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A new convenient procedure for the thionation of carbonyl compounds utilizing tetrachlorosilane–sodium sulfide

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ABSTRACT

A combination of tetrachlorosilane (TCS) and sodium sulfide in acetonitrile is found to be an efficient thionating reagent for aromatic aldehydes in the absence of catalysis to give the corresponding thioaldehydes as trimers in good yields. Under cobalt(II) chloride catalysis, α,β-unsaturated ketones react with TCS–Na_2S to give the respective disulfides in good yields via the intermediacy of β-mercaptoketones at ambient temperature.

Organosulfur compounds are important intermediates for the synthesis of various biologically active molecules as well as in industry.[1] Thionation of carbonyl compounds is widely applied for the synthesis of organosulfur compounds.[2] A variety of thionating reagents have been described in the literature.[3] Synthetically, Lawesson's reagent (LR)[4] and P_4S_{10},[5a] either alone or with additives,[5b–d] are the most effective sulfurating reagents. However, aside from its high cost, LR has the major disadvantage of being extremely sensitive to moisture and it is very difficult to prepare and handle it in pure form,[6] and the by-products derived from the reagent itself cannot, in general, be removed by any extractive procedure and must be separated by column chromatography. Thiosilanes, particularly hexamethyldisilathiane (HMDST),[7] have been used as thionating reagents, often under catalysis. They exhibit specific reactivity due to the unique and complementary properties of sulfur and silicon, and have thus emerged as very useful reagents in synthetic organic chemistry.[8] However, organothiosilanes are good reagents for carbonyl functionalization[9] as they react with activated carbonyl compounds through cleavage of the Si–S bond and addition to the C=O group; the uncatalyzed thiosilane addition is still not a facile process, and requires high temperatures and long reaction times.[10] On the other hand, silyl sulfides were found to react slowly with α,β-unsaturated ketones at elevated temperature but, in the presence of cyanide, thiolate, or fluoride ions, the addition process occurs very efficiently to afford 1,4-adducts.[11] The development of novel synthetic strategies for thionation, which have advantages with respect to mild reaction conditions, cleaner reactions, and simple isolation of the product, is of interest. In this context, and in conjunction with our interest[12] in exploring the utility of in situ reagents based on tetrachlorosilane (TCS)[13] in organic synthesis, we report herein a new in situ thiosilane system derived from cheap and readily available tetrachlorosilane and sodium sulfide that converts aromatic aldehydes into their corresponding thioaldehydes, which are obtained as trimers, in good yield at room temperature using acetonitrile as a solvent without any catalyst. Also, under these exceptionally mild conditions, α,β-unsaturated ketones react with the $SiCl_4$–Na_2S reagent in the presence of a catalytic amount of $CoCl_2 \cdot 6H_2O$ to give β-mercaptoketone derivatives that subsequently auto-oxidize to give the respective disulfides. However, no reaction was observed with aryl methyl ketones.

The reaction of aldehydes with $SiCl_4$–Na_2S proceeds without further addition of any catalyst giving good yields of the corresponding thioaldehydes which were obtained as trimers (Scheme 1, Table 1). The structures of the isolated trithioaldehydes were assigned based on their spectral analyses as well as by comparison of their melting points with reported values.[14]

The driving force for the present reaction is the net formation of the stronger Si–O bond, where the difference in Si–O and Si–S bond energies is ≈34 kcal,[15] and therefore promotes the easy addition of

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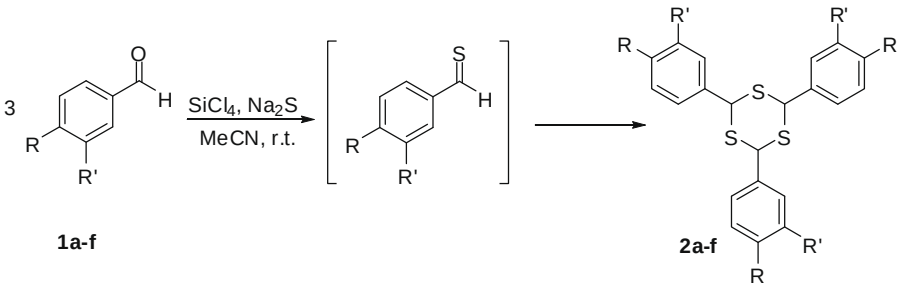


1a, 2a; R' = R = H
1b, 2b; R' =H, R = Me
1c, 2c; R' = H, R = OMe
1d, 2d; R' = H, R = Cl
1e, 2e; R' = H, R = Br
1f, 2f; R' = Br, R = H

Scheme 1.

