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Synthesis and Selected Reactions of 2(3)-Furoyl Phosphonates Functionalyzed at the Neighbor Position of the Furan Ring

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Abstract—Reactions of 2-and 3-furoyl chlorides having chloromethyl or butylthiomethyl group in the adjacent position of the furan ring as well as of analogous *N*-morpholinomethylfuroyl chloride hydrochlorides with triethyl phosphite have been studied. The synthesized chloromethylfuroyl phosphonates have given the corresponding products of nucleophilic substitution in the reactions with sodium azide and potassium thiocyanate in the case of 4-chloromethyl-3-furoyl phosphonate. In the reaction of 3-chloromethyl-2-furoyl phosphonate with sodium azide, cleavage of the P–C bond takes place simultaneously with nucleophilic substitution. Potassium thiocyanate forms 3-thiocyanatomethyl-2-furoyl phosphonate in the reaction with this substance. The synthesized stable furoyl phosphonates enter the Wittig reaction with resonance-stabilized phosphoranes to give phosphorylated furylalkenes. If these compounds carry a chloromethyl group in the furan ring, they react with sodium azide and potassium thiocyanate to give the corresponding products of nucleophilic substitution. Analogously, aminomethyl derivatives have been obtained in the reaction with morpholine at room temperature.

Keywords: furoyl chlorides, Arbuzov reaction, furoyl phosphonates, Wittig reaction, nucleophilic substitution

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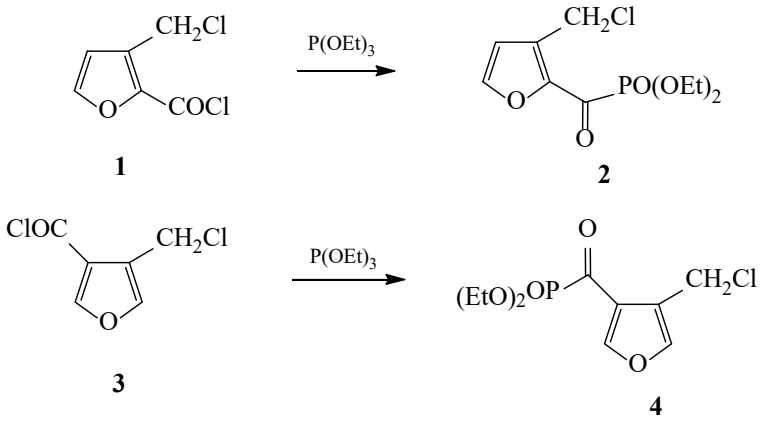
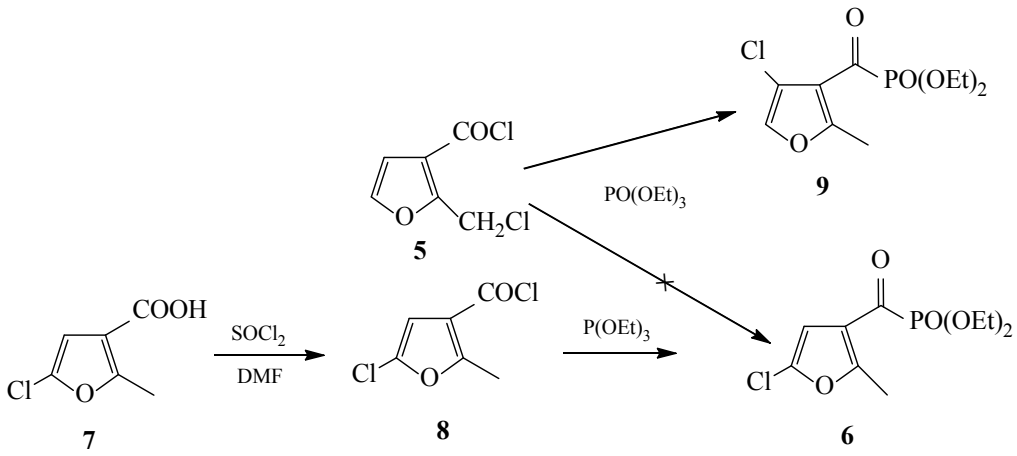
We have recently investigated the methods of synthesis and chemical properties of furoyl phosphonates bearing a functional group remote from the phosphorus-containing substituent [1, 2]. Extending those studies, we turned to furoyl phosphonates with a substituent adjacent to the acyl phosphonate group. This study aimed to elucidate the influence of the neighbor substituent on the course of the Arbuzov reaction and to investigate nucleophilic substitution reactions in such furoyl phosphonates when the adjacent substituent was a chloromethyl group. It was also proposed to study the features of the Wittig reaction with resonance-stabilized phosphoranes for the above-mentioned furoyl phosphonates, as well as the nucleophilic substitution reactions of phosphorylated chloromethylfurylalkenes formed via the Wittig process.

Acyl chlorides **1**, **3**, and **5** were chosen as the starting compounds for the preparation of chloromethylfuroyl phosphonates. The reaction was carried out at the acid

Scheme 1.



Scheme 2.



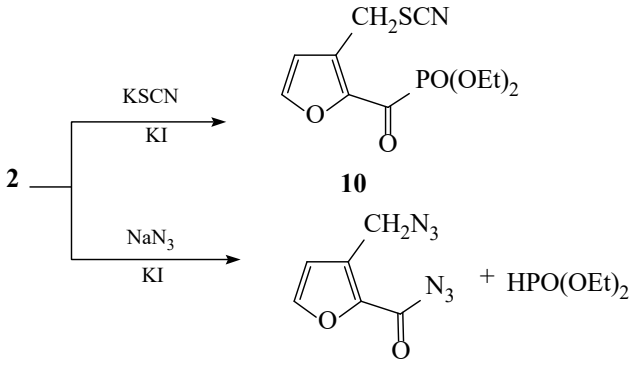
chloride : triethyl phosphite molar ratio of 1 : 1.05 in benzene at room temperature. In the case of acid chlorides **1** and **3**, the corresponding furoyl phosphonates **2**, **4** were obtained in 96 and 98% yield, respectively (Scheme 1). The ^{1}H NMR spectrum of compound **2** contained two signals of chloromethyl group at 4.76 and 4.82 ppm. The furan ring proton H^4 was also revealed by two signals at 6.78 ppm (br. s) and 6.80 ppm (d, J_{HH} = 2.6 Hz). The only broadened signal of the H^5 furan ring proton was located at 7.66 ppm.

The reaction of 2-chloromethyl-3-furoyl chloride **5** under those conditions occurred differently. A stable substance with bp 144–146°C (1 mmHg) was isolated from the reaction mixture. Chemical shift of phosphorus in that substance was –2.33 ppm, characteristic of acyl phosphonates. Its ^{1}H NMR spectrum contained a signal of the methyl group protons at 2.59 ppm, and the signal of the furan ring proton was located at 7.06 ppm. The ^{13}C NMR spectrum contained the signals of the furan ring carbon atom nuclei at 121.16 (C^4), 122.63 (C^3, $^2J_{PC}$ = 68.7 Hz), 142.76(C^5), and 162.54 ppm (C^2, $^3J_{PC}$ = 14.5 Hz). The signal of the carbonyl group carbon atom nucleus was found at 193.12 ppm ($^1J_{PC}$ = 184.1 Hz). High-resolution mass spectrometry data showed that the molecule contained one chlorine atom. We suggested that the formed substance was 2-methyl-5-chloro-3-furoyl phosphonate **6** and carried out its counter synthesis starting from the reported 2-methyl-5-chloro-3-furoic acid **7** [3]. Its refluxing in benzene with thionyl chloride in the presence of DMF led to the formation of labile acid chloride **8** with bp 69°C (1 mmHg) in 24% yield (Scheme 2). The NMR spectra contained the signal of the furan ring proton at 6.56 ppm, and the signals of the furan ring carbon atoms nuclei were located at 108.34 (C^4), 120.25 (C^3), 135.88 (C^5), and 160.82 ppm (C^2).

The Arbuzov reaction of acid chloride **8** with triethyl phosphite was carried out at room temperature in benzene and led to the formation of furoyl phosphonate **6** in 98% yield (Scheme 2). It turned out to be labile and could not be distilled in vacuum. While handling, it was split with air moisture with liberation of diethyl hydrogen phosphite and acid **7**. The NMR spectra contained a signal of phosphorus nucleus at –2.19 ppm, a broadened signal of the methyl group was observed at 2.55 ppm, and the signal of the furan ring proton H^3 was found at 6.95 ppm. The signals of the furan ring carbon atoms nuclei were located at 107.16 (C^4, $^3J_{PC}$ = 2.0 Hz), 122.06 (C^3, $^2J_{PC}$ = 68.8 Hz), 135.57 (C^5), and 160.36 ppm (C^2, $^3J_{PC}$ = 14.5 Hz). The signal of the carbonyl group carbon atom was found at 193.24 ppm ($^1J_{PC}$ 184.2 Hz). Hence, stability and spectral properties of the obtained compounds were clearly different. That is why the substance obtained from acid chloride **5** via the Arbuzov reaction was considered to be 2-methyl-4-chloro-3-furoyl phosphonate.

Furoyl phosphonates **2** and **4** were involved in nucleophilic substitution reactions with potassium thiocyanate and sodium azide. The reaction of compound **2** with potassium thiocyanate was carried out in acetonitrile at room temperature (Scheme 3). The thiocyanate : phosphonate molar ratio was 2 : 1, potassium iodide was used as catalyst (10 mol %). Thiocyanate **10** was the reaction product (83% yield). The formation of the C–S bond was confirmed by means of NMR spectroscopy. The signal of protons of the H_2CS fragment was located at 4.33 ppm,

Scheme 3.



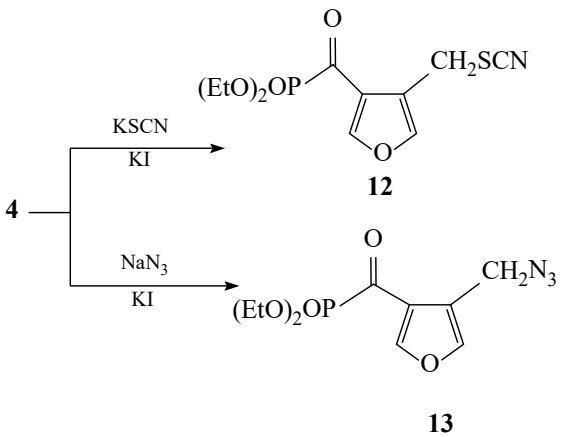
and the signal of the corresponding carbon atom was observed at 28.27 ppm. The signal of the CN carbon atom was revealed at 111.68 ppm.

The reaction with sodium azide was carried out similarly, but the process was complete in a week because of low solubility of azide in acetone (Scheme 3). It turned out that the cleavage of the P–C bond with the elimination of sodium diethyl phosphite occurred, along with substitution of halogen. Sodium diethyl phosphite reacted with air moisture to give diethyl hydrogen phosphite (PH, 6.79 ppm, $^1J_{PH}$ = 692.8 Hz, δ_P 7.33 ppm). The formation of the azidomethyl group was confirmed by the presence of the signal of the methylene group protons at 4.64 ppm and the signal of the corresponding carbon atom at 45.60 ppm. Chemical shifts of the azido group nitrogen atoms were evaluated by means of NH-correlations, N^1 249 and N^2 73 ppm, in agreement with the reference data [4]. The IR spectrum contained an absorption band at 2102 cm^{-1}, characteristic of aliphatic azido group [5]. The formation of acylazido group via the cleavage of the P–C bond was confirmed by the presence of the bands at 2141 (acyl azide) and 1687 cm^{-1} (C=O), in good agreement with the reference data [6] on furoyl azides. Overall, the obtained data allowed assignment of structure **11** to the obtained diazide. Since we failed to remove diethyl hydrogen phosphite from compound **11**, its yield (70%) was calculated on the basis of relative intensities of the signals of furan and diethyl hydrogen phosphite in the ^1H NMR spectrum and total mass of the sample.

