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Remarkable reactivity enhancement with Sb···N inter-coordination of ethynyl-1,5-azastibocines in Pd-catalyzed cross-coupling reactions with organic halides

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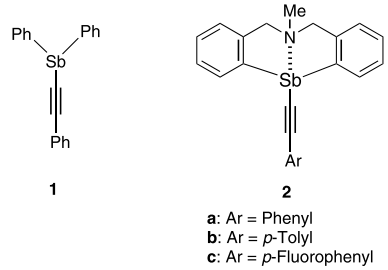
Abstract—The reaction of 12-arylethynyl-6-methyl-5,6,7,12-tetrahydrodibenzo[*c*,*f*][1,5]-azastibocines with organic halides such as acyl halides and aryl halides in the presence of $PdCl_2(PPh_3)_2$ as a catalyst led to the formation of cross-coupling products, alkynyl ketones and diaryl acetylenes, in good yields. The reactivity of the ethynyl group on the 1,5-azastibocines was far superior to that on diphenyl(phenylethynyl)stibane, which brought about marked improvement in the reaction conditions (lower temperature and shorter reaction time) and in the yields of the cross-coupling products. Single-crystal X-ray analysis of the ethynyl-1,5-azastibocine showed the presence of intramolecular Sb···N interaction which should be responsible for the remarkable reactivity enhancement of the 1,5-azastibocines for this type of reaction.

The chemistry of organoantimony compounds has attracted much interest over the years on account of their widespread use for organic synthesis. [1] For example, many organoantimony compounds have been reported to be useful for a wide range of carbon–carbon bond-forming reactions, such as Wittig-type condensation,[2] transition metal-catalyzed self-[3] and cross-coupling reactions,[4–7] carbonylations,[8] and photoreactions[9] as substrates, and for transition metal-catalyzed asymmetric reaction as chiral auxiliaries.[10] However, most of the antimony compounds substantially used are restricted to peraryl antimony(III) and (V) derivatives due to their easy accessibility and simple handling with high stability. In the course of our studies on the synthesis of new organoantimony compounds and their utilization as synthetic reagents for organic synthesis,[9b,10,11] we have recently reported that the reaction of diphenyl(phenylethynyl)stibane **1** with acid halides in the presence of a Pd-catalyst resulted in cross-coupling reaction to give alkynyl ketones, in good to moderate yields.[12] As a continuation of our studies on this type of coupling reaction, we now disclose that treatment of 12-arylethynyl-6-methyl-5,6,7,12-tetrahydrodibenzo[*c*,*f*]-[1,5]azastibocines **2a**–**c** with organic halides such as acyl halides **3** and aryl halides **5** affords the corresponding ethynyl derivatives **4** and **6** through the same type of coupling reaction. In the reaction of the ethynyl-1,5-azastibocines **2a**–**c**, significant reactivity enhancement of the ethynyl groups toward the coupling reaction was observed, in comparison with the reaction by use of the ethynylstibane **1** (Fig. 1).

The key starting compounds, ethynyl-1,5-azastibocines **2a**–**c**,[13] could be easily prepared from bis(*o*-bromobenzyl)methyl amine via 12-bromo-6-methyl-5,6,7,12-tetrahydrodibenzo[*c*,*f*][1,5]-azastibocine, by a similar



1 **2**

a: Ar = Phenyl
b: Ar = *p*-Tolyl
c: Ar = *p*-Fluorophenyl

Figure 1.

Keywords: antimony compounds; alkynyl stibane; 1,5-azastibocine; coupling reactions; palladium catalyst.

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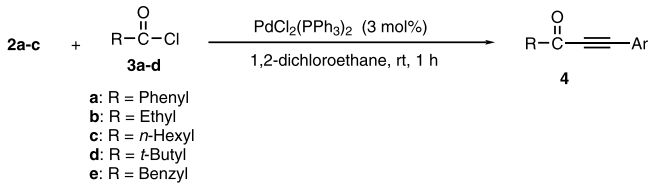
Table 1. Palladium-catalyzed coupling reaction of 1,5-azastibocines **2a–c** with acyl chlorides **3a–e**[a]



Entry	Sb reagent	Acid chloride	Yield of **4** (%)[b]
1	**2a**	**3a**	86 (87)[c]
2	**2b**	**3a**	81 (80)[d]
3	**2c**	**3a**	84 (76)[d]
4	**2a**	**3b**	78 (37)[c]
5	**2a**	**3c**	79 (47)[c]
6	**2a**	**3d**	63 (26)[c]
7	**2a**	**3e**	72 (33)[c]

[a] The reaction was carried out with Sb reagent (**2**: 1 mmol), **3** (1.2 mmol), and $PdCl_2(PPh_3)_2$ (3 mol%) in 1,2-dichloroethane (5 ml) at rt for 1 h under argon atmosphere.

