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CHEMISTRY

Mono- and Di(dechloromethylthioylation) of Dichloromethylarenes with *S*-Methyl Diethylthiophosphinate

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Abstract—The attack of the thiol sulfur atom (P–SMe) on the methine carbon as the main route of the new reaction of dichloromethylarenes with *S*-methyl diethylthiophosphinate has been predicted and experimentally confirmed on the basis of the electronic structure of the *S*-alkyl esters of P(IV) acids. The processes of the mono- and di(dechloromethylthioylation) of dichloromethyl group have been realized. A new approach to the synthesis of the arenecarbaldehyde dimethyl dithioacetals has been developed avoiding the use of gaseous highly toxic methyl mercaptan.

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The reaction of ambident (P=O, P–O) nucleophiles, methyl esters of P(IV) acids, with dichloromethylarenes resulting in aromatic aldehydes and acid anhydrides has been described in the literature [1, 2]. However, there are no data on the reaction of substituted benzylidene chlorides with ambident (P=O, P–S) nucleophiles, in particular, *S*-methyl diethylthiophosphinate.

The aim of this work is to predict and confirm experimentally the main route of the new reaction of *S*-methyl diethylthiophosphinate **Ia** with dichloromethylarenes **II** and the synthesis of arenecarbaldehyde dimethyl dithioacetals without using highly toxic gaseous methyl mercaptan.

We revealed a new reaction of *S*-methyl diethylthiophosphinate **Ia** with dichloromethylarenes **II**. Theoretically, we could assume two reaction routes: *a* and *b* (Scheme 1). We suppose two possible variants of dechloromethylthioylation reaction (route *a*): without charge separation via synchronous four-membered cyclic electron transfer **A** and through charge separation via intermediate formation of sulfonium cation **B**. The further substitution of chlorine atom in compounds **III** by methylthio group should result in dithioacetal **V** and diethylphosphinoyl chloride **IV** (route *a*).

An alternative route is the attack of phosphoryl oxygen at the methine carbon atom of *gem*-dichloride **II** (route *b*). Initially formed quasiphosphonium salt **VI** eliminates methyl chloride to give dechlorodiethylthiophosphinyloxylation product **VII**. The latter, like its oxygen analog $ArCH(Cl)OP(O)Et_2$, seems to be unstable and decomposes into arenecarbaldehyde **VIII** and diethylphosphinothioyl chloride **IX**.

To select the most probable route from *a* and *b*, we focused our attention on the electron structure of *S*-alkyl esters of P(IV) acids $R^1R^2P(O)SR$ **Ia–Ie**. Table 1 shows vertical ionization potentials (IP) of the upper occupied molecular orbitals of *S*-alkyl esters of P(IV) acids [3].

The data of Table 1 shows that IP n_S for all compounds **I** are considerably lower (9.03–9.30 eV) than IP $p_{\pi,0}$ (9.81–10.54 eV), that is, the electron donating ability of MeS group is considerably higher than that of the P=O group. Therefore, we draw a conclusion that route *a* is the most probable route of this reaction (Scheme 1). We selected compound **Ia** for study because, in contrast to compounds **Ic–Ie**, it has only two electron donating centers: SMe and P=O.

Table 1. Vertical ionization potentials of n_s, $p_{\pi,0}$, and n_0 orbitals of *S*-alkyl esters of P(IV) acids **Ia–Ie**

No.	Compound	IP n_s, eV	IP $p_{\pi,0}$, eV	IP n_0, eV
Ia	$MeSP(O)Et_2$	9.17*	9.87*	–
Ib	$EtSP(O)Et_2$	9.03	9.81	–
Ic	$MeSP(O)(OEt)_2$	9.12	10.48	11.23
Id	$EtSP(O)(OEt)_2$	9.26	10.54	10.95
Ie	EtSP(O)(OMe)Me	9.30	10.12	10.70

* Values obtained from the additivity of IP of n_s and $p_{\pi,0}$ orbitals of compounds **Ib**, **Ic**, and **Id**.

