Pergamon

Tetrahedron Letters 44 (2003) 5205–5207

TETRAHEDRON
LETTERS

Copper(I) *tert*-butoxide-promoted stereospecific alkylation of β-hydroxymethylvinylsilanes with alkyl halides

Haruhiko Taguchi, Akira Tsubouchi and Takeshi Takeda*

Department of Applied Chemistry, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

Received 7 April 2003; revised 16 May 2003; accepted 19 May 2003

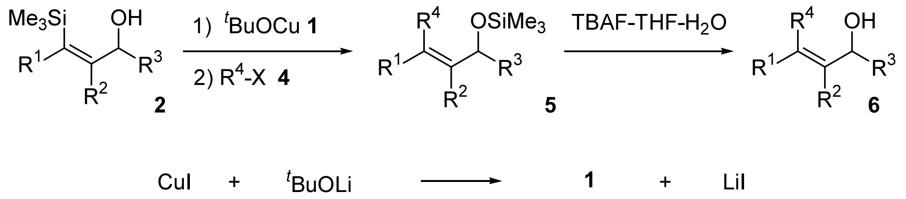
Abstract—Stereospecific alkylation of (*Z*)-β-hydroxymethylvinylsilanes proceeded by treatment with copper(I) *tert*-butoxide and alkyl halides. Tri- and tetra-substituted allylic alcohols were obtained with complete retention of configuration. © 2003 Elsevier Science Ltd. All rights reserved.

Transition metal promoted coupling reactions of vinylsilane derivatives with organic halides have been studied as a method for the construction of highly substituted olefinic compounds.[1] Vinylsilanes possessing fluorine,[2] alkoxy,[3] or hetaryl[4] groups on the silicon atom react with aryl or vinyl halides in the presence of palladium(0) catalyst. These reactions also require the additional activation of vinylsilane with a fluoride ion. Alternatively Denmark and co-workers reported the palladium(0)-catalyzed coupling reaction of 1-(1-alkenyl)silacyclobutanes with aryl and vinyl halides assisted by fluoride ion.[5]

Despite the above extensive investigations, successful coupling of vinylsilanes with organic halides other than aryl and vinyl halides is limited only to the palladium(0)-catalyzed[2] or copper(I) salt-promoted[6] allylation of certain vinylsilanes. Recently, we reported the copper(I) *tert*-butoxide **1** promoted allylation,[7] arylation,[8] and vinylation[8] of (*Z*)-γ-trimethylsilylallylic alcohols **2** (Scheme 1). We assume that the vinylcopper(I) species **3** is generated by silyl group migration from sp^2 carbon to oxygen in these reactions (Scheme 2). On the basis of this assumption, we further studied the reaction of organocopper intermediate **3** and found its unusually high reactivity toward primary alkyl halides.

Initially, we investigated the reaction of (*Z*)-γ-trimethylsilylallylic alcohols **2** with reactive organic halides. The vinylsilanes **2** were successively treated with a slight excess of copper(I) *tert*-butoxide **1** and benzyl bromide **4a** in DMF–THF to produce the silyl ethers **5** and their hydrolysis with *N*,*N*,*N*,*N*-tetrabutylammonium fluoride (TBAF) gave the tri- or tetrasubstituted olefins **6** with complete retention of configuration (Table 1). In the case of the primary alcohol **2d**, the use of palladium catalyst $Pd(PPh_3)_4$ slightly improved the yield (entry 5). When chloromethyl methyl ether **4b** was employed, the further *O*-alkylation also proceeded and the MOM ether **7** was obtained as a major product (entry 6).

The following is a typical experimental procedure. To a DMF (1 ml) suspension of copper(I) iodide (63 mg,

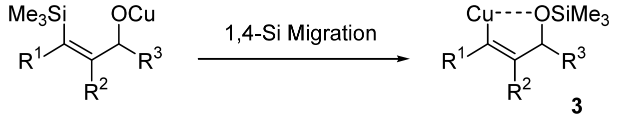


Scheme 1. Copper(I) *tert*-butoxide **1** promoted reaction of (*Z*)-γ-trimethylsilylallylic alcohols **2** with organic halides **4**.

