Sequential Interaction of Enamine with *0,0*-Dialkyldithiophosphoric Acid and Electrophilic Reagent

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Abstract—The adduct of *O*,*O*-dialkyldithiophosphoric acid and enamine reacts exothermically with an electrophilic reagent. In the case of sulfenyl bromide, the iminium salt reduced at the C–Br bond and bis(dialkoxythiophosphorylthio)-disulfide have been formed, experimentally evidencing the reaction of 2-halogenated ald- and ketimines with dithioic acid via the intermediate formation of enamine.

Keywords: enamines, O,O-dialkyldithiophosphoric acid, sulfenyl bromide, bis(dialkoxythiophosphorylthio)-disulfide

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We have earlier shown for the first time that the interaction of *N*-alkyl-2-bromo-2-methyl- (**1a**, **1b**) [1–3], 2-phenyl-2-chlor- (**1c**) [4], 2,2-dichlor- (**1d**), or -dibromaldimide (**1e**) [5–6] and 2-chloro-2-methyl-1-phenylketimine **1f** [4] with *O*,*O*-dialkyldithiophosphoric acids **2** yields initially the iminium salt: ald- or ketiminium dithiophosphate **3**. The presence of excess of acid **2** has led to the reduction of the cation of salt **3** at the C–Hlg bond, the major products being the reduced iminium salt **4** and bis(dialkoxythiophosphorylthio) disulfide **5** (Scheme 1) [1–6]. The suggested scheme of salt **3** reduction involves the halophilic elimination under the action of *O*,*O*dialkyldithiophosphate anion (RO)₂P(S)S[–] and intermediate formation of *O*,*O*-dialkylthiophosphorylsulfenyl halide $(RO)_2P(S)SHlg$ **6** and bipolar ion **7a**, the latter being one of the resonance structures of enamine **7b** with separated charges [4–6]. Protonation of structure **7** and trapping the dithiophosphate anion with sulfenyl halide **6** affords the final products **4** and **5** (Scheme 1).

The reaction of O, O-dialkyldithiophosphoric acids **2** with enamines has not been described in the literature. We studied it in order to experimentally confirm the reduction of salt **3** via the intermediate enamine formation. Since the enamines bearing primary and secondary amine groups are unstable, we utilized the enamines with tertiary amine group. The enamines containing a nitrogen-

Scheme 1.

$$MeC(X)(Y)CZ=NR^{1} + (R^{2}O)_{2}P(S)SH \longrightarrow MeC(X)(Y)CZ=N^{+}H_{3}R^{1} (R^{2}O)_{2}P(S)S^{-}$$

$$1 \qquad 2 \qquad 3$$

$$MeC(X)CZ=N^{+}HR^{1} \longrightarrow MeC(X)=CZ-NHR^{1}] + (R^{2}O)_{2}P(S)SY$$

$$\frac{(R^{2}O)_{2}P(S)SH}{7a} \qquad MeCH(X)CZ=N^{+}HR^{1} (R^{2}O)_{2}P(S)S^{-} + (R^{2}O)_{2}P(S)SY$$

$$\longrightarrow MeCH(X)CZ=N^{+}HR^{1} Y + (R^{2}O)_{2}P(S)SSP(S)(OR^{2})_{2}$$

$$4 \qquad 5$$

 $X = Me, Y = Br, Z = H, R^{1} = i - Pr (1a), t - Bu (1b); X = Ph, Y = Br, Z = H, R^{1} = t - Bu (1c); X = Y = Cl, Z = H, R^{1} = t - Bu (1d); X = Y = Br, Z = H, R^{1} = t - Bu (1e); X = Me, Y = Cl, Z = Ph, R^{1} = i - Pr (1f); R^{2} = i - Pr (2a), Et (2b).$



containing heterocycle such as morpholine [4-(2-methyl-1-propen-1-yl)perhydro-1,4-oxazine **8** and 4-(cyclopenten-1-yl-1)perhydro-1,4-oxazine **9**] (Scheme 2) were readily available.

Since the formation of disulfide 5 involved sulfenyl halide 6, we investigated the sequential interaction of enamines 8 and 9 with acid 2 and compound 6 (Scheme 3).

