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Specific Features of Reactions of Halomethyl Derivatives of 2-Isobutylfuran with Nucleophiles

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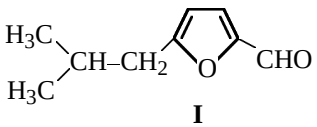
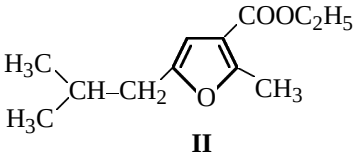
Abstract — 3,4- and 3,5-bis(chloromethyl)-2-isobutylfurans react with sodium diethyl phosphite by the Michaelis–Becker reaction scheme to form phosphonates whose yield significantly depends on the location of the halomethyl group in the furan ring. 3,4-Bis(chloromethyl)-2-isobutyl-5-methylfuran under analogous conditions gives a diphosphonate, while in 3,5-bis(chloromethyl)-2-isobutylfuran phosphorylation of the α-chloromethyl group competes with dehydrochlorination leading to a chloromethylated alkene, the second process being preferred. Further phosphorylation involves only one chloromethyl group of the alkene. Ethyl 5-(bromomethyl)-2-isobutylfuran-3-carboxylate reacts with sodium acetate to give a substitution product, while its isomer with the reverse location of the substituents eliminates hydrogen bromide exclusively. In the latter case, the acetate is formed only as a minor product.

We previously studied some reactions of haloalkyl derivatives of 2-isobutylfuran with electron-acceptor substituents in the ring. It was established that the substitution of halogen under the action of a phosphorus nucleophile may be accompanied by transfer of the reaction center [1] and also by elimination of hydrogen halide.

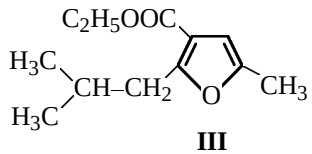
In the present work we developed a procedure for preparing chloromethyl derivatives of 2-isobutylfuran, containing no electron-acceptor group that imparts thermal stability to these compounds, and studied their phosphorylation. As starting materials we used the fairly readily available aldehyde **I** and ethyl furancarboxylates **II** and **III**.



I



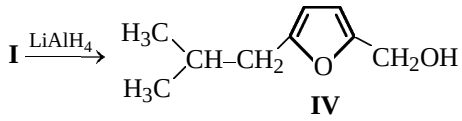
II



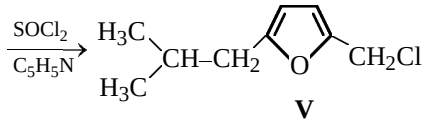
III

In the first stage of this work we proposed to reduce them to corresponding alcohols, to substitute the hydroxy group by chlorine, and to involve the resulting compounds in the Michaelis–Becker reaction.

Aldehyde **I** was reduced with excess lithium aluminum hydride in ether. Alcohol **IV** proved to be rather stable and easily purified product. It was treated with thionyl chloride in ether in the presence of pyridine at 10°C to give chloride **V**.



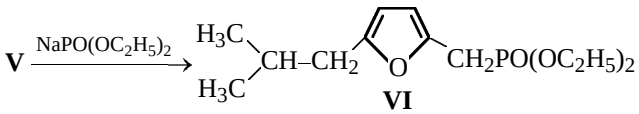
IV



V

The latter compound can be distilled in a vacuum [bp 58°C (1 mm Hg)], but in the free state it darkens in air over the course of 10–15 min. Therefore, distilled chloride **V** was handled as a benzene solution in a refrigerator for no more than 2 h.

Phosphorylation of product **V** was carried out with sodium diethylphosphite in benzene at 80°C for 7 h. Phosphonate **VII** was isolated by vacuum distillation in 42% yield.



VI

The structure of compound **VII** was confirmed by

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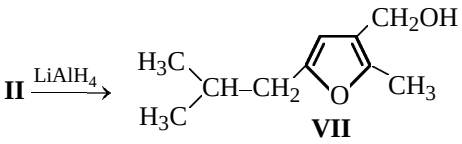
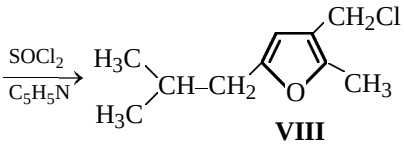
means of ^{1}H NMR spectroscopy. It is interesting to note that we observed long-range coupling between the phosphorus atom and the H^3 ring proton (J_{HP} 2 Hz).