Keywords: alkylation; copper(I) *tert*-butoxide; γ-silylallylic alcohol; silyl migration.

* Corresponding author. Tel.: +81 42 388 7034; fax: +81 42 388 7034; e-mail: takeda-t@cc.tuat.ac.jp

doi:10.1016/S0040-4039(03)01251-6



3

Scheme 2. Formation of vinylcopper(I) species **3** by silyl group migration from *sp*^{2} carbon to oxygen.

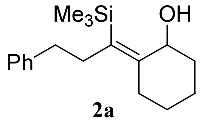
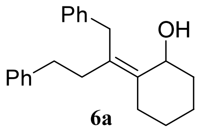
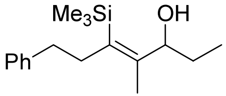
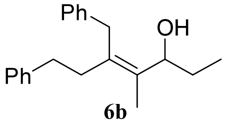
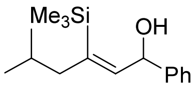
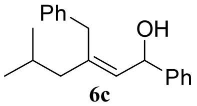
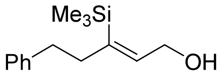
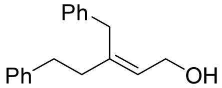
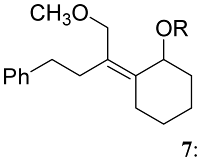
0.33 mmol) was added a THF solution of lithium *tert*-butoxide (1 M, 0.36 ml, 0.36 mmol) at 0°C under argon, and the reaction mixture was stirred for 20 min at room temperature. A DMF (1 ml) solution of (*Z*)-2-[3-phenyl-1-(trimethylsilyl)propane-1-ylidene]cyclohexanol (**2a**) (86 mg, 0.30 mmol) and a DMF (1 ml) solution of benzyl bromide (**4a**) (103 mg, 0.60 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 (3 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 1N 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 70 mg (76%) of (*Z*)-2-(1,4-diphenylbutane-2-ylidene)cyclohexanol (**6a**).

It is of special interest that the alkylation proceeds even when the primary alkyl iodides are employed (Table 2). As shown in entry 6, we observed that the yield of **6** was improved when the reaction took place in the presence of additional equivalents of lithium iodide in certain cases, though a full equivalent of lithium iodide was formed during the preparation of copper(I) *tert*-butoxide **1**. Without hydrolysis, the corresponding silyl ether **5** was isolated (entries 7 and 8).

It is well known that vinylcopper(I) species are unreactive toward organic halides other than allylic, propargylic, and activated alkenyl halides.[9] Although the detail of the alkylation mechanism is unclear at present, the unusual high reactivity of **3** generated by the silyl migration is attributable, at least in part, to the activation by intramolecular coordination of oxygen to copper as depicted in Scheme 2.

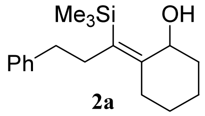
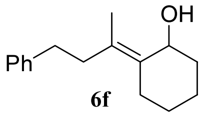
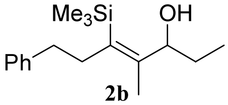
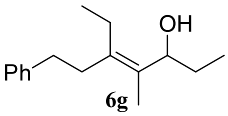
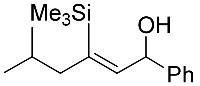
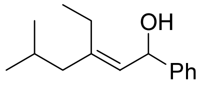
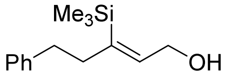
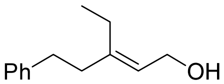
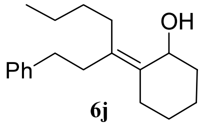
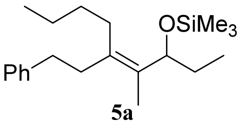
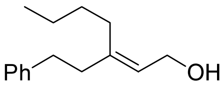
In conclusion, we have developed the first alkylation of vinylsilane derivatives with alkyl halides. Further study on the copper(I) *tert*-butoxide-promoted reactions of a variety of organosilicon compounds possessing a hydroxy group is now in progress.

