

Studies on Organophosphorus Compounds. XVII.*

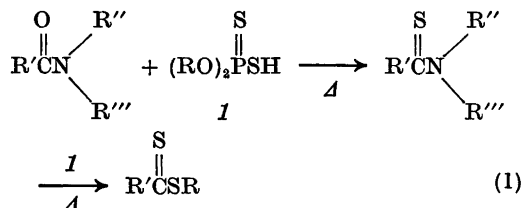
About *O,O*-Diethyl Dithiophosphoric Acid as Thiation and Alkylation Agent. A New Route to Dithiocarboxylic Esters and (Ethylthio) Heterocycles

J. PERREGAARD,** B. S. PEDERSEN and S.-O. LAWESSON

Department of Organic Chemistry, University of Aarhus, DK-8000 Aarhus C, Denmark

By heating thioesters with *O,O*-diethyl dithiophosphoric acid, **2**, at about 120 °C the corresponding dithioesters are produced in appreciable yields. Extended reaction time causes formation of ethyl dithiocarboxylic esters. Also common esters produce, after reaction with **2**, thiono- and/or dithiocarboxylic esters provided the reaction temperature is higher (140 °C). Potential hydroxyheterocycles (2- and 4-hydroxypyridine, saccharin) and **2** give the corresponding (ethylthio) heterocycles.

In a preceding paper thiation and alkylation properties of *O,O*-dialkyl dithiophosphoric acids, **1**, were established in reactions with carboxamides.¹ Thus thio-carboxamides were prepared from carboxamides and **1** after a relatively short reaction time while prolonged heating afforded the corresponding alkyl dithiocarboxylic esters.



Similarly Oae *et al.* have shown that ketones and aldehydes were transformed into the cor-

responding thiocarbonyl compounds or the trimers of these.² This paper will describe further applications of *O,O*-diethyl dithiophosphoric acid, **2** (*1*, R = Et), in reactions with carbonyl containing compounds such as carboxylic esters, thio-carboxylic esters and some potential hydroxy heterocycles.

RESULTS AND DISCUSSION

Thio-carboxylic esters react smoothly in neat **2** at 120 °C to give dithiocarboxylates in good yields (Table 1). Further heating resulted in formation of appreciable amounts of ethyl dithiocarboxylates. In one case this was dramatically demonstrated in product distribution by reaction of phenyl thiobenzoate with **2** during different reaction times (see Table 2). Most of the reaction mixtures were contaminated with ethyl dithiocarboxylates if total conversion of starting materials was desired.

In an attempt to prepare thionocarboxylic esters we also reacted carboxylic esters with **2**. To get any conversion of the starting materials higher reaction temperatures were needed than in the previous reactions. Thus reaction of ethyl benzoate afforded a mixture of the expected ethyl thionobenzoate (45 %) and ethyl dithiobenzoate (11 %), while the only product isolated from reaction of ethyl heptanoate was ethyl dithioheptanoate (66 %). Whether the formation of dithiocarboxylic esters results from alkylation of or rearrangement³ of pri-

* Part XVI, See Ref. 1.

** Present address: GGU, Østervoldgade 10, DK-1350 Copenhagen K. Denmark.

Table 1. Synthesis of dithiocarboxylates^a $\text{RCOSR}' + 2 \rightarrow \text{RCSSR}'$

R	R'	Reaction time/h	Reaction temp./°C	Yield of 3	B.p./mmHg or m.p., °C		H NMR (CDCl ₃)
					Found	Lit.	
C ₆ H ₅	CH ₃	8	120	79	146/15	142/12 ⁶	2.7 (s, 3 H); 7.1–8.0 (m, 5 H)
C ₆ H ₅	CH ₂ CH ₃	7	120	92	150/12	97/0.5 ⁷	1.4 (t, 3 H); 3.4 (q, 2 H); 7.2–8.2 (m, 5 H)
C ₆ H ₅	CH ₂ C ₆ H ₅	6	120	81	156–57/0.2	159–60/0.3 ⁷	4.6 (s, 2 H); 7.1–8.2 (m, 10 H)
C ₆ H ₅	C ₆ H ₅	8	120	59	62	60–61 ⁷	7.2–7.7 (m, 8 H) 8.0–8.3 (m, 2 H)
CH ₃	CH ₂ C ₆ H ₅	5	125	66	85–88/0.4 ^b		2.8 (s, 3 H) 4.4 (s, 2 H) ~7.3 (m, 5 H)
CH ₃	C ₆ H ₅	9	120	85	63–65/0.5 ^b		2.8 (s, 3 H); ~7.4 (m, 5 H)
CH ₃ CH ₂ CH ₃	CH ₂ CH ₃	7	120	95	73–75/10	75/9 ⁸	1.0 (t, 3 H); 1.3 (t, 3 H); 1.8 (m, 2 H); 2.9 (t, 2 H);

^a 0.02 mol of thiolcarboxylate and 15 ml of 2 were used in each experiment.

