2078 *Russian Chemical Bulletin, International Edition, Vol. 60, No. 10, pp. 2078—2080, October, 2011*

Reaction of 3-methoxy-2-methylphenol with 2-ethoxyvinylphosphonic dichloride

Yu. M. Sadykova,[a]* **N. V. Dalmatova,**[b] **A. R. Burilov,**[a] **M. A. Pudovik,**[a] **and A. B. Dobrynin**[a]

[a]*A. E. Arbuzov Institute of Organic and Physical Chemistry Kazan Scientific Center of the Russian Academy of Sciences,*
8 ul. Akad. Arbuzova, 420088 Kazan, Russian Federation.
Fax: +7 (843) 273 2253. E-mail: sadykova@iopc.ru
[b]*Kazan State Technological University,*
68 ul. K. Marksa, 420015 Kazan, Russian Federation

Condensation of 2-ethoxyvinylphosphonic dichloride with 3-methoxy-2-methylphenol in dioxane in the presence of trifluoroacetic acid results in 5,13-dimethoxy-4,14-dimethyl-1-phospha-2,16-dioxatetracyclo[7.7.1.$0^{3,8}$.$0^{10,15}$]heptadeca-3,5,7,10,12,14-hexaene 1-oxide and 2-hydroxy-7-methoxy-8-methyl-2-oxobenzo[*e*]-1,2-oxophosphorine.

Key words: 2-ethoxyvinylphosphonic dichloride, 3-methoxy-2-methylphenol, 2-methylresorcin, condensation reaction, bicyclic phosphonates.

There are plenty of works devoted to the development of methods for the synthesis and studies of properties of the phosphorus-containing cage-like structures, whose framework is formed from three endocyclic P—O (see Refs 1—7), P—N (see Ref. 8), or P—C bonds (see Ref. 9). At the same time, there are virtually no information on the synthesis of the cage-like compounds formed with simultaneous involvement of endocyclic P—O and P—C bonds. The synthesis of phosphonates containing both P—O and P—C bonds is only mentioned in the works[10—13] dealing with the chemistry of carbophosphatranes. However, the method of their preparation is laborious enough, it includes several steps, and the final products are obtained in low yields.

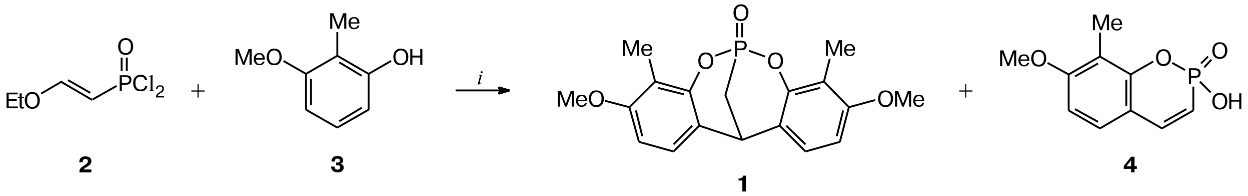
We have developed an original one-step method for the synthesis of phosphonate **1** of a cage-like structure by the condensation of 2-ethoxyvinylphosphonic dichloride[14] **2** with 3-methoxy-2-methylphenol[15] **3** in dioxane in the presence of trifluoroacetic acid (Scheme 1).

It should be noted that the reaction under study gives not only a bicyclic phosphonate **1** as the final product, but also phosphorine **4**, the ratio **1** : **4** = 2 : 1 (see Scheme 1). It is obvious that the reaction proceeds through the intermediate formation of chlorophosphorine **5** (Scheme 2), which has a chemical shift around δ 10 in the ^{31}P NMR spectrum of the reaction mixture and is easily transformed into phosphorine **4** in the process of isolation. Compounds of such a type have been described, and it was noted that the corresponding to them chlorides readily undergo hydrolysis upon the action of water.[16]

The condensation of phenol **3** and 2-ethoxyvinylphosphonic dichloride **2** in the ratio 2 : 1 leads to an insignificant (about 5%) increase in the yield of the cage-like compound **1**.