Ester **II** is easily reduced with lithium aluminum hydride in ether to give alcohol **VII**. The latter is stable and easily purified by vacuum distillation.



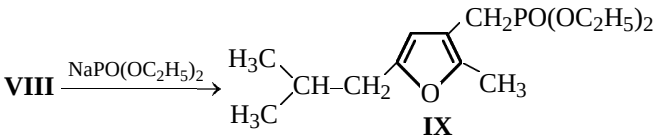
VII



VIII

Under the action of thionyl chloride in ether in the presence of pyridine it forms chloride **VIII** that is a fairly stable compound and can be distilled in a vacuum [bp 70°C (1 mm)]. The yield of chloride **VIII** is 59%, while its analog **V** was obtained in 46% yield. Free chloride **VIII** gradually darkens in air and, therefore, was not handled for a long time.

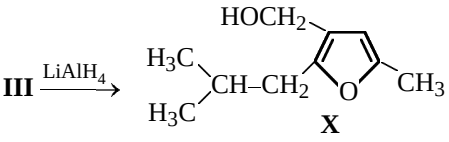
Phosphorylation of compound **VIII** with sodium diethyl phosphite was carried out in benzene at 80°C for 14 h. Phosphonate **IX** was obtained in 73% yield.



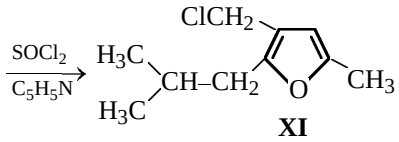
IX

The structure of product **IX** was confirmed by ^{1}H NMR spectroscopy. No long-range coupling constant between the phosphorus atom and the ring proton was observed.

Ester **III** was reduced with lithium aluminum hydride into stable alcohol **X**.



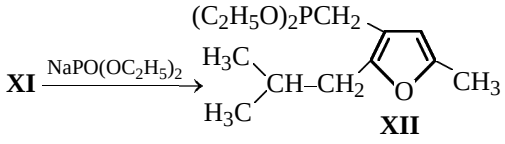
X



XI

Alcohol **X** was converted into chloride **XI** by treatment with thionyl chloride in ether in the presence of pyridine. The yield of chloride **XI** is 71%. This product is relatively stable and can be distilled in a vacuum [bp 64–66°C (1 mm Hg)], but it darkens in air.

Compound **XI** was phosphorylated with sodium diethyl phosphite at 80°C in benzene for 16 h. The yield of phosphonate **XII** is 47%. Its structure was confirmed by ^{1}H NMR spectroscopy. No coupling between the phosphorus atom and the furan ring proton was observed.

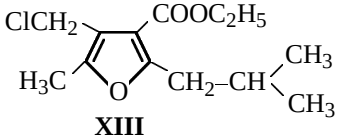


XII

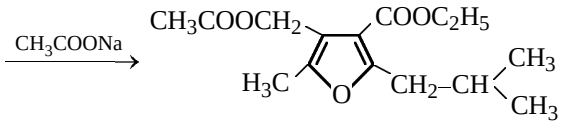
Hence, the β-chloromethyl derivatives of 2-isobutylfuran are more thermally stable than the α-chloromethyl product. Shielding of the β-chloromethyl group with the neighboring substituent increases thermal stability, which is confirmed by the yields and properties of chlorides **VIII** and **XI**. The yield of phosphonate in the Michaelis–Becker reaction also depends on the stability of the starting substrate and steric hindrances created by the neighboring substituents. The shielding effect of the isobutyl group decreases the yield of phosphonate 1.6-fold.

In the second stage of this work we tried to develop a synthetic approach to bis(halomethyl) derivatives of 2-isobutylfuran. It was proposed to compare the chemical properties of halomethyl groups in the α- and β-positions of the ring and to find out conditions under which elimination of hydrogen halide becomes possible.

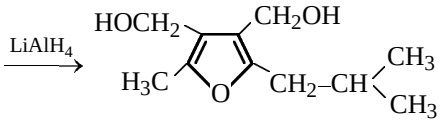
Reaction of chloromethyl derivative **XIII** with sodium acetate gave acetate **XIV**. Reduction of the latter with lithium alumohydride in ether afforded diol **XV**.



