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# Some Transformations of Mono- and Dichloro(diethoxyphosphoryl)acetaldehydes

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**Abstract**—Addition of ethanol and diethyl phosphonate to the carbonyl group of 2,2-dichloro-2-(diethoxyphosphoryl)-acetaldehyde has been studied, and the corresponding α-chloro ether, acetal, and phosphorylated metrifonate have been obtained. α,α-Dichloro-α-phosphoryl carbonyl compounds have been found to undergo haloform cleavage by the action of bases. Perkow reaction of mono- and dichloro(diethoxyphosphoryl)acetaldehydes with triethyl phosphite afforded diethyl 2-(diethoxyphosphoryl)ethenyl phosphates.

**Keywords:** (diethoxyphosphoryl)acetaldehyde, alkoxyvinylphosphonates, haloform type cleavage, chloro ethers, acetals, metrifonate

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α-Phosphorylated aldehydes are convenient starting materials for solving fundamental problems of organophosphorus chemistry. In recent time, halo-substituted α-phosphorylated aldehydes have attracted much attention since the presence of halogen atoms in aldehyde molecules gives rise to additional coordination sites and opens synthetic routes to various organophosphorus compounds.

2-Chloro-2-(diethoxyphosphoryl)acetaldehyde has been synthesized in a low yield by reaction of chloromethylphosphonate with ethyl formate in the presence of metallic sodium [1]. A simple preparative synthesis of mono- and dichloro(diethoxyphosphoryl)acetaldehydes **1** and **2** by low-temperature chlorination of (diethoxyphosphoryl)acetaldehyde with molecular chlorine was later reported in [2, 3]. Recent systematic studies of phosphorylated monochloro aldehydes made it possible to obtain a number of heterocyclic systems that are difficult to access by other methods [4–6]. Acetaldehydes **1** and **2** can be regarded as phosphorylated chloral derivatives, and study of their reactivity is important for organic synthesis.

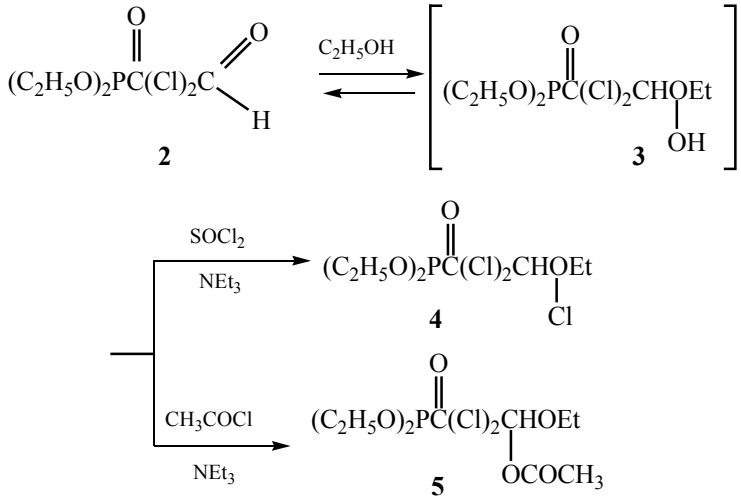
Herein we report some transformations of aldehydes **1** and **2** in reactions with ethanol, ethanolic sodium hydroxide, diethyl phosphonate, triethyl phosphite, and dry sodium ethoxide, which involved the carbonyl group of the substrate.

Aldehyde **2** readily adds ethanol to give hemiacetal **3** which is stable at room temperature; on heating above 50°C, compound **3** decomposed into the initial aldehyde and ethanol. The structure of **3** was confirmed by the IR spectrum which lacked carbonyl stretching band but contained $\nu_{OH}$ band at 3300–3600 $cm^{-1}$, as well as by some chemical transformations (Scheme 1). In particular, treatment of **3** with thionyl chloride on cooling gave diethyl 1,1,2-trichloro-2-ethoxyethylphosphonate (**4**) as a result of substitution of the hydroxy group by chlorine. Compound **4** was stable even on prolonged heating (120–150°C, 2 h). The acylation of **3** with acetyl chloride in the presence of triethylamine furnished acetate **5**. α-Chloro ether **4** was also synthesized independently by passing molecular chlorine through 2-ethoxyethenylphosphonic dichloride heated to 120°C; this reaction involved successive chlorination of the double bond, dehydrochlorination, and further chlorination with the formation of 1,1,2-trichloro-2-ethoxyethylphosphonic dichloride (**6**), and alcoholysis of the latter in the presence of a tertiary amine afforded phosphonate **4** (Scheme 2). It should be noted that compounds **4** and **5** exhibit enhanced fibrinolytic activity.

