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# Synthesis and Properties of (1,3-Dioxolan-2-yl)furans

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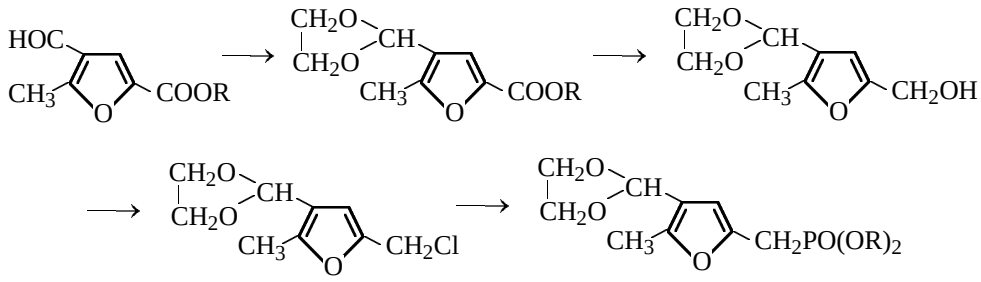
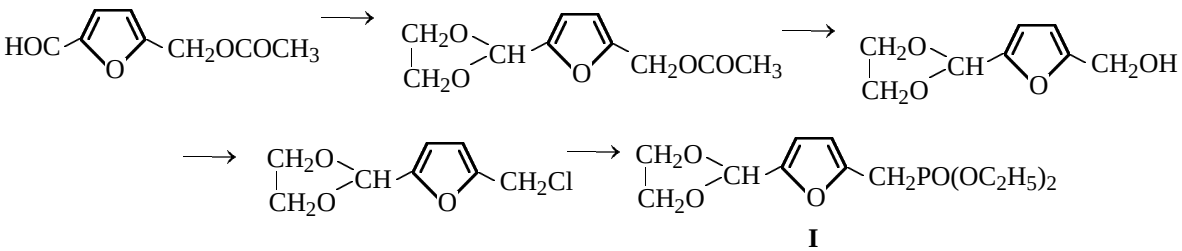
**Abstract** — Reaction of formylfurancarboxylates with excess ethylene glycol in the presence of *p*-toluenesulfonic acid gives rise to (1,3-dioxolan-2-yl)furancarboxylates. Reduction of these products with lithium aluminum hydride proceeds with preservation of the dioxolane ring. Except for 5-(1,3-dioxolan-2-yl)(hydroxymethyl)-2-methyl-3-furan, the obtained alcohols are unstable. Chlorides derived from them decompose under conditions of the Michaelis–Becker reaction, and no phosphorylation products are formed. By contrast, the above-mentioned stable alcohol by treatment with thionyl chloride in the presence of pyridine is converted to a fairly stable chloromethylfuran. The latter compound reacts with sodium diethyl phosphite in benzene to form the corresponding phosphonate that exists as a 1 : 4 mixture of two spectroscopically discernible conformers.

The problem of synthesis of phosphorus-containing aldehydes of the furan series has not yet been solved. It was previously shown that 2-(diethoxyphosphorylmethyl)furan is the only to undergo Vilsmeier formylation [1]. At the same time, chloromethyl- and bromomethylfurfurals do not form phosphonates under conditions of the Arbuzov reaction [2]. In view of the aforesaid, we set ourselves the task to develop a procedure for preparing halomethylfurans with protected aldehyde group and to involve them into the Michaelis–Becker reaction. For protective we chose the dioxolanyl group, since it is sufficiently stable in the presence of reductants and is not split in anhydrous media in the presence of such acidic agents as pyridine hydrochloride. An overall scheme of the transformations is presented below.




One of the isomers of the target phosphorylated products, dioxolane **I**, we previously prepared from 5-acetoxymethylfurfural by the following scheme [3]:




**I**

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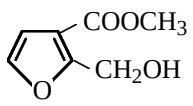
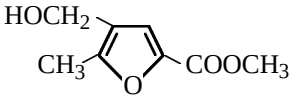
Approaches to other dioxolanylphosphonates of this series were not previously developed.

