Mg-Promoted Reductive Cross Coupling of Carbonyl Compounds with Trimethylsilyl Chloride

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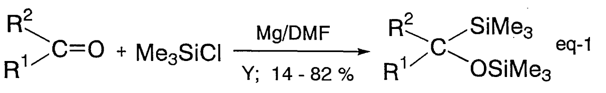
Mg-promoted cross-coupling of aromatic carbonyl compounds with trimethylsilyl chloride (TMSCl) in DMF at room temperature brought about reductive carbon-silicon bond formation to give the corresponding α-trimethylsilylalkyl trimethylsilyl ethers selectively in good yields. The reaction may be initiated through electron transfer from Mg metal to the carbonyl compounds.

Effective formation of a carbon-silicon bond is one of the most attractive subjects in organic synthesis[1] because of much usefulness and important function of organosilicon compounds. Selective introduction of a silyl group to a carbonyl carbon atom has been, however, not readily accomplished due to Brook rearrangement in the course of nucleophilic addition of a trialkylsilyl anion to aldehydes or ketones.[2,3]

We now wish to report a facile method for selective carbon-silicon bond formation through Mg-promoted reductive cross-coupling of carbonyl compounds with TMSCl in DMF at room temperature to give the corresponding α-trimethylsilylalkyl trimethylsilyl ethers (**3**) in good yields (eq-1).



$$R^1R^2C{=}O + Me_3SiCl \xrightarrow[Y;\ 14-82\,\%]{Mg/DMF} R^1R^2C(SiMe_3)(OSiMe_3) \qquad \text{eq-1}$$

1a-n **2** **3a-n**

R^1; Aryl or Heterocycles. R^2; H, Alkyl, or Alkoxyl.

A typical procedure is as follows. A solution containing TMSCl[4] (**2**, 8 mmol) and Mg turnings[4] (15 mmol) in 60 ml of dry DMF was stirred under a nitrogen atmosphere. A DMF solution of benzaldehyde (**1a**, 10 mmol / 5 ml) was dropwise added to the solution for 1 h at room temperature, which was then stirred for about 4 h. After that, the reaction mixture was poured into 200 ml of a saturated aqueous ammonium chloride solution and was extracted by three 100-ml portions of ether. Usual work-up and subsequent column chromatography or distillation of the residue gave α-trimethylsilyl-α-trimethylsiloxytoluene (**3a**) in a good yield with formation of a small amount of the homo-coupling by-product, 1,2-diphenyl-1,2-ethanediol.

Among a variety of reactive metals such as Zn, Al, and Mg, Mg showed the best result in the present reaction, and no or little formation of **3a** was observed when Zn or Al was employed instead of Mg. It may be noteworthy that any reactions did not occur to recover **1a** quantitatively when TMSCl was absent in the reaction system. This reductive cross-coupling reaction was also considerably influenced by a relative ratio of Mg, **2**, and **1a**. The best result for formation of **3a** was obtained when the relative proportion of Mg : **2** : **1a** was 3 : 8 : 1.

Table 1. Reductive Mg-promoted silylation of aldehydes, ketones, and esters

Entry	R^1	R^2	Isolated yield of **3** (%)	
a	C_6H_5	H	**3a**	82
b	o-ClC_6H_4	H	**3b**	79
c	m-ClC_6H_4	H	**3c**	75
d	p-ClC_6H_4	H	**3d**	73
e	p-BrC_6H_4	H	**3e**	37[a]
f	p-$CF_3C_6H_4$	H	**3f**	54
g	o-$CH_3OC_6H_4$	H	**3g**	78
h	o-$C_2H_5OC_6H_4$	H	**3h**	75
i	3,4,5-$(CH_3O)_3C_6H_2$	H	**3i**	71
j	2-thienyl	H	**3j**	52
k	C_6H_5	CH_3	**3k**	66
l	C_6H_5	C_2H_5	**3l**	14[b]
m	2-thienyl	CH_3	**3m**	42
n	C_6H_5	OC_2H_5	**3n**	56

[a] Bis(4-bromophenyl)-1,2-ethanediol was also obtained in a 26% yield.

[b] 4-Trimethylsilylpropiophenone was also obtained in a 20% yield.

Under the similar reaction conditions a variety of trimethylsilylated adducts **3a-n** were efficiently obtained in good to excellent yields.[5] It was quite interesting that the present reaction readily proceeded with not only aromatic aldehydes but also aromatic ketones and esters. The α-trimethylsilylalkyl trimethylsilyl ethers were readily hydrolyzed in an acidic aqueous solution to the corresponding α-trimethylsilyl alcohols.