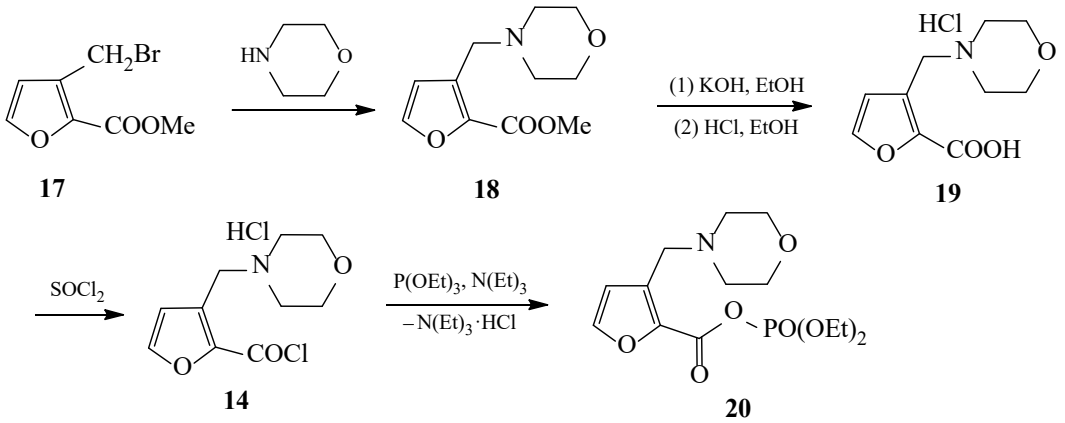
Chloromethylfuroyl phosphonate **4** was completely converted to thiocyanatomethyl derivative **12** under the analogous conditions (24 h, yield 99%) (Scheme 4). The reaction of compound **4** with sodium azide was completed in 48 h at room temperature, the azidomethyl derivative **13** was formed in 88% yield. It was decomposed when heated above 50°C.

Further, we decided to investigate the applicability of the Arbuzov reaction for obtaining of aminomethylfuroyl phosphonates starting from aminomethylfuroyl chlorides hydrochlorides analogously to [2]. Hydrochlorides **14**–**16** were prepared from halomethyl derivatives of the corresponding furoates (Scheme 5). The reaction scheme is exemplified by the synthesis of compound **14**. The reaction of bromide **17** with morpholine was carried out at room temperature in benzene during 10 h, the obtained amino ester **18** was hydrolyzed for 8 h with ethanolic solution of potassium hydroxide at 80°C and then treated with 2 mol of hydrogen chloride solution in ethanol. Crystalline hydrochloride of the amino acid **19** was isolated via evaporation of the ethanolic solution and treatment of the residue with 1 : 1 vol/vol mixture of acetone and ethyl acetate. For conversion into acid chloride **14**, it was refluxed for 6 h in thionyl chloride.

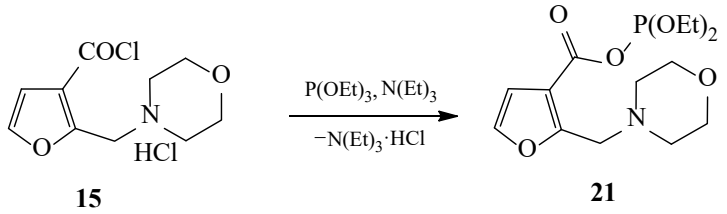
Scheme 4.



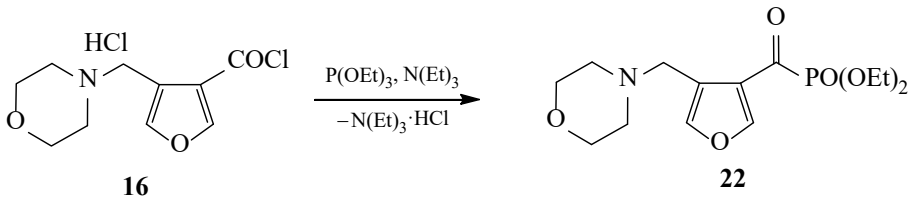
Scheme 5.



Scheme 6.



Scheme 7.



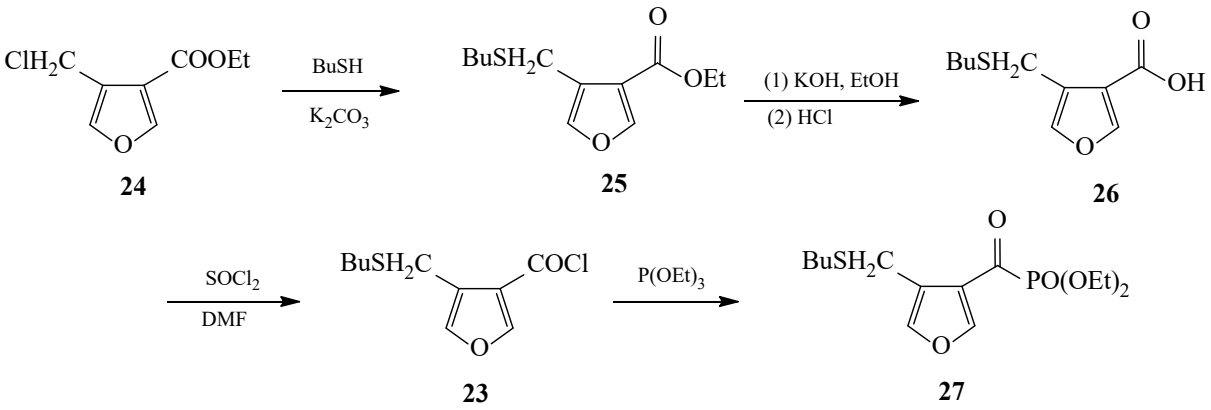
The reaction of furoyl chloride hydrochloride **14** with triethyl phosphite was carried out in benzene at the acid chloride : phosphite molar ratio of 1 : 1.02 in the presence of 1 mol of triethylamine at room temperature for 12 h. The major reaction product occurred to be mixed anhydride of furoic and phosphoric acids **20**, which was isolated in 78% yield (Scheme 5). The signal of the phosphorus in its NMR spectrum was observed at 0.98 ppm, and singlet of the carbonyl carbon atom nucleus was found at 151.51 ppm.

The reaction of acid chloride **15** was carried out similarly, but the major product was mixed anhydride of furoic and phosphorous acids **21** (yield 65%, Scheme 6). Chemical shift of phosphorus in that compound was 138.74 ppm, in good agreement with the reported data on mixed anhydrides of carboxylic and phosphorous acids [7]. The ^{13}C NMR spectrum contained the signal of the carbonyl carbon atom nucleus at 160.54 ppm.

Furoyl chloride **16** formed furoyl phosphonate **22** in 86% yield under the same conditions (Scheme 7). The signal of phosphorus nucleus in the ^{31}P NMR spectrum was found at –3.19 ppm, the doublet of carbonyl carbon atom was located at 194.06 ppm ($^1J_{PC}$ = 179.5 Hz), and the doublet of the C^3 carbon atom of the furan ring was observed at 125.59 ppm ($^2J_{PC}$ = 69.4 Hz).

Hence, the reaction of morpholinomethylfuroyl chroride hydrochloride with triethyl phosphite proceeded likely via two pathways. One of them consisted in dealkylation of triethyl phosphite with triethylamine hydrochloride to give ethyl chloride and ester salt of diethyl phosphite. The phosphorus atom of the latter preferably existed in the three-coordinate state. Further nucleophilic substitution of chlorine yielded mixed ester anhydride of carboxylic and phosphorous acid. Depending on the ease of oxidation, that compound was found as such (product **21**) or as the phosphate (product **20**). The alternative

Scheme 8.



pathway was the Arbuzov reaction (product **22**). In the case of 2,3-disubstituted furans, the first pathway was the major one, whereas the second pathway was predominant for the 3,4-disubstituted substrates.

The next stage of this study was investigation of furoyl phosphonates bearing a butylthiomethyl substituent adjacent to the acyl phosphonate position. The synthesis of the starting acid chlorides was carried out according to the same scheme which is shown in Scheme 8 for compound **23**. Halomethylfuroate **24** gave butylthiomethyl derivative **25** in 84% yield when treated with butanethiol at the halide : thiol molar ratio = 1 :1.1 in acetonitrile at 30–40°C in the presence of solid potassium carbonate. The product hydrolysis with ethanolic potassium hydroxide solution followed by acidifying gave acid **26** in 67% yield. Subsequent treatment with thionyl chloride in benzene in the presence of DMF at boiling led to furoyl chloride **27** in 96% yield. Acid chloride **28** was obtained similarly. In the case of acid **30**, the reaction with thionyl chloride was complex. Singlet of protons of the furan-CH_2S fragment and triplet of protons of the SCH_2 of butyl substituent were absent in the ^1H NMR spectrum of the obtained compound. Instead of those, several multiplets were observed at 3.6–3.9 ppm. While handling, that sample was rapidly converted into fragile insoluble mass evidencing the formation of a crosslinked polymer.

Acid chlorides **23** and **28** reacted with triethyl phosphite at room temperature via the Arbuzov scheme to give acyl phosphonates **27**, **29** bearing butylthiomethyl group in the positions 4 or 2 of the furan ring (Scheme 9). Yield of obtained compounds was 96 and 95%, respectively.

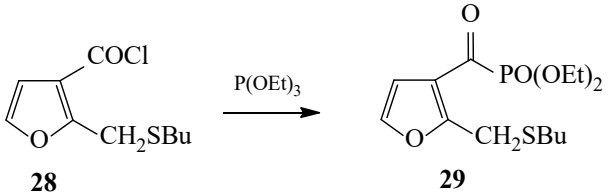
Hence, a series of 2- and 3-furoyl phosphonates having functional group in the adjacent position of the furan ring was prepared via the Arbuzov reaction. The effect of the substituent on the reaction with triethyl phosphite was revealed only for morpholinomethylfuroyl chlorides.

The synthesized furoylphosphonates were introduced in the Wittig reaction with resonance-stabilized phosphoranes (Scheme 10). The reaction was carried out in boiling benzene, the phosphonate : phosphorane molar ratio being 1 : 1.1. The reaction progress was monitored by ^{31}P NMR spectroscopy following gradual decrease in the intensity of the acyl phosphonate phosphorus signal.

