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Synthesis of (4-Hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylphosphine Oxide and Its Reactions with Aprotic Nucleophilic Reagents

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Abstract—Reaction of (4-hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylchlorophosphonium chloride with trimethyl orthoformate affords (4-hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylphosphine oxide. The latter undergoes dehydrochlorination under the action of trimethyl orthoformate and *O*-methyl diethylphosphinate, and with diphenylchloro- and triphenyl phosphines it gives the corresponding phosphonium salts.

Keywords: diphenylphosphine oxide, dehydrochlorination, phosphines, phosphonium salts, trimethyl orthoformate

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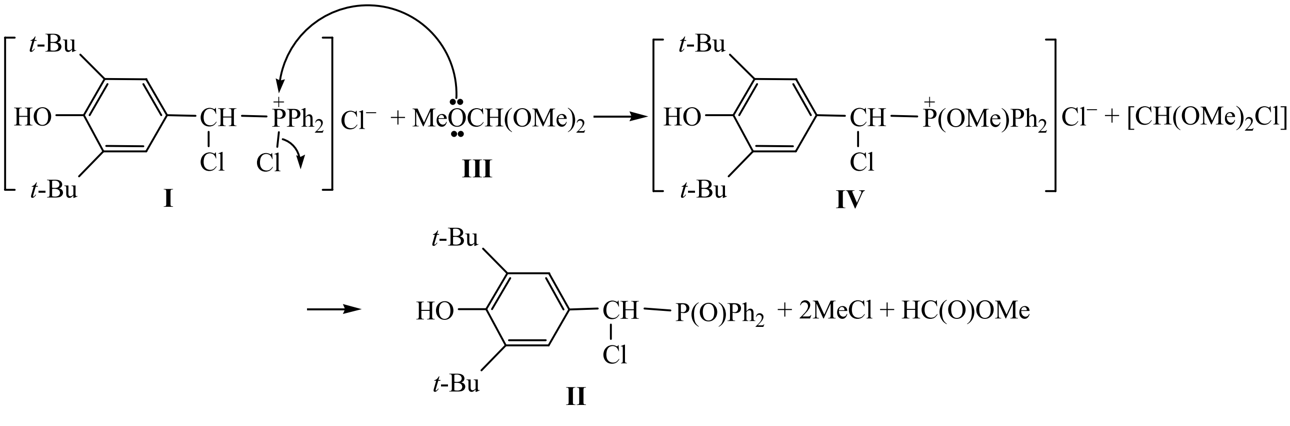
It was found previously that the reaction of equimolar amounts of 4-hydroxy-3,5-di-*tert*-butylbenzylidene chloride with diphenylchlorophosphine led to the formation of (4-hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylchlorophosphonium chloride (**I**) [1]. This salt under the action of sulfur dioxide or air moisture forms (4-hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylphosphine oxide (**II**). It is a promising starting reagent for the synthesis of phosphorylated derivatives of sterically hindered phenols which may exhibit antioxidant and biological activity.

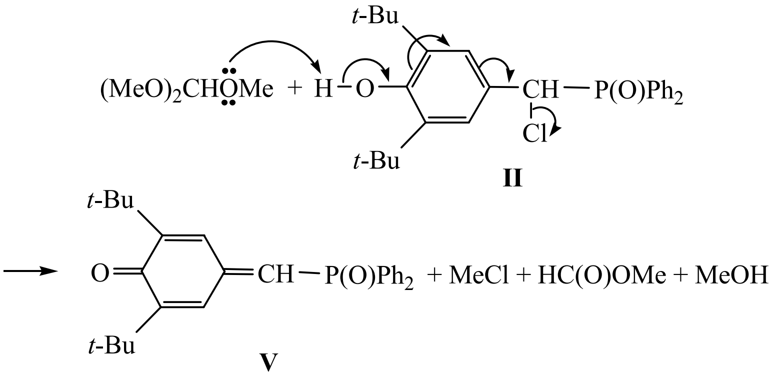
We have found that salt **I** reacts with trimethyl orthoformate **III** with heat evolution. The main product of the reaction of equimolar amounts of compounds **I** and **III** is phosphine oxide **II**. We presume that trimethyl orthoformate substitutes the phosphorus-bound chlorine atom with a methoxy group. Intermediate quasiphosphonium salt **IV** is stabilized by the formation of (4-hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylphosphine oxide (**II**) (Scheme 1).

