Phosphorylation of 3,4-Dichloro-5-hydroxy-2(5*H*)-furanone with Tributylphosphine

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Abstract—The reaction of 3,4-dichloro-5-hydroxy-2(5*H*)-furanone with 2 mol of tributylphosphine involves substitution of both chlorine atoms to form an unstable diphosphonium salt. The latter undergoes partial hydrolysis with cleavage of one of the P–C bonds, yielding finally a monophosphorylation product. A probable reaction pathway is considered in terms of quantum chemistry.

Our previous studies on phosphorylation of 3,4-dichloro-5-hydroxy-2(5*H*)-furanone (mucochloric acid) (**I**) with phosphites, phosphines, and other trivalent phosphorus derivatives established that the reaction direction and the structure and composition of the reaction products much depend on the nature of substituents on the σ^3 -P atom [1]. This method of phosphorylation of halocyclenes allowed preparation of various 4- and 5-monophosphorylation products, such as oxofurylphosphonates, phosphonium salts, and phosphabetaines [2–4]. Attempted substitutions of both chlorine atoms in mucochloric acid most frequenly failed: Diphosphorylation products could not be isolated pure. Only one diphosphorylated furanone derivative was described, prepared by the reaction of



lithium diphenylphosphide with a mucochloric acid ester [5].

Triphenylphosphine reacts with mucochloric acid (I) to give phosphonium salt II whose structure was established by X-ray diffraction analysis [3, 4]. All attempts to obtain a diphosphorylation product by treatment of the monophosphonium salt with a second triphenylphosphine molecule or by reaction of furanone II with two mol of triphenylphosphine led to formation of two products by two concurrent pathways. One of them, $\mathbf{II} \rightarrow \mathbf{III}$, is equilibrium formation of diphosphonium salt III which, however, could not be isolated pure because of the easy convertion to monophosphorylation product II. The same result was obtained for the reaction of furanone I with two mol of triphenylphosphine. Besides, the second mole of triphenylphosphine can act as a base and effect dehydrochlorination of monophosphonium salt II to betaine IV.



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In the present work we studied the possibility of synthesis of a diphosphonium salt by reaction of furanone **I** with tributylphosphine, a more nucleophilic σ^3 -P derivative than triphenylphosphine. The phosphorylating power of tributylphosphine was previously demonstrated on an example of another halocyclane, 2-*N*-phenyl-4,5-dichloropyridazinone [6].

It was found that the reaction of Bu₃P with furanone I in a 1:1 ratio gives [3-chloro-2,5-dihydro-5hydroxy-2-oxofuran-4-yl]tributylphosphonium chloride (V) as a viscous undistillable liquid, $\delta_{\rm P}$ 64.4 ppm (Scheme 2). The IR spectrum of the product contains absorption bands at 1800 (C=O) and 1650 cm⁻¹ (C=C). The presence of the chloride ion was proved by the formation of an AgCl precipitate on treatment with an AgNO₃ solution. The ¹H NMR spectrum contains a group of signals belonging to the (C₄H₉)₃P group, as well as signals at 3.75 s (OH) and 4.1 ppm (CH; ³J_{PH} 9 Hz).

Quantum-chemical calculations (PM3 method) of the enthalpies of formation of the monophosphonium salts which can be formed by phosphorylation of furanone **I** with tributylphosphine gave evidence to show that β -phosphorylated furanone **Va** is slightly more favorable than the alternative, α -phosphorylation product **Vb**.



These data strongly suggest that the phosphine σ^3 -P atom is quaternized by substitution of the chlorine atom on C⁴ rather than on C³, which was earlier observed in all reactions of σ^3 -P derivatives with mucochloric acid [2, 3].

Treatment of monophosphorylated furanone V with triethylamine caused separation of triethylamine hydrochloride. It was filtered off, and the mother

liquor was examined by spectral methods. In its IR spectrum, instead of the disappeared bands at 1800 and 1650 cm⁻¹ related to the C=O and C=C groups of the furan ring, a broad strong band was observed at 1620–1640 cm⁻¹, which, according to [3], can be assigned to vibrations of phosphabetaine system **VI**. It is not be excluded that the phosphabetaine exists in equilibrium with phosphorane **VII**, as evidenced by the appearance of a weak singlet signal at δ_p –5.8 ppm in the phosphorane region. The quantum-chemical calculations showed that phosphabetaine **VI** is more stable than phosphorane **VII**. The enthalpies of formation of these structures are –140.6 and –129.1 kcal/mol, respectively.