Compound **1** is a white crystalline substance, soluble in DMSO and in the acetone—water mixture. The structures and composition of the products obtained were confirmed by the ^{1}H and ^{31}P NMR and IR spectroscopic data, elemental analysis, as well as by X-ray crystallography. According to the X-ray diffraction data for the crystal of compound **1** (Fig. 1), the bond distances in the bicyclic system are within the standard values for these

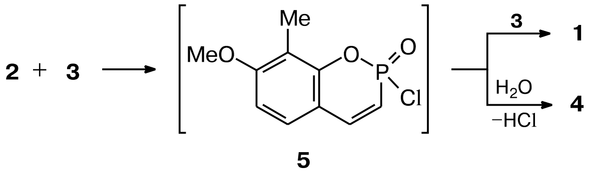
Scheme 1



i. CF$_3$COOH, dioxane.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2041—2043, October, 2011.

Scheme 2



types of bonds. The phosphorus atom has a tetrahedral configuration. The heterocycles, forming the bicyclic system, are in the C-*sofa* conformation; the five-atomic fragment P(2)O(1)C(16)C(11)C(10) is planar. The heterocyclic fragments are turned with respect to each other by 71.33°. The earlier described carbon compound[17] with similar structure also has the rings in the *sofa* conformation. Due to the intermolecular hydrogen bonds of the C—H...O-type involving the phosphoryl and methoxy groups, the corrugated layers are formed, which, in turn, form a bilayer structure directed along the 0*a* axis.

The crystalline compound **4** is readily soluble in ethanol and DMSO. The structure of product **4** was established by X-ray diffraction analysis (Fig. 2). The heterocycle has the conformation of distorted boat, the five-atomic fragment O(1)C(8A)C(4A)C(4)C(3) is planar within 0.056(3) Å, the phosphorus atom P(2) comes out of this plane by 0.3396(7) Å. In the crystal **4**, the phosphoryl group forms a classic hydrogen bond of the O—H...O-type with the hydroxy group of a neighboring molecule, due to which an infinite chain of molecules is formed along the 0*a* axis.

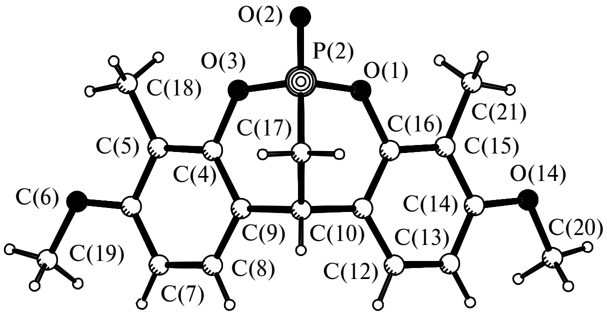


Fig. 1. Geometry of the molecule **1** in crystal.

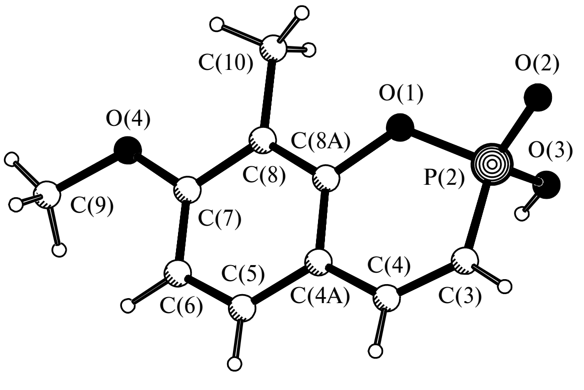
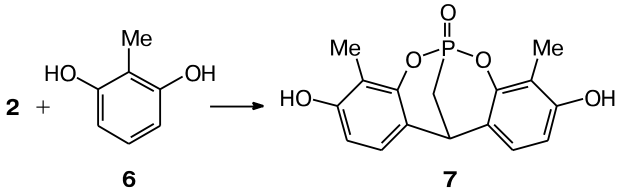


Fig. 2. Geometry of the molecule **4** in crystal.

The condensation of 2-ethoxyvinylphosphonic dichloride **2** with 2-methylresorcin **6** in dioxane in the presence of trifluoroacetic acid gives bicyclic phosphonate **7** as the only product in 80% yield (Scheme 3).

