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Thiostannylation of arynes with stannyl sulfides: synthesis and reaction of 2-(arylthio)arylstannanes†

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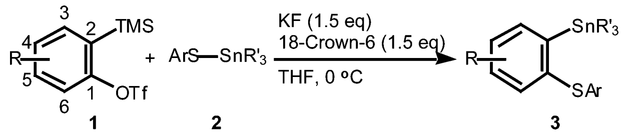
Arynes were found to insert into a sulfur–tin σ-bond of stannyl sulfides to give a variety of 2-(arylthio)arylstannanes, whose carbon–tin bonds were applicable to further transformations.

Addition reactions of an element–element σ-bond to arynes have high synthetic significance, since both elements can be introduced into the carbon–carbon triple bond simultaneously, leading to the formation of polysubstituted arenes in a regioselective manner.[1] In particular, reactions using metallic reagents would be much more attractive in that the resulting carbon–metal bond can be applied to further carbon–carbon bond formation and/or introduction of a functional group. However, only a limited number of reports[2] has been available on the additions of a metal–element bond to arynes thus far, probably due to kinetic instability of arynes causing undesirable side reactions. Recently, we have demonstrated that the additions of a carbon–tin[3a] or silicon–silicon[3b] bond to arynes take place selectively using a palladium catalyst. Herein we report that a sulfur–tin bond of stannyl sulfides adds to arynes without an added catalyst to provide synthetically useful 2-(arylthio)arylstannanes straightforwardly (eqn. (1)). The thiostannylation products thus obtained are convertible into diverse polysubstituted arenes by utilizing their carbon–tin bonds.

(1)

Benzyne, generated *in situ* from 2-(trimethylsilyl)phenyl triflate[4] (**1a**) and a fluoride ion (KF/18-Crown-6), was treated with (tributylstannyl) phenyl sulfide (**2a**) in THF at 0 °C (Table 1, entry 1). The reaction furnished the thiostannylation product, tributyl[2-(phenylthio)phenyl]tin (**3aa**), in 54% yield along with diphenyl sulfide (25%) and tributyl(2-fluorophenyl)tin (6%). In addition to simple benzyne, 4,5-disubstituted arynes (from **1b–1d**) and 2,3-naphthalyne (from **1e**) also provided the corresponding thiostannylation products (**3ba–3ea**) in good yields (entries 2–5). The reaction of sterically congested 3,6-dimethoxybenzyne (from **1f**) or 3,6-dimethylbenzyne (from **1g**) proceeded efficiently as well, giving 61% or 45% yield of the products (entries 6 and 7). Furthermore, stannyl sulfides bearing a *p*-anisyl (**2b**) or *o*-tolyl (**2c**) group could participate in the reaction (entries 8 and 9), and (trimethylstannyl) phenyl sulfide (**2d**) reacted smoothly with benzyne to afford **3ad** in 56% yield (entry 10).[5]

Table 1 Thiostannylation of symmetrical arynes[a]



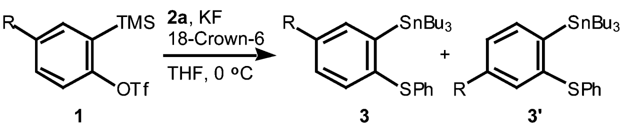
Entry	R	**1**	Ar	R′	**2**	Time (h)	Yield (%)[b]	**3**
1	H	**1a**	Ph	Bu	**2a**	9	54	**3aa**
2	4,5-Me_2	**1b**				24	58	**3ba**
3	4,5-$(CH_2)_3$–	**1c**				24	58	**3ca**
4	4,5-$(CH_2)_4$–	**1d**				29	52	**3da**
5	4,5-$(CH)_4$–	**1e**				19	62	**3ea**
6	3,6-$(MeO)_2$	**1f**				24	61	**3fa**
7	3,6-Me_2	**1g**				51	45	**3ga**
8	H	**1a**	4-$MeOC_6H_4$	Bu	**2b**	3	49	**3ab**
9	H	**1a**	2-MeC_6H_4	Bu	**2c**	4	39	**3ac**
10	H	**1a**	Ph	Me	**2d**	4	56	**3ad**

[a] The reaction was carried out in THF (1 mL) at 0 °C using **1** (0.30 mmol), **2** (0.20 mmol), KF (0.30 mmol) and 18-Crown-6 (0.30 mmol). [b] Isolated yield based on the stannyl sulfide.

We next investigated the thiostannylation of unsymmetrical arynes (Scheme 1). Thus, when 4-substituted arynes (from **1h–1j**) were allowed to react with **2a**, almost equal amounts of regioisomeric products (**3** and **3′**) were produced, indicating that the present reaction certainly proceeds through an aryne intermediate. In marked contrast, the reaction of 4-fluorobenzyne (from **1k**) afforded **3ka** as a major product, where the tributylstannyl moiety was introduced into the *meta*-position of the fluoro substituent. Methoxy or phenyl group in 3-substituted arynes (from **1l** or **1m**) controlled the regioselectivities perfectly to offer **3la** or **3ma** as the sole product, whereas the reaction of 3-methylbenzyne (from **1n**) gave a mixture of **3na** and **3′na** in *ca.* 1 : 1 ratio.

