ORGANIC LETTERS

2007
Vol. 9, No. 11
2231−2233

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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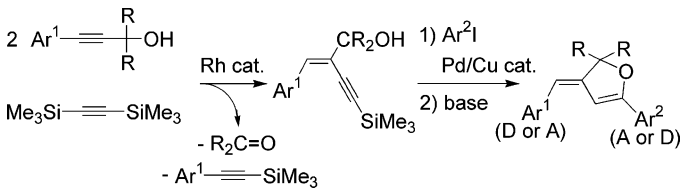
Received April 4, 2007

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**,

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

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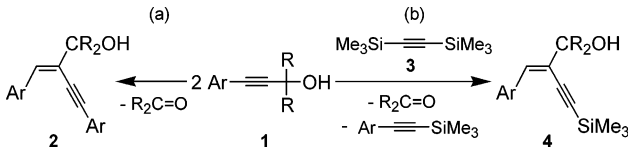
10.1021/ol070799k CCC: $37.00
Published on Web 05/04/2007

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

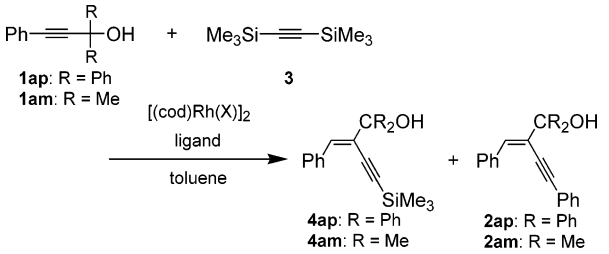
Scheme 1



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.

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]

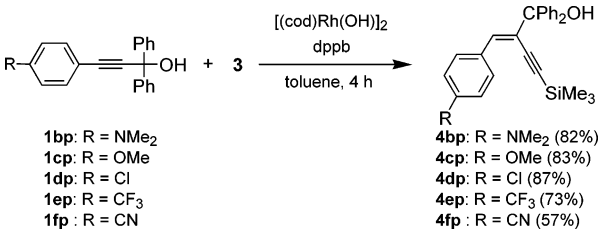


entry	X	R	ligand	time (h)	**4**, % yield[b]	**2**, % yield[b]
1	OH	Ph	dppb	2	64[e]	16
2[c]	OH	Ph	dppb	4	99 (98)[e]	trace
3[c,f]	OH	Ph	dppb	4	76[e]	16
4[c]	OH	Ph	dppp	4	76 (71) (96:4)[g]	trace
5[c]	OH	Ph	dppe	9	64 (57) (89:11)[g]	3
6[c]	OH	Ph	PPh_3[d]	8	43 (37)[e]	8
7[c]	OH	Ph		4	32	20
8[c]	Cl	Ph		8	6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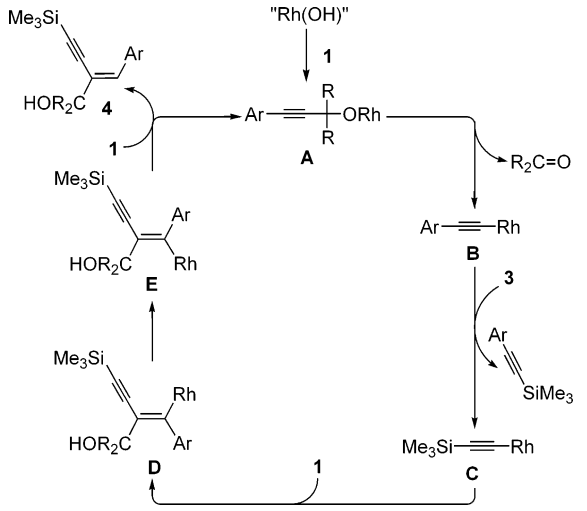
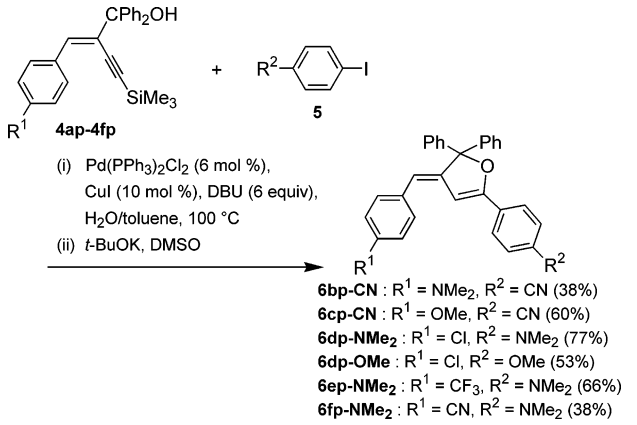
Scheme 3



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.

Acknowledgment. This work was supported by a Grant-in-Aid from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. We thank Ms. Y. Miyaji for the measurement of NMR spectra and Mr. H. Moriguchi and Mr. H. Yamada for MS spectra (Osaka University).

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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