Development of New Catalytic Reactions Triggered by Addition of Organorhodium Species onto Alkynes

Masahiko Shimada

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Preface

The studies presented in this thesis have been carried out under the direction of Professor Masahiro Murakami at Kyoto University during 2002-2008. The studies are concerned with catalytic carbon–carbon bond-forming reaction triggered by addition of organorhodium species onto alkynes.

The author would like to express his sincerest gratitude to Professor Masahiro Murakami for his constant support and encouragement during the course of this work. His supervision of enthusiasm gave the author a fulfilling research life.

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Masahiko Shimada

Department of Synthetic Chemistry and Biological Chemistry
Graduate School of Engineering
Kyoto University

Contents

List of Abbreviations

Ac	acetyl
Ar	aryl
binap	2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
Bn	benzyl
Bu	butyl
CI	chemical ionization
cod	1,5-cyclooctadiene
d	doublet (NMR)
DMF	*N*,*N*-dimethylformamide
DMPU	*N*,*N'*-dimethylpropyleneurea
EI	electron ionization
Et	ethyl
equiv	equivalent(s)
FAB	fast atom bombardment
HRMS	high resolution mass spectra
i	iso
J	coupling constant (NMR)
LDA	lithium diisopropylamide
LHMDS	lithium hexamethyldisilazide
m	multiplet (NMR)
Me	methyl
n	normal
nbd	2,5-norbornadiene
NMR	nuclear magnetic resonance
Ph	phenyl
Pr	propyl
q	quartet (NMR)
quint	quintet (NMR)
rt	room temperature
s	secondary
s	singlet (NMR)
t	tertiary
t	triplet (NMR)
THF	tetrahydrofuran
Tf	trifluoromethanesulfonyl
TMS	trimethylsilyl
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
Ts	4-methylphenylsulfonyl

General Introduction

Organic synthesis plays an important role in modern human life because it is closely related to the development of pharmaceutical, agrochemeical, and material sciences. Since the emergence of transition-metal catalyst, there has been an innovative progress in synthetic organic chemistry. In particular, the emphasis is put on transition-metal catalyzed carbon–carbon bond-forming processes, where a lot of challenging issues, such as stereoselective construction of complicate molecules and activation of inert reaction sites, have been achieved by utilizing transition metals.

The author's research work focused on oragnorhodium(I) intermediates which were exploited for organic synthesis. The details are described in this thesis, which consists of five chapters. Prior to details, he wishes to mention the background and give a brief summary.

(1) Rhodium(I)-catalyzed addition reactions of organoboron reagents to unsaturated functionality.

Organoboronic acids and their esters are relatively non-toxic, easily accessible, mostly stable toward air and water, and hence, are often used as the organometallic reagent.[1] In particular, the palladium-catalyzed cross-coupling reaction of organoboronic acids has found wide applications in industrial processes as well as in laboratory syntheses. Miyaura et al. reported in 1997 that arylboronic acids underwent conjugate addition to α,β-unsaturated ketones in the presence of a rhodium catalyst.[2] Since then, interest in the rhodium(I)-catalyzed addition of organoboron species to unsaturated functionalities has grown dramatically as its utility for the carbon–carbon bond formation has become increasingly clear.[3] An organorhodium(I) species generated from organoborons by transmetalation is reactive enough to add intermolecularly to relatively polar unsaturated functionalities like carbonyl,[4] imino,[5] and cyano[6] groups as well as to less polar alkynes[7] and alkenes[8] (Figure 1). In most of these reactions, the formal oxidation state of rhodium remains +1 throughout the catalytic cycle. A catalytically active Rh(I)–OR' species is often generated by protonolysis of an organorhodium(I) intermediate with a proton source like water. In this regard, rhodium-catalyzed carbon–carbon bond-forming reactions differ from most palladium-catalyzed systems, in which a Pd(II)/Pd(0) redox process is operative.

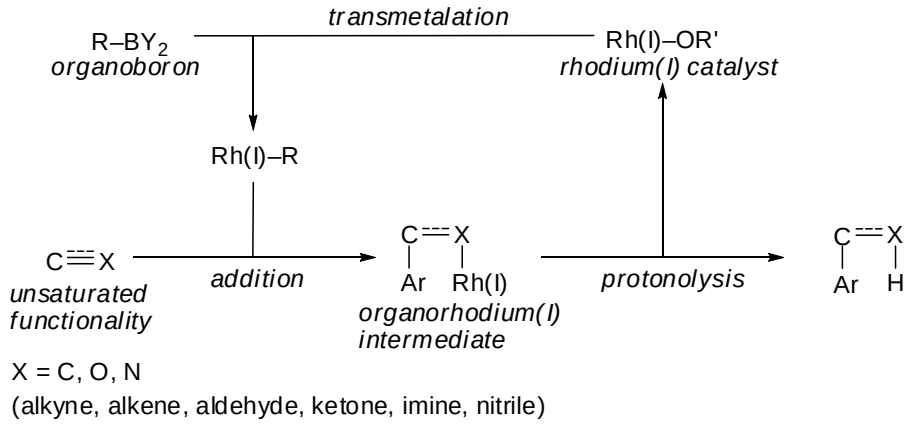


Figure 1. General reaction pathway of Rh(I)-catalyzed addition of organoborons

(2) Cascade reactions triggered by addition of organoborons

Cascade reactions which consist of multiple carbometalation steps provide powerful methods for the construction of structurally complex molecules in an efficient and atom-economical manner.[9] In recent years, the use of rhodium(I)-catalyzed addition of organoborons in cascade reactions has increased significantly,[10] as a complement to well-studied and valuable palladium-catalyzed cascade sequences.[11] When an acceptor molecule contains two or more electrophilic functionalities, the primary one (EF^1), which is more reactive toward an organorhodium(I) intermediate than the others, provides a newly generated organorhodium(I) species by intermolecular addition (Figure 2). The second carborhodation onto the subordinate electrophilic functionality (EF^2) in an intramolecular manner is then triggered to form a cyclic skeleton. The author selected alkynes as the entry point for incorporation of an active Csp^2–Rh linkage and the results are described in the beginning four chapters of this thesis.

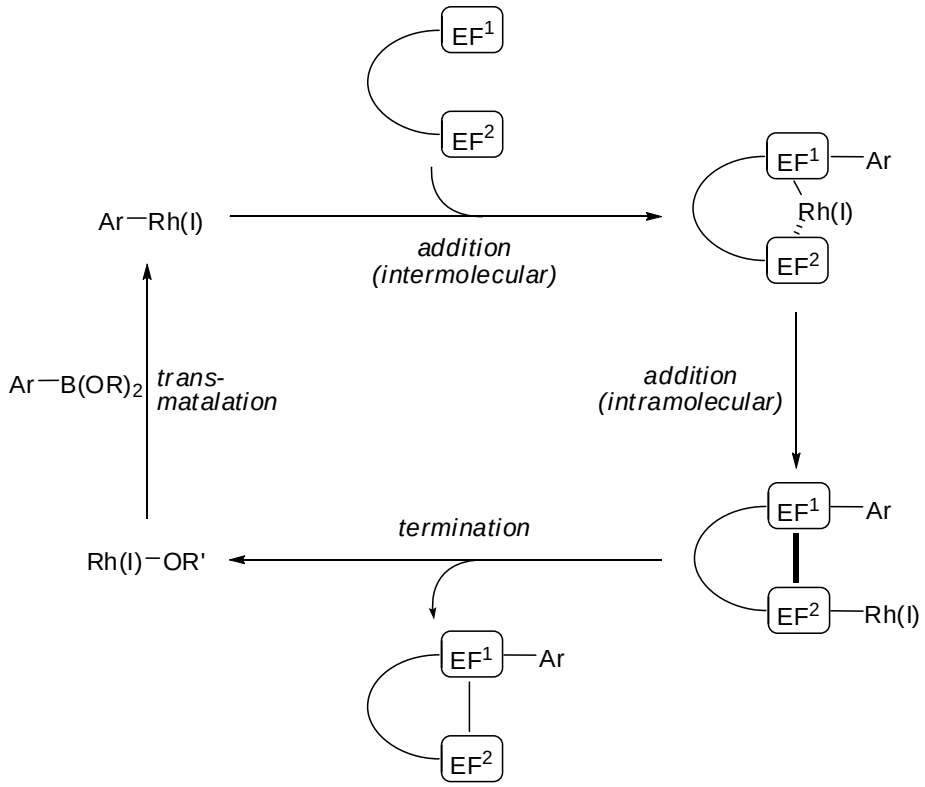
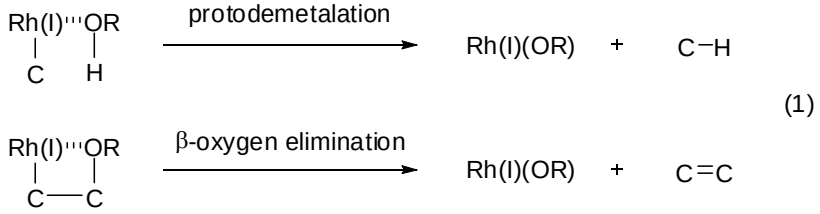


Figure 2. Concept of cascade cyclization triggered by addition of Ar–Rh(I)

(3) β-oxygen elimination of organorhodium(I) intermediates

In general, hydroxo- or alkoxorhodium(I) species are preferred for the transmetalation step of organoborons.[8b,12] This is presumably because the hydroxo and alkoxo ligands on rhodium are nucleophilic enough to coordinate to the boronic compound, facilitating transmetalation between rhodium and boron. The concomitant formation of a thermodynamically stable boronic acid derivative contributes to the driving force of the entire reaction. Thus, regeneration of the Rh(I) –OR species is indispensable for the purpose of performing the addition of oranoborons in a catalytic sense. There are two methodologies available for straightforward generation of such the species from an intermediate organorhodium(I). One is protodemetalation by a proton source like water (as depicted in Figure 1), the other is β-oxygen elimination from β-oxy-substituted organorhodium(I) [Eq. (1)].[13]

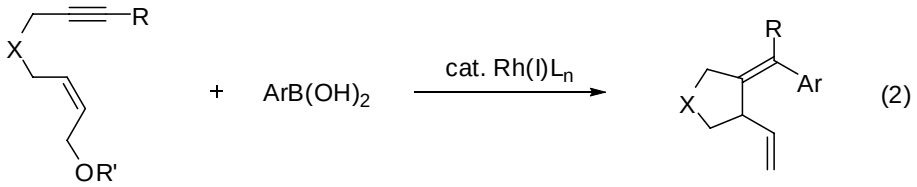


(1)

The β-oxygen elimination process has received much less consideration than the protodemetalation process, although β-elimination serves as an important step in many transition-metal catalyzed reactions. For the termination step of cascade processes, β-oxygen elimination has an advantage over protodemetalation that can possibly intercept propagation of multiple carbon–carbon bond formations at any intermediate stage. The author studied the cascade reaction through β-oxygen elimination of organorhodium(I) intermediates and the results are described in chapter 1 and 2. In addition, another example using a β-oxygen elimination process is shown in chapter 5

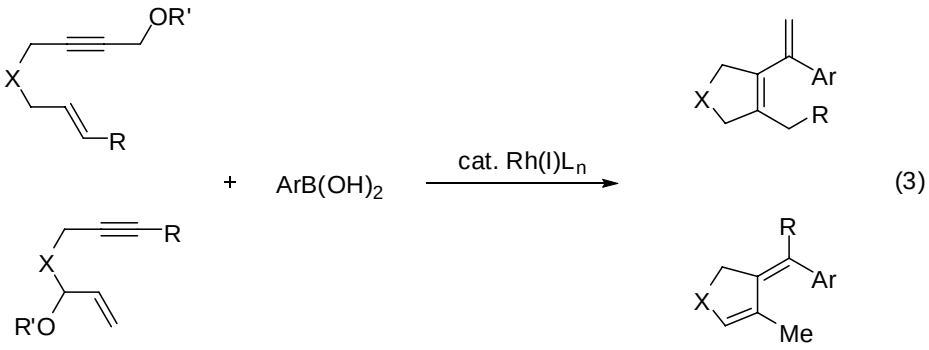
(4) Summary of each chapter

In chapter 1, the author describes the reaction of 1,6-enynes having an allylic ether moiety with arylboronic acids [Eq (2)]. This reaction contains multiple carbon–carbon bond forming steps to afford the cyclized product. An initial intermolecular addition of an arylrhodium(I) species across the carbon–carbon triple bond furnished the alkenylrhodium(I) intermediate, which underwent the following intramolecular carborhodation. The resultant β-alkoxy-substituted organorhodium(I) intermediate gave the product and a catalytically active alkoxorhodium(I) species by β-oxygen elimination.



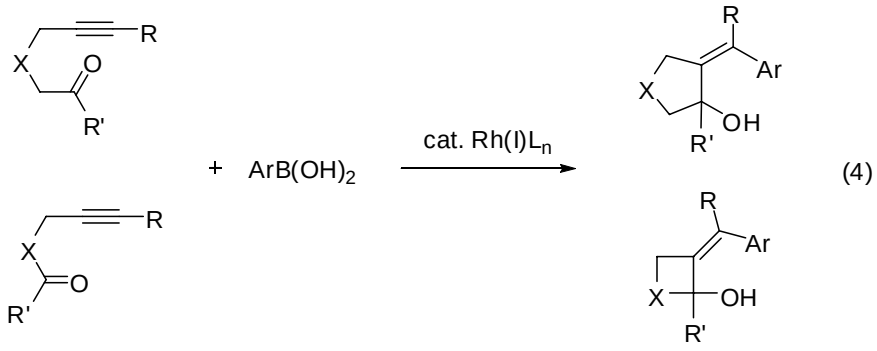
(2)

The different cyclization processes of 1,6-enynes with arylboronic acids are shown in chapter 2. In the presence of a rhodium(I)-diolefin catalyst, arylboronic acids and 1,6-enynes attached with a propargyl or an inner allyl ether moiety produced the cyclic 1,3-diene derivatives in good yields [Eq. (3)]. The successive carborhodations of the aryl- and alkenylrhodium(I) species were the same as the case of chapter 1. The forming alkyl rhodium(I) intermediates, however, did not have any oxygen-substituent at their β-position. This induced the shift of rhodium via a β-hydride elimination/hydrorhodation process. Finally, β-oxygen elimination terminated the reaction affording the product along with a catalytically active alkoxorhodium(I).



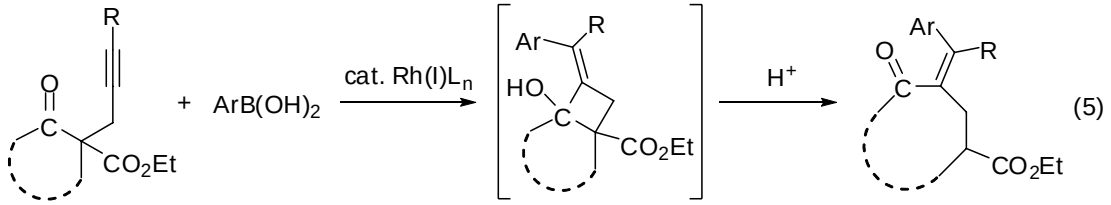
(3)

The author also examined the nucleophilic addition of organorhodium(I) intermediate onto carbonyl functionalities. He found that some alkynones were suitable substrates for his purpose. Chapter 3 describes rhodium(I)-catalyzed synthesis of cycloalkanol derivatives from 5- or 4-alkyn-1-ones and arylboronic acids. The formation of the products occurred through nucleophilic carborhodation of alkenylrhodium(I) intermediates to the ketonic carbonyl group and ensuing hydrolysis.



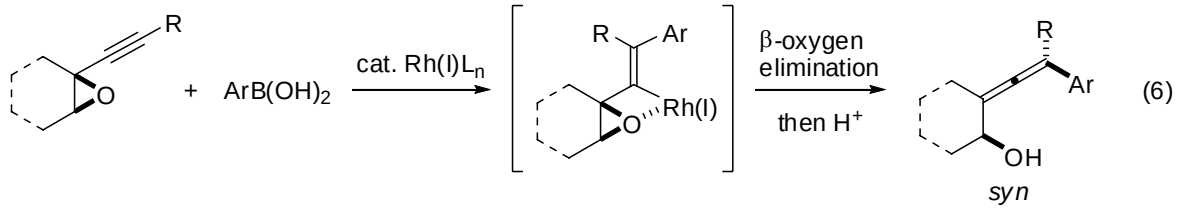
(4)

In chapter 4, the author wishes to report 1,3-acyl migration reaction induced by addition of an arylrhodium(I) species [Eq. (5)]. In the presence of a rhodium(I) catalyst, acetylenic β-ketoesters which were structurally different from the 4-alkyn-1-ones shown in chapter 3 by the ester function, intermediately gave the similar cyclobutanols. Retro-aldol reaction under an acidic condition gave isomerized α,β-unsaturated ketone derivatives in moderate to good yields. This transformation is considered as an acyl 1,3-migration accompanied by arylation of the alkyne moiety.



(5)

Finally, the author shows another example concerning β-oxygen elimination of organorhodium(I) intermediates in chapter 5. The rhodium(I)-catalyzed reaction of alkynyl oxiranes with arylboronic acids provided *syn*-configured α-allenols with excellent diastereoselectivity [Eq. (6)]. The alkenylrhodium(I) intermediate generated by regioselective addition of an arylrhodium(I) species underwent β-oxygen elimination and subsequent protonolysis to afford the product. This result indicates that precoordination of the oxygen atom of the oxirane ring to rhodium has great contribution to the high stereoselection as well as high reactivity.



(6)

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Chapter 1

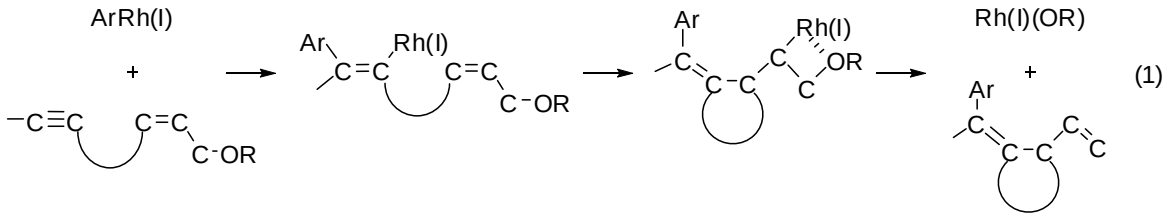
Rhodium-Catalyzed Cyclization of 1,6-Enynes Triggered by Addition of Arylboronic Acids

Abstract

The reaction of arylboronic acids with 1,6-enynes having an allylic ether moiety was catalyzed by a rhodium(I) complex to produce cyclopentanes possessing a tetrasubstituted *exo* olefin and a pendent vinyl group. The reaction was initiated by the regioselective addition of an arylrhodium(I) species to the carbon–carbon triple bond of a 1,6-enyne. The resulting alkenylrhodium(I) intermediate subsequently underwent intramolecular carborhodation to the allylic double bond in a 5-*exo*-trig mode. β-Elimination of the methoxy group afforded the cyclization product and the catalytically active methoxorhodium(I) species. The use of alkyl Grignard reagents instead of arylboronic acids as an organometallic nucleophile was also examined.

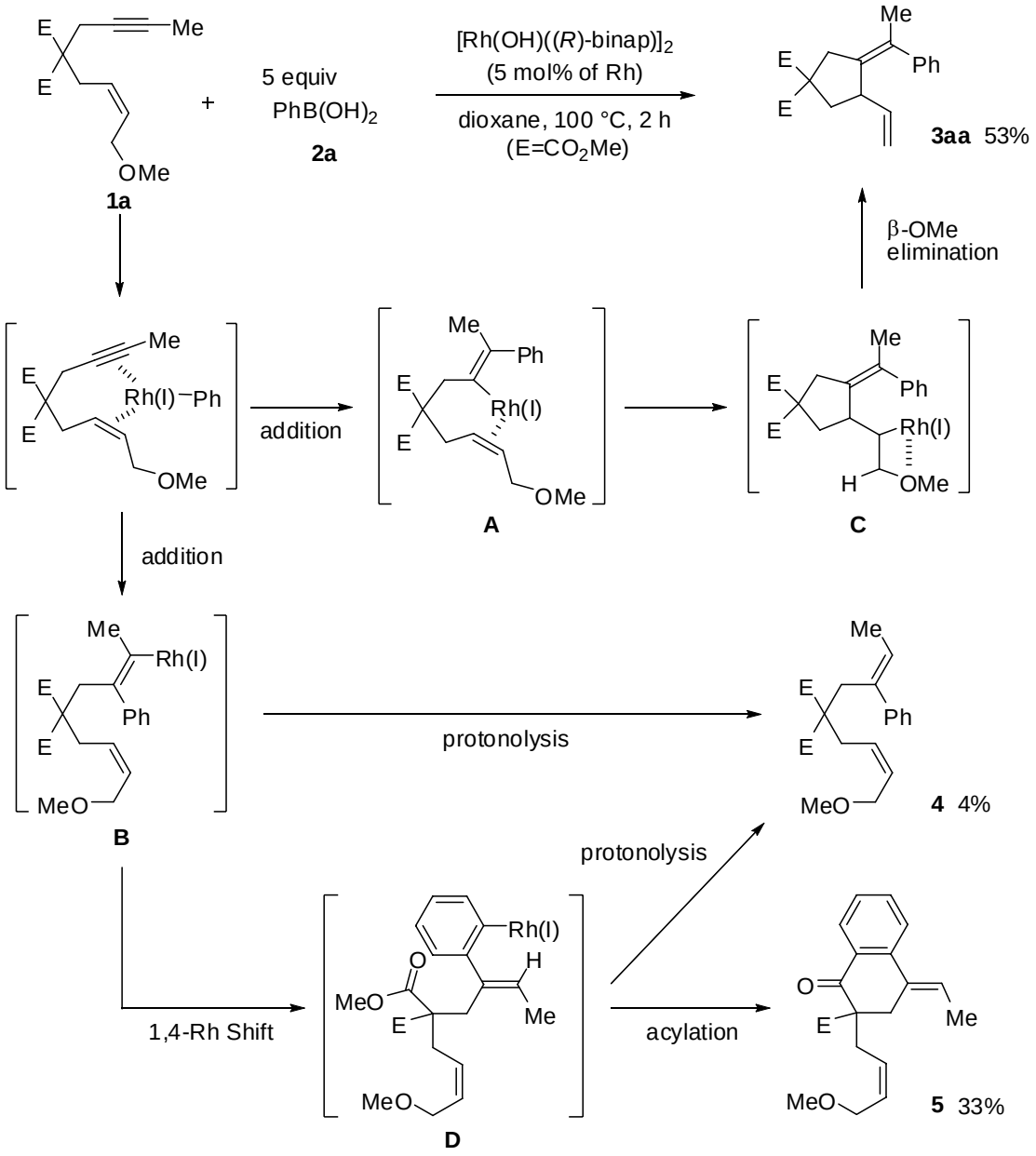
Introduction

The rhodium(I)-catalyzed addition of arylboronic acids to alkenes or alkynes has recently emerged as a useful synthetic protocol for the formation of carbon–carbon bonds in organic chemistry.[1] Unlike most palladium-catalyzed carbon–carbon bond forming reactions which involve a Pd(II)/Pd(0) redox process,[2] the formal oxidation state of rhodium remains +1 through the reaction. In the course of the addition reaction, the intermediate organorhodium(I) species is easily protodemetalated by a proton source (HX) that is present as a co-solvent or additive, regenerating the catalytically active Rh(I)–X species to promote the next catalytic cycle.[3] The intermediate complexes are rarely used for further carbon–carbon bond formation in spite of their potential usefulness. Recently a few reports on cyclization reactions involving the second carbon–carbon bond-forming process have appeared, wherein a catalytic rhodium(I) species was also regenerated by protodemetalation.[4] The author then envisaged that the ensuing carbon–carbon bond formation would be feasible in a catalytic sense if an allylic ether were placed at an appropriate position in the molecule. The intermediate organorhodium complex formed by the intramolecular addition to the allylic carbon–carbon double bond may undergo a facile β-alkoxy elimination.[5,6] The resulting alkoxorhodium(I) would be suitable to participate in the next catalytic cycle through transmetalation with an arylboronic acid.[3f,7] Thus, the author designed a multiple carbon–carbon bond-forming reaction [Eq. (1)].[8,9] Described in this chapter is that a rhodium complex catalyzes cascade reaction of 1,6-enynes with arylboronic acids. The use of alkyl Grignard reagents instead of arylboronic acids as a nucleophilic main-group organometal was also examined.



Results and discussions

The auther examined a reaction of **1a** with phenylboronic acid (**2a**). A mixture of **1a** and **2a** (5 equiv) in 1,4-dioxane was heated at 100 °C in the presence of $[Rh(OH)((R)\text{-binap})]_2$ (5 mol% of Rh) (Scheme 1). The 1,6-enyne **1a** was consumed in 2 h, and after chromatographic isolation, three phenylated products **3aa**, **4**, and **5** were obtained in 53%, 4%, and 33% yield, respectively (see below for asymmetric induction).



Scheme 1. Reaction of 1,6-enyne **1a** with phenylboronic acid (**2a**) catalyzed by $[Rh(OH)((R)\text{-binap})]_2$.

In this model reaction, the catalytic cycle is initiated by transmetalation of hydroxorhodium(I) with phenylboronic acid (**2a**) to generate phenylrhodium(I) and boronic acid. The phenylrhodium(I) species undergoes 1,2-addition across the carbon–carbon triple bond of **1a** in a *syn* fashion, giving the regioisomeric alkenylrhodium(I) intermediates **A** and **B** depending on the direction of 1,2-addition. With the major regioisomer **A**, intramolecular carborhodation to the neighboring allylic double bond occurs in a 5-*exo*-trig mode, furnishing the (cyclopentylmethyl)rhodium(I) intermediate **C**. Subsequent β-elimination of the methoxy group generates the cyclization product **3aa** with release of methoxorhodium(I) which promotes the next catalytic cycle, as hydroxorhodium(I) has done in the initial cycle. It should be noted that, with the organorhodium(I) intermediate **C**, β-oxygen elimination predominates over β-hydride elimination. This preference for β-oxygen elimination sharply contrasts with the palladium-catalyzed Heck-type carbopalladation/cyclization reaction of a similar 1,6-enyne substrate, in which an organopalladium(II) intermediate undergoes β-hydride elimination rather than β-oxygen elimination.[9c] On the other hand, the minor regioisomer **B** is subject to either protonolysis giving the product **4** or 1,4-shift of rhodium onto the phenyl ring.[10] In the latter case, the resultant arylrhodium(I) **D** is subsequently acylated by the neighboring ester group to afford α-tetralone **5** or hydrolyzed to afford **4**.[11]

The reaction of **1a** with **2a** was examined under various conditions (Table 1). A better regioselectivity of the initial 1,2-addition of a phenylrhodium(I) across the carbon–carbon triple bond was observed at room temperature than at 100 °C (entries 1 and 2). The ligand of rhodium also influenced the regioselectivity. The use of cycloocta-1,5-diene (COD) as the ligand led to the selective formation of **3aa** [**3aa**:(**4**+**5**)=>95:5, entries 3–6]. In particular, the reaction at room temperature using the COD ligand proceeded efficiently to afford **3aa** in 72% yield even with the use of two equivalents of **2a** and a lower loading of the catalyst (entry 6). It is conceivable that the stronger π-acidic and less sterically demanding character of the COD ligand led to the highly regioselective addition of the phenylrhodium(I) species.