With the purpose of synthesis of new phosphorylated derivatives of sterically hindered phenols

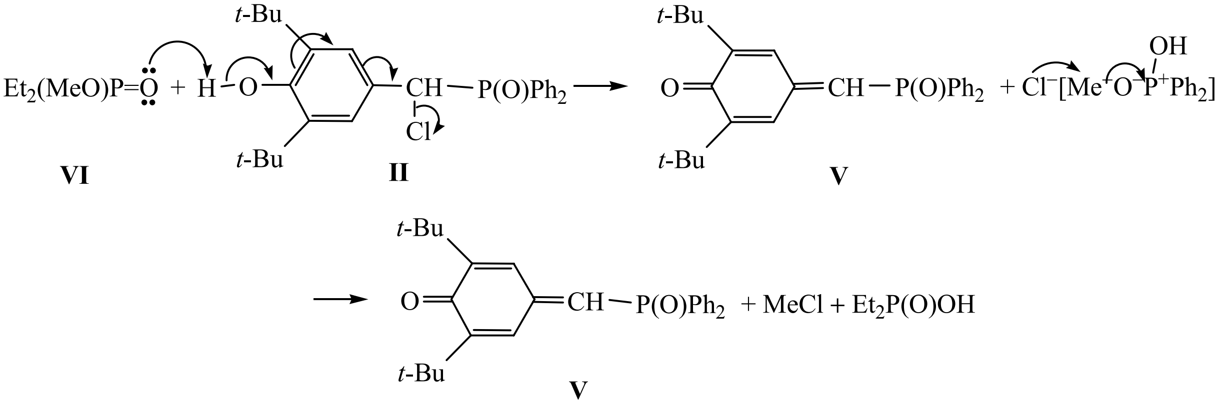
Scheme 1.



Scheme 2.



Scheme 3.



phosphine oxide **II** was involved in the reaction with a series of aprotic nucleophilic reagents like trimethyl orthoformate, *O*-methyl diethylphosphinate, diphenylchlorophosphine, and triphenylphosphine.

We have found that trimethyl orthoformate **III** in the reaction with compound **II** shows a dehydrochlorinating activity. Heating of phosphine oxide **II** with a large excess of orthoester **III** at 110–120°C for 2.5–3 h leads to the formation of 4-(diphenylphosphinylmethylene)-2,6-di-*tert*-butylcyclohexadien-2,5-one (**V**) (Scheme 2).

The result of the reaction between compounds **II** and **III** is a rare example of dehydrochlorinating reactivity of trialkyl orthoformates. Formerly, we discovered this property of the orthoethers on the examples of their interaction with tetra- and pentabromoethanes to form tri- and tetrabromoethylenes [2].

The sequence of chemical transformations presented above suggests that compound **V** may be synthesized by a direct reaction of salt **I** with a large excess of trimethyl orthoformate. This we confirmed experimentally. Refluxing a suspension of salt **I** in benzene with trimethyl orthoformate in 1 : 15 molar ratio for 2.5–3 h gives 4-(diphenylphosphinylmethylene)-2,6-di-*tert*-butylcyclohexadien-2,5-one (**V**) in a good yield.

