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Author(s)	Yoshida, Hiroto; Kubo, Teruhiko; Kuriki, Hitoshi; Osaka, Itaru; Takaki, Ken; Ooyama, Yousuke
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Relation	



Ligand-Free Copper-Catalyzed Cyano- and Alkynylstannylation of Arynes

Hiroto Yoshida,* Teruhiko Kubo, Hitoshi Kuriki, Itaru Osaka, Ken Takaki and Yousuke Ooyama

This paper is dedicated to Professor Tamejiro Hiyama on the occasion of his 70th birthday.

Abstract: A carbon–carbon triple bond of arynes was found to undergo cyanostannylation with a tin cyanide under CuCN catalysis to afford diverse *ortho*-cyanoarylstannanes in high yield. The copper catalyst was also effective for alkynylstannylation of arynes, and the resulting alkynylstannylated products were demonstrated to be convertible into biologically active compounds and a dye for dye-sensitized solar cell.

Much attention has been riveted on the development of metal-catalyzed addition reactions of cyano-containing σ -bonds across unsaturated carbon–carbon bonds, because these attractive reactions allow a versatile cyano functional group and another valuable functionality including boron,^[1] carbon,^[2] nitrogen,^[3] oxygen,^[4] silicon,^[5] sulfur,^[6] germanium^[7] or bromine^[8] to be installed synchronously into carbon frameworks in regio- and stereoselective manners. In view of the remarkable synthetic utility of organostannanes,^[9] whose carbon–tin bonds are facilely convertible into carbon–carbon and carbon–heteroatom bonds, the catalytic cyanostannylation of unsaturated carbon–carbon bonds with tin cyanides, which have been mainly used as nucleophilic cyanating reagents or catalysts with carbon electrophiles,^[10] is certainly of high synthetic value, however, this transformation has thus far remained untapped except for the platinum-catalyzed *trans*-addition to acetylenedicarboxylates.^[11] We report herein that the unprecedented cyanostannylation of a transient carbon–carbon triple bond of arynes^[12,13] smoothly occurs under copper catalysis,^[14,15] and that the copper catalyst is also effective for alkynylstannylation of arynes.^[16]

The cyanostannylation has proven to proceed successfully by treating a THF solution of tributyltin cyanide (**1a**) and benzyne, generated from 2-(trimethylsilyl)phenyl triflate (**2a**)^[17] and a fluoride ion (KF/18-crown-6), with copper(I) cyanide (5 mol %) to give tributyl(2-cyanophenyl)stannane (**3aa**) in 72% yield (Figure 1). The striking feature of the present reaction is that no additional ligand is necessary for the smooth transformation: widely available CuCN efficiently promoted the cyanostannylation of such symmetrical arynes as 2,3-naphthalene (from **2b**) and 4,5-dialkylbenzenes (from **2c** or **2d**). The reaction of 3-bromobenzene (from **2e**) or 3-methoxybenzene (from **2f**) took place with perfect regioselectivity to afford the cyanostannylated products (**3ae** and **3af**) bearing the cyano group at the *meta* position to the

substituents,^[18] where the reactive C–Br bond remained intact in the former case. On the other hand, a mixture of regioisomers (**3ag** and **3'ag**) was formed from **2g** or **2'g** in almost the same yield and regioselectivity, verifying the cyanostannylation included the formation of a common intermediate, 4-methylbenzyne.

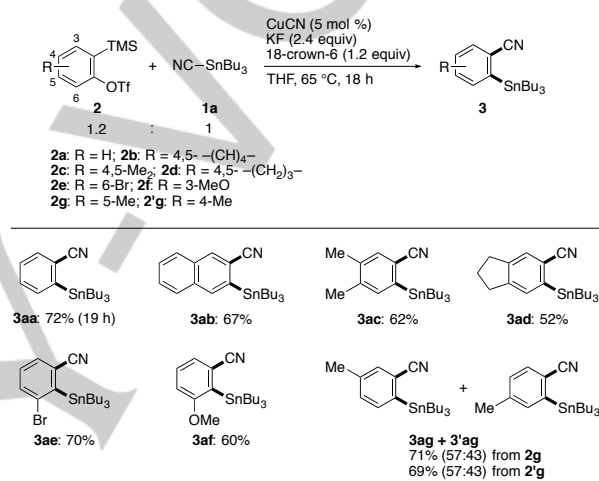


Figure 1. CuCN-catalyzed cyanostannylation of arynes. Conditions: **1a** (0.30 mmol), **2** (0.36 mmol), CuCN (0.015 mmol), KF (0.72 mmol), 18-crown-6 (0.36 mmol), THF (3 mL), 65 °C. Regioisomeric ratio was determined by ¹H NMR.