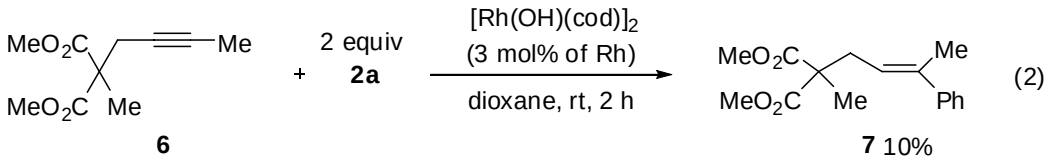
Table 1. Reaction of 1,6-enyne **1a** with **2a** in the presence of Rh(I) complex

1a + **2a** —Rh(I) catalyst, dioxane, 2 h→ **3aa** + **4** + **5**

entry	**2a** (equiv)	Rh(I) complex (mol% of Rh)	temp (°C)	**3aa**/(**4**+**5**) [a]	yield of **3aa** (%) [b]
1	5	$[Rh(OH)((R)\text{-binap})]_2$ (5)	100	59:41	53
2	5	$[Rh(OH)((R)\text{-binap})]_2$ (5)	rt	73:27	66
3	5	$[Rh(OH)(cod)]_2$ (5)	100	> 95:5	60
4	5	$[Rh(OH)(cod)]_2$ (3)	100	> 95:5	69
5	2	$[Rh(OH)(cod)]_2$ (3)	100	> 95:5	60
6	2	$[Rh(OH)(cod)]_2$ (3)	rt	> 95:5	72

[a] Ratio determined by ^{1}H NMR spectroscopy. [b] Yields of isolated products.

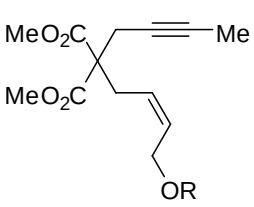
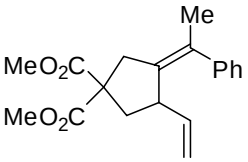
For comparison, an analogous reaction was carried out using substrate **6** lacking an olefin moiety.[4d] Almost no reaction occurred at room temperature when (*R*)-BINAP was used as the ligand. The addition reaction using the COD ligand proceeded only sluggishly at room temperature, and in 2 h, formed the 1,2-adduct **7** in 10% yield [Eq. (2)]. These contrasting results indicates that the olefin moiety of **1a** intramolecularly coordinates to rhodium to facilitate the initial 1,2-addition.



(2)

Next, the author examined the effect of the leaving group placed at the allylic position (Table 2). The addition/cyclization reaction successfully occurred with substrates **1b** and **1c** having a free hydroxyl group and a silyl ether at the allylic position, respectively (entries 1 and 2). The reaction of the allylic acetate **1d**, however, was considerably slower and the starting material remained after 2 h (entry 3). The lower reactivity of the acetate **1d** can be ascribed to the lower nucleophilicity of the acetoxy ligand which results from β-elimination. The transmetalation step between rhodium and boron would be slower with the less nucleophilic acetoxy ligand. In addition, the lower reactivity of **1d** suggests that an oxidative addition mechanism involving π-allyl-rhodium intermediate is unlikely.

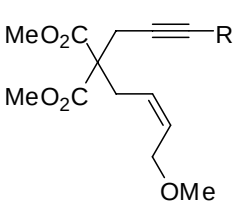
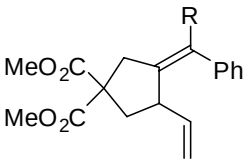
Table 2. Rhodium(I)-catalyzed arylative cyclization: effect of the leaving group at the allylic position [a]

entry	substrate		product	yield (%) [b]
				
1	**1a**	R = Me	**3aa**	72
2	**1b**	R = H		63
3	**1c**	R = TBS		78
4	**1d**	R = Ac		37 [c]

[a] Reaction condition: **1** (0.2 mmol), **2a** (0.4 mmol), $[Rh(OH)(cod)]_2$ (3 mol% of Rh) in dioxane, room temperature, 2 h. [b] Yields of isolated products. [c] The starting material remained.

The regiochemistry of the initial 1,2-addition of phenylrhodium(I) to the carbon–carbon triple bond is influenced by the alkyne substituent (Table 3). A good regioselectivity was observed with the ethyl-substituted **1e** which gave a slightly better yield of **3** than methyl-substituted **1a** (entries 1 and 2). The reaction of phenyl and trimethylsilyl substituted alkynes **1f** and **1g** gave the corresponding products **3fa** and **3ga** in low yield, due to a lower regioselectivity of the initial 1,2-addition of a phenylrhodium(I) species (entries 3 and 4).

Table 3. Rhodium(I)-catalyzed arylative cyclization: effect of the alkyne substituent. [a]

entry	substrate		product	time (h)	yield (%) [b]
					
1	**1a**	R = Me	**3aa**	2	72
2	**1e**	R = Et	**3ea**	2	80
3	**1f**	R = Ph	**3fa**	9	15 [c,d]
4	**1g**	R = TMS	**3ga**	5	20 [c,d]

[a] Reaction condition: **1** (0.2 mmol), **2a** (0.4 mmol), $[Rh(OH)(cod)]_2$ (3 mol% of Rh) in dioxane, room temperature. [b] Yields of isolated products. [c] Compounds corresponding to **4** and **5** were formed. [d] The starting material remained.

A variety of arylboronic acids **2** were subjected to the cascade reaction of **1a** with a rhodium/diene catalyst (Table 4). Both electron-donating and -withdrawing arylboronic acids **2b**–**2f** were suitably reactive (entries 1–5). In cases of sterically bulkier *o*-tolylboronic acid (**2g**) and 1-naphthylboronic acid (**2h**), the corresponding products **3ag** and **3ah** were obtained in good yield as a mixture of atropisomers (entries 6 and 7). However, no reaction occurred when methylboronic acid was used instead of arylboronic acids under the same conditions.

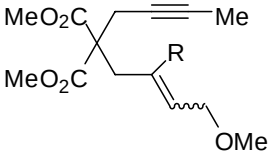
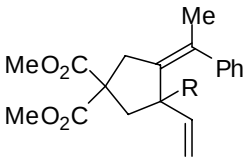
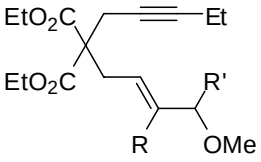
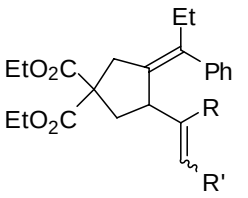
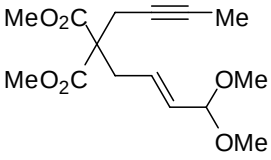
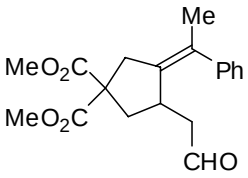
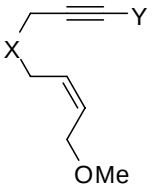
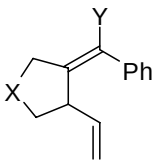
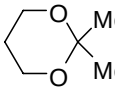
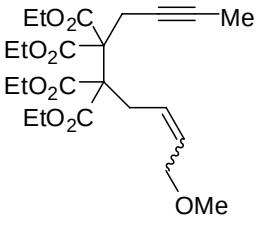
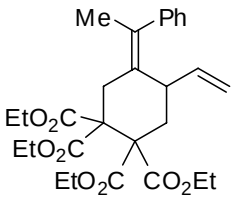
Table 4. Rhodium(I)-catalyzed arylative cyclization: scope of arylboronic acid. [a]

entry	$ArB(OH)_2$		product	time (h)	yield (%) [b]
1	**2b**	Ar = 4-F-C_6H_4	**3ab**	2	77
2	**2c**	Ar = 4-NO_2-C_6H_4	**3ac**	6	82
3	**2d**	Ar = 4-Me-C_6H_4	**3ad**	10	68
4	**2e**	Ar = 3-MeO-C_6H_4	**3ae**	2	77
5	**2f**	Ar = 3-Cl-C_6H_4	**3af**	2	77
6	**2g**	Ar = 2-Me-C_6H_4	**3ag**	8	80 [c]
7	**2h**	Ar = 1-naphthyl	**3ah**	13	81 [c]

[a] **1a** (0.2 mmol), **2** (0.4 mmol), $[Rh(OH)(cod)]_2$ (3 mol% of Rh) in dioxane, room temperature.
[b] Yields of isolated products. [c] Mixture of atropisomers (52:48 for **3ag**, 62:38 for **3ah**).

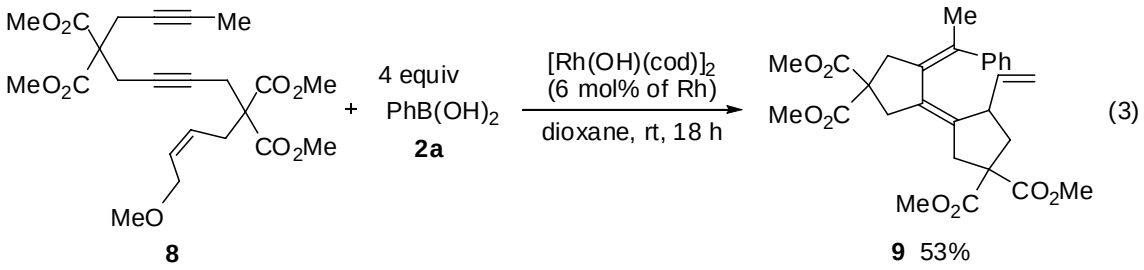
Other examples of the rhodium-catalyzed cascade reaction of 1,6-enynes are listed in Table 5. 1,6-Enyne **1h** having an *E*-olefin was also converted to the product **3aa** in good yield (entry 1). Even substrates **1i** and **1j** equipped with tri-substituted olefins reacted well (entries 2 and 3). The reaction of substrate **1k** afforded the product **3ka** as a mixture of *cis* and *trans* isomers (entry 4). Substrate **1l** having a dimethyl acetal moiety at the allylic position gave the aldehyde **3la** in 70% yield after acidic hydrolysis of the resultant enol ether (entry 5). A variety of functionalized linkers including ether and sulfone were tolerated (entries 6–12). The reaction of aza-1,6-enyne **1t** bearing a sulfonamide group in the linker gave the product **3ta** in only 27% yield due to a lower regioselectivity of the initial 1,2-addition (entry 13). The reaction of 1,7-enyne **1u** possessing a tether longer by one carbon worked far less efficiently, giving the six-membered ring product **3ua** only in 32% yield (entry 14).

Table 5. Rhodium(I)-catalyzed arylative cyclization: scope of the substrate. [a]

entry	substrate		product		time (h)	yield (%) [b]
1		**1h** R = H		**3aa**	2	75
2		**1i** R = Me [c]		**3ia**	23	61
3		**1j** R = Me, R' = H		**3ja**	17	71 [d]
4		**1k** R = H, R' = Me		**3ka**	6	79 [e]
5		**1l**		**3la**	2	70
6		**1m** X = $C(CO_2t\text{-}Bu)_2$, Y = Me		**3ma**	2	69
7		**1n** X = $C(CH_2OMe)_2$, Y = Me		**3na**	2	81
8		**1o** X = $C(CH_2OAc)_2$, Y = Me		**3oa**	5	69
9		**1p** X = $C(CH_2OBn)_2$, Y = Me		**3pa**	5	72
10		**1q** X = $C(CH_2OBn)_2$, Y = Et		**3qa**	16	79
11		**1r** X =  , Y = Me		**3ra**	4	72
12		**1s** X = $C(SO_2Ph)_2$, Y = Me		**3sa**	16	70 [d]
13		**1t** X = NTs, Y = Me		**3ta**	12	27 [d,f]
14		**1u** [g]		**3ua**	4	32

[a] Reaction condition: **1** (0.2 mmol), **2a** (0.4 mmol), $[Rh(OH)(cod)]_2$ (3 mol% of Rh) in dioxane, room temperature, unless otherwise noted. [b] Yields of isolated products. [c] *E*/*Z* = 9:1. [d] **2a** (0.8 mmol) and $[Rh(OH)(cod)]_2$ (6 mol% of Rh) were used. [e] A 59:41 mixture of geometrical isomers were obtained. [f] Compounds corresponding to **4** and **5** were formed. [g] *E*/*Z* = 1:4.

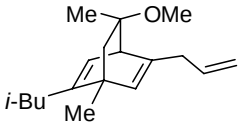
Thus, the cascade reaction was prompted by the carborhodation of a carbon–carbon triple bond and the intermediate alkenylrhodium(I) species successively participated in the second carbon–carbon bond formation. The author then examined a cascade addition/cyclization process using enediyne **8**. When **8** was treated with phenylboronic acid (**2a**) in the presence of $[Rh(OH)(cod)]_2$ (6 mol% of Rh) for 18 h, bicyclic triene derivative **9** was obtained in 53% yield through three successive carborhodation processes followed by β-oxygen elimination [Eq. (3)].



(3)

Next, the asymmetric version was examined using chiral ligands (Table 6). The (*R*)-BINAP ligand brought forth an excellent level of asymmetric induction on the product **3aa** (94% *ee*, entry 1). However, the product selectivity was moderate due to a low regioselectivity associated with the use of phosphine ligands (vide supra). The use of $[Rh(OH)((R)\text{-binap})]_2$ at room temperature slightly increased both chemical yield and enantioselectivity (66% yield, 97% *ee*; entry 4). On the other hand, a better product ratio was observed with a moderate enantioselectivity of 61% *ee* when the chiral diene ligand developed by Carreira was used (entry 5).[12]

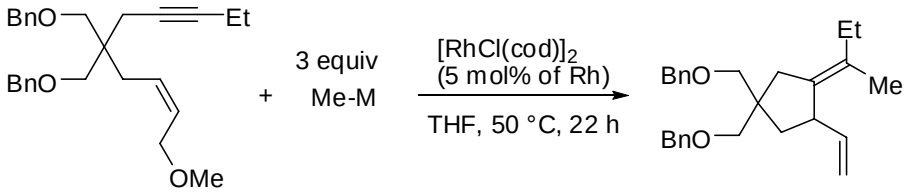
Table 6. Asymmetric arylative cyclization catalyzed by rhodium(I) complex. [a]

entry	**1**	Rh(I) complex (Rh/ligand = 1:1)	temp (°C)	time (h)	**3aa**/(**4**+**5**) [b]	**3aa** (%) [c]	ee (%) [d]
1	**1a**	$[RhCl(C_2H_4)_2]_2$ / (*R*)-BINAP	100	2	64:36	53	94
2	**1a**	$[RhCl((R)\text{-binap})]_2$	100	2	64:36	66	89
3	**1a**	$[Rh(OH)((R)\text{-binap})]_2$	100	2	59:41	60	92
4	**1a**	$[Rh(OH)((R)\text{-binap})]_2$	rt	2	73:27	69	97
5	**1a**	$[RhCl(C_2H_4)_2]_2$ / 	90	5	85:15	60	61
6	**1q**	$[Rh(OH)((R)\text{-binap})]_2$	rt	35	n.d. [e]	72	87

[a] Reaction condition: **1** (0.2 mmol), **2a** (1.0 mmol), Rh(I) complex (5 mol% of Rh) in dioxane. [b] Ratio determined by ^{1}H NMR spectroscopy. [c] Yields of isolated products. [d] Determined by chiral HPLC (OD-H column). [e] Not determined.

As mentioned above, methylboronic acid failed to undergo the cascade reaction with 1,6-enynes (entry 1, Table 7). Since here have been limited examples in which an sp^3 carbon–rhodium linkage intermolecularly adds to unsaturated functionalities,[13,14] the author then examined the use of other organometallic reagents for installation of a methyl group. The model substrate **1q**, lacking ester groups, was reacted with a methyl-metal reagent in the presence of $[RhCl(cod)]_2$ (5 mol% of Rh) at 50 °C for 22 h. Methyllithium and dimethylzinc failed to participate in the catalytic cyclization (entries 2 and 3), although the reason was unclear. On the other hand, methylzinc chloride and trimethylaluminum afforded the cyclized product **10qa** in 25% and 29% yield, respectively (entries 4 and 5). Notably, the use of MeMgCl efficiently promoted the reaction to give the methylated cyclization product **10qa** in 72% yield (entry 6).

Table 7. Rhodium(I)-catalyzed methylative cyclization with methyl-metal reagents.



1q **10qa**

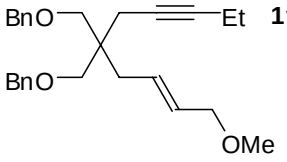
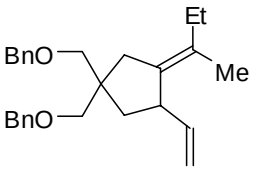
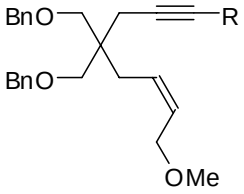
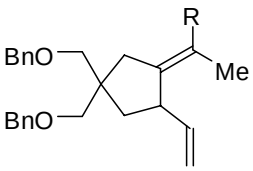
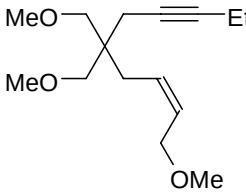
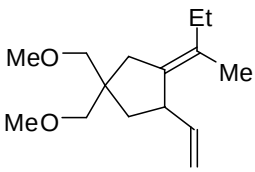
entry	Me-M	yield (%) [a]	entry	Me-M	yield (%) [a]
1	$MeB(OH)_2$	0	4	MeZnCl	25
2	MeLi	0	5	Me_3Al	29
3	Me_2Zn	0	6	MeMgCl	72

[a] Yields of isolated products.

Mechanistically, the reaction might proceed via a methylrhodium(I) species, which is generated by transmetalation of $[RhCl(cod)]_2$ with MeMgCl.[15] Then, the rhodium-catalyzed cascade of addition/cyclization/β-oxygen elimination follows as with the case of arylboronic acids. However, no 1,2-addition across the carbon–carbon triple bond took place when 4-octyne was reacted with MeMgCl in the presence of the rhodium catalyst. At this stage, an oxidative cyclization mechanism involving a five-membered ring rhoda(III)cycle can hardly be ruled out.[16]

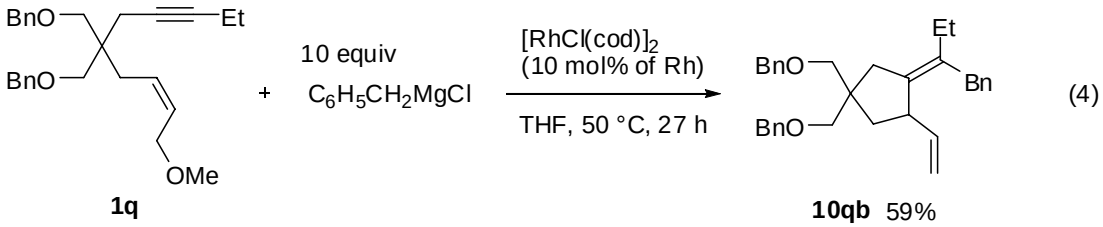
The author examined the reaction of other enyne substrates with MeMgCl (Table 8). The cascade reaction successfully occurred with substrates **1v** having an *E*-olefin (entry 1). The reaction tolerated various substituents on the alkyne terminus, including phenyl group **1w** and trimethylsilyl group **1x** (entries 3 and 4).

Table 8. Rhodium(I)-catalyzed methylative cyclization of 1,6-enynes **1** with methyl Grignard reagent. [a]

entry	substrate		product		time (h)	yield (%) [b]
1		**1v**		**10qa**	12	71
2		**1p** R = Me		**10pa**	20	70
3		**1w** R = Ph [c]		**10wa**	9	72
4		**1x** R = TMS		**10xa**	48	50 [d]
5		**1y**		**10ya**	20	60

[a] Reaction condition: **1** (0.12 mmol), MeMgCl (0.36 mmol), $[RhCl(cod)]_2$ (5 mol% of Rh) in dioxane, 50 °C, unless otherwise noted. [b] Yields of isolated products. [c] A 62:38 mixture of geometrical isomers. [d] $[RhCl(cod)]_2$ (10 mol% of Rh) was used.

The reaction of $C_6H_5CH_2MgCl$ gave the cyclized product **10qb** in 59% yield [Eq. (4)]. Aliphatic Grignard reagents possessing β-hydrogen, like *n*-BuMgCl and *i*-PrMgCl, failed to participate in the cascade reaction, affording a mixture of unidentified products.



(4)

Conclusion

The author has developed new cyclization reactions of 1,6-enynes with arylboronic acids catalyzed by rhodium, wherein a methoxorhodium(I) is regenerated by β-elimination of the methoxy group at the allylic position. The COD ligand shows a good regioselectivity in the addition of an organorhodium(I) species to the carbon–carbon triple bond. These findings would lead to a rational design of rhodium-catalyzed cascade processes involving multiple carbon–carbon bond formation. Furthermore, the potential of MeMgCl as the source of a methyl group in the rhodium-catalyzed cascade reaction is revealed.

Experimetal section

General

All rhodium(I)-catalyzed reactions were carried out under an inert atmosphere. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) spectrometer using $CHCl_3$ (^{1}H, δ = 7.26 ppm) and $CDCl_3$ (^{13}C, δ =77.0 ppm) as an internal standard. High resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck).

Materials

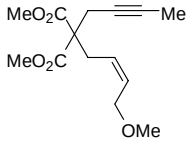
Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $[Rh(OH)(cod)]_2$[17], $[RhCl(cod)]_2$[18], $[RhCl(C_2H_4)_2]_2$[19] and $[Rh(OH)(binap)]_2$[3f] were prepared according to the reported procedures. 1,4-Dioxane was distilled over sodium-benzophenone ketyl prior to use. THF was dried and deoxygenized using an alumina/catalyst column system (Glass Contour Co.).

Starting Materials:

Malonate-tethered 1,6-enynes **1a**, **1c-m** were prepared from malonic esters by the successive alkylations with the corresponding propargyl bromides/allyl bromides in the presence of NaH in a

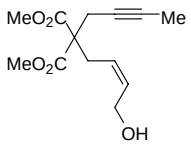
THF solution. Desi1ylation of **1c** (TBAF in THF) gave **1b**. 1,7-Enyne **1u** was also prepared from tetraethyl 1,1,2,2-ethanetetracarboxylate by the same procedure as 1,6-enynes. 1,6-Enynes **1n-r**, **1v-y** were synthesized by reduction of the corresponding malonate-tethered 1,6-enynes ($LiAlH_4$ in Et_2O) and ensuing protection of the resultant diol moieties by standard methods. Bis-phenysulfonyl derivative **1s** was synthesized by the reaction of 5,5-bis-(phenylsulfonyl)pent-2-yne and (*Z*)-1-bromo-4-methoxybut-2-en under the reported condition.[20] Nitrogen-atom-tethered **1t** was prepared from *N*-(but-2-ynyl)-4-methylphenylsulfonamide and (*Z*)-4-methoxybut-2-en-1-ol according to the literature.[21]

Dimethyl 2-(but-2-ynyl)-2-[(*Z*)-4-methoxybut-2-enyl]malonate (1a)



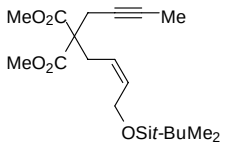
IR (neat): 2956, 1738, 1437, 1293, 1211, 1115 cm^{-1}; ^1H NMR: δ = 1.75 (t, *J* = 2.7 Hz, 3H), 2.72 (q, *J* = 2.5 Hz, 2H), 2.82 (d, *J* = 8.1 Hz, 2H), 3.32 (s, 3H), 3.72 (s, 6H), 4.01 (d, *J* = 6.6 Hz, 2H), 5.30–5.41 (m, 1H), 5.64–5.75 ppm (m, 1H); ^{13}C NMR: δ = 3.5, 23.0, 30.3, 52.7, 57.0, 58.0, 68.0, 73.3, 79.0, 125.7, 131.0, 170.4 ppm; elemental analysis: calcd for $C_{14}H_{20}O_5$: C 62.67, H 7.51; found: C 62.82, H 7.56.

Dimethyl 2-(but-2-ynyl)-2-[(*Z*)-4-hydroxybut-2-enyl]malonate (1b)



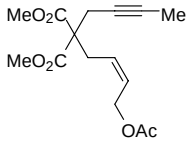
IR (neat): 3409, 2955, 1737, 1439, 1294, 1210 cm^{-1}; ^1H NMR: δ = 1.77 (t, *J* = 2.6 Hz, 3H), 2.74 (q, *J* = 2.5 Hz, 2H), 2.85 (dd, *J* = 7.8, 1.2 Hz, 2H), 3.74 (s, 6H), 4.20 (dd, *J* = 7.2, 1.2 Hz, 2H), 5.29–5.41 (m, 1H), 5.76–5.87 (m, 1H); ^{13}C NMR: δ = 3.5, 23.1, 30.1, 52.8, 57.0, 58.1, 73.3, 79.3, 125.4, 133.1, 170.4; HRMS (CI): *m/z* calcd for $C_{13}H_{19}O_5$: 255.1233 $[M+H]^+$; found 255.1229.

Dimethyl 2-(but-2-ynyl)-2-[(*Z*)-4-(*tert*-butyldimethylsilyloxy)but-2-enyl]malonate (1c)



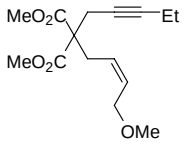
IR (neat): 2955, 1740, 1437, 1293, 1254, 1210 cm^{-1}; ^1H NMR: δ = 0.07 (s, 6H), 0.89 (s, 9H), 1.75 (t, *J* = 2.6 Hz, 3H), 2.72 (q, *J* = 2.6 Hz, 2H), 2.79 (d, *J* = 7.8 Hz, 2H), 3.72 (s, 6H), 4.72 (dd, *J* = 6.3, 1.5 Hz, 2H), 5.14–5.26 (m, 1H), 5.63–5.73 (m, 1H); ^{13}C NMR: δ = –5.2, 3.5, 18.4, 22.9, 25.9, 30.3, 52.7, 57.0, 59.4, 73.3, 78.9, 122.8, 134.7, 170.4; HRMS (CI): *m/z* calcd for $C_{19}H_{33}O_5Si$: 369.2097 $[M+H]^+$; found 369.2096.

