

Facile Preparation of Copper(I) Halide-Dimethyl Sulfide Complex and Its Application

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A preparative method of Me_2SCuX ($\text{X} = \text{Cl}, \text{Br}$) via one-pot reaction was developed from common chemicals such as benzyl halide, DMSO, and $\text{Cu}(0)$. In the reaction mixture small molecules such as methyl halide and dimethyl sulfide *etc.* were efficiently generated *in situ*, resulting in the formation of Me_2SCuX . Oxidation of $\text{Cu}(0)$ in reacting with both benzyl halide (starting material) and methyl halide (*in situ* generated product) to $\text{Cu}(I)$ followed by complexing with dimethyl sulfide (*in situ* generated product) could explain the formation of Me_2SCuX . In particular we found out that heterogeneous reaction of Me_2SCuX and arenediazonium tetrafluoroborate in acetonitrile was so effective to afford corresponding bromoaromatics under mild conditions.

Key Words : Copper(I) halide-dimethyl sulfide complex, DMSO, Benzyl halide

Introduction

Copper(I) halide-dimethyl sulfide complex (Me_2SCuX , $\text{X} = \text{Cl}, \text{Br}$) has been utilized in organic reactions as a versatile reagent. Among the many examples, use of Me_2SCuX to prepare organocuprates seems to be a representative.¹ Me_2SCuX is also known to exert catalytic activities in reactions such as in isomerization of 3,4-dichloro-1-butene to 1,4-dichloro-2-butene.²

Though commercially available Me_2SCuX might seem to serve the purposes in general, when much purer Me_2SCuX is required, it needs to be freshly and carefully prepared to avoid side reactions resulting from the presence of impurities such as $\text{Cu}(II)$ and other metal salts. In regards to this House *et al.* described that lithium organocuprate reagents, made from organolithium and $\text{Cu}(I)$ salt, were decomposed by small amounts of other metal salts such as $\text{Cu}(II)$ during the process of preparing thermally unstable cuprates.³

Considering that the general preparative method of Me_2SCuX requires both Me_2S and CuX , these impurities are obviously originated from the CuX , as was documented in the literature. That is, Wuts described that rather old and impure samples and even some freshly supplies of CuBr contained various amounts of impurities, presumably CuBr_2 and various oxides. And he suggested that these impurities in CuBr were quite soluble in methanol and therefore could readily be washed out.⁴ And he used purified CuBr to make Me_2SCuX . However Theis *et al.*, dissatisfied with the previous method comprising tedious steps to remove colored impurities such as Cu , CuX_2 , and oxides present in CuX , proposed another method that CuBr free of other impurities might be obtained by reducing CuBr_2 with sodium sulfite.⁵

Recently Park *et al.* reported that trimethylsulfonium bromide was obtained from a solution of benzyl bromide in DMSO upon heating.⁶ And they proposed that *in situ*

generated dimethyl sulfide and methyl bromide resulted the formation of trimethylsulfonium bromide. Herein we would like to report a preparative method of Me_2SCuX by adding $\text{Cu}(0)$ to the aforementioned solution of benzyl halide in DMSO. Looking into the literature there is a precedent publication very similar to our findings but using either inorganic acid (HX) or alkyl halides instead of benzyl halides we used.⁷ The Me_2SCuX prepared by our method was satisfactorily pure, readily discerned by its color as was described earlier by House *et al.*, *i.e.* each of CuCl_2 and CuBr_2 forms dark green and dark red solution respectively with dimethyl sulfide.³

In addition to this we have found out that Me_2SCuBr prepared by this method was very effective in displacing diazonium tetrafluoroborate group to afford bromoaromatics particularly under mild conditions. That is, the reactions were completed within 5 min at room temperature under neutral organic media (refer results and discussions).

Experimental Section

Materials. Unless stated otherwise, most of reagents were prepared and some of reagents and solvents purchased were used as received without further purification.

Preparation of Me_2SCuX ($\text{X} = \text{Cl}, \text{Br}$). Standard procedure (using benzyl bromide). To a solution of benzyl bromide (2.38 mL, 20 mmol) in DMSO (10 mL) was added $\text{Cu}(0)$ (0.64 g, 10 mmol). The reaction mixture was maintained at 120 °C for 5 h. After the solution was cooled to room temperature was added water until no more solid appeared. The complex Me_2SCuBr was separated just by decantation. The complex obtained was stirred in acetone to remove DMSO, followed by filtration. The pale silver crystalline complex was dried under vacuum and weighed (1.58 g, 77%), mp 127-129 °C (dec.) (lit³ mp 124-129 °C (dec.)); ¹H NMR (DMSO-*d*₆) δ 2.1 (s); IR (KBr) 2991, 2919, 1438, 1417, 1040, 987.