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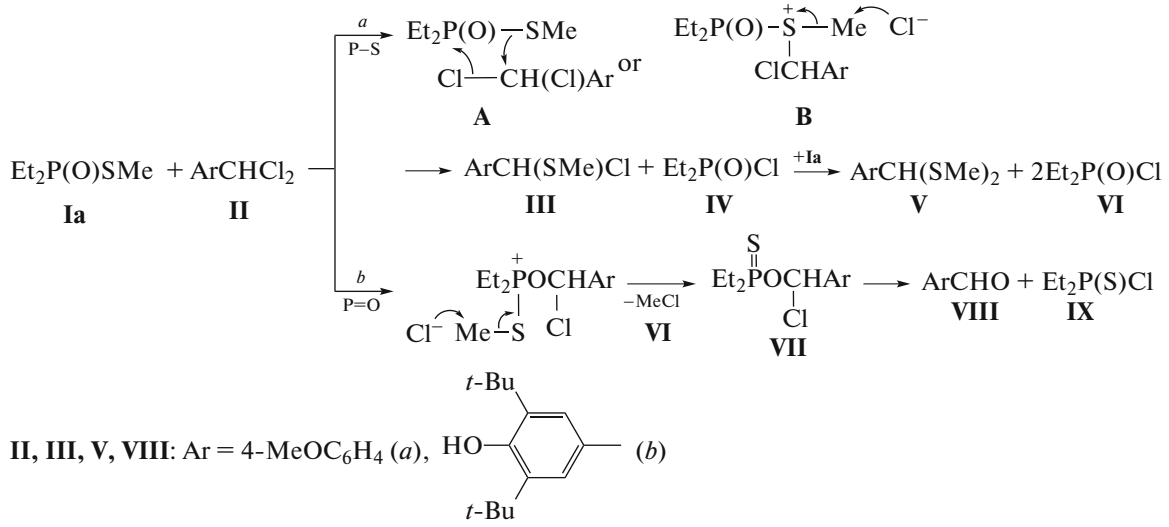


Scheme 1.

Experiments confirmed the realization of route *a* for this reaction. The reaction of dichloromethylarenes **II** with *S*-methyl diethylthiophosphinate **Ia** at the 1 : 1 ratio was carried out at 80–100°C. According to ^{1}H and ^{31}P NMR spectra, the reaction of 4-methoxybenzylidene chloride **IIa** with ester **Ia** leads mainly to a mixture of compound **IV** (δ_P 75.0 ppm) and **IIIa** (δ_H 6.32 ppm, s, CH; 2.40 ppm, s, SMe). This fact indicates the primary attack of the thiol sulfur atom on the methine carbon of the *gem*-dichloride **IIa**.

The attack of the phosphoryl oxygen on the methyne carbon of dichloride **II** seems to be absent because the ^{1}H and ^{31}P NMR spectra of reaction mixtures contain no signals at δ_H 10 ppm (Ar<u>CH</u>O **VIII**) and δ_P 108.8 ppm ($Et_2P(S)Cl$ **IX**).

When compounds **Ia** and **II** react in the 2.5 : 1 ratio or when reaction mixture at the 1 : 1 ratio was mixed with the additional equivalent of phosphinate **Ia** and heated for 1.5–3 h, the process resulted in the di(dechloromethylthioylation) of compound **II** to form dithioacetals **V**, which were isolated in individual state (Scheme 2).

Compounds **V** were commonly obtained with the use of methyl mercaptan and its different mercaptides [4–6]. Only work [7] reported their synthesis by the electrolysis of dithioacetic esters, which were prepared using toxic CS_2 and organomagnesium compounds [8].