Scheme 3



i. CF_3COOH, dioxane.

The structure and composition of the thus obtained bicyclic phosphonate **7** were confirmed by the ^1H and ^{31}P NMR and IR spectroscopic data, elemental analysis data, as well as by mass spectrometry.

Experimental

^1H NMR spectra were recorded on a Bruker AVANCE-600 spectrometer (600 MHz) relative to the signals for the residual protons of the deuterated solvent (DMSO-d_6), ^{31}P NMR spectra were recorded on a Bruker MSL-400 NMR Fourier-spectrometer (100.62 MHz) relative to the external standard, 85% H_3PO_4, at 20 °C. IR spectra were recorded on a Vector 22 IR Fourier-spectrometer (Bruker) in the range of frequencies 400—3800 cm^{-1}. The samples were studied as emulsions in Nujol. The mass spectrum was recorded on a MAT-212 mass spectrometer (Finnigan) with the resolution 1000 (EI, 60 eV, ionization current 0.3 mA), direct injection of the substance into the source of ions. The precise determination of the ion masses was performed at the resolution 10000 by the alignment method. Melting points were measured on a BOCIUS heating stage. Elemental analysis was performed on a EuroVector 3000 instrument. X-ray diffraction studies were performed in the Department of X-ray diffraction studies of the Community Center of the Spectroanalytical Center on the basis of the Laboratory of Diffraction Methods of Studies in the A. E. Arbuzov IOPhCh KazSC RAS. The structure was solved by the direct method using the SIR program[18] and refined first in the isotropic and then in the anisotropic approximation using the SHELXL-97 program.[19] The hydrogen atoms of the hydroxy groups were found from the differential series of electron density, hydrogen atoms at the carbon atoms were placed to the calculated positions and refined using the riding model. All the calculations were performed using the WinGX program package.[20] Analysis of intermolecular contacts, including hydrogen bonds in crystals, were performed using the PLATON program.[21]

5,13-Dimethoxy-4,14-dimethyl-2,16-dioxa-1-phosphatetracyclo[7.7.1.0^{3,8}.0^{10,15}]heptadeca-3,5,7,10,12,14-hexaene 1-oxide (1) and 2-hydroxy-7-methoxy-8-methyl-2-oxabenzo[*e*]-1,2-oxaphosphorine (4). 2-Ethoxyvinylphosphonic dichloride (**2**) (1.2 g, 0.0064 mol) was added dropwise to a mixture of 3-methoxy-2-methylphenol (**3**) (0.88 g, 0.0064 mol) and trifluoroacetic acid (0.48 mL, 0.0064 mol) in dioxane (14 mL). The reaction mixture was heated at 60 °C for 25 h, a precipitate that formed was filtered off, washed with DI water, dried *in vacuo* until the weight was constant to obtain compound **1** (1.2 g, 54.5%), m.p. 218 °C. Found (%): C, 62.42; H, 5.11; P, 8.52. $C_{18}H_{19}O_5P$. Calculated (%): C, 62.43; H, 5.49; P, 8.96. ^{1}H NMR, δ: 2.01 (s, 6 H, CH_3); 2.59 (dd, 2 H, PCH_2, $^3J_{H,H}$ = 4.1 Hz, $^2J_{P,H}$ = 16.39 Hz); 3.74 (s, 6 H,OCH_3); 4.71 (dt, 1 H, CH, $^3J_{H,H}$ = 3.76 Hz, $^3J_{P,H}$ = = 35.58 Hz); 6.70 (d, 2 H, *meta*-CH_{arom}, $^3J_{H,H}$ = 8.54 Hz); 7.28 (d, 2 H, *ortho*-CH_{arom}, $^3J_{H,H}$ = 8.54 Hz). ^{31}P NMR, δ: 13.31. IR, ν/cm^{-1}: 1271 (P=O), 1613 (arom.).

