# Reaction of esters of P<sup>III</sup> acids with 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone\*

M. B. Gazizov, \* R. K. Ismagilov, L. P. Shamsutdinova, A. L. Tarakanova, and R. F. Karimova

Kazan National Research Technological University, 68 ul. K. Marksa, 420015 Kazan, Russian Federation. Fax: +7(843) 231 9505. E-mail: mukattisg@mail.ru

A reaction of P<sup>III</sup> acid esters with 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone leads to the formation of phosphorylated phosphorus ylides, 3,3',5,5'-tetra-*tert*-butylstilbenequinone, and diphosphorylated sterically hindered phenols. The schemes for the formation of these products through the primary key intermediates of betaine and phosphorus ylide structures were suggested.

**Key words:** 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dien-1-one, phosphorylated phosphorus ylides, diphosphorylated sterically hindered phenols.

A combination in the molecule of 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone of a polar system of conjugated double bonds and a chlorine atom with good leaving properties suggests its high reactivity with respect to different nucleophiles. It became easily available after discovering the dehydrochlorination reaction of 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride upon treatment with triethylamine and other bases.<sup>1</sup>

The high reactivity of 4-chloromethylidenequinone is mainly due to the energetically favorable process of transformation of a quinoid system of bonds to more stable aromatic. Its molecule has two reaction centers: the oxygen atom of the carbonyl group exhibiting protonaccepting properties and the electrophilic carbon atom of the chloromethylidene unit capable of undergoing attack by different nucleophiles.

Only several works were devoted to the studies of this compound. Thus, it was shown that it is capable to quantitatively add anhydrous HCl in the hexane solution with the formation of 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride.<sup>1</sup> Its reactions with amines were also described.<sup>2</sup> It is interesting that in this case the same products appeared as in the reaction of 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride with these amines. For example, the reaction of 4-chloromethylidenequinone with diethylamine leads to 2,6-di-*tert*-butyl-4-(diethylamino-methylidene)cyclohexa-2,5-dienone, while the reaction with aniline gives the corresponding azomethine. The 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone pyridinium salt can be obtained by the direct reac-

\* Dedicated to Academician of the Russian Academy of Sciences O. G. Sinyashin on the occasion of his 60th birthday. tion with pyridine. Based on these results, a conclusion has been drawn that 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone is an intermediate compound in the reactions of 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride with amines. Apart from that, it was found that 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride and 4-chloromethylidenequinone have a strong tendency to the transformation to the corresponding aldehyde upon treatment with water and alcohols.

The purpose of the present work is the development of a new method for the synthesis of diphosphorus-containing derivatives of sterically hindered phenols. To achieve this, we used the earlier unknown reaction of  $P^{III}$ acid esters **1** with 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone (**2**).

We for the first time studied the reaction of triethyl phosphite (1a) and O-ethyl diphenylphosphinite (1b) with compound 2. The main reaction products are phosphorylated phosphorus ylides 3a,b, stilbenequinone 4, and diphosphorylated sterically hindered phenols 5a,b (Scheme 1).

We suppose that initially the  $P^{III}$  acid ester 1 adds to highly electrophilic 4-chloromethylidenequinone 2 with the formation of the intermediate of betaine structure 6, which undergoes conversion to ylide 7 as a result of proton transfer to the O-anionic center (Scheme 2).

The intermediates 6 and 7 are the key structures for the explanation of further chemical transformations.

The betaine intermediate 6 undergoes intramolecular electron transfer and eliminates a chloride anion to be converted to a quasiphosphonium compound 8, which stabilizes to phosphorylated methylidenequinone 9, following the scheme of the second step in the Arbuzov—

Published in Russian in Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 12, pp. 2943–2947, December, 2016.

<sup>1066-5285/16/6512-2943 © 2016</sup> Springer Science+Business Media, Inc.





R = OEt (a), Ph (b)







Michaelis reaction. The addition of the  $P^{III}$  acid ester to compound 9 leads to phosphorylated betaine 10, undergoing conversion to phosphorylated ylide 3 after 1,6-proton shift (Scheme 3).

The transformation of intermediate compounds **9** to ylides **3** (see Scheme 3) upon treatment with  $P^{III}$  acid esters, <sup>3-6</sup>, as well as tertiary phosphines, <sup>7-9</sup> has been earlier confirmed experimentally.