Dimethyl 2-(but-2-ynyl)-2-[(*Z*)-4-acetyloxybut-2-enyl]malonate (1d)



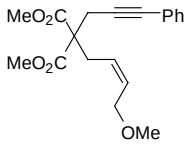
IR (neat): 2957, 1738, 1437, 1375, 1293, 1216 cm^{-1}; ^1H NMR: δ = 1.74 (t, *J* = 2.4Hz, 3H), 2.04 (s, 3H), 2.71 (q, *J* = 2.6 Hz, 2H), 2.84 (dd, *J* = 8.0, 0.8 Hz, 2H), 3.72 (s, 6H), 4.65 (dd, *J* = 6.6, 1.2 Hz, 2H), 5.36–5.49 (m, 1H), 5.64–5.76 (m, 1H); ^{13}C NMR: δ = 3.4, 20.9, 23.0, 30.2, 52.8, 56.9, 60.2, 73.0, 79.3, 127.5, 128.1, 170.2, 170.8; HRMS (CI): *m/z* calcd for $C_{15}H_{21}O_6$: 297.1338 $[M+H]^+$; found 297.1332.

Dimethyl 2-[(*Z*)-4-methoxybut-2-enyl]-2-(pent-2-ynyl)malonate (1e)



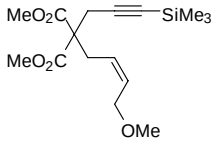
IR (neat): 2995, 1735, 1437, 1293, 1211, 1115 cm^{-1}; ^1H NMR: δ = 1.09 (t, *J* = 7.7 Hz, 3H), 2.13 (qt, *J* = 7.7, 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 2H), 2.80–2.86 (m, 2H), 3.33 (s, 3H), 3.73 (s, 6H), 4.00–4.06 (m, 2H), 5.31–5.42 (m, 1H), 5.65–5.76 (m, 1H); ^{13}C NMR: δ = 12.4, 14.1, 22.9, 30.3, 52.7, 57.1, 58.0, 68.0, 73.6, 85.1, 125.7, 131.0, 170.3; HRMS (CI): *m/z* calcd for $C_{15}H_{23}O_5$: 283.1545 $[M+H]^+$; found 283.1543.

Dimethyl 2-[(*Z*)-4-methoxybut-2-enyl]-2-(3-phenylprop-2-ynyl)malonate (1f)



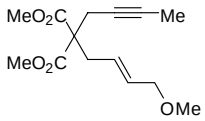
IR (neat): 2953, 1738, 1437, 1294, 1211, 1113 cm^{-1}; ^1H NMR: δ = 2.88 (d, *J* = 8.1 Hz, 2H), 2.98 (s, 2H), 3.25 (s, 3H), 3.74 (s, 6H), 4.01 (dd, *J* = 6.6, 1.5 Hz, 2H), 5.32–5.43 (m, 1H), 5.66–5.76 (m, 1H), 7.22–7.28 (m, 3H), 7.30–7.36 ppm (m, 2H); ^{13}C NMR: δ = 23.6, 30.5, 52.9, 57.1, 58.0, 68.0, 83.6, 84.2, 123.0, 125.5, 128.0, 128.2, 131.3, 131.6, 170.2 ppm; HRMS (CI): *m/z* calcd for $C_{19}H_{23}O_5$: 331.1545 $[M+H]^+$; found: 331.1544.

Dimethyl 2-[(*Z*)-4-methoxybut-2-enyl]-2-(3-trimethylsilylprop-2-ynyl)malonate (1g)



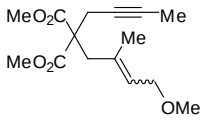
IR (neat): 2957, 1740, 1437, 1211, 1115, 1028 cm^{-1}; ^1H NMR: δ = 0.14 (s, 9H), 2.80 (s, 2H), 2.84 (d, *J* = 7.8 Hz, 2H), 3.33 (s, 3H), 3.73 (s, 6H), 4.03 (dd, *J* = 6.5, 1.4 Hz, 2H), 5.28–5.41 (m, 1H), 5.66–5.77 (m, 1H); ^{13}C NMR: δ = 0.0, 24.0, 30.3, 52.8, 57.0, 58.1, 68.0, 88.3, 101.2, 125.5, 131.3, 170.0; HRMS (CI): *m/z* calcd for $C_{16}H_{27}O_5Si$: 327.1628 $[M+H]^+$; found 327.1624.

Dimethyl 2-(but-2-ynyl)-2-[(*E*)-4-methoxybut-2-enyl]malonate (1h)



IR (neat): 2950, 1738, 1439, 1283, 1210, 1114 cm^{-1}; ^1H NMR: δ = 1.76 (t, *J* = 2.7 Hz, 3H), 2.73 (q, *J* = 2.5 Hz, 2H), 2.79 (d, *J*=7.2 Hz, 2H), 3.29 (s, 3H), 3.73 (s, 6H), 3.86 (d, *J* = 5.7 Hz, 2H), 5.45–5.58 (m, 1H), 5.62–5.74 (m, 1H); ^{13}C NMR: δ = 3.7, 23.3, 35.3, 52.9, 57.5, 57.9, 72.9, 73.4, 79.3, 127.2, 131.7, 170.6; HRMS (CI): *m/z* calcd for $C_{14}H_{21}O_5$: 268.1389 $[M+H]^+$; found 268.1389.

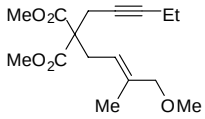
Dimethyl 2-(but-2-ynyl)-2-(4-methoxy-2-methylbut-2-enyl)malonate (1i)



Mixture of geometrical isomers (*E*:*Z*=9:1)

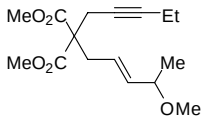
IR (neat, mixture): 2955, 1738, 1437, 1289, 1203, 1088 cm^{-1}; ^1H NMR (*E* isomer): δ = 1.59 (br s, 3H), 1.76 (t, *J*=2.6 Hz, 3H), 2.74 (q, *J* =2.5 Hz, 2H), 2.83 (br s, 2H), 3.31 (s, 3H), 3.73 (s, 6H), 3.92 (dd, *J*=6.3, 0.6 Hz, 2H), 5.43–5.53 (m, 1H); ^{13}C NMR (*E* isomer): δ = 3.5, 17.3, 23.0, 41.4, 52.6, 57.0, 57.8, 68.8, 73.5, 79.3, 127.2, 133.9, 170.8; HRMS (CI): *m/z* calcd for $C_{14}H_{19}O_4$: 251.1283 $[M–OMe]^+$; found 251.1289.

Dimethyl 2-[(*E*)-4-methoxy-3-methylbut-2-enyl]-2-(pent-2-ynyl)malonate (1j)



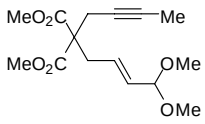
IR (neat): 2980, 1736, 1449, 1289, 1198, 1096 cm^{-1}; ^1H NMR: δ = 1.08 (t, *J* = 7.5 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 6H), 1.69 (br s, 3H), 2.12 (qt, *J* = 7.4, 2.4 Hz, 2H), 2.73 (t, *J* = 2.3 Hz, 2H), 2.83 (d, *J* = 7.8 Hz, 2H), 3.24 (s, 3H), 3.78 (s, 2H), 4.10–4.28 (m, 4H), 5.18–5.26 (m, 1H); ^{13}C NMR: δ = 12.4, 13.9, 14.07, 14.12, 22.9, 30.2, 57.1, 57.3, 61.4, 73.9, 78.3, 84.8, 120.9, 136.6, 170.1; HRMS (CI): *m/z* calcd for $C_{18}H_{29}O_5$: 325.2015 $[M+H]^+$; found 325.2014.

Dimethyl 2-[(*E*)-4-methoxypent-2-enyl]-2-(pent-2-ynyl)malonate (1k)



IR (neat): 2980, 1738, 1289, 1198, 1098, 1071 cm^{-1}; ^1H NMR: δ = 1.09 (t, *J* = 7.5 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 6H), 2.13 (qt, *J* = 7.4, 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 2H), 2.75–2.81 (m, 2H), 3.23 (s, 3H), 3.58–3.73 (m, 1H), 4.10–4.28 (m, 4H), 5.38–5.52 (m, 2H); ^{13}C NMR: δ = 12.4, 14.1, 14.2, 21.5, 22.9, 34.9, 55.8, 57.2, 61.4, 73.6, 77.7, 85.0, 125.8, 136.9, 169.9; HRMS (CI): *m/z* calcd for $C_{18}H_{29}O_5$: 325.2015 $[M+H]^+$; found 325.2017.

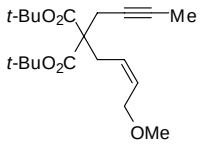
Dimethyl 2-(but-2-ynyl)-2-[(*E*)-4,4-dimethoxybut-2-enyl]malonate (1l)



IR (neat): 2955, 1738, 1437, 1202, 1130, 1053 cm^{-1}; ^1H NMR: δ = 1.75 (t, *J* = 2.4 Hz, 3H), 2.74 (q, *J* = 2.6 Hz, 2H), 2.82 (d, *J* = 7.2 Hz, 2H), 3.28 (s, 6H), 3.73 (s, 6H), 4.71 (d, *J* = 4.2 Hz, 1H), 5.52–5.73 ppm (m, 2H); ^{13}C NMR: δ = 3.5, 23.1, 35.0, 52.6, 52.7, 57.1, 73.0, 79.1, 102.4, 128.4,

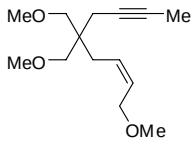
131.6, 170.3 ppm; HRMS (CI): *m/z* calcd for $C_{15}H_{23}O_6$: 299.1495 $[M+H]^+$; found: 299.1493.

Di(*tert*-butyl) 2-(but-2-ynyl)-2-[(*Z*)-4-methoxybut-2-enyl]malonate (1m)



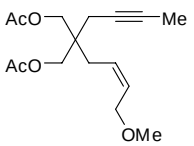
IR (neat): 2975, 1728, 1368, 1300, 1143, 1115 cm^{-1}; ^1H NMR: δ = 1.45 (s, 18H), 1.75 (t, *J* = 2.7 Hz, 3H), 2.61 (q, *J* = 2.5 Hz, 2H), 2.73 (d, *J* = 7.5 Hz, 2H), 3.34 (s, 3H), 4.06 (dd, *J* = 6.3, 1.5 Hz, 2H), 5.31–5.43 (m, 1H), 5.64–5.75 (m, 1H); ^{13}C NMR: δ = 3.4, 22.7, 27.8, 30.0, 57.5, 57.9, 68.2, 74.0, 78.4, 81.5, 126.3, 130.5, 169.2; HRMS (CI): *m/z* calcd for $C_{20}H_{33}O_5$: 353.2328 $[M+H]^+$; found 353.2332.

(*Z*)-5,5-Bis(methoxymethyl)-1-methoxynon-2-en-7-yne (1n)



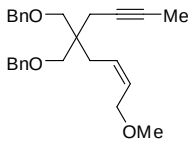
IR (neat): 2921, 2361, 1459, 1198, 1109 cm^{-1}; ^1H NMR: δ = 1.79 (t, *J* = 2.4 Hz, 3H), 2.11 (q, *J* = 2.7 Hz, 2H), 2.15 (d, *J* = 7.2 Hz, 2H), 3.19 (d, *J* = 9.0 Hz, 2H), 3.23 (d, *J* = 9.3 Hz, 2H), 3.32 (s, 6H), 3.33 (s, 3H), 4.02 (d, *J* = 5.7 Hz, 2H), 5.53–5.70 (m, 2H); ^{13}C NMR: δ = 3.6, 22.2, 29.7, 42.3, 57.9, 59.2, 68.2, 74.2, 75.5, 77.3, 128.0, 129.1; HRMS (CI): *m/z* calcd for $C_{13}H_{21}O_2$: 209.1542 $[M–OMe]^+$; found 209.1542.

(*Z*)-5,5-Bis(acetyloxymethyl)-1-methoxynon-2-en-7-yne (1o)



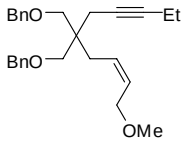
IR (neat): 2922, 1747, 1368, 1231, 1105, 1042 cm^{-1}; ^1H NMR: δ = 1.78 (t, *J* = 2.6 Hz, 3H), 2.06 (s, 6H), 2.19 (q, *J* = 2.5 Hz, 2H), 2.24 (d, *J* = 8.1 Hz, 2H), 3.33 (s, 3H), 3.94–4.04 (m, 6H), 5.47–5.63 (m, 1H), 5.65–5.80 (m, 1H); ^{13}C NMR: δ = 3.5, 20.9, 22.3, 29.5, 40.5, 58.0, 65.4, 68.0, 73.8, 78.7, 126.4, 130.2, 170.7; HRMS (CI): *m/z* calcd for $C_{16}H_{25}O_5$: 297.1702 $[M+H]^+$; found 297.1702.

(*Z*)-5,5-Bis(benzyloxymethyl)-1-methoxynon-2-en-7-yne (1p)



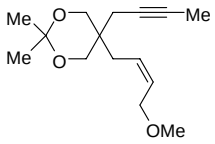
IR (neat): 2859, 1497, 1455, 1366, 1102, 1028 cm^{-1}; ^1H NMR: δ = 1.76 (t, *J* = 2.6 Hz, 3H), 2.16–2.25 (m, 4H), 3.27 (s, 3H), 3.35 (d, *J* = 9.0 Hz, 2H), 3.39 (d, *J* = 8.7 Hz, 2H), 3.99 (d, *J* = 5.1 Hz, 2H), 4.50 (s, 4H), 5.52–5.69 (m, 2H), 7.21–7.36 (m, 10H); ^{13}C NMR: δ = 3.6, 22.4, 29.8, 42.6, 57.9, 68.3, 71.7, 73.2, 75.6, 77.4, 127.3, 128.1, 128.2, 129.1, 138.7; HRMS (CI): *m/z* calcd for $C_{26}H_{33}O_3$: 393.2430 $[M+H]^+$; found 393.2436.

(*Z*)-5,5-Bis(benzyloxymethyl)-1-methoxydec-2-en-7-yne (1q)



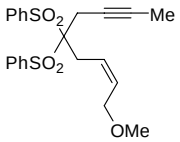
IR (neat): 2861, 1497, 1455, 1366, 1102, 1028 cm^{-1}; ^1H NMR: δ = 1.10 (t, *J* = 7.4 Hz, 3H), 2.14 (qt, *J* = 7.6, 2.3 Hz, 2H), 2.18–2.26 (m, 4H), 3.28 (s, 3H), 3.35 (d, *J* = 9.0 Hz, 2H), 3.40 (d, *J* = 8.7 Hz, 2H), 4.00 (d, *J* = 4.8 Hz, 2H), 4.50 (s, 4H), 5.53–5.70 (m, 2H), 7,21–7.39 (m, 10H); ^{13}C NMR: δ = 12.5, 14.4, 22.3, 29.7, 42.6, 57.9, 68.2, 71.7, 73.2, 75.8, 83.6, 127.3, 128.1, 128.2, 129.1, 138.7; HRMS (CI): *m/z* calcd for $C_{27}H_{35}O_3$: 407.2586 $[M+H]^+$; found 407.2590.

5-(But-2-ynyl)-5-[(*Z*)-4-methoxybut-2-enyl]-2,2-dimethyl-1,3-dioxane (1r)



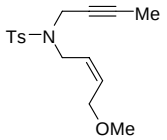
IR (neat): 2992, 1452, 1372, 1258, 1198, cm^{-1}; ^1H NMR: δ = 1.40 (s, 3H), 1.41 (s, 3H), 1.79 (t, *J* = 2.3 Hz, 3H), 2.18–2.28 (m, 4H), 3.34 (s, 3H), 3.61 (d, *J* = 11.7 Hz, 2H), 3.67 (d, *J* = 11.7 Hz, 2H), 4.03 (d, *J* = 6.3 Hz, 2H), 5.48–5.78 (m, 2H); ^{13}C NMR: δ = 3.5, 22.6, 23.0, 24.6, 30.4, 36.0, 58.0, 66.7, 68.0, 74.9, 78.2, 98.0, 126.9, 129.9; HRMS (CI): *m/z* calcd for $C_{15}H_{25}O_3$: 253.1804 $[M+H]^+$; found 253.1806.

(*Z*)-5,5-Bis(phenylsulfonyl)-1-methoxynon-2-en-7-yne (1s)



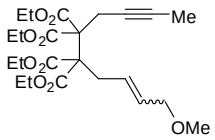
IR (nujol): 1333, 1308, 1146, 1076 cm^{-1}; ^1H NMR: δ = 1.64 (t, *J* = 2.7 Hz, 3H), 3.10 (d, *J* = 6.0 Hz, 2H), 3.16 (q, *J* = 2.5 Hz, 2H), 3.33 (s, 3H), 3.97 (d, *J* = 6.0 Hz, 2H), 5.75–5.94 (m, 2H), 7.54–7.61 (m, 4H), 7.67–7.74 (m, 2H), 8.06–8.13 (m, 4H); ^{13}C NMR: δ = 3.7, 20.9, 27.7, 58.3, 68.3, 70.6, 81.9, 88.9, 123.5, 128.5, 130.7, 131.5, 134.6, 136.7; HRMS (CI): *m/z* calcd for $C_{22}H_{25}O_5S_2$: 433.1143 $[M+H]^+$; found 433.1143.

(*Z*)-5-(4-methylbenzenesulfonyl)-1-methoxy-5-azanon-2-en-7-yne (1t)



IR (nujol): 1597, 1340, 1161, 1094 cm^{-1}; ^1H NMR: δ = 1.55 (t, *J* = 2.4 Hz, 3H), 2.43 (s, 3H), 3.31 (s, 3H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.97–4.04 (m, 4H), 5.46–5.58 (m, 1H), 5.72–5.83 (m, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR: δ = 3.3, 21.5, 36.4, 43.1, 58.1, 67.7, 71.8, 81.6, 126.6, 127.9, 129.3, 131.8, 136.0, 143.3; HRMS (CI): *m/z* calcd for $C_{16}H_{22}NO_3S$: 308.1320 $[M+H]^+$; found 308.1321.

Tetraethyl 1-methoxydec-2-en-8-yne-5,5,6,6-tetracarboxylate (1u)

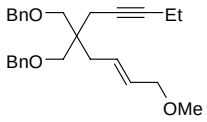


Mixture of geometrical isomers (*E*:*Z*=1:4)

IR (neat, mixture): 2984, 1732, 1368, 1206, 1097, 1036 cm^{-1}; ^1H NMR (mixture): δ = 1.19–1.13 (m, 12H), 1.69–1.77 (m, 3H), 2.86 (d, *J* = 6.9 Hz, 0.4H), 2.98 (d, *J* = 6.9 Hz, 1.6H), 3.00–3.09 (m, 2H), 3.27 (s, 0.6H), 3.33 (s, 2.4H), 3.82 (d, *J* = 5.7 Hz, 0.4H), 4.00 (d, *J* = 6.3 Hz, 1.6H), 4.06–4.32 (m, 8H), 5.53–5.93 (m, 2H); ^{13}C NMR (mixture): δ = 3.6, 13.79, 13.83, 22.6, 22.8, 29.6, 34.6, 57.6, 58.0, 61.55, 61.63, 61.66, 61.71, 62.03, 62.08, 62.12, 62.4, 68.2, 72.7, 74.60, 74.63, 77.9, 78.1, 127.7, 129.0, 129.7, 130.9, 168.76, 168.82, 168.9, 169.0; HRMS (CI, mixture): *m/z* calcd for $C_{23}H_{35}O_9$:

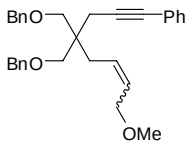
455.2281 $[M+H]^+$; found 455.2269 (major isomer) and 455.2271 (minor isomer).

(*E*)-5,5-Bis(benzyloxymethyl)-1-methoxydec-2-en-7-yne (1v)



IR (neat): 2857, 1455, 1364, 1102, 1028 cm^{-1}; ^1H NMR: δ = 1.09 (t, *J* = 7.4 Hz, 3H), 2.13 (qt, *J* = 7.4, 2.4 Hz, 2H), 2.18–2.24 (m, 4H), 3.28 (s, 3H), 3.35 (d, *J* = 9.0 Hz, 2H), 3.39 (d, *J* = 8.7 Hz, 2H), 3.84 (d, *J* = 5.4 Hz, 2H), 4.50 (s, 4H), 5.53–5.73 (m, 2H), 7.22–7.36 (m, 10H); ^{13}C NMR: δ = 12.5, 14.4, 22.4, 34.7, 42.3, 57.6, 71.9, 73.1, 73.2, 75.8, 83.7, 127.28, 127.34, 128.2, 129.5, 129.7, 138.8; HRMS (CI): *m/z* calcd for $C_{27}H_{35}O_3$: 407.2586 $[M+H]^+$; found 407.2591.

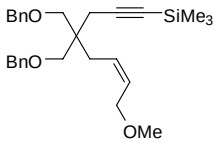
5,5-Bis(benzyloxymethyl)-1-methoxy-8-phenyloct-2-en-7-yne (1w)



Mixture of geometrical isomers. (62:38)

IR (neat, mixture): 2861, 1491, 1455, 1364, 1102, 1028 cm^{-1}; ^1H NMR (major isomer): δ = 2.32 (d, *J* = 6.6 Hz, 2H), 2.50 (s, 2H), 3.26 (s, 3H), 3.43 (d, *J* = 9.0 Hz, 2H), 3.47 (d, *J* = 9.0 Hz, 2H), 4.02 (d, *J* = 5.1 Hz, 2H), 4.53 (s, 4H), 5.57–5.74 (m, 2H), 7.21–7.40 (m, 15H); ^{13}C NMR (major isomer): δ = 23.1, 30.0, 43.0, 58.0, 68.3, 71.8, 73.3, 82.5, 87.0, 123.9, 127.3, 127.6, 127.9, 128.1, 128.2, 129.4, 131.5, 138.6; ^1H NMR (minor isomer): δ = 2.30 (d, *J* = 6.6 Hz, 2H), 2.49 (s, 2H), 3.28 (s, 3H), 3.43 (d, *J* = 9.0 Hz, 2H), 3.47 (d, *J* = 9.0 Hz, 2H), 3.85 (d, *J* = 5.1 Hz, 2H), 4.52 (s, 4H), 5.57–5.77 (m, 2H), 7.21–7.40 (m, 15H); ^{13}C NMR (minor isomer): δ = 23.2, 35.0, 42.7, 57.6, 72.0, 73.1, 73.3, 82.6, 87.0, 124.0, 127.3, 127.4, 127.5, 128.1, 128.2, 129.4, 129.9, 131.5, 138.7; HRMS (CI, mixture): *m/z* calcd for $C_{31}H_{35}O_3$: 455.2586 $[M+H]^+$; found 455.2588.

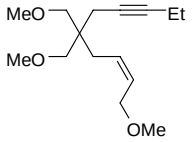
(*Z*)-5,5-Bis(benzyloxymethyl)-1-methoxy-8-trimethylsilyloct-2-en-7-yne (1x)



IR (neat): 2859, 2174, 1455, 1364, 1250, 1102 cm^{-1}; ^1H NMR: δ = 0.13 (s, 9H), 2.24 (d, *J* = 6.6 Hz,

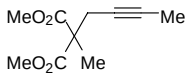
2H), 2.30 (s, 2H), 3.28 (s, 3H), 3.36 (d, J = 9.0 Hz, 2H), 3.40 (d, J = 8.7 Hz, 2H), 4.00 (d, J = 5.4 Hz, 2H), 4.49 (s, 4H), 5.52–5.70 (m, 2H), 7.22–7.36 (m, 10H); ^{13}C NMR: δ = 0.2, 23.5, 29.8, 42.6, 58.0, 68.2, 71.7, 73.3, 86.7, 104.2, 127.3, 127.4, 127.9, 128.2, 129.3, 138.7; HRMS (CI): *m/z* calcd for $C_{28}H_{39}O_3Si$: 451.2668 $[M+H]^+$; found 451.2662.

(*Z*)-5,5-Bis(methoxymethyl)-1-methoxydec-2-en-7-yne (1y)



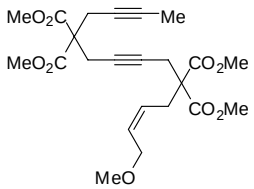
IR (neat): 2887, 1459, 1320, 1198, 1109 cm^{-1}; ^{1}H NMR: δ = 1.13 (t, J = 7.2 Hz, 3H), 2.10–2.23 (m, 6H), 3.20 (d, J = 8.7 Hz, 2H), 3.24 (d, J = 9.0 Hz, 2H), 3.32 (s, 6H), 3.34 (s, 3H), 4.03 (d, J = 5.4 Hz, 2H), 5.53–5.72 (m, 2H); ^{13}C NMR: δ = 12.5, 14.4, 22.2, 29.7, 42.3, 57.9, 59.2, 68.2, 74.2, 75.7, 83.6, 128.1, 129.1; HRMS (CI): *m/z* calcd for $C_{15}H_{27}O_3$: 255.1960 $[M+H]^+$; found 255.1961.

Dimethyl 2-(but-2-ynyl)-2-methylmalonate (6)



IR (neat): 2955, 1736, 1437, 1252, 1206, 1115 cm^{-1}; ^{1}H NMR: δ = 1.52 (s, 3H), 1.75 (t, J = 3.0 Hz, 3H), 2.73 (q, J = 2.7 Hz, 2H), 3.73 (s, 6H); ^{13}C NMR: δ = 3.5, 19.9, 26.2, 52.7, 53.5, 73.6, 78.8, 171.6; HRMS (CI): *m/z* calcd for $C_{10}H_{15}O_4$: 199.0970 $[M+H]^+$; found 199.0974.

(*Z*)-5,5,10,10-Tetramethoxycarbonyl-1-methoxytetradeca-2-ene-7,12-diyne (8)

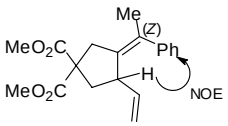


IR (neat): 2957, 1739, 1437, 1329, 1294, 1239 cm^{-1}; ^{1}H NMR: δ = 1.74 (t, J = 2.6 Hz, 3H), 2.75 (t, J = 2.4 Hz, 2H), 2.78 (d, J = 7.8 Hz, 2H), 2.87 (q, J = 2.5 Hz, 2H), 2.93 (t, J = 2.3 Hz, 2H), 3.34 (s, 3H), 3.73 (s, 6H), 3.74 (s, 6H), 4.01 (dd, J = 6.6, 1.5 Hz, 2H), 5.28–5.40 (m, 1H), 5.64–5.75 (m, 1H); ^{13}C NMR: δ = 3.5, 22.88, 22.93, 30.2, 52.8, 52.9, 56.7, 56.9, 58.0, 67.9, 72.9, 77.7, 77.8, 79.1, 125.5, 128.3, 131.1, 169.3, 170.1; HRMS (CI): *m/z* calcd for $C_{23}H_{31}O_9$: 451.1968 $[M+H]^+$; found 451.1979.