XIII



XIV

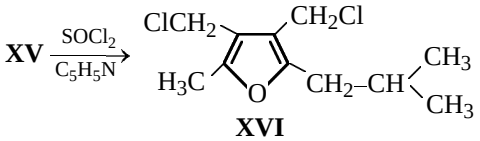


XV

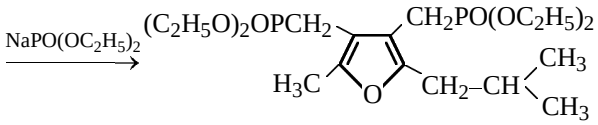
The latter compound is a syrup undistillable in a vacuum and gradually darkening in air. The hydroxy-

methyl groups in diol **XV** give one signal (δ 4.41 ppm) in the ^{1}H NMR spectrum.

Treatment of diol **XV** with thonyl chloride in ether in the presence of pyridine gives chloride **XVI** that can be distilled in a vacuum but darkens in air. The yield of product **XVI** is 62%.



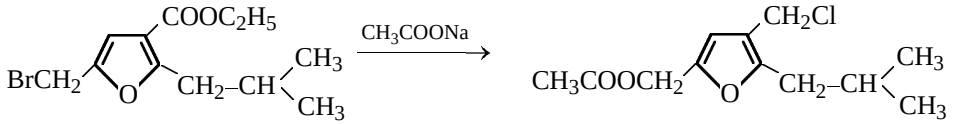
XVI



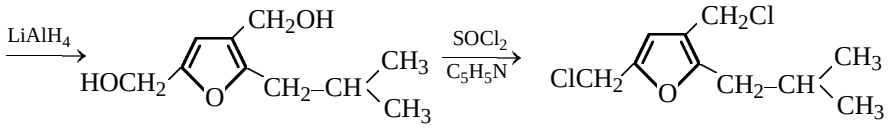
XVII

This compound was reacted with two mol of sodium diethyl phosphite in benzene. The process was carried out at 80°C for 15 h. Diphosphonate **XVII** was isolated by vacuum distillation in 65% yield. The ^{1}H NMR spectrum of the product contained two doublets of equal intensity at δ 2.90 and 2.92 ppm (J_{HP} 20 Hz). We failed to establish whether these signals relate to two different CH_2P groups in the furan ring or to two different conformers of diphosphonate **XVII**. The long-range J_{HP} constants for the methyl group and the isobutyl methylene group are different (3 and 2 Hz, respectively).

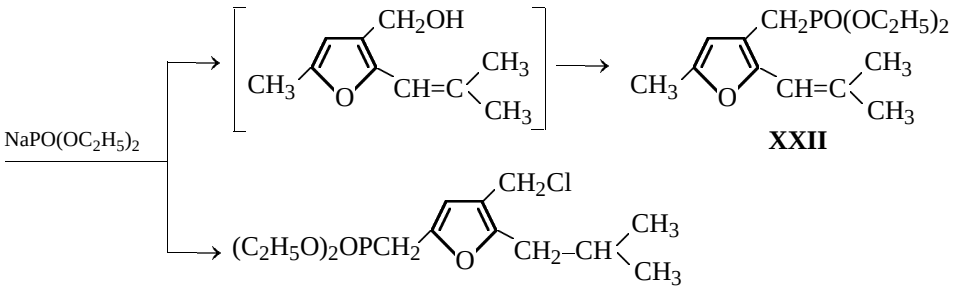
Reaction of unstable bromide **XVIII** with sodium acetate gives acetate **XIX** in low yield. This product was reduced with lithium alumohydride to unstable diol **XX** that was immediately treated with thionyl chloride in ether in the presence of pyridine. The resulting dichloride after removal of pyridine hydrochloride was immediately subjected to fast vacuum distillation to obtain compound **XXI** in low yield [bp 89–90°C (1 mm)]. This compound was immediately reacted with two mol of sodium diethyl phosphite. The process was carried out at 80°C for 10 h. Vacuum distillation of the reaction mixture gave a fraction with bp 135°C (1 mm Hg). Its ^{1}H NMR spectrum contained two sets of signals. The main product was characterized by two singlets at δ 1.79 and 1.92 ppm, a signal at δ 2.19 ppm from the methyl group at the furan ring, a doublet at δ 2.60 ppm (J_{HP} 21 Hz), a broadened singlet at δ 5.76 ppm (CH=), and a signal of the furan ring proton at δ 5.98 ppm. The ^{1}H NMR spectrum of the minor product contained signals of the isobutyl group, a signal of the CH_2P fragment (δ 2.93 ppm, J_{HP} 20 Hz), a signal of the CH_2Cl group (singlet at δ 4.30 ppm), and a doublet of the furan ring proton (δ 6.09 ppm, J_{HP} 3 Hz). According to the spectral data, the ratio of the reaction products was estimated at 2.2 : 1. The process can be described by the following scheme.