The structure of ylides **3** was confirmed by the <sup>31</sup>P and <sup>1</sup>H NMR spectroscopy data. The <sup>31</sup>P NMR spectra exhibit two doublets from the nonequivalent phosphorus atoms: **3a**,  $\delta_{P(1)}$  29.20 ( ${}^{2}J_{P,P} = 91.25$  Hz, the phosphonate P atom);  $\delta_{P(2)}$  50.13 ( ${}^{2}J_{P,P} = 91.25$  Hz, the ylide P atom); **3b**,  $\delta_{P(1)}$  27.82 ( ${}^{2}J_{P,P} = 49.4$  Hz, the phosphine oxide P atom),  $\delta_{P(2)}$  50.49 ( ${}^{2}J_{P,P} = 49.4$  Hz, the ylide P atom).





The structure of ylide **3b** is also confirmed by its reaction with 3,5-di-*tert*-butyl-4-hydroxybenzylidene chloride, which, due to the dehydrochlorinating ability of compound **3b**, resulted in the formation of meth-ylidenequinone **2** and diphosphorylated sterically hindered phenol **5b** (Scheme 4).

#### Scheme 4 But Ph OEt But Cl ŹН HO HO CI ő But Bu Ρh 3b But But O But But Ρh ο 2 5b



Scheme 6

Following a parallel pathway, ylide 7a adds to the second molecule of chloromethylidenequinone 2 with the formation of the intermediate 11a containing two chlorine atoms in vicinal position (Scheme 5).

The presence of the electron-withdrawing quasiphosphonium group in compound **11a** facilitates the attack of triethyl phosphite on the positively charged chlorine atom with the formation of a new intermediate, the betaine **12a** (Scheme 6).

An argument in favor of this scheme is the presence in the  ${}^{31}P$  NMR spectrum of the reaction mixtures of a

#### Scheme 5



singlet at  $\delta_{^{31}P}$  –1.37 corresponding to the phosphorus atom in diethyl chlorophosphate.

The double bond of the intermediate 12a, subjected to the electronic influence of the negatively charged oxygen atom, is capable of deprotonating the phenol hydroxy group of other molecule of the same intermediate. The resulting betaine 13 stabilizes *via* the elimination of triethyl phosphite with the formation of a stable system of stilbenequinone 4 (Scheme 7).

The formation of diphosphorylated sterically hindered phenols can be explained by the solvolysis of phosphorylated ylides.<sup>3</sup> The intra- or intermolecular deprotonation of the ethoxy group by the carbanionic center of ylide **3** proceeds with liberation of ethylene and the formation of the stable phosphoryl group.

The experiments showed that the use of an excess of esters 1 with respect to chloromethylidenequinone 2 promotes the formation of ylides 3. In the case of a two-fold excess of chloromethylidenequinone 2, the yield of stilbenequinone 4 depends on the nature of  $P^{\rm III}$  acid ester: the use of triethyl phosphite increases its yield to 38%, while no stilbenequinone 4 is formed at all when *O*-ethyl diphenylphosphinite is used. It is possible that two bulky phenyl groups at the phosphorus atom in ylide 7b, in contrast to the two ethoxy groups in ylide 7a, hinder the nucleophilic attack on 4-chloromethylidenequinone 2 (see Scheme 5). The transformation of ylide 7b to diphosphorylated sterically hindered phenol 5b becomes a predominant direction of the reaction.



Scheme 7



The structure and composition of the synthesized compounds were confirmed by elemental analysis and <sup>1</sup>H and <sup>31</sup>P NMR spectra.

In conclusion, we have developed a new method for the synthesis of sterically hindered phenols **3** and **5** containing two P atoms by the earlier unknown reaction of 2,6-di-*tert*-butyl-4-chloromethylidenecyclohexa-2,5-dienone with P<sup>III</sup> acid esters. The reaction gives 3,3',5,5'-tetra-*tert*-butylstilbenequinone **4** as a side product, which was isolated in the individual state when a two-fold excess of 4-chloromethylidenequinone **2** was used. The schemes suggested for the formation of products **3**, **4**, and **5** include the formation of primary key intermediates of betaine **6** and ylide **7** nature.

## Experimental

<sup>1</sup>H NMR spectra were recorded on Tesla BS-567A (100 MHz), Bruker WP-250 (250 MHz), and Bruker MSL-400 (400 MHz), using SiMe<sub>4</sub>, CDCl<sub>3</sub>, acetone-d<sub>6</sub> as references. <sup>31</sup>P NMR spectra were recorded on Bruker MSL-400 (162 MHz) and Bruker WP-250 (101 MHz), using 85% aqueous H<sub>3</sub>PO<sub>4</sub> as an external standard.

