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Copper(I) *tert*-butoxide-promoted coupling of *o*-(1-hydroxyalkyl)arylsilanes with organic halides

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Abstract—Copper(I) *tert*-butoxide-promoted coupling of arylsilanes possessing a 1-hydroxyalkyl group at the *o*-position with organic halides proceeded to give disubstituted arenes. The results indicate that an intermediary arylcopper species is formed by aromatic C^{sp^2}-to-O silyl migration.

Base-catalyzed silicon migration from carbon to oxygen has been extensively studied and widely used in organic synthesis.[1] Although 1,4 aromatic sp^2 carbon to oxygen silyl migration is an attractive way for the preparation of an arylcarbanion species, only a limited number of studies have been done on such reactions. Keay and coworkers investigated the 1,4 C-to-O silyl migration of 2-trialkylsilyl-3-(hydroxymethyl)furans and thiophenes using sodium hydride, potassium hydride, vinylmagnesium bromide, and alkyllithiums. They concluded that any reactive species at C-2 of these arenes formed by the silyl migration is rapidly protonated by the unreacted alcohol before its reaction with electrophiles.[2] Preparation of aryllithiums via silyl migration was achieved only with the use of arene chromium tricarbonyl complexes. Moser et al. investigated the addition of alkyllithiums[3] or lithium enolates[4] to an *o*-trimethylsilylbenzaldehyde chromium tricarbonyl complex and the reactions of aryl anions generated by silyl migration of the resulting alkoxides. This process eliminates the protonation of the aryl anion, and it is obvious that the silyl group migration is facilitated by the stabilization of the anion with the electron-withdrawing chromium tricarbonyl moiety.

Our recent observations on the copper(I) *tert*-butoxide **1**-promoted 1,4 C^{sp^2}-to-O silyl migration of (*Z*)-γ-trimethylsilyl allylic alcohols[5] prompted us to investigate straightforward preparation of an arylmetal species by silyl migration via copper(I) alkoxides. In this communication we wish to describe a copper(I) *tert*-butoxide **1**-promoted C-to-O silyl migration of *o*-(1-hydroxyalkyl)arylsilanes **2** and the reaction of the resulting arylmetal species **3** with organic halides **4** (Scheme 1).

A successive treatment of the benzyl alcohol **2a** with a slight excess of copper(I) *tert*-butoxide, prepared from lithium *tert*-butoxide and copper(I) iodide, and methallyl chloride **4a** (1.2 equiv) produced the trimetylsilyl ether of *o*-methallylbenzyl alcohol **5a**. Desilylation of the silyl ether **5a** with tetrabutylammonium fluoride (TBAF) gave the alcohol **6a** in 54% yield (entry 1, Table 1). The combined use of 1.2 equiv of lithium *tert*-butoxide and 0.5 equiv of copper(I) iodide increased the yield of **6a** by 75% (entry 2). The reaction proceeded even when a catalytic amount of the copper salt was used though the yield was unsatisfactory (entry 3). Similar reactions of allyl and prenyl chlorides **4b** and **c** were also performed to produce the allylation products **6b** and **c**. The latter reaction gave the formal S_N2 product with good regioselectivity. The present method for the preparation of an arylmetal species is successfully applied to the naphthalenemethanol derivatives **2d** and **e** (entries 8–10).

Contrary to the reaction of **2a**, the primary benzyl alcohol **2b** reacted with methallyl chloride **4a** to produce the allylation product **6d** only in moderate yield and a substantial amount of *o*-trimethylsilylbenzaldehyde **7** was isolated as a by-product (entry 6). The formation of

Keywords: alkylation; allylation; arylsilane; copper(I) *tert*-butoxide; silyl migration.

