Palladium-catalysed dimerisation–distannylation of arynes: synthesis and reaction of 2,2′-distannylbiaryls†

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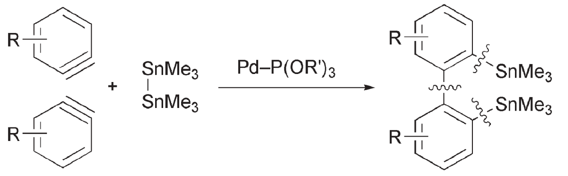
Two molar amounts of arynes were found to insert into a Sn–Sn bond of a distannane in the presence of a sub-stoichiometric amount of a palladium-phosphite complex, affording straightforwardly 2,2′-distannylbiaryls.

The transition metal-catalysed cross- or homocoupling reactions of aryl halides (pseudohalides) and/or arylmetal reagents have proven to be the most powerful and popular method for the synthesis of biaryls, which constitute an important class of such invaluable organic compounds as pharmaceuticals, agrochemicals, dyes and functional materials.[1] Although a wide variety of biaryls can efficiently be constructed depending upon the coupling reactions, these methods are usually unsuitable for the synthesis of metallated biaryls, being potent synthetic intermediates. Hence, development of new methodology for assembling biaryl skeletons is challenging, and allows efficient access to largely unexploited classes of biaryls.[2]

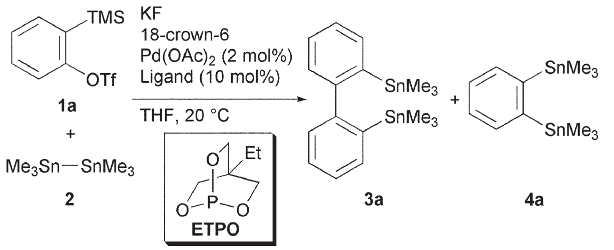
We have recently reported the palladium-catalysed insertion reactions of arynes into an element–element σ-bond, that is, carbostannylation (C–Sn σ-bond),[3] disilylation (Si–Si σ-bond)[4] and distannylation (Sn–Sn σ-bond),[5] which afford diverse 1,2-disubstituted arenes in a straightforward manner.[6,7] Since then we have been studying ligand effects on the insertion reactions, and have found dimerisation–distannylation of arynes occurs in the presence of a palladium–phosphite complex. Herein we disclose the first demonstration of an insertion reaction into an element–element σ-bond being accompanied by dimerisation of arynes, which offers a new method to assemble biaryl skeletons with introducing two stannyl moieties into their 2- and 2′-positions (eqn (1)).[8]



(1)

First, a palladium-catalysed reaction of *in situ*-generated benzyne (from **1a** and KF/18-crown-6)[9] with hexamethyldistannane (**2**) was examined using various ligands (Table 1). By use of a bicyclic phosphite, ETPO (4-ethyl-2,6,7-trioxa-1-phosphabicyclo-[2.2.2]octane),[10] we observed that insertion of two molar amounts of benzyne into the Sn–Sn σ-bond took place predominantly to afford 2,2′-bis(trimethylstannyl)biphenyl (**3a**) and 1,2-bis-(trimethylstannyl)benzene (**4a**) in 62% and 15% yield, respectively (entry 1).[11] In sharp contrast, the reaction with *t*-OcNC (1,1,3,3-tetramethylbutyl isocyanide) gave **4a** as the major product (entry 2).[5] Other ligands were also surveyed, however, none of them were found to be suitable for the dimerisation–distannylation, except for the case with trimethylphosphite, which provided a 16% yield of **3a** (entries 3–8).[12,13]

Table 1 Ligand effect on the reaction of benzyne with **2**[a]



Entry	Ligand	Time/h	Yield of **3a**[b] (%)	Yield of **4a**[b] (%)
1	ETPO	22	62	15
2	*t*-OcNC	3	Trace	42
3	$P(OMe)_3$	4	16	18
4	$P(Oi\text{-}Pr)_3$	19	0	10
5	$P(OPh)_3$	26	0	19
6	PPh_3	6	0	0
7	$P(C_6F_5)_3$	13	0	0
8[c]	None	3	0	16

[a] The reaction was carried out in THF (2 mL) at 20 °C using **1a** (0.66 mmol), **2** (0.22 mmol), KF (1.32 mmol) and 18-crown-6 (1.32 mmol) in the presence of $Pd(OAc)_2$ (4.4 μmol) and a ligand (0.022 mmol). [b] Isolated yield based on **2**. [c] $Pd(dba)_2$ was used instead of $Pd(OAc)_2$.