Table 1
Reaction of aryl aldehydes with the TCS–Na_2S reagent

Entry	Substrate	Time (h)	Product	Yield[a] (%)
1	Benzaldehyde	9	**2a**	82
2	4-Methylbenzaldehyde	10	**2b**	77
3	4-Methoxybenzaldehyde	8	**2c**	79
4	4-Chlorobenzaldehyde	12	**2d**	68
5	4-Bromobenzaldehyde	14	**2e**	72
6	3-Bromobenzaldehyde	18	**2f**	63

[a] Yield of isolated product.

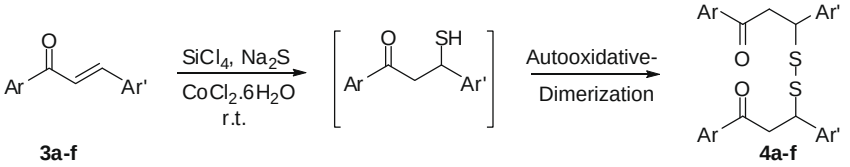
thiosilane to the carbonyl group of the aldehyde with formation of the thermodynamically controlled products.

Applying the present reaction to aryl methyl ketones failed to yield the corresponding thioketones even with the use of a catalyst and/or by heating. This led us to attempt the reaction with α,β-unsaturated ketones, the reason being that the 1,4-addition might be a favorable process (Scheme 2). Thus, α,β-unsaturated ketones were found to react with TCS–Na_2S in the presence of a catalytic amount of $CoCl_2{\cdot}6H_2O$ to give the 1,4-adducts (presumably the thiols **C**, Scheme 3) but, as is well known, such thiols undergo autooxidative dimerization easily to give disulfides **4**.[16] It is noteworthy to mention that no reaction was observed in the absence of either the catalyst or $SiCl_4$. The generality of the process was examined by applying the reaction to various examples of α,β-unsaturated ketones; however, bischalcones gave a complex mixture with no preparative value. For example, dibenzalacetone and 2,6-bis(4-methoxybenzal)cyclohexanone gave no distinct products (Scheme 2, Table 2).

The structure of disulfides **4** was supported by analytical and spectral data. In the IR spectra of **4**, the absorption at 1670–1680 cm^{-1} attributed to the carbonyl stretching of the saturated system showed a clear shift compared to the corresponding starting α,β-unsaturated ketone. The ^1H NMR spectrum of **4f,** for example, showed two doublets at δ 3.46 and δ 3.29 as well as two triplets at δ 4.42 and δ 4.16. These were assigned to the C-2 and C-3 protons, respectively.