The interaction with enamine **8** with acid **2** gave the product of addition at the double bond **12**. We suggested that acid **2** first protonated enamine **8** at the nitrogen atom, affording the ammonium salt: 4-(2-methyl-1-propenyl)-perhydro-1,4-oxazinium diisopropoxydithiophosphate **10** which was converted into the iminium salt: 4,4-(2-methylpropane-1,1-diyl)perhydro-1,4-oxazinium dithiophosphate **11a**, via prototropy salt **11a** was transformed into the product of acid **2** addition to enamine

8: *O*,*O*-diisopropyl[1-(perhydro-1,4-oxazin-4-yl)-2-methylpropylthio]dithiophosphate **12a**.

The formation of salts **10** and **11a** could not be observed experimentally. However, 4-(cyclopentene-1,1-diyl)perhydro-1,4-oxazinium diisopropoxydithiophosphate **11b** analogous to salt **11a** was isolated (Scheme 4). The formation of product **12b** was not observed under the reaction conditions.

The addition of sulfenyl bromide 6 to the mixture led to exothermic reaction with the formation of disulfide 5 and reduction product 13 of the hypothetic analog 14 of the iminium salt 3 initially formed from compounds 1 and 2 (Scheme 5).

Such experimental outcome of sequential three-component interaction of enamine, dithioacid, and sulfenyl bromide was an evidence of the reaction of *N*-alkyl-2-haloald(ket)imines **1** with *O*,*O*-dialkyldithiophosphoric acids **2** via the intermediate formation of enamine **7**.

To elaborate novel methods of synthesis of polyfunctional organic compounds, we extended the range of the electrophilic agents: propionyl chloride **15** and α -bromoether **16** were introduced in the reaction instead of sulfenyl bromide **6** (Scheme 6).

Me₂C=CH O (*i*-PrO)₂PSS⁻ (i-PrO)₂PSSH 8 10 2a Me₂CH-CH=N Me₂CH-(i-PrO)₂PSS P(OPr-i) 11a (i-PrO)₂P(S 12a $+ [(i-PrO)_2P(S)S]_2$ Br⁻ Me₂CH--CH 13a 5a Scheme 4. $(i-PrO)_2P(S)S$ $SP(S)(OPr-i)_2$ 11b 12b

Scheme 3.

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$$Me_2C(Hlg) - CH = N O (RO)_2P(S)S^{-14}$$

The obtained propionylthio derivative **17** has not been described in the literature. However, *O*,*O*-dialkyl-*S*acetyl dithiophosphates (RO)₂P(S)SCOMe **19** including (i-PrO)₂P(S)SCOMe **19a** have been known. Compounds **19** have been obtained via several methods: reaction of potassium (RO)₂P(S)SK or lead [(RO)₂P(S)S]₂Pb salt of dialkyldithiophosphoric acid with acetyl chloride [7]; addition of sulfur to dialkyl-*S*-acetylphosphites (RO)₂PSCOMe [8]; and interaction of acetonitrile MeCN with acid **2** in the presence of acetic acid [9]. Hence, we elaborated a novel method of synthesis of *O*,*O*dialkylalkanoylthio dithiophosphates.

Moreover, we suggested a novel method of preparation of O,O-diethyl(methoxymethylthio) dithiophosphate **18** (Scheme 6) which has been earlier obtained via methylation of O,O-diethyl(hydroxymethylthio)dithiophosphate (EtO)₂P(S)SCH₂OH **19** using diazomethane [10].

It should be noted that sequential interaction of enamine with *O*,*O*-diisopropoxydithiophosphoric acid and *O*,*O*-diisopropoxythiophosphorylsulfenyl bromide as the electrophile gave bis(diisopropoxythiophosphorylthio) disulfide and the iminium salt reduced at the C–Br bond, experimentally evidencing the formation of the enamine intermediate in the reactions of 2-haloald(ket)imines with dithioacids. Novel methods of the P,S-containing organic compounds were elaborated.

EXPERIMENTAL

¹H and ¹³C NMR spectra were recorded using Tesla BS-567A (100 MHz) and AVANCE 400WB (400.13 and 100.61 MHz) instruments in CDCl₃. The chemical shifts relative to TMS were determined using residual protons and carbon signals of the deuterated solvent. ³¹P

NMR spectra were recorded using AVANCE 400WB (161.98 MHz) instrument, the chemical shifts were reported relative to 85% H₃PO₄ as external reference.

