ORGANIC LETTERS

2007
Vol. 9, No. 20
4081−4083

Gold-Catalyzed Cyclization of (*ortho*-Alkynylphenylthio)silanes: Intramolecular Capture of the Vinyl–Au Intermediate by the Silicon Electrophile

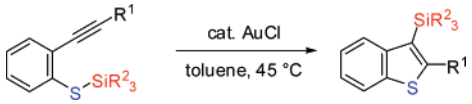
Itaru Nakamura,* Takuma Sato, Masahiro Terada, and Yoshinori Yamamoto

Department of Chemistry, Graduate School of Science, Tohoku University,
Sendai 980-8578 Japan

itaru-n@mail.tains.tohoku.ac.jp

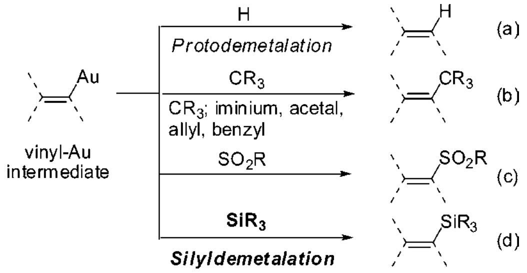
Received August 10, 2007

ABSTRACT



The gold-catalyzed cyclization of (*ortho*-alkynylphenylthio)silanes 1 produced the corresponding 3-silylbenzo[*b*]thiophenes 2 in good to excellent yields. For example, the reaction of [2-(1-pentynyl)phenylthio]triisopropylsilane 1a, [2-(*p*-anisylethynyl)phenylthio]triisopropylsilane 1e, and [2-(phenylethynyl)phenylthio]triisopropylsilane 1g in the presence of 2 mol % of AuCl in toluene at 45 °C gave 2a, 2e, and 2g in 98, 99, and 97% yields, respectively. This reaction proceeds through intramolecular capture of the vinyl–Au intermediate by the silicon electrophile, so-called silyldemetalation.

Scheme 1. Capture of the Vinyl−Gold Intermediate by Various Electrophiles: (a) Proton (Protodemetalation), (b) Carbon Electrophiles, (c) Sulfonyl Groups, and (d) Silicon Electrophiles (Silyldemetalation)



Gold-catalyzed reactions have rapidly gained great importance as a synthetic method in organic chemistry.[1] For a large number of gold-catalyzed reactions, the catalytic cycle is completed by trapping of a vinyl−Au intermediate with a proton, so-called *protodemetalation* (Scheme 1, type a).[1a,2] Recently, several groups, including ourselves, have disclosed that such intermediates can also be captured by carbon electrophiles, such as iminium, α-alkoxyalkyl, allyl, and benzyl groups, in an intramolecular fashion (type b).[3] We also recently reported that a vinyl−Au intermediate can be trapped by sulfur electrophiles in a gold-catalyzed intramolecular aminosulfonylation reaction (type c).[4] In this communication, we report that a vinyl−Au intermediate can be intramolecularly captured by silicon electrophiles (type d); the gold-catalyzed cyclization of (*ortho*-alkynylphenylthio)-

---

(1) For a review of Au-catalyzed reactions: (a) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (b) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (c) Hashmi, A. S. K.; Huchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. (d) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (e) Asao, N. *Synlett* **2006**, 1645. (f) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, 4555. (g) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200. (h) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990.

(2) For example: (a) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 11364. (b) Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1141. (c) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912. (d) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962.

(3) (a) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804. (b) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4473. (c) Dubé, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 12062.

(4) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 2284.

