Communication

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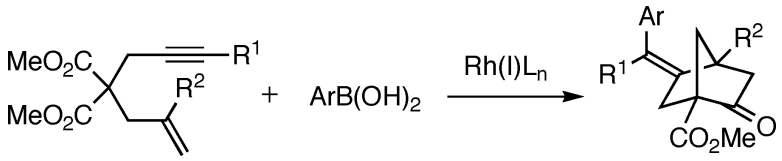
J. Am. Chem. Soc., **2005**, 127 (5), 1390-1391• DOI: 10.1021/ja043123i • Publication Date (Web): 13 January 2005



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Ketone Synthesis by Intramolecular Acylation of Organorhodium(I) with Ester

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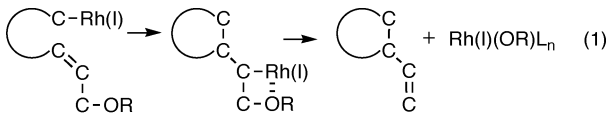
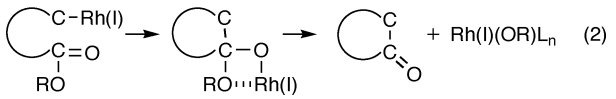
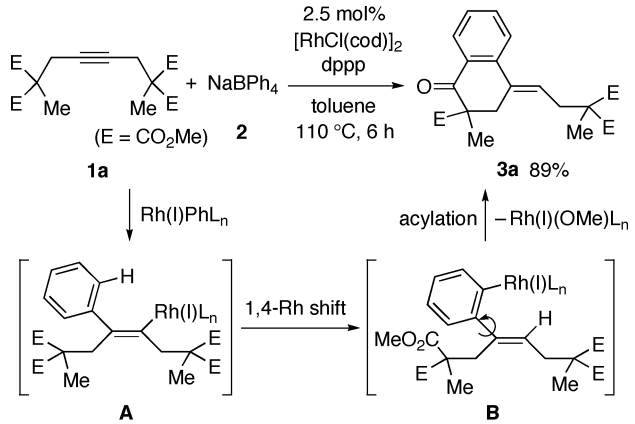
Rhodium(I)-catalyzed addition reactions using arylboron reagents have gained much interest in organic chemistry due to their unique reactivities and stereoselectivities.[1] It is supposed that the formal oxidation state of rhodium remains 1+ throughout the catalytic cycle unlike most palladium-catalyzed carbon−carbon bond-forming reactions of organoboranes which involve a redox cycle.[2] There are two important steps required to achieve a catalytic cycle in addition to the carbon−carbon bond-forming step, i.e. regeneration of the catalytically active rhodium(I) species from the product and transmetalation of the rhodium(I) species with the arylboron reagent. The counteranion of the regenerated rhodium(I) species should be nucleophilic enough to facilitate transmetalation with the arylboron reagent. It has been shown that rhodium(I) hydroxides and alkoxides are suitable for this purpose.[3] We have recently developed a rhodium-catalyzed cyclization reaction with arylboronic acids, wherein a rhodium(I) alkoxide is generated by β-elimination with an alkoxyl group placed at the allylic position (eq 1).[4] We then envisaged that the acylation of the organorhodium(I) intermediate with an ester group would result in the formation of a ketone[5] and a catalytically active rhodium(I) alkoxide. Whereas organorhodium(I) species are known to undergo nucleophilic addition to aldehydes,[6] ketones,[7] imines,[8] and acid anhydrides,[9] there have been no reports on acylation with esters due to their low nucleophilicities. In this communication, we describe new cyclization reactions that are triggered by the rhodium-catalyzed addition of an arylboron reagent onto a carbon−carbon triple bond. The addition prompts intramolecular acylations with an ester group to form cyclic ketones (eq 2).





