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A new reagent for the efficient synthesis of disulfides from alkyl halides

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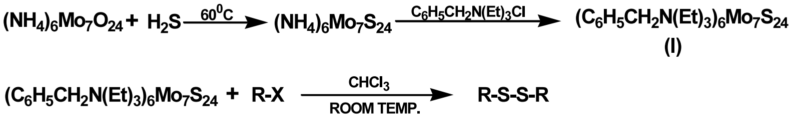
Abstract—Benzyltriethylammonium tetracosathioheptamolybdate [$(C_6H_5CH_2N(Et)_3)_6Mo_7S_{24}$] has been found to be a superior sulfur transfer reagent for the conversion of alkyl halides to the corresponding disulfides in excellent yields under very mild reaction conditions. © 2003 Elsevier Science Ltd. All rights reserved.

Disulfides are versatile building blocks for the synthesis of various organo-sulfur compounds,[1] and they also play important roles in biological and chemical processes.[2] Various methods have been reported in the literature[3] for the synthesis of disulfides from thiols[3,4] which make use of various oxidizing agents. Oxidizing agents ranging from molecular oxygen[5] to halogens and derivatives,[6] metal oxides[7] and oxo-peroxo salts[8] have been utilized to oxidize thiols to disulfides. The most commonly used method for the direct conversion of alkyl halides to disulfides has been by using Na_2S/S.[9] Nevertheless the methods currently available for the preparation of disulfides often involve many steps and the transformation is usually effected at 70–90°C for a long period of time (20–30 h)[9] giving only moderate yields of the corresponding disulfide. There is current interest in sulfur containing compounds of molybdenum and tungsten because of their involvement in bioinorganic chemistry and catalysis.[10,11] Organic ligand complexes,[12] thioanions[13] and polymeric heteronuclear clusters[14] formed in molybdenum–sulfur complexes have generated interest for both synthetic and theoretical chemists, although very few studies have been reported on their reactivity with organic substrates.[15,16]

In this communication, we report our initial findings on the efficient sulfur transfer reaction of tetracosathioheptamolybdate, $MO_7S_{24}^{6-}$, with alkyl halides. The work reported[17] earlier involved the use of a cation substituted ammonium molybdate for the conversion of alkyl halides to disulfides. Although the reagent is good in terms of reactivity, the main disadvantage is that it is very expensive and the starting material for its preparation is also costly and available only in research quantities. Another disadvantage is that the sulfur transfer reaction has been performed using equimolar or a slight excess of the reagent with respect to alkyl halide, making the method over-all very expensive. In order to increase the scope and utility of the suflur transfer reagent, we have synthesized three new reagents, i.e. [$(C_6H_5CH_2N(Et)_3)_6Mo_7S_{24}$] (**I**), [$(CH_3(CH_2)_{15}N(Me)_3)_6$-$Mo_7S_{24}$] (**II**), [$(C_5H_5N(CH_2)_{15}CH_3)_6Mo_7S_{24}$ (**III**), which were prepared from commercially available ammonium heptamolybdate, and studied the reaction of (**I**) with a variety of organic halides (1:0.183) in chloroform at room temperature (30°C) to afford the corresponding disulfides in excellent yields. The reactivities of the reagents decrease in the following order [$(C_6H_5CH_2N(Et)_3)_6Mo_7S_{24}$]>[$(C_5H_5N(CH_2)_{15}CH_3)_6Mo_7S_{24}$> $(CH_3(CH_2)_{15}N(Me)_3)_6Mo_7S_{24}$. It is evident that the



$$(NH_4)_6Mo_7O_{24} + H_2S \xrightarrow{60^0C} (NH_4)_6Mo_7S_{24} \xrightarrow{C_6H_5CH_2N(Et)_3Cl} (C_6H_5CH_2N(Et)_3)_6Mo_7S_{24}$$

(I)

$$(C_6H_5CH_2N(Et)_3)_6Mo_7S_{24} + R\text{-}X \xrightarrow[\text{ROOM TEMP.}]{CHCl_3} R\text{-}S\text{-}S\text{-}R$$

Keywords: disulfide; sulfur transfer reagent; alkyl halide.

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more polarisable and more nucleophilic the reagent, the more facile the reaction becomes.