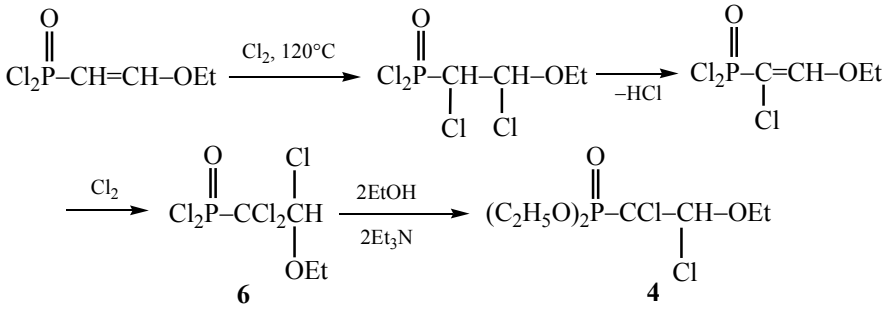
Phosphorylated dichloroacetaldehyde **2** readily reacted with diethyl phosphonate (Abramov reaction) to afford hydroxy bis-phosphonate **7** (Scheme 3); the latter can be regarded as phosphorylated metrifonate derivative which may be used as insecticide in agriculture.

Haloform type cleavage of the $C^{\alpha}$–$C^{\beta}$ bond of aldehyde **2** by the action of ethanolic sodium hydroxide or

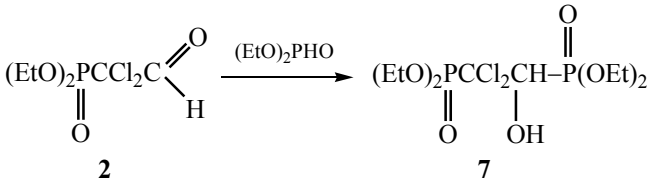
**Scheme 1.**



**Scheme 2.**



**Scheme 3.**



morpholine produced diethyl (dichloromethyl)phosphonate (**8**). In the reaction with morpholine, morpholine-4-carbaldehyde was also formed (Scheme 4). In contrast, the reaction of **2** with solid sodium ethoxide in boiling diethyl ether (heterogeneous conditions) involved cleavage of the P–C bond with the formation of triethyl phosphate (**9**) and sodium 2,2-dichloroethen-1-olate; treatment of the latter with dilute aqueous HCl gave dichloroacetaldehyde (**10**) (Scheme 5).

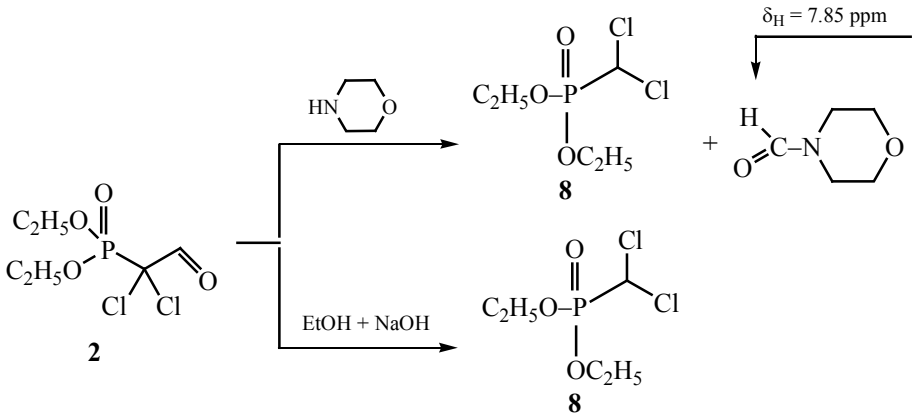
Like chloral, Perkow reaction of mono- and dichloro aldehydes **1** and **2** with triethyl phosphite afforded 2-(diethoxyphosphoryl)ethenyl diethyl phosphates **11a** and **11b** (Scheme 6). According to the $^1$H NMR data, the C=C double bond in **11a** has *E* configuration ($^3J_{HH}$ = 14.0 Hz).

Thus, the chemical reactivity of chlorinated (diethoxyphosphoryl)acetaldehydes **1** and **2** is similar to the reactivity of trichloroacetaldehyde. They add nucleophiles at the carbonyl group, undergo haloform type cleavage, and react with trialkyl phosphites according to Perkow. Cleavage of the P–C bond with the formation of triethyl phosphate was observed in the reaction with solid sodium ethoxide.

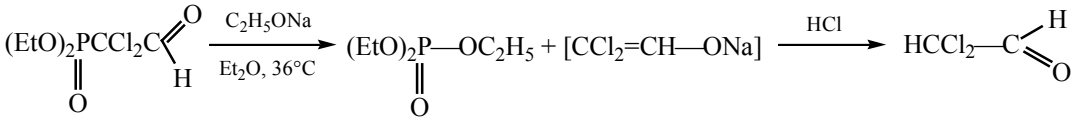
## EXPERIMENTAL

The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker-300 spectrometer at 300 and 75 Hz, respectively, using hexamethyldisiloxane as internal standard. The IR spectra were recorded in mineral oil on a Specord 75-IR instrument.