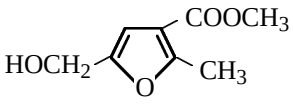
Hydroxymethylfurans **II**–**V** were used as starting compounds. They were oxidized to the corresponding aldehydes. Previously [4] this reaction was carried out with active manganese dioxide in benzene, but it was found that the yield and purity of the final products strongly depend on the quality of manganese dioxide, which is hardly controlled. Therefore, the procedure involving an aqueous pyridine solution of chromic acid was used. Compounds **II**–**V** were oxidized at room temperature, and the target aldehydes **VI**–**IX** were obtained in satisfactory yields without admixture of the starting alcohol. This result could not be achieved with manganese dioxide.



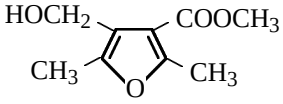

**II**



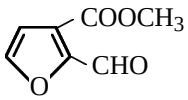

**III**



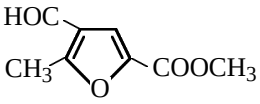

**IV**



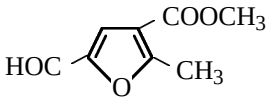

**V**



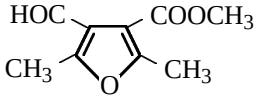

**VI**




**VII**



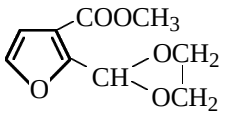

**VIII**



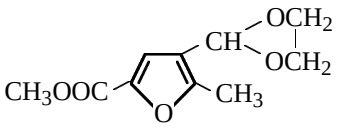

**IX**

Hydroxymethylfurans **II** and **III** are rather labile and form significant amounts of polymers on distillation. We tried to oxidize crude products obtained by alkaline methanolysis of the corresponding acetoxymethyfurans. In occurred that here aldehydes **VI** and **VII** are also formed in almost the same yields.

Acetalization of aldehydes **VI**–**XI** was carried out with excess freshly distilled ethylene glycol in benzene in the presence of *p*-toluenesulfonic acid. The evolving water was removed by azeotropic distillation with a Dean–Stark trap. Aldehydes **VI** and **VII** under these conditions gave 1,3-dioxolanes **X** and **XI**, while compounds **VII** and **IX** did not react. Aldehyde **IX** proved to be so passive that it could not even be involved in condensation with malonic acid in pyridine, which is usually quite facile with furancarbaldehydes.

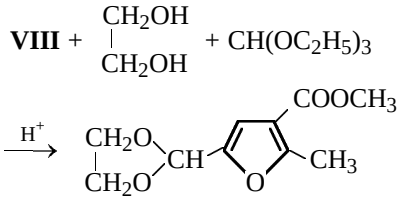



**X**

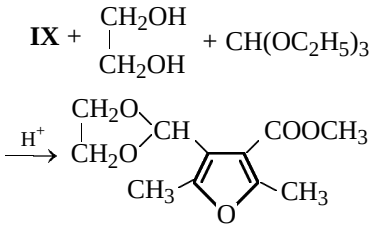



**XI**

To shift the acetalization equilibrium for aldehydes **VIII** and **IX** to dioxolane formation, we tried triethyl orthoformate as dehydrating agent [6]. This method proved to be effective, and dioxolanes **XII, XIV** were prepared in 47% and 57% yields, respectively. Diethyl acetals were not formed.




**XII**

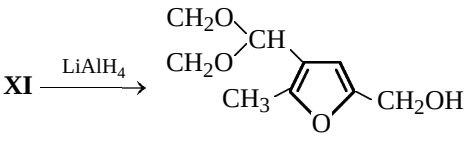



**XIII**

Further we studied reduction of the obtained compounds with lithium aluminum hydride. The reaction was carried out in ether by addition of a solution of dioxolane in absolute ether to a boiling suspension of lithium aluminum hydride in ether with vigorous stirring.

