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Synthesis and Aminomethylation of 2-Isobutyl-3- and 4-Diethoxyphosphorylmethylfurans

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Abstract — Synthetic procedure for preparing 2-isobutyl-3- and 4-furancarboxylic acyl chlorides is developed. Reduction of these compounds with lithium alumohydride leads to corresponding alcohols which under treating with thionyl chloride in the presence of pyridine form chloromethyl derivatives. The latter compounds are phosphorylated with sodium diethyl phosphite under the Michaelis–Becker reaction conditions to give corresponding phosphonates. Reaction of compounds obtained with dimethyl(chloromethyl)amine proceeds at the free α-position of the furan ring and delivers aminophosphonates. These substances do not evolve dimethylamine even under the conditions of vacuum distillation (145–150°C, 1 mm Hg).
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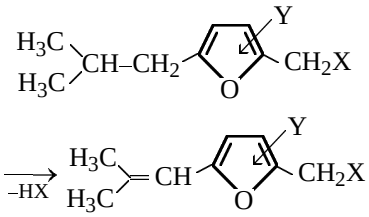
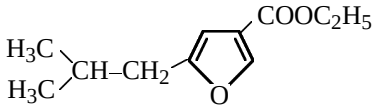
We have found previously [1,2] that 2-isobutylfuran halomethyl derivatives can eliminate hydrogen chloride to give furylalkenes as is shown below.



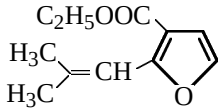
Developing the studies of this unusual reaction we decided to look for some other functional groups which are capable of furylalkene formation by elimination of a volatile products. Investigation of 2-aminomethylated diethoxyphosphorylmethylfurans [3] showed that on handling or during the vacuum distillation these compounds eliminate dimethylamine in a noticeable amount. Therefore we assumed that in the case of 2-isobutyl-5-dimethylaminomethylfurans the conditions can be found which are favorable for dimethylamine elimination leading to the phosphonates with unsaturated side chain. Compounds of such structure are valuable synthons for constructing the carbon frame of furan-containing terpenes for instance using the Wittig–Horner reaction.

At the same time synthetic approaches to these compounds were not developed so far. We propose to use alkyl 2-isobutylfurancarboxylates **I** and **II** as the starting compounds.

Synthesis of compound **I** was assumed to carry out according to the following typical procedure.