O,O-Diisopropyl[1-(perhydro-1,4-oxazin-4-yl)-2methylpropylthio] dithiophosphate (12a). A solution of 2.14 g (0.01 mol) of acid 2a in 10 mL of CCl₄ was added dropwise to a solution of 1.41 g (0.01 mol) of enamine 8 in 5 mL of CCl₄, maintaining the reaction mixture temperature at 0–5°C. The temperature was increased to ambient, and the mixture was kept during 1 day. The solvent was evaporated under reduced pressure to afford 3.27 g (92%) of crystalline product with purity 96%, mp 78-79°C. ¹H NMR spectrum, δ , ppm: 1.12 d (6H, CHMe₂, ${}^{3}J_{HH} =$ 6.6 Hz), 1.32 d (12H, Me_2 CHO, ${}^3J_{HH} = 6.3$ Hz), 2.16 m $(1H, CHMe_2), 2.72 t (4H, NCH_2, {}^{3}J_{HH} = 4.7 Hz), 3.70 t$ (4H, OCH₂), 3 ${}^{3}J_{HH}$ = 4.7 Hz), 4.73 septet (2H, CHOP, ${}^{3}J_{\text{HH}} = 6.3 \text{ Hz}$), 4.97 d (1H, CHN, ${}^{3}J_{\text{HH}} = 10.2 \text{ Hz}$). ¹³C NMR spectrum, δ_{C} , ppm: 20.98 (CHMe₂), 23.73 d $(Me_2CHO, {}^{3}J_{PC} = 5.0 \text{ Hz}), 32.81 (CHMe_2), 49.84 (NCH_2),$ 63.72 (SCH), 66.33 (OCH₂), 72.47 d (POCH, ${}^{2}J_{PC}$ = 7.5 Hz). ³¹P NMR spectrum: δ_P 98.9 ppm. Found, %: C 47.16; H 8.23; N 3.61. C₁₄H₃₀NO₃PS₂. Calculated, %: C 47.30; H 8.51; N 3.94.

Sequential reactions of enamine 8 with acid 2 and electrophiles 6, 15, or 16. a. Interaction with O,O-diisopropylthiophosphorylsulfenyl bromide 6. A solution of 1.84 g (0.013 mol) of acid 2a in 10 mL CCl₄ was added dropwise to a solution of 2.79 g (0.013 mol) of enamine 8 in 10 mL of CCl_4 maintaining the reaction mixture temperature at 0–5°C. The mixture temperature was then raised to ambient, and the mixture was stirred during 5 h. The ³¹P NMR spectrum contained a strong resonance signal at $\delta_{\rm P}$ 98.9 ppm assigned to phosphorus atom in compound 12a. A solution of sulfenyl bromide 6 in CCl₄ prepared from 2.77 g (0.0065 mol) of disulfide 5 and 1.04 g (0.0065 mol) of bromine was added dropwise at -15°C. The mixture was heated to ambient and kept overnight. The precipitate was filtered off and dried to give 2.45 g (85%) of iminium salt 13a. ¹H NMR spectrum,



δ, ppm: 1.39 d (6H, CH**Me**₂, ${}^{3}J_{HH}$ = 6.7 Hz), 3.24 m (1H, CHMe₂), 3.96 m (4H, OCH₂), 4.03 m (4H, N⁺CH), 9.39 d (1H, CHN⁺, ${}^{3}J_{HH}$ = 8.5 Hz). 13 C NMR spectrum, δ_{C} , ppm: 19.50 (CH**Me**₂), 30.62 (CHMe₂), 51.89 and 59.14 [N⁺(CH₂)₂], 66.35 [O(CH₂)₂], 180.1 (CHN⁺). Found, %: C 42.63; H 6.98; N 6.01. C₈H₁₆BrNO. Calculated, %: C 43.26; H 7.26; N 6.31.

4.3 g (78%) of disulfide **5** was isolated from the mother liquor via the solvent evaporation, mp 92°C (mp 91.5–93°C [11]). ¹H NMR spectrum, $\delta_{\rm H}$, ppm: 1.40 d and 1.42 d (24H, Me₂CH, ³*J*_{HH} = 6.4 Hz), 4.90 d. sept (4H, CHOP, ³*J*_{HH} = 6.4, ³*J*_{PH} = 12.0 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 23.75 d (CH₃, ³*J*_{PC} = 4.5 Hz), 23.57 d (CH₃, ³*J*_{PC} = 5.5 Hz), 74.76 d (CH, ²*J*_{PC} = 6.7 Hz). ³¹P NMR spectrum: $\delta_{\rm P}$ 81.70 ppm.