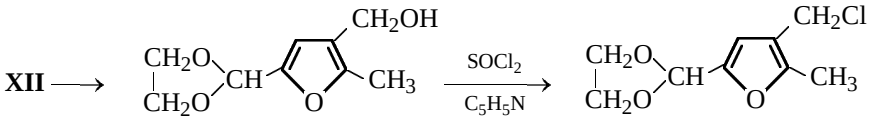
The reduction of dioxolane **XI** gave an unstable product that distilled with strong decomposition at 146–150°C (2 mm) and completely polymerized within 1–1.5 h at room temperature. Because of the fast gel formation in solution, we failed to obtain high-quality $^1$H NMR spectra of this compound. On treatment of the latter with 1 mol of thionyl chloride in

ether in the presence of pyridine with cooling, heat evolution and pyridine hydrochloride formation were observed. The pyridine hydrochloride was separated, and the filtrate was evaporated to give a dark brown oil which polymerized within 1 h at room temperature. Treatment of the product sodium diethyl phosphite in benzene, too, resulted in polymer formation only. Thus, the reduction of dioxolane **XI** gives an alcohol with a probable structure **XIV**, but rigorous structural assessment is prevented by the high lability of the product.

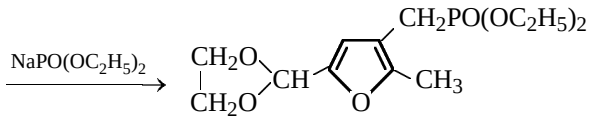


**XIV**

Dioxolane **XII** is reduced with lithium aluminum hydride to form alcohol **XV** in 51% yield. It is a stable viscous oil which can be distilled in a vacuum without decomposition.

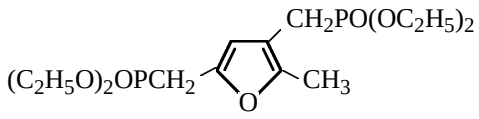


**XV** **XVI**



**XVII**

Treatment of product **XVI** with thionyl chloride in the presence of pyridine in ether gives chloride **XVI** which appreciably decomposes and darkens on distillation. Pure compound **XVI** can be handled for some days. However, we failed to obtain high-quality $^1$H NMR spectra of this compound, since its solutions always contain admixtures of oligomeric products. Chloride **XVI** reacts with sodium diethyl phosphite in benzene under reflux. Strong heat evolution is observed at the beginning of the reaction and strong foaming takes place over the course of 2 h. Sodium chloride is precipitated as particles covered with a sticky tar-like film. The reaction time is 8 h. Vacuum distillation of the decanted organic phase gives phosphonate **XVII** in 23% yield. Its $^1$H NMR spectrum contains doubled signals of the methyl group at the furan ring and of the $CH_2P$ group at the phosphorus atom. The intensity ratio of the upfield and downfield signals in both cases is 1:4. Hence, phosphonate **XVII** exists as a mixture of two conformers with equal $\delta_P$ values (22.8 ppm).

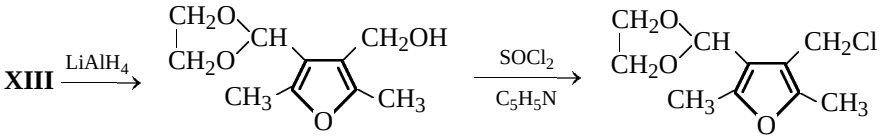


**XVIII**

The same effect we previously observed with compound **XVIII** with analogous location of bulky substituents. Note that in both cases the existence of spectrally discernible conformers was found in compounds having bulky substituents in the 2 and 4 positions, i.e. when the substituents can not form a common conjugation system with the furan ring. In ketones, alkyl carboxylates, nitriles, amides, and phenyl derivatives this effect has never been observed.

