FORMATION OF ALKOXYPHOSPHORANES IN REACTION OF SUBSTITUTED 0-AMINOMETHYLPHENOLS WITH TRIALKYL PHOSPHITES

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The reaction of trialkyl phosphites with phenolic Mannich bases leads to the formation of the esters of alkoxybenzylphosphonic acids [1]. It was postulated that alkoxyphosphoranes are formed as intermediate products of this reaction, which, however, could not be isolated.

The most stable should be the alkoxyphosphoranes with substituents in the benzene ring that are ortho to the oxygen of the phosphorane ring, since the steric factors of the substituent can be manifested to substantial degree in this case [2], i.e., its ability to sterically shield the oxygen of the phosphorane ring. Starting with this, we reacted some phenolic Mannich bases that have a substituent ortho to the phenolic hydroxyl. The corresponding alkoxyphosphoranes are formed when o-substituents are present, which could be identified; the phosphorane is also formed from 2-diethylaminomethyl-4-cyclohexylphenol.

When 2-ethylaminomethyl-4-isopropyl-6-methylphenol is reacted with triethyl phosphite the ${}^{31}P$ signal of a pentacovalent compound (+31 ppm) was recorded in the ${}^{31}P$ NMR spectrum of the reaction mixture, the intensity of which signal decreases as the reaction progresses, with a simultaneous increase in the signal of the phosphorus nucleus of the end reaction product, namely 2-ethoxy-2-oxo-5-isopropyl-7-methyl-1-oxa-2-phosphaindan, $\delta_{31}P - 42$ ppm.

The structure of the obtained phosphoranes is confirmed by the elemental analysis data (Table 1), and by the IR spectra, in which the absorption band of the phosphoryl group in the 1250-1260 cm⁻¹ region is absent. The ³¹P chemical shifts of the synthesized phosphoranes are found in the positive region, which is characteristic of structures with a pentacovalent phosphorus [3, 4], The alkoxyphosphoranes can be distilled in a high vacuum without decomposition, but, like other compounds of this type [5], they are unstable to heat, and react easily with compounds that contain a labile hydrogen atom.

We made a detailed study of the properties of 2,2,2-triethoxy-7-methyl-1-oxa-2-phosphaindan (I). The compound is isomerized completely at 185-190° to the diethyl ester of ethoxybenzylphosphonic acid, $\delta_{31}P-26$ ppm. The hydrolysis of (I) proceeds in two steps and, if an equimolar ratio of the reactants is used, can be stepped at the step of forming the diethyl ester of 2-hydroxy-3-methylbenzylphosphonic acid (II), $\delta_{31}P-30$ ppm.



Aliphatic alcohols transesterify two of the ethoxyl groups in (I). 2-Ethoxy-2-oxo-7-methyl-1-oxa-2-phosphaindan (III), δ_{31P} -45 ppm, is formed when (I) is reacted with phenol, CH₃COOH, aniline or malonic ester. In the ³¹P NMR spectra of the reaction mixtures, taken after heating, but before fractional distillation, the signal δ_{31P} -30 ppm was recorded, which, according to [6], corresponds to phosphonate (II).

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The property of the alkoxyphosphoranes to react with compounds that contain a labile hydrogen atom was used to trap the intermediate phosphoranes in the reaction with those phenolic Mannich bases that give highly reactive pentacovalent compounds with the trialkyl phosphites. In these experiments only the signals of the phosphorus nuclei of the end reaction products, namely the esters of alkoxybenzylphosphonic acids, are recorded on the ³¹P NMR spectra. The Mannich bases from p- and m-cresol, 4-chlorophenol [1], and 4-bromo- and 3-chlorophenol, belong in this class. Thus, the reaction of the m- and p-cresol Mannich bases with triethyl phosphite in the presence of aniline gives the corresponding phosphaindans with a tetracoordinated phosphorus in the ring, which confirms the possibility of the intermediate formation of alkoxyphosphoranes.

The obtained data make it possible to assume that the reactions of trialkyl phosphites with phenolic Mannich bases proceed through the pentacovalent compounds, which are found in equilibrium with their bipolar form, the phosphonium betaine. The formation of the different end products depends on the stability of the intermediate alkoxyphosphorane, which is determined by the substituent in the benzene ring, and its position relative to the oxygen of the phosphorane ring. When speaking of the stability of pentacovalent compounds it must be kept in mind that they are capable of thermal isomerization, hydrolysis, and reacting with the amines that are liberated in the reaction process (see scheme below).



EXPERIMENTAL METHOD

The ³¹P NMR spectra were taken on a KGU-4 instrument (10.2 MHz) relative to 85% H₃PO₄ (external standard). The low-boiling fractions, which were distilled off during the reaction course, were studied by the GLC method on a "Khrom-3" instrument (120°, carrier gas = helium, and stationary phase = polymethylsiloxane).