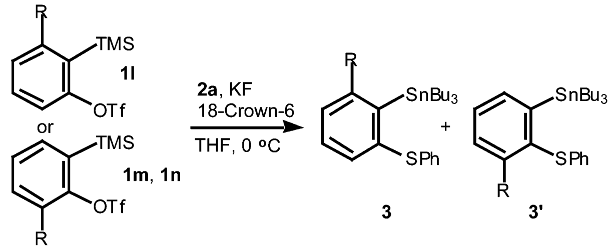
The thiostannylation would be triggered by a nucleophilic attack of a sulfur atom of a stannyl sufide as depicted in Scheme 2.[6,7] The resulting zwitterion (**4**) then undergoes an intramolecular nucleophilic substitution at the stannyl moiety to afford the product (*path A*). Owing to a strong electron-withdrawing effect of a fluorine

4-Substituted Arynes



R	Time (h)	Yield (%)	**3** : **3'**	Product
Me (**1h**)	5	63	*ca.* 1 : 1	**3ha**, **3'ha**
Ph (**1i**)	24	52	*ca.* 1 : 1	**3ia**, **3'ia**
MeO (**1j**)	6	55	*ca.* 1 : 1	**3ja**, **3'ja**
F (**1k**)	48	21	72 : 28	**3ka**, **3'ka**

3-Substituted Arynes



R	Time (h)	Yield (%)	**3** : **3'**	Product
MeO (**1l**)	27	62	> 99 : 1	**3la**
Ph (**1m**)	24	61	> 99 : 1	**3ma**
Me (**1n**)	5	57	*ca.* 1 : 1	**3na**, **3'na**

Scheme 1 Thiostannylation of unsymmetrical arynes.

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b4/b405883f/

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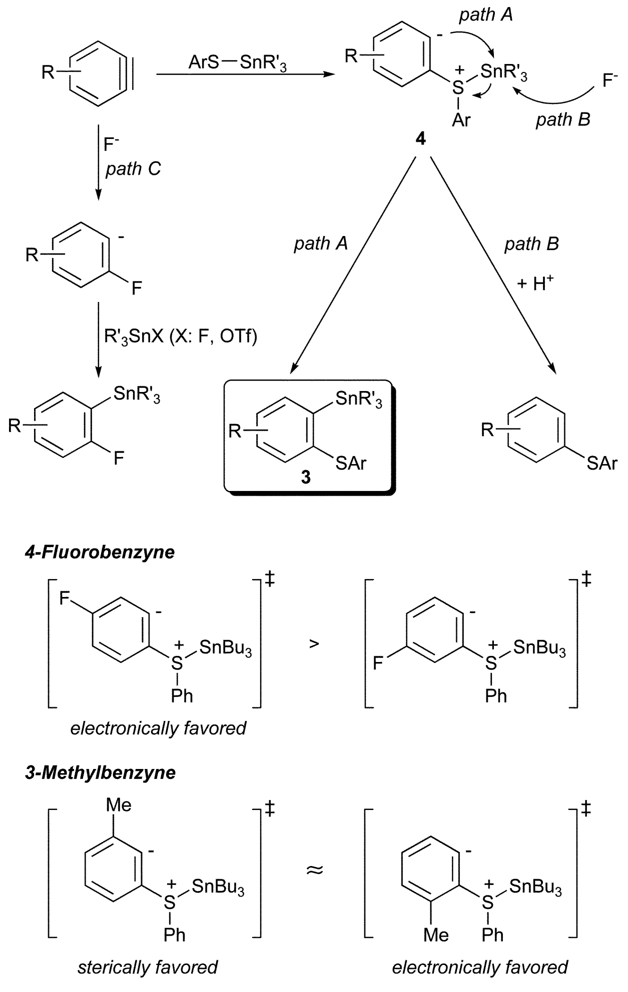
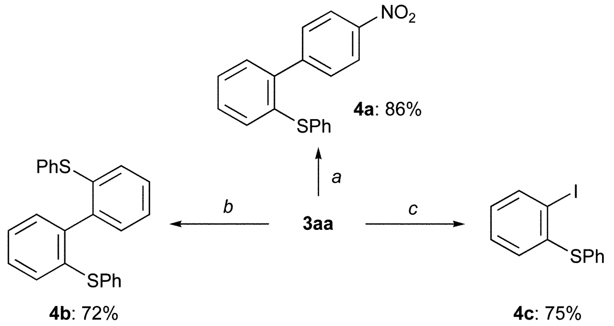
atom in 4-fluorobenzyne, the developing negative charge at the *meta* position (*vs. para*) is stabilized to a greater extent in the transition state for the addition of a sulfur moiety to 4-fluorobenzyne, which leads to the predominant production of **3ka**.[8] In contrast, electronic effects of other substituents in 4-subsituted arynes are so slight that equal addition to both ends of the triple bond takes place. The exclusive formation of **3la** or **3ma** would be attributable to disfavored steric repulsion between a substituent (MeO or Ph) in the aryne and **2a**, which prevents the sulfur atom approaching the *ortho* position of the substituent. In the case of 3-methylbenzyne, the steric effect should compete with the electron-donating effect of the methyl group which prefers generation of the anion in **4** at the *meta* position, and a mixture of **3na** and **3′na** is formed.[6] A diaryl sulfide should arise from a nucleophilic attack of a fluoride ion to a stannyl moiety (*path B*), and formation of a (2-fluoroaryl)tin can be ascribed to a reaction of a 2-fluoroaryl anion with a stannyl electrophile (*path C*).[9]

