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Reactions of α-Haloaldehydes with Triethyl Phosphorotrithioite

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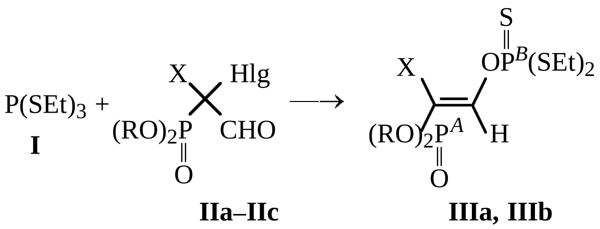
Abstract—Triethyl phosphorotrithioite reacts with linear and cyclic α-mono- and α,α-dihaloaldehydes by the Perkow reaction scheme to form *O*-vinyl phosphorotrithioates. It was established that catalytic amounts of zinc chloride much accelerate the reaction.

Reactions of thioesters of P(III) acids with carbonyl compounds are sufficiently thoroughly studied [1–3]. However, reactions of normal thioesters of phosphorous acids with α-halocarbonyl compounds have scarcely been explored. As shown in [4, 5], reactions of mixed *O,S*-esters of phosphorous acids with chloral involve the P–O bond and leave out the P–S bond; therewith, the products of the reactions of trialkyl phosphorotrithioites with chloral have not been identified.

With the purpose of establishing the pathway of the reaction and the nature of the products we have studied the reaction of triethyl phosphorotrithioite (**I**) with various α-haloaldehydes.

It was found that the major products of the reaction of compound **I** with functionalyzed α-haloaldehydes are *O*-vinyl esters of phosphorotrithioic acid. Phosphoryl-substituted mono- and dihaloaldehydes **IIa**–**IIc** react with phosphorotrithioite **I** at 100–110°C.

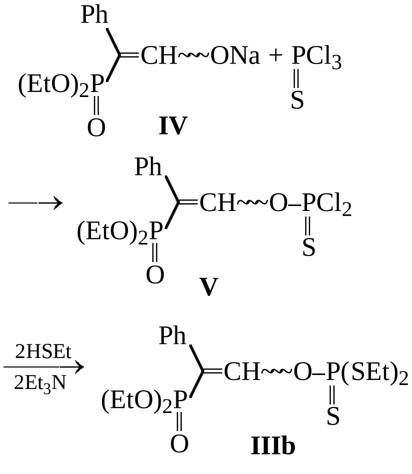


R = *i*-Pr, X = Hlg = Cl (**a**); R = Et, X = Ph, Hlg = Cl (**b**), Br (**a**).

In the ^{1}H NMR spectra of compounds **IIIa, IIIc**, the vinyl proton signal is observed at δ 7.6–7.8 ppm as a doublet ($^3J_{P^AH}$ 12 Hz, $^3J_{P^BH}$ 12.5 Hz). Based on the results in [6, 7], where the doublet with $^3J_{PH}$ 12–18 Hz was assigned to the methylene proton *cis* to the phosphinoyl group and the doublet with $^3J_{PH}$ 41 Hz, to the corresponding *trans*-proton, we suggested that bisphosphorylated product **IIIa** has a *Z* structure and compound **IIIb**, an *E* structure. That means that the vinyl proton is *cis* to the phosphinoyl group.

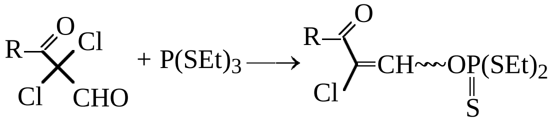
The ^{31}P NMR spectra of compounds **IIIa** and **IIIb** contain by two signals at δ_P 6 (**IIIa**) or 16 (**IIIb**) and 112 ppm, which provides evidence for the presence of phosphinoyl and phosphinothioyl fragments in the molecule.

To confirm the structure of the obtained compounds, independent synthesis of bisphosphorylated product **IIIb** was performed by the reaction of enolate **IV** with phosphorus sulfochloride and ethanethiol.



