A Convenient Synthesis of Novel Unsymmetrical Acyl Thioacyl Disulfides and Acyl *O,O*-Dialkylthiophosphoryl Disulfides

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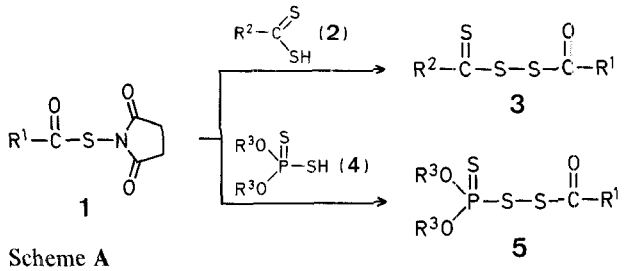
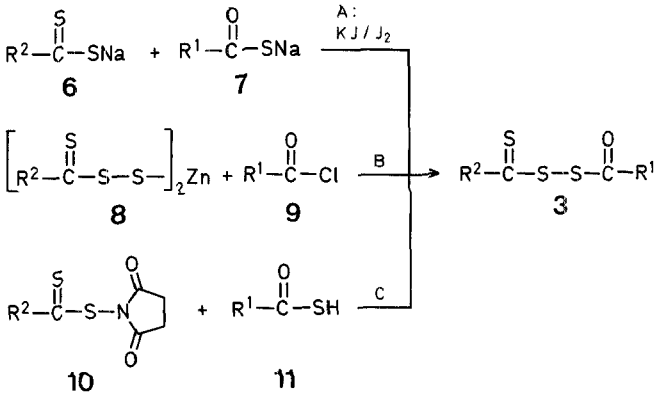
It is well known that symmetrical bis[acyl][1] and bis[thioacyl] disulfides[2] can be readily obtained by the iodine- or toluenesulfonyl chloride-oxidation of the corresponding thio- or dithiocarboxylic acids. However, the preparation of unsymmetrical acyl thioacyl disulfides **3**, compounds of considerable spectroscopical and practical interest, has not been reported. Recently, a convenient preparation of *N*-(aroylthio)-succinimides **1**, valuable cationic thioaroylating agents for mercaptans and thiobenzoic acids, was developed in our laboratory[3]. We now describe two further synthetic applications of reagent **1**: the preparations of acyl thioacyl disulfides **3** and acyl *O,O*-dialkylthiophosphoryl disulfides **5**. These unsymmetrical disulfides are readily obtained from the reaction of the corresponding dithio acids **2** or *O,O*-dialkyl dithiophoshoric acids **4** with *N*-(aroylthio)-succinimides **1** (Scheme **A**).



Scheme **A**

The results are summarized in Tables 1 and 2. The structures of the products were established on the basis of I.R., U.V.-visible, ^{1}H-N.M.R., and mass spectral data together with microanalytical data. The experimental procedures are simple. The yields of **3** are almost quantitative, but those of **5** are low because of the loss during isolation by preparative T.L.C. At present, these methods seem to be limited to the aromatic derivatives of **3** (R^1, R^2 = aryl) and **5** (R^1 = aryl), because no appropriate purification method for the oily aliphatic products formed has yet been found.

Three other routes (A–C, Scheme **B**) for the preparation of **3** have also been investigated under various reaction conditions. These methods, however, have been found to be unpractical from the points of view of yields and purification procedures; the route A leads to the formation of bis[acyl] disulfides and bis[thioacyl] disulfides together with **3**. The separation of **3** from the reaction mixture by fractional crystallization, or column or thin layer chromatography has been found to be very difficult. No formation of **3** from routes B[4] and C[5] was observed.



Scheme **B**

The unsymmetrical disulfides **3** and **5** obtained are very stable in the solid state and in the solution. They can be kept at room temperature for over a year. The n→π* transitions of the C=S group in **3**, without exception, show the hypsochromic shifts of ca. 3–5 nm compared with those of corresponding bis[thioacyl] disulfides.