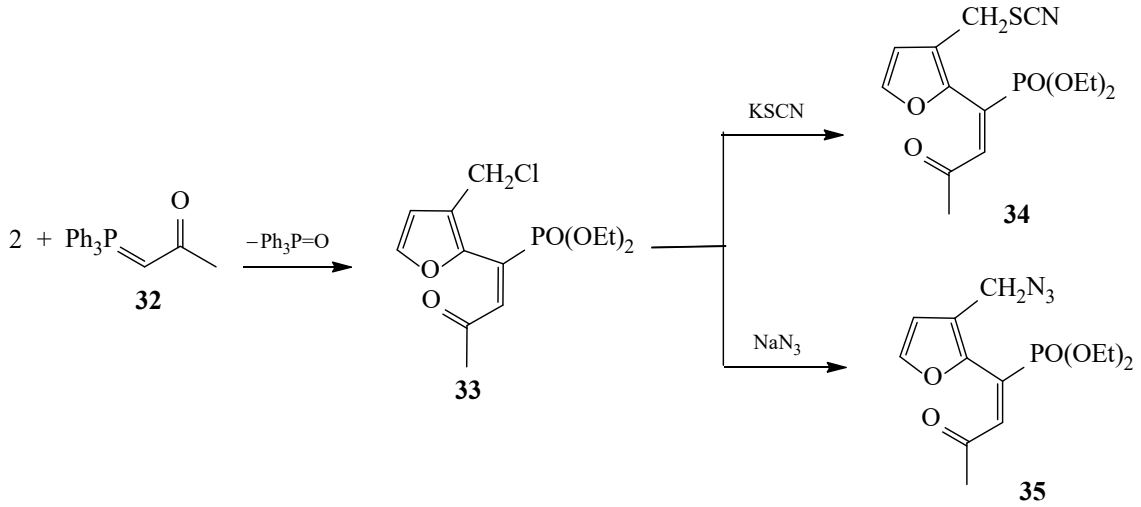
The reaction was complete in 9–10 h, no certain dependence on the structure of substrate and nature of the phosphorane was found. The reaction proceeded stereoselectively to give the compounds with *trans*-location of the phosphonate and carbonyl group with respect to the double bond.

The reaction of acyl phosphonate **2** with acetylmethylenetriphenylphosphorane **32** resulted in the formation of unsaturated ketone **33**. The signal of the phosphorus nucleus of that compound was observed at 12.71 ppm, the signal of the protons of the ketone methyl group was located at 2.05 ppm, and a doublet of olefinic proton was observed at 7.13 ppm (J_{PH} = 22.0 Hz). A broad signal of the carbon atom of the ketone methyl group was found at 29.68 ppm, a doublet of the C^1 carbon atom at the double bond was observed at 131.77 ppm ($^2J_{PC}$ = 3.1 Hz), a doublet of the C^1 carbon atom at the double bond was found

Scheme 9.



Scheme 10.



at 128.97 ppm ($^1J_{PC}$ = 179.0 Hz), and a doublet of the carbon atom of the ketone carbonyl group was observed at 198.67 ppm ($^3J_{PC}$ = 20.2 Hz).

Considering that thiocyanatomethylfuroyl phosphonate **10** decomposed under the probed conditions of the Wittig reaction, and analogous azidomethyl derivative was not formed via nucleophilic substitution of chlorine in compound **2**, we involved the unsaturated ketone **33** in the reactions with potassium thiocyanate and sodium azide (Scheme 10). The substitution was carried out in acetonitrile at the phosphonate : nucleophile molar ratio of 1 : 2 in the presence of 10 mol % of potassium iodide. The reaction of potassium thiocyanate with halomethylketone **33** was complete during a day at room temperature and proceeded exclusively at the sulfur atom. Thiocyanate **34** was isolated in 54% yield. The formation of thiocyanate group was confirmed by the presence of the signal of thiocyanatomethyl group protons at 4.21 ppm, the signal of the corresponding carbon atom at 29.51 ppm, and the signal of the carbon atom of the –SCN fragment at 112.68 ppm.

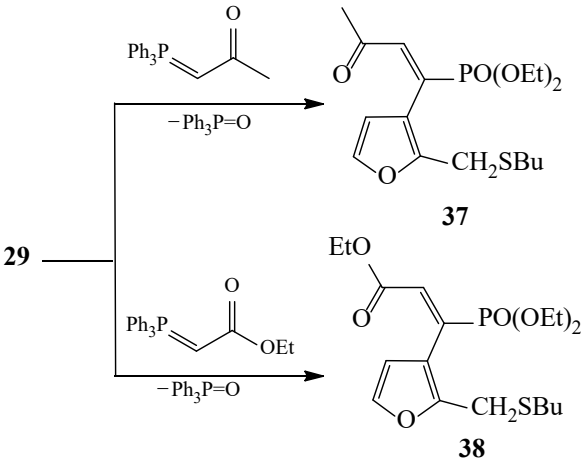
The reaction of compound **33** with sodium azide was carried out at 70°C due to low solubility of the azide in acetonitrile. The reaction was complete in 9 h and was accompanied by considerable decomposition. The signal of the azidomethyl group protons in the NMR spectrum of the product was revealed at 4.25 ppm, and that of the corresponding carbon atom was found at 45.59 ppm.

2-Butylthiomethyl-3-furoyl phosphonate **29** reacted with acetylmethylene- **32** and ethoxycarbonylmethylenetriphenylphosphorane **36** under the above-described conditions. The yield of 4-furylbut-3-en-2-one **37** was 80%, and that of 3-(furyl)acrylate **38** was 86% (Scheme 11). Those substances were stable in air and in solutions at moderate heating.

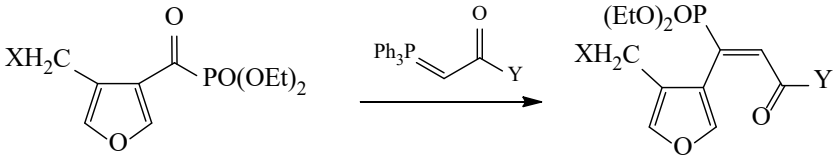
4-Substituted 3-furoyl phosphonates **4**, **12** and **27** were also introduced in the reactions with phosphoranes **32** and **36** under the above-used conditions. The yield of the chloromethyl (**39**, **40**) and butylthiomethyl (**42**, **43**) derivatives was of 80–90%, while the yield of thiocyanatomethyl derivative **41** was as low as 54% (Scheme 12).

Chloromethyl derivatives **39**, **40** were involved in the nucleophilic substitution reactions with amines. It was found that those reactions were complicated at elevated temperatures, but at 25°C smooth substitution of chlorine with morpholine residue occurred. The corresponding unsaturated aminophosphonates of the furan series **44**, **45** were

Scheme 11.



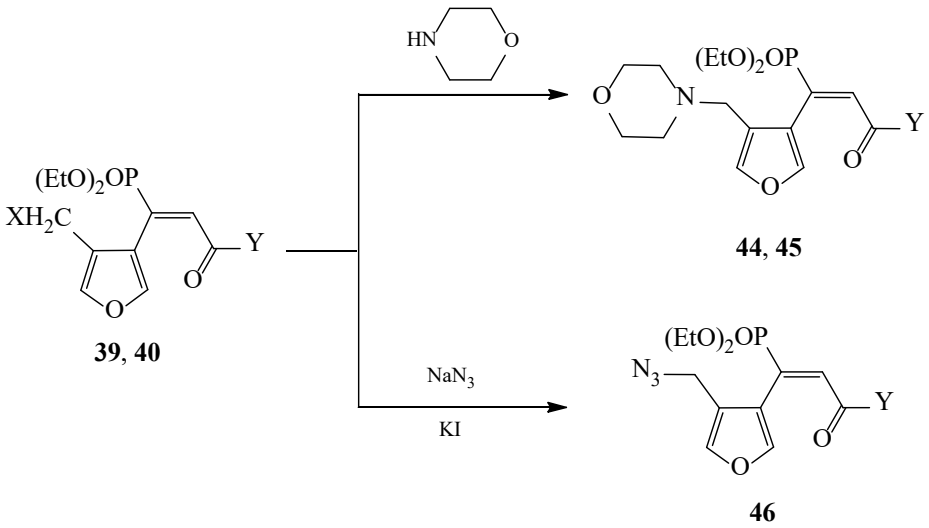
Scheme 12.



4, **12**, **27** **39**–**43**

Y = Me, OEt; X = Cl (**4**), NCS (**12**), BuS (**27**); X = Cl, Y = Me (**39**), OEt (**40**); X = NCS, Y = Me (**41**); X = BuS, Y= Me (**42**), OEt (**43**).

Scheme 13.



39, **40** **44**, **45** **46**

X = Me (**39**, **44**, **46**), OEt (**40**, **45**).

obtained in 85 and 55% yield, respectively (Scheme 13). Lower yield of ester **45** as compared to ketone **44** could be due to its partial hydrolysis during isolation.

Chloromethylketophosphonate **39** was also introduced in the reaction with sodium azide. Considering that thermal lability of furoyl phosphonate **13** did not permit its use in the Wittig reaction, the above-mentioned process was the only approach to the corresponding unsaturated azidomethylfurylphosphonates. As before, the reaction was carried out at the chloride : azide : potassium iodide molar ratio of 1 : 2 : 0.1. In was found that the reaction product was decomposed in acetonitrile at 80°C, but the substitution proceeded smoothly in acetone at 20°C and was complete in a week. The phosphorylated azidoketone **46** was isolated in 95% yield (Scheme 13). The signal of the azidomethyl group protons in its NMR spectrum was observed at 4.18 ppm, and the signal of the corresponding carbon atom was found at 44.82 ppm.

Hence, the presence of the adjacent group in the furan ring of furoyl phosphonates significantly influenced the course of the Arbuzov reaction in the case of functionalized furoyl chlorides as well as the Wittig reaction in the case of furoyl phosphonates. It is found that in the case of 2-chloromethyl-3-furoyl chloride the Arbuzov reaction was accompanied by the shift of the halogen from the side chain to the position 4 of the furan ring. It was established that hydrochlorides of *N*-morpholinomethylfuroyl chlorides showed dual reactivity in the reaction with triethyl phosphite. 2,3-Disubstituted furans formed mixed anhydrides of phosphorous and carboxylic acid which were further oxidized into the derivatives of phosphoric acid, but 3,4-disubstituted isomer formed furoyl phosphonate. The presence of sulfide group in the side chain did not affect the course of the Arbuzov reaction.

Azidomethyl and thiocyanatomethyl groups might decrease thermal stability of furoyl phosphonates as well as of phosphorylated alkenes, which prevented the use of the Wittig reaction for the preparation of certain representatives of such furylalkenes. An alternative approach to those substances was using the analogous

chloromethyl derivatives in nucleophilic substitution reactions. In certain cases, they proceeded smoothly only at room temperature in polar aprotic solvents, the duration being prolonged.

EXPERIMENTAL

^{1}H, ^{13}C, ^{31}P, and ^{15}N NMR spectra were recorded using a Bruker AVANCE-400 spectrometer [400.13 MHz (^{1}H), 100.16 MHz (^{13}C), 161.67 MHz (^{31}P), and 40.54 MHz (^{15}N)]. IR spectra were recorded using a Shimadzu IR Tracer 100 spectrometer with a DCIR Specas adapter (diamond window). High-resolution mass spectra were measured using a Bruker MicrOTOF mass spectrometer. Melting points were measured using a Boëtius apparatus.

2-Methyl-5-chloro-3-furoyl chloride (8). 0.4 mL of thionyl chloride and 1 drop of DMF were added to a suspension of 0.90 g of 2-methyl-5-chloro-3-furoic acid in 10 mL of benzene. The formed mixture was refluxed for 8 h, the volatile products were distilled off, and the residue was distilled in vacuum. Yield 0.20 g (20%), colorless oil, bp 69°C (1 mmHg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.60 s (3H, CH_3-furan), 6.56 s (1H, H^4-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.30 (CH_3-furan), 108.34 (C^4-furan), 120.25 (C^3-furan), 135.88 (C^5-furan), 160.82 (C^2-furan), 161.03 (C=O).

