JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

COMMUNICATION

pubs.acs.org/JACS

Photochemically Promoted Transition Metal-Free Cross-Coupling of Acylsilanes with Organoboronic Esters

Kazuta Ito, Hiroto Tamashima, Nobuharu Iwasawa, and Hiroyuki Kusama*

Department of Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

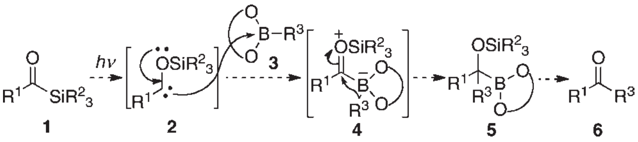
S Supporting Information

ABSTRACT: Intermolecular carbon—carbon bond formation between acylsilanes and organoboronic esters was achieved by photoirradiation under almost neutral, transition metal-free conditions. In this reaction, siloxycarbenes generated by photoisomerization of acylsilanes reacted with boronic esters to give the formal B—C bond insertion intermediates, which underwent unique rearrangement to afford the cyclic α-alkoxyboronic esters. Acidic treatment of the resulting crude products under air furnished the cross-coupled ketones in good yields.

Acylsilanes have long been known to undergo a 1,2-shift of the silyl group by photolysis to generate siloxycarbenes.[1] This photochemical isomerization normally proceeds under neutral conditions at ambient temperature and is potentially useful for carbene-mediated organic synthesis. Siloxycarbenes exhibit nucleophilic character and are known to react with acidic H—X bonds such as alcohols (X = O), HCN, and malononitrile (X = C) to furnish the formal insertion products.[2,3] Watanabe and Nagai reported a formal insertion of siloxycarbenes into Si—H bonds of mono- and diarylsilanes, which was proposed to proceed via the zwitterionic species bearing a pentacoordinate silicate moiety, 1,2-hydride shift of which gave the final products.[4] However, it is surprising that only a limited number of substrates have been applied to the above-mentioned transformations and that few reports have appeared, to date, utilizing photochemically generated siloxycarbenes for C—C bond formation[5] except for the specific reactions with olefins[6] and an aldehyde.[7]

We envisioned that organoboronic esters **3** would participate in a formal B—C insertion via a mechanism similar to that of the Si—H insertion mentioned above,[4b] where the last step would be a 1,2-shift of organyl groups R^3 attached to the B atom, and the resulting insertion products **5** would be converted to the corresponding ketones **6** by appropriate oxidative treatment (Scheme 1). Herein, we report photochemically promoted acyl—aryl, acyl—alkenyl, and acyl—alkyl coupling reactions between acylsilanes and boronic esters without the use of transition metal catalyst.

Scheme 1



First, a mixture of 4-methoxybenzoyltrimethylsilane (**1a**) and 4-(trifluoromethyl)phenylboronic acid neopentyl glycol ester (**3a**) was irradiated in degassed acetonitrile with a 500-W superhigh-pressure Hg lamp at room temperature (Scheme 2).[8] As a result, a 1:1 adduct between **1a** and **3a** was observed in the crude materials in ~30% yield (determined by ^{1}H NMR analysis). This adduct was unstable toward purification by preparative TLC (silica gel) under air, and the benzophenone derivative **6aa** was finally isolated in 30% yield.[9] Careful analysis of the crude mixture by ^{1}H, ^{13}C, and HMBC spectra revealed that the structure of the primary product was not the initially assumed **5aa** but the seven-membered ring compound **7aa**, which is thought to be formed via a unique rearrangement of the siloxy and the alkoxy groups from the B—C insertion product **5aa.**[10,11]

Since the expected carbon—carbon bond formation was realized simply by photoirradiating the mixture of **1a** and **3a** at room temperature, we then optimized the reaction conditions to improve the yield of the cross-coupling product **6aa.**[12,13] Among the solvents examined (2 equiv of **3a** was used), nonpolar solvents such as benzene, cyclohexane, and hexanes gave the desired products in satisfactory yields (75%, 86%, and 80% yields, respectively),[14] while ethereal solvents such as Et_2O and THF did not improve the yield (46% and 35% yields, respectively).[14] In hexanes, the amount of the boronic ester employed could be reduced to only a slight excess. Furthermore, when the reaction was conducted in the presence of 4 Å molecular sieve (MS4A) in a closed vessel, the yield of **7aa** in the crude mixture was improved to 95% (determined by ^{1}H NMR analysis). Acidic treatment (1 M HCl in THF at rt under air) of thus-obtained crude mixture followed by silica gel chromatography gave the ketone **6aa** in 91% yield (Table 1, entry 1).[15]