Typical procedure for rhodium-catalyzed cyclization of 1,6-enynes with arylboronic acids:

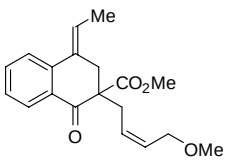
To an oven-dried, argon-purged flask was added $[Rh(OH)(cod)]_2$ (1.37 mg, 0.3 μmol, 0.03 equiv of Rh) and arylboronic acid (0.4 mmol, 2.0 equiv), followed by 1 mL of 1,4-dioxane. A solution of substrate (0.2 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL) was added to the reaction mixture at room temperature. After complete consumption of substrate, the reaction was quenched with water. The aqueous layer was extracted with ethyl acetate three times, and the combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the purified product.

(*Z*)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-vinylcyclopentane (3aa)



The *Z* configuration of the *exo* double bond was assigned on the basis of the observed NOE. $[\alpha]^{23}_{D}$ = +58.6 (*c* = 0.95, $CHCl_3$) (97% *ee*); IR (neat): 2953, 1732, 1435, 1254, 1204, 1069 cm^{-1}; ^1H NMR: δ = 1.98–2.02 (m, 3H), 2.14 (dd, *J* = 13.2, 6.3 Hz, 1H), 2.52 (ddd, *J* = 13.1, 7.9, 1.0 Hz, 1H), 3.04 (d, *J* = 16.8 Hz, 1H), 3.15 (dt, *J* = 16.5, 1.8 Hz, 1H), 3.33–3.45 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 4.56 (dt, *J* = 17.1, 1.5 Hz, 1H), 4.63 (dt, *J* = 10.2, 1.5 Hz, 1H), 5.37 (ddd, *J* = 17.1, 10.2, 6.9 Hz, 1H), 7.09–7.28 (m, 5H); ^{13}C NMR: δ = 22.2, 38.9, 40.5, 45.4, 52.7, 52.9, 58.8, 113.9, 126.2, 127.8, 131.4, 136.1, 139.6, 143.5, 172.2, 172.4; elemental analysis: calcd for $C_{19}H_{22}O_4$: C 72.59, H 7.05; found: C 72.78, H 7.07; HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 93:7, flow rate = 0.6 mL min^{-1}): *t* = 8.04 min (major), *t* = 9.47 min (minor).

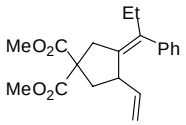
Methyl 4-[(*E*)-ethylidene]-2-[(*Z*)-4-methoxybut-2-enyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (5)



IR (neat): 2923, 1738, 1688, 1437, 1210, 1113 cm^{-1}; ^1H NMR: δ = 1.90 (d, *J* = 6.9 Hz, 3H), 2.69–2.80 (m, 3H), 3.26–3.33 (m, 1H), 3.31 (s, 3H), 3.65 (s, 3H), 3.98 (d, *J*=5.9 Hz, 2H), 5.54–5.74

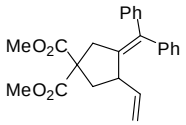
(m, 2H), 6.36 (q, *J* = 7.0 Hz, 1H), 7.33 (td, *J* = 7.4, 1.4 Hz, 1H), 7.50 (td, *J* = 7.4, 1.4 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 8.32 (dd, *J* = 7.7, 1.1 Hz, 1H); ^{13}C NMR: δ = 14.2, 31.9, 33.3, 52.5, 58.0, 58.7, 68.1, 123.7, 124.8, 127.0, 127.5, 127.9, 129.6, 129.9, 130.4, 133.8, 141.7, 171.7, 194.8; HRMS (CI): *m/z* calcd for $C_{19}H_{23}O_4$: 315.1596 $[M+H]^+$; found 315.1584.

(*Z*)-1,1-Dimethoxycarbonyl-3-(1-phenylpropylidene)-4-vinylcyclopentane (3ea)



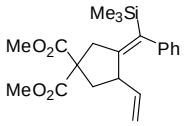
IR (neat): 2957, 1738, 1435, 1262, 1204, 1171 cm^{-1}; ^{1}H NMR: δ = 0.91 (t, *J* = 7.5 Hz, 3H), 2.08 (dd, *J* = 12.9, 6.0 Hz, 1H), 2.20–2.48 (m, 2H), 2.53 (dd, *J* = 13.2, 8.1 Hz, 1H), 3.09 (s, 2H), 3.25–3.36 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 4.48 (dt, *J* = 16.8, 1.5 Hz, 1H), 4.59 (dt, *J* = 9.9, 1.8 Hz, 1H), 5.35 (ddd, *J* = 17.1, 10.5, 6.9 Hz, 1H), 7.03–7.08 (m, 2H), 7.16–7.27 (m, 3H); ^{13}C NMR: δ = 12.5, 29.2, 38.1, 40.0, 45.0, 52.7, 52.8, 58.9, 113.6, 126.2, 127.7, 128.5, 135.3, 138.4, 139.5, 142.0, 172.1, 172.3; HRMS (EI): *m/z* calcd for $C_{20}H_{24}O_4$: 328.1675 $[M]^+$; found 328.1674.

1,1-Dimethoxycarbonyl-3-(diphenylmethylene)-4-vinylcyclopentane (3fa)



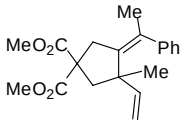
IR (neat): 2953, 1734, 1267, 1206, 1167, 1075 cm^{-1}; ^{1}H NMR: δ = 2.08 (dd, *J* = 13.2, 7.2 Hz, 1H), 2.66 (ddd, *J* = 12.9, 8.1, 1.8 Hz, 1H), 2.94 (dd, *J* = 16.5, 1.8 Hz, 1H), 3.24 (dd, *J* = 16.5, 2.4 Hz, 1H), 3.68–3.75 (m, 1H), 3.70 (s, 3H), 3.72 (s, 3H), 4.57 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.66 (dt, *J* = 10.2, 1.2 Hz, 1H), 5.48 (ddd, *J* = 17.1, 10.2, 6.9 Hz, 1H), 7.08–7.32 (m, 10H); ^{13}C NMR: δ = 39.7, 40.3, 45.4, 52.8, 59.2, 114.0, 126.56, 126.62, 128.0, 129.0, 129.3, 138.1, 138.9, 139.3, 141.8, 142.6, 171.9, 172.0; HRMS (EI): *m/z* calcd for $C_{24}H_{24}O_4$: 376.1675 $[M]^+$; found 376.1674.

(*E*)-1,1-Dimethoxycarbonyl-3-(phenyltrimethylsilylmethylene)-4-vinylcyclopentane (3ga)



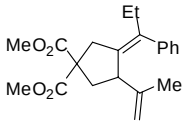
IR (neat): 2955, 1737, 1435, 1252, 1206, 1073 cm^{-1}; ^1H NMR: δ = 0.06 (s, 9H), 1.98 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.55 (dd, *J* = 13.4, 8.6 Hz, 1H), 3.12 (s, 2H), 3.21–3.32 (m, 1H), 3.74 (s, 3H), 3.77 (s, 3H), 4.45 (d, *J* = 17.1 Hz, 1H), 4.60 (d, *J* = 10.3 Hz, 1H), 5.41 (ddd, *J* = 17.1, 10.2, 7.1 Hz, 1H), 6.81 (d, *J* = 7.2 Hz, 2H), 7.05–7.14 (m, 1H), 7.15–7.25 (m, 2H); ^{13}C NMR: δ = –0.1, 38.8, 40.5, 46.2, 52.8, 59.2, 113.5, 125.1, 127.6, 139.4, 139.5, 143.6, 151.7, 171.96, 172.01; HRMS (EI): *m/z* calcd for $C_{21}H_{28}O_4Si$: 372.1757 $[M]^+$; found 372.1757.

(*Z*)-1,1-Dimethoxycarbonyl-4-methyl-3-(1-phenylethylidene)-4-vinylcyclopentane (3ia)



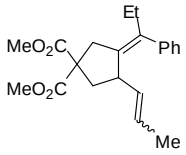
IR (neat): 2953, 1740, 1435, 1256, 1204, 1171 cm^{-1}; ^1H NMR: δ = 0.79 (s, 3H), 1.92–1.98 (m, 3H), 2.25 (d, *J* = 13.5 Hz, 1H), 2.47 (dd, *J* = 13.4, 1.1 Hz, 1H), 3.16 (dd, *J* = 17.4, 1.2 Hz, 1H), 3.31 (dt, *J* = 17.6, 1.3 Hz, 1H), 3.71 (s, 3H), 3.75 (s, 3H), 4.69 (dd, *J* = 10.5, 1.2 Hz, 1H), 4.76 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.58 (dd, *J* = 17.4, 10.8 Hz, 1H), 7.02–7.09 (m, 2H), 7.12–7.25 (m, 3H); ^{13}C NMR: δ = 24.4, 25.3, 40.3, 49.1, 49.3, 52.7, 52.9, 57.1, 111.1, 126.1, 127.4, 128.5, 131.1, 138.7, 143.6, 145.5, 172.3, 172.9; HRMS (EI): *m/z* calcd for $C_{20}H_{24}O_4$: 328.1675 $[M]^+$; found 328.1667.

(*Z*)-1,1-Dimethoxycarbonyl-3-(1-phenylpropylidene)-4-(2-prop-2-enyl)cyclopentane (3ja)



IR (neat): 2965, 1732, 1445, 1254, 1181, 1071 cm^{-1}; ^1H NMR: δ = 0.92 (t, *J* = 7.5 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.45 (s, 3H), 2.10 (dd, *J* = 13.1, 7.1 Hz, 1H), 2.23–2.49 (m, 2H), 2.47 (ddd, *J* = 13.3, 8.3, 1.4 Hz, 1H), 3.04 (d, *J* = 16.2 Hz, 1H), 3.17 (dd, *J* = 16.1, 1.4 Hz, 1H), 3.24–3.33 (m, 1H), 4.11–4.29 (m, 4H), 4.31–4.36 (m, 1H), 4.37–4.42 (m, 1H), 7.01–7.09 (m, 2H), 7.10–7.26 (m, 3H); ^{13}C NMR: δ = 12.6, 14.0, 14.2, 19.4, 29.1, 38.7, 38.9, 48.7, 59.2, 61.4, 61.5, 111.6, 126.0, 127.6, 128.2, 135.5, 138.1, 142.2 , 145.7, 171.6, 171.8; HRMS (EI): *m/z* calcd for $C_{23}H_{30}O_4$: 370.2144 $[M]^+$; found 370.2143.

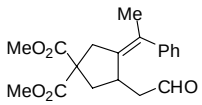
1,1-Dimethoxycarbonyl-3-[(*Z*)-1-phenylpropylidene]-4-(prop-1-enyl)cyclopentane (3ka)



Mixture of geometrical isomers. (59:41)

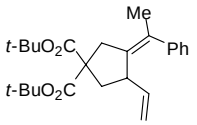
IR (neat, mixture:): 2979, 1732, 1445, 1256, 1179, 1094 cm^{-1}; ^1H NMR (major isomer): δ = 0.90 (t, *J* = 7.5 Hz, 3H), 1.21–1.32 (m, 9H) 1.97 (dd, *J* = 13.1, 7.1 Hz, 1H), 2.17–2.32 (m, 1H), 2.32–2.44 (m, 1H), 2.49 (dd, *J* = 13.1, 8.3 Hz, 1H), 3.05 (s, 2H), 3.13–3.25 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.72 (dq, *J* = 15.0, 6.4 Hz, 1H), 4.84–4.94 (m, 1H), 6.99–7.05 (m, 2H), 7.11–7.17 (m, 3H); ^{13}C NMR (major isomer): δ = 12.5, 14.09, 14.13, 17.7, 29.2, 38.1, 40.5, 44.4, 59.0, 61.41, 61.45, 124.5, 126.0, 127.6, 128.6, 132.4, 136.3, 137.8, 142.0, 171.8, 171.9; HRMS (EI, major isomer): *m/z* calcd for $C_{23}H_{30}O_4$: 370.2144 $[M]^+$; found 370.2153. ^1H NMR (minor isomer): δ = 0.89 (t, *J* = 7.4 Hz, 3H), 1.04 (d, *J* = 5.1 Hz, 3H), 1.26 (t, *J* = 7.3 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.80 (dd, *J* = 13.1, 8.0 Hz, 1H), 2.15–2.30 (m, 1H), 2.31–2.46 (m, 1H), 2.58 (ddd, *J* = 13.1, 8.3, 1.2 Hz, 1H), 3.05 (d, *J* = 16.2 Hz, 1H), 3.12 (d, *J* = 16.2 Hz, 1H), 3.54–3.65 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.85–4.98 (m, 2H), 6.99–7.05 (m, 2H), 7.10–7.16 (m, 1H), 7.18–7.26 (m, 2H); ^{13}C NMR (minor isomer): δ = 12.1, 12.5, 14.1, 14.2, 29.3, 38.3, 38.9, 40.7, 59.1, 61.4, 61.5, 122.1, 125.9, 127.7, 128.6, 132.8, 136.8, 137.7, 142.1, 171.78, 171.81; HRMS (EI, minor isomer): *m/z* calcd for $C_{23}H_{30}O_4$: 370.2144 $[M]^+$; found 370.2153.

(*Z*)-1,1-Dimethoxycarbonyl-4-(formylmethyl)-3-(1-phenylethylidene)cyclopentane (3la)



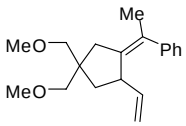
IR (neat): 2955, 2726, 1722, 1435, 1261, 1203 cm^{-1}; ^1H NMR: δ = 1.91 (dd, *J* = 13.5, 7.7 Hz, 1H), 1.97 (br s, 3H), 2.04 (ddd, *J* = 17.7, 9.3, 2.1 Hz, 1H), 2.11 (ddd, *J* = 17.4, 4.2, 1.2 Hz, 1H), 2.68 (ddd, *J* = 13.4, 8.3, 1.6 Hz, 1H), 3.01 (dt, *J* = 16.7, 1.9 Hz, 1H), 3.13 (d, *J* = 16.5 Hz, 1H), 3.29–3.43 (m, 1H), 3.75 (s, 3H), 3.78 (s, 3H), 7.09–7.14 (m, 2H), 7.17–7.25 (m, 1H), 7.26–7.34 (m, 2H), 9.32–9.34 (m, 1H); ^{13}C NMR: δ = 22.6, 35.0, 39.3, 40.0, 47.8, 52.85, 52.91, 58.8, 126.8, 127.5, 128.5, 131.0, 136.5, 143.2, 172.0, 172.1, 201.3; HRMS (CI): *m/z* calcd for $C_{19}H_{23}O_5$: 331.1545 $[M+H]^+$; found 331.1547.

(*Z*)-1,1-Di(*tert*-butyloxycarbonyl)-3-(1-phenylethylidene)-4-vinylcyclopentane (3ma)



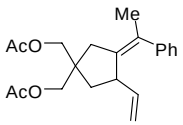
IR (neat): 2979, 1728, 1370, 1258, 1165, 1144 cm^{-1}; ^1H NMR: δ = 1.46 (s, 9H), 1.48 (s, 9H), 1.97 (dd, *J* = 12.9, 6.0 Hz, 1H), 2.00 (d, *J* = 1.5 Hz, 3H), 2.46 (dd, *J* = 12.9, 8.4 Hz, 1H), 2.90–3.06 (m, 2H), 3.30–3.42 (m, 1H), 4.52 (dt, *J* = 17.1, 1.6 Hz, 1H), 4.59 (ddd, *J* = 10.0, 1.7, 1.1 Hz, 1H), 5.40 (ddd, *J* = 17.2, 10.0, 7.3 Hz, 1H), 7.08–7.19 (m, 3H), 7.20–7.30 (m, 2H); ^{13}C NMR: δ = 22.2, 27.9, 38.6, 40.2, 45.4, 60.2, 81.1, 81.2, 113.5, 126.1, 127.8, 127.9, 130.9, 136.9, 140.1, 143.7, 170.9, 171.1; HRMS (FAB): *m/z* calcd for $C_{25}H_{35}O_4$: 399.2535 $[M+H]^+$; found 399.2536.

(*Z*)-1,1-Bis(Methoxymethyl)-3-(1-phenylethylidene)-4-vinylcyclopentane (3na)



IR (neat): 2975, 1458, 1447, 1198, 1109 cm^{-1}; ^1H NMR: δ = 1.45 (dd, *J* = 13.2, 6.3 Hz, 1H), 1.80 (ddd, *J* = 13.2, 8.7, 0.9 Hz, 1H), 1.98 (br s, 3H), 2.26 (dt, *J* = 16.2, 1.8 Hz, 1H), 2.43 (d, *J* = 16.5 Hz, 1H), 3,24 (d, *J* = 9.3 Hz, 1H), 3.28 (d, *J* = 9.0 Hz, 1H), 3.32–3.36 (m, 3H), 3.36 (s, 3H), 3.38 (s, 3H), 4.47–4.59 (m, 2H), 5.43 (ddd, *J* = 17.4, 10.2, 7.2 Hz, 1H), 7.11–7.29 (m, 5H); ^{13}C NMR: δ = 22.3, 37.7, 38.4, 44.9, 46.4, 59.3, 59.4, 75.5, 77.0, 112.4, 125.9, 127.7, 128.0, 130.6, 139.0, 141.6, 144.1; HRMS (CI): *m/z* calcd for $C_{19}H_{26}O_2$: 286.1933 $[M]^+$; found 286.1928.

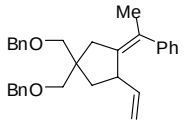
(*Z*)-1,1-Bis(acetoxymethyl)-3-(1-phenylethylidene)-4-vinylcyclopentane (3oa)



IR (neat): 2953, 1744, 1379, 1364, 1229, 1038 cm^{-1}; ^1H NMR: δ = 1.49 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.84 (ddd, *J* = 13.6, 8.6, 1.0 Hz, 1H), 1.98 (br s, 3H), 2.08 (s, 3H), 2.09 (s, 3H), 2.31 (d, *J* = 16.1 Hz, 1H), 2.47 (d, *J* = 16.2 Hz, 1H), 3.30–3.43 (m, 1H), 3.98 (d, *J* = 10.8 Hz, 1H), 4.03 (d, *J* = 11.1 Hz, 1H), 4.08 (s, 2H), 4.52 (dt, *J* = 16.9, 1.6 Hz, 1H), 4.60 (dt, *J* = 10.1, 1.4 Hz, 1H), 5.41 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1H), 7.09–7.21 (m, 3H), 7.22–7.30 (m, 2H); ^{13}C NMR: δ = 20.9, 22.4, 37.4, 38.3, 44.4,

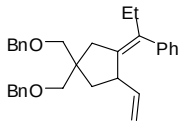
44.6, 66.2, 67.8, 113.1, 126.2, 127.8, 131.8, 137.2, 140.8, 143.6, 171.0, 171.1; HRMS (CI): *m/z* calcd for $C_{21}H_{26}O_4$: 342.1831 $[M]^+$; found 342.1824.

(*Z*)-1,1-Bis(benzyloxymethyl)-3-(1-phenylethylidene)-4-vinylcyclopentane (3pa)



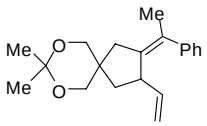
IR (neat): 2855, 1495, 1455, 1364, 1100, 1028 cm^{-1}; ^1H NMR: δ = 1.48 (dd, *J* = 13.2, 6.9 Hz, 1H), 1.85 (dd, *J* = 13.2, 8.7 Hz, 1H), 1.95 (br s, 3H), 2.27 (dt, *J* = 16.2, 1.8 Hz, 1H), 2.49 (d, *J* = 16.2 Hz, 1H), 3.19–3.32 (m, 1H), 3.36 (d, *J* = 9.0 Hz, 1H), 3.41 (d, *J* = 9.0 Hz, 1H), 3.49 (s, 2H), 4.44 (dd, *J* = 17.1, 1.2 Hz, 1H), 4.51 (dd, *J* = 10.2, 0.9 Hz, 1H), 4.53 (s, 2H), 4.55 (s, 2H), 5.38 (ddd, *J* = 17.2, 10.1, 7.1 Hz, 1H), 7.02–7.08 (m, 2H), 7.11–7.18 (m, 1H), 7.19–7.38 (m, 12H); ^{13}C NMR: δ = 22.4, 37.8, 38.6, 44.9, 46.6, 72.6, 73.1, 73.2, 74.5, 112.4, 125.9, 127.3, 127.4, 127.5, 127.7, 128.0, 128.2, 130.5, 138.9, 139.1, 141.6, 144.2; HRMS (CI): *m/z* calcd for $C_{31}H_{35}O_2$: 439.2637 $[M+H]^+$; found 439.2642.

(*Z*)-1,1-Bis(bezyloxymethyl)-3-(1-phenylpropylidene)-4-vinylcyclopentane (3qa)



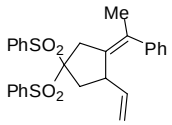
$[\alpha]^{27}_D$ = +50.7 (*c* = 1.33, $CHCl_3$) (87% *ee*); IR (neat): 2857, 1455, 1364, 1100, 1028 cm^{-1}; ^1H NMR: δ = 0.87 (t, *J* = 7.5 Hz, 3H), 1.45 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.83 (dd, *J* = 13.2, 8.7 Hz, 1H), 2.16–2.44 (m, 3H), 2.51 (d, *J* = 15.9 Hz, 1H), 3.10–3.23 (m, 1H), 3.36 (d, *J* = 9.0 Hz, 1H), 3.41 (d, *J* = 9.0 Hz, 1H), 3.49 (s, 2H), 4.39 (dt, *J* = 17.1, 1.5 Hz, 1H), 4.49 (d, *J* = 10.2 Hz, 1H), 4.53 (s, 2H), 4.54 (s, 2H), 5.37 (ddd, *J* = 17.2, 10.1, 7.3 Hz, 1H), 6.97–7.03 (m, 2H), 7.11–7.39 (m, 13H); ^{13}C NMR: δ = 12.8, 29.2, 36.8, 38.2, 44.7, 46.7, 72.6, 73.2, 74.6, 112.1, 125.9, 127.3, 127.37, 127.42, 127.5, 127.6, 128.2, 128.7, 137.4, 138.4, 138.8, 138.9, 141.5, 142.7; HRMS (CI): *m/z* calcd for $C_{32}H_{37}O_2$: 453.2794 $[M+H]^+$; found 453.2793; HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 99.8:0.2, flow rate = 0.6 mL min^{-1}): *t* = 15.98 min (major), *t* = 17.99 min (minor).

(*Z*)-8,8-Dimethyl-2-(1-phenylethylidene)-3-vinyl-7,9-dioxaspiro[4.5]decane (3ra)



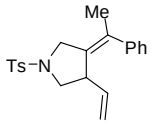
IR (neat): 2992, 2857, 1383, 1370, 1200, 1069 cm^{-1}; ^1H NMR: δ = 1.41 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.443 (s, 3H), 1.447 (s, 3H), 1.77 (ddd, *J* = 13.2, 8.4, 0.6 Hz, 1H), 2.00 (br s, 3H), 2.32 (d, *J* = 16.8 Hz, 1H), 2.65 (d, *J* = 16.8 Hz, 1H), 3.25–3.38 (m, 1H), 3.59 (dd, *J* = 11.4, 1.2 Hz, 1H), 3.67 (d, *J* = 11.7 Hz, 1H), 3.69 (dd, *J* = 11.1, 1.2 Hz, 1H), 3.76 (d, *J* = 11.4 Hz, 1H), 4.56 (dt, *J* = 17.1, 1.7 Hz, 1H), 4.62 (dt, *J* = 10.2, 1.3 Hz, 1H), 5.44 (ddd, *J* = 17.0, 10.1, 6.8 Hz, 1H), 7.10–7.20 (m, 3H), 7.21–7.30 (m, 2H); ^{13}C NMR: δ = 22.3, 22.4, 25.3, 38.7, 39.5, 40.6, 44.7, 68.6, 69.7, 97.8, 113.0, 126.0, 127.75, 127.82, 131.3, 137.9, 141.3, 143.9; HRMS (CI): *m/z* calcd for $C_{20}H_{26}O_2$: 298.1933 $[M]^+$; found 298.1933.

(*Z*)-3-(1-Phenylethylidene)-1,1-bis(phenylsulfonyl)-4-vinylcyclopentane (3sa)



IR (nujol): 1330, 1314, 1148, 1080 cm^{-1}; ^1H NMR: δ = 1.89 (s, 3H), 2.53 (dd, *J* = 15.3, 7.2 Hz, 1H), 2.77 (ddd, *J* = 15.2, 8.5, 1.6 Hz, 1H), 3.09 (d, *J* = 18.3 Hz, 1H), 3.57 (dt, *J* = 18.0, 2.2 Hz, 1H), 3.58–3.70 (m, 1H), 4.33 (d, *J* = 16.8 Hz, 1H), 4.53 (d, *J* = 10.2 Hz, 1H), 5.33 (ddd, *J* = 17.0, 10.1, 8.3 Hz, 1H), 7.01–7.05 (m, 2H), 7.15–7.29 (m, 3H), 7.58–7.66 (m, 4H), 7.70–7.79 (m, 2H), 8.06–8.13 (m, 4H); ^{13}C NMR: δ = 22.7, 36.3, 37.6, 45.9, 92.5, 114.2, 126.6, 127.8, 128.0, 128.7, 128.8, 131.00, 131.06, 132.5, 134.3, 134.5, 134.7, 136.1, 137.2, 138.7, 142.6; HRMS (CI): *m/z* calcd for $C_{27}H_{27}O_4S_2$: 479.1351 $[M+H]^+$; found 479.1354.

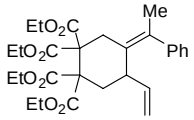
(*Z*)-3-(1-Phenylethylidene)-1-(4-methylbenzenesulfonyl)-4-vinylpyrrolidine (3ta)



IR (neat): 2984, 1599, 1495, 1338, 1163, 1096 cm^{-1}; ^1H NMR: δ = 1.91 (br s, 3H), 2.46 (s, 3H), 3.17 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.23–3.33 (m, 1H), 3.26 (dd, *J* = 9.2, 2.3 Hz, 1H), 3.85 (d, *J* = 14.1

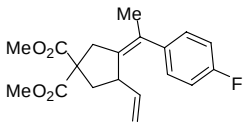
Hz, 1H), 4.01 (dt, *J* = 14.0, 1.4 Hz, 1H), 4.63 (dt, *J* = 17.1, 1.4 Hz, 1H), 4.76 (dt, *J* = 10.1, 1.1 Hz, 1H), 5.53 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1H), 7.04–7.11 (m, 2H), 7.16–7.29 (m, 3H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.71–7.78 (m, 2H); ^{13}C NMR: δ = 21.6, 21.8, 45.2, 50.5, 53.8, 115.0, 126.8, 127.4, 127.9, 128.0, 129.6, 131.7, 132.8, 132.9, 137.5, 142.3, 143.6; HRMS (CI): *m/z* calcd for $C_{21}H_{24}O_2NS$: 354.1528 $[M+H]^+$; found 354.1525.

