Heteroatom Chemistry
Volume 15, Number 5, 2004

A Novel Reduction of Sodium Alkyl Thiosulfates with $InCl_3$(cat.)/Sm(0) System in Aqueous Media: Facile Synthesis of Disulfides

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Received 14 November 2003; revised 9 February 2004

ABSTRACT: *A novel reduction of sodium alkyl thiosulfates with $InCl_3$(cat.)/Sm(0) system in aqueous media has been developed, which generates the corresponding disulfides in good yields.* © 2004 Wiley Periodicals, Inc. Heteroatom Chem 15:376–379, 2004; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20023

INTRODUCTION

Disulfides are important reagents and intermediates for the preparation of several compounds in organic synthesis [1]. A variety of methods for the synthesis of disulfides have been described. For example, the oxidation of thiols [2]; the nucleophilic substitution of sulfenylthiocyanates [3], thiolsulfonates [4], sulfenylhydrazo compounds [5], and sulfenimides [6] with thiols; and the reduction of sulfonic acids and sodium sulfonates [7], and sulfenyl, sulfinyl, and sulfonyl derivatives [8] are most common ones. However, because these methods suffer from using either foul smelling thiols, or harsh reaction conditions, in addition to only moderate yields and waste handling problems, developing milder and environmentally friendly methods for the preparation of disulfides is desirable.

In the last decade, indium has emerged as a suitable and valuable reagent for accomplishing Barbier-type reactions, Reformatsky reactions, Michael-additions and cross-aldol reactions in aqueous media [9,10]. More recently, the huge potential of indium metal as a broad-scope reducing agent for organic functional groups has also received much attention [11]. Because it is inert toward water and acid solutions, indium metal promoted organic reactions are generally carried out in water or in aqueous media, providing an optimal "green chemistry" reaction [12]. However, the disadvantage of metallic indium powder mediated reactions is that in some cases the indium powder and organic substrate clump together, making the mixture difficult to stir.

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Contract grant sponsor: National Natural Science Foundation of China.
Contract grant number: 20372024, 20172018.
Contract grant sponsor: Excellent Scientist Foundation of Anhui Province, China.
Contract grant number: 2001040.
Contract grant sponsor: Natural Science Foundation of the Education Department of Anhui Province, China.
Contract grant number: 2002kj254zd.
Contract grant sponsor: Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry, China.
Contract grant number: 2002247.
Contract grant sponsor: Excellent Young Teachers Program of MOE, China.
Contract grant number: 2024.

The first ionization potential of metallic samarium is 5.63 eV, similar to that of metallic lithium (5.39 eV). Also metallic samarium is stable in air and has a stronger reducing power ($Sm^{3+}/Sm = -2.41$ V). These properties prompted us to use it as reducing agent to reduce In(III) to its low valent species to promote the reaction. Here, we wish to report a novel method for the preparation of disulfides through the reduction of sodium alkyl thiosulfates with zero valent indium generated in situ from the reaction of $InCl_3$ with Sm(0) in aqueous solution at room temperature. The reaction affords the corresponding disulfides in good yields.

$$RSSO_3Na \xrightarrow[\text{THF-}H_2O(1:2)]{InCl_3(\text{cat.})/Sm(0)} RSSR$$

RESULTS AND DISCUSSION

Our initial experiments investigated the effect of amount of indium(III) chloride and samarium metal on the reduction of sodium alkyl thiosulfates in aqueous media. The results are summarized in Table 1. Sodium dodecyl thiosulfate was chosen as a model compound for this study.

From Table 1, it is evident that indium(III) chloride and samarium metal are essential to the reduction of sodium alkyl thiosulfates. The reaction cannot occur in the absence of indium(III) chloride or samarium metal. The amount of indium(III) chloride and samarium metal has been examined. The results show that only a catalytic amount of indium(III) chloride (5–10% mol) is needed for the reaction in the presence of stoichiometric amount of samarium metal. In the presence of $InCl_3$ (5–10% mol), less than stoichiometric amount of samarium metal cannot afford the high yields of reductive homo-coupling products because of insufficient low valent indium species generated in situ from the reaction of metallic samarium with indium(III) chloride. The reaction works smoothly in aqueous media (containing 66.7% water by volume) because of the good solubility of sodium dodecyl thiosulfate (reactant) and the poor solubility of disulfide (product) in this co-solvent.

Under optimized reaction conditions, a variety of sodium alkyl thiosulfates were successfully reduced with $InCl_3$ (10% mol)-Sm reductive system followed by a homo-coupling process to generate the corresponding disulfides in good yields. The results are listed in Table 2.

