into dimethyl phosphite and 2-dimethylphosphino-2-hydroxyhexan-5-one, for which ring—chain tautomerism with the formation of a cyclic hemiacetal is possible; dehydration of the latter leads to the dihydrofuran derivative [40]:

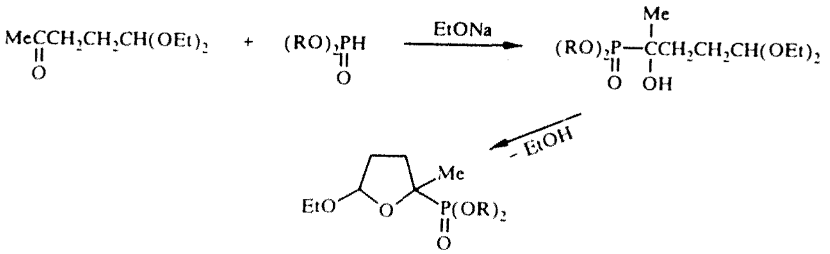


The reaction of allylcarbanions, produced from halogen-substituted allylphosphonates, with aldehydes gives a mixture of linear and cyclic products, among which phosphorylated 2,3-dihydrofuran was detected (yield 35-65%) [41].

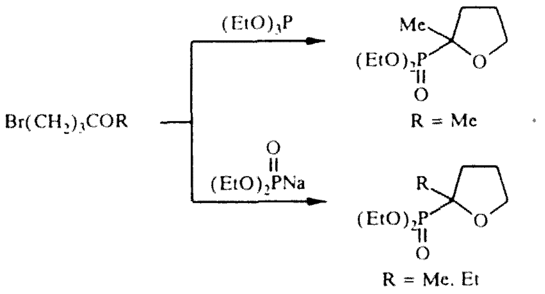


X = Cl, Br; R = H, Me; R^1 = Ph, *p*-ClC_6H_4, *p*-$MeOC_6H_4$

At 50-60°C in the presence of sodium alcoholates, dialkyl phosphonates react at the carbonyl group of levulinaldehyde diethyl acetal with the formation of α-hydroxy compounds, which undergo cyclization as a result of the elimination of alcohol. The yield of the tetrahydrofuran derivatives of phosphorus amounts to 35-40% [42].

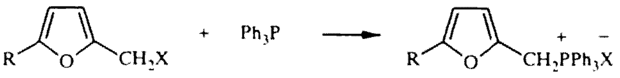


1-Bromo-4-pentanone reacts with triethyl phosphite when heated to 120-140°C and forms the rearranged product of the Arbuzov reaction with a 79% yield [43]. 1-Bromo-4-pentanone and 1-bromo-4-hexanone also form cyclic products with sodium diethyl phosphite [43].



1.2. Synthesis of Compounds of Type II

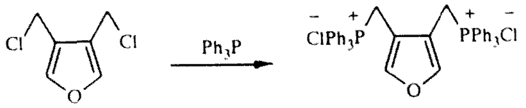
Among the compounds of type II, in which the phosphorus atom is separated from the furan ring by one carbon atom, phosphonium salts have found greatest use in organic synthesis. They are usually obtained with high almost quantitative yields by heating 2- and 3-furylmethyl chlorides [44-56], bromides [57-62], and iodides [63] with triphenylphosphine in benzene, toluene, and dimethylformamide. Compounds with various functional groups in the furan ring [46-53, 58-61, 63] and with two phosphonium groups in the molecule [54-56], compounds in which the furan ring is separated from the phosphorus atom by several methylene groups [64], and derivatives of benzofuran [65], dihydrofuran [57], and tetrahydrofuran [57] have been obtained in this way.



X = Cl; R = H [44 – 47], Me [46], NO_2 [47, 53], CHO [48 – 50], COOMe [51, 52]

X = Br; R = H [57], COMe [58], CH=CHCOAr [59], NO_2 [60, 61]

X = I; R = NO_2 [63]



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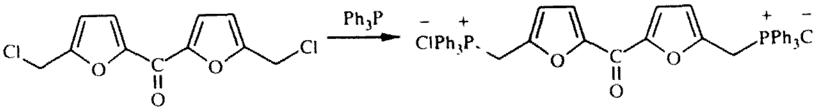

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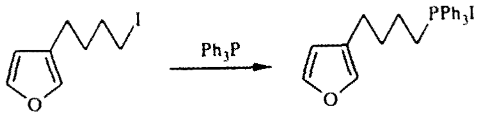

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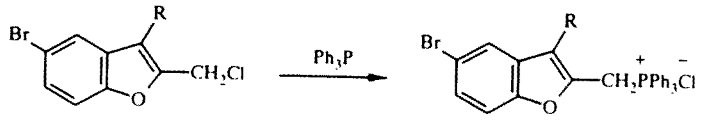

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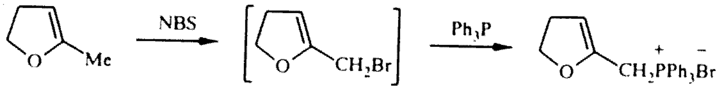

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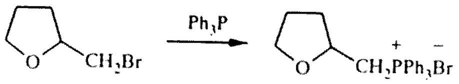
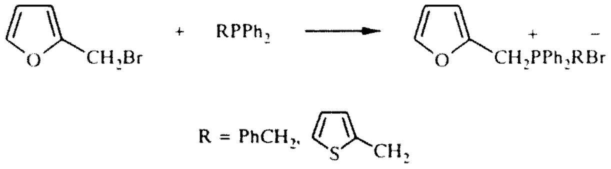
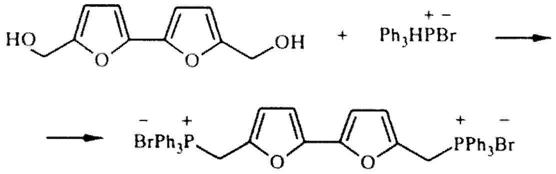


[57]

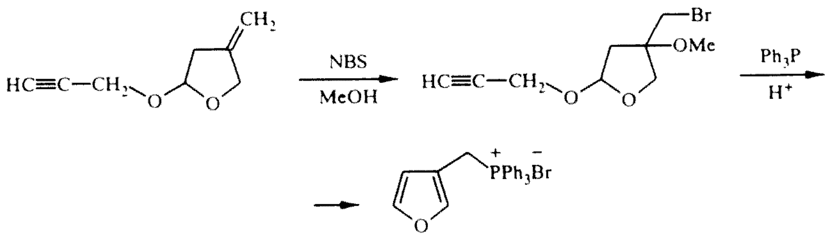
In addition to triphenylphosphine, 2-thenyldiphenyl- and benzyldiphenylphosphine were also used in the reaction with furfuryl bromide [62].



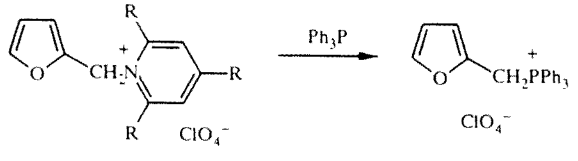
A phosphonium salt was also obtained with a low yield (22%) from 5,5′-bifurfuryl alcohol and triphenylphosphonium bromide [66, 67].



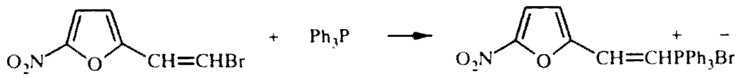
Treatment of 2-(2-propynyloxy)-4-methylenetetrahydrofuran with N-bromosuccinimide in methanol and then with triphenylphosphine in dimethylformamide in an acidic medium gave 3-furylmethyltriphenylphosphonium bromide [68].



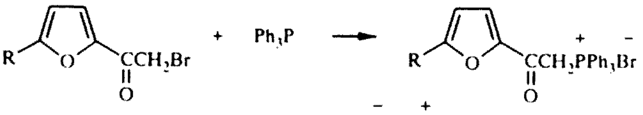
If furfurylpyridinium perchlorates are fused with triphenylphosphine (80°C), a triphenylphosphonium salt is formed with a 98% yield [69].



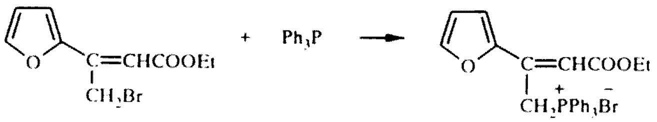
1-(5-Nitro-2-furyl)-2-bromoethylene [70], furyl [47, 58, 71, 72] and benzofuryl [73] bromomethyl ketones, and ethyl 4-bromo-3-(2-furyl)but-2-enoate [74] quaternize triphenylphosphine just as easily and with high yields (~90%).



[70]

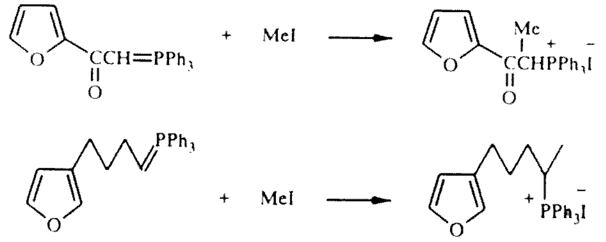


R = H [71, 72], NO$_2$ [47], $\overset{-}{Br}Ph_3\overset{+}{P}CH_2$ [58]

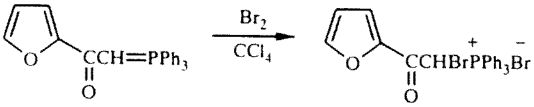


[74]

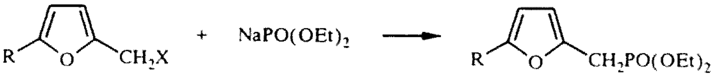
Another method of obtaining phosphonium salts with several carbon atoms between the furan ring and the phosphorus atom involves heating triphenylphosphoranes with an excess of methyl iodide without a solvent or in benzene. The yields of the C-methylation products amount to 80-87% [64, 75].



In reaction with bromine in carbon tetrachloride, furoylmethylenetriphenylphosphorane forms a phosphonium bromide with a quantitative yield [76].

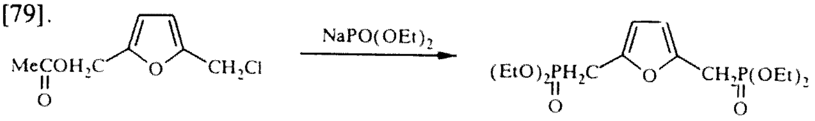


The synthesis of 5-substituted furfurylphosphonates was realized by the Michaelis—Becker reaction from halogenomethylfurans and sodium diethyl phosphite by heating in benzene [77-82].

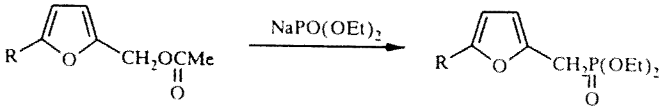


X = Cl, Br; R = H [80, 81], Me [77, 78, 82], COOEt [77, 82], ROCH$_2$ (R = Me, Et, Pr, Bu) [79], RO(CH$_2$)$_n$OCH$_2$ [78], (RO)$_2$CH [78]

In a number of cases, phosphorylation is accompanied by reduction of the bromomethyl group to a methyl group (5-ethoxycarbonylfurfuryl bromide), and sometimes this process becomes the only process [78]. 5-Acetoxymethylfurfuryl chloride reacts with sodium diethyl phosphite with substitution of the chlorine atom and the acetoxy group, but the monosubstitution product was not isolated [79].

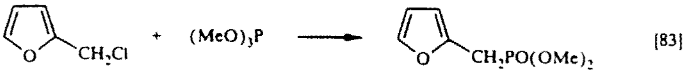


Furfurylphosphonates were obtained with small yields by the reaction of the acetates of furfuryl alcohols with sodium diethyl phosphite [79].



R = H, Me

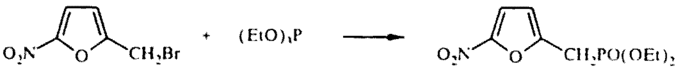
In addition to the Michaelis—Becker reaction, the reaction of trialkyl phosphites with various halogen derivatives of furans (the Arbuzov reaction) has been used for the synthesis of furfurylphosphonates [88, 83, 84], tetrahydrofurylphosphonates [81], furoylmethylphosphonates [85-87], and furoylphosphonates [88, 89].



[83]

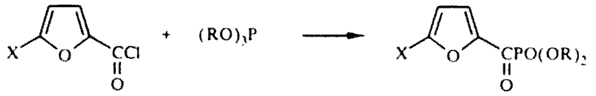
TABLE 1. Yields of the β-Ketophosphonate in Relation to the Halogen and the Temperature

X	T °C	Yield of β-ketophosphonate, %	Yield of enol phosphate	X	T °C	Yield of β-ketophosphonate %	Yield of enol phosphate
Cl	70	—	100	I	20	74	26
Br	20	68	32	I	50	94	6
Br	50	82	18	I	70	94	6
Br	70	84	16				



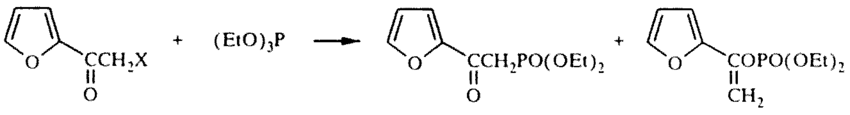
[80]

[81]

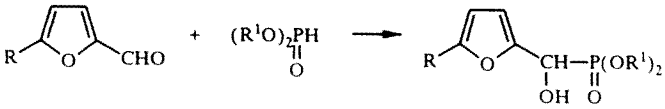


[88, 89]

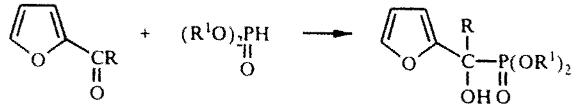
The direction of the reaction of triethyl phosphite with 2-furyl halogenomethyl ketone is affected by the nature of the halogen [85, 87]. Whereas chloroacetylfuran reacts with the quantitative formation of the enol phosphate, and bromoacetylfuran gives a mixture of enol phosphate and β-ketophosphate, the iodine derivative mainly forms the β-ketophosphonate (Table 1).



Furfural and its 5-substituted derivatives [90-99], and also methyl 2-furyl and phenyl furyl ketones [100], react with the dialkyl phosphonate in an equimolar ratio in the presence of sodium ethoxide or methoxide with the formation of furylhydroxymethylphosphonate esters with yields of 40-70%.

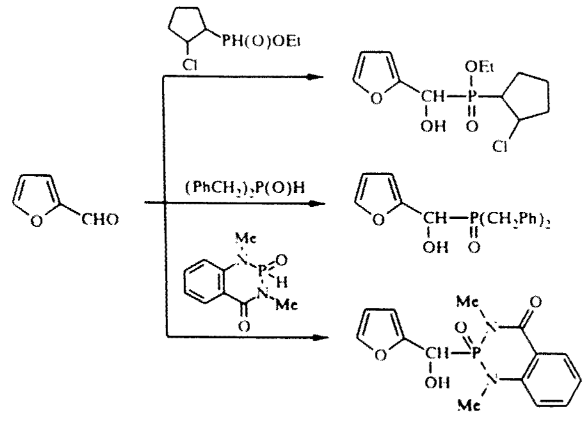


R = H, Me, Br, NO$_2$, m-NO$_2$C$_6$H$_4$; R^1 = C$_n$H$_{2n+1}$(n = 1...4, 6...10, 12, 14, 16), ClCH$_2$CH$_2$, Cl$_3$CCMe$_2$

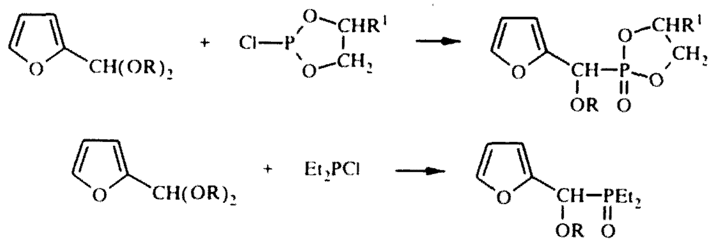


R = Me, Ph; R^1 = Me, Et

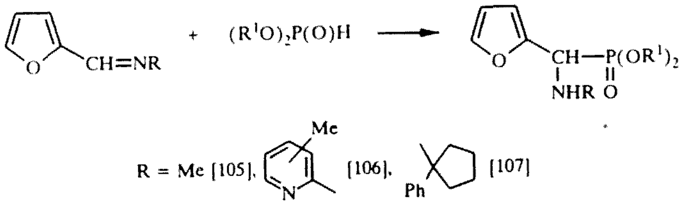
Ethyl 2-chlorocyclopentylphosphinate [101], dibenzylphosphine oxide [102], and 1,2-dimethyl-1H-1,3,2-benzodiazaphosphorin-4-one 2-oxide [103] also add at the carbonyl group of furfural when heated [101, 103] or under the influence of an alkaline catalyst [102].