Using benzyl chloride. The standard procedure above was repeated except benzyl chloride (2.40 mL, 20 mmol) instead of benzyl bromide to give complex Me_2SCuCl (0.30 g, 19%), mp 120-125 °C (dec.) (lit.³ mp 118-124 °C (dec.)); ^1H NMR ($\text{DMSO-}d_6$) δ 2.0 (s).

Using 4-methylbenzyl bromide. The standard procedure above was repeated except the use of 4-methylbenzyl bromide (0.93 g, 5.0 mmol), DMSO (4.0 mL) and $\text{Cu}(0)$ (0.16 g) to give Me_2SCuBr (0.45 g, 88%).

Using 2-methylbenzyl bromide. The standard procedure above was repeated except the use of 2-methylbenzyl bromide (1.34 mL, 10 mmol), DMSO (8.0 mL) and $\text{Cu}(0)$ (0.32 g) to give Me_2SCuBr (0.91 g, 89%).

Using 2-chlorobenzyl bromide. The standard procedure above was repeated except the use of 2-chlorobenzyl bromide (1.30 mL, 10 mmol), DMSO (8.0 mL) and $\text{Cu}(0)$ (0.32 g) to give Me_2SCuBr (0.80 g, 78%).

Using 4-nitrobenzyl bromide. The standard procedure above was repeated except the use of 4-nitrobenzyl bromide (2.17 g, 10 mmol), DMSO (8.0 mL) and $\text{Cu}(0)$ (0.32 g) to give Me_2SCuBr (0.87 g, 85%).

Using 2-nitrobenzyl bromide. The standard procedure above was repeated except the use of 2-nitrobenzyl bromide (2.17 g, 10 mmol), DMSO (8.0 mL) and $\text{Cu}(0)$ (0.32 g) to give Me_2SCuBr (0.89 g, 87%).

Preparation of diazonium tetrafluoroborate⁸

Benzenediazonium tetrafluoroborate (standard procedure): To a 250 mL two-neck round-bottom flask was added aniline (6.6 mL, 72.5 mmol), conc. HCl (30 mL) and water (15 mL), followed by heating for 30 min. After the reaction mixture was cooled to 0-5 °C using ice-bath, solution of sodium nitrite (6.0 g, 87 mmol) in water (20 mL) was added dropwise. When the addition was completed, any insoluble solid was filtered off, followed by addition of sodium tetrafluoroborate (15.8 g, 145 mmol). The precipitate was filtered, washed with cold water, ethanol, and ether respectively to obtain pale beige crystalline solid (9.76 g, 57%), mp 98-102 °C (dec.).

3-Nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 3-nitroaniline (10.0 g, 72.5 mmol) to obtain pale beige crystalline solid (14.8 g, 87%), mp 161-167 °C (dec.).

4-Bromobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-bromoaniline (12.47 g, 72.5 mmol) to obtain pale beige crystalline solid (13.6 g, 80%), mp 113-115 °C (dec.).

3,4-Dimethylbenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 3,4-dimethylaniline (8.78 g, 72.5 mmol) to obtain pale beige crystalline solid (5.0 g, 30%), mp 94-96 °C (dec.).

4-Nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-nitroaniline (10.0 g, 72.5 mmol) to obtain pale beige crystalline solid (17.0 g, 99%), mp 138-141 °C (dec.); ^1H NMR ($\text{DMSO-}d_6$) δ 9.0 (dd, $J = 9.5$ Hz, $J = 2.4$ Hz, 2H), 8.8 (dd, $J = 9.5$ Hz, $J = 2.4$ Hz, 2H).

3-Chloro-6-methoxy-4-nitrobenzenediazonium tetrafluoro-

borate: The standard procedure above was repeated except the use of 3-chloro-6-methoxy-4-nitroaniline (7.30 g, 36.3 mmol), sodium nitrite (3.0 g, 43.5 mmol), and sodium tetrafluoroborate (7.90 g, 72.5 mmol) to obtain pale beige crystalline solid (1.83 g, 20%), mp 153-155 °C (dec.).

2-Methoxybenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 2-methoxyaniline (8.78 g, 72.5 mmol) to obtain pale beige crystalline solid (1.43 g, 16%).

