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Vinylcyclopropanation of Olefins via 3-Methoxy-1-propenylrhodium(I)

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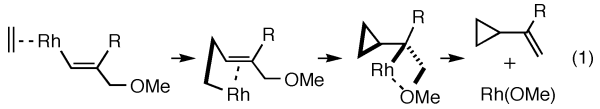
Vinylcyclopropanes (VCPs) have attracted significant attention in organic chemistry due to the occurrence of VCP moieties in a large number of natural and artificial biologically active compounds.[1] In addition, VCPs are valuable synthetic intermediates,[2] resulting in an ever-increasing demand for innovative methods for the synthesis of VCPs.[3] We report herein a new approach to the VCP substructure, which consists of multiple carborhodation steps,[4] including an intramolecular 3-*exo-trig* cyclization, and a termination step with β-oxygen elimination[5] (eq 1).



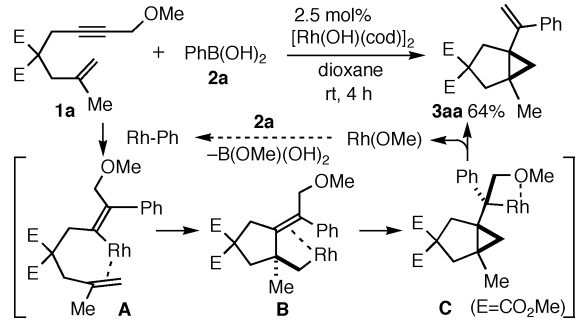
(1)

Recently, we found that an organorhodium(I) species adds intramolecularly to an allylic ether in a 5-*exo-trig* mode, followed by β-oxygen elimination to afford a vinylcyclopentane.[6] The resulting alkoxyrhodium(I), which is formed along with the vinylcyclopentane, then engages in transmetalation with an organoboron reagent to promote the ensuing catalytic cycle. We next designed 1,6-enyne **1** bearing a propargyl ether moiety in order to examine whether a similar intramolecular addition process would be feasible in a 3-*exo-trig* mode. This reaction would obviously be far less favorable due to the developing ring strain. Thus, a solution of **1a** and phenylboronic acid (**2a**, 3 equiv) in dioxane was stirred in the presence of $[Rh(OH)(cod)]_2$ (0.05 equiv of Rh) at room temperature for 4 h. After chromatography, 1-(1-phenylvinyl)-bicyclo[3.1.0]hexane **3aa** was isolated in 64% yield (Scheme 1).[7] We propose the following mechanism consisting of successive triple C−C bond formations. Phenylrhodium(I) species, generated by the transmetalation of rhodium(I) with phenylboronic acid (**2a**), adds across the carbon−carbon triple bond of **1a** to afford the alkenylrhodium(I) species **A**.[8] Then, intramolecular carborhodation of the pendent double bond occurs in a 5-*exo-trig* mode to form the (cyclopentylmethyl)rhodium(I) intermediate **B**. The second intramolecular carborhodation back to the allylic double bond occurs in a 3-*exo-trig* mode to form the alkylrhodium(I) intermediate **C**.[9] Finally, β-elimination of the methoxy group affords product **3aa** along with a catalytically active methoxyrhodium(I) species.

A control experiment was carried out using 1,6-enyne **4** lacking a methoxy moiety in order to gain an insight into the effect of the methoxy group (Scheme 2). No cyclopropane formation was observed with **4**. Instead, the (cyclopentylmethyl)rhodium(I) intermediate **D**, which corresponds to **B** in Scheme 1, led to the formation of cyclopentane **5** and 2-norbornanone **6** by hydrolysis and intramolecular acylation with the ester group, respectively.[5c,d]

It is conceivable that the three-membered ring closure from **B** to **C** is facilitated by developing coordination of the methoxy group to rhodium.[10] Formation of the methoxyrhodium(I) species by β-oxygen elimination would drive the reaction further forward.[11] The methoxyrhodium(I) then undergoes transmetalation with **2a** to generate methyl dihydrogen borate together with a phenylrhodium(I), which joins the next catalytic cycle again. We assume that the formation of the thermodynamically stable methyl dihydrogen borate makes a large contribution to the driving force of the entire reaction.

Scheme 1



Scheme 2

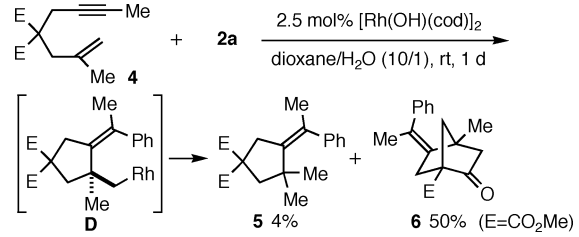
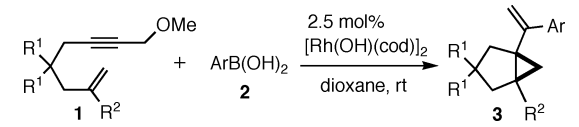


Table 1. Rhodium-Catalyzed Arylative Cyclization of **1** with **2**[a]



entry	**1**	R^1	R^2	Ar (**2**)	**3**	yield (%)[b]
1	**1a**	MeO_2C	Me	4-FC_6H_4 (**2b**)	**3ab**	60
2	**1a**	MeO_2C	Me	3-ClC_6H_4 (**2c**)	**3ac**	65
3	**1a**	MeO_2C	Me	3-$MeOC_6H_4$ (**2d**)	**3ad**	68
4	**1b**	$MeOCH_2$	Me	Ph (**2a**)	**3ba**	73
5	**1c**	$TBSOCH_2$	Me	Ph (**2a**)	**3ca**	60
6	**1d**	MeO_2C	*n*-Bu	Ph (**2a**)	**3da**	61[c]

[a] See Supporting Information for details. [b] Isolated yield. [c] With 10 mol % of $[Rh(OH)(cod)]_2$, 70 °C.