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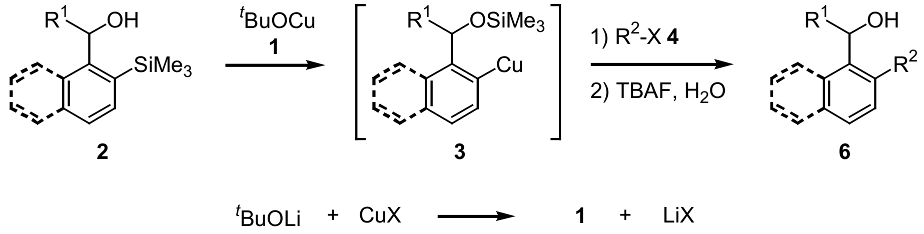
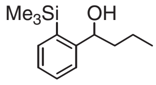
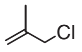
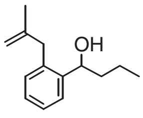
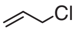
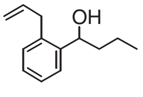
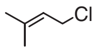
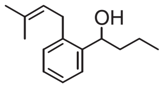
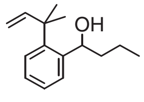
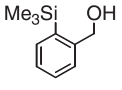
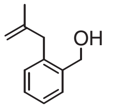
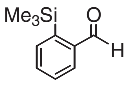
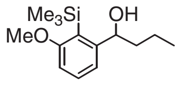
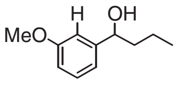
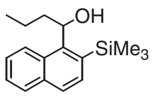
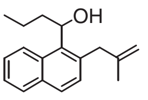
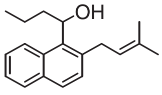
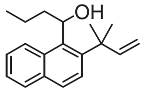
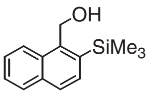
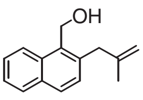


Scheme 1. Copper(I) *tert*-butoxide **1**-promoted reaction of *o*-(1-hydroxyalkyl)arylsilanes **2** with organic halides **4**.

Table 1. Copper(I) *tert*-butoxide-promoted allylation of *o*-(1-hydroxyalkyl)arylsilanes **2**[a]

Entry	Arylsilane **2**	Allyl chloride **4**	Time (h)	Product (yield/%)
1[b]	 **2a**	 **4a**	2	 **6a** (54)
2	**2a**	**4a**	2	**6a** (75)
3[c]	**2a**	**4a**	4	**6a** (60)
4	**2a**	 **4b**	2	 **6b** (66)
5[d]	**2a**	 **4c**	4	 **α-6c** (52)  **γ-6c** (12)
6[b]	 **2b**	**4a**	10	 **6d** (23)  **7** (24)
7	 **2c**	**4a**	3	 **8** (74)
8	 **2d**	**4a**	2	 **6e** (72)
9[d]	**2d**	**4c**	4	 **α-6f** (64)  **γ-6f** (1)
10	 **2e**	**4a**	12	 **6g** (79)

[a] All the reactions were performed with a similar procedure as described in the text, unless otherwise noted.

[b] 1.2 equiv of lithium *tert*-butoxide and 1.1 equiv of copper(I) iodide were used.

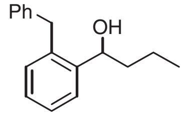
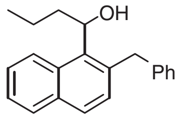
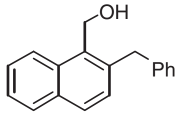
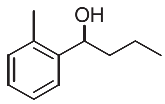
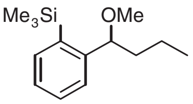
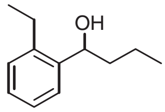
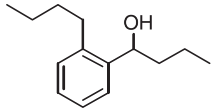
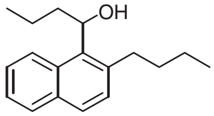
[c] 1.2 equiv of lithium *tert*-butoxide and 0.2 equiv of copper(I) iodide were used.

[d] The products **α-6** and **γ-6** were obtained as a mixture.

7 would be attributable to thermal degradation of the copper(I) alkoxide of **2b**. Such oxidation of alcohols via copper(I) alkoxides was reported by Whitesides et al.[6] Substitution at the *ortho* position of the silylbenzene moiety largely retards the allylation: in preference to allylation, protodesilylation proceeded to afford the alcohol **8** in 74% yield when the *o*-silyl benzylic alcohol **2c** bearing a neighboring methoxy group was employed (entry 7). It was confirmed that the silyl migration did proceed in this case by isolation of the trimethylsilyl ether of **8** in 59% yield without hydrolysis.

