A Facile KF/Al_2O_3-mediated, One-pot Synthesis of Symmetrical Trithiocarbonates from Alkyl Halides and Carbon Disulfide

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A facile, efficient, and convenient method has been developed for the one-pot synthesis of symmetrical trithiocarbonates from carbon disulfide and various alkyl halides in the presence of KF/Al_2O_3 in DMF at room temperature.

In recent years, synthesis of symmetrical and unsymmetrical dialkyl trithiocarbonates has attracted much attention, since they represent an important class of key compounds that have been used for various applications, especially for the preparation of insecticides, pesticides in agriculture and as lubricating additives.[1] Furthermore, radical polymerization with thiocarbonylthio reversible addition–fragmentation chain-transfer (RAFT) agents[2–4] is arguably one of the most versatile processes for living free-radical polymerization displaying superior flexibility with respect to monomers and reaction conditions. For instance, dibenzyl trithiocarbonate (DBTTC) derivatives are focused as RAFT agents,[4,5] which enables controlled free-radical polymerization of various vinyl monomers to afford polymers with narrow polydispersities and controlled molecular weights.

Some procedures for preparation of trithiocarbonates have been developed including reactions of thiols with thiophosgene,[6] arylchlorothioformates with alkanethiols,[7] sodium trithiocarbonates with alkyl halides,[8] benzenethiols and alkyl halides with carbon disulfide in the presence of a phase-transfer catalyst.[9] Another general method involves the dialkylation of the trithiocarbonate anion with halides, using phase-transfer catalysts or at elevated temperature.[10] However, various disadvantages such as synthetic inconvenience, unavailability of starting materials, use of large excess of highly toxic or stinky chemicals, and formation of unwanted side products such as sulfides, etc. encountered in the reported methodologies necessitate the development of a more efficient and convenient method. Very recently, Wood and co-workers reported the synthesis of symmetrical trithiocarbonates using 1,1′-thiocarbonyl diimidazole (TCDI) and primary thiols;[11] this method, however, needs an inert atmosphere and elevated temperature (60 °C) and gives moderate yields of the product. In a recent report, symmetrical trithiocarbonates were obtained from various alkyl halides with carbon disulfide and cesium carbonate under ambient conditions;[12] but, this reagent is rather expensive.

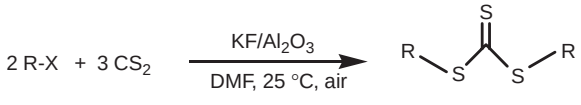
The potassium fluoride on alumina continues to attract much interest from organic chemists due to the versatility of use in synthetic chemistry.[13] Its benefit have been achieved by taking advantage of the strongly basic nature of KF/Al_2O_3 which has allowed it to replace organic bases in a number of reactions.[14–17] The high efficacy and ease of product isolation prompted us to investigate its use for preparation of a variety of trithiocarbonates. We report here an efficient one-pot synthesis of symmetrical dialkyl trithiocarbonates by reaction of alkyl halides with CS_2 at room temperature in an aerial atmosphere catalyzed by KF (40% by weight)/Al_2O_3.

The experiments were initially conducted with benzyl bromide and carbon disulfide, as a model reaction, at various molar ratios, solvents, and temperatures under an aerial atmosphere. It was found that equimolar amounts (3 mmol) of benzyl bromide and CS_2 in dry dimethylformamide (DMF) produced the desired product in 68% yield within 17 h at room temperature. Under the same reaction conditions, another experiment was also carried out with molar ratio of benzyl bromide:CS_2 = 1:1.5, for which the isolated yield of the product was 92%. Therefore, we decided to perform our study at this molar ratio in dry DMF at 25 °C.

To establish the generality of this process, various alkyl halides were added to stirred mixture of carbon disulfide and KF/Al_2O_3 in DMF at 25 °C (Scheme 1).