[b] Isolated yield. The values in parentheses show the yields of **4** when the reaction was performed at 80°C for 2–8 h using **1** instead of **2** as an alkynylation reagent.

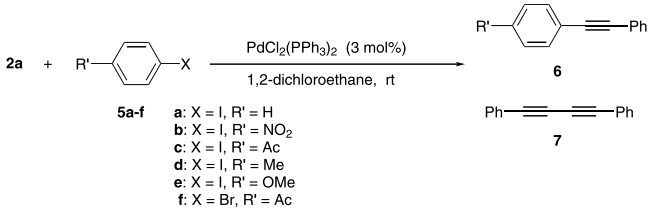
[c] See ref. 12.

[d] At 80°C for 5 h.

procedure reported by Akiba and co-workers.[14] In order to elaborate the reaction with the 1,5-azastibocines **2a–c**, we first examined the transition metal-catalyzed reaction of **2a–c** with acyl chlorides **3a–e**, and the results are summarized in Table 1. The 1,5-azastibocines **2a–c** on treatment with benzoyl chloride **3a** by use of $PdCl_2(PPh_3)_2$ as a catalyst in 1,2-dichloroethane at room temperature brought about cross-coupling reaction to give alkynyl ketones **4** in good yields. By comparison with the ethynylstibane **1**, the ability of the ethynyl-1,5-azastibocines **2a–c** was far superior as an alkynylation agent for this type of coupling reaction from the standpoint of the reaction conditions; the reaction temperature and the reaction time for **2a** being at rt for 1 h, whereas those for **1** being at 80°C for 2.5 h (entries 1–3).[12] Moreover, in the reaction of **2a** with aliphatic acyl chlorides **3b–e**, the reaction conditions as well as the yields of the cross-coupling products **4** were more satisfactory than those of **1** (entries 4–7). In all these reactions, a catalytic amount of diaryl-1,3-butadiynes **7** (2–3%) was isolated, and the antimony reagent was recovered as its chloride in 40–50% yield after chromatographic separation of the reaction mixture. These coupling reactions might proceed through a classical Stille-type coupling cycle shown previously,[12] and it is likely that **2** accelerates transformation of $RCOPdL_2Cl$ into $RCOPdL_2$–≡–Ar which is the presumed intermediate for the formation of the coupling product RCO–≡–Ar.

The remarkable high ability of **2a–c** as an alkynylation agent was also disclosed by the reaction of the ethynyl-1,5-azastibocine **2a** with aryl halides **5a–f**. As shown as entry 1 in Table 2, the reaction of **1** with iodobenzene **5a** at 80°C for 24 h gave cross-coupling product **6a** and homo-coupling product **7** in 16 and 47% yields, respectively. On the other hand, the same reaction by use of **2a** instead of **1** afforded **6a** in 58% yield as a main product under far milder reaction conditions than the formers. It was also apparent that the yields of the cross-coupling products **6** were highly dependent on the electronic nature of the aryl iodides **5a–e**. The aryl iodides bearing electron-attracting substituents such as nitro and acetyl groups on the *p*-position on **5** improved not only the reactivity of the iodides but also the yields of the coupling products **6**, whereas those having electron-donating substituents showed lower reactivity. Furthermore, the reaction of **2a** with *p*-bromo-

Table 2. Palladium-catalyzed coupling reaction of 1,5-azastibocine **2a** with aryl halides **5a–f**[a]



Entry	Sb reagent	Aryl halide	Temp.	Time (min)	Yield (%)[b]	
					6	**7**
1	**1**	**5a**	80°C	24 h	16	47
2	**2a**	**5a**	rt	5	58	7
3	**2a**	**5b**	rt	5	95	3
4	**2a**	**5c**	rt	5	98	<1
5	**2a**	**5d**	rt	5	57	12
6	**2a**	**5e**	rt	20	66	10
7	**2a**	**5f**	rt	20	43	16

[a] The reaction was carried out with Sb reagent (**1** or **2a**: 1 mmol), aryl halide (**5**: 1.2 mmol), and $PdCl_2(PPh_3)_2$ (3 mol%) in 1,2-dichloroethane (5 ml) under argon atmosphere.