The arylative vinylcyclopropanation reaction was carried out with a variety of substrate combinations of **1** and **2**, with the results listed in Table 1. The corresponding 1-(1-arylvinyl)bicyclo[3.1.0]-hexanes **3** were synthesized in yields ranging from 60 to 73%.

Preliminary results using chiral phosphine ligands are shown in eq 2. A good level of asymmetric induction was observed with the BINAP-type ligands.

We next extended the VCP forming procedure to an intermolecular variant; 2-(3-methoxypropenyl)benzo[1,3,2]dioxaborole (**7**),[12] which was readily synthesized by hydroboration of 3-methoxypropyne with catecholborane (HBCat),[13] was exploited for the vinyl-

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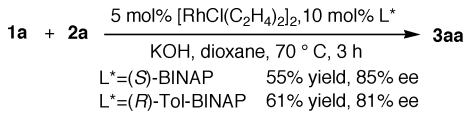
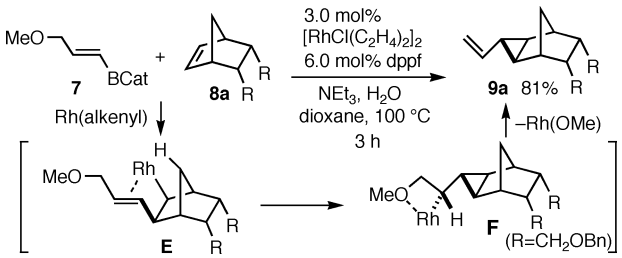


(2)

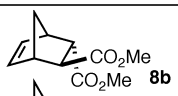
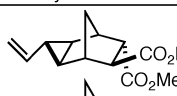
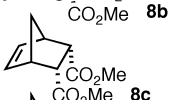
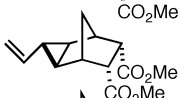
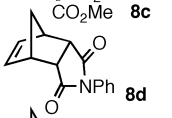
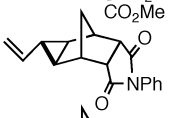
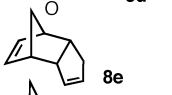
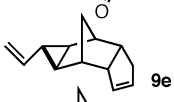
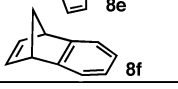
cyclopropanation of norbornene derivatives **8** (Scheme 3).[14] Thus, a dioxane solution of **7** (3 equiv) and H_2O (1.5 equiv) was added in portions to a dioxane solution of norbornene **8a**, $[RhCl(C_2H_4)_2]_2$ (0.06 equiv of Rh), dppf (0.06 equiv), and NEt_3 (10 equiv) at 100 °C. After heating the solution for 3 h, 3-*exo*-vinyltricyclo[3.2.1.0^{2,4}]-octane **9a** was isolated as a single stereoisomer in 81% yield by chromatography. We assume that the reaction is initiated by addition of an alkenylrhodium(I) species onto the alkene from the *exo* side,[5a] giving the norbornylrhodium(I) intermediate **E**. Then, intramolecular carborhodation to the allylic double bond occurs in a 3-*exo-trig* mode. For this ring-closing step to take place with **E**, the conformational orientation of the carbon−carbon double bond shown is preferred over the alternative one,[15] leading to the stereoselective formation of **F**. β-Oxygen elimination of the methoxy group produces **9a** and a methoxyrhodium(I) species.

Scheme 3



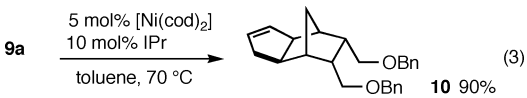
The vinylcyclopropanation of other norbornene derivatives **8b**−**8f** afforded the corresponding products **9b**−**9f** in yields ranging from 44 to 85% (Table 2). It should be noted that, with the cyclopentadiene dimer (**8e**), the vinylcyclopropanation occurred selectively at the norbornene double bond (entry 4).

Table 2. Rhodium-Catalyzed Vinylcyclopropanation of **8** with **7**[a]

entry	substrate **8**	cycloadduct **9**	yield (%)[b]
1	 **8b**	 **9b**	75
2	 **8c**	 **9c**	85
3	 **8d**	 **9d**	71
4	 **8e**	 **9e**	78
5	 **8f**	 **9f**	44

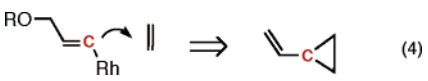
[a] See Supporting Information for details. [b] Isolated yield.

Finally, the rearrangement of VCPs to cyclopentenes was examined to demonstrate the additional synthetic utility of this process. Treatment of **9a** with the nickel catalyst reported recently[16] led to cyclopentene **10** cleanly in good yield and with complete retention of stereochemistry (eq 3).



(3)

In summary, new cyclization reactions forming VCPs were developed wherein an alkenylrhodium(I) possessing a methoxy substituent at the allylic position as a potential leaving group formally acts as an allylic carbene equivalent (eq 4). By this protocol, a VCP was installed in a complex cyclic structure in a single operation via successive multiple carbon−carbon bond formations.



(4)

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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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