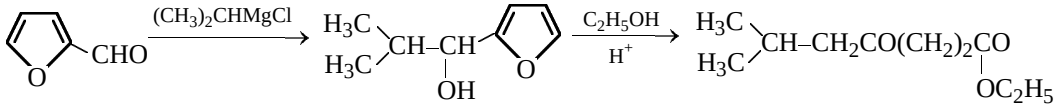


I

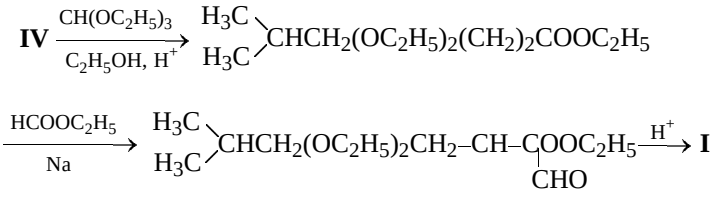


II

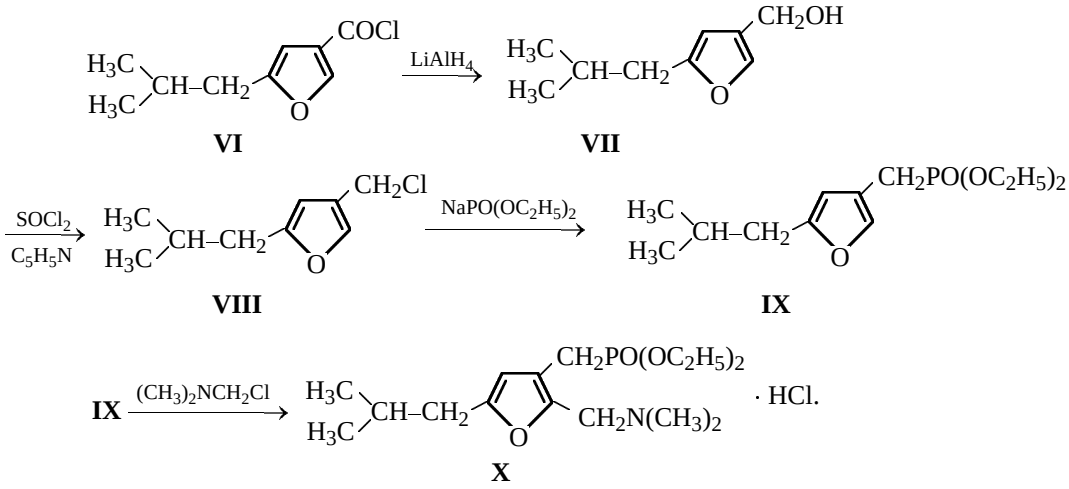
Reaction of isopropylmagnesium chloride with 2-furaldehyde leads to secondary alcohol **III** which by means of the Markwald rearrangement can be converted to ketoester **IV** [4]. The latter product is ketalyzed for protecting the ketone carbonyl group and then is formylated with ethyl formate under the conditions of the Claisen reaction [5]. Aldehyde **V** thus obtained could be involved in cyclization in acidic medium delivering furan **I**.



III **IV**



However it occured that two last steps of this synthesis proceed with a complication. The aldehyde **V** sodium derivative is a strong emulgator, and at working up the reaction mixture for separation a large amount of unreacted ketal is transfered into the water phase. After acidification the target product **V** is formed but its purification by vacuum distillation can not provide removing of this admixture. The ester **I** obtained is therefore substantially contaminated with aliphatic compounds. Separation of pure furan can be achieved olny by alkaline hydrolysis, isolation of the mixture of acids, and treating it with thionyl chloride in presence of DMF. The acyl chloride **VI** obtained after distillation in a vacuum according to ^{1}H NMR data was free from noticeable amounts of admixtures. The acyl chloride **VI** reduction was carried out with lithium alumohydride in ether at 36°C. The alcohol **VII** obtained (yield 65%) is a stable compound with no tendency of polymerization. Treating the alcohol **VII** with thionyl chloride in ether in the presence of pyridine was carried out at 17–25°C for 5 h. Vacuum distillation afforded stable chloride **VIII** in 65% yield. This product can be distilled in a vacuum without tarring and does not darken on air at room temperature. The chloride **VIII** phosphorylation was carried out with sodium diethyl phosphite at 80°C in benzene for 14 h. Phosphonate **IX** was isolated by vacuum distillation in 71% yield.



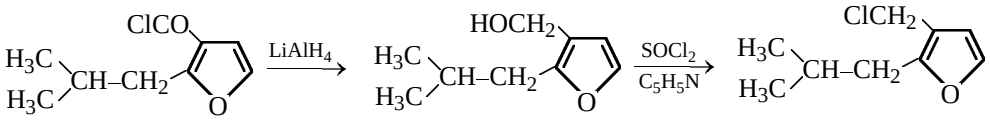
Aminomethylation of compound **IX** was carried out with dimethyl(chloromethyl)amine analogously to [3] in acetonitrile at 80°C for 6 h. We failed to isolate obtained aminophosphonate hydrochloride **X** in the crystalline form. The syrup-like salt **X** was prepared in 83% yield and characterized by the ^{1}H and ^{31}P NMR spectra.

For the isolation of free amine **Xa** the product obtained was dissolved in ethanol and treated with the equivalent amount of sodium ethylate in ethanol. After removing sodium chloride the aminophosphonate **Xa** was isolated by vacuum distillation, bp 145°C (1 mm Hg). The product yield was 48% only, nevertheless, we could not detect formation of the deamination product with the expected boiling point about 120°C (1 mm Hg) or dimethylamine in a significant amount which should be condensed in a trap cooled with liqiud nitrogen. That means that dimethylamine elimination does not take place. Decrease in the aminophosphonate yield may be probably caused by dealkylation of the phosphorus-containing group in the presence of traces of sodium ethoxide. This is confirmed indirectly by the fact that

only the mechanical losses were observed at the repeated distillation of phosphonate **Xa**.