XVIII **XIX**



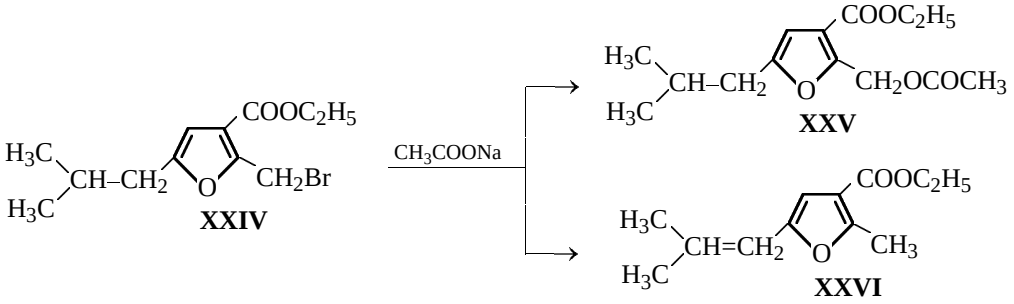
XX **XXI**



XXII **XXIII**

The first stage of the reaction of dichloride **XXI** with sodium diethyl phosphite proceeds in two directions. The main pathway is dehydrohalogenation accompanied by prototropic isomerization to form a double bond stabilized by two methyl groups. The competing Michaelis–Becker reaction provides phosphonate **XXIII**. The second stage of the main reaction involves chlorine substitution in the β-chloromethyl group to give phosphorylated furylalkene **XXII**. No bisphosphonate was detected among the reaction products, which points to a low reactivity of the chlorometyl group in compound **XXIII**.

The discovery of such unusual chemical properties of dichloride **XXI** stimulated us to develop a procedure for preparing its isomer with the reverse location of the substituents, starting from bromide **XXIV**. It was previously shown that this compound reacts with trimethyl phosphite to form substitution products, that is phosphonates [1]. The chemical behavior of this compound in reactions with other nucleophiles has not been studied. To substitute bromine with the acetoxy group we reacted bromide **XXIV** with sodium acetate by the above-mentioned procedure. It occured that under these conditions the main reaction pathway becomes dehydrobromination, rather than bromine substitution. As a result, we obtained a 3.1 : 1 mixture of alkene **XXV** and acetate **XXVI** (by ^{1}H NMR data). We failed to isolate individual compounds from this mixture by vacuum distillation.



Hence, the 3,4-bis(chloromethyl) derivative of 2-isobutylfuran enters nucleophilic substitution only. Contrary to that, compounds containing an α-halomethyl group under the action of nucleophiles are capable of eliminating hydrogen halide with transfer of the reaction center to form a stable dimethylvinyl group. Electron-acceptor substituents in the nearest position of the furan ring facilitate this process.

Analysis of the ^{1}H NMR spectra of the obtained phosphonates shows that coupling between the phosphorus atom and the proton in the ring or in the α -position of the side chain is transmitted through 4 or 5 bonds and involves the C^2–C^3 bond of the furan ring only. This agrees with the previously mentioned anisotropism of substituent effect transmittance in the furan series [3].

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on Tesla BS-487C (80 MHz) and Tesla BS-497C (100 MHz) spectrometers in CCl_4 or $CDCl_3$ against internal HMDS. The phosphorus chemical shifts were calculated from INDOR spectra.