The reaction of two mol of Bu_3P with mucochloric acid **I** in chloroform was accompanied by appearance of two strong doublets at δ_P 37.5 and 42.2 ppm (${}^3J_{PP}$ 11 Hz), implying formation of diphosphoniofuranone **VIII**. All attempts to isolate this product pure failed.

Nevertheless, this reaction in ether resulted in isolation of a white crystalline compound (mp 165–167°C after recrystallization in air; δ_P 36.6 ppm). It was identified as tributyl(2,5-dihydro-4,5-dihydroxy-2oxofuran-3-yl)phosphonium chloride (**IX**). The observation in its IR spectrum of strong bands at 1690 (C=O) and 1620 cm⁻¹ (C=C), as well as a broad diffuse band at 2250–2400 cm⁻¹ belonging to the hydroxy group involved in a strong hydrogen bond with the chloride ion confirms the proposed structure. The formation of such an H complex we reported previously [6].

The formation of furanone **IX** is best explained by a scheme offered for the formation of a structurally structure phosphonium salt obtained from tributylphosphine and 2-*N*-phenyl-4,5-dichloropyridazone [6] (Scheme 3, all H_f^0 values are in kcal/mol).

According to this scheme, the first stage of the reaction of furanone I with a twofold excess of Bu_3P involves substitution of two chlorine atoms to form an unstable diphosphonium intermediate **VIII**. During workup of the reaction mixture, partial hydrolysis with atmospheric moisture occurs, accompanied by P-C⁴ bond cleavage and formation of a stable final



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product **IX**. The preferred cleavage of the $P-C^4$ bond which is in the β position to the carbonyl group was confirmed by the reaction of 2-*N*-phenyl-4,5-dichloropyridazone with tributylphosphine. The structure of the product was established by X-ray diffraction [6]. Analogous process is likely to occur with diphosphonium salt **VIII**.

If the reaction of furanone **I** with two moles of Bu_3P was carried out under argon, then, along with salt **X**, a product with δ_P 77 ppm and tributylphosphine oxide (δ_P 43 ppm) could be isolated from the mother liquor [7]. The product with δ_P 77 ppm was assigned the structure of betaine (ylide) **X**. Its IR spectrum contained two strong C=O bands (1800 and 1770 cm⁻¹) and a C=C band at 1620 cm⁻¹.

The formation of monophosphorylated dihydroxyfuranone **IX** and its dehydrochlorination product **X** can also explained in terms of Scheme 3. The formation of a phosphine oxide was previously observed in the reaction of triphenylphosphine with mucochloric acid while recrystallization of a phosphabetaine [4]. The dehydrochlorination of a phosphonium salt (analogous to **IX**) and the formation of a stable betaine (ylide) was also previously observed in reactions of similar pyridazinone derivatives [8].

By PM3 quantum-chemical calculations of various

structures presented in Scheme 3 we could evaluate, in terms of enthalpy, the probability of separate stages. Thus, the first stage, that is formation of diphosphorylation product VIII, is thermodynamically unfavorable ($\Delta\Delta H_{\rm f}$ +83.87 kcal/mol); this stage is probably driven by solvation effects which were not considered in the calculations. At the same time, hydrolysis of product **VIII** with HCl evolution and tributylphosphine oxide formation (the latter can also be formed by oxidation of the starting Bu₃P with atmospheric oxygen) yields product **IX** which is thermodynamically favorable ($\Delta\Delta H_{\rm f}$ –20.51 kcal/mol). Subsequent dehydrochlorination of phosphonium salt **IX** to form betaine (ylide) **X** ($\Delta\Delta H_{\rm f}$ –2.80 kcal/mol) is also favorable. Analysis of the structure of this intermediate points to a considerable delocalization of electron density in this molecule. The charge distribution can be presented as follows:



Evidently, inspite of the strong difference in the reactivity of halogen-containing α , β -unsaturated carbonyl O- and N-containing heterocyclic com-

pounds: 3,4-dichloro-5-hydroxy-2(5*H*)-furanone and 2-*N*-phenyl-4,5-dichloro-3-pyridazinone, especially toward P-nucleophiles [6, 8], furanones and pyridazinones react with tributylphosphine, as well as with lithium diphenylphosphide [9], in a principally similar way.