The CuCN catalytic system has turned out to be also effective for the alkynylstannylation of arynes (Figure 2).^[19] Thus treatment of tributyl(hexyn-1-yl)stannane (**1b**) with **2a** under similar conditions to those of the cyanostannylation provided a 77% yield of alkynylstannylated product **3ba**, and symmetrical arynes (from **2b–2d**) were convertible into the respective products (**3bb–3bd**) in good yields. It should be noted that the regioselectivity with 3-bromobenzene (from **2e**) and 3-methoxybenzene (from **2f**) could totally be regulated to furnish *meta*-alkynylated products **3be** and **3bf**,^[18] being in marked contrast to the result with the previous iminophosphine–palladium-catalyzed alkynylstannylation.^[16] In addition, preferential addition of the alkynyl group to the β -position was observed with 1,2-naphthalene (from **2h**),^[20] and the intermediacy of arynes was also confirmed by the reaction of 4-methylbenzyne (from **2g**) or 4-methoxybenzyne (from **2i**), in which a regioisomeric mixture was generated in almost equal ratio. Other alkynylstannanes with alkyl (**3ca** and **3da**), aryl (**3ea**), alkenyl (**3fa**) or propargyl ether (**3ga**) moiety could participate in the reaction (Figure 3), and furthermore high functional group compatibility was demonstrated by use of alkynylstannanes having a C–Cl bond (**3ha** and **3ia**), ester (**3ja**), hydroxy (**3ka**) or acetal (**3la**) moiety. Although the reaction mixture inevitably contains a fluoride ion for aryne generation, a

[a] Prof. Dr. Hiroto Yoshida, Teruhiko Kubo, Hitoshi Kuriki, Prof. Dr. Itaru Osaka, Prof. Dr. Ken Takaki, Prof. Dr. Yousuke Ooyama
Department of Applied Chemistry, Graduate School of Engineering
Hiroshima University
Higashi-Hiroshima (Japan)
E-mail: yhiroto@hiroshima-u.ac.jp

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C(sp)–Si bond of **3ma** was found to be tolerable throughout the reaction.

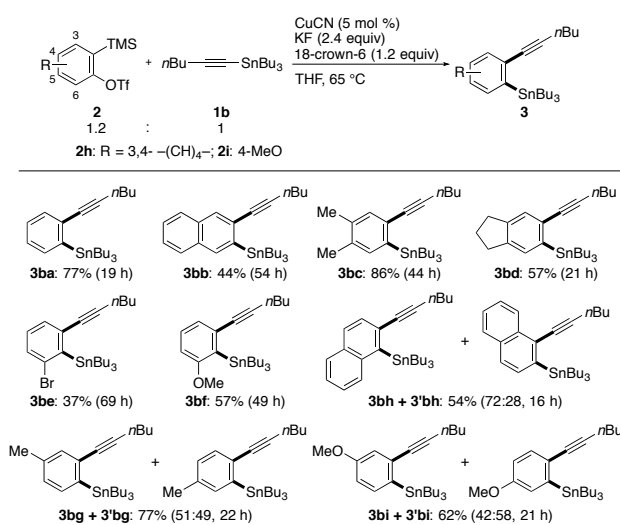


Figure 2. CuCN-catalyzed alkynylstannylation with hexynylstannane. Conditions: **1b** (0.30 mmol), **2** (0.36 mmol), CuCN (0.015 mmol), KF (0.72 mmol), 18-crown-6 (0.36 mmol), THF (3 mL), 65 °C. Regioisomeric ratio was determined by ¹H or ¹¹⁹Sn NMR.

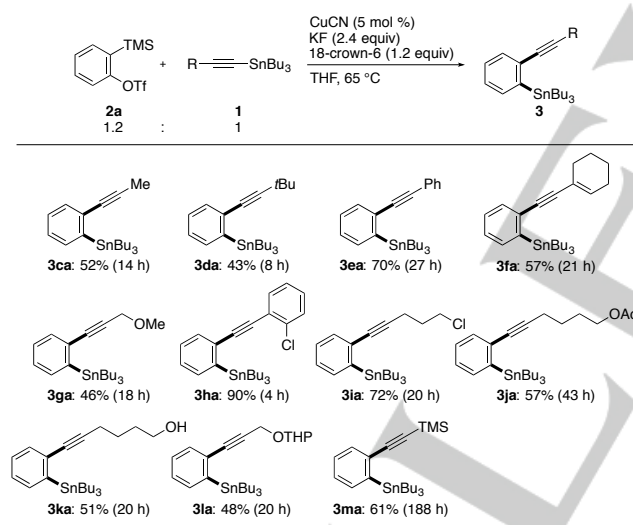
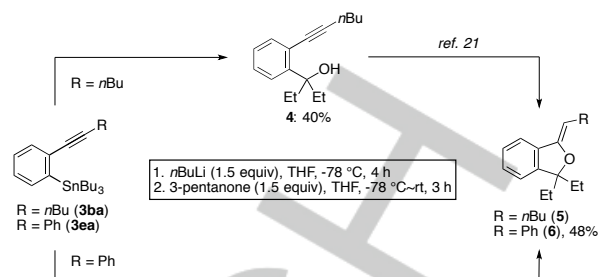