Synthesis of (*N*-morpholino)methyl derivatives of alkyl furoates (*general procedure*). 25 mmol of morpholine was added with stirring to a solution of 10 mmol of alkyl halomethylfuroate in 40 mL of benzene. When the chloride was consumed, the reaction mixture was refluxed for 8 h with stirring. The bromomethyl compounds reacted within 10 h at room temperature. After the reaction was complete, the obtained mixture was extracted with 10% hydrochloric acid (3×10 mL), aqueous extract was washed with 7 mL of ethyl acetate and then treated with sodium carbonate under vigorous stirring to pH 9–10. The formed oil was extracted with chloroform (3×15 mL), the extract was washed with 10 mL of brine and dried over sodium sulfate. Chloroform was distilled off, and the residue was kept in vacuum (1 mmHg) at room temperature.

Methyl 3-(*N*-morpholinomethyl)2-furoate (18) was obtained from methyl 3-bromomethyl-2-furoate. Yield 62%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.46 br. s (4H, NCH_2-morpholine), 3.68 br. s (4H, OCH_2-morpholine), 3.73 s (2H, NCH_2-furan), 3.89 s (3H, CH_3O), 6.58 br. s (1H, H^4-furan), 7.47 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 51.67 (CH_3O), 52.98 (NCH_2-furan), 53.50 (NCH_2-morpholine), 66.94 (OCH_2-morpholine), 113.94 (C^4-furan), 131.96 (C^3-furan), 140.59 (C^5-furan), 145.14 (C^2-furan), 159.60 (C=O).

Ethyl 2-(*N*-morpholinomethyl)-3-furoate was obtained from ethyl 2-bromomethyl-3-furoate. Yield 87%, light yellow oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, CH_3, J_{HH} = 7.2 Hz), 2.52 t (4H, NCH_2-morpholine, J_{HH} = 4.4 Hz), 3.68 t (4H, OCH_2-morpholine, J_{HH} = 4.4 Hz), 3.91 s (2H, NCH_2-furan), 4.27 q (2H, CH_2O, J_{HH} = 7.2 Hz), 6.66 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.33 d (1H, H^5-furan, J_{HH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.29 (CH_3-ester), 46.33 (NCH_2-furan), 53.54 (NCH_2-morpholine), 60.33 (CH_2O-ester), 66.64 (OCH_2-morpholine), 110.69 (C^4-furan), 116.73 (C^3-furan), 141.80 (C^5-furan), 157.06 (C^2-furan), 163.60 (C=O).

Ethyl 4-(*N*-morpholinomethyl)-3-furoate was obtained from ethyl 4-chloromethyl-3-furoate. Yield 65%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (3H, CH_3, J_{HH} = 7.2 Hz), 2.50 t (4H, NCH_2-morpholine, J_{HH} = 4.4 Hz), 3.62 s (2H, NCH_2-furan), 3.68 t (4H, OCH_2-morpholine, J_{HH} = 4.4 Hz), 4.27 q (2H, CH_2O, J_{HH} = 7.2 Hz), 7.35 br. s (1H, H^5-furan), 7.90 d (1H, H^2-furan, J_{HH} = 1.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.30 (CH_3-ester), 52.03 (NCH_2-furan), 53.52 (NCH_2-morpholine), 60.20 (CH_2O-ester), 67.01 (OCH_2-morpholine), 118.34 (C^3-furan), 121.53 (C^4-furan), 142.46 (C^5-furan), 148.83 (C^2-furan), 163.41 (C=O).

Hydrolysis of alkyl (*N*-morpholinomethyl)furoates (*general procedure*). 15 mol of anhydrous potassium hydroxide was added to a solution of 10 mmol of (*N*-morpholinomethyl)furoate in 50 mL of ethanol. The formed mixture was refluxed for 8 h with stirring, saturated solution of hydrogen chloride in ethanol containing 25 mmol of hydrogen chloride was added, and the mixture was stirred for 30 min. Potassium chloride was filtered off and washed with 20 mL of ethanol. The obtained ethanolic solution was evaporated to dryness, and the residue was triturated with a solvent specified below for each substance. The obtained crystals were filtered off and dried in air to constant mass.

3-(*N*-Morpholinomethyl)-2-furoic acid hydrochloride (19) was crystallizes from 1 : 1 acetone–ethyl acetate. Yield 93%. Decomposes at 200°C. ^{1}H NMR spectrum (DMSO-d_6) δ, ppm: 3.06 br. t (4H, NCH_2-morpholine, J_{HH} = 4.4 Hz), 3.13 br. t (4H, OCH_2-morpholine, J_{HH} =

4.4 Hz), 4.51 s (2H, NCH_2-furan), 7.18 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.98 d (1H, H^5-furan J_{HH} = 2.0 Hz), 11.95 br. s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 50.29 (NCH_2-furan), 51.32 (NCH_2-morpholine), 63.40 (OCH_2-morpholine), 115.46 (C^4-furan), 122.12 (C^3-furan), 143.82 (C^5-furan), 146.68(C^2-furan), 159.97 (C=O).

2-(*N*-Morpholinomethyl)-3-furoic acid hydrochloride was crystallized from 2 : 1 acetone–ethyl acetate. Yield 67%. Decomposes at 185°C. ^1H NMR spectrum (DMSO-d_6) δ, ppm: 3.20 br. s (4H, NCH_2-morpholine), 3.83 br. s (4H, OCH_2-morpholine), 4.64 s (2H, NCH_2-furan), 6.83 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.93 d (1H, H^5-furan J_{HH} = 2.0 Hz), 9.73 br. s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 42.97 (NCH_2-furan), 51.36 (NCH_2-morpholine), 63.53 (OCH_2-morpholine), 111.92 (C^4-furan), 121.50 (C^3-furan), 145.67 (C^5-furan), 148.48(C^2-furan), 164.04 (C=O).

4-(*N*-Morpholinomethyl)-3-furoic acid hydrochloride was crystallized from ethyl acetate. Yield 95%. Decomposes above 250°C. ^1H NMR spectrum (DMSO-d_6) δ, ppm: 3.09 br. s (4H, NCH_2-morpholine), 3.90 br. s (4H, OCH_2-morpholine), 4.40 s (2H, NCH_2-furan), 8.14 d (1H, H^5-furan, J_{HH} = 1.6 Hz), 8.42 d (1H, H^2-furan, J_{HH} = 1.6 Hz), 11.44 br. s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 48.58 (NCH_2-furan), 51.05 (NCH_2-morpholine), 63.15 (OCH_2-morpholine), 113.77 (C^4-furan), 119.05 (C^3-furan), 147.48 (C^5-furan), 150.23 (C^2-furan), 164.57 (C=O).

Synthesis of (*N*-morpholinomethyl)furoyl chlorides hydrochlorides (*general procedure*). Hydrochloride of the corresponding (*N*-morpholinomethyl)furoic acid (10 mmol) was suspended in 30 mL of thionyl chloride. The obtained mixture was refluxed with vigorous stirring for 8 h. After removal of thionyl chloride, the residue was triturated with hexane. The formed crystals were filtered off, washed with hexane, and kept in vacuum (1 mmHg) for 20 min at room temperature. The obtained compounds were completely hydrolyzed with residual moisture while dissolution in DMSO. Due to that, their spectral data were identical to those of corresponding acid hydrochlorides.

3-(*N*-Morpholinomethyl)-2-furoyl chloride hydrochloride (14). Yield 88%, mp 165°C (ethyl acetate–hexane 1 : 3).

2-(*N*-Morpholinomethyl)-3-furoyl chloride hydrochloride (15). Yield 79%, light grey crystals, mp 146°C (hexane).

4-(*N*-Morpholinomethyl)-3-furoyl chloride hydrochloride (16). Yield 97%, white crystals, mp 182°C (hexane).

Synthesis of butylthiomethyl derivatives of alkyl furoates (*general procedure*). 11 mmol of butanethiol and 22 mmol of anhydrous potassium carbonate were added to a solution of 10 mmol of halomethylfuroate in 40 mL of acetonitrile. The reaction mixture was stirred at 30–40°C for 3–4 h until complete liberation of carbon dioxide. Inorganic salts were filtered off and washed with 10 mL of acetonitrile. The formed solution was evaporated, the residue was dissolved in 30 mL of chloroform and washed with 20 mL of water and 20 mL of brine. After drying over calcium chloride, chloroform was distilled off, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

Ethyl 4-(butylthiomethyl)-3-furoate (25) was obtained from ethyl 4-chloromethyl-3-furoate. Yield 84%, light yellow oil. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.91 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.34 t (3H, CH_3, J_{HH} = 7.2 Hz), 1.40 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz, 1.57 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.50 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 3.78 s (2H, furan-CH_2S), 4.31 q (2H, CH_2O, J_{HH} = 7.2 Hz), 7.39 d (1H, H^5-furan, J_{HH} = 1.6 Hz), 7.98 d (1H, H^2-furan, J_{HH} = 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.67 (C^4H_3-butyl), 14.27 (CH_3-ester), 22.01 (C^3H_2-butyl), 24.98 (C^1H_2S-butyl), 31.42 (C^2H_2-butyl), 31.68 (furan-CH_2S), 60.30 (CH_2O), 117.50 (C^4-furan), 122.81 (C^3-futan), 141.95 (C^5-furan), 149.09 (C^2-furan), 163.22 (C=O).

Ethyl 2-(butylthiomethyl)-3-furoate was obtained from ethyl 2-bromomethyl-3-furoate. Yield 98%, light yellow oil. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.36 t (3H, CH_3, J_{HH} = 7.2 Hz), 1.38 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.56 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.55 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 4.08 s (2H, furan-CH_2S), 4.31 q (2H, CH_2O, J_{HH} = 7.2 Hz), 6.68 d (1H, H^4-furan, J_{HH} = 1.8 Hz), 7.32 d (1H, H^5-furan, J_{HH} = 1.8 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.62 (C^4H_3-butyl), 14.32 (CH_3-ester), 21.96 (C^3H_2-butyl), 27.06 (C^1H_2S-butyl), 31.47 (C^2H_2-butyl), 31.72 (furan-CH_2S), 60.41 (CH_2O), 110.86 (C^4-furan), 114.51 (C^3-furan), 141.39 (C^5-furan), 158.74 (C^2-furan), 163.53 (C=O).

Methyl 3-(butylthiomethyl)-2-furoate was obtained from methyl 3-bromomethyl-2-furoate; the residue after distillation of chloroform was distilled in a vacuum. Yield 70%, light yellow oil, bp 154°C (1 mmHg). ^1H

NMR spectrum ($CDCl_3$), δ, ppm: 0.86 t (3H, C^4H_3-butyl, J_{HH} = 7.0 Hz), 1.36 sextet (2H, C^3H_2-butyl, J_{HH} = 7.0 Hz), 1.54 quintet (2H, C^2H_2-butyl, J_{HH} = 7.0 Hz), 2.44 t (2H, C^1H_2S-butyl, J_{HH} = 7.0 Hz), 3.90 s (3H, CH_3O), 3.92 s (2H, furan-CH_2S), 6.58 br. s (1H, H^4-furan), 7.47 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.63 (C^4H_3-butyl), 21.94 (C^3H_2-butyl), 25.90 (C^1H_2S-butyl), 31.26 (C^2H_2-butyl), 31.34 (furan-CH_2S), 51.73 (CH_3O), 113.95 (C^4-furan), 132.99 (C^3-furan), 140.08 (C^5-furan), 145.29 (C^2-furan), 159.59 (C=O).