We next investigated the dimerisation–distannylation of various arynes using ETPO as a ligand (Table 2). Similarly to the case of benzyne, 4,5-dimethyl- (from **1b**) or 4,5-diethylbenzyne (from **1c**) reacted with **2**, providing the corresponding 2,2′-distannylbiaryls in 53% or 52% yield (entries 1–3). The reaction was also applicable to cyclohexene- (from **1d**), cyclopentene-condensed aryne (from **1e**) or 4,5-dibutylbenzyne (from **1f**) to give the products in moderate yields (entries 4–6), whereas the yields of the reaction of 4,5-dihexylbenzyne (from **1g**) or 2,3-naphthalyne (from **1h**) were somewhat low (entries 7 and 8). Owing to steric hindrance around the triple bonds, the reaction of 3,6-dimethylbenzyne (from **1i**) was rather sluggish (entry 9), and furthermore, 3,6-dimethoxybenzyne (from **1j**) did not give the dimerisation–distannylation product at all (entry 10).

An unsymmetrical aryne, 4-methylbenzyne (from **1k**), could also participate in the dimerisation–distannylation to afford a 52% yield

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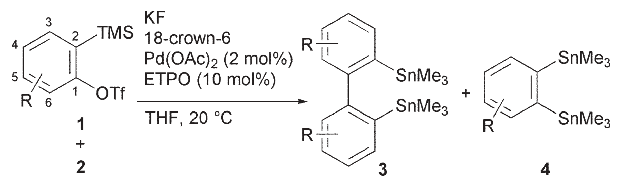
Table 2 Dimerisation–distannylation of arynes[a]

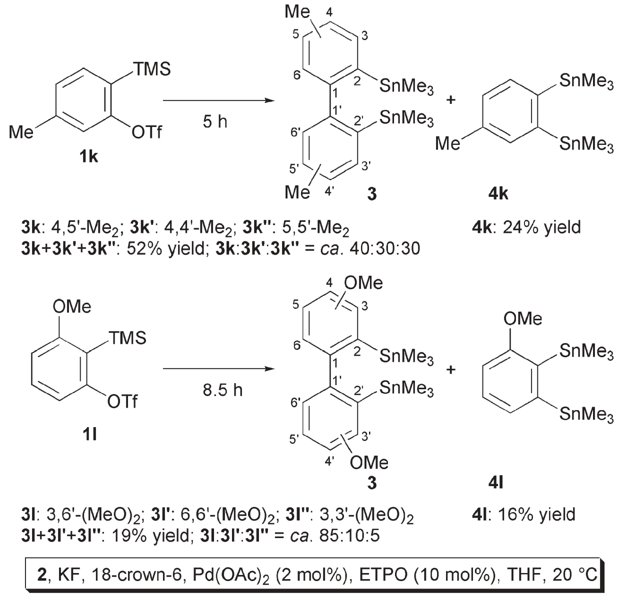


Entry	R in **1**	Time/h	Yield[b] of **3** (%)	Yield of **4**[b] (%)	Products
1	H (**1a**)	22	62	15	**3a**, **4a**
2	4,5-Me_2 (**1b**)	3	53	19	**3b**, **4b**
3	4,5-Et_2 (**1c**)	5	52	17	**3c**, **4c**
4	4,5- –$(CH_2)_4$– (**1d**)	3	54	18	**3d**, **4d**
5	4,5- –$(CH_2)_3$– (**1e**)	8	45	29	**3e**, **4e**
6	4,5-Bu_2 (**1f**)	4.5	41	19	**3f**, **4f**
7[c]	4,5-Hex_2 (**1g**)	2	36	20	**3g**, **4g**
8[d]	4,5- –$(CH)_4$– (**1h**)	2.5	31	26	**3h**, **4h**
9	3,6-Me_2 (**1i**)	18.5	16	4	**3i**, **4i**
10	3,6-$(MeO)_2$ (**1j**)	8	0	0	—