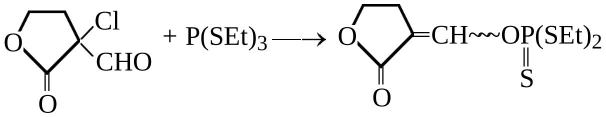
Intermediate phosphorothioic dichloride **V** was not isolated pure and characterized *in situ* by the ^{1}H and ^{31}P NMR spectra of the reaction mixture. Hence, the ^{31}P NMR spectrum contains two signals at δ_P 16 and 55 ppm, assigned to the phosphinoyl and dichlorophosphinothioyl fragments of compound **V**, respectively [8].

The vinyl proton of compound **V** appears in the ^{1}H NMR spectrum of the reaction mixture as a doublet at δ_P 7.7 ppm ($^3J_{PH}$ 12.5 Hz). Linear (**VIa, VIb**) and cyclic (**VII**) carbonyl-containing mono- and dichloroaldehydes also react with triethyl phosphorotrithioite along the Perkow scheme.



VIa, VIb **VIIIa, VIIIb**

R = Ph (**a**), EtO (**b**).



VII **IX**

The ^{1}H NMR spectra of compounds **VIIIa** and **VIIIb** show a =CH–O proton signal at δ 8 ppm as a doublet with $^3J_{PH}$ 12.5 Hz. The methine proton of thiophosphate **IX** appears as two triplets at δ 7.55 ppm ($^4J_{HH}$ 2.5 Hz and $^3J_{PH}$ 12.5 Hz).

The phosphorus signals of the thiophosphoryl groups are observed at δ_P 112 [**VIIIb** and **IX**] and 93 ppm [**VIIIa**].

The IR spectra of *O*-vinyl phosphorotrithioates **III, VIII,** and **IX** agree with the proposed structure. The absorption band at 650–690 cm^{-1} relates to stretching vibrations of the P=S group, the narrow band at 1620–1660 cm^{-1}, to the C=C bond, and the band at 1695–1710 cm^{-1}, to the C=O group. The P=O group of bisphosphoryl compounds **IIIa** and **IIIb** absorbs at 1260 cm^{-1}.

The structure of the synthesized *O*-vinyl phosphorotrithioates suggests formation of geometric isomers. But the ^{1}H and ^{31}P NMR spectra show that the reaction proceeds stereoselectively to form a single isomer. However, the structure of the isolated isomer is impossible to assign unambiguously with the spectral evidence in hand.

Analysis of the ^{31}P and ^{1}H NMR spectra of the reaction mixtures shows that the rate of formation of *O*-vinyl phosphorotrithioates depends on the nature of the α-substituents in the carbonyl compounds. Hence, the most electophilic dichloroacetic aldehydes **IIa** and **VIa, VIb** react with thiophosphite **I** for 1 h. The decreased electrophilicity of the carbonyl carbon atom in monohaloacetaldehydes **IIb, IIc** and **VII** results in that these compounds fail to react without catalyst under prolonged heating (14–16 h), while in the presence of zinc chloride the reaction is complete within 4–8 h. The rate of the reaction of triethyl phosphorotrithioite with haloaldehydes also depends on the nature of the halogen. The reaction with chlorine-substituted carbonyl compound **IIb** is complete within 8 h. On replacement of chlorine by the more readily leaving bromine (aldehyde **IIc**) the reaction time is halved.

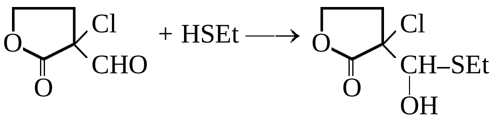
Note that in all the reactions of α-haloaldehydes with triethyl phosphorotrithioite we isolated, along with *O*-vinyl phosphorotrithioates, such by-products as trietyl phosphorotrithioate and triethyl phosphorotetrathioate whose formation is characteristic of reactions of trialkyl phosphorotrithioites with carbonyl compounds [2].

It is known [1,2] that reactions of *S*-esters of P(III) acids with carbonyl compounds are actively catalyzed with acids (specifically, HCl). In this connection we have studied the reaction of triethyl phosphorotrithioite with haloaldehyde **VIa** in the presence of equimolar amount of hydrogen chloride, which proceeds just at room temperature and leads to formation of vinyl phosphate **VIIIa**. In this case, the yield of the product increases by 13%.