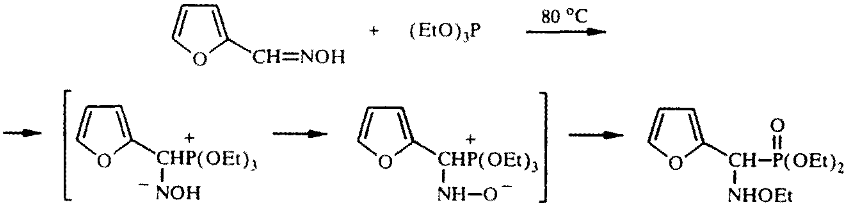
Furfural acetals react with 2-chloro-1,3,2-dioxaphospholanes exothermically and with resin formation. The reagents were therefore mixed with cooling, and the reaction products were quickly distilled. Under these conditions the yields of 2-furylalkoxymethylenephosphonates amounted to 30-60%. In the reaction of dichlorophosphines with acetals, the tertiary phosphine oxides were obtained [104].



With dialkyl phosphonates in the presence of sodium ethoxide, furyl-containing azomethine bases form the products from addition at the C=N bond [105-107].

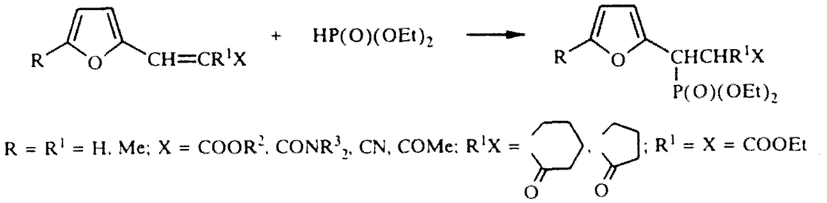


Furfural oxime reacts with triethyl phosphite when heated to 80°C. The reaction takes place at the C=N group and is accompanied by the migration of a proton from the oxygen atom to the nitrogen [108].



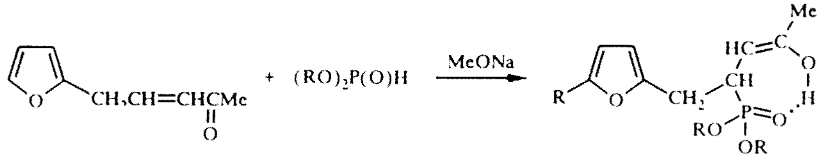
The phosphorylation reactions of various vinylfurans by diethyl phosphonate [109-113], diethyl thiophosphonate [114], trialkyl phosphite [115, 116], ethyldichlorophosphine [117], trimethylsilyloxydiphenylphosphine [118], and hypophosphoric acid [119] have been widely studied.

The addition of diethyl phosphonate to the esters and amides of 3-(2-furyl)acrylic acid [120-122], 3-(2-furyl)acrylonitrile [111], and 2-(2-furyl)vinyl methyl ketone [111] in the presence of sodium ethoxide (alkene—diethyl phosphonate—sodium ethoxide ratios 1:1.25:0.05) takes place exclusively at the C=C double bond with the formation of substituted furfurylphosphonates:

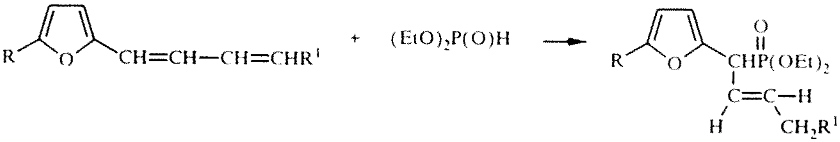


The yield of the reaction products depends on the structure of the initial furylalkene and decreases with the introduction of a methyl group into the furan ring [111]. A reduction in the yield from 40-50 to 1-15% is also observed in the transition from the esters to the amides of the furylacrylic acids. The yield is also small for compounds in which $R^1 \neq H$, e.g., for 2-(1,1-diethoxycarbonylvinyl)furan (32%) and 2-furylmethylenecyclohexan-2-one (40%) [112]. Derivatives of furylacrylic acid with R^1 = Me do not enter into phosphorylation under the given conditions [110].

The results from investigations into the addition of diethyl phosphonate to 2-(2-furyl)vinyl methyl ketone are contradictory [109, 111, 113]. In the earlier paper [109] it was noted that the direction of the reaction is determined by the amount of the catalyst; in the presence of an equimolar amount of sodium methoxide, addition takes place at the C=C bond, while a catalytic amount leads to the product from addition at the carbonyl group. According to data from more recent papers [111, 113], phosphorylation takes place exclusively at the C=C bond. Diethyl phosphonate also adds to the double bond of furfurylvinyl methyl ketone [123], and according to IR and PMR spectroscopy the product has an enolic structure stabilized by a hydrogen bond.

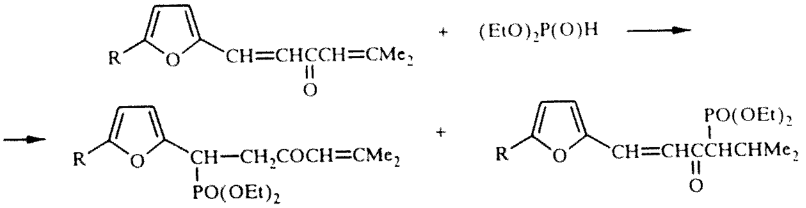


The reaction of diethyl phosphonate with certain conjugated and unconjugated diene derivatives of furan was studied [111, 112]. In the case of the conjugated systems 1,4-addition occurs, and the reaction is stereospecific, since only the E isomer is formed [112].

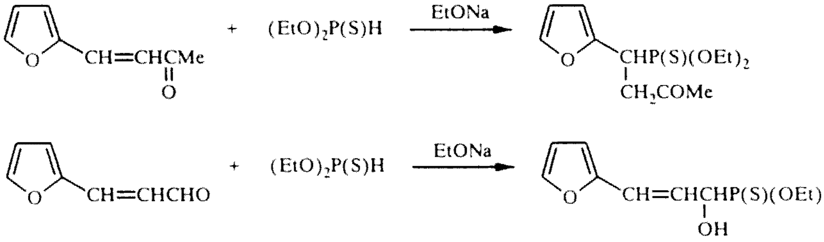


R = H, Me; R¹ = COMe, COOEt

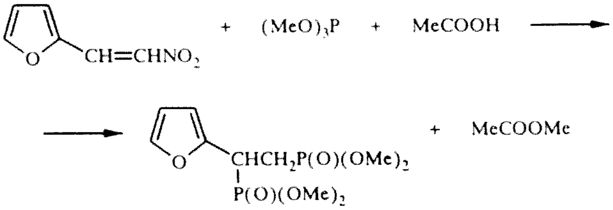
However, if the double bonds are not conjugated, the products from addition at both double bonds are formed [111].



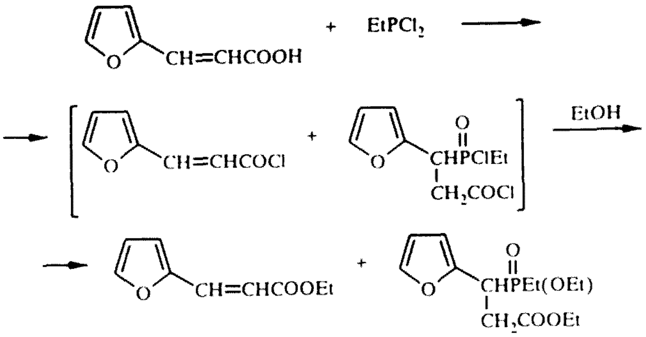
The phosphorylation of 2-furylvinyl methyl ketone by diethyl thiophosphonate in the presence of sodium ethoxide takes place at the C=C double bond and not at the carbonyl group, whereas the product from addition at the carbonyl is formed with furylacrolein [114].



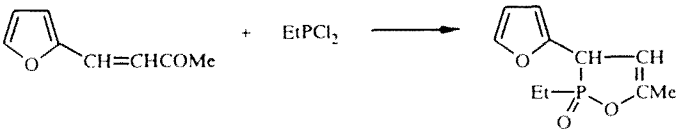
The reaction of trimethyl phosphite with 1-(2-furyl)-2-nitroethylene in acetic acid takes place vigorously with the formation of 1,2-bis(dimethoxyphosphoryl)-1-(2-furyl)ethane [115].



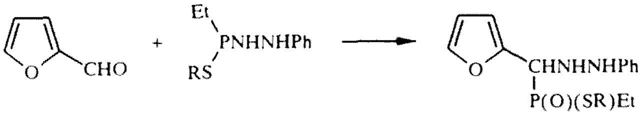
The reaction of ethyldichlorophosphine with furylacrylic acid begins at 80°C. After treatment of the mixture with ethanol ethyl furylacrylate and ethyl ethyl-1-[1-(2-furyl)-2-(ethoxycarbonyl)ethyl]phosphinate were isolated from the reaction products [117].



Intramolecular cyclization occurs in the reaction of ethyldichlorophosphine with 1-(2-furyl)but-1-en-3-one in acetic anhydride [117].

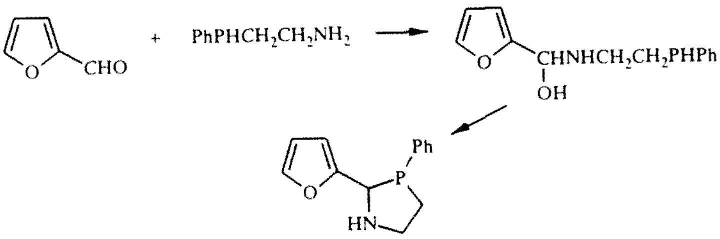


The condensation of furfural with various types of organophosphorus compounds has been used very widely for the synthesis of compounds in which the furan ring is separated from the phosphorus atom by one [120, 121], two [122, 124-128], or a larger number [129] of carbon atoms. The phenylhydrazides of ethylthioalkylphosphinic acids react readily (20-30 min, 30-35°C, yields 71-74%) with furfural according to the following scheme [120]:

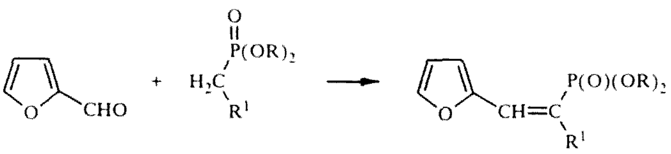


R = Et, Bu

Phenyl(β-aminoethyl)phosphine enters into reaction with furfural with the formation of a linear intermediate product, which then undergoes cyclization with the formation of furyl-substituted phosphazolidine [121]:

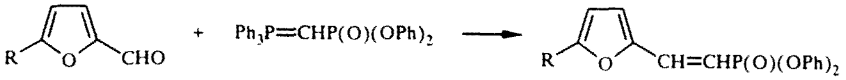


In the presence of various types of catalysts (pyridinium acetate, piperidine, titanium tetrachloride), furfural reacts with the nitrile [122] and ester [124] of dialkoxyphosphorylacetic acid, bisdialkoxyphosphorylmethanol [124], and dialkoxyphosphorylmethyl phenyl ketone [125], i.e., with compounds containing a methylene group with mobile hydrogen atoms. The yields of the reaction products amount to 80-90%.

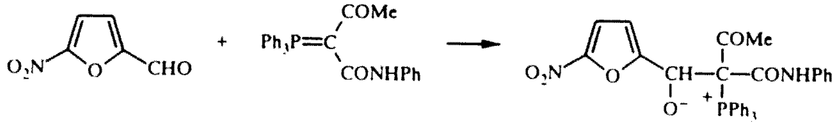


R = Et, R^1 = CN; R = Et, R^1 = COOEt; R = *i*-Pr, R^1 = C(O)(OPr-*i*); R = Et, R^1 = C(O)Ph

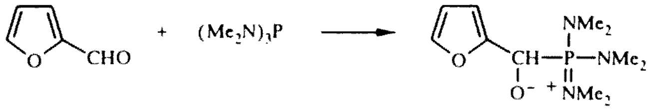
The condensation of furfural and 5-nitrofurfural with diphenoxyphosphorylmethylenetriphenylphosphorane in benzene with gentle heat (65-70°C) for 12-20 h also leads to furylvinylphosphonates (yields 74-80%).



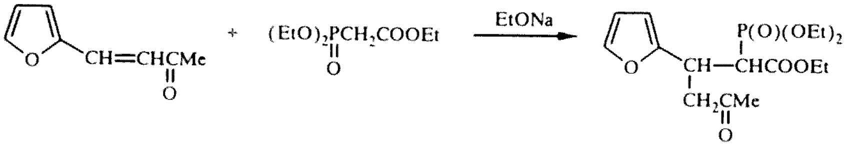
The synthesis of 1-acetyl-1-phenylcarbamoyl-2-(5-nitro-2-furyl)ethylenetriphenylphosphonium betaine was realized by the reaction of 5-nitrofurfural with 1-acetyl-1-phenylcarbamoylmethylenetriphenylphosphorane [127].



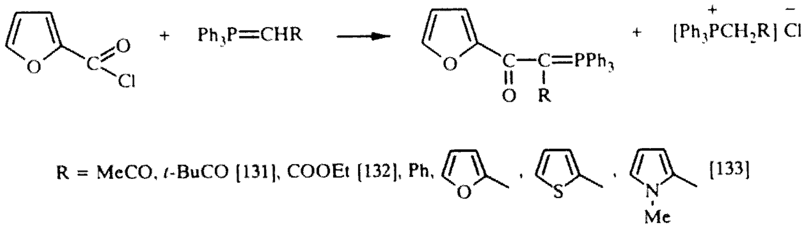
Furfural also forms a 1:1 adduct of the betaine type with tris(dimethylamino)phosphine [128].



The addition of ethyl diethoxyphosphorylacetate to 2-(2-furyl)vinyl methyl ketone takes place when they are heated in a sealed tube at 130-135°C for 10 h in the presence of sodium ethoxide, and ethyl α-diethoxyphosphoryl-β-(2-furyl)-acetobutyrate is formed [130].

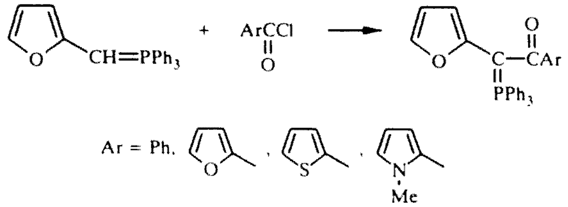


It was established that the various triphenylphosphoranes react with pyromucoyl chloride in benzene at room temperature according to the following scheme [131-134].



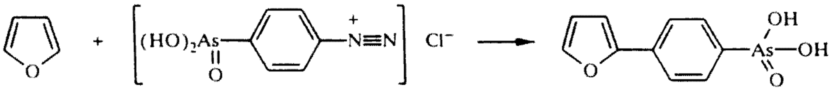
R = MeCO, *t*-BuCO [131], COOEt [132], Ph, [133]

2-Furylmethylenephosphorane also enters into reaction with aroyl chlorides with the formation of 2-furyl(α-aroyl)methylenetriphenylphosphoranes with high yields (70-90%) [133].