(*Z*)-4-(1-Phenylethylidene)-1,1,2,2-tetraethoxycarbonyl-5-vinylcyclohexane (3ua)



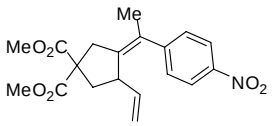
IR (neat): 2982, 1733, 1445, 1267, 1200, 1040 cm^{-1}; ^{1}H NMR: δ = 1.24 (t, *J* = 7.5 Hz, 3H), 1.260 (t, *J* = 7.2 Hz, 3H), 1.264 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.98 (br s, 3H), 2.40 (dd, *J* = 13.8, 2.1 Hz, 1H), 2.82–2.90 (m, 2H), 3.14–3.23 (m, 1H), 3.24 (d, *J* = 15.6 Hz, 1H), 3.96–4.28 (m, 8H), 4.84 (dt, *J* = 17.4, 1.8 Hz, 1H), 4.91 (dt, *J* = 10.7, 2.0 Hz, 1H), 5.61 (ddd, *J* = 17.4, 10.4, 4.4 Hz, 1H), 7.10–7.16 (m, 2H), 7.17–7.31 (m, 3H); ^{13}C NMR: δ = 13.7, 13.8, 14.1, 20.7, 29.8, 34.8, 40.2, 58.5, 59.0, 61.2, 61.35, 61.45, 61.8, 114.0, 126.2, 127.2, 127.6, 128.0, 134.6, 140.4, 144.4, 168.6, 169.3, 170.5, 170.7; HRMS (CI): *m/z* calcd for $C_{28}H_{37}O_8$: 501.2488 $[M+H]^+$; found 501.2485.

(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(4-fluorophenyl)ethylidene]-4-vinylcyclopentane (3ab)



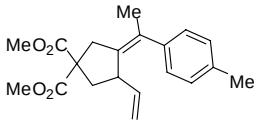
IR (neat): 2955, 1733, 1603, 1509, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.97 (br s, 3H), 2.11 (dd, *J* = 13.2, 6.3 Hz, 1H), 2.52 (dd, *J* = 13.1, 8.0 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 3.13 (dt, *J* = 17.0, 1.7 Hz, 1H), 3.27–3.41 (m, 1H), 3.72 (s, 3H), 3.76 (s, 3H), 4.55 (dt, *J* = 17.1, 1.4 Hz, 1H), 4.62 (d, *J* = 10.2 Hz, 1H), 5.34 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1H), 6.85–6.98 (m, 2H), 7.00–7.14 (m, 2H); ^{13}C NMR: δ = 22.3, 39.0, 40.6, 45.5, 52.7, 52.9, 58.7, 114.1, 114.6 (d, *J* = 20.7 Hz), 129.4 (d, *J* = 8.1 Hz), 130.5, 136.6, 139.3, 139.5, 161.3 (d, *J* = 243.2 Hz), 172.1, 172.3; HRMS (EI): *m/z* calcd for $C_{19}H_{21}FO_4$: 332.1424 $[M]^+$; found 332.1423

(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(4-nitrophenyl)ethylidene]-4-vinylcyclopentane (3ac)



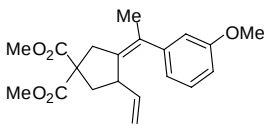
IR (neat): 2953, 1734, 1541, 1509, 1456, 1340 cm^{-1}; ^1H NMR: δ = 2.02 (br s, 3H), 2.13 (dd, *J* = 13.2, 6.6 Hz, 1H), 2.54 (ddd, *J* = 13.2, 6.6, 1.1 Hz, 1H), 3.07 (d, *J* = 17.1 Hz, 1H), 3.16 (dt, *J* = 17.1, 1.8 Hz, 1H), 3.30–3.42 (m, 1H), 3.74 (s, 3H), 3.78 (s, 3H), 4.54 (dt, *J* = 17.1, 1.4 Hz, 1H), 4.62 (dt, *J* = 10.3, 1.2 Hz, 1H), 5.31 (ddd, *J* = 17.2, 10.0, 7.3 Hz, 1H), 7.25–7.31 (m, 2H), 8.08–8.14 (m, 2H); ^{13}C NMR: δ = 21.8, 39.3, 40.8, 45.8, 52.8, 52.9, 58.5, 114.9, 123.2, 128.8, 129.7, 139.0, 146.2, 150.4, 171.8, 172.1; HRMS (EI): *m/z* calcd for $C_{19}H_{21}NO_6$: 359.1369 $[M]^+$; found 359.1374.

(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(4-methylphenyl)ethylidene]-4-vinylcyclopentane (3ad)



IR (neat): 2954, 1734, 1435, 1256, 1204, 1171 cm^{-1}; ^1H NMR: δ = 1.98 (br s, 3H), 2.16 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.31 (s, 3H), 2.51 (ddd, *J* = 13.1, 8.0, 0.9 Hz, 1H), 3.03 (d, *J* = 17.1 Hz, 1H), 3.15 (dt, *J* = 16.8, 1.8 Hz, 1H), 3.35–3.44 (m, 1H), 3.72 (s, 3H), 3.76 (s, 3H), 4.57–4.72 (m, 2H), 5.41 (ddd, *J* = 17.0, 10.4, 6.5 Hz, 1H), 6.99–7.10 (m, 4H); ^{13}C NMR: δ = 21.1, 22.2, 38.9, 40.4, 45.3, 52.7, 52.9, 58.8, 114.0, 127.6, 128.5, 131.2, 135.7, 135.8, 139.7, 140.6, 172.2, 172.4; HRMS (EI): *m/z* calcd for $C_{20}H_{24}O_4$: 328.1675 $[M]^+$; found 328.1670.

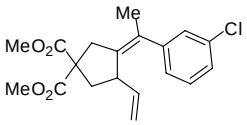
(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(3-methoxylphenyl)ethylidene]-4-vinylcyclopentane (3ae)



IR (neat): 2953, 1734, 1489, 1435, 1260, 1205 cm^{-1}; ^1H NMR: δ = 1.99 (br s, 3H), 2.16 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.51 (ddd, *J* = 13.1, 8.0, 0.9 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 3.15 (dt, *J* = 16.9, 1.8 Hz, 1H), 3.33–3.46 (m, 1H), 3.72 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 4.58–4.71 (m, 2H), 5.42 (ddd, *J* = 17.1, 10.5, 6.6 Hz, 1H), 6.65–6.78 (m, 3H), 7.16 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR: δ = 22.1, 38.9, 40.4, 45.5, 52,7, 52.9, 55.2, 58.7, 111.6, 113.6, 114.0, 120.3, 128.8, 131.2, 136.2, 139.7, 144.9,

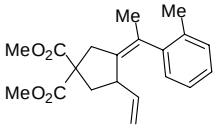
159.1, 172.2, 172.4; HRMS (EI): *m/z* calcd for $C_{20}H_{24}O_5$: 344.1624 $[M]^+$; found 344.1624.

(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(3-chlorophenyl)ethylidene]-4-vinylcyclopentane (3af)



IR (neat): 2953, 1733, 1435, 1259, 1205, 1173 cm^{-1}; ^1H NMR: δ = 1.97 (br s, 3H), 2.12 (dd, *J* = 13.2, 6.5 Hz, 1H), 2.52 (dd, *J* = 13.2, 7.8 Hz, 1H), 3.04 (d, *J* = 17.1 Hz, 1H), 3.13 (dt, *J* = 17.1, 1.5 Hz, 1H), 3.30–3.43 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 4.57 (dt, *J* = 17.0, 1.4 Hz, 1H), 4.64 (dt, *J* = 9.9, 1.4 Hz, 1H), 5.34 (ddd, *J* = 17.2, 10.1, 7.1 Hz, 1H), 6.96–7.02 (m, 1H), 7.08–7.21 (m, 3H); ^{13}C NMR: δ = 22.0, 39.0, 40.7, 45.6, 52.8, 52.9, 58.6, 114.4, 126.1, 126.3, 128.1, 129.1, 130.2, 133.5, 137.3, 139.3, 145.2, 172.0, 172.2; HRMS (EI): *m/z* calcd for $C_{19}H_{21}ClO_4$: 348.1128 $[M]^+$; found 348.1127.

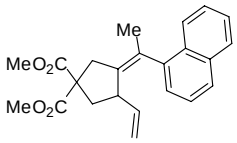
(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(2-methylphenyl)ethylidene]-4-vinylcyclopentane (3ag)



Mixture of atropisomers (52:48)

IR (neat, mixture): 2953, 1736, 1435, 1256, 1204, 1171 cm^{-1}; ^1H NMR (mixture): δ = 1.89 (br s, 1.5H), 1.91 (br s, 1.5H), 2.02 (dd, *J* = 13.5, 8.1 Hz, 0.5H), 2.10 (dd, *J* = 13.2, 6.6 Hz, 0.5H), 2.13 (s, 1.5H), 2.14 (s, 1.5H), 2.48–2.60 (m, 1H), 2.83–2.94 (m, 0.5H), 2.98–3.17 (m, 2H), 3.17–3.29 (m, 0.5H), 3.74 (s, 1.5H), 3.746 (s, 1.5H), 3.754 (s, 1.5H), 3.79 (s, 1.5H), 4.20 (d, *J* = 17.1 Hz, 0.5H), 4.37–4.48 (m, 1H), 4.54 (dt, *J* = 10.1, 1.3 Hz, 0.5H), 5.23 (ddd, *J* = 18.3, 10.2, 8.4 Hz, 0.5H), 5.36 (ddd, *J* = 17.1, 10.2, 7.2 Hz, 0.5H), 6.87–6.96 (m, 1H), 7.01–7.15 (m, 3H); ^{13}C NMR (mixture): δ = 18.8, 19.6, 21.5, 22.1, 38.4, 38.6, 40.1, 40.4, 45.5, 45.8, 52.7, 52.8, 58.9, 113.2, 113.5, 125.1, 125.5, 126.4, 126.5, 128.0, 129.0, 129.6, 129.8, 131.0, 132.2, 134.0, 135.4, 135.9, 136.2, 138.2, 139.5, 142.5, 143.0, 172.1, 172.2, 172.3; HRMS (EI, mixture): *m/z* calcd for $C_{20}H_{24}O_4$: 328.1675 $[M]^+$; found 328.1671.

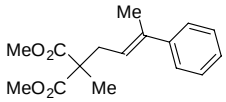
(*Z*)-1,1-Dimethoxycarbonyl-3-[1-(naphthalene-1-yl)ethylidene]-4-vinylcyclopentane (3ah)



Mixture of atropisomers (62:38)

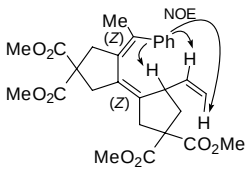
IR (neat, mixture): 2953, 1733, 1435, 1266, 1200, 1169 cm^{-1}; ^1H NMR (mixture): δ = 2.00–2.16 (m, 4H), 2.45 (ddd, *J* = 13.2, 8.0, 1.4 Hz, 0.625H), 2.56 (dd, *J* = 13.2, 7.8 Hz, 0.375H), 2.75–2.88 (m, 0.625H), 3.06–3.41 (m, 2.375H), 3.75 (s, 1.875H), 3.76 (s, 1.125H), 3.82 (s, 1.125H), 3.84 (s, 1.875H), 3.97–4.11 (m, 1.375H), 4.37 (ddd, *J* = 10.2, 1.5, 0.9 Hz, 0.625H), 5.00 (ddd, *J* = 17.1, 10.1, 8.0 Hz, 0.375H), 5.27 (ddd, *J* = 17.2, 10.0, 7.4 Hz, 0.625H), 7.12 (dd, *J* = 7.2, 1.2 Hz, 0.375H), 7.18 (dd, *J* = 7.2, 1.2 Hz, 0.625H), 7.32–7.49 (m, 3H), 7.67–7.87 (m, 3H); ^{13}C NMR (mixture): δ = 22.5, 22.9, 38.8, 38.9, 40.3, 40.5, 45.8, 45.9, 52.8, 52.87, 52.90, 58.88, 58.91, 113.1, 113.4, 124.9, 125.1, 125.2, 125.31, 125.34, 125.4, 125.8, 125.9, 126.0, 126.6, 126.8, 128.0, 128.4, 129.5, 130.2, 130.9, 131.8, 133.5, 133.6, 137.6, 138.1, 138.5, 139.4, 140.9, 141.5, 172.11, 172.14, 172.2, 172.4; HRMS (EI, mixture): *m/z* calcd for $C_{23}H_{24}O_4$: 364.1675 $[M]^+$; found 364.1678.

Dimethyl 2-(but-2-ynyl)-2-methylmalonate (7)



IR (neat): 2953, 1736, 1435, 1244, 1204, 1111 cm^{-1}; ^1H NMR: δ = 1.47 (s, 3H), 2.05 (br s, 3H), 2.80 (d, *J* = 7.5 Hz, 2H), 3.74 (s, 6H), 5.61 (tq, *J* = 7.8, 1.5Hz, 1H), 7.19–7.37 (m, 5H); ^{13}C NMR: δ = 16.2, 20.0, 34.8, 52.6, 53.9, 121.7, 125.8, 126.9, 128.1, 138.7, 143.6, 172.5; HRMS (EI): *m/z* calcd for $C_{16}H_{20}O_4$: 276.1362 $[M]^+$; found 276.1362.

(*Z*)-1,1-dimethoxylcarbonyl-3-{3,3-dimethoxylcarbonyl-5-[(*Z*)-1-phenylethylidene]-cyclopentylidene}-4-vinylcyclopentane (9)

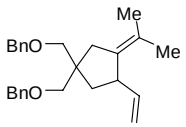


The *Z* and *Z* configuration of two double bonds was assigned on the basis of the observed NOE. IR (neat): 2955, 1732, 1435, 1270, 1204, 1063cm^{-1}; ^{1}H NMR: δ = 1.39–1.52 (m, 1H), 1.82 (dd, *J* = 12.9, 9.3 Hz, 1H), 1.97 (br s, 3H), 2.14 (ddd, *J* = 12.7, 8.3, 1.7 Hz, 1H), 2.72–2.82 (m, 1H), 2.82–2.98 (m, 3H), 3.01–3.11 (m, 2H), 3.64 (s, 3H), 3.65 (s, 3H), 3.74 (s, 3H), 3.76 (s, 3H), 4.61 (dt, *J* = 17.3, 1.7 Hz, 1H), 4.79 (dt, *J* = 10.5, 1.5 Hz, 1H), 5.35 (ddd, *J* = 17.2, 10.6, 6.5 Hz, 1H), 7.08–7.16 (m, 3H), 7.18–7.25 (m, 2H); ^{13}C NMR: δ = 21.3, 39.1, 39.4, 40.9, 41.2, 44.0, 52.59, 52.64, 52.8, 52.9, 56.6, 58.4, 113.4, 126.2, 127.9, 128.0, 130.6, 131.7, 132.5, 135.6, 139.3, 143.8, 171.1, 171.8, 172.1, 172.3; HRMS (CI): *m/z* calcd for $C_{28}H_{32}O_8$: 496.2097 [*M*]$^+$; found 496.2095.

Typical procedure for rhodium-catalyzed cyclization of 1,6-enynes with Grignard reagents:

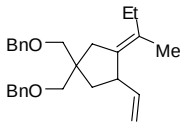
In a N_2-purged glovebox, to an oven-dried screw-capped vial was added $[RhCl(cod)]_2$ (1.5 mg, 3.0 μmol, 0.05 equiv of Rh) and a solution of substrate (0.12 mmol, 1.0 equiv) in THF (1.2 mL) and the reaction mixture was stirred for 5 minutes at room temperature. Then, Grignard reagents (THF solutions, 0.36 mmol, 3.0 equiv) were added to the resulting solution, and heated to 50 °C. After complete consumption of substrate, the reaction was quenched with 1M HCl. The aqueous layer was extracted with ethyl acetate three times, and the combined extracts were washed with sat. $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the purified product.

(*E*)-1,1-Bis(benzyloxymethyl)-3-(prop-2-ylidene)-4-vinylcyclopentane (10pa)



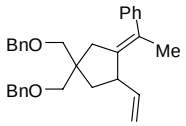
IR (neat): 2855, 1455, 1364, 1100, 1028 cm^{-1}; ^{1}H NMR: δ = 1.49 (dd, *J* = 13.1, 6.8 Hz, 1H), 1.58 (s, 3H), 1.63 (s, 3H), 1.94 (ddd, *J* = 13.4, 8.8, 1.3 Hz, 1H), 2.11 (d, *J* = 15.9 Hz, 1H), 2.35 (d, *J* = 15.6 Hz, 1H), 3.14–3.28 (m, 1H), 3.29 (d, *J* = 9.0 Hz, 1H), 3.33 (d, *J* = 8.7 Hz, 1H), 3.44 (s, 2H), 4.50 (s, 2H), 4.51 (s, 2H), 4.82–4.95 (m, 2H), 5.68 (ddd, *J* = 17.2, 10.0, 7.3 Hz, 1H), 7.22–7.36 (m, 10H); ^{13}C NMR: δ = 20.7, 21.8, 37.5, 39.0, 44.9, 47.0, 72.7, 73.1, 73.2, 74.4, 112.3, 125.2, 127.2, 127.3, 127.4, 128.2, 135.4, 138.9, 139.0, 142.5; HRMS (CI): *m/z* calcd for $C_{26}H_{33}O_2$: 377.2481 [*M*+H]$^+$; found 377.2481.

(*E*)-1,1-Bis(benzyloxymethyl)-3-(but-2-ylidene)-4-vinylcyclopentane (10qa)



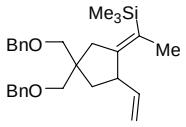
IR (neat): 2857, 1455, 1364, 1098, 1028 cm^{-1}; ^1H NMR: δ = 0.94 (t, *J* = 7.5 Hz, 3H), 1.49 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.57 (br s, 3H), 1.88–2.06 (m, 3H), 2.10 (d, *J* = 16.2 Hz, 1H), 2.39 (d, *J* = 15.9 Hz, 1H), 3.13–3.26 (m, 1H), 3.31 (s, 2H), 3.45 (s, 2H), 4.50 (s, 2H), 4.51 (s, 2H), 4.81–4.98 (m, 2H), 5.68 (ddd, *J* = 17.2, 10.0, 7.3 Hz, 1H), 7.20–7.41 (m, 10H); ^{13}C NMR: δ = 12.6, 17.9, 28.9, 36.7, 38.8, 44.7, 47.0, 72.7, 73.1, 73.2, 74.4, 112.2, 127.2, 127.3, 127.4, 128.2, 131.3, 134.8, 138.9, 142.4; HRMS (CI): *m/z* calcd for $C_{27}H_{35}O_2$: 391.2637 $[M+H]^+$; found 391.2638.

(*E*)-1,1-Bis(benzyloxymethyl)-3-(1-phenylethylidene)-4-vinylcyclopentane (10wa)



IR (neat): 2857, 1495, 1455, 1364, 1100, 1028 cm^{-1}; ^1H NMR: δ = 1.55 (dd, *J* = 13.4, 7.1 Hz, 1H), 1.95 (br s, 3H), 2.05 (dd, *J* = 13.5, 9.0 Hz, 1H), 2.26 (s, 2H), 3.25 (s, 2H), 3.32–3.44 (m, 1H), 3.40 (d, *J* = 8.7 Hz, 1H), 3.43 (d, *J* = 9.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 12.3 Hz, 1H), 4.48 (s, 2H), 4.98 (d, *J* = 10.2 Hz, 1H), 5.04 (d, *J* = 17.1 Hz, 1H), 5.81 (ddd, *J* = 17.2, 9.8, 7.4 Hz, 1H), 7.18–7.39 (m, 15H); ^{13}C NMR: δ = 20.3, 38.5, 38.6, 45.2, 47.3, 72.3, 73.17, 73.20, 74.5, 112.7, 126.0, 127.2, 127.3, 127.4, 127.9, 128.15, 128.18, 130.8, 138.8, 139.3, 141.5, 144.8; HRMS (CI): *m/z* calcd for $C_{31}H_{35}O_2$: 439.2637 $[M+H]^+$; found 439.2641.

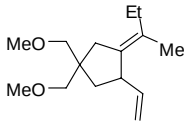
(*E*)-1,1-Bis(benzyloxymethyl)-3-(1-trimethylsilylethylidene)-4-vinylcyclopentane (10xa)



IR (neat): 2857, 1455, 1364, 1248, 1098, 1028 cm^{-1}; ^1H NMR: δ = 0.10 (s, 9H), 1.49 (dd, *J* = 13.4, 9.2 Hz, 1H), 1.62 (br s, 3H), 1.91 (dd, *J* = 13.4, 9.2 Hz, 1H), 2.17 (d, *J* = 15.3 Hz, 1H), 2.44 (d, *J* = 15.6 Hz, 1H), 3.21–3.52 (m, 1H), 3.25 (d, *J* = 9.0 Hz, 1H), 3.30 (d, *J* = 9.0 Hz, 1H), 3.40 (d, *J* = 8.7

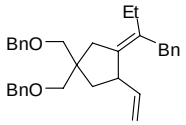
Hz, 1H), 3.49 (d, *J* = 9.0 Hz, 1H), 4.43 (d, *J* = 12.3 Hz, 1H), 4.508 (s, 2H), 4.510 (d, *J* = 12.0 Hz, 1H), 4.85–4.95 (m, 2H), 5.61–5.75 (m, 1H), 7.21–7.36 (m, 10H); ^{13}C NMR: δ = –0.3, 18.3, 38.0, 39.8, 45.5, 47.2, 72.3, 73.2, 74.5, 112.4, 127.2, 127.3, 128.2, 128.5, 138.85, 138.94, 141.4, 152.6; HRMS (CI): *m/z* calcd for $C_{28}H_{38}O_2Si$: 434.2641 $[M]^+$; found 434.2639.

(*E*)-3-(Butan-2-ylidene)-1,1-bis(methoxymethyl)-4-vinylcyclopentane (10ya)



IR (neat): 2874, 1636, 1458, 1198, 1115 cm^{-1}; ^{1}H NMR: δ = 0.93 (t, *J* = 7.5 Hz, 3H), 1.42 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.57 (br s, 3H), 1.88 (ddd, *J* = 13.4, 8.9, 1.2 Hz, 1H), 1.92–2.06 (m, 2H), 2.05 (d, *J* = 15.6 Hz, 1H), 2.30 (d, *J* = 15.9 Hz, 1H), 3.14 (s, 2H), 3.16–3.28 (m, 1H), 3.29 (s, 2H), 3.32 (s, 3H), 3.33 (s, 3H), 4.86–4.96 (m, 2H), 5.70 (ddd, *J* = 17.0, 10.0, 7.1 Hz, 1H); ^{13}C NMR: δ = 12.5, 17.9, 28.8, 36.5, 38.5, 44.6, 46.8, 59.3, 75.2, 77.0, 112.2, 131.4, 134.8, 142.3; HRMS (EI): *m/z* calcd for $C_{15}H_{26}O_2$: 238.1933 $[M]^+$; found 238.1924.

(*Z*)-1,1-Bis(benzyloxymethyl)-3-(1-phenylbut-2-ylidene)-4-vinylcyclopentane (10qb)



IR (neat): 2857, 1495, 1453, 1364, 1100, 1028 cm^{-1}; ^{1}H NMR: δ = 0.86 (t, *J* = 7.5 Hz, 3H), 1.52 (dd, *J* = 13.5, 6.6 Hz, 1H), 1.77–2.05 (m, 3H), 2.20 (d, *J* = 15.6 Hz, 1H), 2.47 (d, *J* = 16.2 Hz, 1H), 3.21–3.40 (m, 4H), 3.44–3.57 (m, 3H), 4.52 (s, 2H), 4.53 (s, 2H), 4.83–4.98 (m, 2H), 5.76 (ddd, *J*=17.2, 9.8, 7.4 Hz, 1H), 7.08 (d, *J*=6.9 Hz, 2H), 7.11–7.37 (m, 13H); ^{13}C NMR: δ = 12.8, 25.9, 36.8, 37.1, 38.9, 44.9, 46.9, 72.7, 73.2, 74.4, 112.6, 125.5, 127.3, 127.4, 128.1, 128.22, 128.25, 128.7, 134.3, 137.5, 138.8, 138.9, 140.7, 142.7; HRMS (CI): *m/z* calcd for $C_{33}H_{39}O_2$: 467.2950 $[M+H]^+$; found 467.2952.

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Chapter 2

Rhodium-Catalyzed Cyclization Reaction of Oxygen-Substituted 1,6-Enynes with Arylboronic Acids

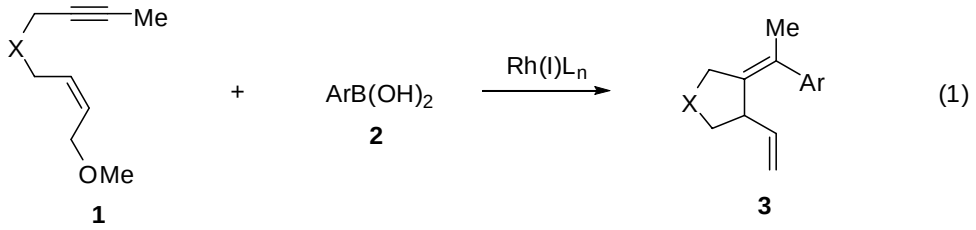
Abstract

Methoxy-substituted 1,6-enynes reacted with arylboronic acids in the presence of a rhodium(I) complex to give arylated cyclization products. The multi-step mechanism consisted of rhodium/boron transmetalation, intermolecular carborhodation, intramolecular carborhodation, β-hydride elimination, hydrorhodation, and β-oxygen elimination. A shift of the position of a carbon–carbon double bond was observed to suggest that the β-hydride elimination/hydrorhodation process took place repeatedly.