We then investigated the effects of steric bulk of the silyl group (Table 1). Although the substrate with a TBS group gave the corresponding ketone **6aa** in high yield (entry 2), a TIPS group dramatically slowed down the reaction, and most of the starting materials were recovered (entry 3).[16]

Concerning the ester moiety of the boronic acid, the reaction of a pinacol ester derivative also gave the coupling product in good yield, but the reaction rate was slower than that of a neopentyl glycolate.[17] These results indicated that the combination of sterically less hindered substrates, acyl*trimethylsilane* and boronic acid *neopentyl glycol ester*, is suitable for the present reaction.

Received: November 15, 2010
Published: February 23, 2011

Scheme 2

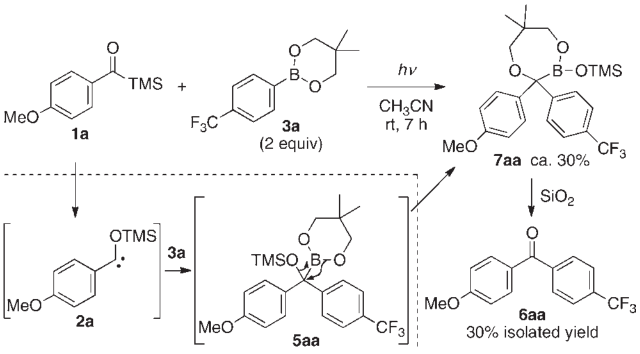
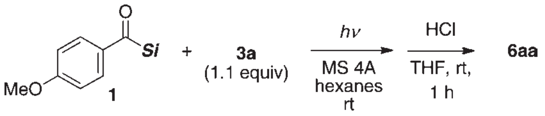


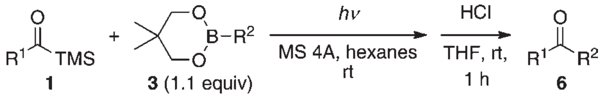
Table 1. Effects of the Silyl Group



entry	*Si*	time/h	yield/%
1	TMS **1a**	1.5	91
2	TBS **1b**	3.5	93
3[a]	TIPS **1c**	12	19

[a] 79% of the starting materials **1c** was recovered.

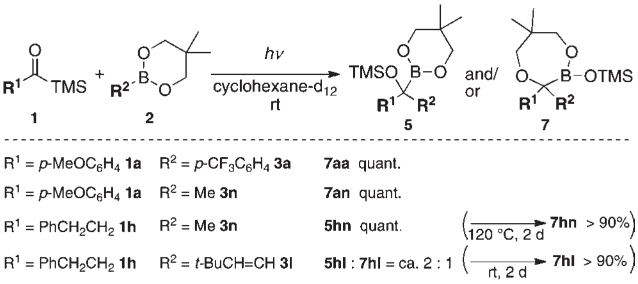
Table 2. Substrate Scope under the Optimum Conditions[a]



entry	R^1	R^2	time/h	yield/%
1	4-MeOC$_6$H$_4$ **1a**	4-ClC$_6$H$_4$ **3b**	4	**6ab** 91
2		4-BrC$_6$H$_4$ **3c**	2	**6ac** 85
3		4-IC$_6$H$_4$ **3d**	2.5	**6ad** 78
4		4-MeCOC$_6$H$_4$ **3e**	3	**6ae** 80
5		4-OHCC$_6$H$_4$ **3f**	1.5	**6af** 52
6[b]		4-O$_2$NC$_6$H$_4$ **3g**	3	**6ag** 55
7		Ph **3h**	5	**6ah** 93
8		4-MeOC$_6$H$_4$ **3i**	3	**6ai** 78
9		2-MeOC$_6$H$_4$**3j**	3	**6aj** 90[c]
10		4-*t*-BuC$_6$H$_4$ **3k**	2	**6ak** 89
11[d,e]		(*E*)-*t*-BuCH=CH **3l**	1.5	**6al** 61
12[d]		*n*-Bu **3m**	3	**6am** 43
13[f]	Ph **1d**	4-F$_3$CC$_6$H$_4$ **3a**	2	**6da** 60
14[e,f]	4-F$_3$CC$_6$H$_4$ **1e**		0.7	**6ea** 63
15[d]	2-MeOC$_6$H$_4$ **1f**		3	**6fa** 63
16[f]	2-thienyl **1g**		4	**6ga** 41
17[g]	PhCH$_2$CH$_2$ **1h**		6	**6ha** 87
18[g]		4-MeOC$_6$H$_4$ **3i**	6	**6hi** 75
19[d,g]		*n*-Bu **3m**	6	**6hm** 76
20[d,g]		Me **3n**	6	**6hn** 78[c]
21[h]	(*E*)-4-CF$_3$C$_6$H$_4$CH=CH **1i**	4-F$_3$CC$_6$H$_4$ **3a**	1	**6′ia** 49[i]