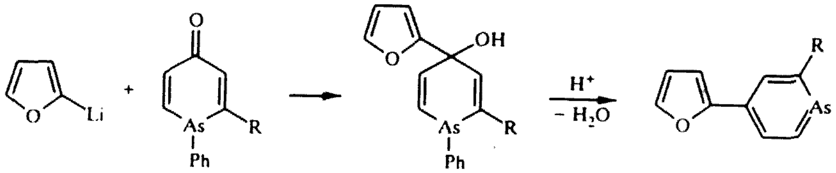


Ar = Ph,

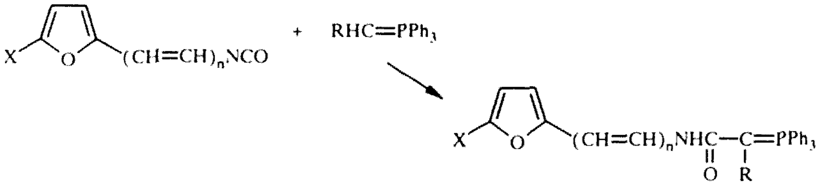
A compound in which the furan ring is separated from the arsenic atom by a benzene ring was obtained through a diazonium salt of arsanilic acid [135-137]. The reaction between furan and the diazo compound takes place in acetone with the vigorous release of nitrogen. In the opinion of the authors [136], the 2-substituted product is formed with greater probability, but this was not strictly proved.



2-Furyllithium reacts with 4-oxo-1,4-dihydroarsenine at the carbonyl group. In an acidic medium, the obtained hydroxy derivative can be aromatized to an arsenine [138].

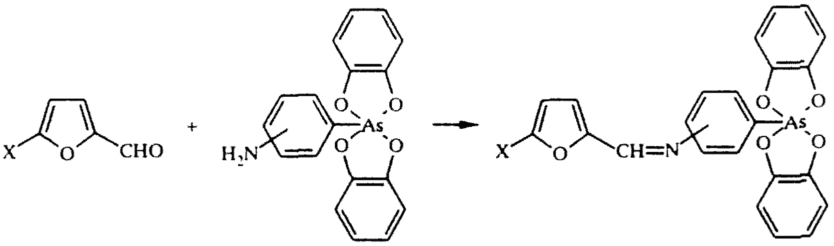


The furan derivatives of phosphorus and arsenic, in which the heterocycle and the element are separated by a carbofunctional chain $(C)_nX(C)_m$ (X = O, N), are very sparse and were synthesized by various methods. Thus, triphenylmethylenephosphoranes $Ph_3P{=}CHR$ react with 2-furyl-, 5-nitro-2-furyl-, and 2-(5-nitro-2-furyl)vinyl isocyanates according to the following scheme [139] (yields 65-75%).

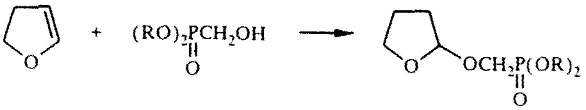


n = 0: X = H, NO_2; R = CN, COOEt, COC_6H_4Br-*p*, COPh, COMe;
n = 1: X = NO_2; R = CN, COOEt

The condensation of furfural and 5-nitrofurfural with derivatives of *ortho-* and *para*-substituted arsanilic acids gave azomethine bases with antiparasitic activity [140].



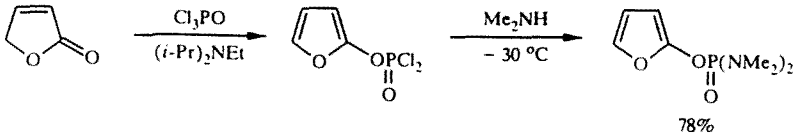
In the reaction of 2,3-dihydrofuran with hydroxymethylphosphonates in the presence of a catalytic amount of concentrated hydrochloric acid, dialkoxyphosphoryl derivatives of tetrahydrofuran are formed [141].



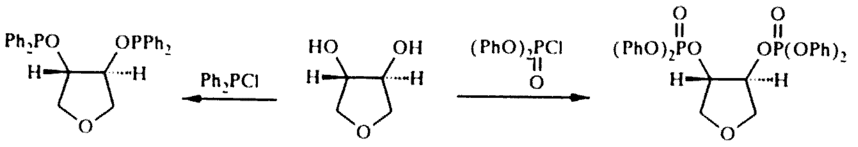
R = Me, Et

1.3. Synthesis of Compounds of Type III

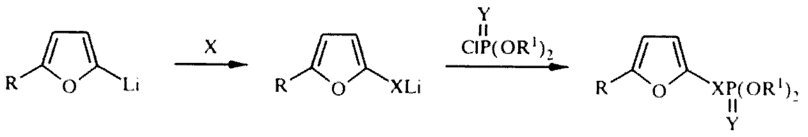
Compounds in which the furan ring and the phosphorus atom are separated by an oxygen atom were obtained with 60-65% yields from 2(5H)-furanone by the action of phosphorus oxychloride in methylene chloride in the presence of ethyldiisopropylamine at room temperature. The chlorine atoms of 2-furyl phosphorodichloridate are easily substituted during reaction with an excess of dimethylamine in ether with cooling to −30°C [142].



Tetrahydrofuran derivatives of type III have also been mentioned in the literature [143]. They were obtained in the reaction of optically active tetrahydrofuran-3,4-diol with diphenylchlorophosphine or diphenyl phosphorochloridate in THF with slight cooling in the presence of pyridine.

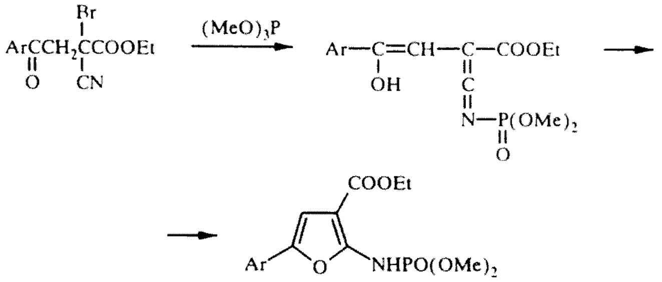


Furyl thiophosphates and furyl selenophosphates were synthesized through lithium furyl sulfide and selenide, which are formed in the reaction of 2-furyllithium with elemental sulfur or selenium. Without isolation they react with dialkyl phosphorochloridate and its thio analog [144, 145].



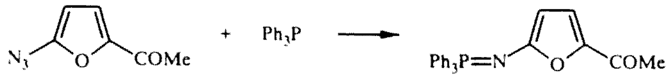
R = H, Me; R^1 = Me, Et; X = S, Se; Y = O, S

Compounds with the C_{furyl}—N—P fragment are also sparse [146-148]. When treated with trimethyl phosphite at room temperature, ethyl α-bromo-α-cyano-γ-aryl-γ-oxopropionates undergo cyclization with the formation of dimethyl (5-aryl-2-furylamino)phosphonates with yields of 66-70% [146].

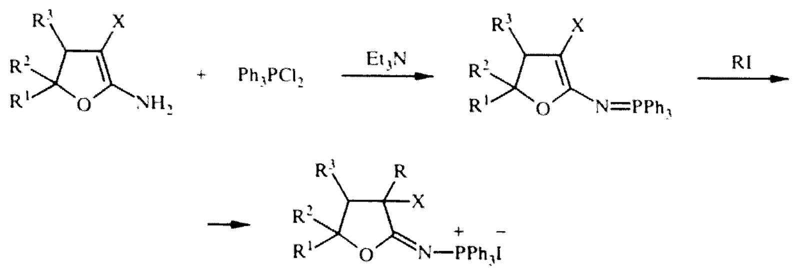


Ar = Ph, *p*-ClC_6H_4

2-Acetyl-5-azidofuran reacts with triphenylphosphine with the release of nitrogen and the formation of triphenyl[(2-acetyl-5-furyl)imino]phosphorane [147].



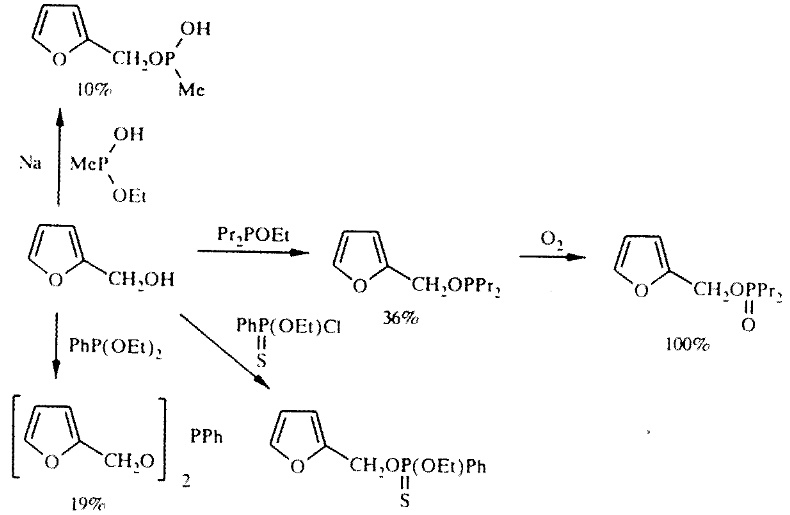
Triphenyliminophosphoranes can also be obtained by the reaction of triphenyldichlorophosphorane with various derivatives of 2-amino-4,5-dihydrofuran in hexachlorohexane in the presence of triethylamine [148]. The iminophosphoranes in turn can be converted into phosphonium salts by the action of alkyl iodides [148].



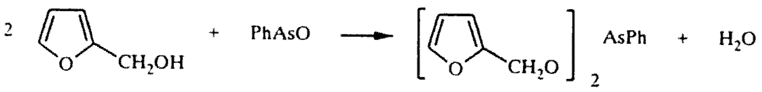
R = Me, Et; R^1 = R^2 = R^3 = H, Me; X = COOEt, CN

The compounds of the third type are represented most widely by the derivatives of tetrahydrofuryl alcohol [149-162], the synthesis of which is usually achieved by treating tetrahydrofuryl alcohol with various phosphorylating agents. As mentioned in a series of papers [151, 155], the synthesis of the analogous compounds of furfuryl alcohol is accompanied by resin formation and by a substantial reduction of the yield [155]. Data on the direct introduction of a phosphorus and arsenic atom into furfuryl alcohol are therefore extremely limited.

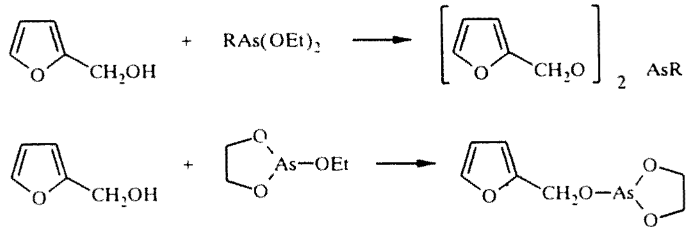
The transesterification of methylphosphonite, phenylphosphonite, and dipropylphosphonite esters by furfuryl alcohol with heat was undertaken in [155]. The product yields were high and amounted to 10-36%. Dipropyl(furfuryloxy)phosphine is oxidized quantitatively to furfuryl dipropylphosphinate. Furfuryl alcohol reacts with ethoxy(thio)phenylchlorophosphorus in the presence of pyridine [163].



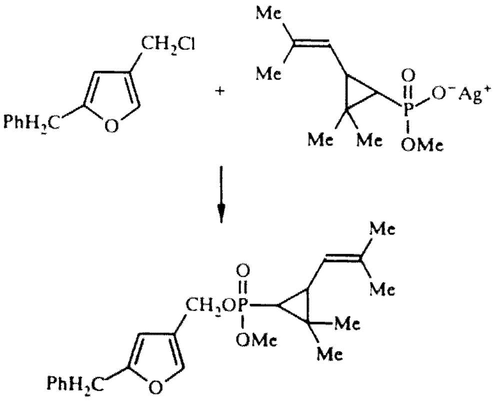
Three different methods have been used for the synthesis of furfuryl arsinites. In the reaction of furfuryl alcohol with trichloroarsine in the presence of a base in absolute ether, it was not possible to isolate furfuryl arsenites on account of resin formation. A phenylarsonite ester was obtained with a good yield when furfuryl alcohol was heated with phenylarsine oxide [164].



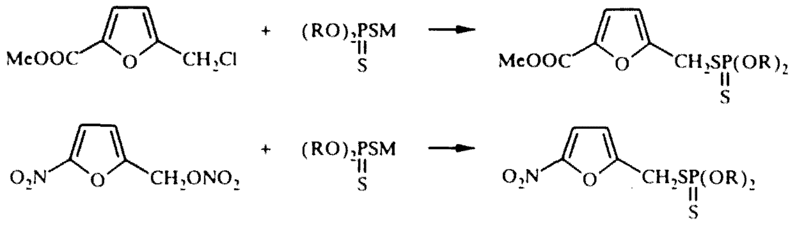
It is also possible to obtain arsonite and arsenite esters during the transformation of the acids of trivalent arsenic [164].



4-(2-Benzyl)furfuryl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropylphosphonate was synthesized with a very low yield (2%) from 2-benzyl-4-furylmethyl chloride and silver phosphonate by heating in acetonitrile [165].

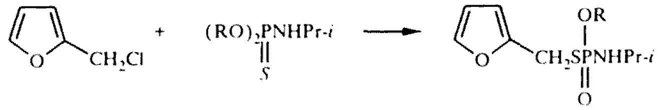


In the reaction of alkali-metal dithiophosphates with 2-methoxycarbonyl-5-chloromethylfuran [166] or 5-nitrofurfuryl nitrate [167, 168] the corresponding O,O-dialkyl S-furfuryl thiophosphates were obtained.

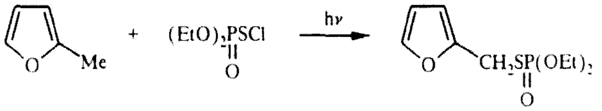


R = Me, Et, Pr, *i*-Pr, *i*-Bu

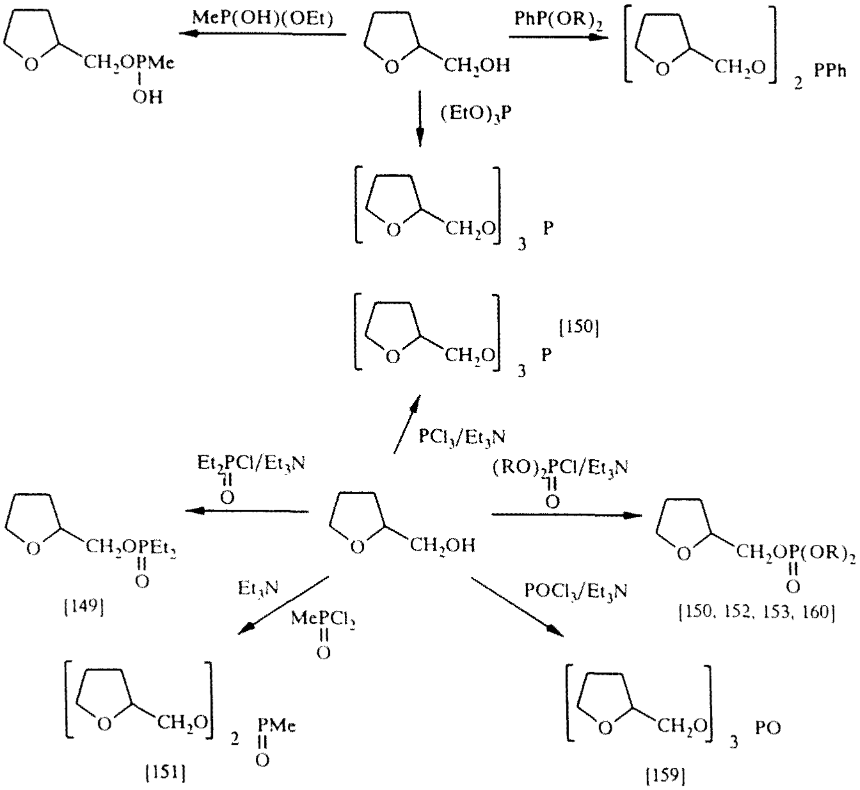
The reaction between furfuryl chloride and dialkyl(isopropylamido)thiophosphate was used for the synthesis of phosphoroamidothioates containing a furfurylthio group [169].



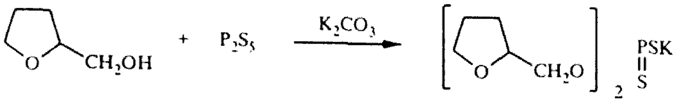
O,O-Diethyl S-furfuryl thiophosphate can be obtained under radical conditions during the ultraviolet irradiation of sylvane and O,O-diethyl S-chlorothiophosphate [170].