4-Methylbenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-methylaniline (8.78 g, 72.5 mmol) to obtain pale beige crystalline solid (2.48 g, 32%).

4-Methoxybenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-methoxyaniline (8.78 g, 72.5 mmol) to obtain pale beige crystalline solid (1.61 g, 18%).

Displacement of diazonium tetrafluoroborate group by Me_2SCuX ($X = \text{Cl, Br}$)

From benzenediazonium tetrafluoroborate (standard procedure): To a 100 mL two-neck round-bottom flask was added benzenediazonium tetrafluoroborate (0.93 g, 4.85 mmol) dissolved in acetonitrile (20 mL), followed by addition of Me_2SCuBr (1.0 g, 4.85 mmol) under stirring. The solution was concentrated, followed by addition of ethyl acetate. After the insoluble material was filtered off the filtrate was concentrated followed by column chromatography to obtain bromobenzene (0.57 g, 75%).

From 3-nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 3-nitrobenzenediazonium tetrafluoroborate (1.15 g, 4.85 mmol) to obtain 3-bromonitrobenzene (0.72 g, 73%), mp 53-54 °C (lit. mp 53-56 °C).

From 4-bromobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-bromobenzenediazonium tetrafluoroborate (1.31 g, 4.85 mmol) to obtain 1,4-dibromobenzene (0.89 g, 78%), mp 88-89 °C (lit. mp 83-87 °C); ^1H NMR ($\text{DMSO-}d_6$) δ 7.5 (s).

From 3,4-dimethylbenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 3,4-dimethylbenzenediazonium tetrafluoroborate (0.90 g, 4.85 mmol) to obtain 1-bromo-3,4-dimethylbenzene (0.187 g, 21%). GC/MS 183 (M^+) 171, 143, 117, 105, 89, 77, 51, 39.

From 4-nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-nitrobenzenediazonium tetrafluoroborate (1.15 g, 4.85 mmol) to obtain 4-bromonitrobenzene (0.98 g, 100%), mp 125-128 °C (lit. mp 124-126 °C); GC/MS 200(M^+) 173, 157, 156, 75, 50, 38; ^1H NMR ($\text{DMSO-}d_6$) δ 7.9 (d, $J = 9.2$ Hz, 2H), 8.2 (d, $J = 9.2$ Hz, 2H).

From 4-nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-nitrobenzenediazonium tetrafluoroborate (0.74 g, 3.1 mmol) and Me_2SCuCl (0.5 g, 3.1 mmol) to obtain 4-chloronitrobenzene (0.30 g, 62%), mp 82-85 °C (lit. mp 80-83 °C); GC/MS 156 (M^+) 157, 127, 111, 113, 85, 75, 63, 50, 37; ^1H

NMR (DMSO- d_6) δ 7.76 (dd, $J = 9.2$ Hz, $J = 2.2$ Hz, 2H), 8.28 (dd, $J = 9.2$ Hz, $J = 2.3$ Hz, 2H).

From 3-chloro-6-methoxy-4-nitrobenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 3-chloro-6-methoxy-4-nitrobenzenediazonium tetrafluoroborate (1.20 g, 5.96 mmol) to obtain 1-bromo-3-chloro-6-methoxy-4-nitrobenzene (0.58 g, 76%), mp 100-102 °C; GC/MS 267 (M^+), 237, 206, 178, 176, 141, 112, 97, 62, 53; ^1H NMR (DMSO- d_6) δ 4.0 (*s*, 3H), 7.4 (*s*, 1H), 8.4 (*s*, 1H).

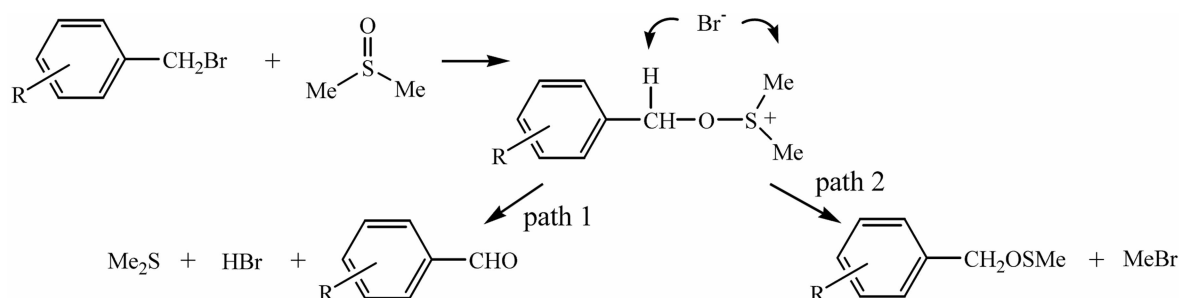
From 2-methoxybenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 2-methoxybenzenediazonium tetrafluoroborate (1.15 g, 4.85 mmol) to obtain 2-bromoanisole (0.13 g, 16%). ^1H NMR (DMSO- d_6) δ 3.7 (*s*, 3H), 6.6-7.3 (*m*, 4H).