Alkaline hydrolysis of alkyl (butylthiomethyl)-furoates (*general procedure*). 12 mmol of potassium hydroxide was added to a solution of 10 mmol of alkyl (butylthiomethyl)furoate in 50 mL of ethanol. The mixture was refluxed for 8 h, and then ethanol was distilled off. The residue was dissolved in 15 mL of water and washed with 8 mL of ethyl acetate. The aqueous solution was acidified with concentrated hydrochloric acid to pH 2–3 and extracted with chloroform (3×15 mL). The extract was dried with sodium sulfate, chloroform was removed, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

4-(Butylthiomethyl)-3-furoic acid (26). Yield 67%, light yellow crystals, mp 62-63°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.93 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.42 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.59 quintet (2H, C^2H_2-butyl, J_{HH} = Hz), 2.53 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 3.80 s (2H, furan-CH_2S), 7.44 (1H, H^5-furan), 8.11 (1H, H^2-furan), 8.91 br. s (1H. OH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.72 (C^4H_3-butyl), 22.03 (C^3H_2-butyl), 24.81 (C^1H_2S-butyl), 31.40 (C^2H_2-butyl), 31.71 (furan-CH_2S), 117.22 (C^3-furan), 122.98 (C^4-furan), 142.37 (C^5-furan), 150.65 (C^2-furan), 168.73 (C=O).

2-(Butylthiomethyl)-3-furoic acid. Yield 69%, light yellow crystals, mp 35°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.38 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.57 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.56 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 4.09 s (2H, furan-CH_2S), 6.72 br. s (1H, H^4-furan), 7.36 br. s (1H, H^5-furan), 11.63 br. s (1H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.62 (C^4H_3-butyl), 21.96 (C^3H_2-butyl), 26.93 (C^1H_2S-butyl), 31.48 (C^2H_2-butyl), 31.78 (furan-CH_2S), 111.02 (C^4-furan), 113.69 (C^3-furan), 141.75 (C^5-furan), 160.56 (C^2-furan), 169.48 (C=O).

3-(Butylthiomethyl)-2-furoic acid. Yield 71%, light yellow crystals, mp 40°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.88 t (3H, C^4H_3-butyl, J_{HH} = 7.0 Hz), 1.37 sextet (2H, C^3H_2-butyl, J_{HH} = 7.0 Hz), 1.56 quintet (2H, C^2H_2-butyl, J_{HH} = 7.0 Hz), 2.65 t (2H, C^1H_2S-butyl, J_{HH} = 7.0 Hz), 3.94 s (2H, furan-CH_2S), 6.64 d (1H, H^4-furan, J_{HH} = 7.0 Hz), 7.57 d (1H, H^5-furan, J_{HH} = 7.0 Hz), 11.63 br. s (1H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.64 (C^4H_3-butyl), 21.96 (C^3H_2-butyl), 25.94 (C^1H_2S-butyl), 31.32 (C^2H_2-butyl), 31.32 (furan-CH_2S), 114.41 (C^4-furan), 135.48 (C^3-furan), 139.36 (C^5-furan), 146.58 (C^2-furan), 164.31 (C=O).

Synthesis of (butylthiomethyl)furoyl chlorides (*general procedure*). 13 mmol of thionyl chloride and 2 drops of DMF were added at vigorous stirring to a solution of 10 mmol of (butylthiomethyl)furoic acid in 40 mL of benzene. The mixture was refluxed with stirring for 8 h, volatile products were removed in vacuum, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

4-(Butylthiomethyl)-3-furoyl chloride (23). Yield 96%, light yellow oil. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.93 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.42 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.58 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.52 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 3.79 s (2H, furan-CH_2S), 7.49 d (1H, H^5-furan, J_{HH} = 1.4 Hz), 8.23 d (1H, H^2-furan, J_{HH} = 1.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.67 (C^4H_3-butyl), 21.97 (C^3H_2-butyl), 24.70 (C^1H_2S-butyl), 31.35 (C^2H_2-butyl), 31.87 (furan-CH_2S), 123.06 (C^4-furan), 128.34 (C^3-furan), 143.36 (C^5-furan), 154.47 (C^2-furan), 159.18 (C=O).

2-(Butylthiomethyl)-3-furoyl chloride (28). Yield 89%, light yellow oil. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.91 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.39 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.56 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.56 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 4.01 s (2H, furan-CH_2S), 6.81 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.37 d (1H, H^5-furan, J_{HH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.62 (C^4H_3-butyl), 21.91 (C^3H_2-butyl), 27.16 (C^1H_2S-butyl), 31.35 (C^2H_2-butyl), 32.04 (furan-CH_2S), 112.78 (C^4-furan), 118.76 (C^3-furan), 141.90 (C^5-furan), 161.56 (C^2-furan), 161.98 (C=O).

Reaction of furoyl chlorides with triethyl phosphite (*general procedure*). 10.5 mmol of triethyl phosphite was added to a solution of 10 mmol of the corresponding furoyl chloride in 30 mL of benzene. The reaction mixture was stirred for 1–2 h and left overnight. On the next day, benzene was distilled off, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

Diethyl 3-chloromethyl-2-furoyl phosphonate (2). Yield 96%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 t (6H, CH_3, J_{HH} = 7.2 Hz), 4.32 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 14.8 Hz), 4.75 s (1H, CH_2Cl), 4.82 s (1H, CH_2Cl), 6.78 br. s (0.5 H, H^4-furan), 6.80 d (0.5 H, H^4-furan, J_{HH} = 2.6 Hz), 7.66 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.39 d (CH_3-phosphonate, $^2J_{PC}$ = 5.8 Hz), 35.90 (CH_2Cl), 36.36 (CH_2Cl), 64.28 d (CH_2OP, $^2J_{PC}$ = 7.1Hz), 115.43 (C^4-furan), 134.19 d (C^3-furan, $^3J_{PC}$ = 8.7 Hz), 147.42 d (C^2-furan, $^2J_{PC}$ = 60.1 Hz), 147.45 d (C^2-furan, $^2J_{PC}$ = 60.1 Hz), 147.79 (C^5-furan), 148.21 (C^5-furan), 187.38 d (C=O, $^1J_{PC}$ = 187.6 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –2.31.

Diethyl 4-chloromethyl-3-furoyl phosphonate (4). Yield 98%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.38 t (6H, CH_3, J_{HH} = 7.2 Hz), 4.21–4.29 m (4H, CH_2OP), 4.72 br. s (2H, CH_2Cl), 7.56 d. t (1H, H^5-furan, J_{PH} = 2.8 Hz, J_{HH} = 1.4 Hz), 8.79 d (1H, H^2-furan, J_{PH} = 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.36 d (CH_3-phosphonate, $^2J_{PC}$ = 5.7 Hz), 36.26 (CH_2Cl), 64.27 d (CH_2OP, $^2J_{PC}$ = 7.1 Hz), 122.15 d (C^4-furan, $^3J_{PC}$ = 10.8 Hz), 124.66 d (C^3-furan, $^2J_{PC}$ = 69.8 Hz), 143.28 (C^5-furan), 155.34 d (C^2-furan, $^3J_{PC}$ = 4.1 Hz), 194.10 d (C=O, $^1J_{PC}$ = 181.6 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.69.

Diethyl 2-methyl-5-chloro-3-furoyl phosphonate (6). Yield 96%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 t (6H, CH_3, J_{HH} = 7.0 Hz), 2.55 s (3H, CH_3-furan), 4.27 d. q (4H, CH_2OP, J_{HH} = 7.0 Hz, J_{PH} = 14.8 Hz), 6.95 s (1H, H^4-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.59 (CH_3-furan), 16.34 d (CH_3-phosphonate, $^2J_{PC}$ = 5.6 Hz), 64.05 d (CH_2OP, $^2J_{PC}$ = 7.1 Hz), 107.16 d (C^4-furan, $^3J_{PC}$ = 2.0 Hz), 122.06 d (C^3-furan, $^2J_{PC}$ = 68.8 Hz), 135.57 (C^5-furan), 160.36 d (C^2-furan, $^3J_{PC}$ = 14.5 Hz), 193.25 d (C=O, $^1J_{PC}$ = 184.2 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –2.18.

Diethyl 2-methyl-4-chloro-3-furoyl phosphonate (9). The residue after removal of solvents was distilled in vacuum. Fraction with bp 144–146°C (1 mmHg) was collected, yield 37%, colorless oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (6H, CH_3, J_{HH} = 7.0 Hz), 2.59 s (3H, CH_3-furan), 4.10 d. q (4H, CH_2OP, J_{HH} = 7.0 Hz, J_{PH} = 14.8 Hz), 7.06 s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.74 (CH_3-furan), 16.36 d (CH_3-phosphonate, $^2J_{PC}$ = 5.7 Hz), 64.07 d (CH_2OP, $^2J_{PC}$ = 7.2 Hz), 121.16 (C^4-furan), 122.63 d (C^3-furan, $^2J_{PC}$ = 68.7 Hz), 142.75 (C^5-furan), 162.54 d (C^2-furan, $^3J_{PC}$ = 14.5 Hz), 193.12 d (C=O, $^1J_{PC}$ = 184.1 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –2.31. Mass spectrum, *m/z*: found 303.0160, calculated for $C_{10}H_{14}ClO_5P$ 303.0167 $[M + Na]^+$.

Diethyl 4-(butylthiomethyl)-3-furoyl phosphonate (27). Yield 96%, yellow syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 t (3H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 1.31–1.41 m (8H, CH_3-phosphonate + C^{3}H$_2$-butyl), 1.55 quintet (2H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 2.49 t (2H, C^{1}H$_2$S-butyl, J_{HH} = 7.2 Hz), 3.78 s (2H, furan-CH_2S), 4.23 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 15.2 Hz), 7.22 d (1H, H^2-furan, J_{PH} = 1.6 Hz), 7.43 s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.66 (C^{4}H$_3$-butyl), 16.35 d (CH_3-phosphonate, $^2J_{PC}$ = 5.6 Hz), 21.96 (C^{3}H$_2$-butyl), 25.21 (C^{1}H$_2$S-butyl), 31.42 (C^{2}H$_2$-butyl), 31.79 (furan-CH_2S), 64.07 d (CH_2OP, $^2J_{PC}$ = 6.9 Hz), 122.37 d (C^4-furan, $^3J_{PC}$ = 11.1 Hz), 125.05 d (C^3-furan, $^2J_{PC}$ = 69.4 Hz), 142.31 d (C^5-furan, $^3J_{PC}$ = 1.1 Hz), 155.43 d (C^2-furan, $^3J_{PC}$ = 4.1 Hz), 194.02 d (C=O, $^1J_{PC}$ = 179.4 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.40.

Diethyl 2-(butylthiomethyl)-3-furoyl phosphonate (27). Yield 95%, yellow syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (1.5H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 0.91 t (1.5H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 1.34 t (3H, CH_3, J_{HH} = 7.2 Hz), 1.39 t (3H, CH_3, J_{HH} = 7.2 Hz), 1.35–1.41 m (2H, C^{3}H$_2$-butyl), 1.55 quintet (1H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 1.56 quintet (1H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 2.54 t (1H, C^{1}H$_2$S-butyl, J_{HH} = 7.2 Hz), 2.56 t (1H, C^{1}H$_2$S-butyl, J_{HH} = 7.2 Hz), 4.00 s (1H, furan-CH_2S), 4.01 s (1H, furan-CH_2S), 4.26 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 14.4 Hz), 6.80 d (1H, H^4-furan, J_{PH} = 2.0 Hz), 7.21 d (1H, H^5-furan, J_{PH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.61 (C^{4}H$_3$-butyl), 16.40 d (CH_3-phosphonate, $^2J_{PC}$ = 5.7 Hz), 21.90 (C^{3}H$_2$-butyl), 21.92 (C^{3}H$_2$-butyl), 27.14 (C^{1}H$_2$S-butyl), 27.61 (C^{1}H$_2$S-butyl), 31.34 (C^{2}H$_2$-butyl), 31.44 (C^{2}H$_2$-butyl), 31.93 (furan-CH_2S), 32.03 (furan-CH_2S), 63.95 d (CH_2OP, $^2J_{PC}$ = 7.1 Hz), 111.41 d (C^4-furan, $^3J_{PC}$ = 2.6 Hz), 120.54 d (C^3-furan, $^2J_{PC}$ = 68.6 Hz), 141.86 (C^5-furan), 160.40 d (C^2-furan, $^3J_{PC}$ = 9.0 Hz), 193.94 d (C=O, $^1J_{PC}$ = 183.5 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –2.09.