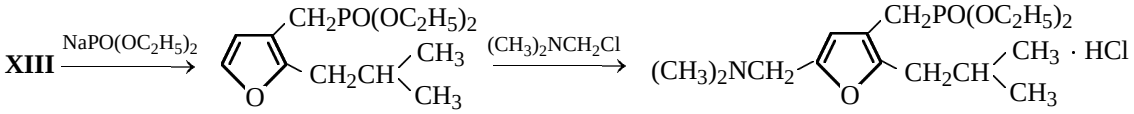
Synthesis of the isomeric phosphonate with isobutyl and diethoxyphosphorylmethyl groups located at the same side of the furan ring was started with the preparation of the ester **II** by the modified Feist–Benary procedure [6] including condensation of chloroacetaldehyde with ethyl isobutyrylacetate in water–pyridine medium. But it occured that the isolated compound **II** was significantly contaminated with aliphatic compounds. They could be removed only by alkaline hydrolysis, extraction of nonhydrolyzed material, and treating the acid mixture obtained with a thionyl chloride excess. This procedure delivered the acyl chloride **XI** with bp 62°C (1 mm Hg) whose ^{1}H NMR spectrum did not contain signals of admixture.

The acyl chloride **XI** reduction was carried out with lithium alumohydride in ether at 36°C. The stable alcohol **XII** obtained was isolated by vacuum distillation in 62% yield. Chloride **XIII** was prepared by treating compound **XII** with thionyl chloride in ether in the presence of pyridine at 15-20°C for 3 h. Reaction product was isolated in 64% yield. It is a stable compound which can be distilled in a vacuum without decomposition and does not darken at room temperature.



XI **XII** **XIII**

The chloride **XIII** phosphorylation was carried out under the Michaelis–Becker reaction conditions with sodium diethyl phosphite in benzene at 80°C for 13 h. Phosphonate **XIV** was isolated by vacuum distillation as a viscous oil with bp 118°C (1 mm Hg) in 72% yield.



XIV **XV**

Phosphonate **XIV** was aminomethylated with dimethyl(chloromethyl)amine in acetonitrile for 6 h. Aminophosphonate hydrochloride **XV** was obtained as a glass-like mass which did not give well formed crystals. It was characterized by ^{1}H amd ^{31}P NMR spectra. The yield of the product was 95%.

For isolation of the free aminophosphonate **XVa** the hydrochloride **XV** was dissolved in ethanol and treated with an equivalent amount of a sodium ethoxide ethanolic solution. Sodium chloride was removed, and the residue was distilled in a vacuum. Aminophosphonate **XVa** was obtained as a viscous oil with bp 151–153°C (1 mm Hg) in 59% yield. The products of dimethylamine elimination or dimethylamine itself were not found. Evidently the reason of the moderate yield similarly to the previous case was the dealkylation of phosphonate group in the presence of sodium ethoxide traces. At repeated distillation of phosphonate **XVa** the mechanical losses were only observed.

Thus, 3- and 4-substituted 2-isobutylfuran derivatives show quite close chemical behavior in the considered reaction sequence. Yields of corresponding isomeric alcohols, chlorides, and phosphonates are similar and the products are equally stable. Aminomethylation of phosphonates **IX** and **XIV** proceeds under the similar conditions. The products obtained have no tendency to eliminate dimethylamine. At the same time in presence of the ethoxide traces dealkylation of phosphonates to esterosalts evidently takes place causing decrease in the yield of free aminophosphonates at their isolation from the salts.

EXPERIMENTAL

The ^{1}H and ^{31}P NMR spectra of compounds obtained were taken on a Bruker AC-200 spectrometer (200.13 MHz ^{1}H; 80.014 MHz ^{31}P) in $CDCl_3$ and in DMSO-d_6 in the case of aminophosphonate hydrochlorides, with internal TMS (^{1}H) and external 85% H_3PO_4 (^{31}P) as references.

