Superbasic system CsOH/DMSO as a reagent for a fast one-step synthesis of symmetrical dialkyl trithiocarbonates

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ABSTRACT

Symmetrical dialkyltrithiocarbonates were readily synthesized in excellent yields by one-pot reaction of carbon disulfide and various alkyl halides under mild reaction conditions in the presence of cesium hydroxide.

Keywords:
Symmetrical trithiocarbonates
Cesium hydroxide
One-pot reaction
Carbon disulfide
Alkyl halides

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1. Introduction

The impact of organosulfur chemistry on modern organic synthesis is indisputable and has played an enormous role in biology, medicine and industry [1].Among them, organic trithiocarbonates constitute an important class of compounds which have been claimed for various applications in industry, synthesis and medicine [2]. They have been widely used as pesticides in agriculture [3],lubricating additives [4], in material science [5], in froth flotation[6] for the recovery of minerals from their ores and for their absorption properties of certain metals [7],intermediates in organic synthesis [8], for protection of thiol functionality [9],and in free radical polymerization reactions [10]. Additionally, they are used in various C–C bond forming reactions [11] which necessitates their preparation through convenient and safe methods.

The synthesis of trithiocarbonates has received considerable attention and several methods have been developed including reactions of thiols with thiophosgene [12],chlorodithioformates [13], or with carbon disulfide and alkyl halides under basic conditions in two-steps [14].Other general method involves the dialkylation of the trithiocarbonate anion with halides, using phase-transfer catalysts or at elevated temperature [15]. In a recent report, 1,1 ́-thiocarbonyl diimidazol (TCDI) and primary thiols were used, under inert atmosphere and elevated temperature (60°C), for synthesis of symmetrical trithiocarbonates [16].Recently, a method for the synthesis of trithiocarbonates was reported using a Cs_2CO_3/CS_2 system [17].In a previous study [18], we investigated the one-pot synthesis of symmetrical dialkyltrithiocarbonates by reaction of alkyl halides with CS_2 at room temperature catalyzed by KF/Al_2O_3. However, each of the above methods has at least one of the following drawbacks: long reaction times, tedious work-up, low yields of product, synthetic inconvenient, employment of highly toxic chemicals with unpleasant odors, unavailability of starting materials, use of 10- to 19- fold molar excess amount of carbon disulfide and bases toward alkyl halides and formation of unwanted side products such as sulfides, etc. Consequently, developing new and convenient methods for the synthesis of symmetrical trithiocarbonates under mild reaction conditions is very valuable.

2. Experimental

All chemicals were purchased from Merck. All products were identified by comparison of their spectral and physical data with those of the known samples. IR spectra were obtained using an ABB FTLA 2000 instrument. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DRX-400 Avance instrument with $CDCl_3$ as solution and the chemical shifts are determined by reference to residual $CHCl_3$ in $CDCl_3$. All compounds were characterized by comparing their physical data with those in the literature.

