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Regio- and Stereoselective Cross-Coupling of *tert*-Propargyl Alcohols with Bis(trimethylsilyl)acetylene and Its Utilization in Constructing a Fluorescent Donor–Acceptor System†

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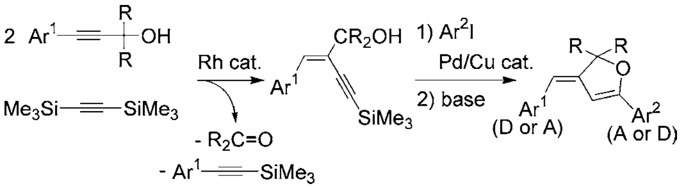
ABSTRACT



1,1-Disubstituted 3-aryl-2-propyn-1-ols undergo regio- and stereoselective cross-coupling on treatment with bis(trimethylsilyl)acetylene in the presence of a rhodium catalyst via cleavage of C(sp)–C(sp^3) and C(sp)–Si bonds to produce the corresponding 2-hydroxymethyl-(*E*)-enynes. The subsequent desilylative Sonogashira coupling followed by base-promoted cyclization affords fluorescent dihydrofuran derivatives.

The catalytic synthesis of π-conjugated enyne compounds has attracted considerable interest, due to the presence of the skeleton in natural products and their utility as versatile building blocks in organic synthesis.[1] While a variety of enynes can now be prepared by the dimerization of alkynes, the selective cross-coupling of two different alkynes is, in general, still difficult owing to the fact that the formation of regio- and stereoisomers as well as homodimers is possible, and thus a major challenge.[2,3] Among the rare, leading examples of the cross-coupling is the palladium-catalyzed reaction of terminal alkynes with internal ones having an electron-withdrawing group.[2] As in this instance, a key alkynylmetal intermediate generated by C(sp)−H bond activation of a terminal alkyne is usually involved in such a reaction.

Meanwhile, various unique and useful catalytic processes involving C−C bond cleavage via β-carbon elimination in metal alcoholate intermediates have recently been developed.[4] In the course of our work on the transformations,[5] we found that in the presence of a rhodium catalyst, γ-arylated *tert*-propargyl alcohols, i.e., ketone-masked aryl acetylenes **1**,

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† This paper is dedicated to the heartfelt memory of the late Professor Yoshihiko Ito of Kyoto and Doshisha Universities.

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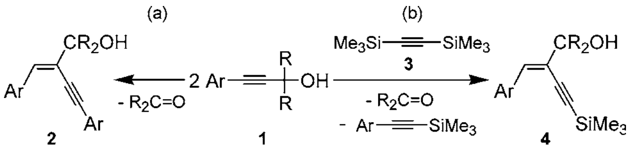
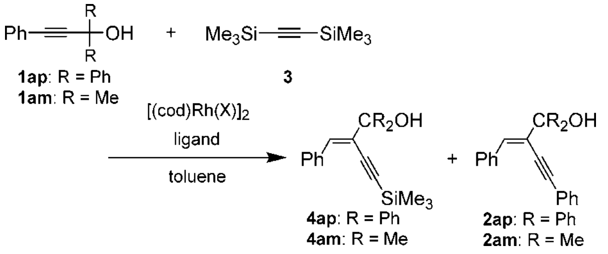
efficiently undergo homocoupling with liberation of a ketone molecule through C(sp)−C(sp^3) bond cleavage to regio- and stereoselectively produce 1,4-diaryl-2-hydroxymethyl-(*E*)-enynes **2** (Scheme 1, a).[5e] Notably, the products readily cyclize in the presence of a base to form dihydrofuran derivatives, some of which exhibit strong fluorescence in the solid state. During the examination of cross-coupling using **1**, we have observed that the propargyl alcohols selectively react with bis(trimethylsilyl)acetylene (**3**) via activation of one of the C(sp)−Si bonds to afford the corresponding 1-aryl-4-trimethylsilyl-(*E*)-enynes **4** (Scheme 1, b). The silyl function has also been subjected to further structural elaboration to lead to a donor−acceptor (D−A) *π*-conjugated system on the dihydrofuran scaffold.