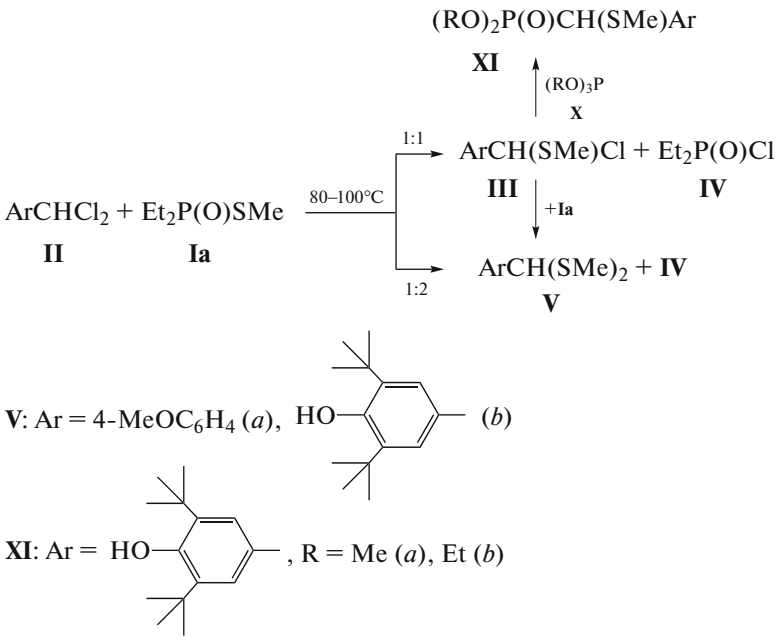
α-Chloroethers **III** were not isolated in pure state. However, their structure was confirmed by their involvement in the reaction with additional equivalent of compound **Ia** (Scheme 2) and trialkyl phosphites **X** (Scheme 2). In the latter reaction, we obtained new phosphorus- and sulfur-containing organic compounds **XI**.

In summary, it should be noted that we revealed new reaction between *S*-methyl diethylthiophosphinate and dichloromethylarenes. First, based on the analysis of electronic structure of *S*-alkyl esters of P(IV) acids, we predicted and then confirmed experimentally the *a* route of the mono- and di(dechloromethylthioylation) reaction of dichloromethyl group to form α-chlorothioether and arenecarbaldehyde dithioacetal. We developed the method of synthesis of arenecarbaldehyde dimethyl dithioacetals avoiding the use of highly toxic gaseous methyl mercaptan.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Tesla BS-567A and a Bruker MSL-400 spectrometers operating at 100 and 400 MHz, respectively, using residual proton signals of the deuterated solvents (DMSO-d_6, acetone-d_6, and $CDCl_3$) as a reference. ^{31}P NMR spectra were recorded on a Bruker MSL-400 spectrometer operating at 162 MHz using 85% H_3PO_4 as an external reference. IR spectra were obtained on a PerkinElmer Spektrum 65 Fourier transform IR spectrophotometer in the range 400–4000 cm^{-1} as Nujol mulls. Reaction dynamics was studied by ^{1}H and ^{31}P NMR spectroscopy.

4-Methoxybenzaldehyde dimethyl dithioacetal Va. (A) A mixture of 3.82 g (0.02 mol) of 4-methoxybenzaldehyde **IIa** and 7.61 g (0.05 mol) of *S*-methyl diethylthiophosphinate **Ia** was heated at 100°C for 4 h. The reaction mixture was treated with 20 mL of diethyl ether, washed with water (2 × 20 mL), and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure, the residue was distilled to give 2.10 g (49%) of compound **Va**, bp 169–170°C (12 mmHg).



Scheme 2.

^{1}H NMR (CCl_4 + $CDCl_3$), δ, ppm: 7.24 and 6.76 (both d, 4H, C_6H_4, $^3J_{HH}$ 8.6), 4.70 (s, 1H, CH), 2.03 (s, 6H, SMe).

For $C_{10}H_{14}OS_2$ anal. calcd. (%): C, 56.03; H, 6.58; S, 29.92.

Found (%): C, 55.88; H, 6.73; S, 29.47.

(B) A mixture of 3.82 g (0.02 mol) of dichloride **IIa** and 3.04 g (0.02 mol) of *S*-methyl diethylthiophosphinate **Ia** was heated at 100°C for 4 h. The ^{1}H NMR spectrum of the reaction mixture showed intense resonance signals at δ_H 6.04 (s, ClCH-S) and 2.32 (s, CHSMe) related to compound **III**. Compound **Ia** 4.57 g (0.03 mol) was added supplementary and the mixture was heated at 100°C for 3 h. The treatment of the reaction mixture by the method A resulted in 2.23 g (52%) of product **Va**.

4-Hydroxy-3,5-di-*tert*-butylbenzaldehyde dimethyl dithioacetal Vb.