2-Isobutyl-4-clhoroformylfuran (VI). *a*. To a Grignard reagent solution prepared from 55 ml of isopropyl chloride and 14.5 g of magnesium in 150 ml of ether 40.6 ml of 2-furaldehyde was added dropwise with stirring and cooling at 25–30°C. Resulting mixture was stirred for 3 h and left overnight. Next day the reaction mixture was treated with saturated water solution of ammonium chloride until separation of organic and inorganic phases was achieved, and diluted with 150 ml of petroleum ether. Organic layer was decanted, and the inorganic salt gel was treated with stirring with 100 ml of petroleum ether. Joined organic extracts were washed with water and dried over sodium sulfate. Solvent was removed, and the residue was distilled in a vacuum to give 45.7 g of the product **III** with bp 46–46°C (1 mm Hg), n_D^{20} 1.4680. ^{1}H NMR spectrum, δ, ppm: 0.725 d (CH_3-isopropyl, J_{HH} 7 Hz), 0.875 d (CH_3-isopropyl, J_{HH} 7 Hz), 1.925 m (CH-isopropyl), 4.000 s (OH), 4.100 d.d (CH-OH); 6.050 s (H^4-furan), 6.150 s (H^3-furan), 6.670 s (H^5-furan).

b. A mixture of 38.8 g of alcohol **III** and 156 ml of ethanol containing 0.5 g of hydrogen chloride was refluxed with stirring for 9 h, ethanol was distilled off at reduced pressure, and the residue was distilled in a vacuum to give 34.1 g of ketoester **IV**, bp 79°C (1 mm Hg), n_D^{20} 1.4260.

c. A mixture of 34.4 g of ketoester **IV**, 29 ml of triethyl orthoformate, 10 ml of absolute ethanol and 0.3 ml of concentrated sulfuric acid was refluxed with stirring for 12 h, the volatile products were distilled off at reduced pressure, and the residue was distilled in a vacuum to give 29.2 g of ketal with bp 78°C (1 mm Hg), n_D^{20} 1.4280.

d. To the vigorously stirred suspension of 2.8 g of sodium foil in 100 ml of toluene 28 g of ketal and 17.4 g of ethyl formate were added dropwise from two different dropping funnels. The component addition rate was regulated to provide simultaneous completion of loading. During the addition the reaction mixture was cooled with water. After the addition was complete the mixture obtained was stirred for 3–4 h to complete disappearance of sodium pieces and then left overnight. On the next day it was treated with 50 ml of water, organic layer was separated and once more extracted with 50 ml of water. Joined water extracts were acidified with hydrochloric acid to pH 1 and stirred at room temperature for 1 h. Then the reaction mixture was extracted with benzene (3×40 ml), the extract was treated with 0.3 ml of perchloric acid, and resulting mixture was refluxed with the Dean–Stark trap until complete separation of water. Toluene was removed at reduced pressure, and the residue was distilled in a vacuum. A fraction boiling in the range 73–79°C (1 mm Hg) was collected, yield 2.5 g.

e. The sample with bp 73–79°C (1 mm Hg), 5.0 g, obtained according to the prceeding procedure was refluxed with stirring with a solution of 3.4 g of potassium hydroxide in 25 ml of water for 3 h. The reaction mixture obtained was extracted with 10 ml of ether to remove nonhydrolized material, and then acidified to pH 1. Obtained oil was extracted 3 times with ether, the extract was dried over calcium chloride, ether was distilled off, and the residue was kept in a vacuum (1 mm Hg) for 1 h at room temperature to give 3.3 g of crude 2-isobutylfuran-4-carboxylic acid as a dark red viscous oil.

f. The sample obtained in the preceeding stage, 3.3 g, was dissolved in 15 ml of benzene, and 2.8 ml of thionyl chloride and 3 drops of DMF were added to it. The mixture obtained was refluxed with stirring for 4 h, benzene was removed at reduced pressure, and the residue was distilled in a vacuum to give 2.8 g of acyl chloride **VI**, bp 67°C (1 mm Hg). ^{1}H NMR spectrum, ($CDCl_3$),δ, ppm: 0.910 d (CH_3-isobutyl, J_{HH} 7 Hz), 1.992 m (CH-isobutyl); 2.440 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 6.210 s (H^3-furan); 7.720 s (H^5-furan).