The trithiocarbonate anion (CS_3^{2-})[18] is known to be prepared by reacting ammonium sulfide, strong aqueous ammonia, aqueous alkali-metal hydroxide, or alkali-metal sulfide with carbon disulfide. When carbon disulfide was added to the suspension of KF/Al_2O_3 in dry DMF, and the mixture was stirred vigorously at 25 °C, the colorless mixture changed to blood red solution within 15 min, indicating the formation of trithiocarbonate anion.[18] In situ alkylation with alkyl halides for the appropriate time (Table 1) followed by filtration, evaporation of DMF, addition of water, and extraction with Et_2O afforded the crude symmetrical trithiocarbonates; further purification can be achieved by preparative TLC.[19] The structures of all the products were established from their analytical and spectral (IR, ^1H and ^{13}C NMR) properties. Potassium fluoride and alumina are both inexpensive and commercially available. We found that this method was applicable for trithiocarbonation of benzyl, allyl, primary, and secondary halides. The results are summarized in Table 1. The procedure worked fine with primary, benzyl ($PhCH_2$) as well as allyl halides (Entries 1, 2, and 5–10, Table 1) to give symmetrical trithiocarbonates in high to excellent yields. The results clearly show the need for longer reaction times for secondary halides (Entries 3, 11, and 12, Table 1), giving the products with lower yields. Under the same reaction conditions, tertiary halides (Entries 4 and 13, Table 1) does not produce the expected trithiocarbonate even after 40–48 h. This represents the S_N2 type nucleophilic reaction.

To conclude, we have developed a new convenient and efficient protocol for the one-pot synthesis of symmetrical trithiocarbonates from carbon disulfide and various alkyl halides in



Scheme 1.

Table 1. Trithiocarbonylation of various alkyl halides

Entry	Alkyl halide	Time/h	Yield[a]/%
1	$PhCH_2Br$	12	92
2	$PhCH_2Cl$	18	90
3	$PhCH(CH_3)Br$	20	79
4	$PhC(CH_3)_2Br$	48	No reaction
5	$CH_2{=}CHCH_2Br$	17	85
6	$CH_2{=}CHCH_2Cl$	20	84
7	CH_3CH_2I	17	93
8	CH_3I	20	87
9	$CH_3(CH_2)_5Br$	18	94
10	$CH_3(CH_2)_7I$	18	95
11	$(CH_3)_2CHBr$	35	70
12	$CH_3CH_2CH(CH_3)Br$	35	75
13	$(CH_3)_3CBr$	40	No reaction

[a]Isolated yields.

the presence of KF/Al_2O_3 at room temperature. This method offers significant advantages over earlier reported procedures in that it avoids the need to apply thiol and toxic thiophosgen, features a simple reaction procedure and mild conditions, easy work-up, ready availability of the reagent, and high yields of the products.

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19 General procedure: A mixture of KF/Al_2O_3 (2 g, 40% by weight)[16] and carbon disulfide (3 mmol) in DMF (5 mL) was vigorously stirred at 25 °C for 15 min; then, alkyl halide (2 mmol) was added to the red blood mixture. The color of the mixture immediately changed from red to yellow. Stirring of the resulting reaction mixture was continued at 25 °C for the appropriate time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the filtrate was evaporated, Et_2O (30 mL) was added and washed with water (2×15 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated to give the crude trithiocarbonate, which was purified by preparative TLC (silica gel, eluent, *n*-hexane).\
Dibenzyl trithiocarbonate: IR (neat): ν_{max} 1602, 1494, 1062 (C=S) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.31–7.20 (m, 10H), 4.58 (s, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 223.2, 135.4, 129.7, 129.2, 128.3, 42.0.
Diallyl trithiocarbonate: IR (neat): ν_{max} 1638, 1062 (C=S) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 5.86–5.77 (m, 2H), 5.27 (dd, 2H, $J = 17.0$, 1.3 Hz), 5.14 (dd, 2H, $J = 10.0$, 1.3 Hz), 3.98 (d, 4H, $J = 6.8$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 222.9, 131.4, 120.1, 40.1.
Diethyl trithiocarbonate: IR (neat): ν_{max} 1078 (C=S) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.31 (q, 4H, $J = 7.4$ Hz), 1.29 (t, 6H, $J = 7.4$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 224.8, 31.5, 13.5.
Di-*n*-octyl trithiocarbonate: IR (neat): ν_{max} 1062 (C=S) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.29 (t, 4H, $J = 7.3$ Hz), 1.63 (quin, 4H, $J = 7.3$ Hz), 1.34 (quin, 4H, $J = 7.0$ Hz), 1.24–1.20 (m, 16H), 0.82 (t, 6H, $J = 6.2$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 225.1, 37.3, 32.2, 29.6, 29.5, 29.4, 28.5, 23.1, 14.6.
Diisopropyl trithiocarbonate: IR (neat): ν_{max} 1078 (C=S) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 4.14 (sept, 2H, $J = 6.9$ Hz), 1.34 (d, 12H, $J = 6.9$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 223.9, 42.1, 22.5.

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