By the analogy with compound **Va**, 0.53 g (43%) of compound **Vb** as colorless crystals, mp 69–70°C, was obtained by the method A from 1.00 g (0.0035 mol) of dichloride **IIb** and 1.58 g (0.0105 mol) of thiophosphinate **Ia**.

^{1}H NMR (CCl_4 + acetone-d_6), δ, ppm: 7.32 (s, 2H, C_6H_2), 5.56 (s, 1H, OH), 4.89 (s, 1H, CH), 2.24 (s, 6H, SMe), 1.59 (s, 18H, CMe_3).

For $C_{17}H_{28}OS_2$ anal. calcd. (%): C, 65.33; H, 9.03; S, 20.52.

Found (%): C, 64.89; H, 9.15; S, 20.13.

(4-Hydroxy-3,5-di-*tert*-buthylphenyl)(methylthio)-methanedimethoxyphosphonate XIa. A mixture of 1.45 g (0.005 mol) of 4-hydroxy-3,5-di-*tert*-butylbenzylidene chloride **IIb** and 1.14 g (0.0075 mol) of *S*-methyl diethylthiophosphinate **Ia** was heated at 80°C for 1 h and allowed to cool to ambient temperature. Trimethyl phosphite **Xa** 1.55 g (0.0125 mol) was added dropwise with stirring to the reaction mixture. Reaction mixture warming and methyl chloride evolution were observed. The reaction mixture allowed to stand overnight, dissolved in 10 mL of diethyl ether, and washed with water (2 × 10 mL). The organic layer was separated and dried with anhydrous sodium sulfate. The solution was filtered and the solvent was removed under reduced pressure. The residue was treated with 10 mL of dry hexane to give 0.86 g (46% over two stages) of compound **XIa** as a colorless powder, mp 130–131°C.

^{1}H NMR (acetone-d_6), δ, ppm: 7.40 (d, 2H, C_6H_2, $^4J_{HH}$ 1.8 Hz), 6.19 (s, 1H, OH), 4.16 (d, 1H, CH, $^2J_{PH}$ 19.3 Hz), 3.80 and 3.57 (both d, 6H, OMe, $^3J_{PH}$ 10.5 Hz), 2.16 (d, 3H, SCH_3, $^4J_{PH}$ 1.0 Hz), 1.49 (s, 18H, CMe_3).

^{31}P NMR, δ_P, ppm: 25.4.

IR (ν, cm^{-1}): 3138 br (OH), 1224 (P=O), 1179 (P–O–C), 752, 634, 622 (C–S–C).

For $C_{18}H_{31}O_4PS$. anal. calcd. (%): C, 57.73; H, 8.34; P, 8.27; S, 8.56.

Found %: C, 57.47; H, 8.63; P, 8.19; 8.05; S, 8.16; 8.31.

(4-Hydroxy-3,5-di-*tert*-buthylphenyl)(methylthio)-methanedimethoxyphosphonate XIb. By the analogy with compound **XIa**, 1.29 g (64%) of compound **XIb**

as a colorless powder, mp 101–104°C, was obtained from 1.45 g (0.005 mol) of dichloride **IIb**, 1.14 g (0.0075 mol) of thiophosphinate **Ia** and 2.08 g (0.0125 mol) triethyl phosphite **Xb**.

^{1}H NMR (acetone-d_6), δ, ppm: 7.38 (d, 2H, C_6H_2, $^4J_{HH}$ 1.8 Hz), 6.21 (s, 1H, OH), 4.36–3.88 (m, 1H, CH; 4H, OCH_2), 2.18 (d, 3H, SMe, $^4J_{PH}$ 1.0 Hz), 1.50 (s, 18H, CMe_3), 1.31 and 1.15 (both t, 6H, Me, $^3J_{HH}$ 7.0 Hz).

^{31}P NMR, δ_P, ppm: 23.1.

For $C_{20}H_{35}O_4PS$ anal. calcd. (%): C, 59.62; H, 8.69; P, 7.71; S, 7.96.

Found (%): C, 59.37; H, 8.76; P, 7.52, 7.46; S, 8.01, 7.85.

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