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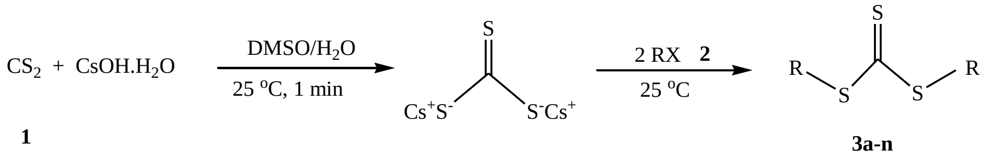
*Typical procedure for preparation of dibenzyltrithiocarbonate**(3a)***: To the solution of $CsOH.H_2O$ (167 mg, 1.0 mmol) in $DMSO:H_2O$ (15:1, 1 mL), carbon disulfide (152 mg, 2.0 mmol) was added and the mixture was stirred at 25 ℃ for 1 min. The color of the mixture immediately changed from light yellow to blood red; then, benzyl bromide (171 mg, 1.0 mmol) was added to the above solution, and the reaction mixture was stirred at that temperature until the reaction was completed (monitored by TLC). On completion of the reaction, the mixture was filtered and evaporated, EtOAc (25 mL) was added and washed with water (2 × 15 mL) and dried over anhydrous $MgSO_4$. The solution was concentrated to give the crude product, which was purified by preparative TLC (silica gel, eluent, *n*-hexane) to afford the pure dibenzyltrithiocarbonate**(3a**, 139 mg, 96%**)** as light yellow oil. Selective data: **3a**, **3b:** IR (neat, ν_{max}):1062 (C=S), 1494, 1602 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.67 (s, 4H), 7.28-7.40 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 41.59, 127.86, 128.77, 129.34, 134.96, 222.80. **3e:** Yellow oil; IR (neat, ν_{max}): 1057 (C=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.92 (t, 6H, J = 6.8 Hz), 1.27-1.35 (m, 8H), 1.40-1.45 (m, 4H), 1.72 (quin, 4H, J = 7.6 Hz), 3.39 (t, 4H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$): δ 14.04, 22.53, 28.02, 28.64, 31.33, 36.88, 224.78. **3g**, **3h:** Light yellow oil; IR (neat, ν_{max}): 1057 (C=S), 1638 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.07 (d, 4H, J = 6.8 Hz), 5.23 (d, 2H, J = 10.0 Hz), 5.36 (d, 2H, J = 17.0, 1.3 Hz), 5.85-5.95 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 39.72, 119.72, 130.97, 222.48. **3j:** Yellow oil; IR (neat, ν_{max}): 1069 (C=S), 1449, 1493, 1596 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.82 (d, 6H, J = 7.6 Hz), 5.39 (q, 2H, J = 7.6 Hz), 7.35-7.41 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 21.41, 50.10, 127.77, 128.44, 128.71, 141.13, 221.44. **3l:** Yellow oil; IR (neat, ν_{max}): 1075 (C=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.99 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 43.86, 228.68. **3m:** Light yellow oil; IR (neat, ν_{max}): 1078 (C=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.03 (t, 6H, J = 7.4 Hz), 1.41 (d, 6H, J = 6.8 Hz),1.66-1.83 (m, 4H), 4.136 (sext,2H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$): δ 11.46, 19.61, 28.81, 47.98, 224.03. **3n:** Light yellow oil; IR (neat, ν_{max}): 1073 (C=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.42 (d, 12H, J = 7.2 Hz), 4.22 (sept, 2H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$): δ 22.07, 41.63, 223.48.

3. Results and Discussion

Cesium hydroxide continues to attract much attention from organic chemists due to the versatility of use in synthetic chemistry; it is non-toxic, and a strong inorganic base (pK_b= –1.76) used as an alternative non-nucleophilic base in several reactions [19]. We have now developed an easy and one-step synthesis of symmetrical dialkyltrithiocarbonates directly from carbon disulfide and alkyl halides using cesium hydroxide monohydrate in dimethyl sulfoxide (DMSO) and H_2O (15:1) at room temperature.

To optimize the reaction with respect to solvent, temperature, time, molar ratios of the components and to maintain the blood red base sensitive trithiocarbonate anion (CS_3^{2-}), we initially examined the reaction of benzyl bromide and carbon disulfide as a model reaction, at various conditions under an aerobic atmosphere (Table 1). The best molar ratios of $CS_2:PhCH_2Br:CsOH.H_2O$ was found to be 2:1:1. Also, the results show that $DMSO:H_2O$ (15:1) is the best solvent (entry 12, Table 1). After optimization, a variety of other alkyl halides were shown to undergo the reaction smoothly, giving the desired products in high to excellent yields (Scheme 1). The results are summarized in Table 2.

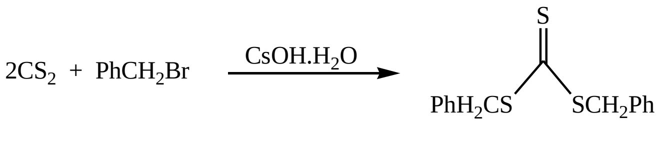


Scheme 1.Trithiocarbonation of alkyl halides in the presence of cesium hydroxide.