^b Elemental analyses were in accordance with the proposed structures.

marily formed thionocarboxylic esters is at present uncertain. Compared to improved tetraphosphorus decasulfide sulfurizations⁴ our method seems to be advantageous in many cases (higher yields) except under conditions when 2 being a pronounced alkylation agent. Such alkylations were found to predominate in reactions of 2 with potential hydroxyhetero-

cycles. Thus 3-ethylthiobenzoisothiazole-*S*-dioxide, 7, was prepared from saccharin, 2-ethylthiopyridine, 8a, from 2-pyridone, and 4-ethylthiopyridine, 8b, from 4-pyridone. A similar alkylative sulfurization of carbostyryl by 2 has been reported by Oae *et al.*⁵

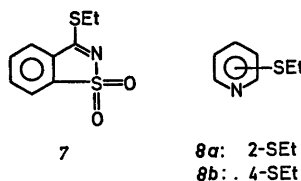
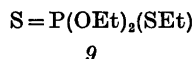


Table 2. Time dependent product distribution.

$\text{PhC} \begin{array}{c} \text{O} \\ \\ \text{SPh} \end{array}$	$\xrightarrow{2}$	$\text{PhC} \begin{array}{c} \text{S} \\ \\ \text{SPh} \end{array}$	+	$\text{PhC} \begin{array}{c} \text{S} \\ \\ \text{SEt} \end{array}$
4		5		6

Reaction time/h	Reaction temp./°C	Yield of		
		4/%	5/%	6/%
8	120	34	58	8
10	120	12	18	67
12	120	—	10	86

Finally, it should be mentioned that *O,O,S*-triethyl dithiophosphate, 9, was isolated in most of our reactions (with the hydroxypyridines and saccharin appreciable amounts of 9 were formed), which shows that 2 itself is alkylated under these reaction conditions.



EXPERIMENTAL

^1H NMR spectra were recorded at 60 MHz on a Varian A-60 spectrometer. TMS was used as internal reference standard. Chemical shift values are expressed in δ values. Mass spectra were recorded on a CEC 21-104 mass spectrometer operating at 70 eV using direct inlet. Silica gel 60 (Merck) was used for column chromatography. Commercial *O,O*-diethyl dithiophosphoric acid was kindly delivered by Cheminova A/S, DK-8260 Lemvig. Elemental analyses were performed by Novo Industry A/S, Copenhagen. M.p.'s and b.p.'s are uncorrected.

Reactions of *thiocarboxylic esters* were performed as indicated in Table 1. The reaction mixtures were neutralized with K_2CO_3 -solution, and H_2O (200 ml) and ether (100 ml) were added. The phases were separated and the H_2O -phase was further extracted with ether (2×100 ml). The combined ether phases were washed with H_2O (2×50 ml), dried (MgSO_4) and the ether evaporated. The dithiocarboxylic esters, **3**, were purified by column chromatography (eluted with light petroleum or 5% v/v ether/light petroleum). The products were characterized by their b.p./m.p. and ^1H NMR spectra (Table 1).

Carboxylic esters. *Ethyl benzoate* (0.02 mol) was heated at 140°C with 15 ml of **2** for 10 h. The reaction mixture was worked up as above affording 2.0 g of product consisting of a mixture of ethyl thionobenzoate (yield 45%) and ethyl dithiobenzoate (yield 11%). These two compounds could not be separated by column chromatography, but they were identified according to ^1H NMR: ^1H NMR (CDCl_3) of ethyl thionobenzoate: 1.5 (t, 3 H); 4.7 (q, 2 H); 7.2–8.2 (m, 5 H). ^1H NMR (CDCl_3) of ethyl dithiobenzoate: 1.4 (t, 3 H); 3.4 (q, 2 H); 7.2–8.2 (m, 5 H). These spectra were in accordance with spectra of separately prepared samples.

Ethyl heptanoate (0.02 mol) was heated at 140°C with 15 ml of **2** for 9 h. The same working-up procedure as above afforded 2.5 g (66%) of ethyl dithioheptanoate. B.p. $79-81^\circ\text{C}/0.2$ mmHg (lit.⁷ b.p. = $71^\circ\text{C}/0.1$ mmHg). ^1H NMR (CDCl_3): 0.9 (t, 3 H); 1.2–2.0 (m, 8 H); 1.3 (t, 3 H); 3.0 (t, 2 H); 3.2 (q, 2 H).