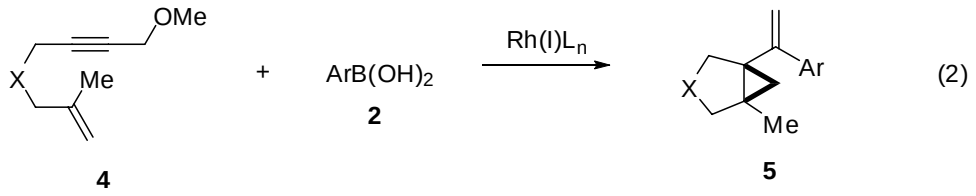
Introduction

A wide range of organoboronic acids and esters are available readily, often even commercially, to promote their use in organic synthesis.[1] While fairly stable toward air and water, they react with rhodium(I) complexes to generate organorhodium(I) species, which subsequently undergo a carborhodation step onto a variety of unsaturated organic functionalities in an intermolecular manner. Thus, the rhodium-catalyzed addition reactions of organoboronic acid derivatives have been intensively studied as a useful method of carbon–carbon bond formation.[2] It has also been shown that multiple carborhodation steps can operate on substrates possessing two or more unsaturated functionalities to form structurally complex cyclic molecules.[3]

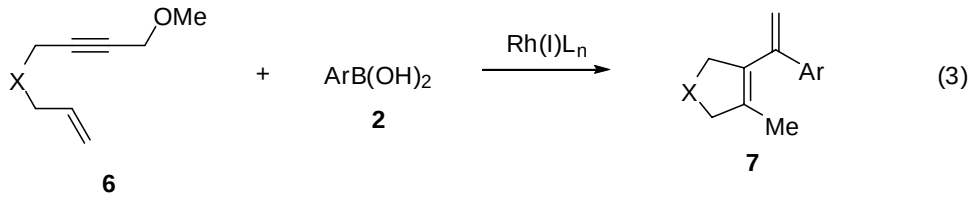
In the preceding chapter, the author described the rhodium-catalyzed arylative cyclization reaction of 1,6-enynes having an allylic ether moiety [eq. (1)].[4]



The synthesis of vinylcyclopropanes from 1,6-enynes to which an oxygen-substituent was attached at the propargylic position was also reported by his laboratory [eq. (2)].[5]



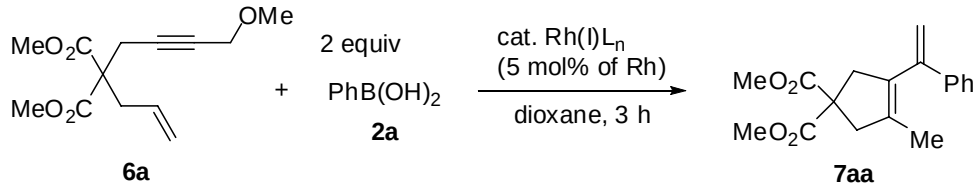
In both cases, a catalytically active methoxorhodium(I) species is regenerated through β-methoxy elimination. During continuous studies on other 1,6-enyne compounds, the author found that a cyclization reaction proceeded by a different pathway to give unexpected cyclic products **7** when the methyl substituent on the alkenyl moiety of **4** was subtracted [eq. (3)]. The small structural change brought a successive β-hydride elimination/hydrorhodation process in the reaction sequence.



Results and discussions

Initially, the author examined several rhodium catalysts (5 mol% of Rh) in the reaction of 1,6-enyne **6a** (1 equiv) with phenylboronic acid (**2a**, 2 equiv) (Table 1). Whereas the employment of Wilkinson's complex catalyzed the reaction only inefficiently, the use of $[RhCl(binap)]_2$ and $[RhCl(cod)]_2$ together with KOH gave the arylative cyclization product **7aa** in 56% and 44% yields, respectively (entries 1–3). Unlike the case of the substrate **4** [Eq. (2)], no formation of vinylcyclopropane substructure was observed. Rhodium(I)-norbornadiene complexes gave better results (entries 4–6), and **7aa** was produced in the best isolated yield of 72% when $[Rh(OMe)(nbd)]_2$[6] was employed at 50 °C without any additional base.

Table 1. Reaction of 1,6-enyne **6a** and phenylboronic acid (**2a**) in the presence of Rhodium(I) catalyst [a]

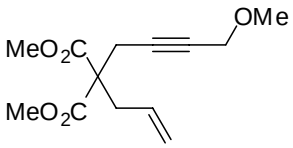
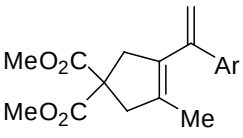
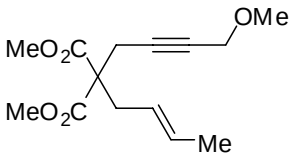
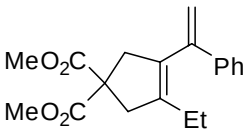
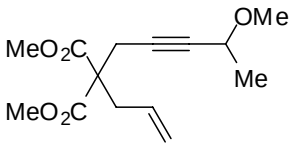
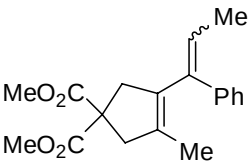
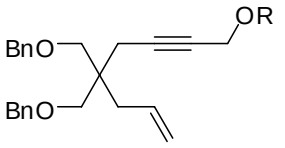
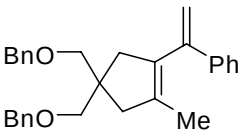


entry	$Rh(I)L_n$	base (0.6 equiv)	temp (°C)	yield (%) [b]
1	$RhCl(PPh_3)_3$	KOH	80	14
2	$[RhCl(binap)]_2$	KOH	80	56
3	$[RhCl(cod)]_2$	KOH	80	44
4	$[RhCl(nbd)]_2$	KOH	80	66
5	$[RhCl(nbd)]_2$	KOH	50	65
6	$[Rh(OMe)(nbd)]_2$	–	50	72

[a] Reaction condition: **6a** (0.2 mmol), **2a** (0.4 mmol), $Rh(I)L_n$ (5 mol% of Rh), KOH (0.12 mmol) in dioxane, 2 h. [b] Yields of isolated products.

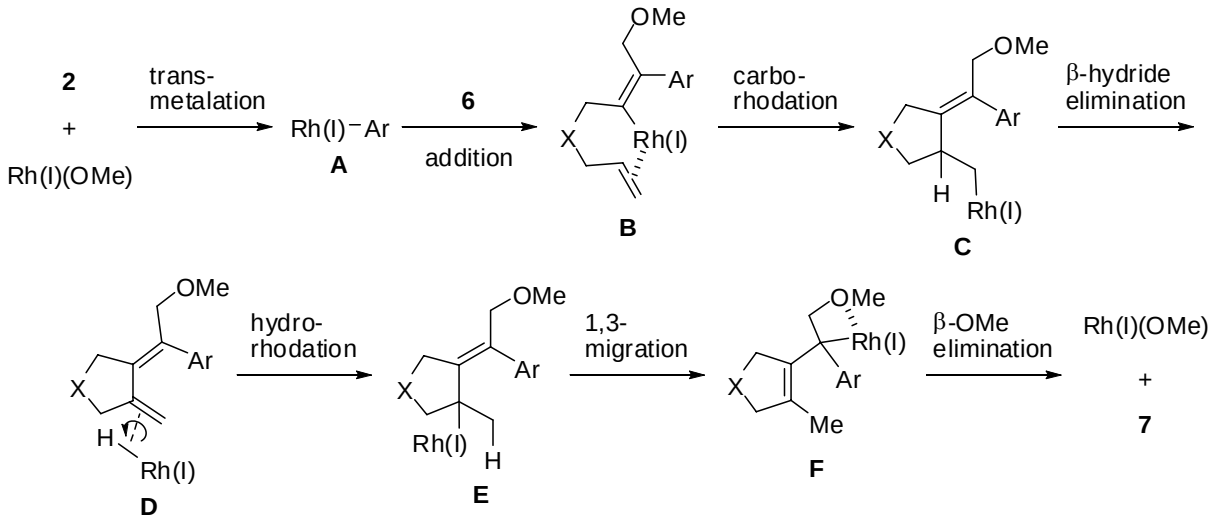
The scope of the reaction was examined by using various combinations of 1,6-enynes **6** and arylboronic acids **2** under the optimized reaction conditions (Table 2). A sterically and electronically diverse array of arylboronic acids reacted with **6a** to give 1-(1-arylvinyl)-2-methylcyclopentenes **7ab**–**7af** in yields ranging from 65 to 71% (entries 1–5). A vicinally disubstituted alkene also participated in the reaction (entry 6). A mixture of *E* and *Z* isomers was produced from substrate **6c** (entry 7). The cyclization reaction also occurred with substrate **6e** having a free hydroxy group at the propargylic position (entry 9).

Table 2. Rhodium(I)-catalyzed reaction of 1,6-enynes **6** and aryllboronic acids **2** [a]

entry	substrate	$ArB(OH)_2$	product	yield (%) [b]
1	 **6a**	**2b** 4-Me-C_6H_4	 **7ab**	67
2		**2c** 3-Me-C_6H_4		**7ac**	66
3		**2d** 2-Me-C_6H_4		**7ad**	65
4		**2e** 3-Br-C_6H_4		**7ae**	71
5		**2f** 3-MeO-C_6H_4		**7af**	69
6	 **6b**	**2a** Ph	 **7ba**	55 [c]
7	 **6c**	**2a** Ph	 **7ca**	74 [d,e]
8	 **6d** R=Me	**2a** Ph	 **7da**	66 [f]
9	**6e** R=H	**2a** Ph		**7da**	54 [d]

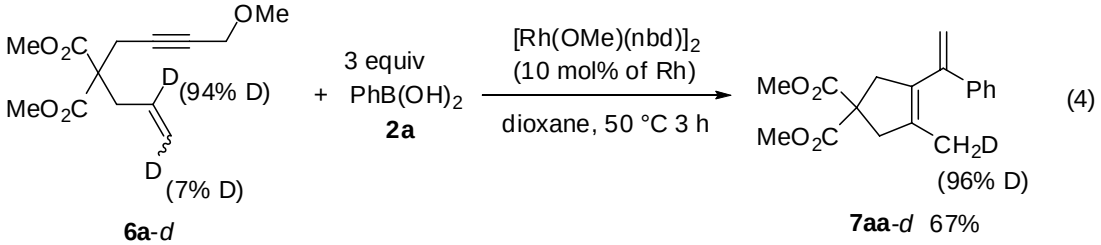
[a] Reaction condition: **6** (0.2 mmol), **2** (0.4 mmol), $[Rh(OMe)(nbd)]_2$ (5 μmol, 5 mol% of Rh) in dioxane, 50 °C, 3-5 h, unless otherwise noted. [b] Yields of isolated products. [c] 80 °C. [d] **2** (0.8 mmol), $[Rh(OMe)(nbd)]_2$ (10 μmol, 10 mol% of Rh). [e] *E*:*Z*=57:43. [f] Room temperature.

The author proposes that the reaction proceeds through the pathway outlined in Scheme 1. Arylrhodium species **A**, generated by transmetalation of an arylboronic acid with a rhodium(I) complex,[7] adds regioselectively across the carbon–carbon triple bond of **6** to afford alkenylrhodium(I) species **B**.[8] Then, intramolecular carborhodation occurs onto the pendent carbon–carbon double bond in a 5-*exo*-trig mode to give (cyclopentylmethyl)rhodium(I) intermediate **C**. β-Hydride elimination is immediately followed up by hydrorhodation with an opposite regiochemistry to accomplish a 1,2-shift of rhodium,[9] leading to the formation of cyclopentylrhodium(I) **E**. Allylic 1,3-migration of rhodium furnishes alkylrhodium(I) **F**. Finally, β-methoxy elimination yields **7** together with a catalytically active methoxorhodium(I) species.[10]



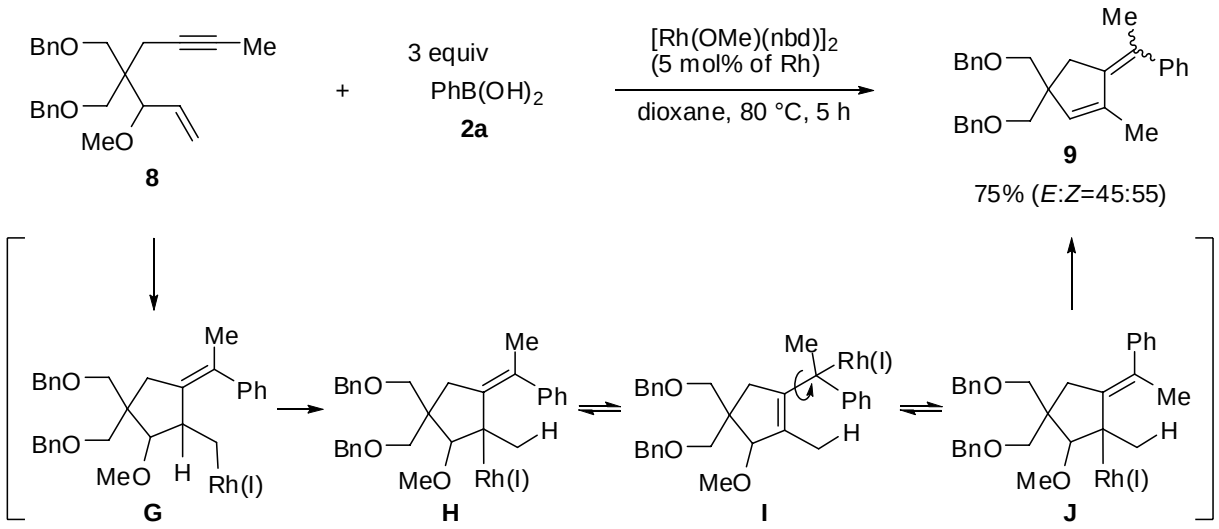
Scheme 1. Proposed mechanism for the formation of **7** from **6**

When deuterated 1,6-enyne **6a**-*d* reacted with phenylboronic acid (**2a**), the vinylic deuterium atom migrated to the methyl carbon of **7aa**-*d* [eq. (4)]. This result supports the involvement of the β-hydride elimination/hydrorhodation sequence in the catalytic cycle.



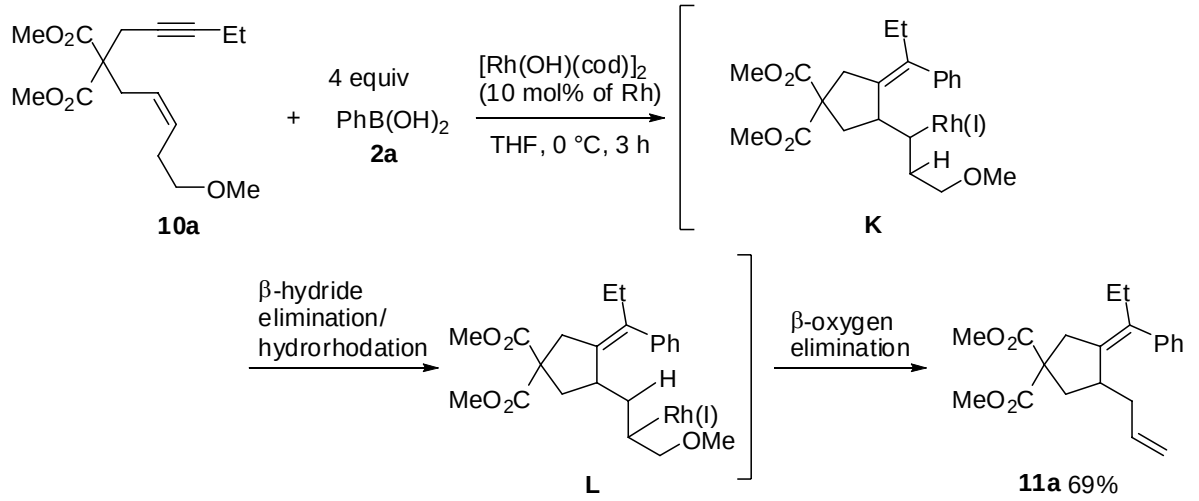
(4)

Variants of the cyclization reaction involving successive β-hydride elimination/hydrorhodation process were found when analogous 1,6-enynes having a methoxy group at different positions were used. The reaction of 1,6-enyne **8** having a methoxy group at the inner allylic position reacted with **2a** at 80 °C to give the cyclized product **9** as a mixture of geometrical isomers (*E*:*Z* = 45:55) in 75% yield (Scheme 2). The author assumes that the mixture arose from equilibration between geometrical isomers **H** and **J** through allylic isomer **I**.



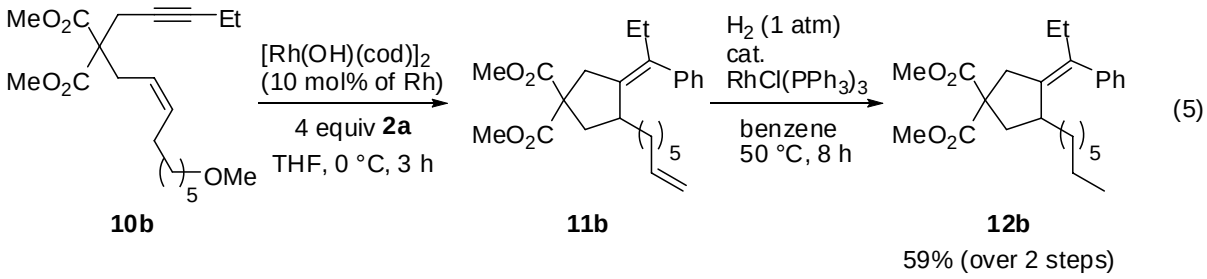
Scheme 2. Rhodium(I)-catalyzed arylative cyclization of 1,6-enyne **8** with phenylboronic acid

The author also studied the reaction of 1,6-enyne **10a** having a methoxy group at the homo-allylic position. An analogous arylative cyclization reaction proceeded to afford intermediate **K**. β-Hydride elimination, hydrorhodation, and β-methoxy elimination successively occurred to afford **11a** in 69% yield when $[Rh(OH)(cod)]_2$ was used as the catalyst (Scheme 3).[11]



Scheme 3. Rhodium(I)-catalyzed arylative cyclization of 1,6-enyne **10a** with phenylboronic acid

In the case of substrate **10b** having a methoxy group at a more remote position of the alkenyl chain, the β-hydride elimination/hydrorhodation process was repeated until β-methoxy elimination formed a terminal olefin [eq. (5)].[12] The product **11b** was accompanied by a certain amount (ca. 30%) of several regioisomers having a carbon–carbon double bond at inner positions. Therefore, to estimate the efficiency of the cyclization reaction, the crude **11b** was subjected to a hydrogenation reaction.



Conclusion

The author has developed new cyclization reactions of methoxy-substituted 1,6-enynes with arylboronic acids catalyzed by a rhodium(I) complex. The reaction proceeds through a multi-step sequence which consists of rhodium/boron transmetalation, intermolecular carborhodation, intramolecular carborhodation, β-hydride elimination, hydrorhodation, and β-oxygen elimination. The observed preference for β-oxygen elimination indicates high affinity of rhodium in the intermediate for the oxygen-substituent.

Experimental Section

General

All rhodium(I)-catalyzed reactions were carried out with standard Schlenk techniques under an argon atmosphere. ^{1}H NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300.07 MHz) spectrometer. ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^{13}C at 75.46 MHz) spectrometer or a JEOL JNM-A400 (^{13}C at 100.40 MHz) spectrometer. NMR data were obtained in $CDCl_3$. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm. Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm. ^{1}H NMR of **7aa**-*d* was obtained in C_6D_6 (the residual proton signal of the solvent at 7.16 ppm was used as an internal standard). High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. Column chromatography was performed with silica gel 60 N (Kanto Chemical Co). Preparative thin-layer chromatography was performed with silica 60 PF_{254} (Merck).

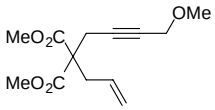
Materials

Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $[Rh(OMe)(nbd)]_2$[6], $[Rh(OH)(cod)]_2$[13], $[RhCl(nbd)]_2$[14], $[RhCl(cod)]_2$[15] and $[RhCl(binap)]_2$[16] were prepared according to the reported procedures. 1,4-Dioxane was distilled over sodium-benzophenone ketyl prior to use. THF was dried and deoxygenized using an alumina/catalyst column system (Glass Contour Co.).

Starting Materials:

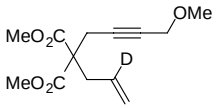
1,6-Enynes **6a**, **6c** and **6b** were prepared from dimethyl 2-allylmalonate or dimethyl (*E*)-crotylmalonate by alkylation with the corresponding propargyl bromides in the presence of NaH in a THF solution. 1,6-Enyne **6e** was synthesized from Dimethyl 2-allyl-2-(prop-2-ynyl)malonate according to the following procedure. Reduction ($LiAlH_4$ in Et_2O) and benzylation (NaH, BnBr, cat. TBAI in THF/DMF (5/1)) gave the intermediate 1,6-enyne, which was reacted with *n*-BuLi, then paraformaldehyde to afford **6e**. Methylation of **6e** (MeOTf, 2,6-di-*t*-Bu-pyridine in CH_2Cl_2) produced **6d**. The synthetic procedure for 1,6-enyne **8** was described below. Diethyl 2-(diethoxymethyl)malonate formed by the reaction of diethyl ethoxymethylenemalonate and NaOEt in EtOH, was treated with 1-bromo-2-butyne in the presence of NaH in a THF solution. The resulting malonate was subjected to reduction ($LiAlH_4$ in Et_2O), benzylation (NaH, BnBr, cat. TBAI in THF/DMF (5/1)) and hydrolysis under an acidic condition (3*N* HCl aq in THF) to afford the hex-4-ynal derivative. The reaction of this aldehyde with vinylmagnesium bromide in a THF solution followed by methylation (MeOTf, 2,6-di-*t*-Bu-pyridine in CH_2Cl_2) produced the desired **8**. 1,6-Enyne **10a**, **10b** were prepared from dimethyl 2-(pent-2-ynyl)malonate and the corresponding allylic bromides (NaH in THF). Deuterated 1,6-enyne **6a**-*d* was prepared from dimethyl 2-(4-methoxybut-2-enyl)malonate and 2-deuterioprop-2-enyl methanesulfonate under the reported reaction condition.[17] 2-Deuterioprop-2-enyl methanesulfonate was prepared from 2-Deuterio-prop-2-en-1-ol[18] according to the literature. [17]

Dimethyl 2-(4-methoxybut-2-ynyl)-2-(prop-2-enyl)malonate (6a)



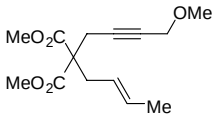
IR (neat): 2955, 2244, 1740, 1642, 1437 cm^{-1}; ^1H NMR: δ = 2.80 (dt, *J* = 7.2, 1.1 Hz, 2H), 2.85 (t, *J* = 2.1 Hz, 2H), 3.34 (s, 3H), 3.74 (s, 6H), 4.06 (t, *J* = 2.1 Hz, 2H), 5.09–5.22 (m, 2H), 5.63 (ddt, *J* = 17.1, 9.9, 7.5 Hz, 1H); ^{13}C NMR (75 MHz): δ = 23.0, 36.6, 52.7, 57.0, 57.3, 59.9, 79.0, 81.1, 119.8, 131.6, 170.1; HRMS (CI): *m/z* calcd for $C_{13}H_{18}O_5$: 254.1154 $[M]^+$; found 254.1160.

Dimethyl 2-(2-dueterioprop-2-enyl)-2-(4-methoxybut-2-ynyl)malonate (6a-*d*)



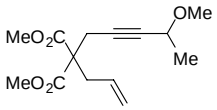
^{1}H NMR: δ = 2.77–2.82 (m, 2H), 2.85 (t, *J* = 2.1 Hz, 2H), 3.34 (s, 3H), 3.74 (s, 6H), 4.06 (t, *J* = 2.1 Hz, 2H), 5.07–5.21 (m, 1.93H), 5.53–5.69 (m, 0.06H); ^{13}C NMR (75 MHz) δ = 23.1, 36.6, 52.7, 57.0, 57.3, 59.9, 79.1, 81.2, 119.7, 131.4 (t, *J* = 23.2 Hz), 170.2; HRMS (FAB): *m/z* calcd for $C_{13}H_{18}O_5D$: 256.1295 $[M+H]^+$; found 256.1293.

Dimethyl 2-[(*E*)-but-2-enyl]-2-(4-methoxybut-2-ynyl)malonate (6b)



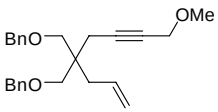
IR (neat): 2955, 1997, 1738, 1435, 1283 cm^{-1}; ^{1}H NMR: δ = 1.58–1.66 (m, 3H), 2.65–2.73 (m, 2H), 2.80 (t, *J* = 2.1 Hz, 2H), 3.31 (s, 3H), 3.70 (s, 6H), 4.03 (t, *J* = 2.1 Hz, 2H), 5.12–5.27 (m, 1H), 5.48–5.64 (m, 1H); ^{13}C NMR (75 MHz): δ = 18.0, 22.9, 35.4, 52.6, 57.1, 57.2, 59.8, 78.8, 81.3, 123.8, 130.5, 170.3; HRMS (CI): *m/z* calcd for $C_{14}H_{21}O_5$: 269.1389 $[M+H]^+$; found 269.1389.

Dimethyl 2-(4-methoxypent-2-ynyl)-2-(prop-2-enyl) malonate (6c)



IR (neat): 2986, 1740, 1642, 1439, 1219, 1206 cm^{-1}; ^{1}H NMR: δ = 1.37 (d, *J* = 6.6 Hz, 3H), 2.80 (dt, *J* = 7.5, 0.9 Hz, 2H), 2.83 (d, *J* = 1.8 Hz, 2H), 3.35 (s, 3H), 3.73 (s, 6H), 4.03 (qt, *J* = 6.6, 1.8 Hz, 1H), 5.09–5.21 (m, 2H), 5.63 (ddt, *J* = 17.1, 9.9, 7.8 Hz, 1H); ^{13}C NMR (75 MHz): δ = 22.2, 22.9, 36.6, 52.7, 56.0, 57.0, 66.7, 79.7, 83.1, 119.7, 131.7, 170.1; HRMS (CI): *m/z* calcd for $C_{14}H_{21}O_5$: 269.1389 $[M+H]^+$; found 269.1386.

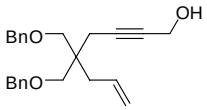
4,4-Bis(benzyloxymethyl)-8-methoxyoct-1-en-6-yne (6d)



IR (neat): 2857, 1638, 1455, 1364, 1096 cm^{-1}; ^{1}H NMR: δ = 2.25 (d, *J*=7.5 Hz, 2H), 2.30–2.36 (m, 2H), 3.32–3.44 (m, 4H), 3.33 (s, 3H), 4.06 (t, *J* = 2.0 Hz, 2H), 4.50 (s, 4H), 5.00–5.15 (m, 2H), 5.68–5.88 (m, 1H), 7.21–7.37 (m, 10H); ^{13}C NMR (75 MHz): δ = 22.5, 36.3, 42.2, 57.2, 60.1, 71.9,

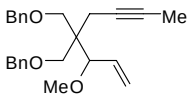
73.2, 77.7, 83.7, 118.0, 127.3, 128.2, 133.8, 138.7; HRMS (CI): *m/z* calcd for $C_{25}H_{30}O_3$: 378.2195 $[M]^+$; found 378.2200.

5,5-Bis(benzyloxymethyl)oct-7-en-2-yn-1-ol (6e)



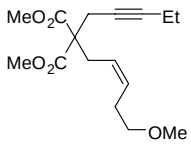
IR (neat): 3420, 2863, 2222, 1638, 1455, 1366 cm^{-1}; ^1H NMR: δ = 1.55 (t, *J* = 6.2 Hz, 1H), 2.23 (d, *J* = 7.5 Hz, 2H), 2.31 (t, *J* = 2.3 Hz, 2H), 3.36 (d, *J* = 8.7 Hz, 2H), 3.40 (d, *J* = 9.0 Hz, 2H), 4.18 (dt, *J* = 6.0, 2.1 Hz, 2H), 4.50 (s, 4H), 5.02–5.13 (m, 2H), 5.78 (ddt, *J* = 17.4, 10.2, 7.5 Hz, 1H), 7.23–7.38 (m, 10H); ^{13}C NMR (75 MHz): δ = 22.5, 36.3, 42.1, 51.3, 71.7, 73.2, 80.3, 83.1, 118.1, 127.3, 127.4, 128.2, 133.8, 138.7; HRMS (EI): *m/z* calcd for $C_{24}H_{28}O_3$: 364.2038 $[M]^+$; found 364.2035.