Finally, synthetic utility of the thiostannylation product has been demonstrated by transformation to variously substituted arenes (Scheme 3). Thus, cross-coupling of **3aa** with 4-nitroiodobenzene gave **4a** in 86% yield. Furthermore, homocoupling[10] or iodolysis of **3aa** afforded biaryl **4b** or aryl iodide **4c**, respectively.



Scheme 2 Plausible reaction pathways.



Reagents and Conditions: (*a*) 4-$NO_2C_6H_4I$ (1.5 eq), CuI (0.75 eq), $Pd(PPh_3)_4$ (0.1 eq), DMF, 50 °C, 16 h ; (*b*) CuCl (1 eq), $CuCl_2$ (1 eq), $Pd(PPh_3)_4$ (0.1 eq), DMSO, 50 °C, 2 h; (*c*) I_2 (1 eq), CH_2Cl_2, r.t., 3 h.

Scheme 3 Transformation of the thiostannylation product.

In conclusion, we have disclosed that the thiostannylation of arynes takes place with stannyl sulfides to offer diverse 2-(arylthio)arylstannanes straightforwardly, which can be utilized for the synthesis of substituted arenes. Further studies on insertion reactions of arynes into other element–element σ-bonds are in progress.

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Notes and references

1 (*a*) Se–Se and Te–Te σ-bond: N. Petragnani and V. G. Toscano, *Chem. Ber.*, 1970, **103**, 1652; (*b*) S–S σ-bond: J. Nakayama, T. Tajiri and M. Hoshino, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 2907; (*c*) N–CO σ-bond: H. Yoshida, E. Shirakawa, Y. Honda and T. Hiyama, *Angew. Chem. Int. Ed.*, 2002, **41**, 3247.

2 (*a*) Si–C σ-bond: Y. Sato, Y. Kobayashi, M. Sugiura and H. Shirai, *J. Org. Chem.*, 1978, **43**, 199; (*b*) Sn–Cl σ-bond: C.-L. Tseng, S.-H. Tung and K.-M. Chang, *Chem. Abs.*, 1964, **61**, 7035; (*c*) B–O σ-bond: C.-L. Tseng, K.-M. Chang and S.-H. Tung, *Chem. Abs.*, 1964, **61**, 16084.

3 (*a*) H. Yoshida, Y. Honda, E. Shirakawa and T. Hiyama, *Chem. Commun.*, 2001, 1880; (*b*) H. Yoshida, J. Ikadai, M. Shudo, J. Ohshita and A. Kunai, *J. Am. Chem. Soc.*, 2003, **125**, 6638.

4 Y. Himeshima, T. Sonoda and H. Kobayashi, *Chem. Lett.*, 1983, 1211.

5 A diaryl sulfide (5–21%) and tributyl(2-fluoroaryl)tin (trace–9%) were formed as by-products in all cases.

6 For a review on the nucleophilic couplings with arynes, see: S. V. Kessar, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Flemming, Pergamon Press, Oxford, 1991, **vol. 4**, pp. 483–515.

7 For reported examples on the nucleophilic couplings of sulfides with arynes, see: (*a*) J. Nakayama, S. Takeue and M. Hoshino, *Tetrahedron Lett.*, 1984, **25**, 2679; (*b*) G. M. Blackburn, W. D. Ollis, C. Smith and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1969, 99.

8 A similar regioselectivity was observed in the nucleophilic couplings with 4-chlorobenzyne: (*a*) J. F. Bunnett and C. Pyun, *J. Org. Chem.*, 1969, **34**, 2035; (*b*) J. F. Bunnett and J. K. Kim, *J. Am. Chem. Soc.*, 1973, **95**, 2254.

9 Treatment of **2a** with KF/18-Crown-6 did not give a thiophenoxide ion, which would add to an aryne, if any. Moreover, destannylation of **3aa** did not occur in the presence of KF/18-Crown-6. These results prompt us to propose *path B* in the formation of a diaryl sulfide.

10 E. Shirakawa, Y. Nakao, T. Tsuchimoto and T. Hiyama, *Chem. Commun.*, 2002, 1962.