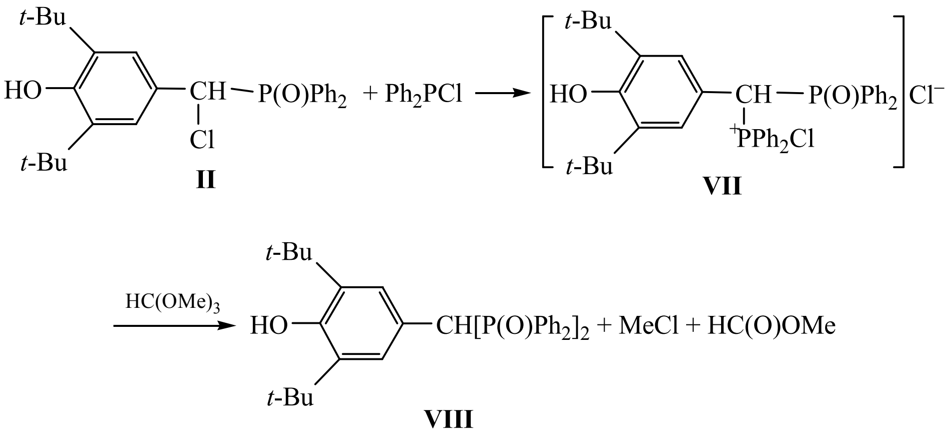
Compound **V** was prepared also by the reaction of phosphine oxide **II** with *O*-methyldiethylphosphinate **VI** (Scheme 3).

Formerly, we discovered dehydrohalogenating reactivy of P(IV) acid esters on an example of interaction of compound **IV** with polybromoethanes [3].

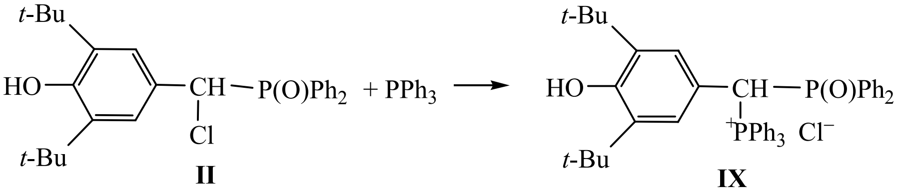
We have also studied the reactions of prosphine oxide **II** with diphenylchlorophosphine and triphenylphosphine, the compounds exhibiting nucleophilic properties [1, 4, 5]. Diphenylchlorophosphine adds compound **II** to give salt **VII**. Treating phosphine oxide **II** with trimethyl orthoformate results in the formation of 4-hydroxy-3,5-di-*tert*-butylphenylmethanebis(diphenylphosphine oxide) (**VIII**) (Scheme 4).

Triphenylphosphine quarternizes phosphine oxide **II** to give (4-hydroxy-3,5-di-*tert*-butylphenyl)(diphenyl-

Scheme 4.



Scheme 5.



phosphinyl)methanetriphenylphosphonium chloride in a high yield (Scheme 5).

The structure of compounds **II, V, VIII** was confirmed by the identity of the IR spectra of the compounds obtained to those of authentic samples, and also by the absence of the melting point depression in the case of mixed samples.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Tesla BS-567A (100 MHz) instrument. ^{31}P NMR spectra were obtained on a CXP-100 (36.5 MHz) spectrometer. Chemical shifts of hydrogen are given with respect to TMS, and of phosphorus, to 85% phosphoric acid.

IR spectra were recorded on a Perkin Elmer Spectrum 65 spectrometer from KBr pellets or mulls in mineral oil.

(4-Hydroxy-3,5-di-*tert*-butylphenyl)chloromethanediphenylphosphine oxide (II). A mixture of 4.18 g (0.008 mol) of salt **I** and 0.87 g (0.008 mol) of orthoester **III** was refluxed for 30 min in 25 mL of benzene until complete dissolution of the starting salt **I**. After removing volatile products in a vacuum 3.03 g (81.8%) of compound **II** was obtained, mp 182–185°C (from toluene). IR spectrum, ν, cm^{-1}: 3410 br (OH), 1239 (P=O). ^{1}H NMR spectrum (CCl_4 + $CDCl_3$), δ, ppm: 1.48 s [18H, $C(CH_3)_3$], 5.45 d (1H, CHP, $^2J_{PH}$ 6.5 Hz), 7.12 d (2H, C_6H_2, $^3J_{HH}$ 2 Hz), 7.40–8.20 m (10H, C_6H_5). ^{31}P NMR spectrum (acetonitrile): δ_P 28.96 ppm.