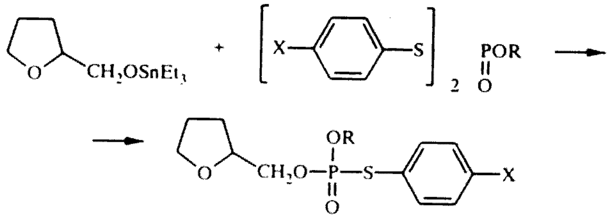
The tetrahydrofuryl esters of trivalent and pentavalent phosphorus acids were synthesized either by transesterification [150, 155] or by the reaction of the chlorine derivatives of phosphorus with tetrahydrofuryl alcohol in the presence of bases (usually triethylamine) [149-161].



Tetrahydrofuryl alcohol also reacts with phosphorus pentasulfide. The obtained dithiophosphoric acid was isolated in the form of the potassium salt [154].

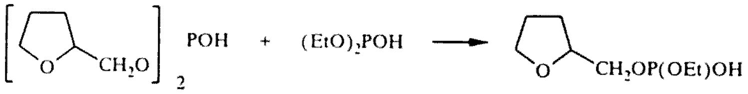


Apart from the substitution of a hydrogen atom in tetrahydrofuryl alcohol by the various phosphorus groups, other extremely uncommon methods of synthesis have also been used. For example, the reaction of O-alkyl S,S-diaryl dithiophosphates with tetrahydrofurfuryloxytriethylstannane gave high yields (67-80%) of the corresponding O,O-dialkyl S-aryl dithiophosphates [162].



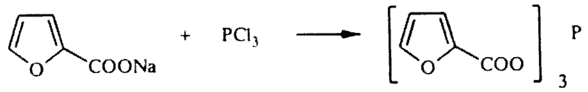
X = Me, Cl; R = Et, c-C_6H_{11}, $Ph(CH_2)_2$

Unsymmetrical dialkyl phosphites are formed in a redistribution reaction. Ethyl tetrahydrofurfuryl phosphite was obtained with a 45% yield by heating a 1:6 mixture of diethyl and ditetrahydrofurfuryl phosphites at 100-120°C for 10-15 h [171].

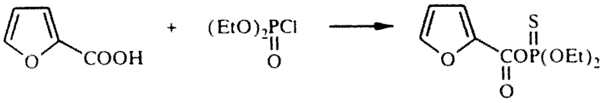


Pyromucic acid and its salts were used for the synthesis of the furoate derivatives of phosphorus [172-174], antimony [175], and bismuth [175].

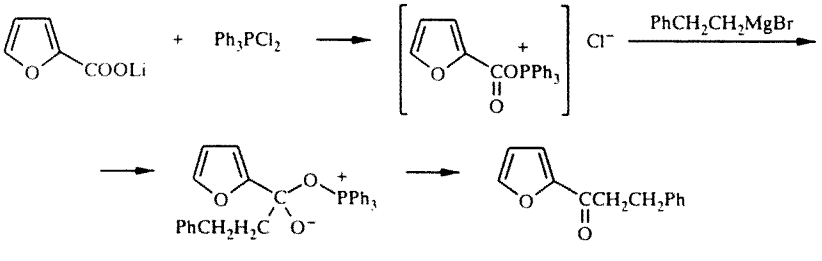
Tris(furoyloxy)phosphine is formed in the reaction of sodium pyromucate with trichlorophosphine in benzene solution with slight cooling. The compound was used for the phosphorylation of alcohols [172].



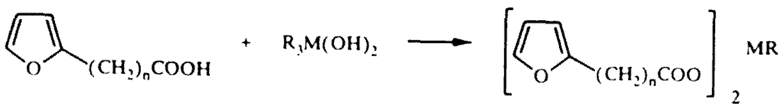
Diethyl 2-furoyl thiophosphate was obtained with a very small yield (4%) in the reaction of pyromucic acid with O,O-diethyl chlorothiophosphate in chlorobenzene solution by the action of pyridine [173].



In reaction with triphenyldichlorophosphorane lithium 2-furancarboxylate gives a high yield of a carboxyphosphonium salt, which gives a betaine and then a ketone when treated with a Grignard reagent [174].

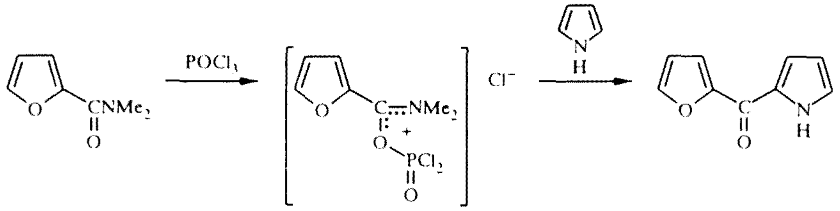


The action of trialkyl- and triaryldihydroxyantimony and the corresponding derivatives of bismuth on 2-furancarboxylic and 2-furylmethanecarboxylic acids gave the corresponding dicarboxylates of antimony and bismuth. It is possible to see a substantial decrease in the yield of the dicarboxylate from 76-78% to 37-48% in the transition from the derivatives of pyromucic acid to the compounds of furylacetic acid [175].

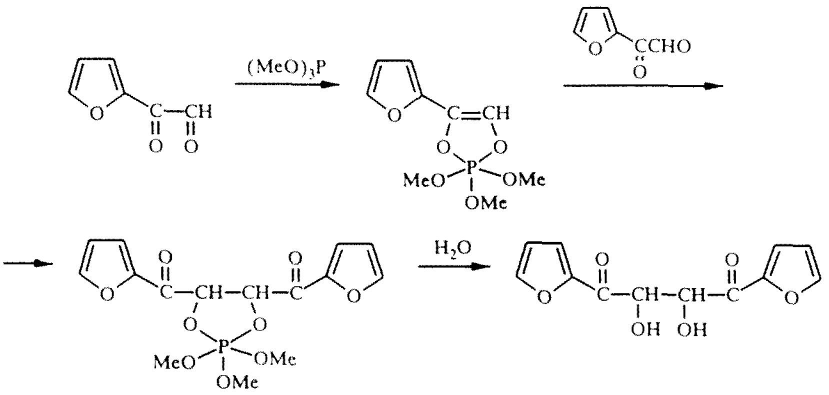


M = Sb; n = 0; R = Me, c-C_6H_{11}, Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 2,4,6-$Me_3C_6H_2$;
n = 1; R = Me, Ph;
M = Bi; n = 0; R = Ph, 4-MeC_6H_4;
n = 1; R = Ph

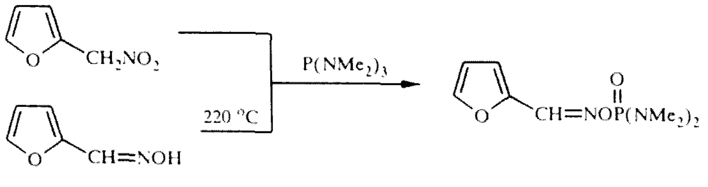
A complex, which was used as a furoylating agent in reaction with pyrrole, was obtained when N,N-dimethylpyromucamide was dissolved in phosphorus oxychloride in the absence of moisture [176].



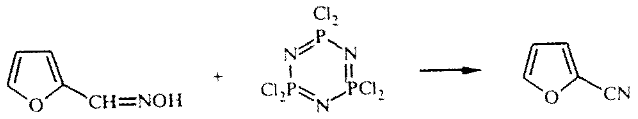
The reaction of furylglyoxal with trimethyl phosphite in a ratio of 2:1 at room temperature takes four days. The obtained product, the hydrolysis of which gave 1,2-bis(2-furoyl)-1,2-dihydroxyethane, contains a 1,3,2-dioxaphospholane ring [177].



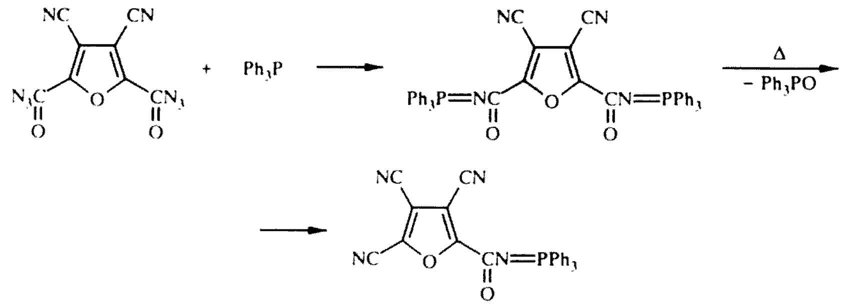
Organophosphorus derivatives of furfural oxime were synthesized by the action of hexamethylphosphorotriamide on a solution of 2-(nitromethyl)furan in dichloromethane in an atmosphere of nitrogen [178] or on the unsubstituted oxime at elevated temperature [179].



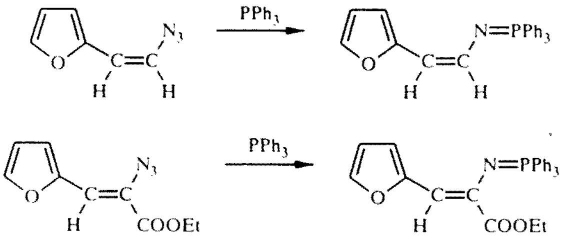
The yield of the reaction product amounted to 50% in the first case and 39% in the second. It should be noted that the derivatives of the oximes are unstable and are easily transformed into the corresponding nitriles. This was the reason for the fact that a phosphorus-containing oxime could not be isolated in the reaction of furfural oxime with 2,2,4,4,6,6-hexachloro-1,3,5,2λ^5,4λ^5,6λ^5-triazatriphosphorin, where the only isolated product of the reaction was 2-cyanofuran [180].



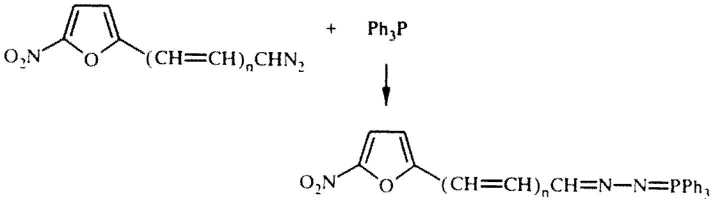
The reaction of triphenylphosphine with various azides has been studied quite widely for the synthesis of iminophosphoranes of the furan series [181-185]. The addition of triphenylphosphine to 3,4-dicyano-2,5-di(azidocarbonyl)furan in benzene solution is accompanied by the release of nitrogen and gives a high yield [181]. When heated, the obtained diiminophosphorane loses one molecule of triphenylphosphine oxide. It was not possible to open the P=N bond at higher temperature.



Various furylvinyl azides react with triphenylphosphine at room temperature [183, 184] or on cooling to 0°C [185]. The reaction usually takes 15-30 min, and the yield of the iminophosphoranes is greater than 90%.

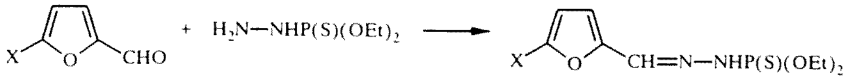


Derivatives of diazomethane with nitrofuryl and nitrofurylvinyl groups also react with triphenylphosphine at room temperature in ether in 15-60 min. The yields of the diazo derivatives of phosphorus amount to 72-75% [186].



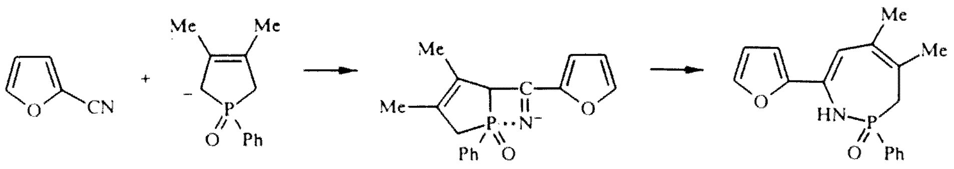
n = 0, 1

The condensation of 5-substituted furfurals with diethyl hydrazinothiophosphate was used for the synthesis of furfurylidenehydrazones with a phosphorus atom at the nitrogen [187, 188].



X = NO_2, Ar

2-Furonitrile reacts with 3,4-dimethyl-1-phenyl-1-oxo-1-phosphole deprotonated at the α position to the phosphorus atom. Initially the anion attacks the carbon atom of the cyano group, and the nitrogen is then inserted into the ring with the formation of 1-aza-2-phosphacyclohepta-4,6-diene [189] with a furyl group at position 7 of the ring (yield 36%).

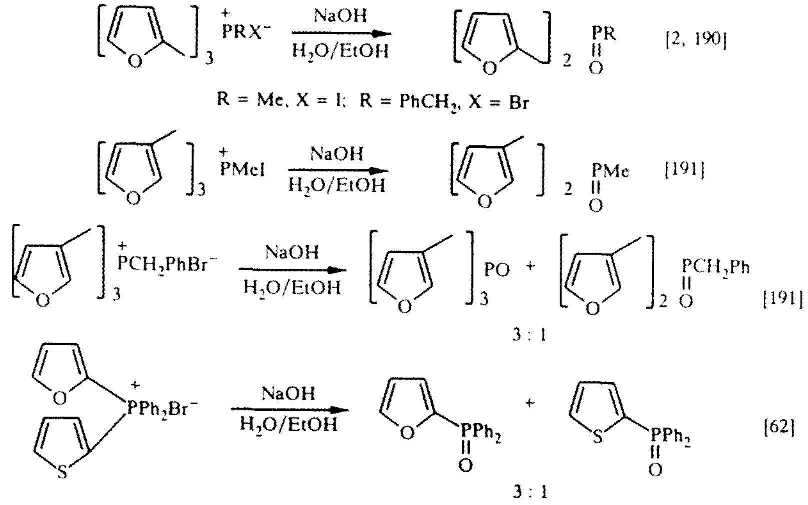


2. CHEMICAL PROPERTIES

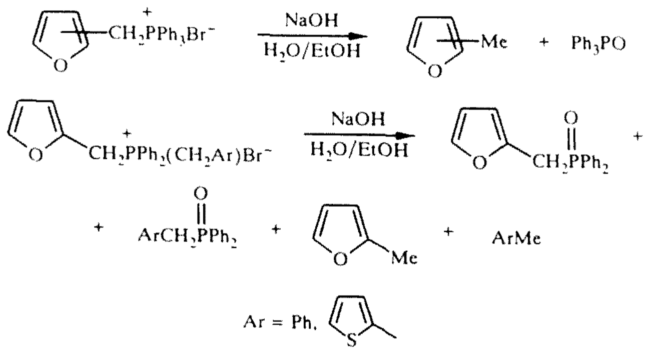
The chemical transformations into which the furan derivatives of phosphorus and arsenic enter can be subdivided into several types: Reactions taking place with cleavage of the C—P and C—As bonds; transformations affecting the furan ring and organic substituents in it; transformations of the functional substituents at the element; transformations involving change in the valence state of the phosphorus and arsenic.

2.1. Cleavage of the C—P and C—As Bonds

On account of the higher stability of the C_{furyl}—M bonds for the compounds of phosphorus and arsenic of type I compared with the analogous compounds of group IVB elements removal of the furan ring was not observed for certain types of compound (phosphines, arsines, furylphosphonic acid). At the same time, cleavage of the P—C bond was observed in furylphosphonium salts during alkaline hydrolysis in aqueous ethanol [2, 62, 190, 191].



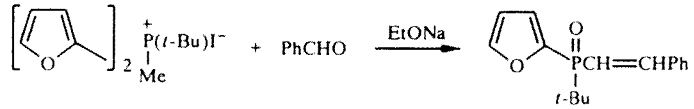
Tri(2-furyl)- and tri(3-furyl)methylphosphonium iodides are hydrolyzed with the loss of furan and the formation of difurylmethylphosphine oxides. Tri(2-furyl)benzylphosphonium bromide undergoes analogous changes, but in the case of tri(3-furyl)benzylphosphonium bromide toluene is eliminated preferentially, and a 1:3 mixture of di(3-furyl)benzylphosphine oxide and tri(3-furyl)phosphine oxide is formed. This fact and also the high rate of hydrolysis of the 2-furyl derivatives compared with the 3-furylphosphonium salts demonstrate the high stability of the 2-furyl carbanion [190, 191]. Cleavage of the C_{furan}—P and $C_{thiophene}$—P bonds is observed during the alkaline hydrolysis of (2-furyl)(2-thienyl)diphenylphosphonium bromide, and as a result of the higher stability of the 2-thienyl carbanion the ratio of the furan and thiophene resulting from the reaction amounts to 1:3 [62].