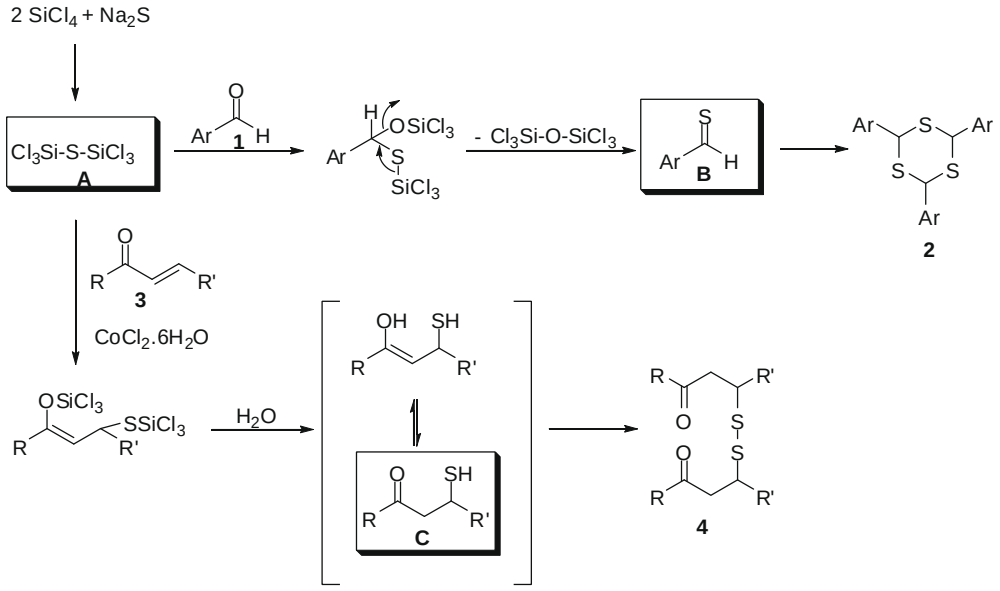
Plausible mechanisms for the present reactions may proceed as depicted in Scheme 3. 1,2-Addition of stoichiometric thiosilane, generated in situ from the reaction of TCS and Na_2S in 2:1 molar ratio, in a similar manner to HMDST preparation[17] (proposed hexachlorodisilathiane **A**; HCDST) to the carbonyl group of the aldehyde **1** yields the transient thioaldehyde **B** which undergoes trimerization to form **2**. By analogy, the proposed hexachlorodisilathiane A reacts with α,β-unsaturated ketones **3** only in the presence of $CoCl_2{\cdot}6H_2O$ catalysis via a 1,4-addition mechanism to give the thiol C which subsequently undergoes autooxidative dimerization to form disulfides **4**.

In conclusion, we have developed a new thiosilane reagent which is generated in situ from readily available and inexpensive tetrachlorosilane and sodium sulfide.[18] The thiosilane reagent acts as a mild and potent thionating reagent for aromatic aldehydes in acetonitrile at room temperature without catalysis giving the corresponding trithioaldehydes in good yields. Under these mild conditions, α,β-unsaturated ketones react with $SiCl_4$–Na_2S using a catalytic amount of $CoCl_2{\cdot}6H_2O$ to give the respective disulfides via a 1,4-conjugate addition mechanism. This new in situ reagent may find additional applications as a substitute for HMDST, poten-



3a, 4a; Ar = Ar' = Ph
3b, 4b; Ar = Ph, Ar' = 4-BrC_6H_4-
3c, 4c; Ar = Ph, Ar' = 4-MeC_6H_4-
3d, 4d; Ar = 4-MeC_6H_4-, Ar' = 4-BrC_6H_4-
3e, 4e; Ar = Ar' = 4-MeC_6H_4-
3f, 4f; Ar 2-thienyl, Ar' = Ph

Scheme 2.



Scheme 3. Plausible mechanisms for the formation of **2** and **4**.

Table 2
Reaction of α,β-unsaturated ketones with the TCS–Na_2S reagent in the presence of $CoCl_2{\cdot}6H_2O$

Entry	Substrate	Time (h)	Product	Yield[a] (%)
1	Benzalacetophenone	12	**4a**	71
2	4-Bromobenzalacetophenone	14	**4b**	63
3	4-Methylbenzal-acetophenone	12	**4c**	72
4	4-Bromobenzal-4′-methylacetophenone	14	**4d**	66
5	4-Methylbenzal-4′-methylacetophenone	12	**4e**	74
6	2-Benzal-2-acetylthiophene	11	**4f**	61
7	Dibenzalacetone	17	—	—
8	2,6-Bis(4-methoxybenzal)cyclohexanone	18	—	—

[a] Yield of isolated product.

tially expanding the synthetic value of tetrachlorosilane in synthetic organic chemistry.