The reduction of dioxolane **XIII** gives alcohol **XIX** in 52% yield. It is a relatively stable compound which only slightly decomposes on vacuum distillation. Compound **XIII** reacts with thionyl chloride in the presence of pyridine to form an unstable chloride **XX** which can be quickly distilled in a vacuum in an amount of 1.5-2 g but quickly darkens just in the receiver. This compound gives no phosphorylation products under conditions of the Michaelis–Becker reaction. Only diethyl hydrogen phosphite could be distilled off from the reaction mixture, while all the furan derivative tarred.

Hence, (dioxolanyl)(hydroxymethyl)furans, despite the fact that the dioxolanyl substituent is a stronger electron acceptor than alkoxyl, are not considerably stabilized. Chloromethyl derivatives of dioxolanylfurans are evidently still more unstable than related (alkoxymethyl)(chloromethyl)furans, because under conditions of the Michaelis–Becker reaction only one




**XIX** **XX**

of the three obtained products gives the corresponding phosphonate, while in the case of alkoxymethylfurans all the six isomeric dialkoxyphosphorylmethylfurans were obtained [7].

## EXPERIMENTAL

The $^1$H NMR spectra were recorded on Tesla BS-487C (80 MHz) and Tesla BS 497C (100 MHz) spectrometers in $CCl_4$. The phosphorus chemical shifts were calculated from INDOR spectra.

**Oxidation of alcohols of the furan series to aldehydes with the Cornforth reagent** *(general procedure).* A solution of 0.06 mol of chromic anhydride in 6 ml of water was added dropwise with stirring and cooling to 20 ml of pyridine at 20–22°C. After 30-min keeping at 20°C, a solution of 0.015 mol of an alcohol in pyridine (1:1) was added dropwise over the course of 10–15 min. The reaction mixture was stirred for 2–3 h and left overnight. The pyridine was removed at reduced pressure (bath temperature 25–30°C), the residue was diluted with equal volume of water, and the resulting material was triturated with chloroform. The chromium hydroxide precipitate that formed was filtered off and washed with chloroform. The chloroform extracts were washed with water, filtered once more if necessary, and dried over calcium chloride. The solvent was removed at reduced pressure, solid target products were triturated with hexane and filtered off, and liquid ones were distilled in a vacuum.

**Metyl 2-formyl-3-furancarboxylate (VI).** Yield 46%, bp 102°C (1.5 mm), mp 77–78°C. $^1$H NMR spectrum, δ, ppm: 3.86 s ($COOCH_3$), 6.78 s (furan $H_4$), 7.63 s (furan $H^5$), 10.15 (CHO).

**Methyl 4-formyl-5-methyl-2-furancarboxylate (VII).** Yield 52%, bp 116°C (1 mm) slowly crystallizing syrup, mp 42°C. $^1$H NMR spectrum, δ, ppm: 2.63 s (furan $CH_3$), 3.79 s ($CH_3OOC$), 7.27 s (furan $H^3$), 9.78 s (CHO).

**Methyl 5-formyl-2-methyl-3-furancarboxylate (VIII).** Yield 74%, syrup. $^1$H NMR spectrum, δ, ppm: 2.36 (furan $CH_3$), 3.76 s ($CH_3OOC$), 6.41 s (furan $H^4$), 9.21 (CHO).

**Methyl 4-formyl-2,5-dimethyl-3-furancarboxylate (IX).** Yield 69%, bp 95°C (1 mm). $^1$H NMR spectrum, δ, ppm: 2.43 s (furan $CH_3$), 3.76 s ($CH_3OOC$), 10.23 s (CHO).