The progress of the reaction of triethyl phosphorotrithioite with aldehyde **VII** in the presence of equimolar amount of hydrogen chloride was controlled by means of ^{31}P and ^{1}H NMR spectroscopy. In the ^{31}P NMR spectrum, signals at δ_P 188 and 211 ppm appear. They are characteristic of diethyl phosphorodithioite and ethyl phosphorodichloridothioite, respectively. In the ^{1}H NMR spectrum, the signal at δ 9.5 ppm, characteristic of the aldehyde proton, disappears and signals at δ 5.2 and 12.5 ppm appear, assigned to the >CH and OH protons of thioacetal **X**. As the temperature rises, the intensity of the signals at δ_P 188 and 211 ppm decreases, and the intensity of the signal at δ_P 56 ppm assigned to phosphorochloridodithioate **XII** increases.

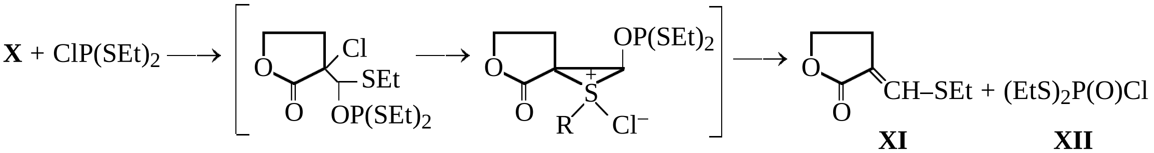
After heating of the reaction mixture at 100°C for 1 h, the proton signals assigned to thioacetal **X** disappear from the ^{1}H NMR spectrum, and a triplet at δ 7.25 ppm ($^4J_{HH}$ 2.5 Hz), characteristic of the vinyl proton of unsaturated thioester **XI** appears. Basing on the spectral data we can propose that in the first stage triethyl phosphorotrithioite reacts with hydrogen chloride to give diethyl phosphorochloridodithioite and ethanethiol [2] which further reacts with aldehyde

$$P(SEt)_3 + HCl \longrightarrow ClP(SEt)_2 + HSEt$$



VII **X**

VII to form thioacetal **X**. As the temperature rises, thioacetal **X** reacts with diethyl phosphorochloridodithioite to give an unstable phosphite which decomposes into unsaturated thioester **XI** and phosphorochloridodithioate **XII** according to the known scheme [9].

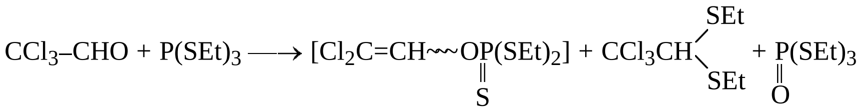

XI **XII**

We failed to isolate compounds **XI** and **XII** pure because of their close boiling points.

As the reaction of phosphorothioites with chloral in the presence of catalysts has not so far been studied, we turned to the reaction of triethyl phosphorotrithioite with chloral in the presence of catalytic amounts of zinc chloride. After heating of the reaction mixture at 100°C for 1 h, signals at δ_P 188 and 210 ppm appear in the ^{31}P NMR spectrum, belonging to diethyl phosphorochloridodithioite and ethyl phosphorodichloridothioite. Evidently, because of the steric overloading of the carbonyl carbon atom, the halogenophilic attack of phosphorus on the chlorine atom, leading to formation of phosphorochloridothioites, takes place. In addition, the ^{31}P NMR spectrum shows signals at δ_P 93 and 63.3 ppm, characteristic of triethyl phosphorotetrathioate and triethyl phosphorotrithioate, and a weak signal at δ_P 112 ppm, assignable to *O*-vinyl phosphorotrithioate **XIII**.

In the ^1H NMR spectrum of the reaction mixture we observed, along with the signals at δ 1.3 (CH_3) and 2.9 ppm ($–SCH_2–$), a singlet at δ 5.5 ppm, related to the proton of chloral dithioacetal **XIV**, and a weak doublet at δ 7.05 ppm ($^3J_{PH}$ 12.5 Hz), characteristic of the proton at the double bond of *O*-vinyl phosphorotrithioate **XIII**.

