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Reactions of 1,2-Imino Alcohols with Phosphoromonochloridites: Formation of 2-Iminoalkyl(phenyl) phosphites

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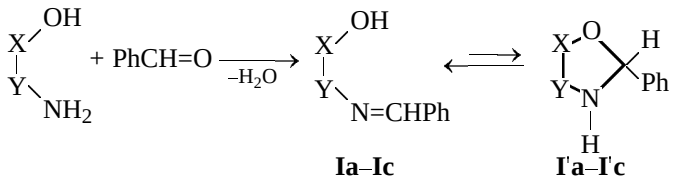
Abstract — 1,2-Imino alcohols existing in a tautomeric equilibrium with the corresponding 1,3-oxazolidines react with phosphoromonochloridites in ether in the presence of triethylamine to form 2-iminoalkyl(phenyl) phosphites as the only reaction products.

Phosphorylation of imino alcohols with Hal–P(III) derivatives is studied insufficiently. Published data [1–4] deal with the phosphorylation of imino phenols with P(III) acid chlorides. It was shown that P(III) imino derivatives primarily formed in these reactions in the presence of organic bases undergo further transformations to give polycyclic phosphoranes as the final products. In the previous paper we reported that phosphorochloridites react with aliphatic 1,2-imino alcohols in the presence of triethylamine to form β-imino phosphites, which under the action of acetic acid readily cyclize to 1,4,2-oxazaphosphorines [5]. These compounds are the only products when these reactions are carried out without introducing additional bases [6, 7]. Imino phosphites stable under the common conditions were recently obtained by alcoholysis of amido esters of P(III) acids with 1,2-imino alcohols [8]. It should be noted that none of the cited works gave due attention to the well-known fact of the existence of imino alcohols, especially 1,2-imino alcohols, as an equilibrium mixture of two tautomers having the open-chain and cyclic (1,3-oxazolidine) structures [9, 10]. In this connection, the probability of the reaction of 1,2-imino alcohols with P(III) halides along at least two pathways with the formation of several reaction products cannot be ruled out.

In this work we studied the reaction of some 1,2-imino alcohols with phosphoromonochloridites in the presence of triethylamine.

1,2-Imino alcohols **Ia**–**Ic** were prepared by the reaction of 1,2-amino alcohols with benzaldehyde in refluxing benzene with the removal of the released water using a Dean–Stark trap. The physicochemical constants of **Ia**–**Ic** were close to the published data (see Experimental).



The ^{1}H NMR spectra of all imino alcohols **Ia**–**Ic** in $CDCl_3$ contain a strong singlet at 8 ppm corresponding to the HC=N proton of the open-chain tautomer. At the same time, in the spectra of imino alcohols **Ia** and **Ib**, weaker signals were observed in the range 5–6 ppm; similarly to [9], these signals can be assigned to the proton at C^2 in 1,3-oxazolidines **I'a** and **I'b**. This proton in **I'a** gives one singlet, and in **I'b**, two singlets in approximately 2 : 1 ratio. In the latter case, the splitting is caused by the existence of

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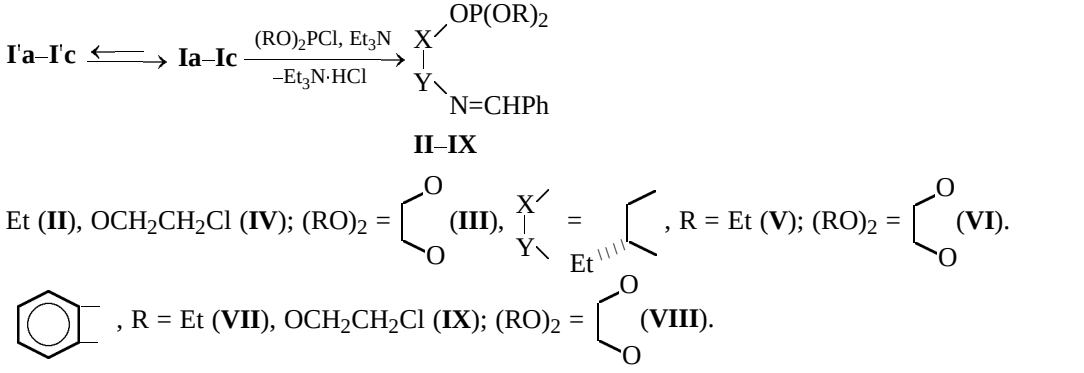
1,3-oxazolidine **I'b** as a mixture of diastereomers (*cis/trans* isomers). The ratio of the tautomers found from the integral intensity of the signals of the indicator protons of the two tautomeric forms is as follows: **Ia/I'a** 10 : 1, **Ib/I'b** 5.5 : 1.