5-Isobutylfurfuryl alcohol (IV). To a suspension of 1.0 g of lithium aluminum hydride in 40 ml of ether, a solution of 4.4 g of 5-isobutyl-2-furaldehyde (**I**) was added dropwise with stirring at a rate providing slight boiling of the reaction mixture. After all aldehyde had been added, the reaction mixture was stirred for 2 h and left overnight. On the next day it was treated with 5 ml of ethyl acetate and then with saturated solution of ammonium chloride until the organic and inorganic phase separated. The ethereal solution was decanted, dried over $CaCl_2$, and distilled in a vacuum to obtain 3.5 g of alcohol **IV**,bp 78°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.82 d (isobutyl CH_3, J_{HH} 7 Hz), 1.92 m (isobutyl CH), 2.30 distorted d (isobutyl CH_2, J_{HH} 7 Hz), 3.74 s (OH), 4.32 s (furan CH_2O). 5.77 d (furan H^4, J_{HH} 2 Hz), 5.92 d (furan H^3, J_{HH} 2 Hz).

2-(Chloromethyl)-5-isobutylfuran (V). To a solution of 9.5 g of alcohol **IV** and 2 ml of pyridine in 30 ml of anhydrous ether, a solution of 1.2 ml of thionyl chloride in 10 ml of ether was added dropwise with stirring at 5–10°C. The reaction mixture was kept for 4 h at room temperature, pyridine hydrochloride was filtered off, the filtrate was evaporated at

reduced pressure, and the residue was distilled in a vacuum to give 1.8 g (46%) of compound **V**, bp 58°C (1 mm Hg). The product was immediately involved in further transformations.

2-(Diethoxyphosphorylmethyl)-5-isobutylfuran (VI). To a solution of sodium diethyl phosphite prepared from 0.24 g of sodium and 2 ml of diethyl hydrogen phosphite in 20 ml of benzene, a solution of 1.8 g of chloride **V** in 3 ml of benzene was added dropwise at 80°C. No heat evolution was observed. The reaction mixture was refluxed with stirring for 8 h, sodium chloride was removed on a centrifuge, and the residue was distilled in a vacuum to give 1.1 g (42%) of phosphonate **VI**, bp 132–134°C (1.5 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.83 d (isobutyl CH_3, J_{HH} 7 Hz), 1.17 t (ethyl CH_3, J_{HH} 7 Hz), 1.90 m (isobutyl CH), 2.34 d (isobutyl CH_2, J_{HH} 7 Hz), 2.96 d (CH_2P, J_{HP} 21 Hz), 3.95 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz), 5.75 d (furan H^4, J_{HH} 3 Hz), 5.97 d.d (furan H^3, J_{HH} 3 Hz, J_{HP} 2 Hz), δ_P 20.0 ppm.

3-(Hydroxymethyl)-5-isobutyl-2-methylfuran (VII). To a suspension of 0.8 g of lithium aluminum hydride in 50 ml of ether, a solution of 4.5 g of furan **II** in 10 ml of ether was added dropwise with stirring at a rate providing slight boiling of reaction mixture. After all furan **II** had been added, the reaction mixture was stirred for 2 h and left overnight. On the next day it was treated with 5 ml of ethyl acetate and then with a saturated solution of ammonium chloride until phase separation. The ethereal solution was decanted and dried over $CaCl_2$. Ether was removed at reduced pressure, and the residue was distilled in a vacuum to give 2.3 g of alcohol **VII**, bp 78°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.82 d (isobutyl CH_3, J_{HH} 7 Hz), 1.67 m (isobutyl CH), 2.07 d (furan CH_3), 2.17 distorted d (isobutyl CH_2, J_{HH} 7 Hz), 4.07 br.s (CH_2–furan + OH), 5.67 s (furan H^4).

3-(Chloromethyl)-5-isobutyl-2-methylfuran (VIII). To a solution of 2.3 g of alcohol **VII** and 1.2 ml of pyridine in 25 ml of ether, a solution of 1 ml of thionyl chloride in 6 ml of ether was added dropwise with stirring at 5–10°C. The reaction mixture was stirred for 4 h at room temperature, pyridine hydrochloride was filtered off, and the filtrate was distilled in a vacuum to give 1.5 g (59%) of chloride **VIII**, bp 70°C (1 mm Hg). The product was immediately involved in further transformations.

