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Copper(I) Bromide - Dimethyl Sulfide Complex - an Alternative to Copper(I) Triflate for Removal of the Thiophenoxide Group

Theodore Cohen*, Craig Shook[1] and Mohan Thiruvazhi

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, USA

Abstract: Commercially available copper(I) bromide - dimethyl sulfide complex is comparable to the far more expensive copper(I) triflate in assisting the removal of the thiophenoxide group from certain substrates.

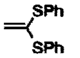
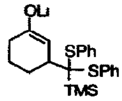
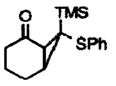
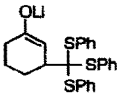
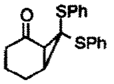
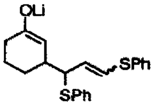
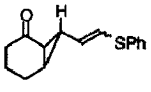
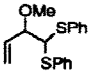
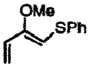
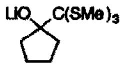
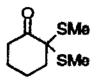
In 1975, the benzene complex of copper(I) triflate[2] was introduced as a specific Lewis acid for the removal of thiophenoxide anions from organic molecules.[3] Such thiophenoxide removal has been used for eliminations to alkenes and dienes,[3,4] ring expansions and chain extensions,[5] a Grob fragmentation,[6] and the formation of cyclopropanes[7] and β-lactams.[8] Knapp has used tetrakis(acetonitrile)copper(I) perchlorate[9] to effect the removal of the thiomethoxide group from deprotonated 1-[tris(methylthio)methyl]cyclopentanol to give a ring expanded product. Although copper(I) perchlorate was found to be more effective than copper(I) triflate for this particular reaction, the former has to be treated with great caution because of its explosive nature at high temperatures;[9a] however, Knapp has suggested that tetrakis(acetonitrile)copper(I) tetrafluoroborate could replace the corresponding perchlorate salt in large-scale reactions.

During the course of our work with 7,7-disubstituted norcarane-2-ones,[10] we discovered that the copper(I) bromide - dimethyl sulfide complex could substitute for copper(I) triflate in their synthesis. In order to survey the scope and limitations of the use of CuBr•Me$_2$S for this purpose, several of the above examples were repeated using this reagent. Table 1 summarizes the results of the comparative study.

It is apparent from the Table that the reactions with CuOTf proceed at lower temperatures than those with CuBr•Me$_2$S and that the substitution of the former by the latter is most successful the more stable the carbocation remaining after removal of the RS group. In some cases (entries 1 and 2), CuBr•Me$_2$S can replace CuOTf with no yield penalty. In some other cases (entries 3 and 4), the use of CuBr•Me$_2$S results in a modest decrease in effectiveness; in entry 4, the reduced yield associated with the use of CuBr•Me$_2$S is the result of a chromatographic purification over silica gel that is required in order to separate the acid-sensitive product (control experiments indicated a 50% loss associated with purification by flash chromatography)[11] from unreacted substrate which is not present in the cleaner reaction using CuOTf. We suggest that the crude yield of the product in entry 4 (CuBr•Me$_2$S) is actually comparable to the corresponding crude yield when CuOTf is employed. The synthesis of (Z)-2-methoxy-1-phenylthio-1,3-butadiene (entry 5) from 4,4-bis(phenylthio)-3-methoxy-1-butene requires vigorous reaction conditions even with CuOTf. With CuBr•Me$_2$S no reaction occurred even under refluxing toluene while 4,4-bis(phenylthio)-3-methoxy-1-butene decomposed under more vigorous conditions (refluxing mesitylene). Entry 6 shows that CuBr•Me$_2$S is almost as efficient as the hazardous tetrakis(acetonitrile)copper(I) perchlorate and the safer-to-handle tetrakis(acetonitrile)copper(I) tetrafluoroborate for the ring expansion shown.

There are several attractive features to the use of CuBr•Me$_2$S. It is safe to handle, commercially available and relatively inexpensive. CuOTf is also commercially available (Alfa) but it is about 24 times more expensive than CuBr•Me$_2$S (Aldrich). Neither of the copper reagents used by Knapp is commercially available. In summary, although CuBr•Me$_2$S cannot replace CuOTf or tetrakis(acetonitrile)copper(I) salts in all cases, due to its availability, low cost, and relative efficiency, it could be used as a practical alternative in a number of reactions.

Table 1 Comparison of CuOTf or Cu(CH_3CN)$_4$ salts with CuBr•Me_2S for removal of thiophenoxide ion

Entry	Substrate	Compound	Reaction conditions with CuOTf[a] (yield)	Reaction conditions with CuBr•Me_2S (yield)
1	MeC(SPh)$_3$		C_6H_6/THF, 25 °C 0.3 h (99%)	C_6H_6/THF, reflux 3 h (93%)
2[b]			THF, -78° C to -23 °C (72%)	THF, -78 °C to 0 °C (71%)
3[b]			THF, -78 °C, 2 h (70%)	THF, -78 °C to 0 °C (62%)
4[b]			THF, -45 °C, 2 h (78%)	THF, 25 °C, 15 h (50%)
5			C_6H_6/THF, reflux 5 h (55-60%)	No reaction
6[c]			Toluene, 75 °C 4h (60-66%)[d]	Toluene, 80 °C 5h (55%)

[a] CuOTf was employed for removal of the thiophenoxide group unless otherwise indicated. [b] The substrate was generated from the reaction of appropriate nucleophiles with 2- cyclohexene-1-one (ref 7, 10). [c] The substrate was obtained from the reaction of the appropriate carbanion with cyclopentanone (ref 9). [d] $CuBF_4$•$4CH_3CN$ or $CuClO_4$•$4CH_3CN$ was employed (ref 9).

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