**Methyl 2-(dioxolan-2-yl)-3-furancarboxylate (X).** A mixture of 4.8 g of aldehyde **VI**, 5 ml of ethylene glycol, 0.1 g of *p*-toluenesulfonic acid, and 50 ml of benzene was refluxed with a Dean–Stark trap for 6 h, after which it was washed with a sodium carbonate solution, dried over calcium chloride, and distilled in a vacuum. Yield 2 g (38%), bp 128–130°C (1 mm). $^1$H NMR spectrum, δ, ppm: 3.75 s ($CH_3OOC$), 4.05 m (dioxolane $OCH_2$), 6.35 s (dioxolane OCHO), 6.55 s (furan $H^4$), 7.27 (furan $H^5$).

**Methyl 4-(dioxolan-2-yl)-5-methyl-2-furancarboxylate (XI).** A mixture of 12.1 g of aldehyde **VII**, 12 ml of ethylene glycol, 0.1 g of *p*-toluenesulfonic acid, and 60 ml of benzene was refluxed with a Dean–Stark trap for 6 h until the water had been removed completely. The resulting mixture was washed with a dulute sodium carbonate solution, dried over calcium chloride, and distilled in a vacuum. Yield 7.8 g (51%), bp 126°C (1 mm). $^1$H NMR spectrum, δ, ppm: 2.31 (furan $CH_3$), 3.73 s ($CH_3O$), 3.88 m (dioxolane $OCH_2$), 5.58 s ($OCH_2O$), 6.98 (furan $H^3$).

**Methyl 5-(dioxolan-2-yl)-2-methyl-3-furancarboxylate (XII).** A mixture of 13.4 g of aldehyde **VIII**, 25 ml of ethylene glycol, 15 ml of triethyl orthoformate, 0.1 g of *p*-toluenesulfonic acid, and 50 ml of chloroform was refluxed with stirring for 10 h and washed with a dilute sodium carbonate solution. The chloroform layer was dried over calcium chloride and distilled in a vacuum. Yield 7.4 g (47%), bp 130–132°C (1 mm). $^1$H NMR spectrum, δ, ppm: 2.50 s (furan $CH_3$), 3.78 s ($CH_3O$), 4.00 m (dioxolane $OCH_2$), 5.74 s (OCHO), 6.59 s (furan $H^4$).

**Methyl 4-(dioxolan-2-yl)-2,5-dimethyl-3-furancarboxylate (XIII).** A mixture of 9.6 g of aldehyde **IX**, 20 ml of ethylene glycol, 10 ml of triethyl orthoformate, 0.1 g of *p*-toluenesulfonic acid, and 100 ml of chloroform was refluxed for 10 h. The resulting mixture was washed with a dilute sodium carbonate solution, dried over calcium chloride, and distilled in a vacuum. Yield 6.8 g (57%), bp 112–114°C (1 mm).

$^1$H NMR spectrum, δ, ppm: 2.21 s (furan $CH_3^2$), 2.38 s (furan $CH_3^5$), 3.71 s ($CH_3O$), 3.84 m (dioxolane $CH_2O$), 5.98 s (OCHO).

**5-(Dioxolan-2-yl)-3-(hydroxymethyl)-2-methylfuran (XV).** To a suspension of 1.3 g of lithium aluminum hydride in 30 ml of anhydrous ether, a solution of 7.4 g of dioxolanylfuran **XII** in 10 ml of anhydrous ether was added dropwise with stirring at a rate sufficient to keep the reaction mixture slightly boiling. After **XII** had been added completely, the reaction mixture was stirred for 1 h, left overnight, and then treated with 10 ml of ethyl acetate and a saturated solution of ammonium chloride until an aqueous aluminum hydroxide gel had formed. The organic layer was decanted, the solvent was removed, and the residue was distilled in a vacuum. Yield 3.31 g (51%), bp 137°C (2 mm). $^1$H NMR spectrum, δ, ppm: 2.13 s (furan $CH_3$), 3.46 s (OH), 3.91 br.s (dioxolane $CH_2$), 4.26 s (furan $CH_2O$), 5.55 s (OCHO), 6.23 s (furan $H^4$).