3-(Diethoxyphosphorylmethyl)-5-isobutyl-2-methylfuran (IX). To a solution of sodium diethyl phosphite prepared from 0.2 g of sodium and 1.5 ml of diethyl hydrogen phosphite in 20 ml of benzene, 1.5 g of chloride **VIII** was added with stirring. The reaction mixture was refluxed for 14 h, sodium chloride was removed on a centrifuge, benzene was evaporated at reduced pressure, and the residue was distilled in a vacuum to give 1.7 g (73%) of phosphonate **IX**, bp 121–124°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.84 d (isobutyl CH_3, J_{HH} 7 Hz); 1.16 t (ethyl CH_3, J_{HH} 7 Hz); 1.82 m (isobutyl CH), 2.12 s (furan CH_3), 2.26 distorted d (isobutyl CH_2, J_{HH} 7 Hz); 2.58 d (CH_2P, J_{HP} 21 Hz); 3.86 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz), 5.78 s (furan H^4), δ_P 23.5 ppm.

4-(Hydroxymethyl)-5-isobutyl-2-methylfuran (X). To a suspension of 0.8 g of lithium aluminum hydride in 50 ml of dry ether, a solution of 4.5 g of furan **III** in 20 ml of of absolute ether was added dropwise at a rate providing slight boiling of reaction mixture. After the addition had been complete, the reaction mixture was stirred for 3 h and left overnight. On the next day it was treated with 10 ml of ethyl acetate, after which a solution of ammonium chloride was added dropwise until phase separation. The organic phase was decanted, dried over calcium chloride, the solvent was removed at reduced pressure, and the residue was distilled in a vacuum to give 2.8 g of alcohol **X**, bp 82°C (2 mm). ^{1}H NMR spectrum, δ, ppm: 0.84 d (isobutyl CH_3, J_{HH} 7 Hz), 1.74 m (isobutyl CH), 2.14 s (furan CH_3), 2.29 m (isobutyl CH_2), 3.26 s (OH), 4.16 s (CH_2OH), 5.76 s (furan H^3).

4-(Diethoxyphosphorylmethyl)-5-isobutyl-5-methylfuran (XII). *a*. To a solution of 2.8 g of alcohol **X** and 1.4 ml of pyridine in 20 ml of ether, a solution of 1.2 ml of thionyl chloride in 5 ml of dry ether was added dropwise with stirring at 5–10°C. After the addition had been complete, the reaction mixture was kept for 3 h at 15–20°C, pyridine hydrochloride was filtered off, ether was removed at reduced pressure, and the residue was distilled in a vacuum to give 2.2 g (71%) of chloride **XI**, bp 64–66°C (1 mm Hg). The product was immediately involved in further transformations.

b. To a solution of sodium diethyl phosphite prepared from 0.3 g of sodium and 2 ml of diethyl hydrogen phosphite in 20 ml of benzene, 2.2 g of chloride **XI** was added in one portion. The resulting mixture was refluxed with stirring at 80°C for 16 h. Sodium chloride was removed on a centrifuge, the solvent was distilled off at reduced pressure, and the residue was distilled in a vacuum to give 1.6 g (47%) of phosphonate **XII**, bp 133°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.82 d (isobutyl CH_3, J_{HH} 7 Hz), 1.24 t (CH_3-ethyl, J_{HH} 7 Hz), 1.84 m (isobutyl CH), 2.10 s (CH_3-furan), 2.26 d.d (isobutyl CH_2, J_{HH} 7 Hz, J_{HP} 2 Hz), 2.54 d (CH_2P, J_{HP} 21 Hz), 3.89 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz), 5.76 s (furan H^3), δ_P 23.7 ppm.

Ethyl 4-(acetoxymethyl)-2-isobutyl-5-methyl-

furan-3-carboxylate (XIV). To a solution of 3.9 g of ethyl 4-(chloromethyl)-2-isobutyl-5-methylfuran-3-carboxylate **XIII** in 30 ml of a mixture of acetic acid and acetic anhydride boiling in the range 130–132°C, 2.5 g of sodium acetate was added. The resulting solution was refluxed with stirring for 16 h and then poured in 100 ml of water and extracted with methylene chloride. The extract was dried over calcium chloride, methylene chloride was distilled off, and the residue was distilled in a vacuum to give 2.9 g of acetate with bp 130–132°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.85 d (isobutyl CH_3, J_{HH} 7 Hz), 1.27 t (ethyl CH_3, J_{HH} 7 Hz), 1.90 br.s (CH_3COO + isobutyl CH), 2.25 s (furan CH_3), 2.70 d (isobutyl CH_2, J_{HH} 7 Hz), 4.15 q (CH_2OOC, J_{HH} 7 Hz), 4.90 s (furan CH_2O).