Table 1. Reaction of the γ-silylallylic alcohols **2** with reactive alkyl halides **4**

Entry	γ-Silylallylic Alcohol **2**	Organic Halide **4** (equiv)	Time (h)	Product	Yield (%)
1	 **2a**	$PhCH_2Br$ (2.0) **4a**	2	 **6a**	76
2	 **2b**	**4a** (2.0)	2	 **6b**	72
3	 **2c**	**4a** (2.0)	6	 **6c**	61
4	 **2d**	**4a** (2.0)	20	 **6d**	59
5[a), b)]	**2d**	**4a** (2.0)	20	**6d**	69
6	**2a**	CH_3OCH_2Cl (2.0) **4b**	4	 **6e**: R = H **7**: R = CH_2OCH_3	22 40

a) ^{t}BuOCu was prepared from ^{t}BuOLi and CuCl . b) The reaction was carried out in the presence of 3 mol% of $Pd(PPh_3)_4$.

Table 2. Reaction of the γ-silylallylic alcohols **2** with primary alkyl iodides **4**

Entry	γ-Silylallylic Alcohol **2**	Alkyl Iodide **4** (equiv)	Time (h)	Product	Yield (%)
1	 **2a**	MeI (2.0) **4c**	6	 **6f**	74
2	 **2b**	EtI (2.0) **4d**	6	 **6g**	84
3	 **2c**	**4d** (1.2)	6	 **6h**	57
4[a]	 **2d**	**4d** (1.2)	24	 **6i**	56
5	**2a**	BuI (2.0) **4e**	4	 **6j**	57
6[b]	**2a**	**4e** (2.0)	4	**6j**	64
7[c]	**2b**	**4e** (2.0)	2	 **5a**	53
8[b), c)]	**2b**	**4e** (2.0)	2	**5a**	67
9[a]	**2d**	**4e** (1.2)	20	 **6k**	46

a) 1.5equiv of CuI were used. b) The reaction was carried out in the presence of additional 1.1 equiv of LiI.
c) The product was isolated without hydrolysis.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) 'Exploitation of Multi-Element Cyclic Molecules' (No. 14044022) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References

1. Hiyama, T. In *Organosilicon Compounds in Cross-coupling Reactions*; Diederich, F.; Stang, P. J., Eds. Metal-catalyzed Cross-coupling Reactions; Wiley-VCH: Weinheim, 1998; p. 421.
2. (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918; (b) Hatanaka, Y.; Goda, K. *J. Organomet. Chem.* **1994**, *465*, 97; (c) Hiyama, T.; Hatanaka, Y. *Pure Appl. Chem.* **1994**, *66*, 1471.
3. (a) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051; (b) Suginome, M.; Kinugasa, H.; Ito, Y. *Tetrahedron Lett.* **1994**, *35*, 8635; (c) Denmark, S. E.; Yang, S.-M. *Org. Lett.* **2001**, *3*, 1749; (d) Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc.* **2002**, *124*, 2102.
4. (a) Itami, K.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 5600; (b) Itami, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 11577; (c) Hosoi, K.; Nozaki, K.; Hiyama, T. *Chem. Lett.* **2002**, 138.
5. (a) Denmark, S. E.; Choi, J. Y. *J. Am. Chem. Soc.* **1999**, *121*, 5821; (b) Denmark, S. E.; Wang, Z. *Synthesis* **2000**, 999.
6. Takeda, T.; Uruga, T.; Gohroku, K. *Chem. Lett.* **1999**, 821.
7. Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *Org. Lett.* **2001**, *3*, 3811.
8. Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *J. Org. Chem.* **2002**, *67*, 8450.
9. Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.