A Convenient Synthesis of Bis[acyl] Disulfides using Phase-Transfer Catalysis

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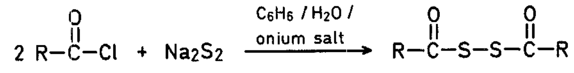
Bis[acyl] disulfides have been synthesized by several procedures, for example oxidation of thiocarboxylate ions[1], treatment of acyl halides with sodium disulfide[2], lithium disulfide[3], or hydrogen disulfide[4]. Acylation of sodium disulfide has been reported to proceed only in low yield. For instance, 4-nitrobenzoyl chloride was allowed to react with sodium disulfide in ethanol to give bis[4-nitro-benzoyl] disulfide in 28% yield[2].

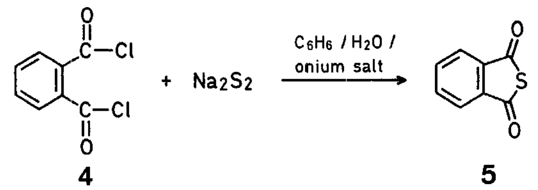
We have applied the phase-transfer method to the acylation of sodium disulfide. We have found that bis[acyl] disulfides **3** were synthesized in high yield simply from the reaction of an acyl chloride **1** with sodium disulfide (**2**) in a two-phase system consisting of benzene, water, and a phase-transfer catalyst. The procedure we describe avoids the use of anhydrous conditions, reduces reaction times, and provides yields superior to the standard method[1].



$$2\ R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + Na_2S_2 \xrightarrow[\text{onium salt}]{C_6H_6\ /\ H_2O\ /} R-\overset{\overset{\displaystyle O}{\|}}{C}-S-S-\overset{\overset{\displaystyle O}{\|}}{C}-R$$

1 **2** **3**

This phase-transfer method also provided an improved route to thiophthalic anhydride (**5**) since this product is formed in high yield when phthaloyl chloride (**4**) is allowed to react with sodium disulfide. Disulfide products were not formed in this particular reaction. Thiophthalic anhydride (**5**) was also prepared in high yield by use of sodium sulfide nonahydrate instead of sodium disulfide.



4 **5**

Hexadecyltributylphosphonium bromide is the most effective among the quaternary salts tested (Table 1). Tetrabutylphosphonium bromide and benzyltriethylammonium chloride are less effective.

Table 1. Catalytic Effect of Quaternary Salts on the Yield of Bis[benzoyl] Disulfide (**3c**)[a]

Quaternary salt	Yield [%]
$[(C_4H_9)_4P]^{\oplus}Br^{\ominus}$	55
$[C_{16}H_{33}P(C_4H_9)_3]^{\oplus}Br^{\ominus}$	83
$[(C_4H_9)_4N]^{\oplus}Br^{\ominus}$	68
$[(C_8H_{17})_3NCH_3]^{\oplus}Cl^{\ominus}$	77
$[C_6H_5CH_2N(C_2H_5)_3]^{\oplus}Cl^{\ominus}$	55

[a] Reaction conditions: 30 min at room temperature.

The yields of isolated diacyl disulfides **3** given in Table 2 are over 85% when using 0.5 molar equivalents of sodium disulfide. Aliphatic acyl chlorides react faster than aromatic acyl chlorides. Particularly, in the case of decanoyl chloride (**1a**) and tetradecanoyl chloride (**1b**), the reactions are complete in 20 min at 0°C. The yield of dibenzoyl disulfide (**3c**) is superior to the yield obtained by the standard method[1]. From the substituted benzoyl chlorides (**1f–k**), the corresponding dibenzoyl disulfides (**3f–k**) are obtained in almost quantitative yield in 150 min at room temperature.

The results from the reaction of phthaloyl chloride (**4**) with sodium disulfide are summarised in Table 3. When the same reaction without the phase-transfer catalyst is carried out in ethanol, the yield of thiophthalic anhydride (**5**) is only 12.5%[2]. Thiophthalic anhydride (**5**) is usually prepared from the reaction of phthalic anhydride with sodium sulfide, and in this procedure phthalic acid is always formed as a by-product along with thiophthalic anhydride[5]. The present procedure using phase-transfer catalysis avoids the formation of phthalic acid and offers yield superior to the usual method[5].