From 4-methylbenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-methylbenzenediazonium tetrafluoroborate (1.15 g, 4.85 mmol) to obtain 4-bromotoluene (0.18 g, 24%), mp 25-28 °C (lit. mp 26-29 °C).

From 4-methoxybenzenediazonium tetrafluoroborate: The standard procedure above was repeated except the use of 4-methoxybenzenediazonium tetrafluoroborate (1.15 g, 4.85 mmol) to obtain 4-bromoanisole (0.14 g, 18%). ^1H NMR (DMSO- d_6) δ 3.7 (*s*, 3H), 6.7 (*d*, 2H), 7.3 (*d*, 2H).

Results and Discussion

Preparation of Me_2SCuX ($\text{X} = \text{Cl}, \text{Br}$). According to our recent findings that dimethyl sulfide and methyl bromide *etc.* were efficiently produced from a solution of benzyl bromide in DMSO upon heating,⁶ we set out hopefully to utilize those *in situ* generated volatile chemicals into a more useful compound. And we were able to obtain Me_2SCuX when we added $\text{Cu}(0)$ to a solution of benzyl bromide (benzyl chloride) and DMSO maintaining at 120 °C for 5 h. Table 1 shows the high isolated yields (77-89%) of the complexes Me_2SCuBr we obtained. However yield of Me_2SCuCl obtained from a solution of benzyl chloride in DMSO was low (18%, entry 2) reflecting the low reactivity of chlorides compared to that of bromides. We have previously noted this similar low reactivity of benzyl chloride compared to that of benzyl bromide in the preparation of trimethylsulfonium halide from a solution benzyl halide in DMSO.⁶



Scheme 1. Pathways in the reaction of benzyl bromide and DMSO.⁶

Table 1. Preparation of Me_2SCuX

Entry	Benzyl halide	Yield (%) ^a
1	$\text{R}_1=\text{R}_2=\text{R}_3=\text{H}, \text{X}=\text{Br}$	77
2	$\text{R}_1=\text{R}_2=\text{R}_3=\text{H}, \text{X}=\text{Cl}$	18
3	$\text{R}_1=\text{NO}_2, \text{R}_2=\text{R}_3=\text{H}, \text{X}=\text{Br}$	85
4	$\text{R}_1=\text{R}_2=\text{H}, \text{R}_3=\text{NO}_2, \text{X}=\text{Br}$	87
5	$\text{R}_1=\text{CH}_3, \text{R}_2=\text{R}_3=\text{H}, \text{X}=\text{Br}$	88
6	$\text{R}_1=\text{R}_2=\text{H}, \text{R}_3=\text{CH}_3, \text{X}=\text{Br}$	89
7	$\text{R}_1=\text{R}_2=\text{H}, \text{R}_3=\text{Cl}, \text{X}=\text{Br}$	78

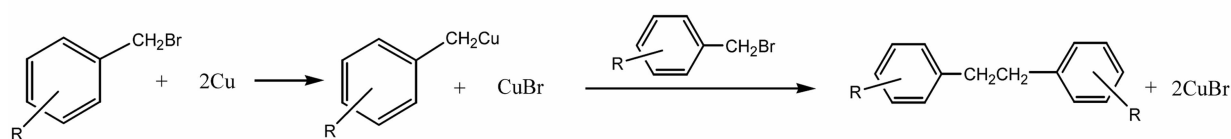
^aIsolated yield.

Remarks needs to be mentioned about the present method of Me_2SCuX . First of all it is unique in that volatile and flammable chemicals (methyl bromide and dimethyl sulfide) are conveniently produced and utilized from common safe chemicals such as bromide, DMSO, and $\text{Cu}(0)$.⁶ Secondly the method is a consecutive one-pot reaction of useful reagents. That is, $\text{Cu}(0)$ is oxidized to $\text{Cu}(I)$, followed by forming complex with dimethyl sulfide, generated *in situ*.