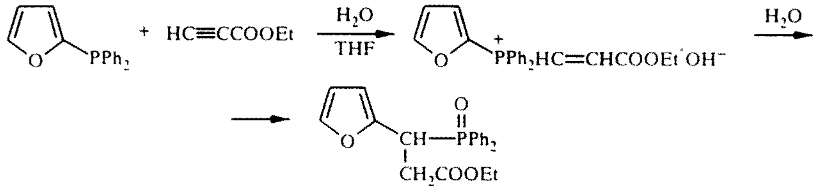
During hydrolysis (2-furylmethyl)triphenylphosphonium bromide and (3-furylmethyl)triphenylphosphonium bromide are transformed into triphenylphosphine oxide and the corresponding methylfurans, and here the 2-substituted derivative is hydrolyzed 100 times faster than the 3-isomer [190, 192]. (2-Furylmethyl)(2-thienylmethyl)diphenylphosphonium bromide and

(2-furylmethyl)benzyldiphenylphosphonium bromide give sylvane with 2-methylthiophene in a ratio of 1.3:1 and sylvane with toluene in a ratio of 7:1 respectively [62].

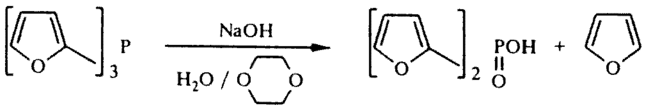
The direction of the reaction between the furyl-containing phosphonium salts and carbonyl compounds in the presence of sodium alcoholates in protic solvents is affected by the structure of the phosphonium ions. Thus, methyldiphenyl(2-furyl)phosphonium [5, 193], methylphenyldi(2-furyl)phosphonium [5], and tri(2-furyl)phosphonium iodides [5, 193] and also *tert*-butylbenzyldi(2-furyl)phosphonium bromide react with benzaldehyde without elimination of the furan ring and with the formation of styrene in the case of the methyl-containing ions or stilbene in the case of the *tert*-butylbenzyl derivative. However, the main product from the reaction of methyl(*tert*-butyl)di(2-furyl)phosphonium iodide with benzaldehyde under the influence of sodium ethoxide in the ethanol—*tert*-butyl(styryl)(2-furyl)phosphine oxide medium is formed by the loss of furan from the vinylphosphonium intermediate [6, 193]:



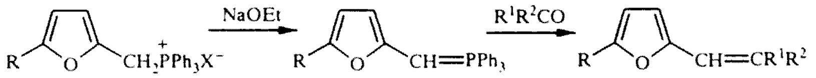
The vinylphosphonium ion, which is formed as intermediate product in the reaction of diphenyl(2-furyl)phosphine with ethyl propiolate in the presence of water in tetrahydrofuran solution, readily forms the product from migration of the 2-furyl group from the phosphorus to the neighboring carbon atom [194] during hydrolysis.

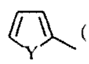


During hydrolysis by a water—dioxane solution of sodium hydroxide, tri(2-furyl)phosphine oxide eliminates furan with the formation of di(2-furyl)phosphinic acid [195]:

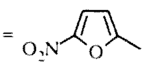


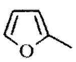
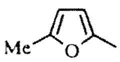
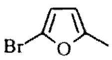
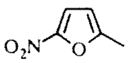
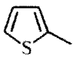
The best-studied reaction for phosphonium compounds of the second type with a furan ring and a phosphorus atom separated by one methylene group or by a large number of carbon atoms, i.e., the Wittig reaction, also takes place with elimination of the organophosphorus substituent. This reaction has been used for the synthesis of furyl-containing olefins by the action of carbonyl compounds on alkylidenephosphoranes, which are in turn obtained by treatment of the phosphonium salts with alkali-metal alcoholates in alcohol solution and are brought into the reaction without isolation. Various unsaturated derivatives of furan were obtained by this method [44-57, 59-61, 63, 65-68, 71, 73, 74, 196-209].

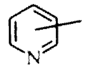
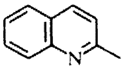
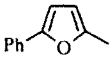


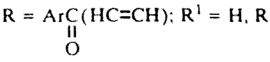
R = H; R¹ = H, R² =  (Y = O, S, Se) [44, 45]; R¹ = H, R² =  [46];

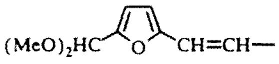
R¹ = H, R² = Ph [57]; R¹, R² = $(CH_2)_5$ [57]. R = COOMe; R¹ = H, R² = XC_6H_4 [51, 52, 199].

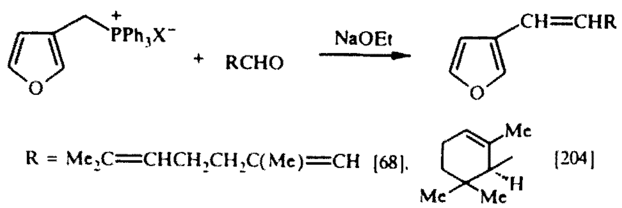
R = COOEt; R¹ = H, R² =  [203]. R = NO_2; R¹ = R² = H [61, 202];

R¹ = H, R² = Ph, , , , , ,

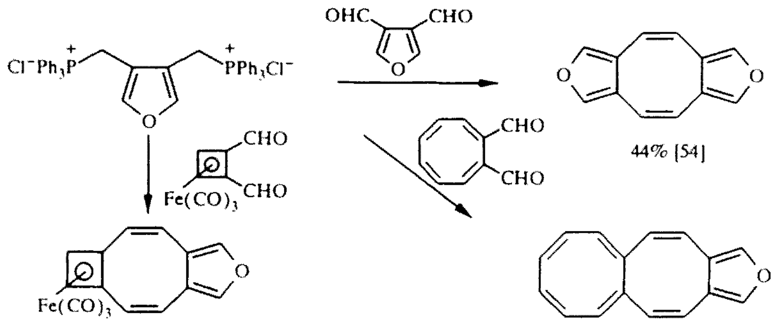
,  [53, 63, 201]; R¹ = H, R² =  [61].


R = $\mathrm{Ar}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}(\mathrm{HC{=}CH})$; R¹ = H, R² = p-$O_2NC_6H_4$ [59].

R = $(MeO)_2CH$; R¹ = H, R² =  [207]



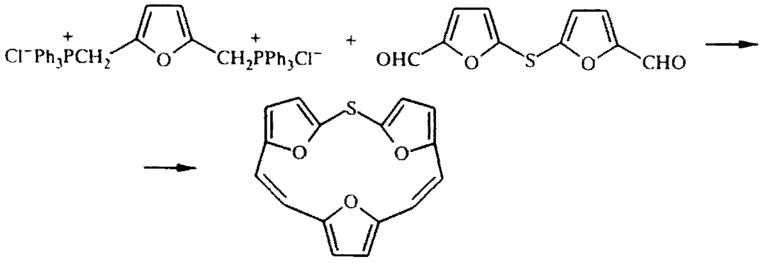
As a rule, a mixture of the *cis* and *trans* isomers is formed in the examples given above with yields of 60-70%. In addition to the linear furyl-containing olefins, various cyclic products were obtained by the Wittig reaction. For this purpose diphosphonium salts of furan [54-56, 66, 67, 196, 205] and also phosphonium salts of furfural [48, 49] were used as starting compounds. The yield of the cyclic adducts is usually small, and it rarely exceeds 20%.



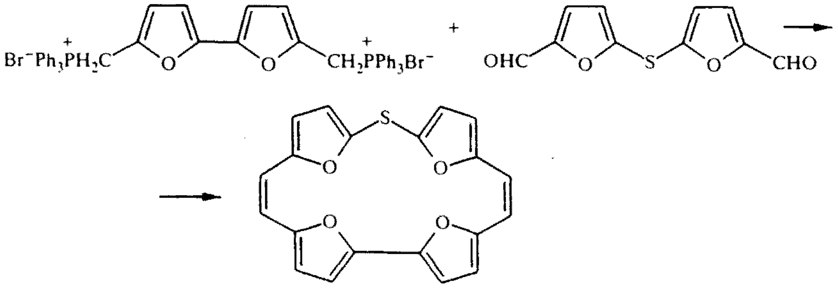
44% [54]

26% [196]

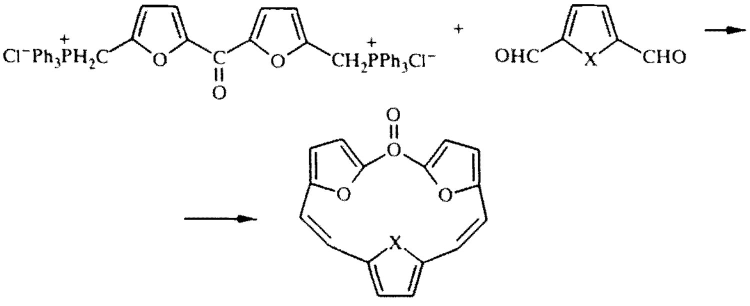
15% [55]



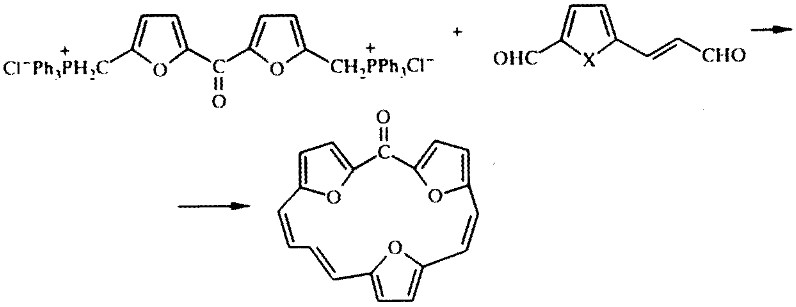
10,1% [66, 67]



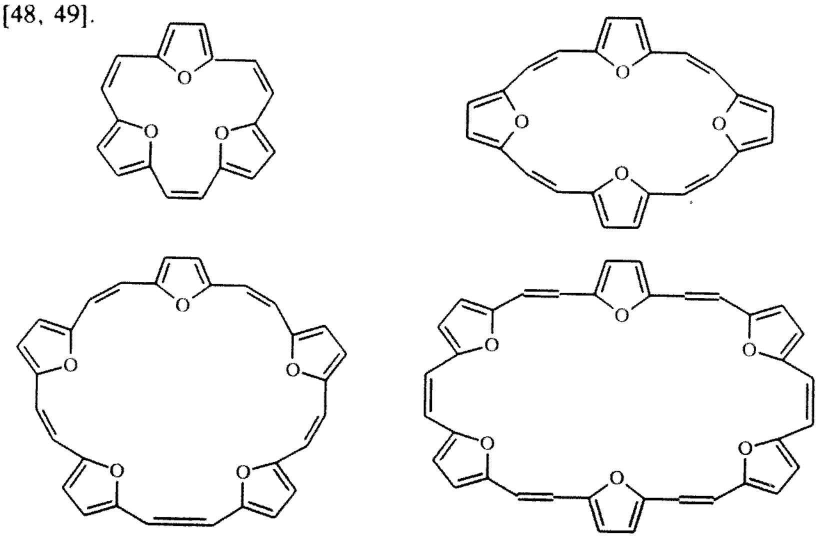
1,3% [66, 67]



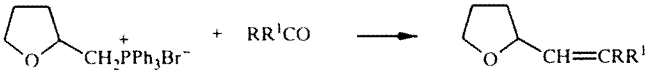
X = O (65%), X = NH (13,8%) [56]

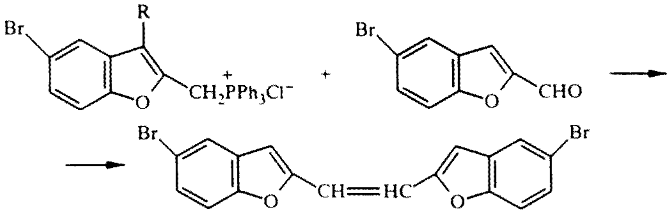


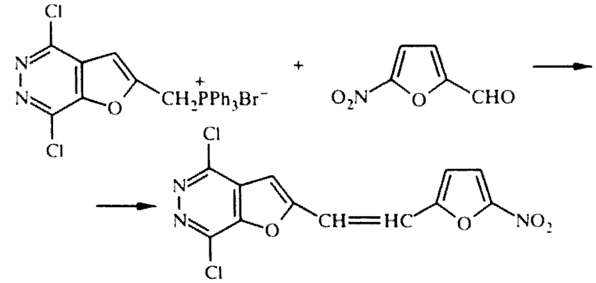
Initially an ylide is formed during the treatment of 5-formylfurfuryltriphenylphosphonium chloride with lithium ethoxide, and it then enters into self-condensation with the formation of a complex mixture, in which the linear condensation products predominate (85%). The cyclic compounds with three-, four-, five-, and six-furanoid systems were isolated with very low yields (0.8-0.07%) [48, 49].

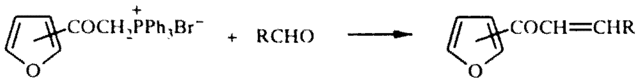


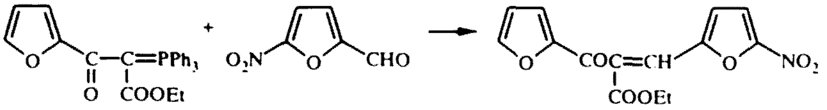
Phosphonium salts of tetrahydrofuran [57], benzofuran [65], furo[2,3-*d*]pyridazine [209], and various furoyl compounds [71, 72, 197, 200, 208] have also been used for the synthesis of unsaturated derivatives of furan.



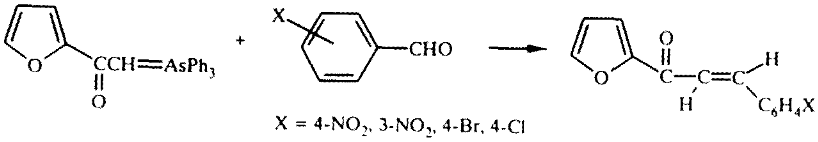




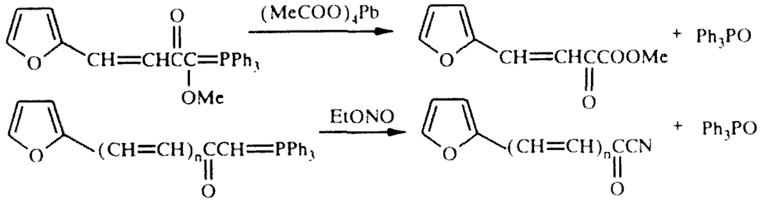




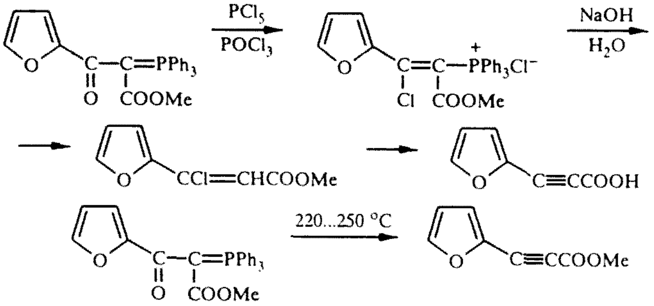
2-Furoylmethylenetriphenylarsorane reacts with *m*- and *p*-substituted benzaldehydes stereoselectively with the formation of the *trans*-products with yields of 96-99% [210].



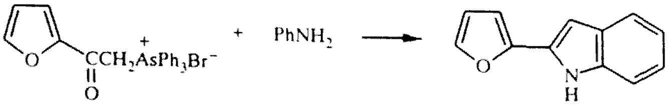
Furyl-containing phosphonium and arsonium salts and also alkylidenephosphoranes and alkylidenearsoranes have been used not only in the synthesis of olefinic derivatives by the Wittig reaction. Alkylidenephosphoranes are easily oxidized by lead tetraacetate [211] and ethyl nitrite [212] with the formation of the esters of β-keto acids and β-ketonitriles respectively.