The o-aminomethylphenols were synthesized from bis-aminomethanes and the appropriate phenols as described in [7]. Their structure was confirmed by the elemental analysis data (Table 2), and by the IR spectra, in which the intense absorption bands of a phenolic hydroxyl in the 3600-3000 cm⁻¹ region are

TABLE 2. R

R	Yield, %	Bp, °C (p, mm of Hg)	n_D^{20}	d_{4}^{20}	Found N,	Calcu- lated N,%
$\begin{array}{l} 4\text{-}C_{6}H_{11}\text{-}cyclo\\ 6\text{-}C_{6}H_{11}\text{-}cyclo\\ 6\text{-}CH_{2}\text{-}CH\text{=}CH_{2}\\ 3\text{-}Cl\\ 4\text{-}Br\\ 4\text{-}Br\\ 6\text{-}CH_{3}\\ 4\text{-}i\text{-}C_{3}H_{7}; 6\text{-}CH_{3} \end{array}$	57,5 64,0 80,0 40,0 50,0 50,0 57,0	120—125 (0,015) 130—133 (0,06) 98—100 (0,015) 78—80 (0,025) 95—98 (0,07) 75—76 (0,01) 82 (mp)	1,5265 1,5260 1,5190 1,5295 1,5450 1,5150 	0,9931 0,9880 0,9874 1,1090 	5,05 5,21 6,27 6,82 5,76 7,05 5,55	5,35 5,35 6,53 6,57 5,69 7,25 5,95

absent, which suggests that the OH group is involved in the intramolecular hydrogen bond with the nitrogen atom of the o-aminomethyl group [8].

 $\frac{2,2,2-\text{Triethoxy-7-methyl-1-oxa-2-phosphaindan (I)}{2,2,2-\text{Triethoxy-7-methyl-1-oxa-2-phosphaindan (I)}} A \text{ mixture of 16.6 g of triethyl phosphite and 19.3 g of 2-diethylaminomethyl-6-methylphenol was heated at 160-170° for 1.5 h, with a simultaneous distillation of the diethylamine liberated in the reaction. After fractional distillation we isolated 24.1 g (74.5%) of (I) with bp 74-75° (0.013 mm); n_D^{20} 1.4970; d_4^{20} 1.0845; \delta_{31} + 27 ppm. Found: C 58.82; H 8.20; P 10.88\%. C_{14}H_{23}O_4P. Calculated: C 58.74; H 8.04; P 10.84\%.$

The properties of the alkoxyphosphoranes, obtained in similar manner from the corresponding oaminomethylphenols, are given in Table 1.

Thermal Isomerization of 2,2,2-Triethoxy-7-methyl-1-oxa-2-phosphaindan (I). Compound (I) $(\delta_{31P} + 27 \text{ ppm})$ was heated in a sealed ampul at 165-190°. After 1 h the appearance of the ³¹P signal (-26 ppm) is observed on the ³¹P NMR spectrum, which becomes predominant as the heating is continued. After 5 h, (I) is isomerized completely to the diethyl ester of 2-ethoxy-3-methylbenzylphosphonic acid, $\delta_{31P} - 26$ ppm.

<u>Hydrolysis of 2,2,2-Triethoxy-7-methyl-1-oxa-2-phosphaindan (I)</u>. To an acetone solution of 14.35 g of (I) was added 0.9 g of water, and the temperature of the mixture rose to 70°. After removal of the volatile products (in vacuo) we obtained 12.4 g (96%) of (II); n_D^{20} 1.5100; δ_{31P} -30 ppm. Found: C 56.13; H 7.50; P 11.49%. C₁₂H₁₉O₄P. Calculated: C 55.85; H 7.36; P 12.01%.

Hydrolysis of Diethyl Ester of 2-Hydroxy-3-methylbenzylphosphonic Acid (II). A mixture of 0.45 g of (II) and 15 g of water was heated at 100° for 15 h. After removal of the volatile products (in vacuo) we obtained 4.8 g (95%) of 2-hydroxy-3-methylbenzylphosphonic acid, which was identified as the monoaniline salt with mp 186-188°. Found: N 4.60; P 10.69%. $C_{14}C_{18}$ NOP. Calculated: N 4.74; P 10.50%.

 $\frac{2-\text{Ethoxy-2,2-dipropoxy-7-methyl-1-oxa-2-phosphaindan.} \text{ A mixture of 7.75 g of (I) and 18.7 g of propanol was heated at 95-105° for 4 h. We isolated 6.12 g (72%) of 2-ethoxy-2,2-dipropoxy-7-methyl-1-oxa-2-phosphaindan with bp 98-102 (0.04 mm); n²⁰_D 1.4938; d²⁰₄ 1.0635; <math>\delta_{31}$ +26 ppm. Found: C 61.24; H 8.44; P 9.92%. C₁₆H₂₇O₄P. Calculated: C 61.15; H 8.60; P 9.87%.

In a similar manner, reaction with hexyl alcohol gave 2-ethoxy-2,2-dihexoxy-7-methyl-1-oxa-2-phosphaindan in 60% yield, with bp 142-145° (0.1 mm); n_D^{20} 1.4820; d_4^{20} 1.0740. Found: C 66.76; H 10.03; P 7.26%. C₂₂H₃₉O₄P. Calculated: C 66.33; H 9.79; P 7.79%.