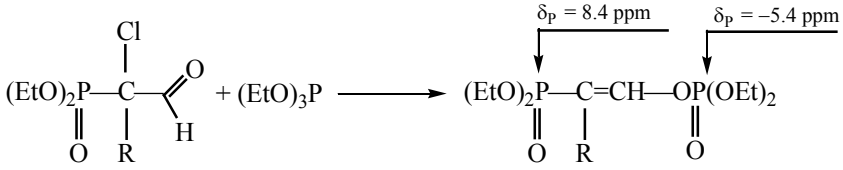
**Scheme 4.**



**Scheme 5.**



**Scheme 6.**



R = H (**1**, **11a**), Cl (**2**, **11b**).

**Diethyl (1,1,2-trichloro-2-ethoxyethyl)phosphonate (4).** A mixture of 10 g of aldehyde **2**, 2.8 mL of ethanol, 5 g of triethylamine, and 50 mL of benzene was cooled to 0–5°C, and 3.2 g of thionyl chloride was added. The mixture was stirred for 3 h at 30–40°C, the precipitate was filtered off, and the filtrate was evaporated. Yield 8.2 g (58%), bp 105–108°C (0.5 mmHg), $d_4^{20}$ = 1.3113, $n_D^{20}$ = 1.4670. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.1–1.25 m (9H, $CH_3$), 3.85–4.02 m (6H, $OCH_2$), 5.85 d (1H, CH, $^2J_{HP}$ = 2.0). Found, %: Cl 33.44; P 9.77. $C_8H_{16}Cl_3O_4P$. Calculated, %: Cl 33.97; P 9.89.

**2,2-Dichloro-2-(diethoxyphosphoryl)-1-ethoxyethyl acetate (5)** was synthesized in a similar way from 25 g of aldehyde **2** and 6.6 g of acetyl chloride using 11 mL of ethanol and 6.7 g of pyridine. Yield 22 g (71%), bp 120–121°C (0.5 mmHg), $d_4^{20}$ = 1.2724, $n_D^{20}$ = 1.4565. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.1 t (3H, $CH_3$, $^3J_{HH}$ = 6.9), 1.25 t (6H, $CH_3$, $^3J_{HH}$ = 7.2), 2.1 s (3H, $CH_3CO$), 3.75 m (2H, $OCH_2$), 4.1 m (4H, $OCH_2$), 5.95 d (1H, CH, $^2J_{HP}$ = 2.0). Found, %: Cl 23.54; P 10.55. $C_{10}H_{19}Cl_2O_6P$. Calculated, %: Cl 21.06; P 10.54.

**(1,1,2-Trichloro-2-ethoxyethyl)phosphonic dichloride (6).** Dry chlorine was passed over a period of 2–3 h through 10 g of 2-ethoxyethenylphosphonic dichloride heated to 120°C. The mixture was then subjected to fractional distillation. Yield 51%, bp 89–90°C (0.2 mmHg), mp 48°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.22 t (3H, $CH_3$, $^3J_{HH}$ = 6.9), 3.75 m (2H, $CH_2O$), 5.75 s (1H). Found, %: P 3.67; Cl 22.14. $C_4H_6Cl_5PO_2$. Calculated, %: P 3.82; Cl 21.90.

**Alcoholysis of (1,1,2-trichloro-2-ethoxyethyl)-phosphonic dichloride (6).** Ethanol, 10 mL, was added with vigorous stirring to a mixture of 5 g (0.02 mol) of phosphonic dichloride **6** and 2.1 g (0.02 mol) of triethylamine in 100 mL of diethyl ether on cooling with ice water. The mixture was stirred for 2 h at room temperature and was then refluxed for 2 h. The precipitate of triethylamine hydrochloride was filtered off, the solvent was

removed from the filtrate, and the product (compound **4**) was isolated by fractional distillation. Yield 3.2 g (64%), bp 106–108°C (0.5 mmHg), $d_4^{20}$ = 1.3134, $n_D^{20}$ = 1.4657.

**Tetraethyl (1,1-dichloro-2-hydroxyethane-1,2-diyl)-diphosphonate (7).** Aldehyde **2**, 6.2 g, was cooled to 5–8°C, and 2.7 g of diethyl phosphate was added with stirring. The mixture was stirred for 3 h at 50–60°C, and was then evacuated at 60–80°C. Yield 5 g (70%). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.15–1.25 m (12H, $CH_3$), 3.95–4.15 m (8H, $OCH_2$), 3.36 d (1H, PCH, $^2J_{HP}$ = 18.0). Found, %: P 16.21; Cl 18.62. $C_{10}H_{22}Cl_2P_2O$. Calculated, %: P 16.02; Cl 18.33.