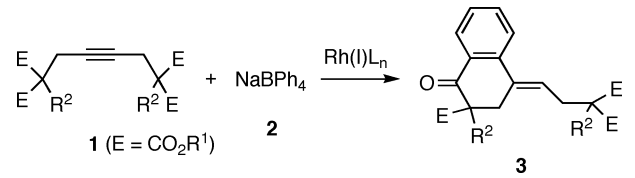
The cyclization of symmetrical acetylenic esters **1** was first examined using phenylboronic acid. The simple 1,2-addition product to the carbon−carbon triple bond was obtained, consistent with the previous reports.[10] On the other hand, the use of sodium tetraphenylborate (**2**) under strictly anhydrous conditions [toluene, $[RhCl(cod)]_2$ (0.05 equiv of Rh), dppp, 110 °C, 6 h][9b] produced the α-tetralone derivative **3a** in 89% yield without formation of the 1,2-addition product. The *E* configuration of the double bond was confirmed by a difference NOE study. We assume the following mechanism: a phenylrhodium(I) species, generated in situ by the transmetalation of a rhodium(I) complex with $NaBPh_4$, adds to the carbon−carbon triple bond in a syn fashion to give the alkenylrhodium(I) intermediate **A**. Then, a 1,4-shift of rhodium takes place to afford 2-(alkenyl)phenylrhodium(I) intermediate **B**,[10a,11] which was protected from protodemetalation by the anhydrous reaction conditions. The acylation of **B** with the ester group affords **3a** with concomitant generation of a catalytically active rhodium(I) methoxide (Scheme 1).

Scheme 1



cod=cycloocta-1,5-diene, dppp=1,3-bis(diphenylphosphino)propane

Table 1. Rhodium-Catalyzed Cyclization of Symmetrical Acetylenic Esters **1** with Sodium Tetraphenylborate (**2**)[a]



entry	**1**	OR^1	R^2	time (h)	**3**	yield (%)[b]
1	**1b**	OEt	Me	23	**3b**	70
2	**1c**	O*i*-Pr	Me	90	**3c**	63
3	**1d**	OMe	*i*-Bu	37	**3d**	81
4	**1e**	OMe	Ph	60	**3e**	69

[a] The reaction was carried out with **1** (0.20 mmol) and **2** (0.24 mmol) in the presence of $[RhCl(cod)]_2$ (0.05 equiv of Rh) and dppp (0.01 mmol) in toluene (1.5 mL) at 110 °C. [b] Isolated yields.

Various symmetrical acetylenic esters **1** underwent the reaction with sodium tetraphenylborate (**2**) (Table 1). The catalytic process worked well with **1b** and **1c** having ethyl and isopropyl ester groups (entries 1 and 2). Isobutyl and phenyl substituents were tolerated as R^2 to give the corresponding products **3d** and **3e** in good yields (entries 3 and 4), while substrates having a hydrogen as R^2 gave a complex mixture.

Interestingly, the reaction of acetylenic ester **1f** possessing a methallyl moiety as R^2 proceeded in a different reaction pathway to give the bicyclo[2.2.1]heptan-2-one derivative **4** in 73% yield (Scheme 2). No formation of the corresponding α-tetralone derivative **3** through a 1,4-shift of rhodium was observed. From the alkenylrhodium(I) intermediate **C**, intramolecular carborhodation to a pendant olefin in a 5-*exo* mode occurs in preference to a 1,4-

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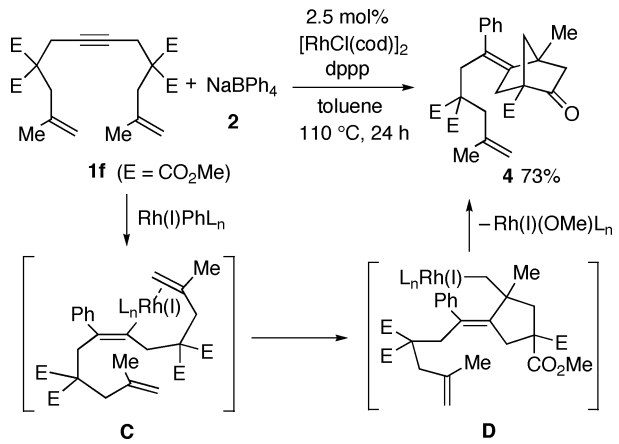
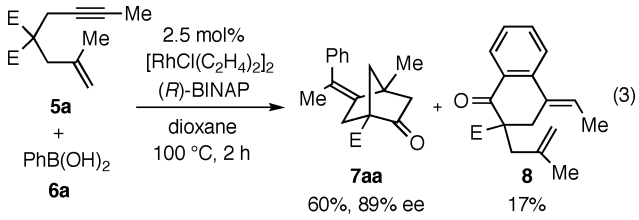
Scheme 2