4-(Diphenylphosphinylmethylene)-2,6-di-*tert*-butylcyclohexadien-2,5-one (V). *a.* A mixture of 1.14 g (0.0025 m) of phosphine oxide **II** and 3.98 g (0.0375 mol) of orthoester **III** was boiled for 3 h at 110–120°C. After cooling of the reaction mixture crystals were formed. They were filtered off to obtain 0.87 g (83.6%) of product **V**, mp 219–221°C (isooctane–toluene) (219–221°C [6]). IR spectrum, ν, cm^{-1}: 1650, 1630 (C=O), 1590 (C=CH), 1250 (P=O). ^{1}H NMR spectrum (CCl_4 + $CDCl_3$), δ, ppm: 1.30 s [18H, $C(CH_3)_3$], 6.45 d (1H, CHP, $^2J_{PH}$ 22.5 Hz), 6.83 s, 8.30 s (2H, HC=C), 7.62 m (10H, C_6H_5).

b. While pouring of 7.96 g (0.075 mol) of orthoester **III** to 2.55 g (0.005 mol) of the salt **I** warming up of reaction mixture to 30°C took place. At the subsequent heating of the reaction mixture to 90–100°C the starting salt dissolved for 15–25 min with the liberation of gaseous methyl chloride. The reaction mixture was boiled for 2.5–3 h, cooled, and 1.45 g of precipitated crystals of product **V** was isolated, yield 69.4%, mp 219–221°C (isooctane–toluene).

c. A solution of 1.82 g (0.04 mol) of phosphine oxide **II** and 0.54 g (0.04 mol) of *O*-methyl diethylphosphinate in 5 mL of benzene was boiled for 5 h. Filtering off the crystalline product which precipitated after cooling and after removing of solvent from the mother liquor gave 1.62 g (91%) of compound **V**, mp 218–220°C (isooctane–toluene).

(4-Hydroxy-3,5-di-*tert*-butylphenyl)(diphenylphosphinyl)methanediphenylchlorophosphonium chloride (VII). A solution of 1.14 g (0.0025 mol) of phosphine oxide **II** and 0.55 g (0.0025 mol) of diphenylchlorophosphine in 20 mL of benzene was boiled for 6 h. The residue after removing off benzene in a vacuum was ground to powder to give 1.69 g of salt **VII**, mp 58–63°C. ^{31}P NMR spectrum (acetonitrile), δ_P, ppm: 27.67 (*P*-phosphine oxide), 34.05 (P-phosphonium). Found, %: Cl 10.65, 10.78; P 9.54, 9.39. $C_{39}H_{42}O_2P_2Cl_2$. Calculated, %: Cl 10.52, P 9.19.

(4-Hydroxy-3,5-di-*tert*-butylphenyl)methanebis-(diphenylphosphine oxide) (VIII). A mixture of 1.69 g (0.0025 mol) of salt **VII** and 0.27 g (0.0025 mol) of orthoester **III** was boiled in 20 mL of benzene. In the course of 1 h a gradual dissolution of starting salt **VII** and liberation of methyl chloride was observed. After removing of volatile products in a vacuum 1.08 g (69.7%) of bisphosphine oxide **VIII** was obtained, mp 258–262°C (toluene) (263–266°C [7]).

[(4-Hydroxy-3,5-di-*tert*-butylphenyl)(diphenylphosphinyl)methane]triphenylphosphonium chloride (IX). A solution of 0.82 g (0.0018 mol) of phosphine oxide **II** and 0.47 g (0.0018 mol) of triphenylphosphine in 25 mL of benzene was boiled for 20 min and allowed to stand for 24 h at room temperature. Colorless crystals of compound **IX** were obtained, 1.02 g (79%), mp 239–241°C. ^{1}H NMR spectrum ($CCl_4 + CDCl_3$), δ, ppm: 1.38 s [9H, $C(CH_3)_3$, 5.12 s (1H, OH), 7.15–8.25 m (25H, C_6H_5), 8.30–8.57 m (2H, C_6H_2), 8.75 d.d (1H, CH, $^2J_{PH}$ 7.23 Hz, $^2J_{PH}$ 4.05 Hz). Found, %: P 8.65, 8.95: Cl 5.05, 5.10. $C_{45}H_{47}O_2P_2Cl_2$. Calculated, %: P 8.64, Cl 4.95.

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