[b] GC yield.

acetophenone **5f** led to the formation of cross-coupling products **6c**, although the reaction of **1** with the bromide did not afford **6c** under the same reaction conditions. It is well known that aryl bromides and chlorides are less reactive than the corresponding aryl iodides in a variety of transition metal-catalyzed cross-coupling reaction.[15]

In order to elucidate the higher ability of the ethynyl-1,5-azastibocines **2a–c** than that of the ethynylstibane **1** as an alkynylation agent, we performed a single crystal X-ray analysis of **2a**. The results are depicted in Figure 2, along with the selected data.[16] The results show the presence of intramolecular interaction between the antimony and nitrogen atoms in **2a**; the distance between the antimony and nitrogen atoms being 2.538(4) Å which corresponds to 68% of the sum of the van der Waals radii of both elements (3.74 Å).[17] The central antimony atom exhibits a *pseudo*-trigonal-bipyramidal structure in the crystal, and C(1) on the ethynyl moiety and the nitrogen lie approximately *trans* to each other, the bond angle of N–Sb–C(1) being 156.1(1)°. The bond distance between antimony and C(1) [2.172(4) Å] occupying an apical position is longer than those of Sb–C(1′) [2.164(4) Å] and Sb–C(1″) [2.167(5) Å]. It has been well documented that apical bonds are slightly longer than equatorial bonds in a large number of Group 14, 15 and 16 hypervalent compounds.[18] Nevertheless, these results imply that an elongation of the Sb-C(1) bond would be developed by the Sb···N coordination, because single crystal X-ray analysis of phenylethynyl(α-naphthyl)(*p*-tolyl)stibane lacking such coordination shows that the bond length of Sb–$C_{(ethynyl)}$ [2.10 Å] is significantly shorter than those of Sb–$C_{(a\text{-naphthyl})}$ [2.165 Å] and Sb–$C_{(p\text{-tolyl})}$ [2.15 Å].[19] The coordination should arise from an effective donation of the pair of electrons on the nitrogen atom to the σ* orbital formed in the opposite direction of the C(1)–Sb bond. We consider that the activation of the ethynyl group on the 1,5-azastibocine **2a–c** for this type of coupling reactions would be induced by the formation of the hypervalent coordination between the nitrogen and antimony atoms. These are comparable results to those attained with several germanium,[20] tin[21] and bismuth[22] compounds having this class of coordination which show similar high reactivity toward this type of coupling reaction. The details including reaction mechanism and substituent effect on nitrogen of the 1,5-azastibocines in the present reactions are under investigation.

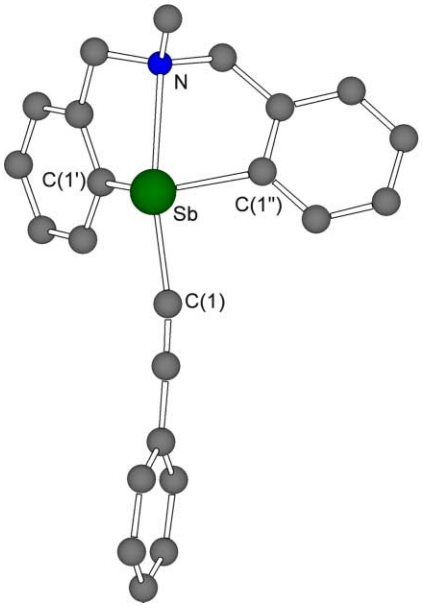


Figure 2. X-Ray structure of **2a**. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å), angles (°), and Sb–N bond distance (Å). Sb–C(1) 2.172(4), Sb–C(1′) 2.167(5), Sb–C(1″) 2.164, C(1)–Sb–C(1′) 92.5(2), C(1)–Sb–C(1″) 91.5(2), C(1′)–Sb–C(1″) 102.9, C(1)–Sb–N 156.1(1), C(1′)–Sb–N 73.2(1), C(1″)–Sb–N 73.8(1), Sb–N 2.538(4).

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