**2,6-Di**-*tert*-butyl-4-(chloromethylidene)cyclohexa-2,5dienone (2) was synthesized according to the known procedure, <sup>1</sup> m.p. 59–61 °C. <sup>1</sup>H NMR (CCl<sub>4</sub> + CDCl<sub>3</sub>),  $\delta$ : 1.25, 1.30 (both s, 18 H, CMe<sub>3</sub>); 6.85 (s, 1 H, CHCl); 6.88 (d, 1 H, CH, <sup>4</sup>J<sub>H,H</sub> = = 2 Hz); 7.45 (d, 1 H, CH, <sup>4</sup>J<sub>H,H</sub> = 2 Hz).

Reaction of triethyl phosphite (1a) with 2,6-di-*tert*-butyl-4chloromethylidenecyclohexa-2,5-dienone (2) at different ratios of

reagents. A (the ratio of reagents 1:1). The addition of ester 1a (0.83 g, 5 mmol) to chloromethylidenequinone 2 (1.26 g, 5 mmol) was accompanied by warming-up and the formation of a dark claret solution. After 3–5 min, a crystalline product precipitated from the reaction mixture. The mixture was allowed to stand at ~20 °C for 6 h, then treated with hexane (2×10 mL). (3,5-Bis-tert-butyl-4hydroxyphenyl)diethoxyphosphoryl(triethoxy)phosphoniomethyl ylide (3a) (0.83 g, 63%) was isolated with impurities of compounds 4 and 5a (<sup>1</sup>H NMR spectroscopy data), m.p. 128–131 °C (heptane; cf. Ref. 3: 131-133 °C). Found (%): C, 56.95; H, 8.70; P, 11.72. C<sub>25</sub>H<sub>46</sub>O<sub>7</sub>P<sub>2</sub>. Calculated (%): C, 57.69; H, 8.91; P, 11.92. <sup>31</sup>P NMR (CDCl<sub>3</sub>),  $\delta$ :  $\delta_{P(1)} = 29.20$  (<sup>2</sup> $J_{P,P} = 91.25$  Hz, phosphonate – P);  $\delta_{P(2)} = 50.13$  (<sup>2</sup>J = 91.25 Hz, ylide – P). <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 1.32 (t, 6 H, POCH<sub>2</sub><u>CH<sub>3</sub></u>, <sup>3</sup> $J_{H,H}$  = 7.5 Hz); 1.40 (t, 9 H, P<sup>+</sup>OCH<sub>2</sub>CH<sub>3</sub>,  ${}^{3}J_{H,H} = 7.5$  Hz); 1.55 (s, 18 H, CMe<sub>3</sub>); 4.08 (q, 4 H, POCH<sub>2</sub>,  ${}^{3}J_{P,H} = {}^{3}J_{H,H} = 7.5$  Hz); 4.32 (q, 6 H, P<sup>+</sup>OCH<sub>2</sub>,  ${}^{3}J_{P,H} = {}^{3}J_{H,H} = 7.5$  Hz); 5.08 (s, 1 H, OH); 7.18 (s, 2 H,  $C_6H_2$ ). Product **3a** upon melting and dissolution in organic solvents (heptane, benzene, chloroform) acquired a reddish violet color characteristic of ylides. The presence in the <sup>1</sup>H and <sup>31</sup>P NMR spectra of compound **3a** of weak resonance signals at  $\delta$  3.32 (t, CH,  ${}^{2}J_{P,H} = 25$  Hz) and  $\delta_{P} 21$  confirmed the presence of small amounts of diphosphonate **5a** isolated earlier in the individual state ( $\delta$ , 3.32,  ${}^{2}J_{P,H} = 25$  Hz,  $\delta_{P}$  21).<sup>10</sup> The colored hexane solution after evaporation of volatile components in vacuo gave 3,3',5,5'-tetrakistert-butyl-4,4'-dihydroxystilbenequinone (4) (0.18 g, 16.6%), an orange precipitate, m.p. 305-308 °C (toluene; cf. Ref. 11: 310-311 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 1.2 (d, 36 H, CMe<sub>3</sub>, <sup>5</sup> $J_{H,H}$  = 2 Hz); 6.97 (d, 1 H, CH,  ${}^{3}J_{H,H} = 2$  Hz); 7.22 (s, 4 H, C<sub>6</sub>H<sub>2</sub>); 7.47 (d, 1 H, CH,  ${}^{3}J_{\rm H,H} = 2$  Hz).

