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# Indium-mediated Reaction in Aqueous Media. Synthesis of Phenacyl Sulfides by Reactions of α-Bromoketones with Sodium Alkyl Thiosulfates†

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Phenacyl sulfides are synthesized in moderate to good yields *via* reaction of α-haloketones with sodium alkyl thiosulfates promoted by indium metal in aqueous media.

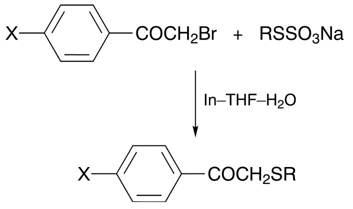
Metal-mediated reactions in aqueous media have recently found considerable application in organic synthesis.[1] Such organometallic-type reactions in aqueous media have many advantages. The most general worth in changing organometallic reactions from strictly anhydrous organic solvents to aqueous media is the ease of reaction in obviating the need for inflammable anhydrous organic solvents and troublesome inert atomospheres. For some reactions, for example, alkylations of carbonyl groups in carbohydrates, it is a great advantage that the substrates do not need first to be converted as they would be when using organic solvents.[2]

The choice of metal in organometallic reactions in aqueous media is however limited,[2] the most commonly used metals being zinc, tin and indium. Bismuth–zinc or $BiCl_3$–Al, $BiCl_3$–Zn and $BiCl_3$–Fe systems are also effective for the allylation of carbonyl compounds and benzotriazole intermediates.[3]

Compared to the use of zinc and tin where acid catalysis, heat or sonication are often required, reactions with indium usually possess the advantage of not needing any promoter, and therefore indium-mediated organometallic reactions in aqueous media have recently found considerable application in organic synthesis. They have been used in the allylation and propargylation of carbonyl compounds,[2,4] the allylation of the carbonyl group in β-oxoesters (which is extremely difficult using organometallic reagents such as allylic magnesium bromide and organolithium compounds because of the acidity of the hydrogen on the carbon inbetween the two carbonyl groups),[5] bis-allylation of 1,3-dibromopropene with carbonyl compounds at the same carbon,[6] reductive coupling of aldimines,[7] *etc.*

Recently, we have reported that allylic and propargyl bromides react with diorganyl diselenides in aqueous media promoted by indium to give allylic and propargyl selenides.[8] This method offers some distinct advantages, such as use of aqueous media and of mild and neutral conditions. However the type of reaction promoted by indium seems to have been somewhat limited. The most useful is the coupling of allylic halides with carbonyl compounds in aqueous media to give the corresponding homoallylic alcohols.

Here we report a novel reaction of α-haloketones with sodium alkyl thiosulfates promoted by indium metal in aqueous media.



In our experiments, we observed that no disulfides were obtained. Thus we suggest that the reaction does not proceed *via* electron transfer from indium to the alkyl thiosulfate but involves an enolate intermediate, although we have not enough proof to clarify this. Unlike other reactions induced by indium, the present reaction is very slow at room temperature and must be conducted at 60–65 °C.

Sulfides are a class of useful synthetic intermediates, and many methods have been reported for their preparation.[12–15] Very recently, our group have reported that an organosamarium reagent reacts with disulfides to afford allyl sulfides.[16] However the reaction must be conducted in strictly anhydrous solvent and under an inert atmosphere. In contrast, the present method circumvents these problems, the reaction being carried out in aqueous tetrahydrofuran solution and in the air. In view of the ready availability of the starting materials, the simplicity of the synthetic procedures, the mild reaction conditions and the moderate-to-good yields of products, we consider that the present procedure provides a novel practical route to phenacyl sulfides.