In the expected range of the NMR spectrum of 1,2-imino alcohol **Ic**, no signals of the protons of the cyclic tautomer **I'c** were observed. This fact shows that 2-(*N*-benzylidenamino)phenol **Ic** under the common conditions in chloroform exists as an open-chain tautomer. In other words, the amount of 1,3-oxazolidine **I'c** in so small that it cannot be detected by NMR spectroscopy. Formation of cyclic tautomer in this case is evidently prevented by the strain appearing in the five-membered ring annelated with the aromatic ring. Another possible reason of the absence of the cyclic tautomer is the decreased nucleophilicity of the phenolic OH group as compared to hydroxy group of aliphatic alcohols, which prevents the intramolecular nucleophilic attack of the hydroxy group of 1,2-imino alcohol at the imine carbon atom. Available data indicate that, on introduction of the electron-accepting CF_3 group to the imine carbon atom, the attack of phenolic hydroxy group at the electrophilic imine carbon atom becomes possible. The corresponding aromatic 1,2-imino alcohol in the crystal has the 1,3-oxazolidine structure [11].

Reactions of imino alcohols **Ia**–**Ic** with phosphoromonochloridites were carried out in anhydrous ether or benzene in the presence of triethylamine. The ^{31}P NMR spectra of all the crude products contain a singlet at 128–140 ppm, i.e., in the range typical of neutral phosphites.



The reaction products were purified by distillation at reduced pressure. In some cases, after filtering off triethylamine hydrochloride and removing the solvent, keeping the crude products in a vacuum was sufficient. The isolated 2-iminoalkenyl(phenyl) phosphites **II**–**IX** are either low-viscous colorless liquids (**II**–**VI**) or light yellow oils (**VII**–**IX**). Their purity and structures were confirmed by ^1H and ^{31}P NMR spectra and also by IR spectroscopy and elemental analysis. The ^{31}P–$\{^1H\}$ NMR spectra of the distilled products contained the singlets in the same range as the spectra of the crude reaction mixture. The ^1H NMR spectra in $CDCl_3$ contained the characteristic singlet of the HC=N proton at δ 8 ppm. The presence of the free imino group was confirmed by the medium-intensity IR absorption band at 1640–1650 cm^{-1}.

Formation of 2-iminoalkyl(phenyl) phosphites **II**–**IX** as the only products in the reaction of phosphoromonochloridites with imino alcohols **Ia**–**Ic**, which exist in a dynamic tautomeric equilibrium with 1,3-oxazolidines **I'a**–**I'v**, is evidently caused by the fact that the OH group in **Ia**–**Ic** is much more reactive than the NH group in **I'a**–**I'c**, and, as the imino alcohols are consumed, the balance **Ia**–**Ic** ⟷ **I'a**–**I'c** shifts to the left until the cyclic tautomer fully disappears. In this connection, it should be noted that phosphorochloridites as electrophilic reagents relative to imino alcohols differ from such electrophiles as isocyanates. Witek *et al*. [12] have shown that 1,2-imino alcohols obtained from ethanolamine and *para*-substituted benzaldehydes react with isocyanates to form only the 1,3-oxazolidine derivatives.

Thus, 1,2-imino alcohols react with phosphoromonochloridites in the presence of an organic base similarly to the usual alcohols to form 2-iminoalkyl(phenyl) phosphites.

EXPERIMENTAL

The ^{1}H NMR spectra of **I**–**IX** and ^{31}P–{^{1}H} NMR spectra of compounds **II**–**IX** in $CDCl_3$ were recorded on Bruker WM-250 (250 MHz, chemical shifts measured relative to residual solvent protons) and Bruker CXP-100 (36.49 MHz, chemical shifts measured relative to external 85% H_3PO_4) spectrometers, respectively. The IR spectra (thin layer for **Ia**, **Ib**, and **II**–**IX**; mull in mineral oil for **Ic**) were obtained on a UR-20 spectrometer. The optical rotation was measured on a Polamat A polarimeter.