Scheme 1



When a mixture of 1,1,3-triphenyl-2-propyn-1-ol (**1ap**) (0.5 mmol) was treated with **3** (3 mmol) in the presence of [(cod)Rh(OH)]$_2$/dppb (4 mol %) in refluxing toluene for 2 h, 2-[(*E*)-benzylidene]-4-trimethylsilyl-1,1-diphenyl-3-butyn-1-ol (**4ap**) was produced along with the homocoupling product **2ap** in 64% and 16% yields (calculated as 2[product]/[**1a**], see below), respectively (entry 1 in Table 1). Addition of **1ap** in a slow manner through a cannula to keep the concentration of **1ap** low could successfully suppress the formation of **2ap** to allow the almost exclusive formation of **4ap** (entry 2). Analysis of the reaction mixture by GC-MS confirmed the formation of 1-phenyl-2-(trimethylsilyl)-acetylene and benzophenone in quantitative yields (0.5 equiv) as the byproducts, which may provide important mechanistic information. Decreasing the amount of **3** to 1.0 mmol still gave 76% of **4ap** (entry 3). The reaction was found to be sensitive to the variation of ligand. The use of dppp or dppe in place of dppb reduced the yield of **4ap** and induced the formation of its (*Z*)-isomer in a small, but considerable amount (entries 4 and 5). The reaction without any phosphine ligand was sluggish (entries 7 and 8). The use of [(cod)-RhCl]$_2$ in place of the hydroxyl complex together with dppb was less effective (entry 9). The reaction of 2-methyl-4-phenyl-3-butyn-2-ol (**1am**) proceeded similarly (entries 10 and 11).

Table 1. Rhodium-Catalyzed Reaction of *tert*-Propargyl Alcohols with Bis(trimethylsilyl)acetylene[a]

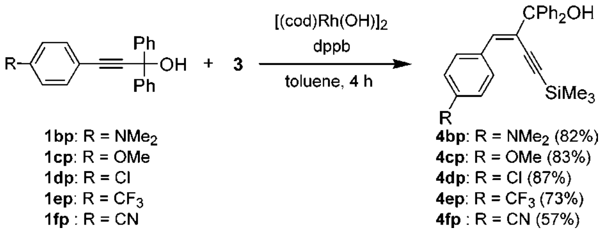


entry	X	R	ligand	time (h)	**4**, % yield[b]	**2**, % yield[b]
1	OH	Ph	dppb	2	64[e]	16
2[c]	OH	Ph	dppb	4	99 (98)[e]	trace
3[c,f]	OH	Ph	dppb	4	76[e]	16
4[c]	OH	Ph	dppp	4	76 (71) (96:4)[g]	trace
5[c]	OH	Ph	dppe	9	64 (57) (89:11)[g]	3
6[c]	OH	Ph	PPh_3[d]	8	43 (37)[e]	8
7[c]	OH	Ph		4	32	20
8[c]	Cl	Ph		8	6	6
9[c]	Cl	Ph	dppb	2	60	trace
10	OH	Me	dppb	4	62[e]	31
11[c]	OH	Me	dppb	4	89 (88)[e]	trace

[a] Reaction conditions: [Rh]:[ligand]:[**1**]:[**3**] = 0.02:0.02:0.5:3.0 (in mmol), in refluxing toluene (4 mL) under N_2. [b] GC yield based on the half amount of **1** used. Value in parentheses indicates isolated yield. [c] Toluene solution of **1** (2 mL, 0.25 mM) was added over 2 h. [d] PPh_3 (0.04 mmol) was used. [e] Exclusively (*E*)-isomer. [f] [**3**] = 1.0 mmol. [g] *E*/*Z* ratio.

The cross-coupling reactions of various 3-(4-substituted phenyl)-1,1-diphenyl-2-propyn-1-ols **1bp**−**1fp** with the disilylacetylene **3** in the double scale of entry 2 in Table 1 gave the corresponding products **4bp**−**4fp** with good isolated yields irrespective of the nature of the 4-substituents (Scheme 2).

Scheme 2



A plausible mechanism for the formation of the enyne **4** is illustrated in Scheme 3, in which neutral ligands are omitted. The first step involves the reaction of **1** with hydroxyrhodium(I) species to form rhodium alcoholate **A** and the successive *β*-carbon elimination with liberation of benzophenone or acetone gives arylalkynylrhodium **B**. Then, the alkynyl exchange between **B** and **3** takes place to from