<u>2-Ethoxy-2-oxo-7-methyl-1-oxa-2-phosphaindan (III)</u>. a) To 8.4 g of (I) was added 1.7 g of CH₃COOH; the temperature of the mixture rose to 90°. The mixture was heated at 115-120° for 1.5 h. The low-boiling fraction contains ethyl acetate and ethanol. After fractional distillation we obtained 3.5 g (57%) of (III) with bp 122-123° (0.04 mm); mp 82-84°. Found: P 14.21%. $C_{10}H_{13}O_3P$. Calculated: P 14.62%.

b) A mixture of 7.17 g of (I) and 2.32 g of aniline was heated at 145-165° for 2 h. The low-boiling fraction contains monoethylaniline and ethanol. After fractional distillation we obtained 3 g (56%) of (III) with mp 85-87°. Found: P 14.35%. $C_{10}H_{13}O_3P$. Calculated P 14.62%.

c) A mixture of 14.4 g of (I) and 4.7 g of phenol was heated at $165-170^{\circ}$ for 6 h. After fractional distillation we isolated 9 g (85%) of (III) with mp 84-86°.

d) A mixture of 7.17 g of (I) and 16 g of malonic ester was heated at 155-165 for 6 h. The low-boiling fraction contains ethanol and ethylmalonic ester. After fractional distillation we isolated 3.9 g (73.6%) of

(III) with mp 85-87°. Found: P 14.16%. C₁₀H₁₃O₃P. Calculated: P 14.62%.

<u>2-Ethoxy-2-oxo-5-isopropyl-7-methyl-1-oxa-2-phosphaindan</u>. A mixture of 6 g of 2-diethylaminomethyl-4-isopropyl-6-methylphenol, 4.1 g of triethyl phosphite and 3 ml of absolute xylene was heated in a nitrogen stream at 160-180° for 2 h. The low-boiling fraction contains diethylamine and ethanol. After distillation we isolated 4.5 g (53.5%) of 2-ethoxy-2-oxo-5-isopropyl-7-methyl-1-oxa-2-phosphaindan with bp 120-121° (0.03 mm); n_D^{20} 1.5100; δ_{31P} -42 ppm; $\nu_{P=O}$ 1280 cm⁻¹. Found: P 11.93%. C₁₇H₂₉O₄P. Calculated: P 12.19%.

Diethyl Ester of 2-Ethoxy-5-bromobenzylphosphonic Acid. A mixture of 34.1 g of 2-diethylaminomethyl-4-bromophenol and 22.8 g of triethyl phosphite was heated at 160-170° for 2 h, with a simultaneous distillation of the diethylamine. After fractional distillation we isolated 20 g (41.4%) of the diethyl ester of 2-ethoxy-5-bromobenzylphosphonic acid with bp 130-133° (0.02 mm); n_D^{20} 1.5290; d_4^{20} 1.3775; δ_{31P} -25 ppm; $\nu_{P=O}$ 1250 cm⁻¹. Found: P 9.31%; MR 78.62. $C_{13}H_{20}O_4$ BrP. Calculated: P 8.82%; MR 78.89.

In a similar manner, from 2-diethylaminomethyl-3-chlorophenol we obtained the diethyl ester of 2-ethoxy-4-chlorobenzylphosphonic acid with bp 139-140° (0.03 mm); n_D^{20} 1.5125; d_4^{20} 1.2092; $\delta_{31}P$ - 26 ppm; $\nu_{P=O}$ 1260 cm⁻¹, yield 45%. Found: P 10.26%; MR 76.09. C₁₃H₂₀O₄PCl. Calculated: P 10.17%; MR 75.99.

2-Ethoxy-2-oxo-5-methyl-1-oxa-2-phosphaindan. A mixture of 9.65 g of 2-diethylaminomethyl-4methylphenol, 8.3 g of triethyl phosphite and 4.65 g of aniline in 20 ml of absolute n-nonane was heated at 155-160° for 5.5 h. The low-boiling fraction contains ethanol and diethylamine. After fractional distillation we obtained 5.7 g (53%) of 2-ethoxy-2-oxo-5-methyl-1-oxa-2-phosphaindan [9] with bp 110-112° (0.006 mm); n_D^{20} 1.5250; δ_{31} P -46 ppm. Found: P 14.68%. $C_{10}H_{13}O_3$ P. Calculated: P 14.62%.

In a similar manner, the reaction of triethyl phosphite with 2-diethylaminomethyl-5-methylphenol gave 2-ethoxy-6-methyl-1-oxa-2-phosphaindan [9] with bp 118-120° (0.006 mm); n_D^{20} 1.5240; δ_{31P} -45 ppm, yield 30% Found: P 14.66%. $C_{10}H_{13}O_3P$. Calculated: P 14.62%.

CONCLUSIONS

1. The formation of stable alkoxyphosphoranes is observed when a phenolic Mannich base, containing o-substituents in the benzene ring, is reacted with trialkyl phosphites.

2. The properties of the alkoxyphosphoranes were studied: hydrolysis, thermal isomerization, and reaction with compounds that contain a labile hydrogen atom. It was shown that these reactions proceed with a rupture of the phosphorane ring.

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