Commercially available halides were chosen to test our procedure. The reaction was carried out at room temperature in chloroform as solvent. Under these conditions, the alkyl halides were effectively and quantitatively converted to the corresponding disulfides proving the efficiency of the new reagent. The results of the sulfur transfer reaction on a variety of halides with (**I**) are summarized in Table 1.

Many factors such as a change in the structure of the reagent, the halide and the structure of the alkyl group, profoundly influence the course of the reaction. For example, labile iodides react quickly, chlorides are rather lethargic and fluorides do not undergo normal reactions at all. Several investigations have been carried out to understand the influence of structural variations of the alkyl moiety. The reactivity order is benzyl halide>primary alkyl halides>secondary alkyl halides>tertiary alkyl halides>aryl halides. While benzyl halides react faster because of the stabilization of incipient positive charge, the non-reactivity of tertiary halides is due to steric hindrance. The reactions of aryl halides with the reagent do not occur favorably under these conditions and result in poor yield of the disulfide.

Thus, in this study we have been able to demonstrate the utility and efficiency of the new sulfur transfer reagent, i.e. benzyltriethylammonium tetracosathioheptamolybdate, for a new carbon–sulfur bond forming reaction. In summary, the use of this reagent offers some advantages such as easy preparation of the reagent, economy, mild reaction conditions and a convenient workup procedure. Furthermore, because of its solubility in organic solvents, this method provides a simple, versatile and general route for the construction of a wide variety of disulfides.

To explore further synthetic utility of this reagent, synthetic and mechanistic studies involving reactions of this reagent with other organic substrates are currently under investigation.

Table 1. Reaction of tetracosathioheptamolybdate (**I**) with alkyl halides

Entry	Substrate	Time (h)	Product	Yield (%)
1	C_2H_5I	6	$(C_2H_5S\text{-})_2$	92
2	C_3H_7I	7	$(C_3H_7S\text{-})_2$	90
3	C_4H_9Cl	14	$(C_4H_9S\text{-})_2$	67
4	C_4H_9Br	10	$(C_4H_9S\text{-})_2$	78
5	C_4H_9I	8	$(C_4H_9S\text{-})_2$	89
6	$C_6H_{13}Br$	10	$(C_6H_{13}S\text{-})_2$	88
7	$C_6H_5CH_2Br$	2	$(C_6H_5CH_2S\text{-})_2$	89
8	*tert*-C_4H_9Br	24	(*tert*-$C_4H_9S\text{-})_2$	>20%
9	$C_6H_5CH_2Cl$	24	$(C_6H_5CH_2S\text{-})_2$	54
10	C_6H_5Cl	48	NR	–

All compounds had satisfactory IR, NMR, and MS data and were compared with authentic samples.

General procedure for the synthesis of reagent (I): Ammonium heptamolybdate (30 g) was dissolved in water (50 ml) and liquid ammonia (135 ml, sp.gr.0.91) was added to give a clear solution. H_2S was passed through this solution for 5 h at 60°C. The reaction mixture containing crystals was cooled to 0°C and washed successively with isopropyl alcohol and ether. The shiny dark brown crystals of ammonium tetracosathioheptamolybdate were dried under vacuum.

To a solution of 32 g of ammonium tetracosathioheptamolybdate in 80 ml of water, a solution of benzyltriethylammonium chloride in 100 ml water was added dropwise. The reaction mixture was stirred at room temperature for a period of 2 h. The solid that separated was filtered, washed with isopropyl alcohol and ether, and dried under vacuum. The dark red crystalline benzyltriethylammonium tetracosathioheptamolybdate (mp 120°C, decomposition) was stored in a desiccator. UV–vis (DMF); $\lambda_{\max}$, 268, 323, 477.

Typical procedure for the synthesis of a disulfide: To a solution of 1.8 mmol of reagent (**I**) in 35 ml of $CHCl_3$, 10 mmol of the alkyl halide in 10 ml $CHCl_3$ was added dropwise over a period of 15 min. The solution was stirred for the time shown in Table 1 at room temperature. The solvent was removed under vacuum and the black residue was extracted with ether. The crude product was purified by column chromatography on silica gel to give the pure disulfide.

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