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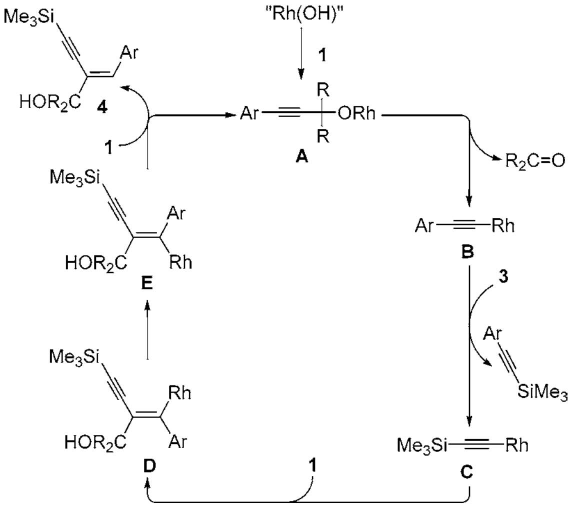
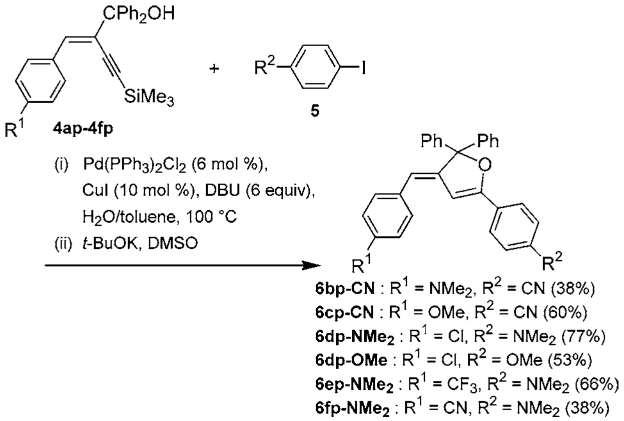
Scheme 3



Scheme 4



silylalkynylrhodium **C** via activation of the C−Si bond,[6] presumably by an oxidative addition−reductive elimination sequence.[7] The successive regioselective insertion of another molecule of **1** to the rhodium−carbon bond affords vinylrhodium **D**. Enyne **4** is formed after the geometrical isomerization of **D** to **E** and protonolysis by **1** with regeneration of **A** as in the case of the homocoupling of **1**. The geometrical isomerization may occur via a zwitterionic form.[8] The interaction of the oxygen with the metal may intervene to stabilize **E**.

The synthetic utility of the cross-coupling products may be demonstrated by the transformation of the silyl group to various aromatic substituents and the subsequent cyclization to produce dihydrofuran derivatives that show solid-state luminescence.[5e,9] Since π-conjugated D−A molecules are often useful as flexible systems with respect to emission range,[10] the dihydrofuran scaffold may allow observation of the change of optical properties depending on the different substituents of the two aromatic rings.

As expected, the arylation of **3** with aryl iodides by a reported method for desilylative Sonogashira coupling,[11] followed by treatment with *t*-BuOK gave the corresponding dihydrofurans **6** in fair to good yields, although the conditions were not optimized (Scheme 4). They showed solid-state fluorescence in a range of 492−589 nm (see Figure S2 in the Supporting Information). Notably, **6cp-CN** showed a relatively strong emission compared to a typical green emitter, tris(8-hydroxyquinolino)aluminum (Alq_3), by a factor of 1.6. Dihydrofurans **6bp-CN** and **6cp-CN**, both of which possess an electron-donating group at R^1 and an electron-withdrawing group at R^2, showed strong fluorescence in solution ($\Phi = 0.76$ and 0.53 in dioxane, respectively). This contrasts with the fact that each of the other compounds **6dp-NMe$_2$**, **6dp-OMe**, **6ep-NMe$_2$**, and **6fp-NMe$_2$** as well as the homocoupling product **2ap** shows only a weak emission in solution. Furthermore, **6bp-CN** showed a large positive solvatochromism of fluorescence ($\lambda_{max} = 508$ nm in hexane; 539 nm in dioxane; 594 nm in MeCN), suggesting a strong intramolecular charge-transfer character in the excited state, while the chromism of **6cp-CN** was very small (see Figure S3 in the Supporting Information). These results indicate that the electronic nature of R^1 and R^2 strongly affects not only the fluorescent wavelength but also the efficiency in both solid and solution.

In summary, we have developed a new, selective alkyne cross-coupling reaction that proceeds via cleavage of C−C and C−Si bonds. The reaction has enabled the construction of a series of π-conjugated D−A systems involving a dihydrofuran skeleton that show intriguing optical properties.

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Supporting Information Available: Standard experimental procedure and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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