2-Isobutyl-4-hydroxymethylfuran (VII). To a suspension of 0.7 g of lithium alumohydride in 60 ml of ether a solution of 2.8 g of the acyl chloride **VI** in 10 ml of ether was added dropwise with stirring at a rate providing slight boiling of reaction mixture. After the addition was complete the reaction mixture was stirred for 1 h and left overnight. On the next day it was treated with 5 ml of ethyl acetate and then with the ammonium chloride saturated solution until the phase separation. Clear etheral solution was decanted, dried over calcium chloride and distilled in a vacuum to give 1.5 g (65%) of alcohol **VII** with bp 62–63°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.86 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.83 m (CH- isobutyl, J_{HH} 7 Hz); 2.36 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 3.11 s (OH); 4.21 s (CH_2OH); 5.83 s (H^3-furan); 7.04 s (H^5-furan).

2-Isobutyl-4-chloromethylfuran (VIII). To a solution of compound **VII**, 1.5 g, in 15 ml of ether 0.8 ml of pyridine was added, and then a solution of 0.7 ml of thionyl chloride in 5 ml of ether was added dropwise with stirring at 17–25°C. Obtained mixture was stirred for 5 h at room temperature, pyridinium chloride was filtered off, ether was removed, and the residue was distilled in a vacuum to give 1.6 g (65%) of chloride **VIII** with bp 56°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.869 d (CH_3-isobutyl, J_{HH} 7 Hz), 1.910 m (CH-isobutyl), 2.400 distotred d

(CH_2-isobutyl, J_{HH} 7 Hz); 4.400 s (CH_2Cl); 6.012 s (H^3-furan); 7.281 s (H^5-furan).

2-Isobutyl-4-(diethoxyphosphorylmethyl)furan (IX). To a solution of sodium diethyl phosphite prepared from 0.2 g of sodium and 1.0 ml of diethyl hydrogen phosphite in 15 ml of benzene, 0.8 g of chloride **VIII** was added in one portion and obtained mixture was refluxed with stirring for 15 h. Sodium chloride was removed on a centrifuge, solvent was evaporated at reduced pressure, and the residue was distilled in a vacuum to give 0.9 g (71%) of phosphonate **IX** with bp 123–125°C (1 mm Hg), n_D^{20} 1.4550. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.869 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.241 t (CH_2-ethyl, J_{HH} 7 Hz); 1.993 m (CH-isobutyl, J_{HH} 7 Hz), 2.400 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 2.870 d (CH_2P, J_{HP} 21 Hz); 4.029 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 5.980 s (H^3-furan); 7.180 d (H^5-furan, J_{HP} 4 Hz). ^{31}P NMR spectrum ($CDCl_3$): δ_P 26.534 ppm.

2-Isobutyl-4-(diethoxyphosphorylmethyl)-5-(dimethylaminomethyl)furan hydrochloride (X). To a solution of 1.7 g of phosphonate **IX** in 15 ml of anhydrous acetonitrile 0.6 g of dimethyl(chloromethyl)amine was added in one portion and resulting mixture was refluxed with stirring at 80°C for 6 h. Then solvent was distilled off at reduced pressure and the residue was kept in a vacuum (1 mm) for 1 h at 25°C. The salt **X** was obtained as a very viscous syrup, yield 1.9 g (83%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.758 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.158 t (CH_3-ethyl, J_{HH} 7 Hz); 1.780 m (CH-isobutyl, J_{HH} 7 Hz); 2.307 d (CH_2-isobutyl, J_{HH} 7 Hz); 2.730 s (CH_3–N); 3.099 d (CH_2P, J_{HP} 20.6 Hz); 3.959 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 4.284 s (CH_2N-furan); 5.939 s (H^3-furan); 9.50 br.s (NH). ^{31}P NMR spectrum (DMSO-d_6): δ_P 25.967 ppm.