[a] Unless otherwise noted, a 500-W superhigh-pressure mercury lamp was used. [b] 436 nm. [c] The crude materials were treated with NaOH/H$_2$O$_2$. [d] 2 equiv of **3** was employed. [e] The crude materials were directly purified by silica gel without acidic treatment. [f] 10 mol % of acridine was added. [g] A 250-W superhigh-pressure mercury lamp was used. [h] 5 equiv of **3** was employed. [i] Yield of the corresponding saturated ketone, 4-CF$_3$C$_6$H$_4$CH$_2$CH$_2$COC$_6$H$_4$-4-CF$_3$ (**6′ia**).

Scheme 3. In Situ NMR Analyses on the Structure and Thermal Behavior of the Products



With the optimum set of reaction conditions in hand (Table 1, entry 1), we next investigated the scope of this novel acyl−aryl cross-coupling reaction (Table 2). With electron-rich aroylsilane **1a**, arylboronic esters of various electronic properties could be employed (entries 1−10). It is noteworthy that arylboronic esters substituted with labile functional groups such as acetyl, formyl, and nitro could be applied because of the neutral conditions (entries 4−6). *o*- And *p*-methoxyphenylboronic esters showed comparable reactivity (entries 8 and 9), but mesitylboronate did not react with **1a** probably due to the steric hindrance around the boron center. An α,*β*-unsaturated and a saturated ketone could be obtained by employing an alkenyl- and an alkylboronic ester, respectively (entries 11 and 12). Although acylsilanes with no electron-donating group exhibited somewhat poorer reactivity, addition of a catalytic amount of acridine as a triplet sensitizer gave satisfactory yields in some cases.[18,19] An ortho-substituted benzoylsilane and a heteroaroylsilane also participated in the cross-coupling (entries 15 and 16). Furthermore, aliphatic acylsilanes including an α,*β*-unsaturated acylsilane were also applicable to give the coupling products in good to high yields (entries 17−21).[20]

To gain insight into the proposed unique rearrangement of the B−C insertion intermediate **5** into the seven-membered ring compound **7**, we then carried out several NMR experiments (Scheme 3, see Supporting Information for details). In the reactions of *aroyl*silanes, the rearranged compound **7** was observed as sole product regardless of the substituent on the boronic ester employed.[21] In contrast, formation of the B−C insertion product **5** was observed in the reactions of the *alkanoyl*silane **1h**. With the *alkyl*boronate **3n**, **5hn** was obtained as an exclusive product, which was stable at room temperature but rearranged to **7hn** at 120 °C. With the *alkenyl*boronate **3l**, a 2:1 mixture of **5hl** and **7hl** was observed just after consumption of **1h**, suggesting that transformation of **5hl** to **7hl** partially occurred under the reaction conditions. Actually, this mixture was almost completely converted to **7hl** at room temperature after 2 days.

These results clearly indicated that the rearrangement of the B−C insertion product **5** to **7** was a thermodynamically favorable pathway[22] and its activation barrier was largely affected by the electronic nature of the substituent. Probably, the driving force of this rearrangement would be to reduce steric hindrance around the Me_3SiO-substituted quaternary carbon of **5**.

In summary, we developed photochemically promoted acyl—aryl, acyl—alkenyl, and acyl—alkyl cross-coupling reactions of acylsilanes with organoboronic esters to afford a wide range of ketones under mild reaction conditions. This is a quite rare example that photochemistry of acylsilanes is efficiently applied for carbon—carbon bond-forming reactions. It is noteworthy that this overall transformation can be achieved without the use of transition metal catalysts.[23,24]

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Experimental procedures and spectral data for the new compounds, NMR data in Scheme 3, and crystallographic data for **8** mentioned in ref 10. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

hkusama@chem.titech.ac.jp

■ ACKNOWLEDGMENT

This research was partly supported by the Sumitomo Foundation and a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