Fractionation of the reaction mixture of phosphorotrithioite **I** with chloral gave thioacetal **XIV** in 35% yield and triethyl phosphorotrithioate in 41% yield.



$$CCl_3–CHO + P(SEt)_3 \longrightarrow [Cl_2C{=}CH\sim\sim O\underset{\underset{S}{\|}}{P}(SEt)_2] + CCl_3CH\begin{matrix}\diagup SEt\\ \diagdown SEt\end{matrix} + \underset{\underset{O}{\|}}{P}(SEt)_3$$

XIII **XIV**

Hence, we established that triethyl phosphorotrithioite reacts with α-halocarbonyl compounds by the Perkow scheme to form *O*-vinyl phosphorotrithioates. Addition of a catalytic amount of zinc chloride to the reaction mixture of phosphorotrithioite **I** with α-monohaloaldehydes significantly accelerates the reaction but does not alter its direction.

The spectral characteristics and elemental analyses of the resulting products are listed in the table.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer in the range ν 400–3800 cm^{-1} for liquid films or suspensions in Vaseline oil between KBr plates. The ^1H NMR spectra were measured on a Tesla BM-567 (100 MHz) against internal HMDS. The ^{31}P NMR spectra were obtained on a Bruker MSL-400 spectrometer (162 MHz) against external 85% phosphoric acid.

Functionalyzed haloaldehydes **II, VI,** and **VII** were prepared according to the procedures in [10].

***S,S*-Diethyl *O*-[2-(diisopropoxyphosphinoyl)-2-phenylvinyl]phosphorotrithioate (IIIa)**. A mixture of 4.28 g of phosphorotrithioite **I** and 5.5 g of aldehyde **IIa** was heated at 100°C for 1 h. Product **IIIa** was purified from admixtures (triethyl phosphorotrithioate, triethyl phosphorotetrathioate) by film distillation [spiral temperature 120°C (0.05 mm Hg)]. Film distillation of the residue [spiral temperature 150°C

IR and ^{1}H and ^{31}P NMR spectra elemental analyses of compounds **III, VIII**, and **IX**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz)	^{31}P NMR spectrum, δ_P, ppm
IIIa	564 (PS), 652 (P=S), 695 (CCl), 995 (POC), 1261 (P=O), 1625 (C=C)	1.25 m (18H, $6CH_3$), 2.9 m (4H, $2SCH_3$), 4.6 m (2H, 2OCH), 7.6 d.d (1H, =CH, $^3J_{P^AH}$ 12, $^3J_{P^BH}$ 12.5)	6, 112
IIIb	555 (PS), 689 (P=S), 1024 (POC), 1261 (P=O), 1640 (C=C)	1.3 m (12H, $4CH_3$), 3.0 m (4H, $2SCH_3$), 4.1 q, (4H $2OCH_2$), 7.4 s (5H, Ph), 7.7 d.d (1H, =CH, $^3J_{P^AH}$ 12, $^3J_{P^BH}$ 12.5)	6, 111.7
VIIIa	558 (PS), 660 (P=S), 690 (CCl), 1199 (POC), 1654 (C=C), 1694 (C=O), 3033 (Ph)	1.3 m (6H, $2CH_3$), 2.9 m (4H, $2SCH_3$), 7.4 s (5H, Ph), 8.0 d (1H, =CH, $^3J_{PH}$ 12.5)	93
VIIIb	556 (PS), 665 (P=S), 704 (CCl), 1066 (POC), 1634 (C=C), 1725 (C=O)	1.3 m (9H, $6CH_3$), 2.9 m (4H, $2SCH_3$), 4.2 m (2H, OCH_2), 8.0 d (1H, =CH, $^3J_{PH}$ 12.5)	112
IX	574 (PS), 659 (P=S), 1020 (POC), 1678 (C=C), 1752 (C=O)	1.3 t (6H, $2CH_3$), 2.9 m (4H, $2SCH_3$), 3.1 t (2H, CH_2), 4.3 t (2H, OCH_2), 7.55 d.t (1H, =CH, $^3J_{PH}$ 12.5, $^4J_{HH}$ 2.5)	112

Table (Contd.)