Reaction of (*N*-morpholinomethyl)furoyl chlorides hydrochlorides with triethyl phosphite (*general procedure*). 11 mmol of triethylamine was added with stirring at room temperature to a suspension of 10 mmol of hydrochloride **14**–**16** in 30 mL of benzene. The reaction mixture was stirred for 20 min at room temperature, and then 10.2 mmol of triethyl phosphite was added. The

mixture was stirred for 3–4 h and left overnight. On the next day, triethylamine hydrochloride was filtered off, the filtrate was evaporated, and the residue was kept in a vacuum (1 mmHg) for 1 h at room temperature.

Mixed anhydride of 3-(*N*-morpholinomethyl)-2-furoic and diethylphosphoric acids (20). Yield 78%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.30 t (6H, CH_3, J_{HH} = 7.0 Hz), 2.53 br. s (4H, NCH_2-morpholine), 3.71 br. s (4H, OCH_2-morpholine), 3.84 s (2H, NCH_2-furan), 4.08 d. q (4H, CH_2OP, J_{HH} = 7.0 Hz, J_{PH} = 15.2 Hz), 6.76 br. s (1H, H^4-furan), 7.42 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.10 d (CH_3-phosphonate, $^2J_{PC}$ = 6.7 Hz), 53.31 (NCH_2-furan), 53.39 (NCH_2-morpholine), 63.58 d (CH_2OP, $^2J_{PC}$ = 5.8 Hz), 66.63 (OCH_2-morpholine), 115.11 (C^4-furan), 128.28 (C^3-furan), 143.83 (C^5-furan), 147.10 (C^2-furan), 153.51 (C=O). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: -0.98.

Mixed anhydride of 2-(*N*-morpholinomethyl)-3-furoic and diethylphosphorous acids (21). Yield 65%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.28 t (6H, CH_3, J_{HH} = 7.2 Hz), 2.57 t (4H, NCH_2-morpholine, J_{HH} = 4.4 Hz), 3.71 t (4H, OCH_2-morpholine, J_{HH} = 4.4 Hz), 3.86 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 14.8 Hz), 3.98 s (2H, NCH_2-furan), 6.74 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.44 d (1H, H^5-furan, J_{HH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.90 d (CH_3-phosphonate, $^2J_{PC}$ = 5.0 Hz), 53.25 (NCH_2-morpholine), 53.34 (NCH_2-furan), 57.99 d (CH_2OP, $^2J_{PC}$ = 11.9 Hz), 66.76 (OCH_2-morpholine), 110.55 (C^4-furan), 115.47 (C^3-furan), 142.52 (C^5-furan), 158.50 (C^2-furan), 160.54 (C=O). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 138.75.

Diethyl 4-(*N*-morpholinomethyl)-3-furoyl phosphonate (22). Yield 86%, light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (6H, CH_3, J_{HH} = 7.2 Hz), 2.51 br. s (4H, NCH_2-morpholine), 3.64 br. s (2H, NCH_2-furan), 3.69 br. s (4H, OCH_2-morpholine), 4.10 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 14.4 Hz), 7.44 s (1H, H^5-furan), 8.14 d (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.36 d (CH_3-phosphonate, $^2J_{PC}$ = 5.5 Hz), 51.70 (NCH_2-furan), 53.48 (NCH_2-morpholine), 53.54 (NCH_2-morpholine), 63.61 d (CH_2OP, $^2J_{PC}$ = 5.8 Hz), 66.94 (OCH_2-morpholine), 67.02 (OCH_2-morpholine), 121.33 (C^4-furan), 125.59 d (C^3-furan, $^2J_{PC}$ = 69.4 Hz), 142.69 (C^5-furan), 155.24 d (C^2-furan, $^3J_{PC}$ = 4.1 Hz), 194.06 d (C=O, $^1J_{PC}$ = 179.5 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.19.

Reaction of chloromethylfuroyl phosphonates with potassium thiocyanate (*general procedure*). 20 mmol of potassium thiocyanate and 1 mmol of potassium iodide were added at room temperature at vigorous stirring to a solution of 10 mmol of chloromethylfuroyl phosphonate **2**,**4** in 30 mL of acetonitrile. The reaction mixture was stirred at room temperature for 24 h, the precipitate was filtered off, and the filtrate was evaporated. The residue was dissolved in 30 mL of chloroform, washed with 10 mL of water and 10 mL of brine, and dried over sodium sulfate. After removal of chloroform, the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

Diethyl 3-(thiocyanatomethyl)-2-furoyl phosphonate (10). Yield 83%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.28–1.38 m (6H, CH_3), 4.29 d. q (4H, CH_2OP, J_{HH} = 7.0 Hz, J_{PH} = 14.8 Hz), 4.29 s (2H, CH_2S), 6.76 d (1H, H^4-furan, J_{HH} = 1.6 Hz), 7.70 d (1H, H^5-furan, J_{HH} = 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.39 d (CH_3-phosphonate, $^2J_{PC}$ = 5.7 Hz), 28.27 (CH_2S), 64.66 d (CH_2OP, $^2J_{PC}$ = 7.2 Hz), 111.67 (SCN), 114.69 d (C^4-furan, $^4J_{PC}$ = 1.3 Hz), 131.40 d (C^3-furan, $^3J_{PC}$ = 8.4 Hz), 148.07 (C^5-furan), 148.19 d (C^2-furan, $^2J_{PC}$ = 59.6 Hz), 187.38 d (C=O, $^1J_{PC}$ = 188.0 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm:–2.68.

Diethyl 4-(thiocyanatomethyl)-3-furoyl phosphonate (12). Yield 99%, light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.37 t (6H, CH_3, J_{HH} = 7.2 Hz), 4.19 s (2H, CH_2S), 4.21–4.28 m (4H, CH_2OP), 7.60 s (1H, H^5-furan), 8.82 (1H, H^2-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.34 d (CH_3-phosphonate, $^2J_{PC}$ = 5.7 Hz), 28.14 (CH_2S), 64.36 d (CH_2OP, $^2J_{PC}$ = 7.1 Hz), 112.29 (SCN), 118.99 d (C^4-furan, $^3J_{PC}$ = 10.8 Hz), 123.88 d (C^3-furan, $^2J_{PC}$ = 68.5 Hz), 143.24 (C^5-furan), 155.77 d (C^2-furan, $^3J_{PC}$ = 4.0 Hz), 194.71 d (C=O, $^1J_{PC}$ = 183.0 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm:–3.22.

Reaction of furoyl phosphonate 2 with sodium azide. 0.43 g (6.6 mmol) of sodium azide and 0.05 g (0.3 mmol) of potassium iodide were added with stirring to a solution of 0.93 g (3.3 mmol) of furoyl phosphonate **2** in 15 mL of acetone. The mixture was stirred at room temperature for a week, the inorganic salts were filtered off, and the filtrate was evaporated. The residue was dissolved in 20 mL of chloroform, the obtained solution was washed with 5 mL of water and 5 mL of brine, and dried over sodium sulfate. Chloroform was removed, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature. Light brown oil, 1.10 g, was obtained. It consisted of 3-(azidomethyl)-2-furoyl azide and diethyl hydrogen phosphite. According to ^{1}H NMR data, molar

ratio of components was 1 : 0.6. Calculated yield of furoyl azide **11** 70%.

Diethyl hydrogen phosphite. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (6H, CH_3, J_{HH} = 7.2 Hz), 4.29 d. q (4H, CH_2OP, J_{HH} = 7.2 Hz, J_{PH} = 16.0 Hz), 6.80 d (P-H, J_{PH} = 692.8 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 7.35.

3-(Azidomethyl)-2-furoyl azide (11). IR spectrum, ν, cm^{-1}: 2102 (N_3 of azidomethyl group), 2141 (N_3 of acyl azide), 1687 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.62 s (2H, CH_2N_3), 6.65 br. s (1H, H^4-furan), 7.54 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 45.64 (CH_2N_3), 113.68 (C^4-furan), 131.71 (C^3-furan), 141.20 (C^5-furan), 146.93 (C^2-furan), 162.90 (C=O). ^{15}N NMR spectrum ($CDCl_3$), δ_N, ppm: 249 (N^1-azidomethyl), 73 (N^3-azidomethyl).

Diethyl 4-(azidomethyl)-3-furoyl phosphonate (13). 1.20 g (18.4 mmol) of sodium azide and 0.15 g (0.9 mmol) of potassium iodide were added with stirring to a solution of 2.60 g (9.2 mmol) of furoyl phosphonate **4** in 25 mL of acetonitrile. The mixture was stirred for 48 h at room temperature and the formed precipitate was filtered off. The filtrate was evaporated, the residue was dissolved in 40 mL of chloroform, washed with 10 mL of water and with 10 mL of brine, and dried over sodium sulfate. Chloroform was removed, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature. Yield 2.33 g (8.1 mmol, 88%), light brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.36 t (6H, CH_3, J_{HH} = 7.2 Hz), 4.08–4.18 m (4H, CH_2OP), 4.49 s (2H, CH_2N_3), 7.49 s (1H, H^5-furan), 8.80 s (1H, H^2-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.32 d (CH_3-phosphonate, $^2J_{PC}$ = 5.6 Hz), 45.01 (CH_2N_3), 64.29 d (CH_2OP, $^2J_{PC}$ = 7.0 Hz), 119.66 d (C^4-furan, $^3J_{PC}$ = 10.8 Hz), 124.81 d (C^3-furan, $^2J_{PC}$ = 69.4 Hz), 142.70 (C^5-furan), 155.44 d (C^2-furan, $^3J_{PC}$ = 4.5 Hz), 194.22 d (C=O, $^1J_{PC}$ = 181.6 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.71.

Reaction of furoyl phosphonates with resonance-stabilized phosphoranes 32 and 36 (*general procedure*). 11 mmol of phosphorane **32** or **36** was added with stirring to a solution of 10 mmol of furoyl phosphonate in 20 mL of benzene. The mixture was refluxed with stirring for 9–10 h, the reaction progress was monitored by means of ^{31}P NMR spectroscopy. After disappearance of the signal of phosphorus nucleus from furoyl phosphonate, the reaction mixture was diluted with 75 mL of hexane, stirred for 30 min, and left overnight. On the next day, the solution was decanted, benzene and hexane were distilled off, and the residue was kept in vacuum (1 mmHg) during 1 h at room temperature.