(2-Furoyl)methoxycarbonylmethylenetriphenylphosphorane was used for the production of 2-furylethynecarboxylic acid [213] and its methyl ester [134]. The acid was synthesized with a yield of 48% in reaction with phosphorus pentachloride followed by alkaline hydrolysis, while its ester was obtained by thermal cleavage of triphenylphosphine oxide with a yield of 75%.

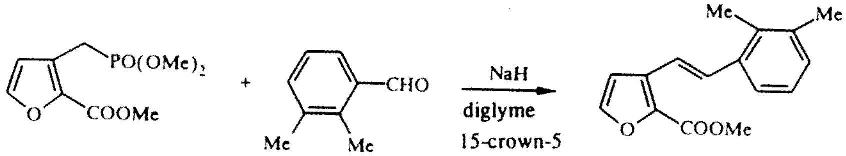


The synthesis of 2-(2-furyl)indole was realized with a yield of 22.8% by the reaction of aniline with (2-furoylmethyl)triphenylarsonium bromide at the carbonyl group followed by cyclization. 1-Aminonaphthalene enters into a similar reaction [210].

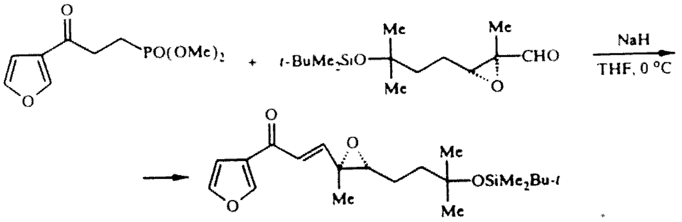


Cleavage of the C—As bond and the formation of Z-triazene were observed during the reaction of phenyl azide with arsenic imide in benzene [214].

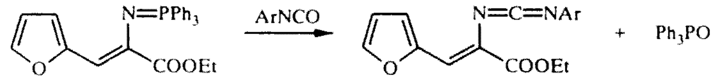
The reaction of the dimethoxyphosphoryl derivatives of furan with aldehydes has been used for the synthesis of olefins with the *trans* configuration at the double bond [83, 215-217]. The reaction of 2-methoxycarbonyl-3-dimethoxyphosphorylmethylfuran with 2,3-dimethylbenzaldehyde under the influence of sodium hydride with gentle heat gives low yields (10%). Only with the addition of catalytic amounts of 15-crown-5 is the yield of *trans*-stilbene increased to 45% [215, 216].



Dimethyl 3-furoylphosphonate reacts with aldehydes in tetrahydrofuran without the addition of crown ethers with cooling to 0°C (yield 92%) [217].

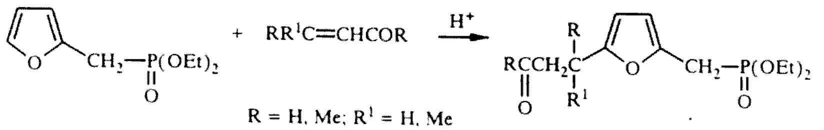


Reactions with the elimination of the phosphorus-containing groups from compounds of type III are extremely rare. Carbodiimides were synthesized by the reaction of the iminophosphoranyl derivative of ethyl furylacrylate with aromatic isocyanates with boiling in dry toluene [185].

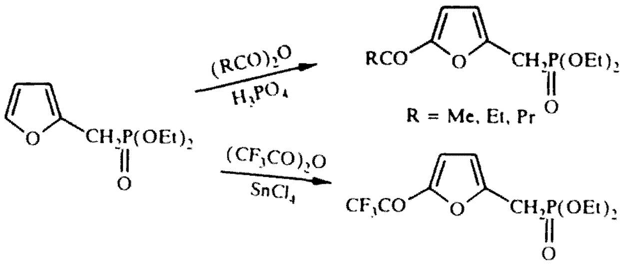


2.2. Reactions Involving the Furan Ring and Organic Substituents

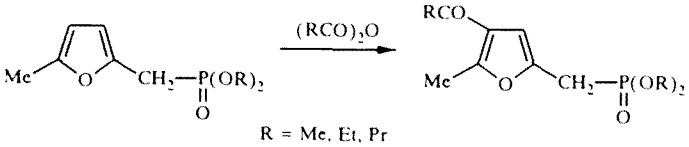
Alkylation [218], nitration [80], and acylation [77, 82, 219, 220] were used for the synthesis of furfurylphosphonates substituted in the furan ring. Diethyl furfurylphosphonate is alkylated by acrolein (16%), crotonaldehyde (39%), and mesityl oxide (44%) in the presence of sulfuric acid. The reaction takes place at position 5 of the furan ring by the usual mechanism of electrophilic substitution [218].



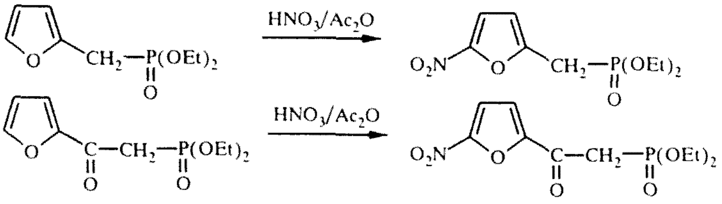
Acetic, propionic, butyric, and trifluoroacetic anhydrides were used as acylating agents in the reaction with furfurylphosphonates, and 85% phosphoric acid was used as catalyst. The reaction was carried out at 90-130°C for the first three anhydrides and at temperatures up to 43°C for trifluoroacetic anhydride. The molar ratios of phosphonate, anhydride, and phosphoric acid were 1:4-6:0.2-0.3. During the acylation of diethyl furfurylphosphonate with acetic, propionic, and butyric anhydrides the 5-acyl derivatives were formed with 53-57% yields, while trifluoroacetic anhydride did not react under these conditions [77, 82, 219]. The use of a small amount of perchloric acid as catalyst led to the appearance of the acyl derivative in the reaction mixture, but strong resin formation was observed in parallel. A more effective catalyst in this case was tin tetrachloride, although it was not possible to avoid the formation of resins. By conducting the reaction at 40-60°C for 5 h with the phosphonate, trifluoroacetic anhydride, and tin tetrachloride in molar ratios of 1:2.4:0.02 it was possible to obtain the 5-trifluoroacetyl derivative with a yield of 43% [220].



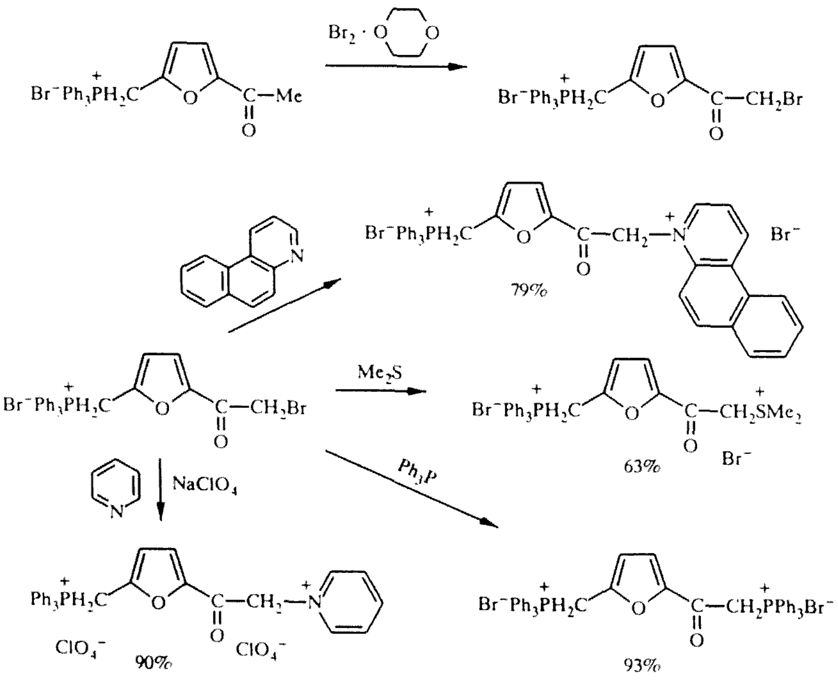
The acylation of 5-methylfurfurylphosphonates takes place with considerably greater difficulty and requires the reaction time to be increased to 12-14 h. The 4-substituted products are formed with yields of 20-40% [220].



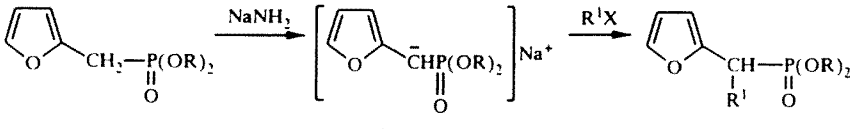
The nitration of furfurylphosphonate and 2-furoylmethylphosphonate was realized successfully with acetyl nitrate (a mild nitrating agent most suitable for furan compounds unstable toward acids) [80, 85]. 5-Nitrofurylphosphonates are formed with yields of about 60%.



5-Acetylfurfuryltriphenylphosphonium bromide is easily brominated at the acetyl group, and the obtained 4-bromoacetylfurfuryltriphenylphosphonium bromide serves as the starting material for the synthesis of the most varied derivatives [58].

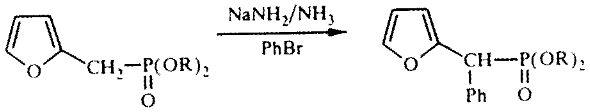


Dialkyl furfurylphosphonates can be alkylated [221] and arylated [222] with alkyl halides and aryl bromides respectively in the presence of sodium amide in liquid ammonia. With equimolar ratios of the phosphonate, alkyl halide, and sodium amide, alkylation only took place at the methylene group and gave 87-97% yields of the monoalkyl products [221].

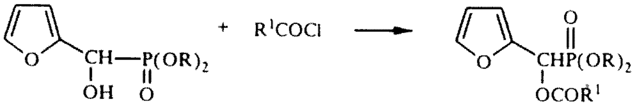


R = Et, *i*-Pr; R^1 = *i*-Pr, Bu, $PhCH_2$

The yields of the arylation products under analogous conditions were considerably lower. Even with an excess of sodium amide (reagent ratios 1:2:3) the yield of the acyl derivatives amounted to 27-37% [222].

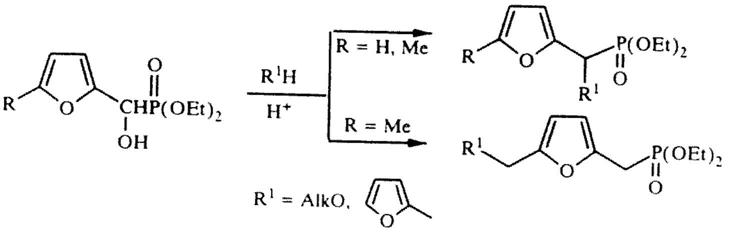


1′-Hydroxyfurfurylphosphonates are acylated by acid chlorides in the presence of triethylamine at room temperature [223] or with gentle heat [224].

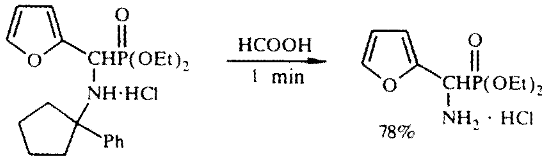


R = Me, Et, Pr, *i*-Pr, Bu, *i*-Bu; R^1 = Me, *i*-Pr, c-C_5H_{11}

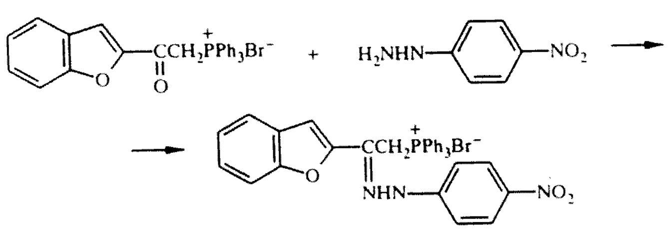
In the presence of such nucleophiles as alcohols or furan in an acidic medium, 5-methyl-1′-hydroxyfurfurylphosphonate forms two types of products, the ratio of which depends on the reaction temperature. With heating to 75°C, preferential substitution at the methyl group occurs [225].



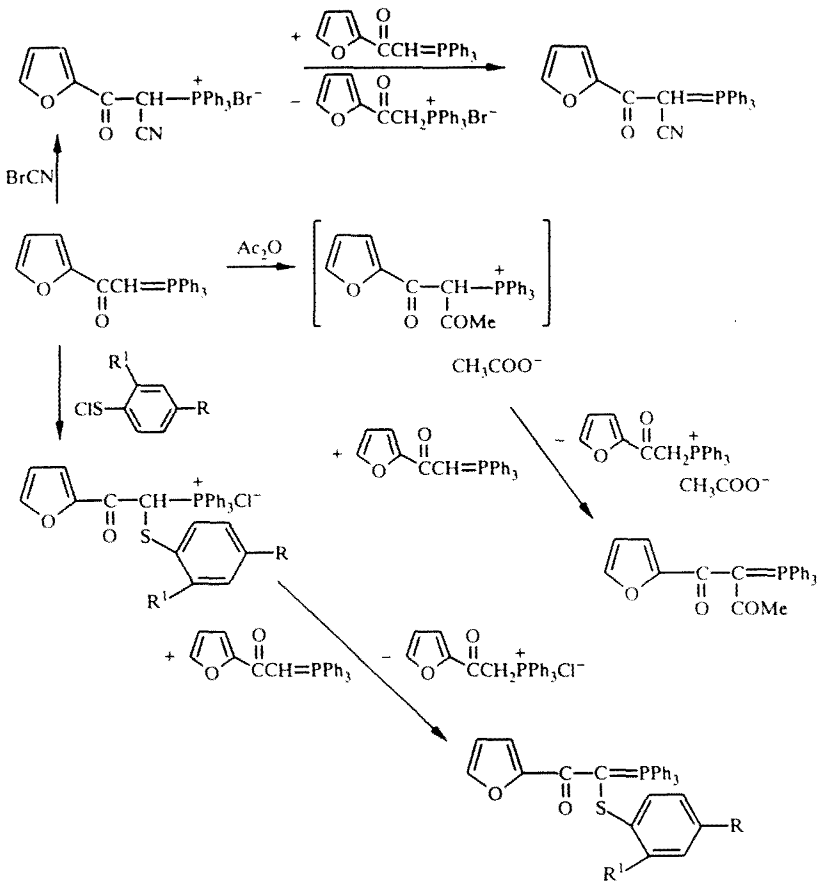
In order to remove the blocking 1-phenylcyclopentyl group from the nitrogen atom in the molecule of 1′-(1-phenylcyclopentylamino)furfurylphosphonate, its hydrochloride was briefly heated in anhydrous formic acid [226].



2-Benzofuroylmethyltriphenylphosphonium bromide enters into condensation with *p*-nitrophenylhydrazine at the carbonyl group when heated and forms phosphoniohydrazones with 60% yields [227].



As mentioned earlier in section 1.2 during discussion of methods for the synthesis of phosphonium salts, furoylmethylenetriphenylphosphorane reacts with methyl iodide [75] and bromine [76]. As a result, α-methyl- and α-bromo-substituted phosphonium salts were obtained with high yields. The reactions of furoylmethylenetriphenylphosphorane with cyanogen bromide [228], arenesulfenyl chlorides [229], and acetic anhydride [133] take place similarly.

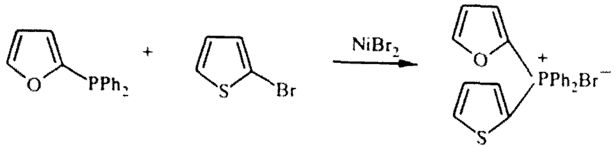


2.3. Chemical Transformations at the Element

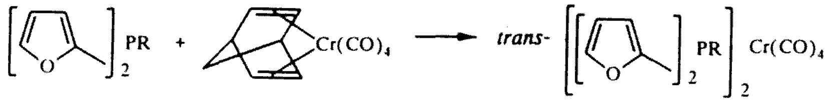
Chemical transformations at the group V element can be divided into two types: Reactions taking place with change of the coordination number of the element and transformations of the functional groups. Reactions of the first type include the numerous transformations of furyl-containing phosphines. These compounds are easily quaternized by alkyl iodides and benzyl bromide [2, 5, 6, 191] when heated in benzene.