The 1,2-imino alcohols **Ia**–**Ic** obtained had the following physicochemical constants. 2-(Benzylidenamino)ethanol **Ia**: bp 94–96°C (0.05 mm), n_D^{20} 1.5725 (published data: bp 135–136.5°C (15 mm) [12]). *R*-(+)-2-(Benzylidenamino)butan-1-ol **Ib** was prepared from *R*-(–)-2-aminobutanol with $[\alpha]_D^{20}$ –7.01 (pure liquid); bp 73°C (0.06) mm, mp 54–55°C, $[\alpha]_D^{20}$ +28.0° (*c* 13.2, MeOH) (published data: bp 55–56°C, $[\alpha]_D^{20}$ +39.30° [13]). 2-(Benzylidenamino)phenol **Ic**: mp 94°C (from benzene); published data: mp 95°C [14]).

2-(Benzylidenamino)ethyl diethyl phosphite II. A solution of 1.80 g of diethyl phosphorochloridite was added dropwise at +5°C under dry argon to a solution of 1.71 g of 2-(benzylidenamino)ethanol **Ia** and 1.20 g of triethylamine in 30 ml of absolute ether. After the addition was complete, the mixture was kept at room temperature for 1.5 h. The precipitate of triethylamine hydrochloride was filtered off, and the solvent was removed in a vacuum. Phosphite **II** was isolated pure by vacuum distillation. Yield 2.66 g (86%), bp 119–121°C (0.25 mm), n_D^{20} 1.5148. IR spectrum, ν, cm^{-1}: 1648 (C=N), 1029 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 1.06 t (6H, $2CH_3$, J_{HH} 7 Hz), 3.67–3.96 m (8H, $4CH_2$), 7.15–7.71 m (5H, C_6H_5), 8.13 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 140.1 s. Found, %: C 58.25; H 7.22; N 4.81; P 11.29. $C_{13}H_{20}NO_3P$. Calculated, %: C 57.99; H 7.43; N 5.20; P 11.52.

2-(Benzylidenamino)ethyl ethylene phosphite III was prepared similarly to **II** from 4.12 g of 2-(benzylidenamino)ethanol **Ia**, 2.79 g of triethylamine, and 3.50 g of ethylene phosphorochloridite. Yield 6.21 g (94%), bp 140–141°C (0.4 mm), n_D^{20} 1.5570. IR spectrum, ν, cm^{-1}: 1647 (C=N), 1018, 1045 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 3.80–4.21 m (8H, $2CH_2CH_2$), 7.24–7.84 m (5H, C_6H_5), 8.22 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 135.8 s. Found, %: C 54.91; H 6.16; N 5.55; P 13.25. $C_{11}H_{14}NO_3P$. Calculated, %: C 55.23; H 5.86; N 5.86; P 12.97.

2-(Benzylidenamino)ethyl bis(2-chloroethyl) phosphite IV was prepared similarly to **II** from 3.57 g of 2-(benzylidenamino)ethanol **Ia**, 2.42 g of triethylamine, and 5.40 g of bis(2-chloroethyl) phosphorochloridite. Yield 6.87 g (88%), bp 195–197°C (0.4 mm), n_D^{20} 1.5285. IR spectrum, ν, cm^{-1}: 1650 (C=N), 1228, 1075 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 3.41–4.01 m (12H, $3CH_2CH_2$), 7.16–7.79 m (5H, C_6H_5), 8.12 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 140.8 s. Found, %: C 46.37; H 5.65; Cl 20.79; N 3.86; P 8.92. $C_{13}H_{18}Cl_2NO_3P$. Calculated, %: C 46.15; H 5.33; Cl 21.00; N 4.14; P 9.17.

2-(*R*)-(*N*-Benzyliden)aminobutyl diethyl phosphite V. A solution of 0.70 g of diethyl phosphorochloridite was added dropwise with stirring at +5°C undr argon to a solution of 0.81 g of *R*-(+)-2-(benzylidenamino)butanol **Ib** and 0.46 g of triethylamine in 30 ml of absolute benzene,. After the addition of the phosphorochloridite was complete, the mixture was kept for 1.5 h at room temperature. The precipitate of triethylamine hydrochloride was filtered off, the solvent was removed at reduced pressure, and the product was dried in a vacuum (1 mm, 50°C) for 0.5 h. Yield 1.15 g (88%), n_D^{20} 1.5148. IR spectrum, ν, cm^{-1}: 1645 (C=N), 1045 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 0.82 t (3H, CH_3CH_2CH, J_{HH} 7.5 Hz), 1.24 t (6H, $2CH_3CH_2O$, J_{HH} 7 Hz), 1.57 m (2H, CH_3CH_2CH), 3.22 m (1H, CH_3CH_2CH), 3.60–4.10 m (6H, $2CH_3CH_2$, $NCHCH_2$), 7.10–7.70 m (5H, C_6H_5), 8.12 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 138.9 s. Found, %: C 60.97; H 8.42; N 5.20; P 10.60. $C_{15}H_{24}NO_3P$. Calculated, %: C 60.61; H 8.08; N 4.71; P 10.44.