**B** (the ratio of reagents 3 : 1). A mixture of ester 1a (1.66 g, 10 mmol) and compound 2 (0.85 g, 3.3 mmol) was heated at 40 °C

for 1 h. The crystals formed upon cooling were treated with hexane to obtain compound **3a** (1.10 g, 62%), m.p. 128-131 °C (heptane).

*C* (the ratio of reagents 1 : 2). A mixture of ester **1a** (0.83 g, 5 mmol) and chloromethylidenequinone **2** (2.52 g, 10 mmol) was heated at 60-80 °C for 2 h. After 48 h, stilbenequinone **4** (0.83 g, 38%) was collected by filtration, m.p. 298–303 °C (toluene).

Reaction of O-ethyl diphenylphosphinite (1b) with 2,6-di-tertbutyl-4-chloromethylidenecyclohexa-2,5-dienone (2) at different ratios of reagents. A (the ratio of 2 : 1 in a hexane solution). The addition of compound 2 (0.63 g, 2.5 mmol) to a solution of ester 1b (1.15 g, 5 mmol) in hexane (3 mL) was accompanied by warmingup and deepening of the color. Trituration of the reaction mixture led to the restructuring of the crystals. The reaction mixture was allowed to stand at 20-25 °C for 24 h, thus obtaining (3,5-bis-tertbutyl-4-hydroxyphenyl)diphenylphosphoryl(diphenyl)ethoxyphosphoniomethyl ylide (3b) (0.95 g, 59%), m.p. 212–215 °C (toluene-heptane, 4 : 1). Found (%): C, 75.35; H, 7.18; P, 9.45. C<sub>41</sub>H<sub>46</sub>O<sub>3</sub>P<sub>2</sub>. Calculated (%): C, 75.92; H, 7.09; P, 9.57. <sup>31</sup>P NMR  $(CDCl_3), \delta: \delta_{P(1)} 27.82 (^2J_{PP} = 49.40 \text{ Hz}, \text{ phosphine oxide}), \delta_{P(2)}$  $50.49 (^2J = 49.4 \text{ Hz}, \text{ ylide})$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 1.30 (s, 18 H, CMe<sub>3</sub>); 1.70 (t, 3 H, CH<sub>3</sub>,  ${}^{3}J_{H,H} = 7$  Hz); 4.80 (q, 2 H, CH<sub>2</sub>,  ${}^{3}J_{P,H} = {}^{3}J_{H,H} = 7$  Hz); 4.95 (s, 1 H, OH); 6.92 (d, 2 H, C<sub>6</sub>H<sub>2</sub>,  ${}^{2}J_{\text{H,H}} = 2 \text{ Hz}$ ; 7.40–8.10 (m, 20 H, C<sub>6</sub>H<sub>5</sub>). The concentration of the toluene-heptane mother liquor gave (3,5-bis-tert-butyl-4hydroxyphenyl)bis(diphenylphosphoryl)methane (5b) (0.26 g, 16.8%), m.p. 260-263 °C (toluene; cf. Ref. 12: 262-264 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>), δ: 1.25 (s, 18 H, CMe<sub>3</sub>); 4.72 (t, 1 H, CH,  ${}^{3}J_{P,H} = 12 \text{ Hz}$ ; 5.10 (s, 1 H, OH); 6.95 (s, 2 H, C<sub>6</sub>H<sub>2</sub>); 7.20-8.30  $(m, 20 H, C_6 H_5).$ 

**B** (the ratio of reagents 3:1 in a toluene solution).Compound **3b** (0.81 g, 78%) was obtained from a mixture of solutions of ester **1b** (1.15 g, 4.5 mmol) in toluene (3 mL) and compound **2** (0.39 g, 1.5 mmol) in toluene (3 mL) (20–25 °C, 48 h), m.p. 209–211 °C (toluene).

*C* (the ratio of reagents 1 : 2 in a hexane solution). A mixture of solutions of ester **1b** (0.58 g, 2.5 mmol) in hexane (5 mL) and compound **2** (1.26 g, 5 mmol) in hexane (5 mL) was refluxed for 1 h. A colorless crystalline product was filtered from the hot solution to obtain compound **5b** (0.53 g, 68%), m.p. 259–262 °C (toluene—heptane, 10 : 1). The starting chloromethylidenequinone **1** (0.21 g), m.p. 56–59 °C (*cf.* Ref. 1: 59–61 °C) was recovered from the reaction hexane solution after cooling.