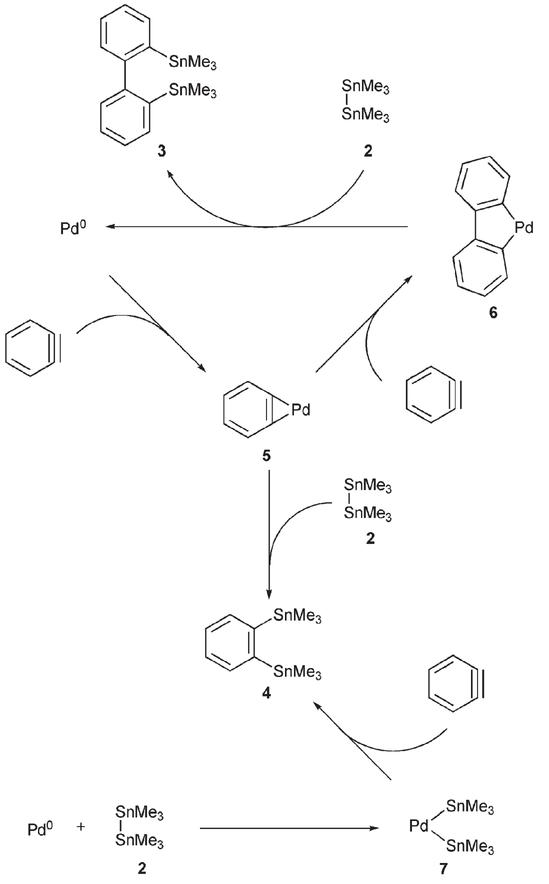
[a] The reaction was carried out in THF (2 mL) at 20 °C using **1** (0.66 mmol), **2** (0.22 mmol), KF (1.32 mmol) and 18-crown-6 (1.32 mmol) in the presence of $Pd(OAc)_2$ (4.4 µmol) and ETPO (0.022 mmol). [b] Isolated yield based on **2**. [c] KF = 2.64 mmol, 18-crown-6 = 2.64 mmol. [d] **1h** = 1.32 mmol, KF = 2.64 mmol, 18-crown-6 = 2.64 mmol.

of a mixture of three regioisomers (**3k**, **3k′** and **3k″**) in the ratio of *ca.* 40:30:30, respectively, which indicates that a substituent at the 4-position of an aryne exerts little effect on the regioselectivity of the reaction (Scheme 1). In sharp contrast, the reaction of 3-methoxybenzyne (from **1l**) proceeded regioselectively, resulting in the predominant formation of **3l** (**3l**:**3l′**:**3l″** = *ca.* 85:10:5).[14]

An aryne is known to readily undergo oxidative cyclisation with a low-valent transition-metal complex.[15] Moreover, neither trimerisation–distannylation products nor higher oligomers were generated in the course of the present study. Hence, the present reaction should be initiated by formation of a palladacyclopropene (**5**) from a palladium–ETPO complex and an aryne (Scheme 2). Subsequent interaction of **5** with a second aryne gives a Pd(2,2′-biphenyl) species (**6**),[16] which reacts further with **2** to afford a distannylbiaryl (**3**).[17] Although a by-product, 1,2-distannylarene **4**, may also be produced from the reaction between **2** and **5**, another pathway involving oxidative adduct **7** is possibly operative in this case as we reported previously.[5] The regioselectivity observed in the reaction of 3-methoxybenzyne can be rationally explained by preferential formation of palladacyclopentadiene **6l**, resulting from insertion of second 3-methoxybenzyne into the sterically less hindered site (*site a*) of **5l** with the orientation which avoids unfavorable steric repulsion between the methoxy group of the incoming aryne and the palladium atom (Scheme 3).