■ REFERENCES

(1) (a) Brook, A. G. *J. Am. Chem. Soc.* **1957**, *79*, 4373–4375. (b) Brook, A. G. *Adv. Organomet. Chem.* **1969**, *7*, 95–155 and references therein. (c) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147–195 and references therein. (d) Bock, H.; Alt, H.; Seidl, H. *J. Am. Chem. Soc.* **1969**, *91*, 355–361. (e) Brown, R. S. *Can. J. Chem.* **1975**, *53*, 2446–2449. (f) Bernardi, F.; Lunazzi, L.; Ricci, A.; Seconi, G.; Tonachini, G. *Tetrahedron* **1986**, *42*, 3607–3610. (g) Barbarella, G.; Bongini, A. *Tetrahedron* **1989**, *45*, 5137–5140. (h) Chimichi, S.; Mealli, C. *J. Mol. Struct.* **1992**, *271*, 133–148. (i) Perrin, H. M.; White, W. R.; Platz, M. S. *Tetrahedron Lett.* **1991**, *32*, 4443–4446.

(2) (a) Brook, A. G.; Duff, J. M. *J. Am. Chem. Soc.* **1967**, *89*, 454–455. (b) Duff, J. M.; Brook, A. G. *Can. J. Chem.* **1973**, *51*, 2869–2883. (c) Bourque, R. A.; Davis, P. D.; Dalton, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 697–699.

(3) Intramolecular C—H insertion reactions of thermally (>250 °C) generated siloxycarbenes have been reported: (a) Bassindale, A. R.; Brook, A. G.; Harris, J. *J. Organomet. Chem.* **1975**, *90*, C6–C8. (b) Shih, C.; Swenton, J. S. *J. Org. Chem.* **1982**, *47*, 2668–2670. (c) Shen, Z.; Dong, V. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 784–786.

(4) (a) Watanabe, H.; Kogure, T.; Nagai, Y. *J. Organomet. Chem.* **1972**, *43*, 285–291. (b) Watanabe, H.; Ohsawa, N.; Sawai, M.; Fukawa, Y.; Matsumoto, H.; Nagai, Y. *J. Organomet. Chem.* **1975**, *93*, 173–179.

(5) A carbamoylsilane has been reported to behave as a siloxyaminocarbene under thermal conditions. Cunico, R. F. *Tetrahedron Lett.* **2001**, *42*, 2931–2932.

(6) (a) Brook, A. G.; Kucera, H. W.; Pearce, R. *Can. J. Chem.* **1971**, *49*, 1618–1621. (b) For the revised reaction mechanism, see: Dalton, J C.; Bourque, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 699–700. See also: (c) Scheller, M. E.; Frei, B. *Helv. Chim. Acta* **1984**, *67*, 1734–1747.

(7) Brook, A. G.; Pearce, R.; Pierce, J. B. *Can. J. Chem.* **1971**, *49*, 1622–1628.

(8) Photoirradiation was carried out through band-pass filter (λ = 436 nm) to ensure that only aroylsilane **1a** could be excited.

(9) Transformation of α-oxygenated boronic esters to the corresponding ketones: (a) Carboni, B.; Ollivault, M.; Le Bouguenec, F.; Carrié, R.; Jazouli, Md. *Tetrahedron Lett.* **1997**, *38*, 6665–6668. (b) Matteson, D. S. In *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Kaufmann, D. E., Matteson, D. S., Eds.; Georg Thieme Verlag: Stuttgart, 2005; Category 1, Vol. 6, pp 607—622. For preparation of α-oxygenated organoboron compounds, see: (c) Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2031–2034. (d) Molander, G. A.; Canturk, B. *Org. Lett.* **2008**, *10*, 2135–2138. (e) Shimizu, M.; Fujimoto, T.; Liu, X.; Minezaki, H.; Hata, T.; Hiyama, T. *Tetrahedron* **2003**, *59*, 9811–9823. (f) Shimizu, M.; Fujimoto, T.; Liu, X.; Hiyama, T. *Chem. Lett.* **2004**, *33*, 438–439. (g) Shimizu, M.; Fujimoto, T.; Liu, X.; Takeda, Y.; Hiyama, T. *Heterocycles* **2008**, *76*, 329–351.

(10) The X-ray analysis of a stable crystalline derivative **8** obtained from 4-bromobenzoyltrimethylsilane and 4-bromophenylboronic acid pinacol ester under the optimum conditions also supported the structure of **7aa**. See SI for details.