**3-(Chloromethyl)-5-(dioxolan-2-yl)-2-methylfuran (XVI).** To a solution of 3.31 g of alcohol **XV** and 1.5 ml of pyridine in 25 ml of anhydrous ether, a solution of 1.3 ml of thionyl chloride was added dropwise with stirring at 0–5°C. The reaction mixture was stirred at room temperature for 4 h, diluted with 30 ml of benzene, the pyridine hydrochloride was filtered off, and the filtrate was distilled in a vacuum. Yield 2.3 g (63%), viscous oil darkening on distillation, bp 112°C (1 mm).

**3-(Diethoxyphosphorylmethyl)-5-(dioxolan-2-yl)-2-methylfuran (XVII).** A solution of 2.3 g of freshly distilled chloride **XVI** in 5 ml of benzene was added with stirring at 70°C to a solution of sodium diethyl phosphite, prepared from 0.3 g of sodium and 2 ml of diethyl hydrogen phosphite in 15 ml of benzene. Slight heat evolution, strong foaming, and precipitation of sodium chloride were observed. The reaction mixture was refluxed for 8 h, the precipitate was removed on a centrifuge, the solvent was distilled off at reduced pressure, and the residue was distilled in a vacuum. Yield 0.8 g (23%), bp 167–168°C (1 mm). $^1$H NMR spectrum, δ, ppm: 1.10 m (ethyl $CH_3$), 2.08 d (furan $CH_3$, minor conformer, $J_{HP}$ 2 Hz) and 2.22 d (furan $CH_3$, major conformer, $J_{HP}$ 2 Hz) (intensity ratio 1 : 4); 2.66 d ($CH_2P$, minor conformer, $J_{HP}$ 20 Hz) and 2.74 d ($CH_2P$, major conformer, $J_{HP}$ 20 Hz) (intensity ratio 1 : 4); 3.90 m ($OCH_2$–$CH_2O$ + $CH_2OP$), 5.64 m (OCHO), 6.22 s (furan $H^4$), $\delta_P$ 22.8 ppm.

**4-(Dioxolan-2-yl)-3-(hydroxymethyl)-2,5-dimethylfuran (XIX) and its reaction with thionyl chloride.** *a.* A solution of 8.4 g of dioxolanylfuran **XIII** in 10 ml of anhydrous ether was added dropwise with stirring to a suspension of 1.4 g of lithium aluminum hydride in 40 ml of anhydrous ether at a rate sufficient to keep the reaction mixture boiling. The reaction mixture was stirred for 3 h at room temperature and left overnight, after which it was treated with 10 ml of ethyl acetate and a saturated solution of ammonium chloride until a compact gel of inorganic compounds and a clear ethereal solution had formed. The solution was decanted, the ether was removed, and the residue was distilled in a vacuum to give 3.87 g (52%) of alcohol **XIX**, bp 122–123°C (1 mm). Distillation of the product was accompanied by certain decomposition. $^1$H NMR spectrum, δ, ppm: 2.15 s (furan $CH_3$), 4.00 s (dioxolane $CH_2O$), 4.20 s ($CH_2OH$), 5.55 s (OCHO).

*b*. To a solution of 3.87 g of alcohol **XIX** and 1.7 ml of pyridine in 25 ml of ether, a solution of 1.5 ml of thionyl chloride in 5 ml of ether was added dropwise with stirring at 10°C. The reaction mixture was stirred at room temperature for 4 h, the pyridine hydrochloride was filtered off, the ether was removed at reduced pressure, and the residue distilled in a vacuum to give 2.0 g of a product with bp 104°C (1 mm) and a melting point of about 40°C. The product quickly darke-ned even in a vacuum. Under conditions of the Michaelis-Becker reaction it gives only polymeric products. Solutions of this compound quickly pass into suspensions of tar-like particles; for this reason, we failed to obtain high-quality $^1$H NMR spectra.

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