The data in Table 2 showed that the sodium alkyl thiosulfates could be easily reduced to the corresponding symmetrical disulfides with $InCl_3$ (10% mol)-Sm system in good yields under aqueous reaction conditions. The chain length of aliphatic substrates would seem to have no influence on the reductive coupling reaction. Substituent effects were also examined in series of sodium benzyl thiosulfates. The results indicated that the reaction is relatively insensitive to the electronic nature of substituents on the aromatic rings. As starting material, the sodium alkyl thiosulfates are readily prepared from the reaction of sodium thiosulfate with suitable alkyl bromide under mild phase transfer catalysis conditions [13].

The possible mechanism for the formation of disulfides from sodium alkyl thiosulfates promoted by indium(III) chloride (cat.) and metallic samarium system involves the reduction and homo-coupling sequence reaction processes. Low valent indium (mainly zero valent indium species) is generated

TABLE 1 Effect of Amount of Indium(III) Chloride and Samarium Metal on the Reductive Homo-Coupling of Sodium Dodecyl Thiosulfate in Aqueous Media[a]

Entry	*Amount of $InCl_3$*	*Amount of Samarium Metal*	*Yield[b] (%)*
1	0 equiv	1.00 equiv	0
2	0.50 equiv	0 equiv	0
3	0.50 equiv	1.00 equiv	81
4	0.25 equiv	1.00 equiv	82
5	0.10 equiv	1.00 equiv	83
6	0.05 equiv	1.00 equiv	80
7	0.10 equiv	2.00 equiv	82
8	0.10 equiv	0.50 equiv	75
9	0.10 equiv	0.25 equiv	45
10	0.10 equiv	0.10 equiv	12

[a] Reaction conditions: sodium dodecyl thiosulfate (1 mmol), THF-H_2O (V/V, 1/2, 5 ml), rt, 4 h.
[b] Isolated yields.

TABLE 2 The Reduction of Sodium Alkyl Thiosulfates to Disulfides with $InCl_3$ (10% mol)-Sm System in Aqueous Media[a]

Entry	*Reactant*	*Product*	*Yield[b] (%)*
1	$n\text{-}C_{16}H_{33}SSO_3Na$	$(n\text{-}C_{16}H_{33}S)_2$	83
2	$n\text{-}C_{12}H_{25}SSO_3Na$	$(n\text{-}C_{12}H_{25}S)_2$	80
3	$n\text{-}C_{10}H_{21}SSO_3Na$	$(n\text{-}C_{10}H_{21}S)_2$	76
4	$n\text{-}C_8H_{17}SSO_3Na$	$(n\text{-}C_8H_{17}S)_2$	78
5	$n\text{-}C_7H_{15}SSO_3Na$	$(n\text{-}C_7H_{15}S)_2$	82
6	$n\text{-}C_6H_{13}SSO_3Na$	$(n\text{-}C_6H_{13}S)_2$	81
7	$n\text{-}C_4H_9SSO_3Na$	$(n\text{-}C_4H_9S)_2$	75
8	$C_6H_5CH_2SSO_3Na$	$(C_6H_5CH_2S)_2$	84
9	$p\text{-}BrC_6H_4CH_2SSO_3Na$	$(p\text{-}BrC_6H_4CH_2S)_2$	82
10	$p\text{-}CH_3C_6H_4CH_2SSO_3Na$	$(p\text{-}CH_3C_6H_4CH_2S)_2$	80

[a] Reaction conditions: sodium alkyl thiosulfate (1 mmol), $InCl_3$ (0.1 mmol), Sm powder (1 mmol), THF-H_2O (V/V, 1/2, 5 ml), rt, 4 h.
[b] Isolated yields.

in situ through the reaction of metallic samarium with indium(III) chloride in the first step, and then sodium alkyl thiosulfate forms an alkyl sulfur free radical (reduction process) with low valent indium under the reaction conditions followed by the cleavage of sulfur–sulfur bond in substrate. It may be assumed that this reduction is also going through a single-electron-transfer (SET) process like another reduction by using indium metal in aqueous media [14]. The generated alkyl sulfur radical reacts with another alkyl sulfur radical (homo-coupling process) to afford symmetrical disulfide [15].

EXPERIMENTAL

All melting points were recorded on a WRS-1A melting point apparatus and are uncorrected. All ^{1}H NMR spectra were recorded on a 60 MHz JEOL MY 60 FT-NMR or a 300 MHz Bruker AZ 300 spectrometer. Chemical shifts are given as δ value with reference to tetramethylsilane (TMS) as internal standard. IR spectra were obtained by using a Nicolet NEXUS 470 spectrophotometer. The reagents were received from commercial supply without purification prior to use. Products were purified by flash column chromatography.