b. Interaction with propanoyl chloride **15.** A solution of 0.92 g (0.01 mol) of acyl chloride **15** in 10 mL of dioxane was added dropwise at -5° C to a mixture prepared from 1.41 g (0.01 mol) of enamine **8** and 2.14 g (0.01 mol) of acid **2a** in 20 mL of dioxane. The reaction mixture was heated to ambient and kept overnight. The precipitate was filtered off and dried to give 1.70 g (96%) of iminium salt **13b**. ¹H NMR spectrum, δ , ppm: 1.40 d (6H, CH**Me**₂, $^{3}J_{HH} = 6.6$ Hz), 3.03 m (1H, CH**Me**₂), 4.04 m (4H, OCH₂), 4.27 m (4H, N⁺CH), 9.90 d (1H, CHN⁺, $^{3}J_{HH} = 8.3$ Hz). Found, %: C 53.79; H 8.87; N 7.53. C₈H₁₆CINO. Calculated, %: C 54.08; H 9.08; N 7.88.

Distilling off the solvent from the mother liquor gave 2.13 g (77%) of *O***,O-diisopropyl-S-propanoylthio dithiophosphate 17**, bp 101–102°C (0.09 mmHg). ¹H NMR spectrum, δ , ppm: 1.18 t (3H, CH₃CH₂, ³J_{HH} = 7.5 Hz), 1.34 d and 1.39 d (12H, CHMe₂, ³J_{HH} = 6.2 Hz), 2.65 q (2H, CH₃CH₂, ³J_{HH} = 7.5 Hz), 4.96 septet (2H, CHOP, ³J_{HH} = 6.2 Hz). ³¹P NMR spectrum: δ_P 76.86 ppm. Found, %: C 39.73; H 7.26; P 11.32. C₉H₁₉O₃PS₂. Calculated, %: C 39.98; H 7.08; P 11.46.

c. Interaction with methoxybromomethane 16. A solution of 3.6 g (0.03 mol) of α -bromoether 16 in 40 mL of CCl₄ was added dropwise at -5° C to a mixture of 4.10 g (0.029 mol) of enamine 8 and 5.39 g (0.029 mol) of acid 2b in 40 mL of CCl₄. The reaction mixture was heated to ambient and kept overnight. The precipitate was filtered off and dried to afford 5.5. g (86%) of iminium salt 13a. Distilling off of the solvent from the mother liquor gave 5.2 g (79%) of *O*,*O*-diethyl(methoxymethylthio)-dithiophosphate 18, bp 75–76°C (0.05 mmHg) {bp 103°C (0.1 mmHg) [10]}. ¹H NMR spectrum, δ , ppm: 1.35 t (6H, CH₃CH₂, ³J_{HH} = 7.1 Hz), 3.38 s (3H, OCH₃),

4.10 q and 4.18 q (4H, CH₂OP, ${}^{3}J_{HH} = 7.1$ Hz), 5.06 d (2H, SCH₂, ${}^{3}J_{PH} = 20.4$ Hz). 13 C NMR spectrum, δ_{C} , ppm: 15.90 (CH₃), 56.95 (OCH₃), 63.75 d (POCH₂, ${}^{2}J_{PC} = 5.6$ Hz), 78.48 d (SCH₂, ${}^{2}J_{PC} = 3.8$ Hz). 31 P NMR spectrum: δ_{P} 94.77 ppm. Found, %: C 31.12; H 6.78; P 13.45. C₆H₁₅O₃PS₂. Calculated, %: C 31.29; H 6.57; P 13.28.

Interaction of 4-(cyclopenten-1-yl-1)perhydro-1,4oxazine 9 with acid 2a. A solution of 2.14 g (0.01 mol) of acid 2a was added dropwise to a solution of 1.53 g (0.01 mol) of enamine 9 in 10 mL of anhydrous CCl_4 under argon maintaining the mixture temperature at 0-5°C. The mixture was heated to ambient and stirred during 5 h. The crystalline precipitate was filtered off and dried to give 3.5 g (95%) of 4-(cyclopentene-1,1-diyl)perhydro-1,4-oxazinium diisopropoxydithiophosphate 11b containing admixture (5%) of morpholinium dithiophosphate. ¹H NMR spectrum, δ, ppm: 1.25 d (12H, **Me**CHOP, ${}^{3}J_{HH} = 6.6$ Hz), 2.13 m (4H, CH₂), 3.22 m [4H, =C(CH₂)₂], 4.09 m [4H, O(CH₂)₂], 4.14 m [4H, N⁺(CH₂)₂], 4.69 septet (2H, CHOP). Found, %: C 48.79; H 7.95; N 4.03. C₁₅H₃₀NO₃PS₂. Calculated, %: C 49.02; H 8.23; N 3.81.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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