The filtrate was concentrated, the oily substance that obtained was dissolved in DI water (10 mL), followed by addition of acetone (5 mL). The white crystals that formed were filtered, washed with acetone, and dried *in vacuo* until the weight was constant to obtain compound **4** (0.6 g, 27%), m.p. 190 °C. Found (%): C, 56.98; H, 5.57; P, 14.16. $C_{10}H_{11}O_3P$. Calculated (%): C, 57.14; H, 5.24; P, 14.76. ^{1}H NMR, δ: 2.09 (s, 3 H, CH_3); 3.84 (s, 3 H, OCH_3); 6.11 (dd, 1 H, CH=, $^3J_{H,H}$ = 12.37 Hz, $^3J_{P,H}$ = = 19.99 Hz); 6.83 (d, 2 H, *meta*-CH_{arom}, $^3J_{H,H}$ = 8.57 Hz); 7.29 (d, 2 H, *ortho*-CH_{arom}, $^3J_{H,H}$ = 8.25 Hz); 7.31 (dd, 1 H, CH=, $^3J_{H,H}$ = 12.67 Hz, $^2J_{P,H}$ = 42.03 Hz). ^{31}P NMR, δ: 6.15. IR, ν/cm^{-1}: 1212 (P=O), 1560 (C=C), 1603 (arom.), 2300 (POH).

5,13-Dihydroxy-4,14-dimethyl-2,16-dioxa-1-phosphatetracyclo[7.7.1.0^{3,8}.0^{10,15}]heptadeca-3,5,7,10,12,14-hexaene 1-oxide (7). 2-Ethoxyvinylphosphonic dichloride (**2**) (2 g, 0.01 mol) was added dropwise to a mixture of 2-methylresorcin (**6**) (1.24 g, 0.01 mol) and trifluoroacetic acid (0.74 mL, 0.01 mol) in dioxane (14 mL). The reaction mixture was heated at 60 °C for 25 h, a precipitate that formed was filtered off, washed with DI water, dried *in vacuo* until the weight was constant. The yield was 1.2 g (80%), m.p. 337—340 °C. Found (%): C, 60.19; H, 4.69; P, 9.83. $C_{16}H_{15}O_5P$. Calculated (%): C, 60.38; H, 4.72; P, 9.75. ^{1}H NMR, δ: 1.99 (s, 6 H, CH_3); 2.57 (dd, 2 H, PCH_2, $^3J_{H,H}$ = = 4.03 Hz, $^2J_{P,H}$ = 16.14 Hz); 4.54 (dt, 1 H, CH, $^3J_{H,H}$ = 4.03 Hz, $^3J_{P,H}$ = 35.58 Hz); 6.51 (d, 2 H, *meta*-CH_{arom}, $^3J_{H,H}$ = 8.43 Hz); 7.04 (d, 2 H, *ortho*-CH_{arom}, $^3J_{H,H}$ = 8.43 Hz); 9.53 (s, 2 H, OH). IR, ν/cm^{-1}: 1269 (P=O), 1613 (arom.), 3250—3550 (OH). ^{31}P NMR, δ: 13.70. MS, *m/z* (I_{rel} (%)): 318 [M]$^+$.

X-ray diffraction studies. Crystals of compound **1** are colorless triclinic prisms, $C_{18}H_{19}O_5P$, M = 346.30, a = 7.382(3) Å, b = 7.459(3) Å, c = 14.986(5) Å, α = 85.072(4)°, β = 89.060(4)°, γ = 89.219(4)°, V = 821.9(5) Å^3, d_{calc} = 1.399 g cm^{-3}, Z = 2, the space group $P\bar{1}$. Intensities of 10944 reflections (1733 from which with $I \geq 2\sigma(I)$) were measured at 20 °C on a Bruker SMART APEX II CCD diffractometer. The final values of the divergence factors: R_{ob} = 0.0662 and R_{wob} = 0.1766 on 2726 independent reflections with $I \geq 2\sigma(I)$, the number of refined parameters 219, R_{int} = 0.062. The complete tables of coordinates, temperature parameters, bond distances, and bond angles were deposited with the Cambrige Structural Database (CCDC 832046).