General Procedure for the Preparation of Disulfides

Under an inert atmosphere of nitrogen, indium(III) chloride (0.1 mmol), metallic samarium powder (1 mmol), and sodium alkyl thiosulfate (1 mmol) were placed in a round-bottomed flask, and THF-H_2O (V/V, 1/2, 5 ml) was added in one portion. The mixture was stirred at room temperature for 4 h. After quenching with dilute hydrochloric acid (0.2 mol/l, 3 ml), the product was extracted with ether (2 × 20 ml). After the organic layer was dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexane–ethyl acetate as eluting agent to give the pure product.

Di(n-hexadecyl)disulfide. mp 50–51°C (Lit. [16] 50°C); IR (KBr) $\nu_{\max}$: 2975, 2950, 2870, 1480, 1380, 725; ^{1}H NMR ($CDCl_3$) δ: 0.86 (t, $J = 7.1$ Hz, 6H), 1.24–1.74 (m, 56H), 2.64 (t, $J = 7.0$ Hz, 4H).

Di(n-dodecyl)disulfide. mp 30°C (Lit. [16] 30°C); IR (KBr) $\nu_{\max}$: 2980, 2960, 2880, 1470, 1385, 720; ^{1}H NMR ($CDCl_3$) δ: 0.86 (t, $J = 7.2$ Hz, 6H), 1.21–1.76 (m, 40H), 2.61 (t, $J = 7.0$ Hz, 4H).

Di(n-decyl)disulfide. Oil [16]; IR (film) $\nu_{\max}$: 2978, 2957, 2868, 1472, 1388, 723; ^{1}H NMR ($CDCl_3$) δ: 0.85 (t, $J = 7.1$ Hz, 6H), 1.18–1.71 (m, 32H), 2.64 (t, $J = 7.1$ Hz, 4H).

Di(n-octyl)disulfide. Oil [16]; IR (film) $\nu_{\max}$: 2975, 2960, 2880, 1460, 1380, 720; ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, $J = 7.0$ Hz, 6H), 1.23–1.74 (m, 24H), 2.62 (t, $J = 7.0$ Hz, 4H).

Di(n-heptyl)disulfide. Oil [16]; IR (film) $\nu_{\max}$: 2972, 2966, 2885, 1469, 1383, 721; ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, $J = 7.1$ Hz, 6H), 1.23–1.72 (m, 20H), 2.65 (t, $J = 7.1$ Hz, 4H).

Di(n-hexyl)disulfide. Oil [16]; IR (film) $\nu_{\max}$: 2977, 2961, 2878, 1466, 1386, 724; ^{1}H NMR ($CDCl_3$) δ: 0.90 (t, $J = 7.2$ Hz, 6H), 1.24–1.70 (m, 16H), 2.58 (t, $J = 7.1$ Hz, 4H).

Di(n-butyl)disulfide. Oil [17]; IR (film) $\nu_{\max}$: 2975, 2956, 2871, 1469, 1380, 720; ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, $J = 7.1$ Hz, 6H), 1.35–1.59 (m, 8H), 2.55 (t, $J = 7.2$ Hz, 4H).

Dibenzyldisulfide. mp 70°C (Lit. [16] 71°C); IR (KBr) $\nu_{\max}$: 3080, 3040, 2980, 2940, 2870, 1610, 1590, 1500; ^{1}H NMR ($CDCl_3$) δ: 3.52 (s, 4H), 6.87–7.33 (m, 10H).

Di(p-chlorobenzyl)disulfide. mp 59°C (Lit. [14] 58°C); IR (KBr) $\nu_{\max}$: 3076, 3033, 2987, 2936, 2874, 1606, 1594, 1500; ^{1}H NMR ($CDCl_3$) δ: 3.51 (s, 4H), 6.92–7.31 (q, 8H).

Di(p-methylbenzyl)disulfide. mp 50–52°C (Lit. [18] 48.5–50°C); IR (KBr) $\nu_{\max}$: 3075, 3028, 2979, 2932, 2872, 1605, 1591, 1498; ^{1}H NMR ($CDCl_3$) δ: 2.35 (s, 6H), 3.56 (s, 4H), 6.92–7.02 (q, 8H).

CONCLUSION

In summary, we have found that indium(III) chloride (10% mol) and metallic samarium powder is a useful reductive system for the reduction of sodium alkyl thiosulfates to disulfides in aqueous media. The remarkable advantages of this reaction are mild, neutral, and environmental-friendly reaction condition, simple operation, and good yields.

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