4-(3-Chloromethylfur-2-yl)-4-(diethoxyphosphoryl)-but-3-ene-2-one (33) was prepared from furoyl phosphonate **2**. Yield 61%, light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.28–1.37 m (6H, CH_3-phosphonate), 2.05 s (3H, CH_3-ketone), 4.07–4.18 m (4H, CH_2O-phosphonate), 4.49 s (2H, CH_2Cl), 6.57 br. s (1H, H^4-furan), 7.13 d (1H, =CH, J_{PH} = 22.0 Hz), 7.52 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.26 d (CH_3-phosphonate, $^2J_{PC}$ = 6.9 Hz), 29.68 br. s (CH_3-ketone), 37.05 (CH_2Cl), 63.24 d (CH_2OP, $^2J_{PC}$ = 5.9 Hz), 63.63 d (CH_2OP, $^2J_{PC}$ = 5.9 Hz), 112.98 d (C^4-furan, $^4J_{PC}$ = 1.5 Hz), 123.37 d (C^3-furan, $^3J_{PC}$ = 5.7 Hz), 128.97 d (=CP, $^1J_{PC}$ = 179.0 Hz), 131.77 d (=CH, $^2J_{PC}$ = 3.1 Hz), 143.95 d (C^5-furan, $^3J_{PC}$ = 2.3 Hz), 144.54 d (C^2-furan, $^3J_{PC}$ = 7.3 Hz), 198.67 d (C=O, $^3J_{PC}$ = 20.2 Hz). ^{31}P NMR ($CDCl_3$), δ_P, ppm: 12.71.

4-(2-Butylthiomethylfur-3-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (37) was prepared from furoyl phosphonate **29**. Yield 80%, yellowish brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 1.32 t (6H, CH_3, J_{HH} = 7.2 Hz), 1.37 sextet (2H, C^{3}H$_2$-butyl, J_{HH} = 7.2 Hz), 1.55 quintet (2H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 2.12 s (CH_3-ketone), 2.59 t (2H, C^{1}H$_2$S-butyl, J_{HH} = 7.2 Hz), 3.63 s (2H, furan-CH_2S), 4.08–4.16 m (4H, CH_2OP), 6.66 d (1H, H^4-furan, J_{PH} = 2.0 Hz), 7.01 d (1H, , =CH, J_{PH} = 23.2 Hz), 7.33 d (1H, H^5-furan, J_{PH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.67 (C^{4}H$_3$-butyl), 15.92 d (CH_3-phosphonate, $^2J_{PC}$ = 7.5 Hz), 16.36 d (CH_3-phosphonate, $^2J_{PC}$ = 6.1 Hz), 21.91 (C^{3}H$_2$-butyl), 27.03 (C^{1}H$_2$S-butyl), 30.45 (CH_3-ketone), 31.35 (C^{2}H$_2$-butyl), 32.38 (furan-CH_2S), 62.95 d (CH_2OP, $^2J_{PC}$ = 6.2 Hz), 112.09 d (C^4-furan, $^3J_{PC}$ = 2.6 Hz), 114.29 d (C^3-furan, $^2J_{PC}$ = 8.2 Hz), 131.98 d (=CH, $^2J_{PC}$ = 2.6 Hz), 132.64 d (=CP, $^1J_{PC}$ = 178.1 Hz), 141.94 (C^5-furan), 150.90 d (C^2-furan, $^3J_{PC}$ = 10.0 Hz), 199.56 d (C=O, $^3J_{PC}$ = 22.1 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.77.

Ethyl 3-(2-butylthiomethylfur-3-yl)-3-(diethoxyphosphoryl)acrylate (38) was prepared from furoyl phosphonate **29**. Yield 86%, yellowish brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (1.5H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 0.91 t (1.5H, C^{4}H$_3$-butyl, J_{HH} = 7.2 Hz), 1.21 t (3H, CH_3-ester, J_{HH} = 7.2 Hz), 1.33 t (6H, CH_3, J_{HH} = 7.2 Hz), 1.33–1.35 m (2H, C^{3}H$_2$-butyl), 1.48 quintet (1H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 1.55 quintet (1H, C^{2}H$_2$-butyl, J_{HH} = 7.2 Hz), 2.47 t (1H, C^{1}H$_2$S-butyl,

J_{HH} = 7.2 Hz), 2.55 t (1H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 3.70 s (1H, furan-CH_2S), 3.74 q (1H, CH_2O-ester, J_{HH} = 7.2 Hz), 3.96 s (1H, furan-CH_2S), 3.99 q (1H, CH_2O-ester, J_{HH} = 7.2 Hz), 4.09–4.20 m (4H, CH_2OP), 6.37 d (0.5H, H^4-furan, J_{PH} = 2.0 Hz), 6.68 d (0.5H, H^4-furan, J_{PH} = 2.0 Hz), 6.89 d (1H, , =CH, J_{PH} = 22.4 Hz), 7.26 d (0.5H, H^5-furan, J_{PH} = 2.0 Hz), 7.38 d (0.5H, H^5-furan, J_{PH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.72 (C^4H_3-butyl), 13.85 (C^4H_3-butyl), 14.00 (CH_3-ester), 14.69 (CH_3-ester), 15.94 d (CH_3-phosphonate, $^2J_{PC}$ = 7.4 Hz), 16.37 d (CH_3-phosphonate, $^2J_{PC}$ = 6.3 Hz), 21.94 (C^3H_2-butyl), 21.96 (C^3H_2-butyl), 27.18 (C^1H_2S-butyl), 27.27 (C^1H_2S-butyl), 31.25 (C^2H_2-butyl), 31.38 (C^2H_2-butyl), 32.08 (furan-CH_2S), 61.00 (CH_2O-ester), 62.97 d (CH_2OP, $^2J_{PC}$ 6.2 Hz), 112.08 d (C^4-furan, $^3J_{PC}$ = 2.5 Hz), 114.34 d (C^3-furan, $^2J_{PC}$ = 8.2 Hz), 133.52 d (=CH, $^2J_{PC}$ = 11.7 Hz), 136.74 d (=CP, $^1J_{PC}$ = 177.8 Hz), 141.45 (C^5-furan), 150.00 d (C^2-furan, $^3J_{PC}$ = 10.2 Hz), 164.26 d (C=O, $^3J_{PC}$ = 28.3 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.14.

4-(4-Chloromethylfur-3-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (39) was prepared from furoyl phosphonate **4**. Yield 84%, brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.16 s (3H, CH_3-ketone), 4.08–4.17 m (4H, CH_2O-phosphonate), 4.49 s (2H, CH_2Cl), 7.08 d (1H, , =CH, J_{PH} = 23.2 Hz), 7.34 br. s (1H, H^5-furan), 7.52 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.30 d (CH_3-phosphonate, $^2J_{PC}$ = 6.3 Hz), 30.70 d (CH_3-ketone, $^4J_{PC}$ = 1.3 Hz), 36.03 (CH_2Cl), 63.11 d (CH_2OP, $^2J_{PC}$ = 6.3 Hz), 117.82 d (C^3-furan, $^2J_{PC}$ = 8.2 Hz), 122.74 d (C^4-furan, $^3J_{PC}$ = 4.3 Hz), 130.91 d (=CP, $^1J_{PC}$ = 179.1 Hz), 131.95 d (=CH, $^2J_{PC}$ = 2.4 Hz), 142.26 d (C^2-furan, $^3J_{PC}$ = 7.3 Hz), 142.55 (C^5-furan), 199.00 d (C=O, $^3J_{PC}$ = 21.5 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm.:14.22.

Ethyl 3-(4-chloromethylfur-3-yl)-3-(diethoxyphosphoryl)acrylate (40) was prepared from furoyl phosphonate **4**. Yield 91%, brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.17 t (3H, CH_3-ester, J_{HH} = 7.0 Hz), 1.29 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 4.06–4.13 m (6H, CH_2O-phosphonate, CH_2O-ester), 4.40 s (2H, CH_2Cl), 6.89 d (1H, =CH, J_{PH} = 22.4 Hz), 7.32 s (1H, H^5-furan), 7.50 s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.90 (CH_3-ester), 16.30 d (CH_3-phosphonate, $^2J_{PC}$ = 6.2 Hz), 35.95 (CH_2Cl), 61.10 (CH_2O-ester), 63.16 d (CH_2OP, $^2J_{PC}$ = 6.3 Hz), 122.94 d (C^4-furan, $^3J_{PC}$ = 5.1 Hz), 124.01 d (C^3-furan, $^3J_{PC}$ = 7.9 Hz), 134.01 d (=CH, $^2J_{PC}$ = 11.1 Hz), 135.34 d (=CP, $^1J_{PC}$ = 179.0 Hz), 141.61 d (C^2-furan, $^3J_{PC}$ = 6.1 Hz), 142.03 (C^5-furan), 164.06 d (C=O, $^3J_{PC}$ = 28.1 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 13.40.

4-(4-Thiocyanatomethylfur-3-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (41) was prepared from furoyl phosphonate **12**. Yield 54%, brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.34 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.20 s (3H, CH_3-ketone), 4.10–4.19 m (4H, CH_2O-phosphonate), 4.14 s (2H, CH_2SCN), 7.09 d (1H, , =CH, J_{PH} = 22.8 Hz), 7.63 br. s (1H, H^5-furan), 7.71 br. s (1H, H^5-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.37 d (CH_3-phosphonate, $^2J_{PC}$ = 5.9 Hz), 28.21 (CH_2SCN), 30.81 d (CH_3-ketone, $^4J_{PC}$ = 1.3 Hz), 63.32 d (CH_2OP, $^2J_{PC}$ = 6.5 Hz), 112.22 (SCN), 117.63 d (C^3-furan, $^2J_{PC}$ = 8.6 Hz), 119.84 d (C^4-furan, $^3J_{PC}$ = 3.8 Hz), 130.35 d (=CP, $^1J_{PC}$ = 180.3 Hz), 131.97 d (=CH, $^2J_{PC}$ = 2.7 Hz), 142.73 d (C^2-furan, $^3J_{PC}$ = 8.0 Hz), 142.87 (C^5-furan), 199.08 d (C=O, $^3J_{PC}$ = 21.0 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 13.82.

4-(4-Butylthiomethylfur-3-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (42) was prepared from furoyl phosphonate **27**. Yield 84%, yellowish brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.31 t (6H, CH_3, J_{HH} = 7.2 Hz), 1.36 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.54 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.15 s (CH_3-ketone), 2.44 t (2H, C^1H_2S-butyl, J_{HH} = 7.2 Hz), 3.49 s (2H, furan-CH_2S), 4.13 d. q (4H, CH_2OP, J_{HH} = 7.3 Hz, J_{PH} = 14.0 Hz), 7.04 d (1H, =CH, J_{PH} = 23.2 Hz), 7.47 br. s (1H, H^5-furan), 7.49 d (1H, H^5-furan, J_{PH} = 2.8 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.67 (C^4H_3-butyl), 13.69 (C^4H_3-butyl), 16.33 d (CH_3-phosphonate, $^2J_{PC}$ = 6.2 Hz), 21.96 (C^3H_2-butyl), 24.96 (C^1H_2S-butyl), 30.57 d (CH_3-ketone, $^4J_{PC}$ = 1.3 Hz), 31.23 (C^2H_2-butyl), 31.43 (furan-CH_2S), 63.01 d (CH_2OP, $^2J_{PC}$ = 6.1 Hz), 118.33 d (C^3-furan, $^2J_{PC}$ = 8.3 Hz), 122.27 d (C^4-furan, $^3J_{PC}$ = 4.3 Hz), 131.58 d (=CP, $^1J_{PC}$ = 178.4 Hz), 131.96 d (=CH, $^2J_{PC}$ = 2.7 Hz), 141.66 (C^5-furan), 141.98 d (C^2-furan, $^3J_{PC}$ = 7.2 Hz), 199.15 d (C=O, $^3J_{PC}$ = 22.0 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.67.