**Diethyl (dichloromethyl)phosphonate (8).** *a*. Aldehyde **2**, 10 g, was added to a solution of 1.6 g of sodium hydroxide in 20 mL of ethanol. Evolution of heat was observed, and a solid precipitated. The precipitate was filtered off, the filtrate was evaporated, and the residue was distilled under reduced pressure. Yield 7 g (88%), bp 77–79°C (0.5 mmHg), $d_4^{20}$ = 1.2808, $n_D^{20}$ = 1.4520. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.5 t (6H, $CH_3$, $^3J_{HH}$ = 7.1), 4.3 m (4H, $OCH_2$, $^3J_{HH}$ = 7.1), 5.5 d (1H, CH, $^2J_{HP}$ = 12.7). $^{13}$C NMR spectrum, $\delta_C$, ppm: 16.61 ($CH_3$), 61.57 (CH), 65.39 ($CH_2$). Found, %: P 14.21; Cl 31.65. $C_5H_{11}Cl_2O_3P$. Calculated, %: P 14.09; Cl 31.81.

*b*. Ethanol, 2.7 mL, was added to a mixture of 12 g of aldehyde **2** and 30 mL of benzene, 5 mL of morpholine was then added, and the mixture was stirred for 2 h at 40–60°C. The solvent was distilled off, and the residue was subjected to fractional distillation under reduced pressure. Yield 13.7 (72%), bp 77–78°C (0.5 mmHg), $d_4^{20}$ = 1.2826, $n_D^{20}$ = 1.4511.

**Reaction of aldehyde 2 with solid sodium ethoxide.** Aldehyde **2**, 23 g, was added to a mixture of 5 g of freshly prepared sodium ethoxide in 20 mL of diethyl ether. The mixture vigorously boiled up on heating to 34°C. The precipitate was filtered off, and triethyl phosphate (**9**) was isolated from the filtrate. Yield 19.6 g (70%), bp 50–51°C (1 mmHg), $d_4^{20}$ = 1.1007, $n_D^{20}$ = 1.4085 [7].

The precipitate was treated with dilute aqueous HCl to obtain 4.9 g (41%) of dichloroacetic aldehyde (**10**), bp 90–92°C, $d_4^{20}$ = 1.3740, $n_D^{20}$ = 1.4290 [8].

**2-(Diethoxyphosphoryl)ethenyl diethyl phosphate (11a).** Triethyl phosphite, 3.5 g (0.02 mol), was added with stirring to a mixture of 6.5 g (0.02 mol) of aldehyde **1** and 100 mL of dioxane cooled to 5–10°C. The mixture was stirred for 1 h at room temperature and for 2–3 h at 60–80°C. The solvent was removed, and the residue was distilled under reduced pressure. Yield 6.4 g (76%), bp 144–145°C (0.1 mmHg), $n_D^{20}$ = 1.4260. $^1$H NMR spectrum ($CDCl_3$) δ, ppm (*J*, Hz): 1.15–1.25 m (12H, $CH_3$, $^3J_{HH}$ = 6.9), 4.01–4.20 m (8H, $OCH_2$), 5.4 d.d (1H, PCH=, $^3J_{HH}$ = 14.0, $^2J_{HP}$ = 10.0), 7.20 d.d.d (1H, =CHO, $^3J_{HH}$ = 14.0, $^3J_{HP}$ = 6.5, 12.0). Found, %: C 37.68; H 10.12; P 19.76. $C_{10}H_{22}O_7P_2$. Calculated, %: C 37.97; H 9.96; P 19.62.

**2-Chloro-2-(diethoxyphosphoryl)ethenyl diethyl phosphate (11b)** was synthesized in a similar way. Yield 7.9 g (82%), bp 147–148°C (0.1 mmHg), $n_D^{20}$ = 1.4480. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.25 t (6H, $CH_3$, $^3J_{HH}$ = 7.2), 1.30 t (6H, $CH_3$, $^3J_{HH}$ = 7.1), 4.02 m (8H, $OCH_2$), 7.2 q (1H, CH=, $^3J_{HP}$ = 9.0). $^{13}$C NMR spectrum, $\delta_C$, ppm (*J*, Hz): 82.6 (PC=, $^1J_{CP}$ = 158.0), 163.5 (=CO, $^2J_{CP}$ = 20.0). Found, %: P 17.54; Cl 10.23. $C_{10}H_{21}ClO_7P_2$. Calculated, %: C 34.23; H 5.99; P 17.68; Cl 10.12.

## CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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