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

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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.

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

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)



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)-

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Table 1.	Cyclization	of (ortho-All	kynylpheny	lthio)silanes	1 <i>a</i>

entry	1	\mathbb{R}^1	${ m SiR^{2}_{3}}$	AuCl (mol %)	time(h)	2	yield (%)
1	1a	<i>n</i> -Pr	$Si(i-Pr)_3$	2	5	2a	98
2	1b	Су	$Si(i-Pr)_3$	25	21	2b	44
3	1c	$4\text{-}i\text{-}\mathrm{Pr}_2\mathrm{NC}_6\mathrm{H}_4$	$Si(i-Pr)_3$	10	18	2c	89
4	1d	2,4-(MeO) ₂ C ₆ H 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	$2\mathbf{g}$	97
8	1ĥ	$4 - F_3 CC_6 H_4$	$Si(i-Pr)_3$	10	21	2h	60
9	1i	2-(1-methylpyrrolyl)	$Si(i-Pr)_3$	10	18	2i	90
10	1j	<i>n</i> -Hex	$Si(i-Pr)_2(s-Bu)$	2	6	2j	quant
11	1k	n-Pr	SiPh ₃	10	2	2k	40

silanes **1** produced 3-silylbenzo[*b*]thiophenes **2** in good to excellent yields (eq 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 AuCl₃, AuCl(CO), and AuBr₃ as the catalyst, instead of AuCl, gave 2a in lower yields, whereas other metal complexes, such as PtCl₂, Pt(PPh₃)₄, PdCl₂, CuCl₂, Ag(OTf), and InCl₃, did not promote the present reaction at all. The reaction of 1a using benzene, hexane, CH2Cl2, 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 (6alkynylbenzodioxol-5-ylthio)silane 11 proceeded smoothly, affording the tricyclic compound 21 in 72% yield (eq 2).



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

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

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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 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 fluorosubstituted substrates **10** and **1p** (eq 4). The reaction of **10** having a fluorine atom at R³ afforded **20** 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 R¹ giving the

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product **2h** in a lower yield (Table 1, entry 8). On the contrary, the reaction of **1p** bearing a fluorine atom at \mathbb{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.

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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.

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