Comp. no.	Found, %		Formula	Calculated, %	
	P	Cl		P	Cl
IIIa	14.47	8.29	$C_{12}H_{25}ClO_4P_2S_3$	14.53	8.32
IIIb	14.05	–	$C_{16}H_{26}O_4P_2S_3$	14.09	–
VIIIa	8.41	9.55	$C_{13}H_{16}ClO_2PS_3$	8.46	9.69
VIIIb	9.19	10.53	$C_9H_{16}ClO_3PS_3$	9.27	10.61
IX	10.35	–	$C_9H_{16}O_3PS_3$	10.40	–

(0.05 mm Hg)] gave 3.83 g (45%) of the target product, n_D^{20} 1.5060.

***S,S*-Diethyl *O*-[2-(diethoxyphosphinoyl)-2-phenylvinyl] phosphorotrithioate (IIIb)**. *a*. A mixture of 4.28 g of phosphorotrithioite **I** and 5.81 g of aldehyde **IIb** was heated at 100–110°C for 8 h in the presence of a catalytic amount of zinc chloride. Distillation of the reaction mixture gave 5.89 g (67%) of product **IIIb**, bp 145–148°C (0.05 mm Hg), n_D^{20} 1.5432.

b. Analogously 4.28 g of phosphorotrithioite **I** and 6.7 of aldehyde **IIc** were heated at 100°C for 4 h to give 6.33 g (72%) of product **IIIb**, bp 145–148°C (0.05 mm Hg), n_D^{20} 1.5434.

Diethyl benzylphosphonate sodium enolate (IV). A mixture of 148 g of ethyl formate and 228 g of diethyl benzylphosphonate was added dropwise with a vigorously stirred and cold (–5–0°C) mixture of 23 g of finely cut metallic sodium, 1.5 l of diethyl ether, and 10 ml of absolute ethanol (for initiation of the reaction). The addition rate was such that the temperature of the reaction mixture was maintained at a temperature of no higher than 5°C. After the addition had been complete, the reaction mixture was kept for 1 h at a decreased temperature, then for 3 days at room temperature, and, finally, for 1.5 h in ether under reflux. Enolate **IV** precipitated and was filtered off, washed with ether (3 × 100), and dried in a water-jet-pump vacuum at 40–60°C. Dry enolate **IV** is a fine cream-colored powder. Yield 250 g (90%).

***S,S*-Diethyl *O*-[2-(diethoxyphosphinoyl)-2-phenylvinyl]phosphorotrithioate (IIIb)**. Enolate **IV**, 5.56 g, was added to a cold (0°C) solution of 3.39 g of phosphorus sulfochloride in 10 ml of ether. The addition rate was such that the temperature of the reaction mixture was maintained at a temperature of no higher than 5°C. After the addition had been complete, the reaction mixture was stirred for 1 h with cooling and for 3 h at room temperature. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 1.3 m (6H, $2CH_2$), 4.0 q (4H, $2OCH_2$), 7.3 s (5H, Ph), 7.7 d (1H, =CH, $^3J_{PH}$ 12.5 Hz). ^{31}P NMR spectrum, δ_P, ppm: 16; 55.7. A day after, the reaction mixture was cooled to 0°C, a mixture of 2.48 g of ethanethiol and 4.40 g of triethylamine was added dropwise to it, and stirring was continued at 0–5°C for 2 h and for 3 h without the cooling bath. The precipitate that formed was filtered off, the solvent was removed from the filtrate, and the residue was distilled to obtain 3 g (34%) of product **IIIb**, bp 145–149°C (0.05 ppm Hg), n_D^{20} 1.5429.