To obtain experimental evidence for this reaction pathway, we reacted mucochloric acid with 2 mol of tributylphosphine and treated the reaction mixture with water. This caused not only $P-C^4$ bond cleavage but also hydrolysis of phosphonium salt IX (or betaine X) with formation of phosphine oxide XI (Scheme 3), δ_p 54 ppm. The IR spectrum of the product contains bands at 1780 (C=O), 1620 (C=C), 1220 (P=O), and 2600–2800 cm^{-1} (OH strongly hydrogen-bonded with P=O). It is known [10] that the tendency of one or another group to cleave on hydrolysis of phosphonium salts depends on the nature of all groups surrounding the phosphorus atom. In the case in hand, hydrolysis is evidently accompanied by cleavage of not only the electron-acceptor oxofuranylphosphonium group by the pathway VIII \rightarrow IX, as is usually observed in nucleophilic substitutions at the phosphonium center, but also of one butyl group, which leads to formation of phosphine oxide XI. Such scheme of hydrolysis of the phosphorylation products of 2-N-phenyl-4,5-dichloropyridazone was described by us previously [6].

EXPERIMENTAL

The IR spectra were recorded on a Specord-75 IR spectrometer at 700–3600 cm⁻¹. The ¹H and ³¹P NMR spectra were recorded on a Unity-300 spectrometer at 300 (¹H) and 121.421 MHz (³¹P) against internal HMDS (¹H) and external 85% orthophosphoric acid. The proton and phosphorus chemical shifts were determined with accuracies of ± 0.05 and ± 0.2 , respectively. The melting points were measured in a Boetius heating block. Quantum-chemical calculations were carried out by means of the MOPAC 6 program [11] on a Pentium-66 MMX computer.

Reaction of 3,4-dichloro-5-hydroxy-2(5*H*)furanone with tributylphosphine in a 1:1 ratio. Tributylphosphine, 0.83 g, was slowly added dropwise with stirring to 0.69 g of mucochloric acid in 40 ml of chloroform. The temperature of the reaction mixture rose by 4°C, and the solution became light yellow. The solvent was removed in a vacuum to leave a viscous yellow liquid, $\delta_{\rm P}$ 64.4 ppm. IR spectrum, v, cm⁻¹: 1800 (C=O); 1650 (C=C). ¹H NMR spectrum (CDCl₃), δ , ppm: 4.1 d (CH, ³J_{HP} 9 Hz), 3.75 s (OH). The product was treated with triethylamine, the triethylamine hydrochloride that precipitated was filtered off, and the filtrate was studied spectroscopically; δ_P -5.8 ppm.

Reaction of 3,4-dichloro-5-hydroxy-2(5*H*)furanone with tributylphosphine in a 1:2 ratio. Tributylphosphine, 5.75 g, was added dropwise with constant stirring to 2.37 g of mucochloric acid in 30 ml of ether. The solvent was removed in part, a white precipitate formed and was filtered off and washed with ether. mp 165–167°C; δ_p 36.6 ppm. IR spectrum, ν , cm⁻¹: 1690 (C=O), 1620 (C=C), 2250–2400 (OH).

Reaction of 3,4-dichloro-5-hydroxy-2(5*H*)furanone with tributylphosphine (1:2) and water. Tributylphosphine, 5.75 g, was added dropwise with constant stirring to 2.37 g of mucochloric acid. Then 20 ml of water was added, and the resulting mixture was thoroughly stirred. The chloroform layer was separated, and the solvent was removed by distillation to leave a viscous dark oil, from which crystals precipitated on standing and again liquefied in air, $\delta_{\rm p}$ 54 ppm. IR spectrum, v, cm⁻¹: 1780 (C=O), 1620 (C=C), 1220 (P=O), 2600–2800 (OH).

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