R^1 = Me, Et, CH_2Ph; R = Me, Ph

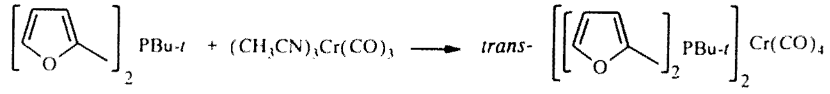
(2-Furyl)diphenylarsine is less active in reaction with methyl iodide. The production of (2-furyl)methyldiphenylarsonium iodide requires prolonged boiling in nitromethane and also an excess of methyl iodide [11]. The quaternization of (2-furyl)diphenylphosphine with 2-bromothiophene was realized with a 40% yield under more rigorous conditions by heating to 160-170°C in the presence of anhydrous nickel dibromide [62].



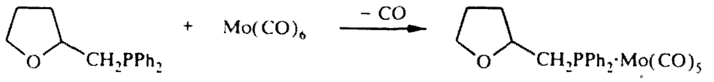
The furylphosphine complexes of chromium [4], molybdenum [4], tungsten [230], rhodium [7], and platinum [231] were synthesized. (η-Bicyclo[2.2.1]hepta-2,5-diene)tetracarbonylchromium reacts with methyl(2-furyl)- and phenyldi(2-furyl)phosphine in hexane solution with the elimination of bicyclo[2.2.1]hepta-2,5-diene. The complexes with phosphine ligands, formed with 35 and 40% yields, have the *trans* configuration [4].



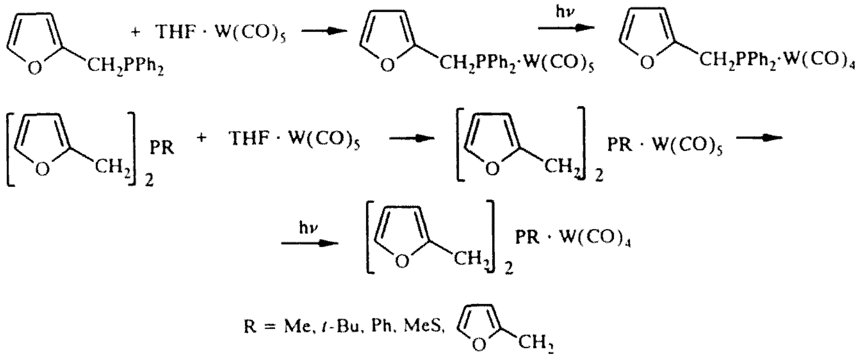
The reaction of tri(acetonitrile)tricarbonylchromium with *tert*-butyldi(2-furyl)phosphine with boiling for 15 h in tetrahydrofuran leads to substitution of two acetonitrile ligands by phosphine and one by carbonyl [4]



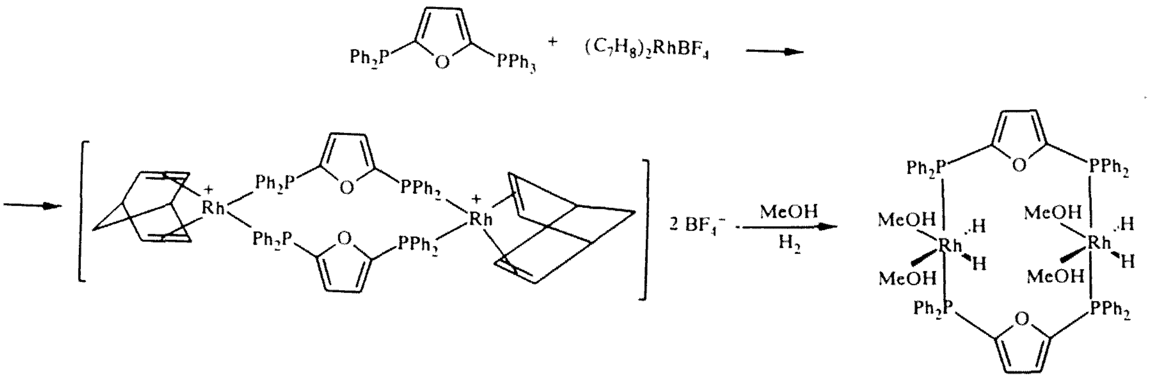
Hexacarbonylmolybdenum and tetrahydrofurfuryldiphenylphosphine in methylcyclohexane solution after 16 h at room temperature give a low yield (20.7%) of the complex tetrahydrofurfuryldiphenylphosphinepentacarbonylmolybdenum [4].



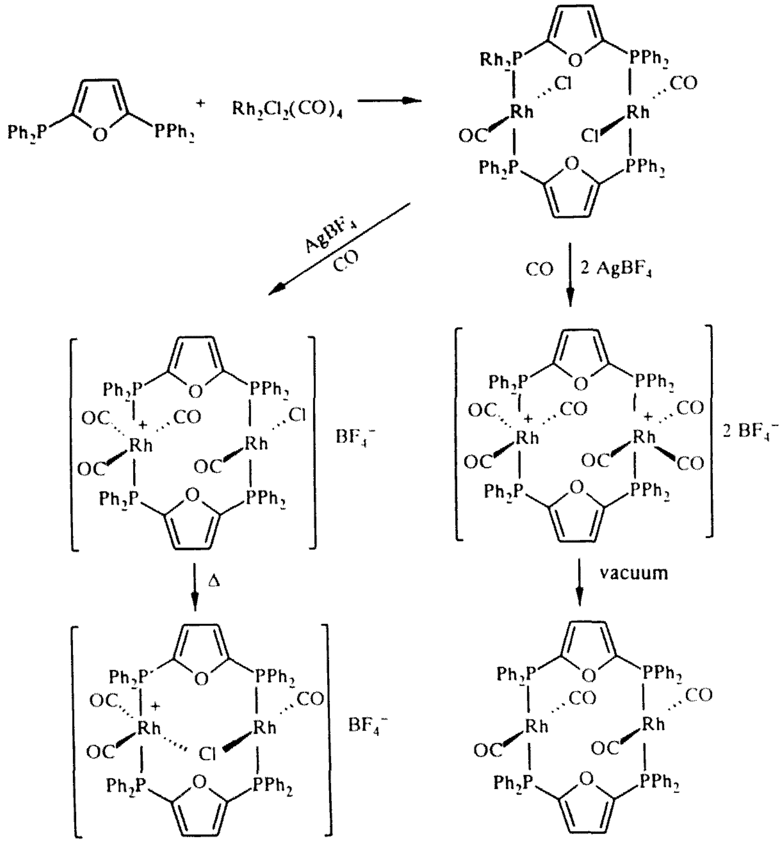
Furfuryldiphenyl-, difurfurylalkyl-, difurfurylaryl-, and trifurfurylphosphines substitute a molecule of tetrahydrofuran in the complex (tetrahydrofuran)pentacarbonyltungsten. Irradiation of ether solutions of the obtained pentacarbonyl complexes leads to the formation of tetracarbonyl derivatives of tungsten [230].



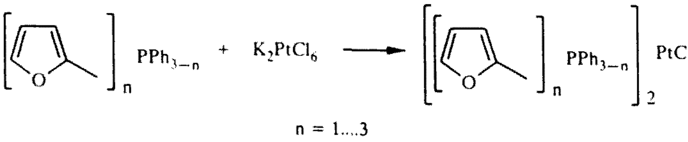
2,5-Bisdiphenylphosphinofuran reacts with bisbicyclo[2.2.1]hepta-2,5-dienerhodium tetrafluoroborate in methylene chloride. According to x-ray crystallographic analysis, the obtained binuclear complex has a centrosymmetric structure with two rhodium atoms attached to a pair of *cis*-located ligands [7]. In cold methanol, bicyclo[2.2.1]hepta-2,5-diene is eliminated from the obtained complex, and a tetrahydride complex with the *trans* structure is then formed after hydrogenation with hydrogen.



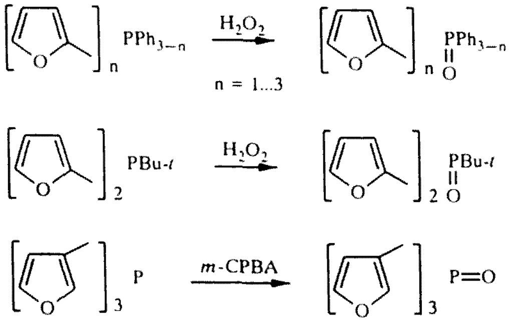
2,5-Bisdiphenylphosphinofuran forms a series of isomers with tetracarbonyl-μ-dichlororhodium. The main product has the *trans* structure and can be carbonylated in the presence of silver fluoroborate [7].



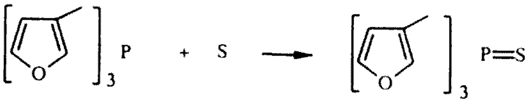
The complexes of platinum with phosphine ligands were obtained in the reaction of a heated solution of the phosphine in ethanol with a cold solution of potassium chloroplatinate in water [231].

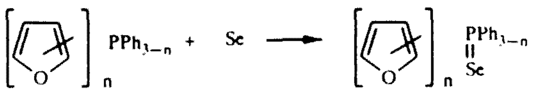


Furyl-containing phosphine oxides can be obtained not only by lithium synthesis [10, 12] or as side products in the Wittig reaction [5] but also by direct oxidation of the phosphines with hydrogen peroxide in acetone [5, 6] or with *m*-chloroperbenzoic acid in chloroform [232].

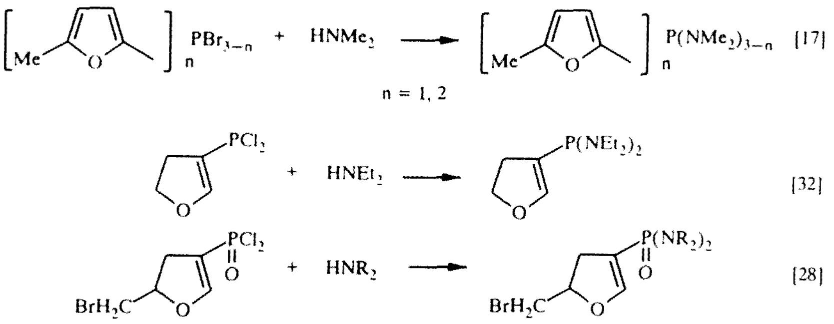


Tertiary phosphines react easily with sulfur [232] and selenium [231] when heated in chloroform.

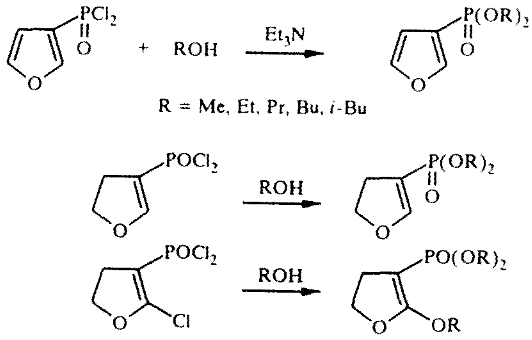




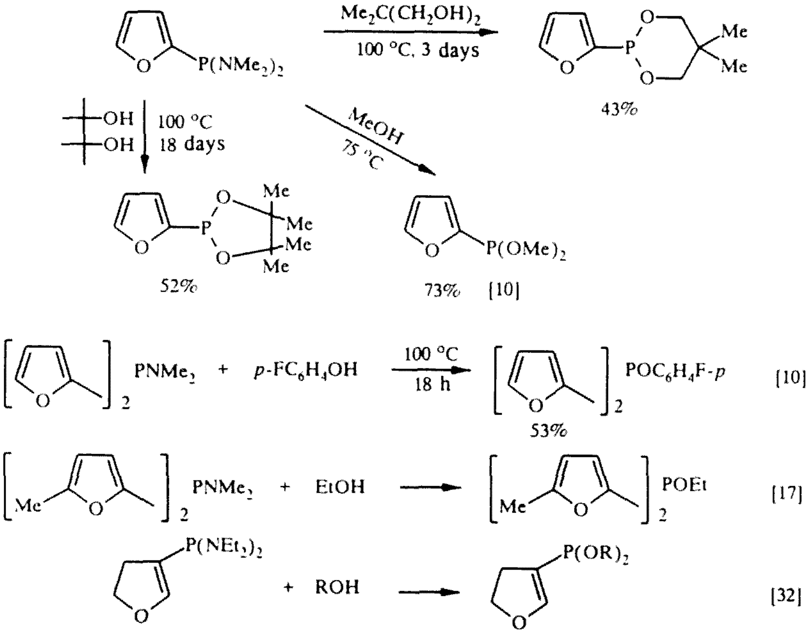
The furyl and dihydrofuryl derivatives of phosphorus with a P—halogen bond react readily with secondary amines. The reaction takes place without complications and with fairly high yields in the case of the compounds both of trivalent [17, 32] and of pentavalent [28] phosphorus.



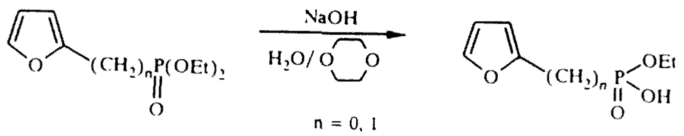
The analogous reaction with alcohols in the presence of triethylamine was conducted for the derivatives of pentavalent phosphorus [27-30, 33].



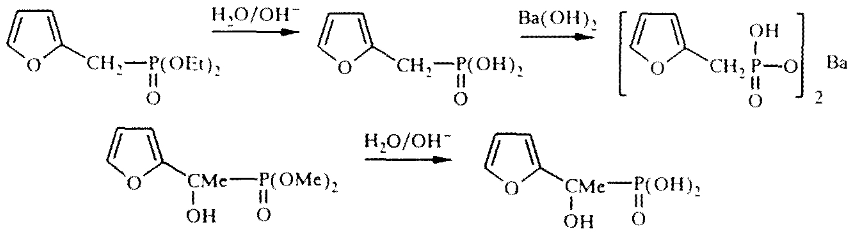
However, it was not possible to obtain phosphonites by such a method on account of their oxidation under these conditions [32, 233]. The best method for the synthesis of phosphonites was alcoholysis of the previously prepared amides [10, 17, 32].



The hydrolysis of derivatives of furyl- and furfurylphosphonic acids was undertaken [14, 81, 100]. During a kinetic investigation of the alkaline hydrolysis of furyl- and furfurylphosphonates by the action of a water—dioxane solution of sodium hydroxide it was established that monoesters are formed as a result of the reaction. Here the rate of hydrolysis of the 2-furylphosphonate is seven times higher than that of the furfurylphosphonate [14].

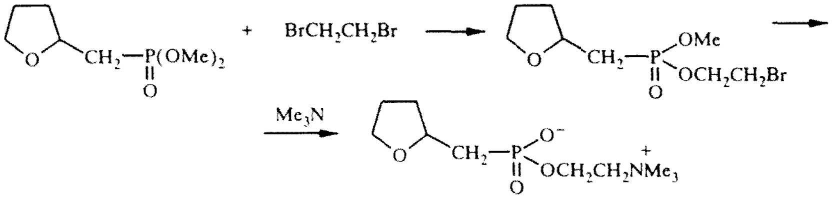


Resinification of the reaction mixture was observed during the acid hydrolysis of diethyl furfurylphosphonate, whereas the phosphonate, analyzed in the form of the barium salt, was obtained during hydrolysis with aqueous alkali [81]. The hydrolysis of hydroxyfurfurylphosphonates takes place similarly [100].

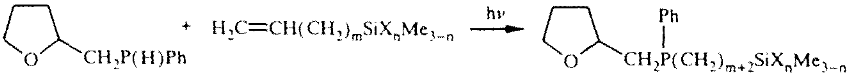


4-(2,3-Dihydrofuryl)dichlorophosphine oxide is hydrolyzed by water with the formation of phosphonic acid, identified in the form of the anilinium salt [27].

The transalkylation of dimethyl tetrahydrofurfurylphosphonate with 1,2-dibromoethane was realized, and ammonolysis of the bromoethyl ester with trimethylamine gave the phosphorus derivative of choline with a yield of 70% [160].



Compounds with a P—H bond can add at the C═C double bond of unsaturated compounds [234, 235]. Thus, silylalkylphosphines were obtained by the photochemical addition of phenyl(tetrahydrofurfuryl)phosphine to allyl- and hexenylsilanes [234].