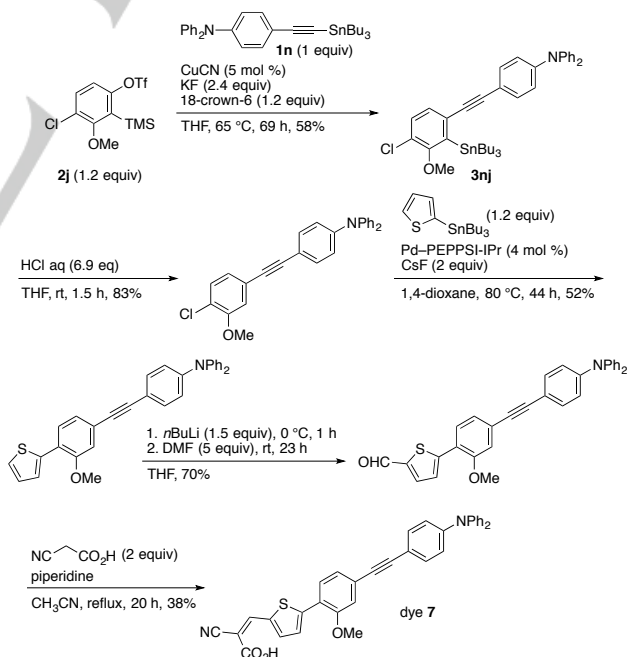
Figure 3. CuCN-catalyzed alkynylstannylation with various alkynylstannane. Conditions: **1** (0.30 mmol), **2a** (0.36 mmol), CuCN (0.015 mmol), KF (0.72 mmol), 18-crown-6 (0.36 mmol), THF (3 mL), 65 °C.

Synthetic versatility of the alkynylstannylation products has been exemplified by transforming **3ba** into tertiary benzylic alcohol **4**, which was reported to be convertible into



Scheme 1. Transformation into antidepressant phthalanes.

dihydroisobenzofuran **5** of antidepressant activity,^[21,22] via tin–lithium exchange followed by capture with 3-pentanone (Scheme 1). Similar treatment of **3ea** was unexpectedly accompanied by cyclization, resulting in the direct production of another potential antidepressant agent **6**.^[22] Moreover, we have also demonstrated that the regioselective alkynylstannylation using **1n** and a chloro-substituted aryne (from **2j**) can be applied to generation of a donor–acceptor diarylalkyne dye (**7**) for a dye-sensitized solar cell (DSSC)^[23] by the Stille coupling–formylation–Knoevenagel condensation sequence (Scheme 2). A DSSC based on **7** showed an η (solar energy-to-electricity conversion yield) value of 1.5% with J_{SC} (short-circuit photocurrent density) of 5.2 mA cm⁻², V_{OC} (open-circuit photovoltage) of 512 mV and ff (fill factor) of 0.56.

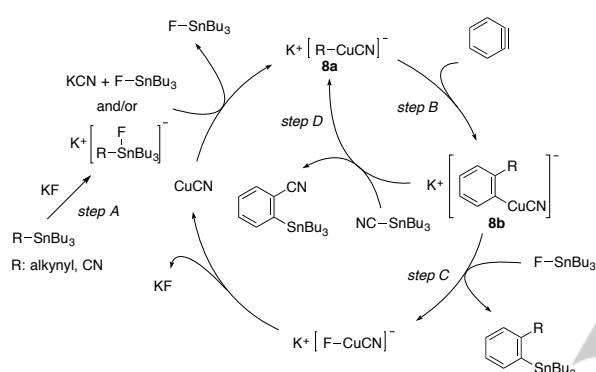


λ_{max}^{abs} (nm) ^a	J_{SC} (mA cm ⁻²)	V_{OC} (V)	ff	η (%)
431	5.20	0.51	0.56	1.50