2-Isobutyl-4-(diethoxyphosphorylmethyl)-5-(dimethylaminomethyl)furan (Xa). To a solution of 1.9 g of the salt **X** in 25 ml of ethanol a solution of sodium ethylate obtained from 0.12 g of sodium and 10 ml of ethanol was added with stirring. After keeping for 20 min at room temperature the sodium chloride formed was removed on a centrifuge, solvent was evaporated at reduced pressure, and the residue was distilled in a vacuun to give 0.8 g (48%) of aminophosphonate **Xa**, bp 145°C (1 mm Hg). ^{1}H NMR spectrum($CDCl_3$), δ, ppm: 0.867 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.249 t (CH_3-ethyl, J_{HH} 7 Hz); 1.913 m (CH-isobutyl, J_{HH} 7 Hz); 2.200 s (CH_3–N); 2.406 distorted d (CH_2-isobutyl, J_{HH} 7 Hz); 2.882 d (CH_2P, J_{HP} 20.6 Hz); 3.368 s (CH_2N); 4.029 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 5.982 s (H-furan).

2-Isobutyl-3-chloroformylfuran (XI). *a*. To a solution of 25.8 g of ethyl isobutyrylacetate in 30 ml of pyridine 20 ml of 50% water solution of chloroacetaldehyde was added in one portion. The mixture obtained was stirred for 9 h at 45°C, poured into 200 ml of water, acidified with hydrochloric acid to pH 1, saturated with salt and extracted with toluene (3 × 80 ml). The extract was washed with water and dried over calcium chloride. Solvent was removed at reduced pressure and the residue was distilled in a vacuum to give 20.7 g of the fraction with bp 53–65°C (1 mm Hg), n_D^{20} 1.4430.

b. The sample obtained in the preceeding stage, 20.8 g, was refluxed with stirring for 4 h with a solution of 20 g of potassium hydroxide in a mixture of 20 ml of water and 30 ml of ethanol. Then ethanol was distilled off, the residue was diluted with 50 ml of water and extracted with petroleum ether. Water layer was acidified with hydrochloric acid to pH 1 and evolved product was extracted with ether. Etherial extract was dried over calcium chloride, ether was distilled off, and the residue was kept in a vacuum (1 mm) at 25°C for 1 h. Crude 1-isobutylfuran-3-carboxylic acid, 7.1 g, was obtained as a mixture of crystals and oil.

c. The compound prepared by the above procedure, 7.1 g, was dissolved in 30 ml of benzene and refluxed with 7 ml of thionyl chloride and 0.2 ml of DMF for 5 h. Distillation of reaction mixture in a vacuum gave 6.6 g of acyl chloride **XI**, bp 62°C (1 mm Hg), n_D^{20} 1.4860. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.927 d (CH_3-isobutyl, J_{HH} 7 Hz); 2.081 m (CH-isobutyl, J_{HH} 7 Hz); 2.841 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 6.748 s (H^4-furan); 7.278 s (H^5-furan).

2-Isobutyl-3-hydroxymethylfuran (XII). To a suspension of 1.7 g of lithium alumohydride in 50 ml of ether a solution of 8.4 g of acyl chloride in 15 ml of ether was added dropwise with stirring and cooling at a rate providing slight boiling of reaction mixture. After the addition was complete the reaction mixture was stirred for 3 h at room temperature and left overnight. On the next day the mixture obtained was treated with 10 ml of ethyl acetate and then with the saturated water solution of ammonium chloride until the phase separation. Organic phase was decanted and the gel-like mixture of inorganic compounds and water was stirred for 10 min with 30 ml of ether. Joined etheral solutions were dried over calcium chloride, ether was removed and the residue was distilled in a vacuum to give 4.3 g (62%) of the alcohol **XII**, bp 61–62°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.883 d (CH_3-isobutyl, J_{HH} 7 Hz);

1.940 m (CH-isobutyl, J_{HH} 7 Hz); 2.467 d (CH_2-isobutyl, J_{HH} 7 Hz); 4.417 s (CH_2OH), 6.350 s (H^4-furan), 7.246 s (H^5-furan).