Crystals of compound **4** are monoclinic, $C_{10}H_{11}O_4P$, M = = 226.16, a = 4.755(3) Å, b = 11.128(4) Å, c = 19.718(3) Å, β = 90.570(12)°, V = 1043.3(8) Å^3, Z = 4, d_{calc} = 1.44 g cm^{-3}, the space group $P2_1/c$. Intensities of 13646 reflections (1345 from which with $I \geq 2\sigma(I)$) were measured at 20 °C on a Bruker SMART APEX II CCD diffractometer (ω/2θ-scanning, θ < 54°, Mo-Kα irradiation, graphite monochromator, R_{int} = 0.0696). The final values of the divergence factors: R_{ob} = 0.050 and R_{wob} = 0.137 (GOOF = 1.029) on 2270 independent reflections with $I \geq 2\sigma(I)$, the number of refined parameters 141, R_{int} = 0.070. The complete tables of coordinates, temperature parameters, bond distances, and bond angles were deposited with the Cambrige Structural Database (CCDC 832047).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 11-03-00416-a).

References

1. E. E. Nifant´ev, I. M. Petrova, *Zh. Obshch. Khim.*, 1968, **38**, 2341 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1968, **38**].
2. R. Filler, H. Novar, *J. Org. Chem*, 1960, **25**, 663.
3. D. B. Denney, J. W. Hanifin, *Tetrahedron Lett.*, 1963, **4**, 2177.
4. K. Taira, D. G. Gorenstein, *Tetrahedron*, 1984, **40**, 3215.
5. M. A. Malenovskaya, A. R. Bekker, S. V. Meshkov, D. A. Predvoditelev, E. E. Nifant´ev, *Zh. Obshch. Khim.*, 1993, **53**, 2458 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1993, **53**].
6. R. S. Edmundson, C. I. Forth, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1980, **8**, 315.
7. R. V. Devis, D. J. Wintergrass, M. N. Janakiraman, E. M. Hyatt, R. A. Jacobson, L. M. Daniels, A. Wroblewski, A. J. Padmakumari, S. K. Das, J. G. Verkade, *Inorg. Chem.*, 1991, **30**, 1330.
8. M. Benhammou, R. Kraemer, H. Germa, J.-P. Majoral, J. Navech, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1982, **14**, 105.
9. A. Ochida, M. Sawamura, *Arkivoc,* 2006, **VII**, 359.
10. J. Kobayashi, K. Goto, T. Kawashima, M. W. Schmidt, S. Nagase, *J. Am. Chem. Soc.*, 2002, **124**, 3703.
11. J. Kobayashi, K. Goto, T. Kawashima, *J. Am. Chem. Soc.*, 2001, **123**, 3387.
12. S. Nakafuji, J. Kobayashi, T. Kawashima, M. W. Schmidt, *Inorg. Chem.*, 2005, **44**, 6500.
13. J. Kobayashi, K. Goto, T. Kawashima, M. W. Schmidt, S. Nagase, *Chem. Eur. J.*, 2006, **12**, 3811.
14. V. V. Kormachev, M. S. Fedoseev, *Preparativnaya khimiya fosfora* [*Preparative Chemistry of Phosphorus*], Publ. UrO RAN, Perm, 1992, p. 189 (in Russian).
15. C. L. Kirkemo, J. D. White, *J. Org. Chem.*, 1985, **50**, 1316.
16. E. N. Varaksina, D. A. Tatarinov, K. Yu. Cherkin, A. V. Nemtarev, V. F. Mironov, A. I. Konovalov, *Phosphorus*, *Sulfur Silicon Relat. Elem.*, 2008, **183**, 566.
17. L. Vijayalakshmi, V. Parthasarathi, N. Dodiab, A. Shahb, *Acta Crystallogr.*, *Sect. E: Struct. Rep. Online*, 2001, **57**, 212.
18. A. Altomare, G. Cascarano, C. Giacovazzo, D. Viterbo, *Acta Crystallogr., Sec. A: Found. Crystallogr.*, 1991, **47**, 744.
19. G. M. Sheldrick, *SHELXL-97, Program for the Refinement of Crystal Structure*, Göttingen University, Göttingen, Germany, 1997.
20. L. J. Farrugia*, J. Appl. Crystallogr.*, 1999, **32**, 837.
21. A. L. Spek, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 1990, **46**, 34.

Received April 4, 2011;
in revised form July 6, 2011