rhodium shift, leading to the formation of the alkylrhodium(I) intermediate **D**. Finally, acylation with the ester group affords the bicyclo[2.2.1]heptan-2-one derivative **4** with generation of the rhodium(I) alkoxide.

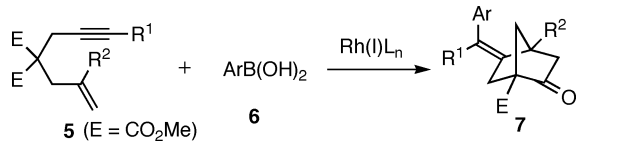
Since bicyclo[2.2.1]heptan-2-one (2-norbornanone) is a unique skeleton which is found in various biological compounds, we next examined the cyclization of unsymmetrical acetylenic ester **5a** in detail. Anhydrous conditions were not required because a proton-labile arylrhodium species is not involved in the catalytic cycle. This permitted the use of arylboronic acids in dioxane. Among phosphine ligands examined, (*R*)-BINAP gave the best yield of **7aa** (60%) with good asymmetric induction (89% ee).[12,13] Apart from **7aa**, the α-tetralone derivative **8** was formed in 17% yield by 1,2-addition of a phenylrhodium(I) species with the opposite regiochemistry (eq 3).



Other representative results for the enantioselective synthesis of bicyclo[2.2.1]heptan-2-one derivatives **7** are summarized in Table 2.[14] Both electron-rich and -deficient arylboronic acids gave good yields of **7** (entries 1 and 2).

In summary, new cyclization reactions that form cyclic ketones were developed wherein an intermediate organorhodium(I) species underwent intramolecular acylation with an ester group.[15] A 2-norbornanone skeleton is constructed in a single operation through successive multiple carbon−carbon bond formations. The reactions ended up with generation of an alkoxyrhodium(I) species to promote the next catalytic cycle.

Table 2. Synthesis of Bicyclo[2.2.1]heptan-2-ones **7**[a]



entry	**5**	R^1	R^2	**6**	Ar	**7**	yield (%)[b]	ee (%)[c]
1	**5a**	Me	Me	**6b**	3-$MeOC_6H_4$	**7ab**	65	80
2	**5a**	Me	Me	**6c**	3-ClC_6H_4	**7ac**	80	94
3	**5b**	Me	*n*-Bu	**6a**	Ph	**7ba**	62[d]	80
4	**5c**	*n*-Bu	Me	**6a**	Ph	**7ca**	64	56

[a] The reaction was carried out with **5** (0.20 mmol) and **6** (1.0 mmol) in the presence of $[RhCl(C_2H_4)_2]_2$ (0.05 equiv of Rh) and (*R*)-BINAP (0.01 mmol) at 100 °C in dioxane (2.0 mL) for 2 h. [b] Isolated yields. [c] The enantiomeric excess determined by HPLC analysis (ref 13). [d] Reaction time 7 h.

Supporting Information Available: Experimental details and selected spectral data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) The results with other phosphine ligands: PPh_3 (0%), P(*t*-Bu)$_3$ (0%), dppp (0%), dppb (50%), dppf (16%), and BIPHEP (51%).

(13) The absolute configuration of the product has not been assigned yet.

(14) The corresponding α-tetralone derivatives were formed in 10−20% yield in addition to **7**.

(15) A report on a similar reaction appeared on the Web during the submission of this manuscript: Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K. Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54.

JA043123I