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Table 2. Bis[acyl] Disulfides **3** prepared

Product No.	R	Reaction conditions time/temperature	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p. [°C]
3a	n-C_9H_{19}	20 min/0 °C	91	51-51.5°	$C_{20}H_{38}O_2S_2$ (374.7)
3b	n-$C_{13}H_{27}$	20 min/0 °C	85	65-66°	$C_{28}H_{54}O_2S_2$ (486.9)
3c	$C_6H_5-CH_2-$	20 min/r.t.	95	58-59°	62°[6]
3d	$C_6H_5-CH{=}CH-$	20 min/r.t.	84	135-135.5°	139°[7]
3e	C_6H_5	60 min/r.t.	94	129-130°	129-130°[1]
3f	4-Cl$-C_6H_4$	60 min/r.t.	98	121-122°	122.5-123°[8]
3g	2-$H_3C-C_6H_4$	150 min/r.t.	98	88-88.5°	$C_{16}H_{14}O_2S_2$ (302.4)
3h	3-$H_3C-C_6H_4$	150 min/r.t.	97	85-86°	$C_{16}H_{14}O_2S_2$ (302.4)
3i	4-$H_3C-C_6H_4$	150 min/r.t.	91	118-119°	118-119°[8]
3j	4-$O_2N-C_6H_4$	150 min/r.t.	85	180-180.5°	183-183.5°[8]
3k	4-$H_3CO-C_6H_4$	150 min/r.t.	70	120-120.5°	119-120°[9]

[a] Satisfactory microanalyses obtained: C ±0.12, H ±0.20, S ±0.26.

Table 3. Preparation of Thiophthalic Anhydride (**5**) from Phthaloyl Chloride (**3**) and Sodium Sulfide

Sodium sulfide [mol-eq.]	Catalyst[a] [mol-eq.]	Time [min]	Yield [%]
1[b]	0.05	30	87
1	0.1	15	85
1	0.05	30	81
1	0.025	30	80

[a] Hexadecyl-tributylphosphonium bromide.

[b] Sodium disulfide used.

The structures of all compounds prepared were confirmed by their I.R. and ^{1}H-N.M.R. spectra and by microanalysis.

Bis[decanoyl] Disulfide (3a); Typical Procedure:

An aqueous solution of sodium disulfide is prepared by heating a mixture of sulfur (0.48 g, 2 mmol) and sodium sulfide nonahydrate (3.61 g, 15 mmol) in water (20 ml) at 90 °C for 15 min with stirring. The aqueous solution of sodium disulfide (**2**) is added dropwise to a mixture of decanoyl chloride (**1a**; 5.70 g, 30 mmol), hexadecyltributylphosphonium bromide (0.76 g, 1.5 mmol), and benzene (30 ml) at 0 °C during 20 min with vigorous stirring. The reaction proceeds exothermically and the aqueous layer changes from brown-red to colorless immediately. The organic layer is separated, washed with water (60 ml), and dried with sodium sulfate. The solvent is removed by evaporation under reduced pressure. The crude product is washed with cold ethanol; yield: 5.1 g (91%); m.p. 50-51 °C; recrystallization from methanol gives pure material; m.p. 51-51.5 °C.

$C_{20}H_{38}O_2S_2$	calc.	C 64.12	H 10.22	S 17.12
(374.7)	found	64.10	10.35	16.86

Thiophthalic Anhydride (5):

A solution of sodium sulfide nonahydrate (2.4 g, 10 mmol) in water (20 ml) is added dropwise into a solution of phthaloyl chloride (**4**; 2.3 g, 10 mmol) and hexadecylphosphonium bromide (0.26 g, 0.5 mmol) in benzene (20 ml) during 30 min at room temperature with vigorous stirring. The organic layer is separated, washed with dilute aqueous hydrochloric acid (40 ml) and water (40 ml), and dried with sodium sulfate. The solvent is removed by evaporation under reduced pressure. The crude product is washed with aqueous methanol; yield: 1.3 g (81%); m.p. 109-111 °C; recrystallization from methanol/water gives a pure sample; m.p. 112-113 °C (Lit.[5], m.p. 114 °C).

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