(11) Related rearrangement reactions: (a) Hesse, G.; Haag, A. *Tetrahedron Lett.* **1965**, 1123–1125. (b) Seyferth, D.; Prokai, B. *J. Am. Chem. Soc.* **1966**, *88*, 1834–1835. (c) See also: Suzuki, A; Nozawa, S.; Miyaura, N.; Itoh, M.; Brown, H. C. *Tetrahedron Lett.* **1969**, 2955–2958.

(12) The photoirradiation was carried out through the super-cold filter (Asahi Optics SC0751) so as not to raise the temperature of the reaction mixture. Since $4\text{-}MeOC_6H_4CHO$, probably due to moisture in the reaction mixture, was observed in the crude mixture, examinations in Tables 1 and 2 were performed in the presence of MS4A. See: Wegert, A.; Behr, J.-B.; Hoffmann, N.; Miethchen, R.; Portella, C.; Plantier-Royon, R. *Synthesis* **2006**, 2343–2348. See also ref 3b.

(13) The reaction of **1a** and **3a** under thermal conditions (microwave, 180 °C in *o*-dichlorobenzene or microwave, 250 °C in decalin) resulted in a complex mixture, and neither **7aa** nor **6aa** could be detected. See ref 3c.

(14) All the reactions were carried out by using degassed solvents. The yields in parentheses are the combined yield of **7aa** and **6aa** determined by ^1H NMR because a small amount of the ketone **6aa** was observed in the crude mixture.

(15) Direct purification of the crude mixture by preparative TLC (silica gel) without acidic treatment gave **6aa** in 81% yield. Both acid and oxygen in the air are responsible for the conversion of **7aa** into **6aa**, but the mechanism of this transformation is unclear at present.

(16) Because of almost quantitative formation of the silyl acetal in 5 min when **1c** was irradiated in MeOH in the presence of 30 mol % of pyridine, formation of the corresponding siloxycarbene from **1c** is fast. In addition, thermal reversion of siloxycarbenes into acylsilanes has been suggested by Brook et al. Thus, this result indicates that the coupling reaction of the siloxycarbene derived from **1c** is suppressed due to the steric hindrance of a TIPS group. See Brook, A. G.; Harris, J. W.; Bassindale, A. R. *J. Organomet. Chem.* **1975**, *99*, 379–383.

(17) The reaction with a catecholate derivative was faster than that with a neopentyl glycolate, but rather sluggish. A diisopropylboronate, an acyclic boronic ester, could be employed, but the reaction was quite slow. See SI for details.

(18) Since siloxycarbenes are generated from the triplet excited state of acylsilanes, the addition of triplet sensitizer is considered to facilitate the formation of **2**. See ref 2c.

(19) The reactions of **1d**, **1e**, and **1g** in the absence of acridine gave the corresponding ketones **6da**, **6ea**, and **6ga** in 57, 16, and 32% yields, respectively.

(20) Saturated ketone **6′ia** is assumed to be formed by protonation at the γ-position of the allylboronic ester moiety of the primary product **7ia**.

(21) In all reactions employing an aroylsilane and/or an arylboronate (Table 2, entries 1—18), ^1H NMR spectra of the crude materials suggested exclusive formation of the rearranged product **7**.

(22) Theoretical calculations (RB3LYP/6-31G(d)//RHF/6-31G) of **5** and **7** bearing phenyl—phenyl, phenyl—methyl, and ethyl—methyl substituents suggested that the rearranged product **7** is thermodynamically more stable than **5** regardless of the substituents on the quaternary carbon.

(23) Transition metal-catalyzed cross-coupling reactions of acylsilanes and stannanes and silylcarbonylation reactions of acylsilanes:

(a) Kang, J.; Choi, Y. R.; Kim, B. J.; Jeong, J. U.; Lee, S.; Lee, J. H.; Pyun, C. *Tetrahedron Lett.* **1990**, *31*, 2713–2716. (b) Tsuji, Y.; Fujihara, T. *Bull. Korean Chem. Soc.* **2007**, *28*, 1902–1909 and references therein. (c) Sakurai, H.; Yamane, M.; Iwata, M.; Saito, N.; Narasaka, K. *Chem. Lett.* **1996**, 841–842. (d) Yamane, M.; Amemiya, T.; Narasaka, K. *Chem. Lett.* **2001**, 1210–1211.

(24) Related metal-free carbon−carbon bond-forming reaction employing tosylhydrazones as a carbene precursor under basic conditions has been reported. See Barluenga, J.; Tomás-Gamasa, M.; Aznar, F.; Valdés, C. *Nature Chem.* **2009**, *1*, 494–499.