3,4-Bis(hydroxymethyl)-2-isobutyl-5-methylfuran (XV). To a suspension of 0.8 g of lithium aluminum hydride in 50 ml of anhydrous ether, a solution of 2.9 g of acetate **XIV** in 10 ml of anhydrous ether was added dropwise with stirring at a rate providing slight boiling of the reaction mixture, after which it stirred for 3 h at room temperature and left overnight. On the next day the reaction mixture was treated with 10 ml of ethyl acetate and then with a saturated solution of ammonium chloride until phase separation. The organic phase was decanted, dried over calcium chloride, ether was distilled off, and the residue was kept for 2 h in a vacuum (1 mm Hg) at room temperature to give 1.9 g of compound **XV** as a yellowish syrup. ^{1}H NMR spectrum, δ, ppm: 0.87 d (CH_3-isobutyl, J_{HH} 7 Hz), 1.87 m (isobutyl CH), 2.19 s (CH_3-furan), 2.39 d (isobutyl CH_2, J_{HH} 7 Hz), 3.65 br.s (OH), 4.41 s (CH_2O).

3,4-Bis(diethoxyphosphorylmethyl)-5-methyl-2-isobutylfuran (XVII). *a*. To a solution of 1.9 g of diol **XV** and 1.4 ml of pyridine in 25 ml of ether, a solution of 1.4 ml of thionyl chloride in 5 ml of ether was added dropwise with stirring at 5–10°C. The reaction mixture was stirred for 3 h at room temperature, pyridine hydrochloride was filtered off, the filtrate was evaporated, and the residue was distilled in a vacuum to give 1.4 g of chloride **XVI**, bp 87°C (1 mm Hg). The product was used immediately after distillation.

b. To a solution of sodium diethyl phosphite prepared from 0.3 g of sodium, and 2.9 ml of diethyl hydrogen phosphite in 25 ml of benzene, 1.4 g of chloride **XVI** was added in one portion. The resulting mixture was boiled with stirring for 11 h, sodium chloride was removed on a centrifuge, benzene was evaporated, and the residue distilled in a vacuum to give 1.7 g (65%) of phosphonate **XVII**, bp 194–196°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 0.85 d (isobutyl CH_3, J_{HH} 7 Hz), 1.25 m (ethyl CH_3), 1.89 m (isobutyl CH), 2.12 d (furan CH_3, J_{HP} 3 Hz), 2.31 d.d (isobutyl CH_2, J_{HH} 7 Hz, J_{HP} 2 Hz), 2.90 d and 2.92 d (CH_2P, J_{HP} 2 Hz), 3.87 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz). δ_P 24.6 ppm.

Ethyl 5-(acetoxymethyl)2-isobutylfuran-3-carboxylate (XIX). A mixture of 11.3 g of crude bromide **XVIII**, 3.4 g of sodium acetate, and 50 ml of a mixture of acetic anhydride and acetic acid boiling in the range 130–132°C was refluxed with stirring at for 14 h and poured into 150 ml of water. The solution was extracted with methylene chloride, solvent was distilled off, and the residue was distilled in a vacuum to give 1.3 g of a product boiling at 82–84°C (1 mm Hg) and comprising mainly ester **III** and 2.5 g of target product **XIX** [bp 128–130°C (1 mm Hg)]. ^{1}H NMR spectrum, δ, ppm: 0.87 d (isobutyl CH_3, J_{HH} 7 Hz), 1.27 t (ethyl CH_3, J_{HH} 7 Hz), 2.02 s (CH_3COO), 1.99–2.03 m (isobutyl CH), 2.80 d (isobutyl CH_2, J_{HH} 7 Hz), 4.20 q (CH_2OOC, J_{HH} 7 Hz), 4.93 s (furan CH_2O), 6.61 s (furan H^4).