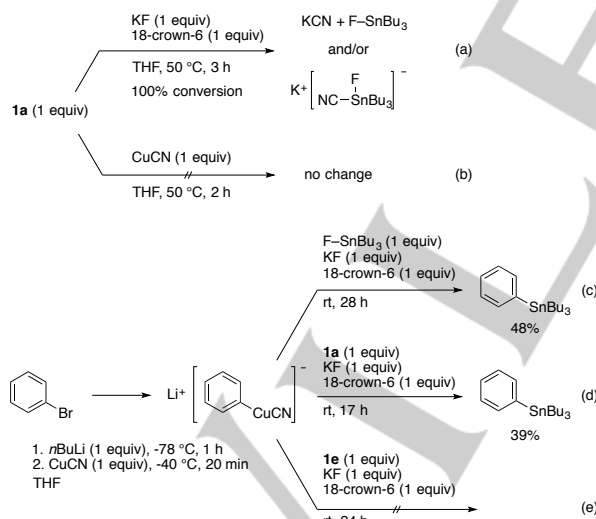
^a In 1,4-dioxane.

Scheme 2. Transformation into a dye for a DSSC.

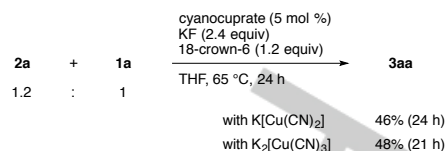
The present cyano(or alkynyl)stannylation may be triggered by formation of a potassium cyanocuprate(I) (**8a**) and tributyltin fluoride via action of a fluoride ion on an organostannane (*step A*, Scheme 3). Positive interaction between **1a** and a fluoride ion, which may imply the formation of tributyltin fluoride and/or cyano(fluoro)stannate, was observed in the ^{119}Sn NMR spectrum, in which the peak of **1a** disappeared completely [Eq. (a) of Scheme 4].^[24] The crucial effect of a fluoride ion on the activation of an organostannane was also confirmed by a stoichiometric reaction of **1a** with CuCN in the absence of a fluoride ion, where **1a** totally remained unchanged [Eq. (b)]. Although we could not obtain direct evidence for the existence of **8a**, potassium dicyanocuprate(I) and dipotassium tricyanocuprate(I), being supposed to be involved in the catalytic cycle, have been demonstrated to exert the catalysis toward



Scheme 3. A plausible catalytic cycle.



Scheme 4. Mechanistic studies.



Scheme 5. Cyanostannylation catalyzed by cyanocuprates.

the cyanostannylation (Scheme 5). In *step B*, the resulting **8a** of high nucleophilicity should be added across an aryne^[18] to give an arylcuprate(I) (**8b**), which is finally transformed into a product (**3**) through capture with a tin fluoride (*step C*). As depicted in Equation (c), a tin fluoride indeed serves as a tin electrophile for capturing an aryl(cyano)cuprate(I), and besides a tin cyanide (**1a**) has also proven to be the tin electrophile [Eq. (d)] in the cyanostannylation (*step D*), whereas a similar pathway is not operative in the alkynylstannylation [Eq. (e)].

In conclusion, we have developed the first cyanostannylation of arynes by use of widely available CuCN as a catalyst, where no additional supporting ligand is needed for the smooth transformation. Under the copper catalysis, arynes were also readily inserted into a C(sp)–Sn bond of alkynylstannanes, and the resulting alkynylstannylation products were demonstrated to be convertible into biologically active molecules and a DSSC dye. Further studies on the copper catalysis toward the carbostannylation using other unsaturated C–C bonds or organostannanes are in progress.

Supporting Information Summary

Synthesis of aryne precursors and alkynylstannanes, detailed experimental procedure, characterization of the products, and ^1H and ^{13}C NMR spectra of the products are available.

Acknowledgements

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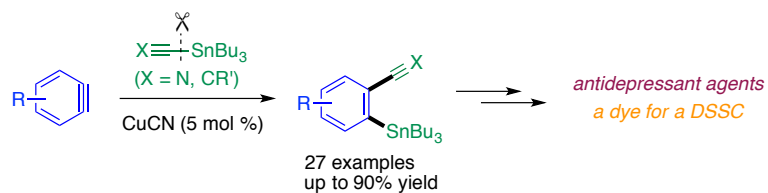
Keywords: alkynylstannylation • arynes • copper • cyanostannylation • dye-sensitized solar cells

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- [24] For ^{119}Sn NMR spectra of the experiments described in Scheme 4, see Supporting Information.

Entry for the Table of Contents

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Cyano- and alkynylstannylation of arynes facilely took place with a ligand-free copper catalyst to provide the respective carbostannylation products, which were transformable into antidepressant agents and a dye for a dye-sensitized solar cell.