4,4-Bis(benzyloxymethyl)-3-methoxyoct-1-en-6-yne (8)



IR (neat): 2919, 2245, 1638, 1455, 1366, 1092 cm^{-1}; ^1H NMR: δ = 1.75 (t, *J* = 2.7 Hz, 3H), 2.34 (q, *J* = 2.7 Hz, 2H), 3.23 (s, 3H), 3.47 (dd, *J* = 9.3, 0.8 Hz, 2H), 3.53 (dd, *J* = 9.0, 3.0 Hz, 2H), 3.66 (d, *J* = 8.7 Hz, 1H), 4.47 (dd, *J* = 12.0, 1.8 Hz, 2H), 4.52 (d, *J* = 12.6 Hz, 2H), 5.12–5.24 (m, 2H), 5.96 (ddd, *J* = 17.1, 10.3, 8.6 Hz, 1H), 7.21–7.35 (m, 10H); ^{13}C NMR (75 MHz): δ = 3.6, 20.6, 45.9, 56.8, 70.48, 70.54, 73.2, 76.3, 84.8, 118.2, 127.15, 127.23, 128.1, 135.9, 138.9; HRMS (CI): *m/z* calcd for $C_{25}H_{30}O_3$: 378.2195 $[M]^+$; found 378.2199.

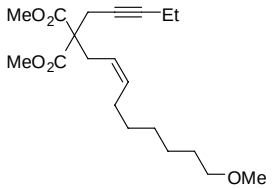
Dimethyl 2- [(*Z*)-5-methoxypent-2-enyl]-2-(pent-2-ynyl)malonate (10a)



IR (neat): 2950, 1740, 1437, 1293, 1210 cm^{-1}; ^1H NMR: δ = 1.08 (t, *J* = 7.5 Hz, 3H), 2.12 (qt, *J* = 7.5, 2.4 Hz, 2H), 2.38 (q, *J* = 6.9 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 2H), 2.83 (d, *J* = 7.8 Hz, 2H), 3.34 (s, 3H), 3.38 (t, *J* = 6.9 Hz, 2H), 3.73 (s, 6H), 5.19–5.32 (m, 1H), 5.52–5.65 (m, 1H); ^{13}C NMR (75 MHz): δ = 12.3, 14.1, 22.9, 27.8, 30.0, 52.6, 57.2, 58.5, 72.1, 73.7, 84.9, 124.3, 130.4, 170.5;

HRMS (CI): *m/z* calcd for $C_{16}H_{25}O_5$: 297.1702 $[M+H]^+$; found 297.1700.

Dimethyl 2-[(*Z*)-9-methoxynon-2-enyl]-2-(pent-2-ynyl)malonate (10b)

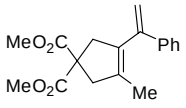


IR (neat): 2932, 1740, 1437, 1293, 1211 cm^{-1}; ^1H NMR: δ = 1.09 (t, *J* = 7.5 Hz, 3H), 1.27–1.40 (m, 6H). 1.51–1.62 (m, 2H), 2.03–2.18 (m, 4H), 2.73 (t, *J* = 2.4 Hz, 2H), 2.80 (d, *J* = 7.8 Hz, 2H), 3.33 (s, 3H), 3.36 (t, *J* = 6.6 Hz, 2H), 3.72 (s, 6H), 5.07–5.19 (m, 1H), 5.49–5.60 (m, 1H); ^{13}C NMR (75 MHz): δ = 12.3, 14.1, 22.8, 26.0, 27.3, 29.2, 29.6, 29.8, 52.6, 57.2, 58.5, 72.8, 73.8, 84.8, 122.1, 134.7, 170.6; HRMS (FAB): *m/z* calcd for $C_{20}H_{33}O_5$: 353.2328 $[M+H]^+$; found 353.2334.

*A typical procedure for the rhodium-catalyzed cyclization of 1,6-enynes **6** with arylboronic acids **2**:*

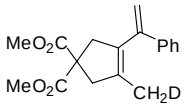
To an oven-dried Schlenk tube was added $[Rh(OMe)(nbd)]_2$ (2.3 mg, 5.0 μmol, 5 mol % Rh), arylboronic acid **2** (0.4 mmol, 2.0 equiv), 1,4-dioxane (1.0 mL), and a solution of 1,6-enyne **6** (0.2 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL). The reaction mixture was stirred at 50 °C for 3–5 h under an argon atmosphere, and then quenched with addition of water (5 mL). The resulting aqueous solution was extracted with ethyl acetate (3 x 10 mL). The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1 or 3:1) to give the corresponding product **7**.

4,4-Dimethoxycarbonyl-1-methyl-2-(1-phenylethenyl)cyclopentene (7aa)



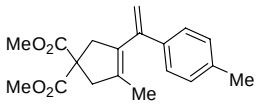
IR (neat): 2955, 1732, 1599, 1435, 1260 cm^{-1}; ^1H NMR: δ = 1.54 (s, 3H), 3.08–3.16 (m, 4H), 3.75 (s, 6H), 5.11 (d, *J* = 1.5 Hz, 1H), 5.43 (d, *J* = 1.5 Hz, 1H), 7.23–7.35 (m, 5H); ^{13}C NMR (75 MHz): δ = 14.9, 44.5, 46.5, 52.8, 57.2, 114.9, 126.9, 127.4, 128.2, 132.4, 134.1, 140.3, 144.7, 172.6; HRMS (CI): *m/z* calcd for $C_{18}H_{20}O_4$: 300.1362 $[M]^+$; found m/z 300.1360.

7aa-*d*



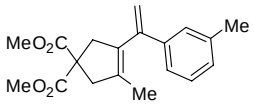
^{1}H NMR (C_6D_6): δ = 1.32–1.44 (m, 2.04H), 3.21–3.24 (m, 2H), 3.75 (s, 6H), 3.39–3.43 (m, 2H), 5.06 (d, *J* = 1.8 Hz, 1H), 5.36 (d, *J* = 1.5 Hz, 1H), 7.03–7.16 (m, 3H), 7.33–7.39 (m, 2H); ^{13}C NMR (75 MHz): δ = 14.7 (t, *J* = 19.7 Hz), 44.5, 46.5, 52.8, 57.2, 114.9, 126.9, 127.4, 128.2, 132.5, 134.1, 140.3, 144.7, 172.6; HRMS (EI): *m/z* calcd for $C_{18}H_{19}O_4D$: 301.1424 $[M]^+$; found m/z 301.1421.

4,4-Dimethoxycarbonyl-1-methyl-2-[1-(4-methylphenyl)ethenyl]cyclopentene (7ab)



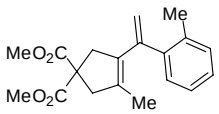
IR (neat): 2953, 1738, 1609, 1512, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.55 (s, 3H), 2.34 (s, 3H), 3.08–3.15 (m, 4H), 3.75 (s, 6H), 5.05 (d, *J* = 1.5 Hz, 1H), 5.40 (d, *J* = 1.5 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz): δ = 14.9, 21.1, 44.5, 46.5, 52.8, 57.3, 114.1, 126.8, 128.9, 132.6, 133.9, 137.2, 137.3, 144.5, 172.6; HRMS (CI): *m/z* calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found 314.1519.

4,4-Dimethoxycarbonyl-1-methyl-2-[1-(3-methylphenyl)ethenyl]cyclopentene (7ac)



IR (neat): 2953, 1734, 1601, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.55 (s, 3H), 2.34 (s, 3H), 3.08–3.15 (m, 4H), 3.75 (s, 6H), 5.08 (d, *J* = 1.5 Hz, 1H), 5.42 (d, *J* = 1.8 Hz, 1H), 7.05–7.12 (m, 3H), 7.16–7.23 (m, 1H); ^{13}C NMR (75 MHz): δ = 14.9, 21.5, 44.5, 46.5, 52.8, 57.3, 114.7, 124.0, 127.6, 128.1, 128.2, 132.6, 134.0, 137.7, 140.2, 144.7, 172.6; HRMS (CI): *m/z* calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found 314.1518.

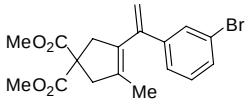
4,4-Dimethoxycarbonyl-1-methyl-2-[1-(2-methylphenyl)ethenyl]cyclopentene (7ad)



IR (neat): 2953, 1734, 1597, 1576, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.22 (s. 3H), 2.13 (s, 3H),

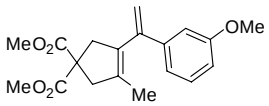
3.02–3.07 (m, 2H), 3.17–3.22 (m, 2H), 3.74 (s, 6H), 5.03 (d, *J* = 1.2 Hz, 1H), 5.25 (d, *J* = 1.2 Hz, 1H), 7.07–7.22 (m, 4H); ^{13}C NMR (75 MHz): δ = 14.4, 19.5, 43.7, 47.6, 52.8, 56.6, 116.2, 125.6, 127.2, 129.0, 129.7, 131.0, 134.0, 135.6, 141.9, 145.4, 172.6; HRMS (CI): *m/z* calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found 314.1513.

2-[1-(3-bromophenyl)ethenyl]-4,4-Dimethoxycarbonyl-1-methylcyclopentene (7ae)



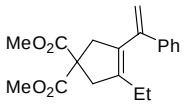
IR (neat): 2953, 1732, 1592, 1559, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.55 (s, 3H), 3.10 (s, 4H), 3.76 (s, 6H), 5.13 (d, *J* = 1.2 Hz, 1H), 5.43 (d, *J* = 1.5 Hz, 1H), 7.14–7.24 (m, 2H), 7.37–7.44 (m, 2H); ^{13}C NMR (75 MHz): δ = 15.0, 44.3, 46.5, 52.9, 57.3, 116.0, 122.4, 125.6, 129.8, 129.9, 130.4, 131.8, 134.9, 142.4, 143.4, 172.5; HRMS (CI): *m/z* calcd for $C_{18}H_{19}O_4Br$: 378.0467 $[M]^+$; found 378.0470.

4,4-Dimethoxycarbonyl-2-[1-(3-methoxyphenyl)ethenyl]-1-methylcyclopentene (7af)



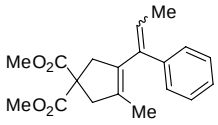
IR (neat): 2953, 1732, 1593, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 1.56 (s, 3H), 3.07–3.16 (m, 4H), 3.74 (s, 6H), 3.81 (s, 3H), 5.10 (d, *J* = 1.8 Hz, 1H), 5.44 (d, *J* = 1.8 Hz, 1H), 6.79–6.92 (m, 3H), 7.18–7.26 (m, 1H); ^{13}C NMR (75 MHz): δ = 14.9, 44.5, 46.5, 52.8, 55.2, 57.2, 112.6, 113.0, 115.0, 119.4, 129.1, 132.4, 134.2, 141.7, 144.5, 159.5, 172.6; HRMS (CI): *m/z* calcd for $C_{19}H_{22}O_5$: 330.1467 $[M]^+$; found 330.1465.

4,4-Dimethoxycarbonyl-1-ethyl-2-(1-phenylethenyl)cyclopentene (7ba)



IR (neat): 2955, 1734, 1435, 1260 cm^{-1}; ^{1}H NMR: δ = 0.93 (t, *J* = 7.8 Hz, 3H), 2.02 (q, *J* = 7.8 Hz, 2H), 3.07–3.15 (m, 4H), 3.75 (s, 6H), 5.09 (d, *J* = 1.8 Hz, 1H), 5.44 (d, *J* = 1.5 Hz, 1H), 7.21–7.37 (m, 5H); ^{13}C NMR (75 MHz): δ = 12.6, 22.0, 43.4, 44.4, 52.8, 57.4, 114.6, 126.7, 127.5, 128.2, 132.1, 139.7, 140.1, 144.5, 172.6; HRMS (CI): *m/z* calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found 314.1513.

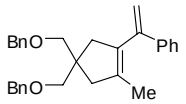
4,4-Dimethoxycarbonyl-1-methyl-2-(1-phenylprop-1-enyl) cyclopentene (7ca)



Mixture of geometrical isomers (*E*:*Z* = 57:43)

IR (neat, mixture): 2953, 1738, 1435, 1260 cm^{-1}; ^1H NMR (*E* isomer): δ = 1.35 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H), 3.03 (s, 2H), 3.05–3.10 (m, 2H), 3.72 (s, 6H), 5.70 (q, *J* = 7.2 Hz, 1H), 7.07–7.36 (m, 5H); (*Z* isomer): δ = 1.58–1.62 (m, 3H), 1.69 (d, *J* = 7.2 Hz, 3H), 2.95–3.00 (m, 2H), 3.10–3.15 (m, 2H), 3.73 (s, 6H), 6.02 (q, *J* = 7.2 Hz, 1H), 7.07–7.36 (m, 5H); ^{13}C NMR, 100 MHz, mixture): δ = 14.5, 14.76, 14.78, 15.3, 43.9, 44.1, 45.4, 47.0, 52.7, 56.9, 57.8, 124.7, 125.0, 126.1, 126.6, 126.8, 128.0, 128.3, 129.2, 130.9, 131.7, 133.4, 133.8, 136.8, 138.1, 139.4, 140.1, 172.7; HRMS (CI, mixture): *m/z* calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found 314.1520.

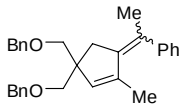
4,4-Bis(benzyloxymethyl)-1-methyl-2-(1-phenylethenyl) cyclopentene (7ea)



IR (neat): 2851, 1948, 1808, 1599, 1495, 1453, 1362 cm^{-1}; ^1H NMR: δ = 1.46 (s, 3H), 2.34–2.46 (m, 4H), 3.49 (s, 4H), 4.54 (s, 4H), 5.05 (d, *J* = 1.8 Hz, 1H), 5.34 (d, *J* = 1.8 Hz, 1H), 7.22–7.37 (m, 15H); ^{13}C NMR (75 MHz): δ = 15.5, 43.6, 45.0, 45.8, 73.2, 74.2, 114.0, 127.0, 127.2, 127.3, 127.4, 128.1, 128.2, 133.4, 135.3, 138.9, 141.1, 146.1; HRMS (CI): *m/z* calcd for $C_{30}H_{32}O_2$: 424.2402 $[M]^+$; found 424.2395.

To an oven-dried Schlenk tube was added $[Rh(OMe)(nbd)]_2$ (1.6 mg, 3.5 μmol, 5 mol % Rh), phenylboronic acid **2a** (52.1 mg, 0.427 mmol, 3.0 equiv), 1,4-dioxane (0.5 mL), and a solution of 1,6-enyne **8** (53.7 mg, 0.142 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL). The reaction mixture was stirred at 80 °C for 5 h under an argon atmosphere, and quenched with addition of water (5 mL). The resulting aqueous solution was extracted with ethyl acetate (3 x 10 mL) and the combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 9:1) to give the corresponding product **9** (44.9 mg, 0.106 mmol, 75%) as a mixture of geometrical isomers (*E*:*Z*=45:55).

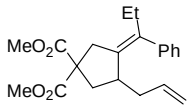
3,3-Bis(benzyloxymethyl)-1-methyl-5-(1-phenylethylidene)cyclopent-1-ene (9)



IR (neat, mixture): 2853, 1734, 1597, 1455, 1362, 1115 cm^{-1}; ^1H NMR (*E* isomer): δ = 2.13 (d, *J* = 0.9 Hz, 3H), 2.19 (s, 3H), 2.26 (s, 2H), 3.33 (d, *J* = 9.3 Hz, 2H), 3.36 (d, *J* = 9.0 Hz, 2H), 4.45 (d, *J* = 12.6 Hz, 2H), 4.50 (d, *J* = 12.6 Hz, 2H), 5.80 (s, 1H), 7.10–7.37 (m, 15H); (*Z* isomer): δ = 1.18 (s, 3H), 1.99 (s, 3H), 2.55 (s, 2H), 3.47 (d, *J* = 9.3 Hz, 2H), 3.50 (d, *J* = 8.4 Hz, 2H), 4.56 (s, 4H), 5.70 (s, 1H), 7.10–7.37 (m, 15H); ^{13}C NMR (75 MHz, mixture): δ = 17.0, 18.6, 20.7, 24.2, 38.7, 39.8, 50.4, 50.5, 73.2, 73.3, 73.7, 74.0, 125.9, 126.1, 127.3, 127.35, 127.40, 127.6, 127.7, 128.17, 128.22, 128.8, 138.3, 138.7, 138.8, 139.2, 139.77, 139.84, 142.0, 142.2, 144.4, 146.7; HRMS (CI, mixture): *m/z* calcd for $C_{30}H_{32}O_2$: 424.2402 $[M]^+$; found 424.2404.

To an oven-dried Schlenk tube was added $[Rh(OH)(cod)]_2$ (4.4 mg, 9.6 μmol, 10 mol % Rh), phenylboronic acid (**2a**, 93.3 mg, 0.765 mmol, 4.0 equiv), THF (0.9 mL) and a solution of 1,6-enyne **10a** (55.2 mg, 0.186 mmol, 1.0 equiv) in THF (1.0 mL). The reaction mixture was stirred at 0 °C for 3 h under an argon atmosphere, and then quenched with addition of water (5 mL). The resulting aqueous solution was extracted with ethyl acetate (3 x 10 mL). The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 7:1) to give the corresponding product **11a** (44.7 mg, 0.131 mmol, 70%).

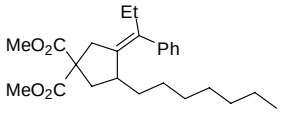
4,4-Dimethoxycarbonyl-1-[(*Z*)-1-phenylpropylidene]-2-(prop-2-enyl)cyclopentane (11a)



IR (neat): 2955, 1738, 1640, 1435, 1258 cm^{-1}; ^1H NMR: δ = 0.88 (t, *J* = 7.5 Hz, 3H), 1.50–1.64 (m, 1H), 1.71–1.82 (m, 1H), 1.89 (dd, *J* = 13.2, 7.5 Hz, 1H), 2.14–2.29 (m, 1H), 2.40 (dq, *J* = 13.8, 7.5 Hz, 1H), 2.49 (ddd, *J* = 13.5, 8.4, 1.7 Hz, 1H), 2.80–2.93 (m, 1H), 2.93 (dt, *J* = 15.9, 1.5 Hz, 1H), 3.09 (dd, *J* = 15.9, 1.5 Hz, 1H), 3.75 (s, 3H), 3.77 (s, 3H), 4.70–4.80 (m, 1H), 4.81–4.88 (m, 1H), 5.45 (ddt, *J* = 17.1, 10.5, 7.5 Hz, 1H), 7.06–7.12 (m, 2H), 7.17–7.25 (m, 1H), 7.26–7.34 (m, 2H); ^{13}C NMR (75 MHz): δ = 12.4, 29.3, 37.8, 38.3, 38.6, 39.7, 52.67, 52.72, 59.0, 116.0, 126.3, 128.1, 128.3, 136.3, 136.7, 137.1, 142.2, 172.2, 172.3; HRMS (CI): *m/z* calcd for $C_{21}H_{26}O_4$: 342.1831 $[M]^+$; found 342.1831.

Arylative cyclization of **10b** (55.8 mg, 0.158 mmol) was carried out according to the same procedure mentioned above to give **11b** (39.1 mg) as a mixture of regioisomers. Consecutively, to an oven-dried Schlenk tube was added $RhCl(PPh_3)_3$ (9.1 mg, 9.8 μmol, 10 mol %) and a solution of **11b** in benzene (4.0 mL). The mixture was degassed by a freeze-pump-thaw method, and then dihydrogen gas was introduced. After stirred at 50 °C for 8 h, the reaction mixture was passed through a Celite® pad. The filtrate was evaporated under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give the corresponding product **12b** (37.6 mg, 0.0939 mmol, 59% (2steps)).

4,4-Dimethoxycarbonyl-1-heptyl-2-[(*Z*)-1-phenylpropylidene]cyclopentane (12b)



IR (neat): 2928, 1738, 1435, 1256, 1171 cm^{-1}; ^1H NMR: δ = 0.78–1.28 (m, 12H), 0.84 (t, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H), 1.85 (dd, *J* = 13.2, 7.2 Hz, 1H), 2.12–2.28 (m, 1H), 2.40 (dq, *J* = 13.5, 7.5 Hz, 1H), 2.53 (ddd, *J* = 13.2, 7.8, 1.2 Hz, 1H), 2.68–2.80 (m, 1H), 2.94 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.08 (dd, *J* = 15.9, 1.5 Hz, 1H), 3.75 (s, 3H), 3.77 (s, 3H), 7.04–7.11 (m, 2H), 7.15–7.23 (m, 1H), 7.24–7.32 (m, 2H); ^{13}C NMR (75 MHz): δ = 12.5, 14.1, 22.6, 26.5, 28.9, 29.0, 29.3, 31.7, 33.8, 38.3, 39.0, 39.9, 52.7, 59.2, 126.1, 128.0, 128.4, 136.4, 137.8, 142.4, 172.3. 172.5; HRMS (EI): Calcd for $C_{25}H_{36}O_4$: 400.2614 $[M]^+$; found. 400.2616

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Chapter 3

Rhodium-Catalyzed Cyclization of Alkynones Induced by Addition of Arylboronic Acids

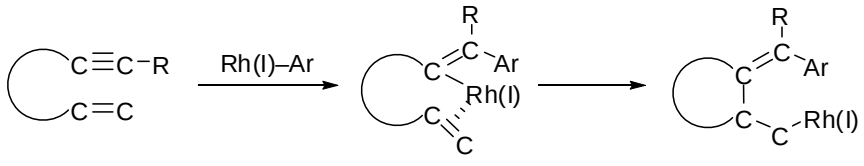
Abstract

Alkynones reacted with arylboronic acids in the presence of a rhodium(I) catalyst to afford four- and five-membered-ring cyclic alcohols equipped with a tetrasubstituted *exo*-cyclic olefin. The cyclic allylic alcohol skeleton was constructed by the carbon–carbon bond formation between the carbonyl group and an alkenylrhodium(I) intermediate formed by the regioselective addition of an arylrhodium(I) species across the carbon–carbon triple bond.

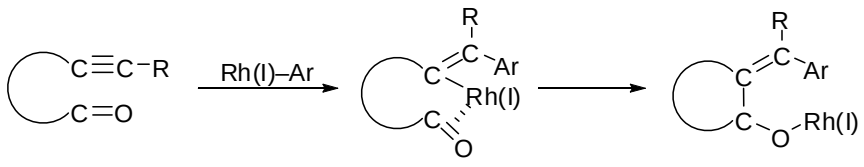
Introduction

Transition-metal-catalyzed cascade reactions involving multiple carbometalation steps serve as a powerful method for the preparation of complex cyclic molecules in an atom-economical manner.[1] A molecule containing two different unsaturated functionalities that can act as an acceptor of an organometallic species is particularly an attractive substrate for such cascade reactions. Recently, rhodium(I)-catalyzed cascade reactions[2] have emerged as a complement to the well-studied palladium-catalyzed cascade sequences.[3] High functional group compatibilities and stereoselectivities have been observed in a number of the rhodium-catalyzed reactions. For the rhodium(I)-catalyzed cascade reactions to start, an alkyne moiety can provide a convenient entry point for incorporation of an active Csp^2–Rh linkage by way of intermolecular carborhodation.[4] The resultant alkenylrhodium(I) species exhibits an enhanced reactivity to the second unsaturated functionality in the molecule than in an intermolecular case.[5]

As shown in the preceding chapters, the rhodium(I)-catalyzed reaction of 1,6-enynes with arylboronic acids gave arylative cyclization products through successive carborhodations of the organorhodium(I) intermediates [Eq (1)]. Like carbon–carbon double and triple bonds, the carbonyl groups of aldehydes and ketones can also accept an organorhodium(I) species to form a carbon–carbon bond.[6] The author envisaged that an analogous sequential addition/cyclization reaction would be feasible with an alkynone, if a carbon–carbon triple bond and a carbonyl group are appropriately arranged in the molecule [Eq (2)]. In this chapter, he wishes to describe the study on the rhodium-catalyzed reaction of alkynones with arylboronic acids.[7]



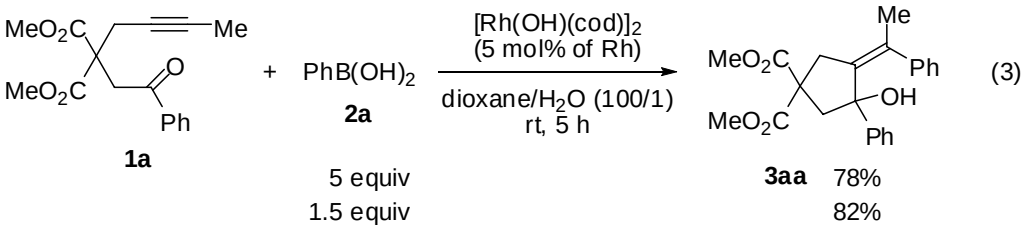
(1)



(2)

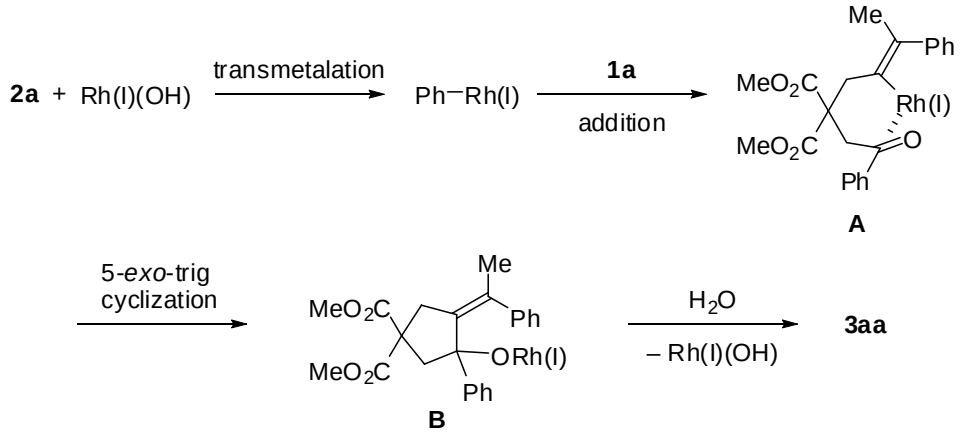
Results and discussions

The author took 5-alkyn-1-ones **1** having a three-carbon tether between the carbon–carbon triple bond and the ketonic carbonyl group as the model substrate and examined the reaction with phenylboronic acid (**2a**). As for a rhodium catalyst, he employed hydroxo(diolefin)rhodium(I) complexes,[8] which successfully catalyzed the cascade reaction of 1,6-enynes with arylboronic acids.[5a] Thus, 5-alkyn-1-one **1a** was treated with **2a** (5.0 equiv) in the presence of $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (100/1) at room temperature for 5 h under an argon atmosphere. Chromatographic isolation afforded cyclopentanol **3aa** equipped with a tetrasubstituted *exo*-cyclic olefin in 78% yield [Eq (3)]. The *Z* configuration of the *exo*-cyclic double bond was corroborated by a difference NOE study. Interestingly, the use of 1.5 equivalents of **2a** was sufficient to obtain a product yield of 82%. However, a lower catalyst loading (1 ~ 3 mol% of Rh) suffered from a poor reproducibility, probably due to deterioration of the catalyst.