Reaction of bis(chloromethyl)furan XXI with sodium diethyl phosphite. *a*. To a suspension of 0.7 g of lithium aluminum hydride in 40 ml of anhydrous ether, a solution of 2.5 g of acetate **XIX** in 15 ml of anhydrous ether was added at a rate providing slight boiling of the reaction mixture. After the addition had been complete, the mixture was stirred for 3 h and left overnight. On the next day it was treated with 10 ml of ethyl acetate and then with a saturated solution of ammonium chloride until phase separation. The organic phase was decanted, dried over calcium chloride, the solvent was removed, and the residue was kept in a vacuum for 2 h (20°C, 1 mm Hg) to give a yellow syrup quickly darkening in air. It was immediately used in further transformations. Yield of diol **XX** 1.4 g.

b. To a solution of 1.4 g of diol **XX** in 30 ml of anhydrous ether, 1.3 ml of pyridine was added, and then a solution of 1.1 ml of thionyl chloride in 10 ml of ether was added dropwise with stirring at 10°C. The reaction mixture was kept for 3 h at room temperature, pyridine hydrochloride was filtered off, ether was distilled off at reduced pressure, and the residue was distilled in a vacuum to give 0.4 g of dichloride **XXI**, bp 89–90°C (1 mm Hg). The product was immediately used in further transformations.

c. To a solution of sodium diethyl phosphite prepared from 0.09 g of sodium and 0.7 ml of diethyl hydrogen phosphite in 10 ml of benzene, a solution of 0.4 g of dichloride **XXI** in 5 ml of benzene was added in one portion. The mixture was refluxed for

9 h, sodium chloride was removed on a centrifuge, benzene was removed at reduced pressure, and the residue was distilled in a vacuum to give 0.3 g of a product boiling at 135°C (1 mm Hg) and comprising phosphonates **XXII** and **XXIII** in a 2.2 : 1 ratio. ^{1}H NMR spectrum, δ, ppm: phosphonate **XXII**: 1.17 t (ethyl CH_3, J_{HH} 7 Hz), 1.79 br.s (*trans*-CH_3), 1.92 s (*cis*-CH_3) 2.19 s (furan CH_3), 2.60 d (CH_2P, J_{HP} 21 Hz), 3.87 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz), 5.76 br.s (HC=), 5.98 s (furan H), δ_P 23.3 ppm; phosphonate **XXIII**: 0.83 d (isobutyl CH_3, J_{HH} 7 Hz), 1.17 t (ethyl CH_3, J_{HH} 7 Hz), 2.31 d (isobutyl CH_2, J_{HH} 7 Hz), 2.93 d (CH_2P–furan, J_{HP} 20 Hz), 3.87 m (CH_2OP, J_{HH} 7 Hz, J_{HP} 11 Hz), 4.30 s (CH_2Cl), 6.09 d (furan H^3, J_{HP} 3 Hz), δ_P 20.5 ppm.

Reaction of ethyl 2-(bromomethyl)-5-isobutylfuran-3-carboxylate with sodium acetate. A mixture of bromide **XXIV** prepared from 10.5 g of ether **II** and 9.4 g of *N*-bromosuccinimide, 10 g of sodium acetate and 60 ml of acetic acid was stirred at 110–120°C for 19 h. The reaction mixture was poured into water, the product was extracted with methylene chloride, dried over sodium sulfate, methylene chloride was removed, and the residue was distilled in a vacuum to give 4.7 g of a fraction boiling at 147–152°C (5 mm Hg) and comprising alkene **XXV** and acetate **XXVI** in a 3.1 : 1 ratio. ^{1}H NMR spectrum, δ, ppm: alkene **XXV**: 1.33 t (ethyl CH_3, J_{HH} 7 Hz), 1.91 s (*trans*-CH_3), 1.98 s (*cis*-CH_3), 2.56 s (furan CH_3), 4.26 q (ethyl CH_2–O, J_{HH} 7 Hz), 5.96 s (HC=), 6.31 s (furan H^4); acetate **XXVI**: 0.96 d (isopropyl CH_3, J_{HH} 7 Hz), 1.33 t (ethyl CH_3, J_{HH} 7 Hz), 2.50 m (isobutyl CH_2 + furan CH_3, overlapping); 4.26 q (ethyl CH_2–O, J_{HH} 7 Hz), 5.28 s (CH_2O–furan), 6.31 s (furan H^4).

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