A facile method for the synthesis of diacyl disulfides

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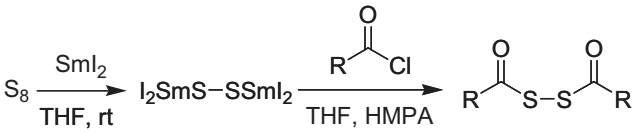
A facile method for the synthesis of diacyl disulfides is reported. Sulfur is reduced with samarium diiodide at room temperature to give samarium disulfides, which react with acyl chlorides in the presence of HMPA to afford the corresponding diacyl disulfides in high yields.

Keywords: diacyl disulfide, samarium diiodide, sulfur, acyl chloride, synthesis

Disulfides are important categories of organic compounds because of the wide existence of their linkage in many molecules such as proteins, peptides, natural products and pharmacologically active compounds.[1] Also, disulfides are an important class of synthetic intermediates in a variety of chemical transformations.[2,3] Much attention has been given to the synthesis of diacyl disulfides from the oxidation of thiocarboxylate ions[4] and treatment of acyl halides with sodium disulfide,[5] lithium disulfide,[6] or hydrogen disulfide.[7] As a modified method, Kadomari *et al.*[8] reported the synthesis of diacyl disulfides from sodium disulfide and acyl halides in a two phase system using an onium salt as a phase transfer agent. Wang *et al.*[9] introduced a convenient method of preparation of diacyl disulfides from acyl chlorides using a sulfur, benzene/NaOH(aq) system with the help of polyethylene glycol as a phase transfer agent. Recently, Tamami and Kiasat[10] reported the synthesis of diacyl disulfides from acyl chlorides in benzene using a polymer supported reagent. However, the above methods suffer from some drawbacks such as low yields, use of strong base, use of aqueous medium, the need for reactions to be carried out under PTC conditions, formation of by products, toxic solvents and hydrolysis of some acyl chlorides under the reaction conditions.

Samarium diiodide as a strong single-electron transfer reducing reagent has been extensively applied in organic synthesis[11] and can reduce elemental sulfur to thiolate anion species.[12] We have previously reported the synthesis of dialkyl disulfides with samarium diiodide.[13] Herein, we wish to report a facile and efficient synthesis of diacyl disulfides under neutral conditions in high yields (Scheme 1).

Sulfur is reduced with samarium diiodide in THF at room temperature to give samarium disulfides, which react with acyl chlorides under reflux in the presence of HMPA to afford the corresponding diacyl disulfides in high yields. In our experiments, we discovered that when the molar ratio of sulfur, samarium and acyl chlorides is 1 : 1.1 : 1.2, diacyl disulfides were obtained in relatively low yields and a small amount of diacyl sulfides was also formed. However, when 1.1 equivalent of sulfur was treated with one equivalent of samarium diiodide and then reacted with 1.2 equivalent of acyl chlorides, diacyl disulfides were formed exclusively in high yields. Aliphatic acyl chlorides react faster than aromatic acyl chlorides. Small amounts of products were observed in the reaction of samarium disulfide with *o*-nitro- or *p*-nitrobenzoyl chloride. The acylation of $(I_2Sm)_2S_2$ gave the diacyl disulfides in low yields in the absence of HMPA.



Scheme 1

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The addition of HMPA as a cosolvent dramatically improved the yields of disulfides. In addition, we treated one equivalent of sulfur with two equivalents of samarium diiodide in a series of reaction conditions to obtain diacyl sulfides. However, unfortunately a mixture of diacyl disulfide and diacyl sulfide was formed. The structures of all compounds prepared were confirmed by m.p., IR, ^{1}H NMR and elemental analyses. The results are summarised in Table 1.

In conclusion, we have reported a neutral and high selective method for the synthesis of diacyl disulfides. The advantages of our method are single product formation, high yields, a non-aqueous medium and neutral conditions.

Experimental

Melting points were determined on a capillary melting point apparatus and are uncorrected. Elemental analyses were obtained using a Carlo-Erba 1106 instrument. IR spectra were recorded with a Perkin Elmer 580 spectrometer. ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer in $CDCl_3$ with TMS as an internal standard. Tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl prior to its use.

General procedure

Samarium powder (150 mg, 1.0 mmol) was placed in a well-dried two-necked round bottom flask containing a magnetic stirrer. Tetrahydrofuran (11 ml) and iodine (279 mg, 1.0 mmol) were added successively under a nitrogen atmosphere. The suspension was stirred at room temperature for 3 h. To the deep blue solution of samarium diiodide formed was added sulfur powder (35.2 mg, 1.1 mmol) and the resulting mixture was stirred at room temperature for 1 h. To the mixture was added successively HMPA (0.5 ml) and acyl chloride (1.2 mmol). The solution was stirred under reflux for the given time (Table 1). After completion of the reaction, the mixture was quenched with saturated sodium bicarbonate solution (20 ml) and extracted with dichloromethane. The extract was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel eluting with petroleum ether/ethyl acetate to afford the corresponding diacyl disulfide in high yields. The products were identified by m.p., elemental analysis, IR, and ^{1}H NMR spectra (for the AA'XX' system of **2**, **3** and **5**, J* = $J_{23} + J_{25}$).