When carbon disulfide (2 mmol) was added to the solution of $CsOH.H_2O$ (1 mmol) in $DMSO:H_2O$ (15:1, 1 mL), and the mixture was stirred vigorously at 25 ℃ for 1 min, the colorless mixture turned blood red immediately, indicating the formation of trithiocarbonate anion (CS_3^{2-}) [20]; in situ alkylation with alkyl halides for the appropriate times (Table 2) afforded the corresponding symmetrical trithiocarbonates. With progress of the reaction, the color of the solution changed from blood red to yellow. The structures of all the products were established from their analytical and spectral (IR, ^1H, and ^{13}C NMR) properties. Primary, secondary, benzylic and allylic halides are converted to the corresponding trithiocarbonates as exclusive and virtually pure products according to TLC and ^1H NMR, in high to excellent yields (Table 2).

Table 1

Screening of the Reaction Conditions[a]



1 **2a** **3a**

Entry	Solvent	$CsOH.H_2O$ (mmol)	Condition	Yield[b] (%)
1	THF	1	25 ℃; 24h	N.R.
2	DMF	1	50 ℃; 24h	51
3	1,4-Dioxane	1	25 ℃; 24h	N.R.
4	$CHCl_3$	1	25 ℃; 24h	N.R.
5	Acetonitrile	1	25 ℃; 24h	42
6	EtOAc	1	25 ℃; 24h	N.R.
7	DME[c]	1	25 ℃; 24h	24
8	Neat	1	25 ℃; 48h	13
9	H_2O	1	50 ℃; 24h	N.R.
10	EtOH	1	50 ℃; 24h	N.R.
11	DMSO	1	25 ℃; 10h	65
12	DMSO:H_2O	1	25 ℃; 5h	96
13	DMSO:H_2O	0.5	25 ℃; 5h	41

[a] Reaction conditions: carbon disulfide (2 mmol), benzyl bromide (1 mmol), solvent (1 mL).

[b] Isolated yields.

[c] 1,2-Dimethoxyethane.

Table 2

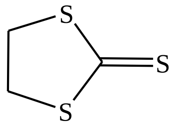
Synthesis of Symmetrical Trithiocarbonates Mediated by $CsOH.H_2O$.

Entry	Alkyl Halide	Time (h)	Product	Yield (%)[a,b]
1	$PhCH_2Br$	5	**3a**	96[18]
2	$PhCH_2Cl$	8	**3b**	94[18]
3	CH_3I	7	**3c**	83[18]
4	CH_3CH_2I	6	**3d**	89[18]
5	$CH_3(CH_2)_4CH_2Br$	10	**3e**	87[18]
6	$CH_3(CH_2)_6CH_2I$	12	**3f**	84[18]
7	$CH_2{=}CHCH_2Br$	5	**3g**	94[18]
8	$CH_2{=}CHCH_2Cl$	6	**3h**	91[18]
9	$4\text{-}BrC_6H_4CH_2Br$	12	**3i**	69[21]
10	$PhCH(CH_3)Br$	12	**3j**	78[18]
11	$PhC(CH_3)_2Br$	24	**3k**	N. R.
12	$BrCH_2CH_2Br$	12	**3l**	86[21]
13	$CH_3CH_2CH(CH_3)Br$	24	**3m**	79[18]
14	$(CH_3)_2CHBr$	16	**3n**	85[18]
15	$(CH_3)_3CBr$	24	**3o**	N. R.

[a] Isolated yields.

[b] References are provided for known compounds.

The procedure worked fine with primary, secondary, benzyl as well as allyl halides. However, under the same reaction conditions, tertiary halides did not produce the expected trithiocarbonates even after 24 h (entries 11 and 15, Table 2). Moreover, 1,3-dithiolane-2-thione (**3l**), a cyclic trithiocarbonate, can also be prepared from 1,2-dibromoethane without formation of any polymeric by-product. The results clearly show that CsOH is an efficient reagent in trithiocarbonation of alkyl halides.



3l

4. Conclusion

In conclusion, cesium hydroxide monohydrate in DMSO/H_2O has been introduced as a potential catalyst for the one-potsynthesis of symmetrical dialkyltrithiocarbonates from various alkyl halides and carbon disulfide. The specific advantages of this methodology include: mild reaction conditions, simple reaction work-up and high to excellent yield of the products without using large excess amount of toxic carbon disulfide.

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