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18. *A typical procedure for the thionation of carbonyl compounds*: A mixture of anhydrous Na_2S (10 mmol) and $SiCl_4$ (20 mmol) in MeCN (15 ml) was stirred for 15 min at ambient temperature. To this mixture, a solution of carbonyl compound (5 mmol) in MeCN (10 ml) was added as well as a catalytic amount of $CoCl_2{\cdot}6H_2O$ (in the case of α,β-unsaturated ketones), and the reaction mixture was stirred at room temperature. On completion (TLC), the mixture was quenched with cold water, extracted with ethyl acetate (for aldehydes) or with $CHCl_3$ (for α,β-unsaturated ketones), dried over anhydrous $MgSO_4$, and the solvent was evaporated under vacuum and the residue was recrystallized to give compound **2** or chromatographed using petroleum ether–ethyl acetate (20:1) as eluent (in most cases) to give pure **4**. *Note:* Sodium sulfide nonahydrate ($Na_2S{\cdot}9H_2O$) was dried by refluxing using dry benzene and a Dean–Stark apparatus for three days. All the prepared trithioaldehydes **2** are known.[14] Disulfides **4** are novel except for **4a**.[19] Data for some representative examples are provided.
Bis-[1-(4-methylphenyl)-3-oxo-3-phenylpropyl]disulfide **4c**: Yield 72%; mp 105 °C; IR (KBr plate) ν 3054, 3027, 2918, 1677 (CO), 1597, 1513, 1447, 1367, 1257, 1208, 819, 760, 687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (m, 4H), 7.58 (m, 2H), 7.53–7.06 (m, 12H), 4.14 (m, 2H), 3.44 (dd, J = 16.76, 7.93 Hz, 2H), 3.38 (dd, J = 16.76, 7.93 Hz, 2H), 2.28 (s, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.66, 138.56, 136.87, 136.66, 132.98, 129.12, 128.00, 127.97, 45.52, 44.12, 21.1; EI-MS (*m/z*, %): 510 (M^+, 7), 255 (13), 223 (25), 119 (100), 77 (91). Anal. Calcd for $C_{32}H_{30}O_2S_2$ (510.892): C, 75.26; H, 5.92; S, 12.56. Found: C, 75.18; H, 6.02; S, 12.67.
Bis-[1,3-bis(4-methylphenyl)-3-oxopropyl]disulfide **4e**: Yield 74%; Purification by recrystallization from diethyl ether; mp 113–115 °C.; IR (KBr plate) ν 3027, 2918, 2859, 1677 (CO), 1605, 1512, 1410, 1367, 1263, 1182, 1116, 810, 726 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.71–7.65 (m, 4H), 7.24–7.12 (m, 10H), 7.05 (d, 2H, J = 7.4 Hz), 4.39 (t, 1H, J = 7.3 Hz), 4.11 (t, 1H, J = 7.3 Hz), 3.46 (d, 2H, J = 7.2 Hz), 3.34–3.27 (m, 2H), 2.36 (s, 6H, 2 × CH_3), 2.28 (s, 6H, 2 × CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 196.15, 142.18, 138.69, 137.07, 136.13, 128.91, 128.35, 127.19, 46.12, 44.57, 23.19, 21.34; EI-MS (*m/z*, %): 538 (M^+, 5), 269 (15), 237 (32), 119 (100), 91 (82). Anal. Calcd for $C_{34}H_{34}O_2S_2$ (538.76): C, 75.79; H, 6.36; S, 11.90. Found: C, 75.84; H, 6.28; S, 11.65.
Bis-[1-phenyl)-3-oxo-3-thienylpropyl]disulfide **4f**: Yield 61%; mp 97 °C; IR (KBr plate, cm^{-1}) ν 3094, 3027, 2920, 1659 (CO), 1599, 1515, 1451, 1413, 1357, 1329, 1237, 1063, 856, 753, 726, 699; ^1H NMR (200 MHz, $CDCl_3$) δ 7.60–7.54 (m, 2H), 7.27–7.15 (m, 10H), 7.10–7.05 (m, 4H), 4.42 (t, 1H, J = 7.0 Hz), 4.16 (t, 1H, J = 7.0 Hz), 3.46 (d, 2H, J = 7.4 Hz), 3.29 (d, 2H, J = 7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.05, 142.10, 141.56, 133,72, 131.53, 128.69, 127.53, 127.29, 127.12, 45.16, 43.88; EI-MS (*m/z*, %): 494 (M^+, 9), 247 (10), 246 (12), 215 (27), 105 (100). Anal. Calcd for $C_{26}H_{22}O_2S_4$ (494.71): C, 63.12; H, 4.48; S, 25.93. Found: C, 63.02; H, 4.29; S, 26.02.
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