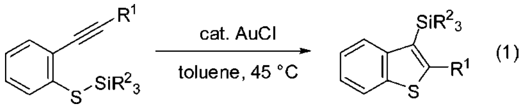
10.1021/ol701951n CCC: $37.00

Table 1. Cyclization of (*ortho*-Alkynylphenylthio)silanes **1**[a]

entry	**1**	R^1	SiR^2_3	AuCl (mol %)	time(h)	**2**	yield (%)[b]
1	**1a**	*n*-Pr	Si(*i*-Pr)$_3$	2	5	**2a**	98
2	**1b**	Cy	Si(*i*-Pr)$_3$	25	21	**2b**	44
3	**1c**	4-*i*-$Pr_2NC_6H_4$	Si(*i*-Pr)$_3$	10	18	**2c**	89
4	**1d**	2,4-$(MeO)_2C_6H_3$	Si(*i*-Pr)$_3$	5	5	**2d**	99
5	**1e**	4-$MeOC_6H_4$	Si(*i*-Pr)$_3$	2	8	**2e**	99
6	**1f**	4-MeC_6H_4	Si(*i*-Pr)$_3$	10	24	**2f**	96
7	**1g**	Ph	Si(*i*-Pr)$_3$	2	19	**2g**	97
8	**1h**	4-$F_3CC_6H_4$	Si(*i*-Pr)$_3$	10	21	**2h**	60
9	**1i**	2-(1-methylpyrrolyl)	Si(*i*-Pr)$_3$	10	18	**2i**	90
10	**1j**	*n*-Hex	Si(*i*-Pr)$_2$(*s*-Bu)	2	6	**2j**	quant
11	**1k**	*n*-Pr	$SiPh_3$	10	2	**2k**	40

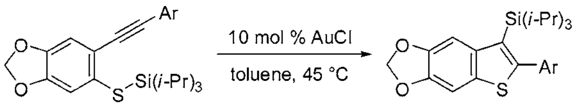
[a] The reaction of **1** (0.4 mmol) was carried out in the presence of catalytic amounts of AuCl in toluene (1 mL) at 45 °C. [b] Isolated yield.

silanes **1** produced 3-silylbenzo[*b*]thiophenes **2** in good to excellent yields (eq 1).



(1)

The results are summarized in Table 1. The reaction of [2-(1-pentynyl)phenylthio]triisopropylsilane **1a** in the presence of 2 mol % of AuCl in toluene at 45 °C for 5 h gave (2-propylbenzo[*b*]thiophen-3-yl)triisopropylsilane **2a** in 98% yield (entry 1). The use of $AuCl_3$, AuCl(CO), and $AuBr_3$ as the catalyst, instead of AuCl, gave **2a** in lower yields, whereas other metal complexes, such as $PtCl_2$, $Pt(PPh_3)_4$, $PdCl_2$, $CuCl_2$, Ag(OTf), and $InCl_3$, did not promote the present reaction at all. The reaction of **1a** using benzene, hexane, CH_2Cl_2, or ethyl acetate, instead of toluene, gave **2a** in similar yields, whereas the use of other solvents, such as acetonitrile and THF, was not effective. The reaction of **1a** at 25 °C afforded **2a** in 63% yield. A higher catalyst loading (25 mol %) was required for the reaction of **1b** bearing a bulky cyclohexyl group at R^1 to obtain **2b** in a moderate yield (entry 2). The reaction of **1c**−**f** having electron-rich aromatic rings at the alkynyl moiety gave the corresponding products **2c**−**f** in excellent yields, whereas the reaction of **1h** bearing an electron-deficient aromatic ring at R^1 produced **2h** in a lower yield (entries 3−8). A pyrrole ring was tolerated in this reaction, as migration of the silyl group to the pyrrole ring was not observed at all (entry 9). A (2-butyl)diisopropylsilyl group showed reactivity similar to a triisopropylsilyl group, and the reaction of **1k** bearing a triphenylsilyl group afforded the desired product **2k** in a lower yield (entries 10 and 11). The reaction of a (6-alkynylbenzodioxol-5-ylthio)silane **1l** proceeded smoothly, affording the tricyclic compound **2l** in 72% yield (eq 2).