Although the detailed role of TMSCl (**2**) in this reaction still remains ambiguous,[6] the reaction mechanism may be depicted as shown in Scheme 1. The reaction may be initiated through one-electron transfer from Mg metal, activated by **2**, to aldehydes **1** to give the corresponding anion radicals **4**. The anion radicals **4** may be then subjected to the first electrophilic attack of **2**, generating the radical species **5**, followed by the fast second electron transfer. Subsequently, the formed anionic cross-coupling intermediates **6** may transformed to the products, α-trimethylsilylalkyl trimethylsilyl ethers, by the second electrophilic attack of **2**.[7]

The products **3a-n** can be easily transformed to many useful compounds such as esters, aldehydes, ketones, alcohols, and ethers.[8] For example, treatment of the product **3k** with $KHSO_4$, and that of the product **3a** with Bu_4NF / p-tolualdehyde gave α-silylstyrene and the mixed diarylethanediol in good yields, respectively (Scheme 2).

The present method may be characterized by high simplicity and convenience of reaction procedure, mild conditions (room temperature and ordinary pressure) and good yields of the products.

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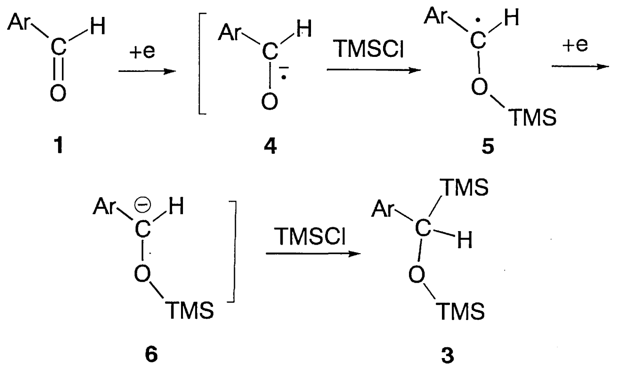
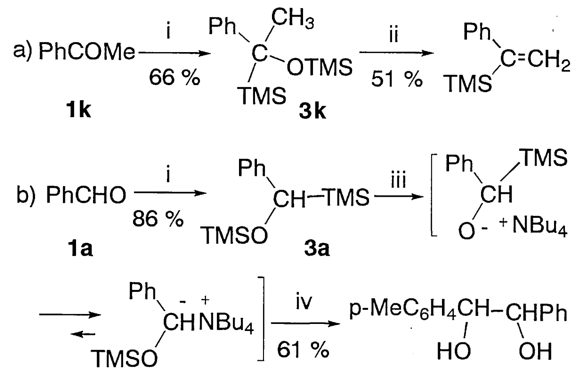
Scheme 1.



Scheme 2.



i : Mg / TMSCl / DMF, ii: $KHSO_4$ /150 °C, iii: Bu_4NF, iv: p-MeC_6H_4CHO / H^+

Reference and Notes

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3 There are some reports for introduction of a TMS group to carbonyl carbons using (trimethylsilyl)lithium or TMSCl in the presence of Mg in HMPA. Their synthetic generality and usefulness, however, have been considerably limited because of special equipment, use of the carcinogenic solvent and expensive reagents, troublesome procedure, and low selectivity. See: J-P. Picard, R. Calas, J. Dunogues, N. Duffaut, J. Gerval, and P. Lapouyade, *J. Org. Chem.*, **44**, 420 (1979); J-P. Picard, A. Ekouya, J. Dunogues, N. Duffaut, and R. Calas, *J. Organometallic Chem.*, **93**, 51 (1972); W. C. Still, *J. Org. Chem.*, **41**, 3063 (1976); R. J. Linderman and A. Ghannam, *J. Org. Chem.*, **53**, 2878 (1988).

4 Trimethylsilyl chloride was freshly distilled before use. Usually commercially available Mg turning for Grignard reagents was used as Mg purchased.

5 All of the products **3** were identified by spectroscopic methods such as ^1H and ^{13}C-NMR, IR, and MS spectra.

6 In this reactions, three kinds of roles for TMSCl may be postulated; that is, activation of **1** as electrophiles by coordination to the oxygen atom of the carbonyl group, stabilization of anion intermediates, and activation of Mg metal.

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