Table 1. Acyl Thioacyl Disulfides **3** prepared

Product No.	R^1	R^2	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (KBr) [cm^{-1}] $\nu_{C=O}$	$\nu_{C=S}$	U.V. (*n*-hexane) λ_{max} [nm] (log ε)	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
3a	C_6H_5	C_6H_5	92	63–67°	$C_{14}H_{10}OS_3$ (290.4)	1690	1230	239 (4.29); 294 (4.14); 529 (2.04)	7.1–7.7 (m, 6H); 7.7–8.2 (m, 4H)
3b	4-H_3C—C_6H_4	C_6H_5	93	99–101°	$C_{15}H_{12}OS_3$ (304.4)	1700	1230	256 (4.43); 292 (4.30); 526 (2.07)	2.35 (s, 3H); 7.1–7.6 (m, 5H); 7.7–8.1 (m, 4H)
3c	C_6H_5	4-H_3C—C_6H_4	93	75–77°	$C_{15}H_{12}OS_3$ (304.4)	1690	1240	241 (4.36); 4.13 (4.34); 524 (2.16)	2.32 (s, 3H); 6.9–7.6 (m, 5H); 7.7–8.1 (m, 4H)
3d	4-H_3C—C_6H_4	4-H_3C—C_6H_4	94	see experimental procedure					
3e	4-Cl—C_6H_4	4-H_3C—C_6H_4	92	80–83°	$C_{15}H_{11}ClOS_3$ (338.9)	1700	1240	257 (4.27); 316 (4.09); 528 (1.90)	2.38 (s, 3H); 7.0–8.2 (m, 8H)
3f	4-H_3CO—C_6H_4	4-H_3CO—C_6H_4	95	79–80°	$C_{16}H_{14}O_3S_3$ (350.5)	1680	1240	290 (4.10); 346 (4.18); 515 (2.11)	3.62 (s, 6H); 6.7–7.1 (m, 4H); 7.9–8.3 (m, 4H)
3g	C_6H_5	4-Cl—C_6H_4	88	48–51°	$C_{14}H_9ClOS_3$ (324.9)	1690	1240	241 (4.35); 3.10 (4.31); 530 (2.12)	7.1–8.2 (m, 9H)
3h	4-H_3C—C_6H_4	4-Cl—C_6H_4	89	85–87°	$C_{15}H_{11}ClOS_3$ (338.9)	1705	1240	257 (4.38); 313 (4.32); 525 (2.15)	2.36 (s, 3H); 7.0–7.5 (m, 4H); 7.7–8.1 (m, 4H)
3i	4-Cl—C_6H_4	4-Cl—C_6H_4	91	65–66°	$C_{14}H_8Cl_2OS_3$ (359.3)	1690	1225	257 (4.40); 310 (4.11); 528 (2.03)	7.2–7.6 (m, 4H); 7.7–8.1 (m, 4H)
3j	4-H_3C—C_6H_4	*i*-C_3H_7	95	oil	$C_{12}H_{14}OS_3$ (270.4)	1705[b]	—	253 (5.06); 303 (3.68); 477 (1.15)	1.30 (d, 6H); 2.32 (s, 3H); 3.6 (m, 1H)

[a] Satisfactory microanalyses obtained: C ±0.29, H ±0.40, S ±0.38; exception: **3j**, C −0.42.
[b] Neat.

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Table 2. Acyl Thiophosphoryl Disulfides **5** prepared

Product No.	R^1	R^3	Yield [%]	n_D^{20}	Molecular formula[a]	I.R. (neat) [cm^{-1}] $\nu_{C=O}$	$\nu_{P=S}$	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
5a	C_6H_5	i-C_3H_7	28	1.5819	$C_{13}H_{19}SO_3P$ (350.4)	1696	652	1.37 (d, 12H); 4.6–5.3 (m, 2H); 7.3–8.2 (m, 5H)
5b	C_6H_5	c-C_6H_{11}	27	1.5919	$C_{19}H_{27}S_3O_3P$ (430.6)	1692	684	0.6–2.4 (m, 20H); 4.4–5.0 (m, 2H); 7.3–8.2 (m, 5H)
5c	4-H_3C—C_6H_4	C_6H_5—CH_2	34	1.6321	$C_{22}H_{21}S_3O_3P$ (460.6)	1700	673	2.42 (s, 3H); 5.31 (d, 4H); 7.1–8.0 (m, 14H)
5d	4-H_3C—C_6H_4	i-C_3H_7	41	see experimental procedure				
5e	4-H_3C—C_6H_4	n-C_4H_9	57	1.5733	$C_{16}H_{25}S_3O_3P$ (420.6)	1697	664	0.6–2.0 (m, 14H); 2.43 (s, 3H); 3.9–4.5 (m, 4H); 7.1–8.0 (m, 4H)
5f	4-H_3C—C_6H_4	n-C_6H_{13}	20	1.5535	$C_{20}H_{33}S_3O_3P$ (448.6)	1703	663	0.6–2.0 (m, 22H); 2.42 (s, 3H); 3.9–4.5 (m, 4H); 7.1–8.1 (m, 4H)
5g	4-H_3C—C_6H_4	c-C_6H_{11}	35	1.5901	$C_{20}H_{29}S_3O_3P$ (444.6)	1704	698	0.7–2.4 (m, 20H); 2.43 (s, 3H); 4.3–5.0 (m, 2H); 7.1–8.0 (m, 4H)
5h	4-H_3C—C_6H_4	C_6H_5	15	1.6260	$C_{20}H_{17}S_3O_3P$ (432.5)	1712	697	2.42 (s, 3H); 6.9–8.0 (m, 14H)