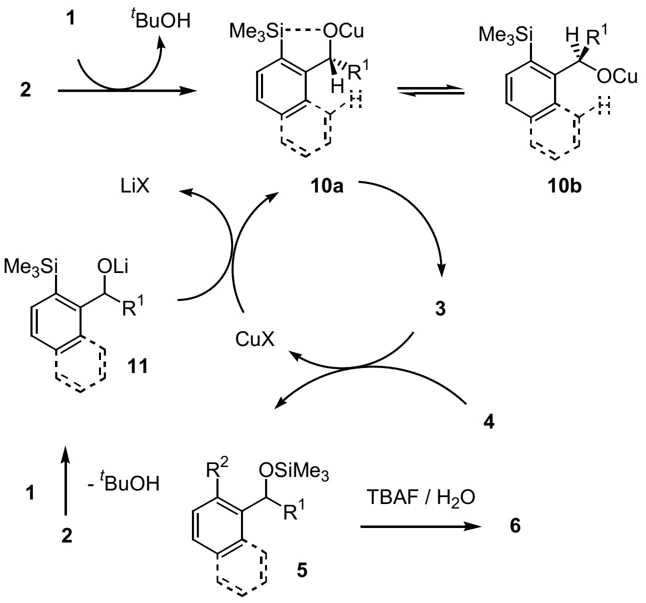
A typical experimental procedure: to a DMF (1 mL) suspension of copper(I) iodide (29 mg, 0.15 mmol) was added a THF solution of lithium *tert*-butoxide (1 M, 0.36 mL, 0.36 mmol) at 0 °C under argon, and the reaction mixture was stirred for 20 min at room temperature. A DMF (1 mL) solution of **2a** (67 mg, 0.30 mmol) and a DMF (1 mL) solution of **4a** (33 mg, 0.36 mmol) were successively added and the mixture was stirred for 2 h. The reaction was quenched by addition of 3.5% NH_3 aqueous solution and the organic materials were extracted with ether and dried over Na_2SO_4. After removal of the solvent, the residue was dissolved in THF (1.8 mL) and a THF solution of TBAF (1 M, 0.3 mL, 0.3 mmol) was added to the solution. The mixture was stirred for 2 h and then diluted with water. The organic materials were extracted with AcOEt, washed with 1 M

Table 2. Copper(I) *tert*-butoxide-promoted alkylation of *o*-(1-hydroxyalkyl)arylsilanes **2**[a]

Entry	Arylsilane **2**	Halide **4**	Time (h)	Product (yield/%)
1	**2a**	$PhCH_2Br$ **4d**	3	 **6h** (57)
2	**2d**	**4d**	2	 **6i** (62)
3	**2e**	**4d**	5	 **6j** (67)
4[b]	**2a**	Me–I **4e**	2	  **6k** (56) **9** (14)
5	**2a**	Et–I **4f**	2	 **6l** (56)
6	**2a**	Bu–I **4g**	2	 **6m** (58)
7	**2d**	**4g**	2	 **6n** (49)

[a] All the reactions were performed with a similar procedure as described in the text, unless otherwise noted.

[b] Five equivalents of methyl iodide were used.



Scheme 2. Plausible pathway for the reaction of *o*-(1-hydroxyalkyl)-arylsilanes **2** with organic halides **4**.

HCl and water, and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by PTLC (hexane/AcOEt = 4:1) to yield 46 mg (75%) of **6a**.

The intermediary organometallic species also reacted with benzyl and alkyl halides. The simple treatment of *o*-trimethylsilylbenzylic alcohols **2** with these halides in the presence of lithium and copper(I) *tert*-butoxides produced alkylation products in good yields (Table 2). When highly reactive methyl iodide was used, the methyl ether **9** was produced as a by-product (entry 4).

Although we have no direct evidence for the formation of an arylcopper species, we tentatively assume that the reaction proceeds via such an intermediate as depicted in Scheme 2. The silyl migration of the copper(I) alkoxide **10**, initially formed from *o*-(1-hydroxyalkyl)arylsilanes **2** and copper(I) *tert*-butoxide **1**, affords the arylcopper species **3**, which reacts with organic halides to give the coupling product **5**. The contrasting results of reactions using the primary alcohols **2b** and **e** ($R^1 = H$) indicate that proper conformation of the copper alkoxide **10** is crucial for the silyl migration. In the case of naphthalenemethanol **2e**, the conformer **10b** is destabilized by the repulsion between the copper alkoxide moiety and the neighboring hydrogen on the naphthalene ring; hence the silyl migration proceeds through the preferred conformation **10a** to produce the arylcopper species **3**. On the other hand the less sterically hindered **10b** is predominant in the benzyl alcohol **2b**, and the silyl migration becomes unfavorable. The copper(I) alkoxide **9** is formed continuously from the lithium alkoxide **11** by the action of copper(I) salt regenerated through the alkylation of arylcopper species **3**.

In conclusion, we have demonstrated that an active arylmetal species can be easily prepared from *o*-(1-hydroxyalkyl)arylsilanes via their copper(I) alkoxides. Further study on the formation of an organometallic species via silyl migration of copper alkoxides is currently in progress.

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