***O*-(2-Benzoyl-2-chlorovinyl) *S,S*-diethyl phosphorotrithioate (VIIIa)**. *a*. A mixture of 4.28 g of phosphorotrithioite **I** and 4.34 g of aldehyde **VIa** was heated at 100°C for 1 h. Product **VIIIa** was purified from admixtures (triethyl phosphorotrithioate and triethyl phosphorotetrathioate) by film distillation [spiral temperature 120°C (0.05 mm Hg)]. The residue was treated with 5 ml of diethyl ether, and the crystals that formed were filtered off, washed with ether, and dried give 3.08 g (42%) of product **VIIIa**, decomp. point 240°C.

b. Through a solution of 4.28 g of phosphorotrithioite **I** and 4.34 g of aldehyde **VIa** in 20 ml of methylene chloride, 0.73 g of hydrogen chloride was bubbled at 20°C. The reaction mixture was left to stand for 2 days, washed with water to pH 6, and dried over $CaCl_2$. The solvent was removed, and the residue was subjected to film distillation. Product **VIIIa** was isolated like in procedure *a*. Yield 4 g (55%), crystals, decomp. point 240°C.

Ethyl 3-[bis(ethylsulfanyl)phosphinothioyloxy]-2-chloroacrylate (VIIIb). A mixture of 6.43 g of phosphorotrithioite **I** and 5.55 g of aldehyde **VIb** was heated at 100°C for 2 h and then subjected to film distillation. Admixtures were removed at the spiral temperature 120°C (0.05 mm Hg), and the product was distilled at the spiral temperature 145°C (0.05 mm). Yield 5.33 g (53%), n_D^{20} 1.5550.

***S,S*-Diethyl *O*-[2-oxotetrahydrofuran-3-ylidenemethyl] phosphorotrithioate (IX)**. A mixture of 6.45 g of phosphorotrithioite **I** and 4.46 g of aldehyde **VII** was heated at 95–100°C for 4 h in the presence of a catalytic amount of zinc chloride. Product **IX** was purified similarly to **VIIIb**. Yield 5 g (56%), n_D^{20} 1.5294.

Reaction of triethyl phosphorotrithioite with α-chloro-α-formyl-γ-butyrolactone (VII) in the presence of hydrogen chloride. Through a solution of 6.43 of phosphorotrithioite **I** and 4.46 g of aldehyde **VII** in methylene chloride, 1.1 g of hydrogen chloride was passed at 20°C. The reaction mixture was left to stand for 2 days. ^{31}P NMR spectrum, δ_P, ppm: 210, 188. Subsequent heating at 100°C for 1 h and distillation gave a fraction [bp 97–98°C (0.05 Hg)] comprising a mixture of unsaturated thioester **XI** and phosphorochloridodithioate **XII**. The ^1H NMR spectrum contains signals of two compounds. Compound **XI** (acetone-d_6), δ, ppm: 1.15 t (3H, CH_3), 2.75 m (4H, CH_2, SCH_2), 4.20 t (2H, OCH_2), 7.25 t (1H, =CH, $^4J_{HH}$ 2.5 Hz). Compound **XII** (acetone-d_6), δ, ppm: 1.15 m (6H, $2CH_3$), 2.75 m (4H, $2SCH_2$). ^{31}P NMR spectrum: δ_P 56 ppm.

Reaction of triethyl phosphorotrithioite with chloral. A mixture of 4.28 g of phosphorotrithioite **I** and 5.88 g of chloral was heated at 100°C in the presence of a catalytic amount of zinc chloride. ^{31}P NMR spectrum, δ_P, ppm: 63 [$(EtS)_3P{=}O$]. 93 [$(EtS)_3P{=}S$], 112 [$(EtS)_2P(S)OCH{=}CCl_2$], 188 [$(EtS)_2PCl$]. After 2 days, excess chloral was removed in a vacuum. Distillation of the residue gave 2.57 g (35%) of thioacetal **XIV**, bp 107°C (0.05 mm Hg), n_D^{20} 1.5400 [^1H NMR spectrum (acetone-d_6), δ, ppm: 1.25 t (6H, $2CH_3$), 2.8 m (4H, $2SCH_2$), 5.55 s (1H, –CH<)] and 1.89 g (41%) of triethyl phosphorotrithioate, bp 140°C (0.05 mm Hg), n_D^{20} 1.5702, δ_P 62 ppm {published data [3]: bp 174°C (10 mm Hg), n_D^{20} 1.5709, δ_P 61 ppm}.

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