[a] Satisfactory microanalyses obtained: C ±0.31, H ±0.31, S ±0.28.

4-Methylbenzoyl 4-Methyl-thiobenzoyl disulfide (3d):
A solution of freshly prepared 4-methyldithiobenzoic acid[6] (**2**; R^2 = 4-H_3C—C_6H_4; 0.35 g, 2 mmol) in tetrahydrofuran (10 ml) is added to *N*-(4-methylbenzoylthio)-succinimide (**1**; R^1 = 4-H_3C—C_6H_4; 0.5 g, 2 mmol) in the same solvent (20 ml) and the mixture is stirred at room temperature for 24 h. The solvent is then evaporated under reduced pressure and the resulting residue is dissolved in ether (~30 ml). This ether solution is first washed with 5% sodium hydrogen carbonate solution and then water, followed by drying with anhydrous sodium sulfate. After evaporation of the solvent, recrystallization of the resulting solid from petroleum ether (b.p. <70 °C) affords **3d** as reddish-pink crystals; yield: 0.60 g (94%); m.p. 106–109 °C.

$C_{16}H_{14}OS_3$	calc.	C 60.34	H 4.43	S 30.21
(318.5)	found	60.58	4.31	29.98

M.S.: m/e = 318 (M^+).

I.R. (KBr): ν = 1705 (C=O); 1240 cm^{-1} (C=S).

U.V. (*n*-hexane): λ_{max} (log ε) = 252 (4.27), 314 (4.23); 525 nm (2.05).

^{1}H-N.M.R. ($CDCl_3$): δ = 2.28 (s, 3H); 2.32 (s, 3H); 7.0–8.1 ppm (m, 8H).

4-Methylbenzoyl *O,O*-Diisopropylthiophosphoryl Disulfide (5d):
A solution of *O,O*-diisopropyl dithiophosphoric acid[7] (**4**; R^3 = i-C_3H_7; 1.3 g, 4.8 mmol) in benzene (20 ml) is added to *N*-(4-methylbenzoylthio)-succinimide[3] (**1**; R^1 = 4-H_3C—C_6H_4; 1.1 g, 4 mmol) in the same solvent (40 ml) and the mixture is stirred at room temperature for 24 h. After evaporation of benzene, the resulting residue is extracted with ether (50 ml), followed by washing of the extract with 5% aqueous sodium hydrogen carbonate solution and then water. The extracts are concentrated to ~1 ml. Preparative T.L.C. [Wakol Gel. B-5F, *n*-hexane/ether (9/1), the product being in the second layer from the top] of this concentrate gives **5d** as a pale yellow oil; yield: 0.65 g (41%); n_D^{20}: 1.5797.

$C_{14}H_{21}S_3O_3P$	calc.	C 46.14	H 5.81
(364.5)	found	45.98	5.59

I.R. (neat): ν = 1704 (C=O); 653 cm^{-1} (P=S).

^{1}H-N.M.R. ($CDCl_3$): δ = 1.39 (s, 12H); 2.43 (s, 3H); 4.6–5.3 (m, 2H); 7.2–8.0 ppm (m, 4H).

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[6] Acids **2** were prepared by concentrated hydrochloric acid acidolysis of the corresponding piperidinium salts: S. Kato, T. Mitani, M. Mizuta, *Int. J. Sulfur Chem.* **8**, 359 (1973).

[7] Acids **4** were prepared (analog to **2**) by concentrated hydrochloric acid acidolysis of the corresponding piperidinium salts: S. Kato, unpublished results.