Reaction of ylide (3b) with 3,5-di-*tert*-butyl-4hydroxybenzylidene chloride. A mixture of solutions of ylide 3b (0.96 g, 1.5 mmol) in benzene (10 mL) and 3,5-di-*tert*-butyl-4hydroxybenzylidene chloride (0.43 g, 1.5 mmol) in benzene (5 mL) was refluxed for 1.5 h. After evaporation of the solvent, the residue was treated with cold hexane to obtain product 5b (0.78 g, 85%), m.p. 259–263 °C (toluene). Chloromethylidenequinone 2 (0.22 g, 56%) was isolated from the hexane solution after evaporation of the solvent, m.p. 58–61 °C (*cf.* Ref. 1: 59–61 °C). <sup>1</sup>H NMR (CCl<sub>4</sub>– CDCI<sub>3</sub>,),  $\delta$ : 1.25, 1.30 (both s, 18 H, CMe<sub>3</sub>); 6.85 (s, 1 H, CHCl); 6.88 (d, 1 H, CH,  ${}^{4}J_{H,H} = 2$  Hz); 7.45 (d, 1 H, CH,  ${}^{4}J_{H,H} = 2$  Hz).

This work was financially supported by the Ministry of Education and Science of the Russian Federation within the Basic Part of the State Assignment No. 2014/56.

### References

- L. K. Popov, F. M. Egidis, V. V. Ershov, *Izv. Akad. Nauk SSSR*, Ser. Khim., 1968, 902 [Bull. Acad. Sci USSR, Div. Chem. Sci. (Engl. Transl.), 1968, 17].
- F. M. Egidis, L. K. Popov, A. A. Volod'kin, V. V. Ershov, M. N. Volkotrub, *Izv. Akad. Nauk SSSR, Ser. Khim*, 1970, 2580 [*Bull. Acad. Sci USSR, Div. Chem. Sci. (Engl. Transl.*), 1970, **19**].
- H. Gross, J. Keitel, B. Costiseella, *Phosphorus, Sulfur, Silicon*, 1992, 70, 331.
- H. Gross, J. Keitel, B. Costisella, *Phosphorus, Sulfur, Silicon*, 1993, 75, 83.
- H. Gross, J. Keitel, B. Costisella, *Phosphorus, Sulfur, Silicon*, 1994, 86, 169.
- M. B. Gazizov, R. K. Ismagilov, L. P. Shamsutdinova, R. F. Karimova, R. B. Zimaletdinov, O. G. Sinyashin, *Russ. J. Gen. Chem. (Engl. Transl.)*, 2009, **79**, 155 [*Zh. Obshch. Khim.*, 2009, **79**, 159].
- Ju. V. Bachtiyarova, M. S. Bondar, V. V. Andriashin, O. N. Kataeva, I. V. Galkina, V. I. Galkin, *Mendeleev Commun.*, 2009, **19**, 37.
- M. S. Bondar´, V. V. Andriyashin, Yu. V. Bakhtiyarova, I. V. Galkina, V. I. Galkin, Sbornik tezisov XV Mezhdunarodnoi Konferentsii po khimii soedinenii fosfora [Abstracts of XV International Conference on Chemistry of Phosphorus Compounds], St-Petersburg, 2008, 336 (in Russian).
- Yu. V. Bakhtiyarova, M. S. Bondar', V. V. Andriyashin, I. V. Galkina, V. I. Galkin, *Tezisy XVIII Mendeleevskogo s"ezda obshchei i prikladnoi khimii [Abstracts of XVIII Mendeleev Summit on General and Applied Chemistry*], Moscow, 2007, V. 1, C. 135 (in Russian).
- R. K. Ismagilov, V. V. Moskva, D. B. Bagautdinova, V. P. Arkhipov, L. Yu. Kopylova, *Zh. Obshch. Khim.*, 1992, **62**, 2488 [*Russ. J. Gen. Chem. (Engl. Transl.*), 1992, **62**].
- Yu. A. Bruk, A. Yu. Rachinsky, *Zh. Obshch. Khim.*, 1964, 34, 2983 [*Russ. J. Gen. Chem. (Engl. Transl.*), 1964, 34].
- M. B. Gazizov, R. K. Ismagilov, L. P. Shamsutdinova, R. Z. Musin, R. F. Karimova, A. A. Bashkirtsev, O. G. Sinyashin, *Russ. J. Gen. Chem. (Engl. Transl.)*, 2010, **80**, 533 [*Zh. Obshch. Khim.*, 2010, **80**, 505].

Received December 28, 2015; in revised form August 2, 2016