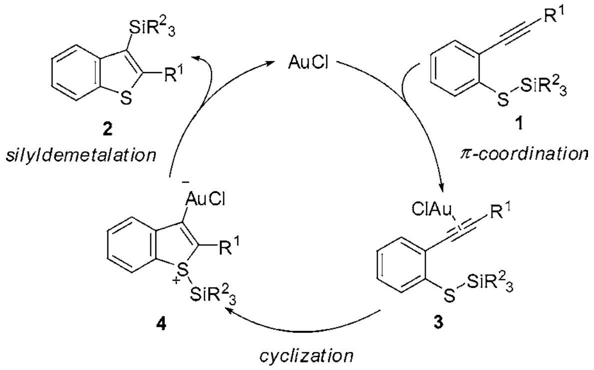
(2)

1l (Ar = 4-$MeOC_6H_4$)

2l (Ar = 4-$MeOC_6H_4$)
72%

The reaction mechanism for this gold-catalyzed cyclization of **1** is illustrated in Scheme 2. The Lewis acidic gold(I) chloride first coordinates to the alkynyl moiety of **1**.[5] The resulting electron-deficient triple bond of **3** undergoes intramolecular nucleophilic attack by the sulfur atom, leading to the silylsulfonium intermediate **4**. A [1,3] migration of the silyl group and subsequent elimination of the AuCl, so-called *silyldemetalation*, gives the product **2**.[6,7]

Scheme 2. Plausible Mechanism



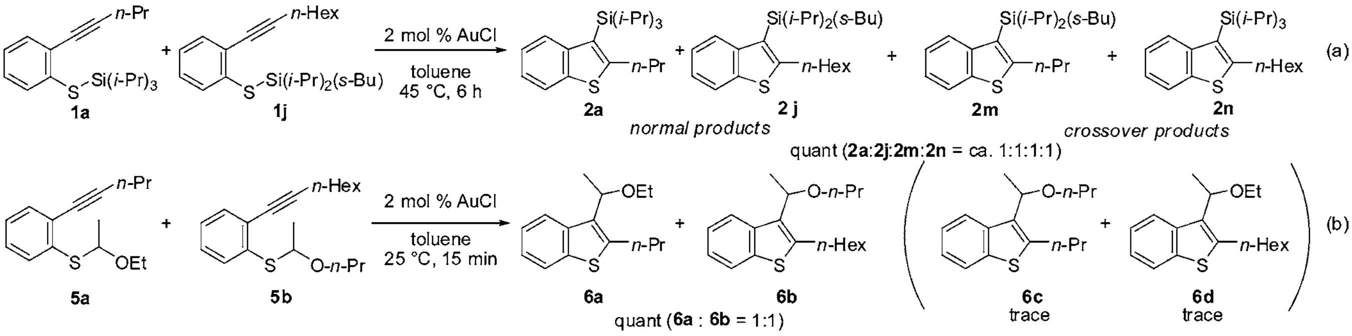
Interestingly, crossover of the silyl group was observed when we mixed **1a** and **1j** under the standard reaction conditions. A resulting 1:1:1:1 mixture of normal products **2a** and **2j** and crossover products **2m** and **2n** was obtained quantitatively (Scheme 3, a). We, however, did not observe any crossover of the silyl group between the starting materials by GC-MS during the progress of the reaction. This result contrasts with the crossover experiment of the gold-catalyzed intramolecular carbothiolation:[3b] the reaction of a mixture

---

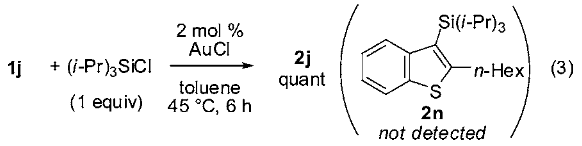
(5) Hüttel, R.; Forkl, H. *Chem. Ber.* **1972**, *105*, 1664.