1: M.p. 132–133°C (lit.[9] 129–130°C); ν_{max} (KBr)/cm^{-1} 3046, 1700, 1682, 1592, 1484; δ_H ($CDCl_3$/TMS): 7.53 (4H, m), 7.66 (2H, m), 8.09 (4H, d, *J* = 9.0 Hz); Anal. Calcd. for $C_{14}H_{10}O_2S_2$: C, 61.3, H, 3.65. Found: C, 61.3, H, 3.7.

2: M.p. 118–119°C (lit.[9] 118–119°C); ν_{max} (KBr)/cm^{-1} 3026, 2918, 1694, 1678, 1603, 1504; δ_H ($CDCl_3$/TMS): 2.44 (6H, s), 7.31 (4H, m,

Table 1 The synthesis of diacyl disulfides

Product No.	Acyl chloride	Product	Time /h	Yield /%[a]
1	PhCOCl	$(PhCOS)_2$	3	96
2	*p*-MeC_6H_4COCl	(*p*-$MeC_6H_4COS)_2$	4	88
3	*p*-ClC_6H_4COCl	(*p*-$ClC_6H_4COS)_2$	4	90
4	*o*-ClC_6H_4COCl	(*p*-$ClC_6H_4COS)_2$	3	85
5	*p*-$MeOC_6H_4COCl$	(*p*-$MeC_6H_4COS)_2$	4	97
6	PhCH=CHCOCl	$(PhCH=CHCOS)_2$	5	83
7	$PhCH_2COCl$	$(PhCH_2COS)_2$	2.5	86
8	CH_3CH_2COCl	$(CH_3CH_2COS)_2$	2.5	98

[a]Yield of isolated product.

*J** = 8.4 Hz), 7.98 (4H, m, *J** = 8.4 Hz); Anal. Calcd. for $C_{16}H_{14}O_2S_2$: C, 63.6, H, 4.6. Found: C, 63.4, H, 4.6.

3: M.p. 122–123°C (lit.[9] 120–121°C); ν_{max} (KBr)/cm^{-1} 3089, 1698, 1680, 1583, 1484; δ_H ($CDCl_3$/TMS): 7.51 (4H, m, *J** = 9.0 Hz), 8.02 (4H, m, *J** = 9.0 Hz); Anal. Calcd. for $C_{14}H_8Cl_2O_2S_2$: C, 49.0, H, 2.3. Found: C, 48.9, H, 2.3.

4: M.p. 87–88°C (lit.[9] 86–87°C); ν_{max} (KBr)/cm^{-1} 3084, 1712, 1697, 1582, 1463; δ_H ($CDCl_3$/TMS): 7.45 (6H, m), 7.89 (2H, d, *J* = 7.69 Hz); Anal. Calcd. for $C_{14}H_8Cl_2O_2S_2$: C, 49.0, H, 2.3. Found: C, 48.9, H, 2.3.

5: M.p. 119–120°C (lit.[9] 120–121°C); ν_{max} (KBr)/cm^{-1} 3118, 2971, 1694, 1687, 1572, 1505; δ_H ($CDCl_3$/TMS): 3.88 (6H, s), 6.98 (4H, m, *J** = 8.7 Hz), 8.06 (4H, m, *J** = 8.7 Hz); Anal. Calcd. for $C_{16}H_{14}O_4S_2$: C, 57.5, H, 4.2. Found: C, 57.7, H, 4.1.

6: M.p. 134–135°C (lit.[8] 135–135.5°C); ν_{max} (KBr)/cm^{-1} 3054, 1701, 1686, 1611, 1574, 1492; δ_H ($CDCl_3$/TMS): 6.88 (2H, s), 6.93 (2H, s), 7.36 (10H, m); Anal. Calcd. for $C_{18}H_{14}O_2S_2$: C, 66.3, H, 4.3. Found: C, 66.2, H, 4.2.

7: M.p. 57–59°C (lit.[8] 58–59°C); ν_{max} (KBr)/cm^{-1} 3086, 2956, 2925, 1734, 1706, 1585, 1495; δ_H ($CDCl_3$/TMS): 4.13 (4H, s), 7.31 (10H, m); Anal. Calcd. for $C_{16}H_{14}O_2S_2$: C, 63.6, H, 4.6. Found: C, 63.6, H, 4.6.

8: Oil; ν_{max} (KBr)/cm^{-1} 2958, 1736, 1710, 1461, 1386; δ_H ($CDCl_3$/TMS): 1.21 (6H, t, *J* = 7.5 Hz), 2.91 (4H, q, *J* = 7.5 Hz); Anal. Calcd. for $C_6H_{10}O_2S_2$: C, 40.45, H, 5.6. Found: C, 40.3, H, 5.6.

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