2-Isobutyl-3-chloromethylfuran (XIII). To a solution of 4.3 g of alcohol **XII** and 2.5 ml of pyridine in 50 ml of ether a solution of 2 ml of thionyl chloride in 5 ml of ether was added dropwise with stirring at 15–20°C. The mixture obtained was kept for 3 h at room temperature, pyridine hydrochloride was filtered off, ether was removed at reduced pressure and the residue was distilled in a vacuum to give 3.1 g (64%) of chloride **XIII** with bp 45°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.930 d (CH_3-isobutyl, J_{HH} 7 Hz); 2.000 m (CH-isobutyl, J_{HH} 7 Hz); 2.505 d.d (CH_2-usobutyl, J_{HH} 7 Hz); 4.449 s (CH_2Cl); 6.374 s (H^4-furan); 7.274 s (H^5-furan).

2-Isobutyl-3-(diethoxyphosphorylmethyl)furan (XIV). To a solution of sodium diethyl phosphite prepared from 0.5 g of sodium and 3.2 ml of diethyl hydrogen phosphite in 40 ml of benzene 3.1 g of chloride **XIII** was added with stirring in one portion at 80°C. Reaction mixture was refluxed with stirring for 14 h, sodium chloride precipitate was removed on a centrifuge, benzene was distilled off at reduced pressure and the residue was distilled in a vacuum to give 3.5 g (72%) of phosphonate **XIV** with bp 118°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.863 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.214 t (CH_3-ethyl, J_{HH} 7 Hz); 1.922 m (CH-isobutyl); 2.389 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 2.806 d (CH_2P, J_{HP} 20 Hz); 3.994 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 6.305 s (H^4-furan); 7.191 s (H^5-furan). ^{31}P NMR spectrum ($CDCl_3$): δ_P 26.524 ppm.

2-Isobutyl-3-(diethoxyphosphorylmethyl)-5-(dimethylaminomethyl)furan (XV). To a solution of 3.2 g of phosphonate **XIV** in 50 ml of dry acetonitrile 1.1 g of dimethyl(chloromethyl)amine was added in one portion, and the mixture was refluxed with stirring at 80°C for 6 h. The homogenic solution formed was evaporated at reduced pressure and the resiue was kept in a vacuum (1 mm) for 3 h at 30°C to give 4.1 g (95%) of the salt **XV** as a glassy mass. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.810 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.192 t (CH_3-ethyl, J_{HH} 7 Hz); 1.926 m (CH-isobutyl); 2.380 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 2.679 s (CH_3–N); 2.739 d (CH_2P, J_{HP} 22 Hz); 3.978 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 4.127 s (CH_2N); 6.613 s (H^4-furan). ^{13}P NMR spectrum (DMSO-d_6): δ_P 25.592 ppm.

2-Isobutyl-3-(diethoxyphosphorylmethyl)-5-(dimethylaminomethyl)furan (XVa). To a solution of 4.1 g of the salt **XV** in 100 ml of ethanol a solution of sodium ethylate prepared from 0.26 g of sodium and 20 ml of ethanol was added with stirring. The mixture obtained was stirred for 20 min, sodium chloride was removed on a centrifuge, ethanol was distilled off at reduced pressure, and the residue was distilled in a vacuum to give 2.2 g (59%) of aminophosphonate **XVa** with bp 151–153°C (1 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.840 d (CH_3-isobutyl, J_{HH} 7 Hz); 1.217 t (CH_3-ethyl, J_{HH} 7 Hz); 1.935 m (CH-isobutyl); 2.100 s (CH_3–N); 2.360 d.d (CH_2-isobutyl, J_{HH} 7 Hz); 2.780 d (CH_2P, J_{HH} 20 Hz); 3.355 s (CH_2N); 3.395 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz); 6.136 s (H^4-furan).

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