$n = 1, 3$; $m = 1, 4$; $X = Cl, MeO$

Ditetrahydrophosphonate reacts at the C═C double bond of acrylamide in the presence of sodium tetrahydrofurfuryl oxide. The direction of the reaction depends substantially on the amount of the catalyst, the reagent ratio, and the presence of a solvent. In the presence of a small amount of the catalyst, a polymeric product is formed. With the reagents in an equimolar ratio and with an excess of sodium tetrahydrofurfuryl oxide and without a solvent, the yield of di(tetrahydrofurfuryl)phosphorylpropionamide amounted to 40%. It was possible to increase the yield to 75% by using a twofold excess of ditetrahydrofurfuryl phosphonate in dioxane [235].

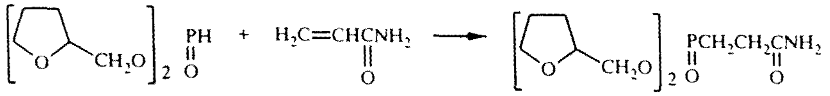
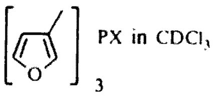


TABLE 2. Data from the PMR Spectra of Derivatives of Tri(3-furyl)phosphine



X	δ^1H, ppm				J, Hz		
	$H_{(2)}$	$H_{(4)}$	$H_{(5)}$	Me	$J_{2,4}$	$J_{2,5}$	$J_{4,5}$
O	7,739	6,576	7,568		0,85	1,56	1,87
S	7,745	6,576	7,556		0,88	1.56	1,87
MeI	8,392	6,993	7,777	3,23	0,96	1,46	2,02
MeI*	8,051	6,827	7,870	2,66	0,99	1,45	2,06

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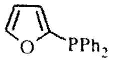
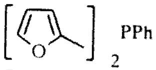
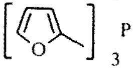
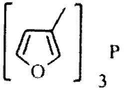
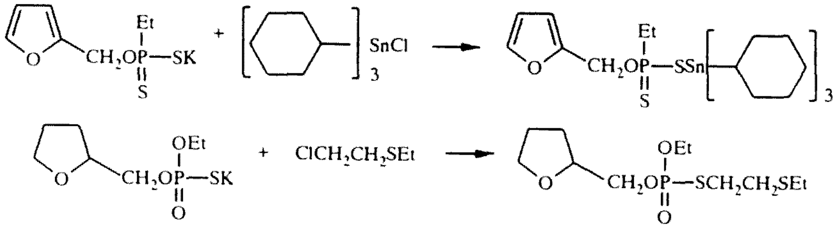
*In CF_3COOH.

TABLE 3. ^{31}P and ^{77}Se NMR Spectra of Furylphosphines, Their Selenides, and Their Platinum Complexes

R_3P	R_3P	R_3PSe			$(R_3P)_2PtCl_2$	
	$\delta^{31}P$, ppm	$\delta^{31}P$, ppm	$\delta^{77}Se$, ppm	$J_{^{77}Se-^{31}P}$, Hz	$\delta^{31}P$, ppm	$J_{^{195}Pt-^{31}P}$ Hz
	-26,6	16,9	-300	754	-1,5	3665
	-50,8	-2,0	-334	774	-18,3	3698
	-76,4	-22,1	-354	793	-36,3	3716
	-81,9	-20,3	-270	745	42,1	3649

The potassium thiophosphates [236] and thiophosphonates [237] substitute the halogen during reaction with alkyl chlorides [236] and chlorostannanes [237].



3. PHYSICOCHEMICAL PROPERTIES

A series of furyl-containing derivatives of phosphorus have been investigated by ^1H [232, 238-240], ^{13}C [241, 242], and ^{31}P [2, 133, 231, 243] NMR spectroscopy.

In the PMR spectra of tri(2-furyl)phosphine [239], tri(5-methyl-2-furyl)phosphine [240], tri(2-furyl)phosphine oxide [238], and dimethyl 2-furylphosphonate [238], the signals of the $H_{(3)}$ and $H_{(5)}$ protons are shifted downfield in relation to unsubstituted furan, indicating descreening of the furan ring in these compounds by the phosphorus atom. The PMR spectra of derivatives of tri(3-furyl)phosphine with the general formula (3-furyl)$_3$PX (X = O, S, MeI) were analyzed [232]. Descreening of all the ring protons of methyltri(3-furyl)phosphonium iodide downfield in relation to tri(3-furyl)phosphine oxide and its sulfur-containing analog was observed (Table 2). The authors [232] attribute this to the ionic nature of the phosphonium compound. The effect of the solvent (deuterochloroform, trifluoroacetic acid) on the proton shifts and the spin—spin coupling

TABLE 4. $\delta^{31}P$ Chemical Shifts of Acylmethylenetriphenylphosphoranes

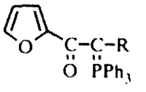
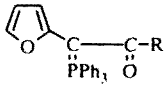
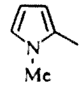
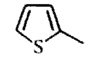
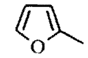
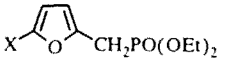
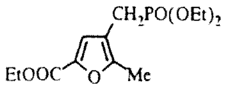
R		
Ph	-17,5	-17,6
	-18,1	-18,4
	-18,7	-18,8
	-19,1	—

TABLE 5. pK_a Values of Furfurylphosphonates



X	$\delta_{(CH2P)}$, ppm	pK_a (DMS)	pK_a (PrOH)
H	3,10	26,8	
Me	3,02	~27	20,5
MeCO	3,30	20,0	18,2
EtOOC	3,26	20,9	
CHO	3,36	~18	
NO_2	3,42	~17	
	2,95	22,3	

constants of methyltri(3-furyl)phosphonium iodide was investigated. The spin—spin coupling constants differ little, but the chemical shifts of the protons of the furan ring and the methyl groups differ substantially.

Some parameters of the spectra of the heavy nuclei of furylphosphines [231, 244], their selenides [231, 244], and their platinum complexes [231, 244] are given in Table 3.

Replacement of the phenyl group in triphenylphosphine ($\delta^{31}P = -4.7$ ppm) by a furyl group leads to an upfield shift of signal for the phosphorus nucleus [231, 244], and the screening of the phosphorus is increased additively with increase in the number of furyl substituents. Similar data were obtained for the selenides R_3PSe and for the platinum complexes $(R_3P)_2PtCl_2$; it is possible to see only a decrease in the contribution from the furyl group to the $\delta^{31}P$ chemical shift in compounds of this type in comparison with furylphosphines.

The quaternization of tri(2-furyl)phosphine with methyl iodide [$\delta^{31}P$ (2-furyl)$_3$PMeI = 15.4 ppm] and benzyl bromide [$\delta^{31}P$ (2-furyl)$_3$PCH$_2$PhBr = 12.8 ppm] is accompanied by a strong downfield shift of the ^{31}P signal [2].

The effect of aromatic substituents on the size of the $\delta^{31}P$ chemical shift in various acylmethylenetriphenylphosphoranes was studied (Table 4) [133]. The screening of the phosphorus atom increases a little in the series of R: Ph < 2-(N-methylpyrrolyl) < 2-thienyl < 2-furyl.

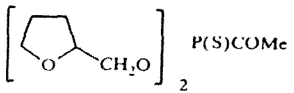
Investigations into the physicochemical characteristics of the furan derivatives of phosphorus by UV methods are also extremely uncommon [12, 77, 82]. Thus, the equilibrium CH acidity of furfurylphosphonates was determined by spectrophotometry in absolute propanol with sodium propoxide as base [82] and in dimethyl sulfoxide by transmetallation [77]. The obtained pK_a values are given in Table 5. However, a series of furfurylphosphonate anions with a methyl, formyl, and nitro group at position 5 of the furan ring proved unstable in dimethyl sulfoxide, and their spectral characteristics were therefore determined with insufficient accuracy [77].

To a first approximation, the conduction of the effect of substituents in the furan ring from position 5 to position 2 was close to that of benzene in the case of p substituents. However, the furfurylphosphonates are 1-2 pK_a units stronger CH acids than the benzyl analogs [77].

The effect of aryl substituents on the position of the frequency of the stretching vibration of the carbonyl group was investigated in a series of aroylmethylenetriphenylphosphoranes, including 2-furoylmethylenetriphenylphosphorane [245], for which ν_{CO} in the crystalline state is 1536 cm^{-1}.

The position of the P═S vibration frequencies in dithiophosphates was determined in [246].

In the derivatives of tetrahydrofuryl alcohol (**1** and **2**) ν_{CO} amounts to 660-680 cm^{-1}.



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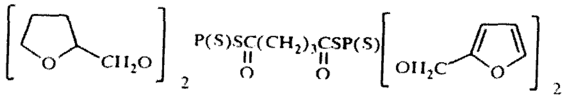
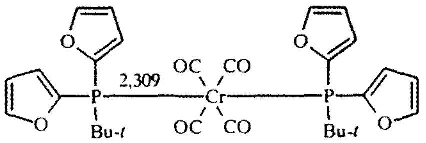


2

An x-ray crystallographic analysis of certain furan derivatives of phosphorus was undertaken [4, 7, 245]. In tri(2-furyl)phosphine selenide, the phosphorus atom has a disordered tetrahedral configuration with average <SePC and <CPC angles of 114.9 and 103.4° respectively. The average lengths of the P—C (1.778 Å) and P—Se (2.094 Å) bonds are significantly shorter than in arylphosphine selenides. The furyl groups are directed in space in such a way that the average O···Se distance is 3.577 Å [245].

In *trans*-di[*tert*-butyldi(2-furyl)phosphine]tetracarbonylchromium, the chromium atom has an octahedral environment [4] with *trans*-located phosphine ligands ($<PCrP^1$ = 180°). The phosphorus atoms are tetracoordinated, and the substituents have a strongly distorted tetrahedral environment. All the $<C_{Fu}PC$ angles are reduced compared with the tetrahedral values and amount to 100.1-101.2°, while the <CrPC angles are increased to 116.9-117.5°. No departures from the norm are observed in the geometry of the furan ring, but the length of the C_{Fu}—P bond is 1.809 Å, which is longer than in tri(2-furyl)phosphine selenide.

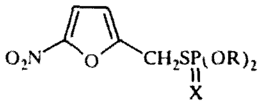


In [7], x-ray crystallographic analysis was only used to obtain evidence for the structure of the binuclear rhenium complex, and its structural parameters were not given in detail.

4. BIOLOGICAL ACTIVITY

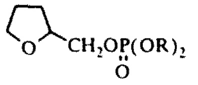
One of the most important types of modern pesticides is the organic compounds of phosphorus, in which substances with various types of biological activity have been found (acaricides, insecticides, nematocides, herbicides). Various forms of pesticidal activity in furan and tetrahydrofuran derivatives have been investigated in this connection.

In the series of O,O-dialkyl S-(5-nitrofurfuryl) thio- and dithiophosphates [167, 168], the compounds with methyl and ethyl substituents (R = Me, X = O; R = Et, X = O, S) exhibited insecticidal activity comparable with malathion toward *Musca domestica L.* [167] and acaricidal activity almost three times the activity of malathion toward *Tetranychus urticae* Koch. All the compounds were ineffective against *Calandra granaria L.*, *Macrosyphoniella sanborni* Theorb., and *Aphis fabae* Scop. [167].



X = O, S; R = Me, Et, Pr, *i*-Pr, *i*-Bu

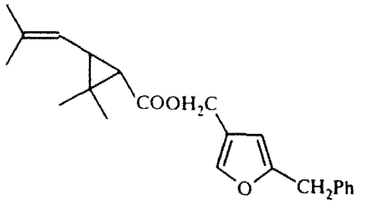
TABLE 6. Insecticidal Activity of Phosphates Against Granary Weevils



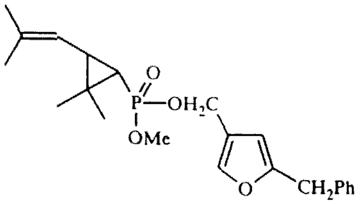
R	Concentration of substance	Mortality of granary weevil in 7 days, %	R	Concentration of substance	Mortality of granary weevil in 7 days, %
Et	0,01	49	*i*-Pr	0,1	54
	0,02	44		0,5	76
	0,05	58		1,0	94
	0,1	76	Bu	0,5	72
	0,5	100 (3 сут)		1,0	72
	1,0	100 (1 сут)			

Phosphate [150] and thiophosphate [237] esters containing a tetrahydrofurfuryl substituent also exhibit insecticidal activity. In this case the compounds with ethyl substituents are more effective than the isopropyl and butyl analogs against granary weevils [150] (Table 6).

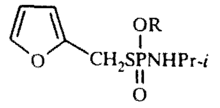
Chrysanthemate esters form a well-known class of natural and synthetic pesticides. However, replacement of the ester group in the synthetic pyrethroid resmethrin (chrysrone, synthrine), used as an insecticide, by phosphoryl leads to almost complete loss of activity against *Musca domestica* and *Lasioderma serricorne* [165].



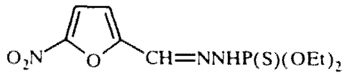
Resmethrin



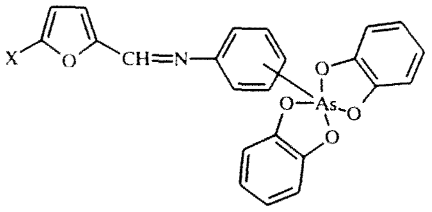
According to data in [169], dialkyl isopropylamidothiophosphates exhibit strong nematocidal activity.



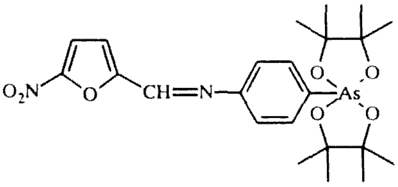
Diethyl 2-(5-nitrofurfurylidene)hydrazinothiophosphate is a coccidiostat and is effective against *Eimeria tenella*. Addition to chicken feed at the rate of 0.022% protects against infection with *Eimeria tenella* by 75% [187].



Azomethine bases of furfural and nitrofurfural containing spiroarsorane fragments are new types of substances with antiparasitic properties [140].



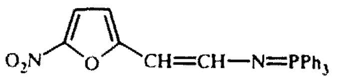
X = H, NO$_2$



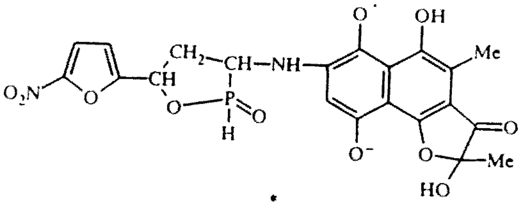
These compounds *in vitro* exhibit antifilariasis activity against *Molinema dessetae*.

The antimicrobial [70, 119, 184, 247] and fungicidal [70] activity of some furan compounds of phosphorus were studied. During comparison of the antimicrobial activity of 5-styryl-2-furoylmethyltriphenylphosphonium bromides and the corresponding triphenylphosphoranes, it was established that the activity of the ylides against the Gram-positive microorganisms *S. aureus* and *B. subtilis* (MSC = 250-500 μg/ml) is 2-4 times lower than that of the phosphonium salts (MSC = 62.5-125 μg/ml) [247]. (MSC is the minimum suppressing concentration.)

The inhibiting concentration of {[2-(5-nitro-2-furyl)vinyl]imino}triphenylphosphorane against the Gram-negative bacteria *Escherichia coli* is 50 μg/ml [184].



The antimicrobial activity of the organophosphorus derivative of the product from hydrolysis of the antibiotic rifamycin S with an unpaired electron at the oxygen atom of the aromatic ring at position 1 is significantly lower than that of the antibiotic itself. The MSC is 0.3-0.5 μg/ml for staphylococcus, 50-100 μg/ml for *Escherichia coli*, and 100 μg/ml for *Proteus* [119].



* * *

The data examined above show that furylphosphines and furylarsines are convenient models for studying the effect of the heterocycle on the cleavage of the $C_{sp}2$—M bond (M = P, As). Furylphosphonium salts can be used successfully in the Wittig reaction for the synthesis of various furylalkenes and cyclic compounds with three, four, five, and six furan rings in a macrocycle. Tris(3-furyl)phosphine favorably replaces triphenylphosphine as ligand in a number of reactions. Representatives of various types of organophosphorus derivatives of furan exhibit insecticidal, antiparasitic, and antibacterial properties.

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