Ethyl 3-(4-butylthiomethylfur-3-yl)-3-(diethoxyphosphoryl)acrylate (43) was prepared from furoyl phosphonate **27**. Yield 86%, yellowish brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 t (1.5H, C^4H_3-butyl, J_{HH} = 7.2 Hz), 1.19 t (3H, CH_3-ester, J_{HH} = 7.2 Hz), 1.36 sextet (2H, C^3H_2-butyl, J_{HH} = 7.2 Hz), 1.53 quintet (2H, C^2H_2-butyl, J_{HH} = 7.2 Hz), 2.45 t (2H, C^1H_2S-butyl,

J_{HH} = 7.2 Hz), 3.44 s (2H, furan-CH_2S), 4.09–4.15 m (6H, CH_2OP, CH_2O-ester), 6.88 d (1H, , =CH, J_{PH} = 22.4 Hz), 7.45 br. s (1H, H^5-furan), 7.47 d (1H, H^2-furan, J_{PH} = 2.8 Hz). ^{13}CNMR spectrum ($CDCl_3$), δ_C, ppm: 13.69 (C^4H_3-butyl), 13.95 (CH_3-ester), 16.34 d (CH_3-phosphonate, $^2J_{PC}$ = 6.1 Hz), 21.97 (C^3H_2-butyl), 27.02 (C^1H_2S-butyl), 31.30 (C^2H_2-butyl), 31.67 (furan-CH_2S), 60.96 (CH_2O-ester), 63.03 d (CH_2OP, $^2J_{PC}$ = 6.2 Hz), 118.23 d (C^3-furan, $^2J_{PC}$ = 7.3 Hz), 122.65 d (C^4-furan, $^3J_{PC}$ = 5.2 Hz), 133.61 d (=CH, $^2J_{PC}$ = 11.5 Hz), 135.87 d (=CP, $^1J_{PC}$ = 178.3 Hz), 141.17 (C^5-furan), 141.28 d (C^2-furan, $^3J_{PC}$ = 6.0 Hz), 164.17 d (C=O, $^3J_{PC}$ = 28.4 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 13.90.

4-(3-Thiocyanatomethylfur-2-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (34). 0.34 g (3.5 mmol) of potassium thiocyanate and 0.34 g (0.17 mmol) of potassium iodide were added to a solution of 0.55 g (1.7 mmol) of phosphonate **33** in 10 mL of acetonitrile. The mixture was stirred for a day at room temperature, the precipitate was filtered off, and the filtrate was evaporated. The residue was dissolved in 20 mL of chloroform, washed with 5 mL of water and with 5 mL of brine, and dried over sodium sulfate. The solvent was removed, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature. Yield 0.32 g (54%), light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.07 s (3H, CH_3-ketone), 4.09–4.17 m (4H, CH_2O-phosphonate), 4.14 s (2H, CH_2SCN), 6.66 d (1H, H^4-furan, J_{HH} = 2.0 Hz), 7.07 d (1H, =CH, J_{PH} = 22.0 Hz), 7.50 d (1H, H^5-furan, J_{HH} = 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.31 d (CH_3-phosphonate, $^2J_{PC}$ = 5.9 Hz), 29.51 (CH_2SCN), 30.96 (CH_3-ketone), 63.26 d (CH_2OP, $^2J_{PC}$ = 5.8 Hz), 112.68 (SCN), 113.07 d (C^4-furan, $^4J_{PC}$ = 1.6 Hz), 121.07 d (C^3-furan, $^3J_{PC}$ = 4.6 Hz), 128.25 d (=CP, $^1J_{PC}$ = 181.0 Hz), 131.88 d (=CH, $^2J_{PC}$ = 3.1 Hz), 144.32 d (C^5-furan, $^4J_{PC}$ = 2.3 Hz), 144.54 d (C^2-furan, $^2J_{PC}$ = 7.1 Hz), 198.92 d (C=O, $^3J_{PC}$ = 19.9 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 12.45.

4-(3-Azidomethylfur-2-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (35). 0.21 g (3.5 mmol) of sodium azide and 0.03 g (0.17 mmol) of potassium iodide were added at room temperature to a solution of 0.52 g (1.6 mmol) of phosphonate **33** in 10 mL of acetonitrile. The mixture was stirred for 9 h at 70°C, and then the precipitate was filtered off. The filtrate was evaporated, the residue was dissolved in 20 mL of chloroform, washed with 5 mL of water and 5 mL of brine, and dried over sodium sulfate. After removal of the solvent, the residue was kept in a vacuum (1 mmHg) for 1 h at room temperature. Yield 0.20 g (38%), light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 t (6H, CH_3-phosphonate, J_{HH} = 7.0 Hz), 2.11 br. s (3H, CH_3-ketone), 4.09–4.20 m (4H, CH_2O-phosphonate), 4.25 br. s (2H, CH_2N_3), 6.61 d (1H, H^4-furan, J_{HH} = 1.2 Hz), 7.14 d (1H, , =CH, J_{PH} = 22.4 Hz), 7.58 d (1H, H^5-furan, J_{HH} = 1.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.35 d (CH_3-phosphonate, $^2J_{PC}$ = 6.5 Hz), 30.97 (CH_3-ketone), 45.57 (CH_2N_3), 63.66 d (CH_2OP, $^2J_{PC}$ = 5.4 Hz), 113.99 (C^4-furan), 121.75 d (C^3-furan, $^3J_{PC}$ = 4.7 Hz), 128.13 d (=CP, $^1J_{PC}$ = 180.7 Hz), 131.81 d (=CH, $^2J_{PC}$ = 2.2 Hz), 144. 48 d (C^5-furan, $^4J_{PC}$ = 2.8 Hz), 145.13 d (C^2-furan, $^2J_{PC}$ = 7.2 Hz), 198.28 d (C=O, $^3J_{PC}$ = 20.9 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 12.87.

4-(4-Azidomethylfur-3-yl)-4-(diethoxyphosphoryl)but-3-en-2-one (46). 1.00 g (15.2 mmol) of sodium azide and 0.03 g (0.17 mmol) of potassium iodide were added at room temperature to a solution of 2.45 g (7.6 mmol) of phosphonate **39** in 50 mL of acetone. The mixture was stirred for a week at room temperature, and then the precipitate was filtered off. The filtrate was evaporated, the residue was dissolved in 60 mL of chloroform, washed with 20 mL of water and 20 mL of brine, and dried over sodium sulfate. After removal of the solvent, the residue was kept in vacuum (1 mmHg) for 1 h at room temperature. Yield 2.37 g (95%) light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.30 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.15 br. s (3H, CH_3-ketone), 4.09–4.14 m (4H, CH_2O-phosphonate), 4.18 br. s (2H, CH_2N_3), 7.14 d (1H, , =CH, J_{PH} = 23.6 Hz), 7.36 br. s (1H, H^5-furan), 7.41 br. s (1H, H^2-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.31 d (CH_3-phosphonate, $^2J_{PC}$ = 6.0 Hz), 30.91 (CH_3-ketone), 44.82 (CH_2N_3), 63.10 d (CH_2OP, $^2J_{PC}$ = 6.2 Hz), 117.75 d (C^3-furan, $^2J_{PC}$ = 7.9 Hz), 120.57 d (C^4-furan, $^3J_{PC}$ = 4.7 Hz), 131.16 d (=CP, $^1J_{PC}$ = 179.3 Hz), 131.93 d (=CH, $^2J_{PC}$ = 2.8 Hz), 141.87 (C^5-furan), 142.11 d (C^2-furan, $^3J_{PC}$ = 6.9 Hz), 198.57 d (C=O, $^3J_{PC}$ = 21.6 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.20.

Reaction of chloromethyl derivatives 39, 40 with morpholine (*general procedure*). 20 mmol of morpholine was added with stirring to a solution of 10 mmol of chloromethylfuran **39** or **40** in 30 mL of benzene. The mixture was left at room temperature for 4 days and then extracted with 5% hydrochloric acid (3×15 mL). The extract was alkalified to pH = 9 by addition of sodium carbonate in small portions with stirring. The mixture was saturated

with sodium chloride and extracted with chloroform (3×20 mL). The extract was dried over sodium sulfate, chloroform was removed, and the residue was kept in vacuum (1 mmHg) for 1 h at room temperature.

4-[4-(*N*-Morpholinomethyl)fur-3-yl]-4-(diethoxyphosphoryl)but-3-en-2-one (44) was prepared from compound **39**. Yield 85%, light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.30 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.16 br. s (3H, CH_3-ketone), 2.86 d (4H, NCH_2-morpholine, J_{HH} = 4.8 Hz), 3.19 s (2H, NCH_2-furan), 3.62 d (4H, OCH_2-morpholine, J_{HH} = 4.8 Hz), 4.05–4.15 m (4H, CH_2O-phosphonate), 6.98 d (1H, , =CH, J_{PH} = 23.6 Hz), 7.38 br. s (1H, H^5-furan), 7.39 d (1H, H^2-furan, J_{HH} = 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 16.34 d (CH_3-phosphonate, $^2J_{PC}$ = 6.1 Hz), 30.66 (CH_3-ketone), 46.40 (NCH_2-furan), 53.66 (NCH_2-morpholine), 62.90 d (CH_2OP, $^2J_{PC}$ = 6.4 Hz), 66.84 (OCH_2-morpholine), 118.65 d (C^3-furan, $^2J_{PC}$ = 7.8 Hz), 121.69 d (C^4-furan, $^3J_{PC}$ = 4.8 Hz), 132.03 d (=CH, $^2J_{PC}$ = 2.6 Hz), 132.06 d (=CP, $^1J_{PC}$ = 178.6 Hz), 141.05 d (C^2-furan, $^3J_{PC}$ = 8.5 Hz), 141.99 (C^5-furan), 198.77 d (C=O, $^3J_{PC}$ = 22.4 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.89.

Ethyl 3-[4-(*N*-morpholinomethyl)fur-3-yl]-3-(diethoxyphosphoryl)acrylate (45) was prepared from compound **40**. Yield 55%, light brown syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 t (3H, CH_3-ester), 1.29 t (6H, CH_3-phosphonate, J_{HH} = 7.2 Hz), 2.85 d (4H, NCH_2-morpholine, J_{HH} = 4.6 Hz), 3.22 s (2H, NCH_2-furan), 3.63 d (4H, OCH_2-morpholine, J_{HH} = 4.6 Hz), 4.04–4.15 m (6H, CH_2O-phosphonate, CH_2O-ester), 6.80 d (1H, =CH, J_{HH} = 22.8 Hz), 7.35 br. s (1H, H^5-furan), 7.38 br. s (1H, H^2-furan). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.98 (CH_3-ester), 16.35 d (CH_3-phosphonate, $^2J_{PC}$ = 6.2 Hz), 46.43 (NCH_2-furan), 53.60 (NCH_2-morpholine), 60.87 (CH_2O-ester), 62.90 d (CH_2OP, $^2J_{PC}$ = 6.1 Hz), 66.95 (OCH_2-morpholine), 118.44 d (C^3-furan, $^2J_{PC}$ = 7.3 Hz), 121.51 d (C^4-furan, $^3J_{PC}$ 5.2 Hz), 132.09 d (=CH, $^2J_{PC}$ = 11.5 Hz), 136.12 d (=CP, $^1J_{PC}$ = 178.9 Hz), 141.01 d (C^2-furan, $^3J_{PC}$ = 6.1 Hz), 141.35 (C^5-furan), 164.17 d (C=O, $^3J_{PC}$ = 28.5 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 14.20.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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