Formation mechanism of Me_2SCuBr . Kornblum reaction is an oxidation of benzyl bromide to benzaldehyde by DMSO in basic aqueous conditions.⁹⁻¹¹ However, in the absence of both a base and water, Kornblum reaction cleanly afforded trimethylsulfonium bromide in excellent isolated yields (65-100%) depending on substituents in benzyl bromide.^{6,12}

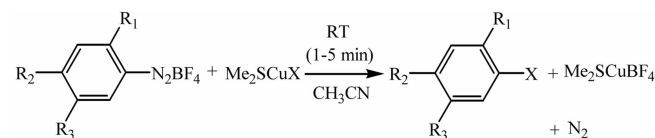
In order to explain high quantitative yields of trimethylsulfonium bromide it was proposed that methyl bromide and dimethyl sulfide were produced not only from the reaction of Kornblum reaction (Scheme 1) but also from decomposition of DMSO itself. That is, the role of DMSO was explained as both an oxidant and a masked precursor for methyl bromide and dimethyl sulfide as was described by Ganem *et al.*¹³ Scheme 1 shows the pathways operating in the reaction of benzyl bromide and DMSO as was proposed by Park *et al.*⁶

In the presence of $\text{Cu}(0)$, however, other simultaneous reactions, in addition to those shown in Scheme 1, proceeded. *i.e.* oxidations of $\text{Cu}(0)$ in reacting with both methyl



Scheme 2. Oxidation of Cu(0) by benzyl bromide.¹⁴

Table 2. Halogenation of diazonium tetrafluoroborate with Me₂SCuX



Entry	Diazonium compounds	Yield (%) ^a
1	R ₁ , R ₂ , R ₃ H, X Br	75
2	R ₁ , R ₂ H, R ₃ NO ₂ , X Br	73
3	R ₁ , R ₃ H, R ₂ Br, X Br	78
4	R ₁ H, R ₂ , R ₃ CH ₃ , X Br	21
5	R ₁ , R ₃ H, R ₂ NO ₂ , X Br	100
6	R ₁ , R ₃ H, R ₂ NO ₂ , X Cl	62
7	R ₁ OCH ₃ , R ₂ NO ₂ , R ₃ Cl, X Br	76
8	R ₁ OCH ₃ , R ₂ , R ₃ H, X Br	16
9	R ₁ , R ₃ H, R ₂ CH ₃ , X Br	24
10	R ₁ , R ₃ H, R ₂ OCH ₃ , X Br	18

^aIsolated yield.

bromide (*in situ* generated product) and benzyl bromide (starting material), similarly as was observed in the literature (Scheme 2).¹¹

In fact we confirmed the formation of bibenzyl in our reaction by GC/MS analysis, strongly supporting the same pathway as shown in Scheme 2. In addition to the benzyl bromide, methyl bromide produced from the reaction of benzyl bromide and DMSO in our conditions (Scheme 1) would also induce oxidation of Cu(0) to CuBr as was shown in Scheme 2. CuBr prepared *in situ* would make a Me₂SCuX by complexing with dimethyl sulfide.

Application of Me₂SCuX (X = Cl, Br). We carried out Sandmeyer reactions with Me₂SCuX and arenediazonium tetrafluoroborates.^{8a} Sandmeyer reactions generally conducted in aqueous conditions, are utilized for many purposes such as in hydroxylation and halogenation *etc.*¹⁵ The present study revealed that Me₂SCuX freshly prepared by our method was very effective in displacing tetrafluoroborate group with halogen under mild conditions and in acetonitrile, *i.e.* the reactions were completed within 5 min at room temperature with vigorous evolution of nitrogen as is shown in Table 2. Considering the heterogeneous reaction mixture due to low solubility of Me₂SCuX in acetonitrile,

the moderate to high isolated yields in Table 2 support the very efficient reaction between Me₂SCuX and arenediazonium tetrafluoroborates.

Conclusion

We were able to discover another preparative method of Me₂SCuX (X = Cl, Br) *via* one-pot reaction from safe and common chemicals such as Cu, benzyl halide, and DMSO. Also we found out that heterogeneous reaction of Me₂SCuX and arenediazonium tetrafluoroborate in acetonitrile was so rapid and effective to afford corresponding bromoaromatics. For an instance 100% isolated yield was obtained from the reaction of Me₂SCuBr and 4-nitrobenzenediazonium tetrafluoroborate.

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