Hydroxyheterocycles. *Saccharin* (0.02 mol) was heated at 130°C with 15 ml of **2** for 3 h. The reaction mixture was then neutralized with K_2CO_3 -solution, and H_2O (200 ml) and CH_2Cl_2 (100 ml) were added. The phases were separated and the H_2O -phase was further extracted with CH_2Cl_2 (2×100 ml). The combined CH_2Cl_2 -phases were washed with H_2O (2×50 ml), dried (MgSO_4) and the CH_2Cl_2 evaporated. The residue was refluxed in ether (50 ml) and upon cooling 3-ethylthiobenzoisothiazole-*S*-dioxide, **7**, precipitated. 4.1 g (93%) were filtered off. M.p. 187°C . (lit.⁹ m.p. $183-184^\circ\text{C}$). ^1H NMR (CDCl_3): 1.5 (t, 3 H); 3.4 (q, 2 H); 7.6–7.8 (m, 4 H).

2-Pyridone (0.02 mol) was heated at 120°C with 15 ml of **2** for 30 min. The same working-up procedure as for dithiocarboxylates afforded 1.0 g (36%) of 2-ethylthiopyridine, **8a**. B.p. $90-92^\circ\text{C}/16$ mmHg (lit.¹⁰ b.p. $205-207^\circ\text{C}$). ^1H NMR (CDCl_3): 1.3 (t, 3 H); 3.1 (q, 2 H); 6.8–7.5 (m, 3 H); 8.3–8.4 (m, 1 H).

4-Pyridone (0.02 mol) was heated at 120°C with 15 ml of **2** for 15 min. The same working-up procedure as for dithiocarboxylates afforded 1.2 g (43%) of 4-ethylthiopyridine, **8b**. B.p. $122^\circ\text{C}/23$ mmHg (lit.¹¹ b.p. $123-126^\circ\text{C}/23-24$ mmHg). ^1H NMR (CDCl_3): 1.4 (t, 3 H); 3.0 (q, 2 H); 7.0–7.1 (m, 2 H); 8.3–8.4 (m, 2 H).

A second compound (3–4 g) was isolated in all reactions of potential hydroxyheterocycles, which was identified as *O,O,S*-triethyl dithiophosphate, **9**. B.p. $120-121^\circ\text{C}/15$ mmHg (lit.¹² b.p. $128^\circ\text{C}/20$ mmHg). ^1H NMR (CDCl_3): 1.4 (t, 9 H); ~ 2.8 (m, 2 H); ~ 4.1 (m, 4 H). MS *m/e* (% rel. int.): 214 (M^+ , 14), 186 [(EtO)₂PSSH, 42], 158 ($\text{M}-2\text{C}_2\text{H}_5$, 42), 153 ($\text{M}-\text{SET}$, 12), 142 (17), 125 (31), 121 (78), 113 (28), 109 (29), 97 (100), 93 (71), 65 (95). A GLC chromatogram showed only one peak.

REFERENCES

1. Perregaard, J., Thomsen, I. and Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **86** (1977) 321.
2. Oae, S., Nakanishi, A. and Tsujimoto, N. *Chem. Ind. London* (1972) 575.
3. Janssen, M. J. In Patai, S., Ed., *The Chemistry of Carboxylic Acids and Esters*, Wiley, New York 1969, p. 705.
4. Scheeren, J. W., Ooms, P. H. J. and Nivard, R. J. F. *Synthesis* (1973) 149.
5. Nakanishi, A. and Oae, S. *Tetrahedron* **29** (1973) 2023.
6. Mayer, R., Scheithauer, S. and Kunz, D. *Chem. Ber.* **99** (1966) 1393.
7. Leon, N. H. and Asquith, R. S. *Tetrahedron* **26** (1970) 1719.
8. Schuijl, P. J. W., Brandsma, L. and Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **85** (1966) 889.
9. Meadow, J. R. and Cavagnol, J. C. *J. Org. Chem.* **16** (1951) 1582.
10. Backer, H. J. and Buisman, J. A. K. *Recl. Trav. Chim. Pays-Bas* **64** (1945) 102.
11. Vompe, A. F. and Monich, N. V. *Dokl. Akad. Nauk SSSR* **170** (1966) 89.
12. Pishchimuka, P. S. *J. Russ. Phys.-Chem. Soc.* **44** (1912) 1406; *Chem. Abstr.* **7** (1913) 987.

Received January 28, 1977.