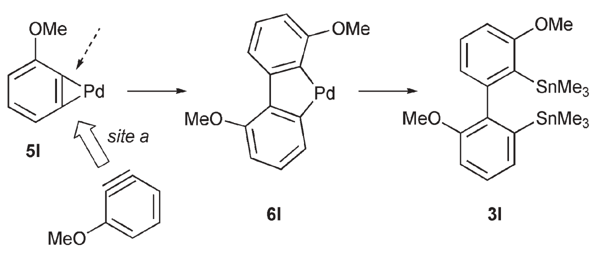


Scheme 1 Dimerisation–distannylation of unsymmetrical arynes.

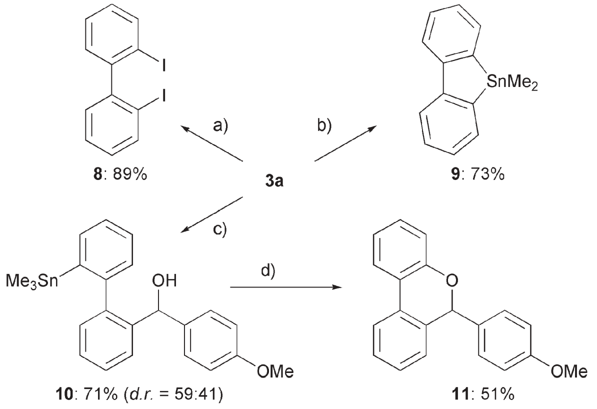


Scheme 2 Catalytic cycle for the dimerisation–distannylation.

Synthetic utility of the dimerisation–distannylation product has been demonstrated by transformation to variously substituted biaryls (Scheme 4). Thus, iododestannylation of **3a** gave 2,2′-diiodobiphenyl (**8**) in 89% yield. Furthermore, an aryl anion, generated from **3a** with methyllithium, underwent intramolecular



Scheme 3 Regioselectivity in the reaction of 3-methoxybenzyne.



Reagents and conditions: a) I_2 (2.1 eq), CH_2Cl_2, 20 °C, 1.5 h; b) MeLi (1.5 eq), THF, 0 °C, 1.5 h; c) MeLi (1.5 eq), THF, -78 °C, 1 h, then 4-$MeOC_6H_4CHO$ (3 eq), -78 °C to 20 °C, 18 h; d) $CuCl_2$ (1 eq), DMSO, 50 °C, 8 h.

Scheme 4 Synthesis of substituted biaryls using **3a**.

cyclisation at 0 °C to produce a 73% yield of 9,9-dimethyl-9-stannafluorene (**9**). On the other hand, the aryl anion could be trapped by 4-methoxybenzaldehyde at −78 °C to afford stannyl-substituted benzhydrol **10** as a mixture of diastereomers (ratio = 59:41) in 71% yield, which was further convertible into a dibenzopyran derivative (**11**) *via* intramolecular arylation of the hydroxyl moiety in the presence of copper(II) chloride.[18]

In conclusion, we have disclosed the first example of an insertion reaction of two molar amounts of arynes into an element–element σ-bond, which is efficiently catalysed by a palladium–ETPO complex. Based upon the present reaction, diverse 2,2′-distannylbiaryls, which are hardly accessible by conventional methods, can be obtained straightforwardly.[19] Moreover, the resulting products have been demonstrated to be convertible into variously substituted biaryls utilizing their carbon–tin bonds. Studies on the improvement of the yield and selectivity of products and on details of the reaction mechanism as well as on expansion of the reaction scope are in progress.

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12 We also examined an ETPO-type ligand bearing such a substituent as H, Me, Ph or *t*-Bu at its 4-position, however, none of them improved the yield and selectivity of **3a**.

13 Other reaction conditions employed for optimisation: *solvent*: DME, *n*-Bu_2O; *temperature*: 0 °C, 50 °C; *Pd source*: $Pd(dba)_2$, $Pd(acac)_2$, $Pd(\eta^5\text{-}C_5H_5)(\eta^3\text{-}C_3H_5)$, $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$.

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