[2-(*R*)-(Benzylidenamino)butyl]ethylene phosphite VI was prepared similarly to **II** from 2.70 g of *R*-(+)-2-(benzylidenamino)butanol **Ib**, 1.54 g of triethylamine, and 1.93 g of ethylene phosphorochloridite. Yield 3.20 g (80%), bp 163–165°C (0.4 mm), n_D^{20} 1.5386. IR spectrum, ν, cm^{-1}: 1645 (C=N), 1015, 1048 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, CH_3, $^3J_{HH}$ 7.5 Hz), 1.65 m (2H, CH_3CH_2), 3.22 m (1H, CH_2CHN), 3.93 m (4H, OCH_2CH_2O), 4.11 m (2H, OCH_2CH), 7.40–7.78 (5H, C_6H_5), 8.26 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 135.2 s. Found, %: C 57.97; H 6.42; N 5.20; P 11.50. $C_{13}H_{18}NO_3P$. Calculated, %: C 58.43; H 6.74; N 5.24; P 11.61.

2-(Benzylidenamino)phenyl diethyl phosphite VII was prepared similarly to **V** from 1.13 g of 2-(benzylidenamino)phenol **Ic**, 0.58 g of triethylamine, and 0.90 g of diethyl phosphorochloridite. Yield 1.70 g (93%), n_D^{20} 1.5912. IR spectrum, ν, cm^{-1}: 1628 (C=N), 1025 (P–O–C). ^{1}H NMR spectrum, δ, ppm: 1.28 t (6H, $3CH_3$, J_{HH} 7 Hz), 4.06 m (4H, $2CH_2$),

6.80–7.35 m (4H, C_6H_4), 7.45–7.93 m (5H, C_6H_5), 8.48 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 133.1 s. Found, %: C 64.10; H 6.50; N 4.63; P 9.97. $C_{17}H_{20}NO_3P$. Calculated, %: C 64.35; H 6.32; N 4.42; P 9.78.

2-(Benzylidenamino)phenyl ethylene phosphite VIIII was prepared similarly to **V** from 3.15 g of 2-(benzylidenamino)phenol **Ic**, 1.61 g of triethylamine, and 2.02 g of ethylene phosphorochloridite. Yield 4.21 g (92%), n_D^{20} 1.6348. IR spectrum, ν, cm^{-1}: 1625 (C=N), 1015 (P–O–C). ^1H NMR spectrum, δ, ppm: 3.83–4.26 m (4H, OCH_2CH_2O), 6.95–7.26 m (4H, C_6H_4), 7.36–7.97 m (5H, C_6H_5), 8.43 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 128.8 s. Found, %: C 62.97; H 4.49; N 5.20; P 11.22. $C_{15}H_{14}NO_3P$. Calculated, %: 62.72; H 4.88; N 4.88; P 10.88.

2-(Benzylidenamino)phenyl bis(2-chloroethyl) phosphite IX was prepared similarly to phosphite **V** from 3.49 g of 2-(benzylidenamino)phenol **Ic**, 1.79 g of triethylamine and 4 g of bis(2-chloroethyl) phosphorochloridite. Yield of **IX** 6.70 g (98%), n_D^{20} 1.5994. IR spectrum, ν, cm^{-1}: 1626 (C=N), 1021, 1074 (P–O–C). ^1H NMR spectrum, δ, ppm: 3.60 t (4H, $2ClCH_2$, J_{HH} 6.0 Hz), 4.17 m (4H, $2OCH_2$), 6.80–7.24 m (4H, C_6H_4), 7.42–7.87 m (5H, C_6H_5), 8.41 s (1H, HC=N). ^{31}P NMR spectrum, δ_P, ppm: 132.6 s. Found, %: C 52.61; H 4.91; Cl 18.78; N 3.42; P 7.75. $C_{17}H_{18}Cl_2NO_3P$. Calculated, %: C 52.85; H 4.66; Cl 18.39; N 3.63; P 8.03.

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