(6) Migration of silyl groups: (a) Kira, M.; Iwamoto, T. In *Chemistry of Silicon Compounds*; Rappoport, Z., Apeloig, Y., Eds.; John Wiley & Sons Ltd.: Chichester, UK, 2001; p 853. (b) Anderson, G.; Cameron, D. W.; Feutrill, G. I.; Read, R. W. *Tetrahedron Lett.* **1981**, *22*, 4347. (c) Yamabe, T.; Nakamura, K.; Shiota, Y.; Yoshizawa, K.; Kawauchi, S.; Ishikawa, M. *J. Am. Chem. Soc.* **1997**, *119*, 807. (d) Takahashi, M.; Kira, M. *J. Am. Chem. Soc.* **1997**, *119*, 1948. (e) Ward, B. D.; Orde, G.; Clot, E.; Cowley, A. R.; Gade, L. H.; Mountford, P. *Organometallics* **2005**, *24*, 2368. (f) Seregin, I. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2006**, *128*, 12050.

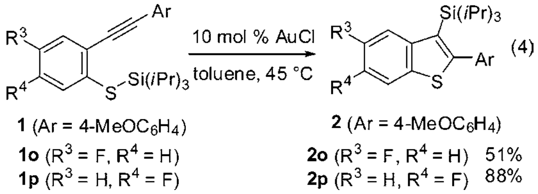
Scheme 3. Crossover Experiments (a) Thiosilylation and (b) Carbothiolation



of the *O,S*-acetals **5a** and **5b** in the presence of catalytic amounts of AuCl gave the products **6a** and **6b** derived from each starting material, and only trace amounts of the crossover products **6c** and **6d** were observed by GC-MS (Scheme 3, b). Because the reaction of **1j** in the presence of 1 equiv of chlorotriisopropylsilane afforded **2j** as a sole product and **2n**, which could be obtained by the reaction with TIPSCl, was not observed by NMR and GC-mass spectroscopic analysis (eq 3), the possibility that the chlorine atom mediated crossover of the silyl group was ruled out.[8] Presumably, the much lower migration ability of the silyl group compared to that of the carbon migrating groups led to a longer lifetime for the silylsulfonium intermediate **4**, resulting in crossover of the silyl groups between two kinds of reactive intermediate **4** in situ.



To study the electronic effect on both the alkynyl moiety and the silylthio group, we carried out the reaction of fluoro-substituted substrates **1o** and **1p** (eq 4). The reaction of **1o** having a fluorine atom at R^3 afforded **2o** in a lower yield (51%), indicating that a decrease in electron density of the triple bond by the electron-withdrawing fluorine atom at the *meta*-position of the alkynyl moiety interferes with π-coordination to the gold catalyst, thus diminishing the reactivity for the cyclization.[9] This result corresponds with that of **1h** having a 4-(trifluoromethyl)phenyl group at R^1 giving the product **2h** in a lower yield (Table 1, entry 8). On the contrary, the reaction of **1p** bearing a fluorine atom at R^4 gave **2p** in a good yield (88%), suggesting that a decrease in nucleophilicity of the sulfur atom by the fluorine atom at the *meta*-position of the silylthio group did not significantly affect the cyclization step.



In conclusion, we are now in a position for synthesizing 3-silylbenzo[*b*]thiophenes in good to excellent yields. It should be noted that the present reaction proceeds through *trans* sulfur−silicon bond addition, so-called *thiosilylation*.[10] The present reaction proceeded under mild conditions without the formation of undesired byproducts, making this methodology useful for the synthesis of highly functionalized 3-silylbenzo[*b*]thiophenes in an environmentally benign manner.

Acknowledgment. This work was financially supported by a Grant-in-Aid for Scientific Research from the Japan Society for Promotion in Science (JSPS).

Supporting Information Available: Experimental procedures and characterization of the products **2** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL701951N

---

(7) Yoshikawa, E.; Gevorgyan, V.; Asao, N.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6781.

(8) Heydari, A.; Alijanianzadeh, R. *Chem. Lett.* **2003**, 226.

(9) Asao, N.; Asano, T.; Ohishi, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4817.

(10) Platinum-catalyzed thiosilylation proceeds in a cis fashion. Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1998**, *120*, 8249.