**Table 1** Conditions, products, yields and mps

| Entry | X | R | Reaction time (*t*/h) | Product | Yield (%)[a] | Mp (*T*/°C) (Lit.) |
|---|---|---|---|---|---|---|
| **a** | H | $PhCH_2$ | 18 | $PhCOCH_2SCH_2Ph$ | 80 | 86–88(89)[9] |
| **b** | H | $C_{16}H_{33}$ | 15 | $PhCOCH_2SC_{16}H_{33}$ | 83 | 40–41 |
| **c** | H | $C_{12}H_{25}$ | 15 | $PhCOCH_2SC_{12}H_{25}$ | 87 | 32–34(34–35)[10] |
| **d** | H | $C_{10}H_{21}$ | 15 | $PhCOCH_2SC_{10}H_{21}$ | 82 | oil[11] |
| **e** | H | $C_8H_{17}$ | 15 | $PhCOCH_2SC_8H_{17}$ | 81 | oil |
| **f** | H | $C_7H_{15}$ | 15 | $PhCOCH_2SC_7H_{15}$ | 80 | oil |
| **g** | Br | $PhCH_2$ | 18 | *p*-$BrC_6H_4COCH_2SCH_2Ph$ | 78 | 158–159 |
| **h** | Br | $C_{12}H_{25}$ | 15 | *p*-$BrC_6H_4COCH_2SC_{12}H_{25}$ | 81 | 104–106 |

[a] Yields of isolated phenacyl sulfides based on $RSSO_3Na$.

## Experimental

*Typical Procedure.*—In a 50 mL round-bottomed flask fitted with a reflux condenser were placed indium (1 mmol) in the form of small grains cut from a bar of indium metal, sodium alkyl thio-

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**Table 2** Spectral data and elemental analyses

| Compd. | $\delta_H$ | $\nu_{max}$ (C═O)/cm$^{-1}$ | Found (required) (%) | |
|---|---|---|---|---|
| | | | C | H |
| **b** | 0.83 (t, 3 H), 1.22–1.63 (m, 28 H) 2.48 (t, 2 H), 3.53 (s, 2 H), 7.33–8.01 (m, 5 H) | 1700 | 76.75(76.60) | 10.72(10.63) |
| **e** | 0.85 (t, 3 H), 1.24–1.75 (m, 12 H) 2.54 (t, 2 H), 3.60 (s, 2 H), 7.28–8.05 (m, 5 H) | 1682 | 72.91(72.73) | 9.15(9.08) |
| **f** | 0.86 (t, 3 H), 1.25–1.75 (m, 10 H) 2.50 (t, 2 H), 3.51 (s, 2 H), 7.26–8.00 (m, 5 H) | 1690 | 72.25(72.00) | 8.87(8.79) |
| **g** | 3.40 (s, 2 H), 3.56 (s, 2 H) 7.13–7.90 (m, 9 H) | 1705 | 56.26(56.10) | 4.16(4.05) |
| **h** | 0.85 (t, 3 H), 1.22–1.68 (m, 20 H) 2.43 (t, 2 H), 3.52 (s, 2 H), 7.43, 7.60, 7.73, 7.86 (q, 4 H) | 1700 | 60.47(60.18) | 7.87(7.77) |

sulfate (1 mmol), $\alpha$-bromoacetophenone (1.25 mmol), THF (20 mL) and water (1 mL). The mixture was stirred at room temperature for 2 h, then continued to stir under slight refluxing until the indium grains were almost consumed and the solution became turbid. The solution was cooled to room temperature and extracted with diethyl ether (30 mL × 2) after brine (10 mL) had been added. The Organic layer was dried ($Na_2SO_4$) and the solvents were evaporated *in vacuo*. The product was separated from the residue through preparative TLC (silica gel) with light petroleum (bp 30–60 °C)–cyclohexane–diethyl ether as eluent.

All mps are uncorrected. IR spectra were obtained on a PE 683 spectrometer. $^1$H NMR spectra were recorded in $CCl_4$ on a JEOL PMX 60 si spectrometer using $Me_4Si$ as internal standard. Analytical data were obtained on a Carlo Erba 1106 instrument.

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