(3)

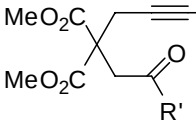
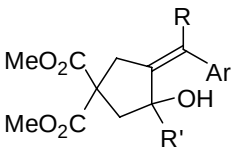
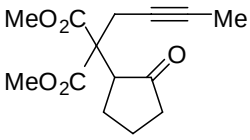
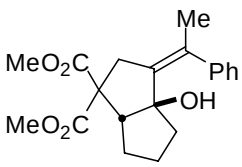
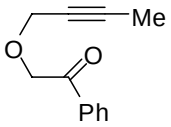
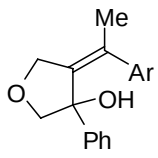
The proposed reaction pathway is depicted in Scheme 1. A phenylrhodium(I) species is initially generated by transmetalation of hydroxorhodium(I) with **2a**. The ketonic carbonyl group directs the regioselective *cis* carborhodation across the carbon–carbon triple bond.[9] The resulting alkenylrhodium(I) intermediate **A** undergoes intramolecular nucleophilic addition to the carbonyl group in a 5-*exo* mode, forming the rhodium(I) alkoxide **B**. Finally, the product **3aa** was released by protodemetalation with regeneration of the catalytically active hydroxorhodium(I) species. Of note is that carborhodation onto the carbon–carbon triple bond and the ketonic carbonyl group proceeds at room temperature.



Scheme 1. Proposed reaction pathway of 5-alkyn-1-one **1a** with phenylboronic acid (**2a**)

The results obtained with a variety of 5-alkyn-1-ones **1** and arylboronic acids **2** are summarized in Table 1. The catalytic process worked well with a sterically and electronically diverse array of arylboronic acids **2b**–**2g** to give the corresponding products **3ab**–**3ag** in 69–82% yields (entries 1–6). 5-Alkyn-1-ones **1b** and **1c** also gave the corresponding products **3ba** and **3ca** in good yields (entries 7 and 8). In the case of 5-alkyn-1-al **1d**, a phenylrhodium(I) initially formed preferentially added to the carbon–carbon triple bond even in the presence of an aldehydic carbonyl group to give the secondary allylic alcohol **3da** in 62% yield (entry 9). The reaction of substrate **1f** with an ether tether gave the product **3fa** in only 21% yield due to the lower regioselectivity of the initial 1,2-addtion of a phenylrhodium(I) species (entry 11). The author assumes that the high regioselectivity of the initial 1,2-addition observed with **1a**–**1e** is to be ascribed not only to the carbonyl coordination but also to the steric effects of the two alkyl substituents flanking the carbon–carbon triple bond. The tether substituent connected to a carbonyl group through the malonate ester was considerably bulkier than the other with **1a**–**1e**.[10] The corresponding steric contrast of **1f** was not sufficient to cause a regioselective addition.

Table 1. Rhodium-catalyzed reaction of 5-alkyn-1-ones **1** with arylboronic acids **2**. [a]

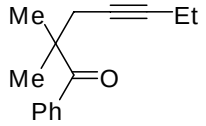
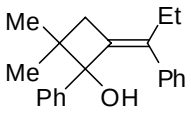
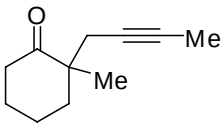
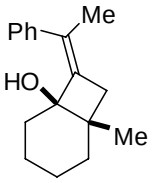
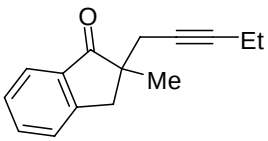
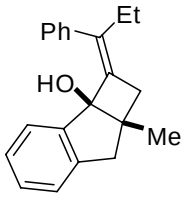
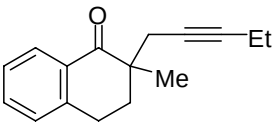
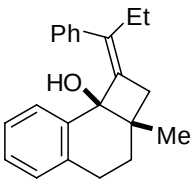
entry	substrate		$ArB(OH)_2$	product		yield (%) [b]
1		**1a** R=Me, R'=Ph	**2b** 4-F-C_6H_4		**3ab**	76
2			**2c** 4-NO_2-C_6H_4		**3ac**	78
3			**2d** 4-Me-C_6H_4		**3ad**	69
4			**2e** 3-MeO-C_6H_4		**3ae**	77
5			**2f** 3-Cl-C_6H_4		**3af**	82
6			**2g** 2-Me-C_6H_4		**3ag**	80 [c]
7		**1b** R=*n*-Bu, R'=Ph	**2a** Ph		**3ba**	82
8		**1c** R=Me, R'=Me	**2a** Ph		**3ca**	72
9		**1d** R=Me, R'=H	**2a** Ph		**3da**	62
10		**1e**	**2a** Ph		**3ea**	82
11		**1f**	**2a** Ph		**3fa**	21

[a] Reaction condition: **1** (0.2 mmol), **2** (1.0 mmol), $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (2.0 mL/20 μL), room temperature, 2-5 h. [b] Yields of isolated products. [c] A 56:44 mixture of atropisomers.

Next, an analogous cyclization in a 4-*exo*-trig mode was examined (Table 2). Thus, 4-alkyn-1-one **4a** having a two-carbon tether was treated with phenylboronic acid (**2a**, 5.0 equiv) under conditions similar to those used for **1**. Chromatographic isolation afforded cyclobutanol **5aa** in 67% yield together with a small amount of 1,2-addition product (6%) (entry 1). It was noteworthy that an intermediate alkenylrhodium(I) species underwent intramolecular nucleophilic carbonyl addition in a 4-*exo*-trig mode, although such four-membered-ring formation would suffer from developing ring strain. The minor product was formed by the 1,2-addition of a phenylrhodium(I) species to the carbon–carbon triple bond with the opposite regiochemistry and subsequent protonolysis. Similar results were obtained with the reactions of 4-alkyn-1-ones **4b**–**4d** possessing cyclic structures, which afforded the corresponding bicyclic products **5ba**–**5da** in

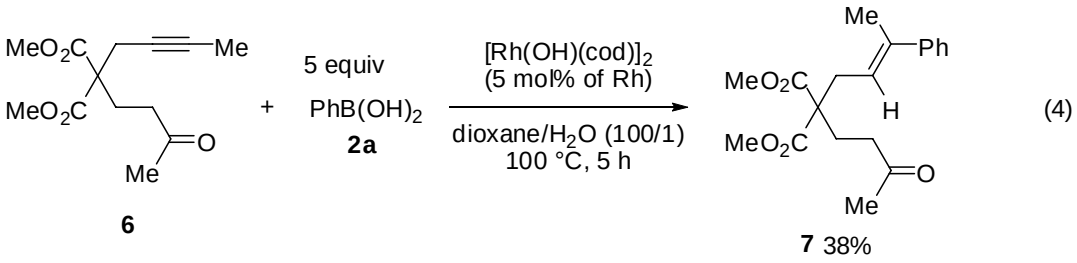
58–61% yields (entries 2–4). The regioselectivities observed with 4-alkyn-1-ones were generally lower than those of 5-alkyn-1-ones.

Table 2. Rhodium-catalyzed reaction of 4-alkyn-1-ones **4** with phenylboronic acid (**2a**). [a]

entry	substrate		product		yield (%) [b]
1		**4a**		**5aa**	67 [c]
2		**4b**		**5ba**	58
3		**4c**		**5ca**	58
4		**4d**		**5da**	61

[a] Reaction condition: **4** (0.25 mmol), **2a** (1.25 mmol), $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (2.5 mL/25 μL), room temperature, 6-25 h. [b] Yields of isolated products.
[c] Obtained as a mixture with 1,2-adduct (6%).

In the case of 6-alkyn-1-ones **6** having a four-carbon tether, even the initial 1,2-addition of a phenylrhodium(I) species failed to occur at room temperature. When the reaction temperature was raised to 100 °C, 1,2-addition took place but the resultant alkenylrhodium(I) intermediate failed to add the carbonyl group, giving the hydrolyzed compound **7** as the major product [Eq. (4)].



(4)

The contrasting results obtained with **1**, **4**, and **6** indicate that, with alkynones **1** and **4**, coordination of the carbonyl group to rhodium facilitates the 1,2-addition to the alkyne moiety and subsequent intramolecular nucleophilic addition to the carbonyl group and that the accelerating effect by coordination significantly depends on the tether length.[5e] Of note was that the four-membered ring formation was facile whereas the six-membered ring formation failed.

Conclusion

Rhodium(I)-catalyzed cyclization reactions of alkynones have been developed. An alkenylrhodium(I) intermediate induced by the regioselective addition of an arylrhodium(I) species across the carbon–carbon triple bond at room temperature subsequently undergoes intramolecular carbonyl addition in 4-*exo* and 5-*exo*-trig modes to construct the carbocyclic alcohols under similar reaction conditions. An addition reaction of ordinary alkynes with arylboronic acids requires heating over 80 °C.[4,9] The presence of the carbonyl group as the secondary acceptor functionality greatly contributes to the high reactivity.

Experimental Section

General

All rhodium(I)-catalyzed reactions were carried out with standard Schlenk technique under an argon atmosphere. Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300.07 Hz and ^{13}C at 75.46 Hz) spectrometer. NMR data were obtained in $CDCl_3$ otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm. Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.00 ppm. High resolution

mass spectra were recorded on a JOEL JMS-SX102A spectrometer. IR spectra were recorded on a Shimadzu FTIR-8100 spectrometer.

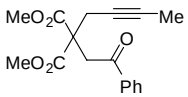
Materials

Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $[Rh(OH)(cod)]_2$ was prepared according to the reported procedure.[11] 1,4-Dioxane was distilled over sodium-benzophenone ketyl prior to use.

Starting Materials:

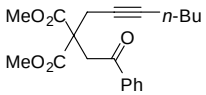
Malonate-tethered 5-alkyn-1-ones **1a**-**c** was prepared by the reaction of dimethyl 2-(alk-2-ynyl)-malonate derivatives with the corresponding α-bromoketones in the presence of NaH in a THF solution. Alkynal **1d** was prepared by the following procedure. Dimethyl 2-(2,2-dimethoxy-ethyl)malonate which was synthesized from dimethyl malonate and 2-bromo-1,1-dimethoxyethane (NaOMe, in MeOH), was reacted with 1-bromobut-2-yne (NaH, in THF) followed by hydrolysis under an acidic condition (trifluoroacetic acid, $CHCl_3/H_2O$) to afford **1d**. Cyclopentanone derivative **1e** was prepared by successive alkylation of dimethyl malonate with α-chloro-cyclopentanone (NaH, in THF/DMF), then 1-bromobut-2-yne (NaH, in THF). Oxygen-atom-tethered **1f** was prepared from 1-bromobut-2-yne and 1-phenylethane-1,2-diol according to the reported prodedure.[12] 4-Alkyn-1-one **4a** was prepared from isobutyrophenone and 1-bromo-pent-2-yne (LDA, in THF/DMPU), and cyclic variants (**4b-d**) were also synthesized by analogous manner.

Dimethyl 2-(but-2-ynyl)-2-(2-oxo-2-phenylethyl)malonate (1a)



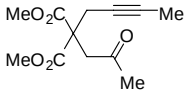
IR (neat): 2955, 1740, 1688, 1435, 1291, 1208 cm^{-1}; ^1H NMR: δ = 1.71 (t, *J* = 2.4 Hz, 3H), 3.04 (q, *J* = 2.5 Hz, 2H), 3.76 (s, 6H), 3.89 (s, 2H), 7.44–7.52 (m, 2H), 7.56–7.63 (m, 1H), 7.98–8.04 (m, 2H); ^{13}C NMR: δ = 3.5, 23.8, 41.1, 53.1, 54.9, 73.7, 79.4, 128.1, 128.6, 133.4, 136.4, 170.1, 196.8; HRMS (EI): *m/z* calcd for $C_{17}H_{18}O_5$: 302.1154 $[M]^+$; found 302.1155.

Dimethyl 2-(hept-2-ynyl)-2-(2-oxo-2-phenylethyl)malonate (1b)



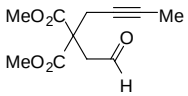
IR (neat): 2955, 1743, 1688, 1435, 1291, 1207 cm^{-1}; ^{1}H NMR: $\delta = 0.84$ (t, J = 7.1 Hz, 3H), 1.22–1.45 (m, 4H), 2.02–2.13 (m, 2H), 3.05 (t, J = 2.4 Hz, 2H), 3.76 (s, 6H), 3.90 (s, 2H), 7.43–7.53 (m, 2H), 7.55–7.63 (m, 1H), 7.98–8.06 (m, 2H); ^{13}C NMR: δ = 13.6, 18.3, 21.8, 23.8, 30.9, 41.1, 53.0, 55.0, 74.6, 84.1, 128.1, 128.6, 133.4, 136.4, 170.1, 196.8; HRMS (CI) *m/z* calcd for $C_{20}H_{25}O_5$: 345.1702 $[M+H]^+$; found 345.1706.

Dimethyl 2-(but-2-ynyl)-2-(2-oxo-propyl)malonate (1c)



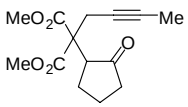
IR (nujol): 2909, 1748, 1715, 1291, 1258, 1204 cm^{-1}; ^{1}H NMR: δ = 1.75 (t, J = 2.7 Hz, 3H), 2.18 (s, 3H), 2.92 (q, J = 2.5 Hz, 2H), 3.32 (s, 2H), 3.72 (s, 6H); ^{13}C NMR: δ = 3.5, 23.8, 30.2, 45.5, 53.0, 54.7, 73.6, 79.2, 169.9, 205.4; HRMS (CI): *m/z* calcd for $C_{12}H_{17}O_5$: 241.1076 $[M+H]^+$; found 241.1075.

Dimethyl 2-(but-2-ynyl)-2-(2-oxo-ethyl)malonate (1d)



IR (nujol): 2757, 1737, 1291, 1200, 1092, 1057 cm^{-1}; ^{1}H NMR: δ = 1.74 (t, J = 2.6 Hz, 3H), 2.90 (q, J = 2.5 Hz, 2H), 3.21 (d, J = 1.2 Hz, 2H), 3.75 (s, 6H), 9.74 (t, J = 1.1 Hz, 1H); ^{13}C NMR: δ = 3.5, 24.4, 46.2, 53.2, 54.3, 73.1, 79.9, 169.6, 198.7; HRMS (CI): *m/z* calcd for $C_{11}H_{15}O_5$: 227.0919 $[M+H]^+$; found 227.0915.

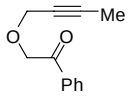
Dimethyl 2-(but-2-ynyl)-2-(2-oxo-cyclopentyl)malonate (1e)



IR (neat): 2955, 1723, 1435, 1245, 1145, 1048 cm^{-1}; ^{1}H NMR: δ = 1.66–1.99 (m, 2H), 1,76 (t, J = 2.7 Hz, 3H), 2.01–2.13 (m, 1H), 2.17–2.41 (m, 3H), 2.78 (dq, J = 16.8, 2.6 Hz, 1H), 2.89 (dq, J =

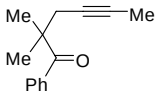
17.0, 2.6 Hz, 1H), 2.92–3.01 (m, 1H), 3.755 (s, 3H), 3.764 (s, 3H); ^{13}C NMR: δ = 3.6, 20.6, 24.4, 26.6, 37.9, 52.6, 52.7, 52.8, 58.5, 74.2, 78.9, 169.7, 170.3, 216.5; HRMS (CI): *m/z* calcd for $C_{14}H_{19}O_5$: 267.1232 $[M+H]^+$; found 267.1235.

But-2-ynyloxymethyl phenyl ketone (1f)



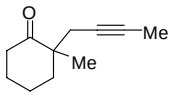
IR (nujol): 2923, 1701, 1449, 1229, 1157, 1121 cm^{-1}; ^{1}H NMR: δ = 1.86 (t, *J* = 2.3 Hz, 3H), 4.32 (q, *J* = 2.4 Hz, 2H), 4.85 (s, 2H), 7.43–7.52 (m, 2H), 7.55–7.63 (m, 1H), 7.91–7.98 (m, 2H); ^{13}C NMR: δ = 3.4, 58.8, 71.4, 74.1, 83.5, 127.6, 128.5, 133.3, 134.6, 195.6; HRMS (FAB): *m/z* calcd for $C_{12}H_{13}O_2$: 189.0916 $[M+H]^+$; found 189.0909.

2,2-Dimethyl-1-phenylhept-4-yn-1-one (4a)



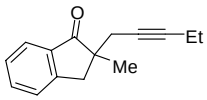
IR (neat): 2975, 1678, 1468, 1320, 1215, 1159 cm^{-1}; ^{1}H NMR: δ = 1.09 (t, *J* = 7.5 Hz, 3H), 1.39 (s, 6H), 2.14 (qt, *J* = 7.6, 2.4 Hz, 2H), 2.52 (t, *J* = 2.6 Hz, 2H), 7.35–7.49 (m, 3H), 7.60–7.67 (m, 2H); ^{13}C NMR: δ = 12.4, 14.2, 25.3, 30.4, 47.8, 76.1, 84.4, 127.3, 128.0, 130.6, 139.0, 208.3; HRMS (CI): *m/z* calcd for $C_{15}H_{19}O$:215.1436 $[M+H]^+$; found 215.1438.

2-(But-2-ynyl)-2-methylcyclohexanone (4b)



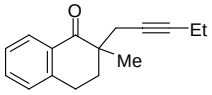
IR (neat): 2936, 1709, 1453, 1375, 1127, 1073 cm^{-1}; ^{1}H NMR: δ = 1.18 (s, 3H), 1.67–1.96 (m, 9H), 2.25–2.50 (m, 4H); ^{13}C NMR: δ = 3.5, 21.2, 22.5, 27.4, 27.9, 38.0, 38.6, 48.2, 75.4, 78.0, 214.5; HRMS (CI): *m/z* calcd for $C_{11}H_{17}O$: 165.1279 $[M+H]^+$; found 165.1277.

2-Methyl-2-(pent-2-ynyl)indan-1-one (4c)



IR (neat): 2975, 1715, 1609, 1466, 1374, 1300 cm^{-1}; ^1H NMR: δ = 0.93 (t, *J* = 7.5 Hz, 3H), 1.27 (s, 3H), 2.02 (qt, *J* = 7.5, 2.4 Hz, 2H), 2.40 (t, *J* = 2.6 Hz, 2H), 2.92 (d, *J* = 17.1 Hz, 1H), 3.35 (d, *J* = 17.1 Hz, 1H), 7.33–7.40 (m, 1H), 7.42–7.48 (m, 1H), 7.60 (td, *J* = 7.2, 1.2 Hz, 1H), 7.73–7.78 (m, 1H); ^{13}C NMR: δ = 12.3, 14.1, 23.3, 28.0, 40.1, 48.8, 75.6, 83.6, 124.3, 126.5, 127.3, 134.9, 135.7, 152.8, 209.8; HRMS (EI): *m/z* calcd for $C_{15}H_{16}O$: 212.1201 $[M]^+$; found 212.1200.

2-Methyl-2-(pent-2-ynyl)-3,4-dihydro-2*H*-naphthalen-1-one (4d)

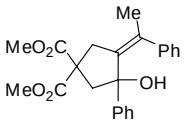


IR (neat): 2934, 1682, 1601, 1456, 1323, 1221 cm^{-1}; ^1H NMR: δ = 1.10 (t, *J* = 7.5 Hz, 3H), 1.25 (s, 3H), 2.06 (dt, *J* = 13.6, 5.6 Hz, 1H), 2.16 (qt, *J* = 7.4, 2.4 Hz, 2H), 2.25 (ddd, *J* = 13.5, 8.4, 6.0 Hz, 1H), 2.45 (dt, *J* = 16.6, 2.4 Hz, 1H), 2.53 (dt, *J* = 16.8, 2.4 Hz, 1H), 2.90–3.10 (m, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.46 (td, *J* = 7.5, 1.4 Hz, 1H), 8.04 (dd, *J* = 7.5, 1.2 Hz, 1H); ^{13}C NMR: δ = 12.5, 14.3, 21.4, 25.5, 27.4, 33.1, 44.6, 75.6, 84.3, 126.6, 128.0, 128.7, 131.3, 133.1, 143.4, 201.4; HRMS (EI): *m/z* calcd for $C_{16}H_{18}O$: 226.1358 $[M]^+$; found 226.1358.

*General procedure for arylative cyclization of 5-alkyn-1-ones **1**:*

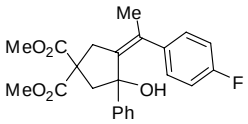
To an oven-dried, Ar-purged flask was added $[Rh(OH)(cod)]_2$ (2.28 mg, 5 μmol, 5 mol% of Rh), arylboronic acid **2** (1.0 mmol, 5.0 equiv), and 1,4-dioxane (1 mL). A solution of substrate **1** (0.2 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL) and H_2O (20 μL) was added to the reaction mixture at room temperature. After complete consumption of substrate was observed, water was added. The aqueous layer was extracted with ethyl acetate three times. The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product **3**.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-phenylethylidene]cyclopentane (3aa)



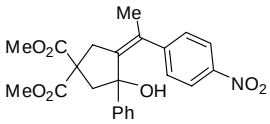
IR (nujol): 3546, 2920, 1732, 1444, 1240, 1202 cm^{-1}; ^1H NMR: δ = 2.00 (br s, 3H), 2.45 (s, 1H), 2.70 (d, *J* = 14.1 Hz, 1H), 2.76 (dd, *J* = 14.1, 1.5 Hz, 1H), 3.13 (dq, *J* = 17.0, 1.9 Hz, 1H), 3.63 (d, *J* = 16.5 Hz, 1H), 3.70 (s, 3H), 3.82 (s, 3H), 6.63–6.71 (m, 2H), 6.87–7.03 (m, 8H); ^{13}C NMR: δ = 23.9, 40.5, 52.9, 53.0, 53.2, 57.5, 82.0, 125.2, 125.9, 126.0, 127.2, 127.5, 127.7, 134.9, 141.5, 141.9, 146.1, 171.8, 172.7; HRMS (FAB): *m/z* calcd for $C_{23}H_{24}O_5$: 380.1624 $[M]^+$; found 380.1624.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(4-fluorophenyl)-ethylidene]-cyclopentane (3ab)



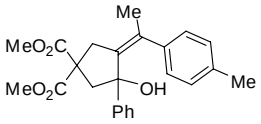
IR (nujol): 3555, 1732, 1509, 1260, 1254, 1213 cm^{-1}; ^1H NMR: δ = 1.96 (br s, 3H), 2.64–2.72 (m, 2H), 2.75 (dd, *J* = 14.4, 1.8 Hz, 1H), 3.15 (dq, *J* = 17.3, 2.0 Hz, 1H), 3.59 (d, *J* = 17.1 Hz, 1H), 3.72 (s, 3H), 3.83 (s, 3H), 6.54–6.68 (m, 4H), 6.94–7.05 (m, 5H); ^{13}C NMR: δ = 23.9, 40.5, 52.9, 53.1, 53.5, 57.5, 82.0, 114.2 (d, *J* = 20.9 Hz), 125.2, 126.0, 127.2, 129.5 (d, *J* = 8.1 Hz), 134.1, 137.7 (d, *J* = 3.5 Hz), 142.0, 145.8, 161.0 (d, *J* = 244.7 Hz), 171.7, 173.2; HRMS (FAB): *m/z* calcd for $C_{23}H_{23}FO_5$: 398.1530 $[M]^+$; found 398.1531.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(4-nitrophenyl)-ethylidene]-cyclopentane (3ac)



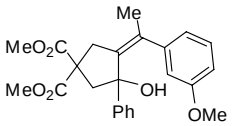
IR (nujol): 3528, 1732, 1597, 1518, 1347, 1256 cm^{-1}; ^1H NMR (C_6D_6): δ = 1.60 (br s, 3H), 2.74 (d, *J* = 14.4 Hz, 1H), 2.88 (dd, *J* = 14.3, 2.3 Hz, 1H), 3.18–3.29 (m, 2H), 3.32 (s, 3H), 3.39 (s, 3H), 3.63 (d, *J* = 17.7 Hz 1H), 6.45–6.52 (m, 2H), 6.68–6.75 (m, 3H), 6.83–6.90 (m, 2H), 7.53–7.59 (m, 2H); ^{13}C NMR (C_6D_6): δ = 23.0, 40.9, 52.6, 52.9, 54.4, 58.0, 82.1, 122.3, 125.7, 126.3, 127.5, 129.3, 133.2, 143.9, 145.4, 146.3, 148.7, 171.4, 173.9; HRMS (FAB) *m/z* calcd for $C_{23}H_{23}NO_7$: 425.1475 $[M]^+$; found 425.1472.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(4-methylphenyl)-ethylidene]-cyclopentane (3ad)



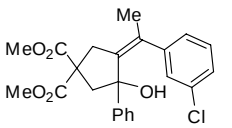
IR (nujol): 3546, 1733, 1514, 1247, 1200, 1092 cm^{-1}; ^1H NMR: δ = 1.98 (br s, 3H), 2.16 (s, 3H), 2.40 (s, 1H), 2.71 (d, *J* = 14.1 Hz, 1H), 2.76 (dd, *J* = 14.1, 1.2 Hz, 1H), 3.13 (dq, *J* = 16.8, 1.8 Hz, 1H), 3.61 (d, *J* = 16.8 Hz, 1H), 3.67 (s, 3H), 3.82 (s, 3H), 6.55 (d, *J* = 7.8 Hz, 2H), 6.73 (d, *J* = 7.8 Hz, 2H), 6.97–7.05 (m, 5H); ^{13}C NMR: δ = 21.0, 23.9, 40.4, 52.8, 53.0, 57.4, 82.1, 125.3, 125.9, 127.2, 127.5, 128.2, 134.7, 135.6, 138.9, 141.2, 146.4, 171.8, 172.6; HRMS (FAB): *m/z* calcd for $C_{24}H_{26}O_5$: 394.1780 $[M]^+$; found 394.1778.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(3-methoxyphenyl)ethylidene]-cyclopentane (3ae)



IR (neat): 3563, 2955, 1733, 1597, 1457, 1067 cm^{-1}; ^1H NMR: δ = 1.99 (br s, 3H), 2.48(s, 1H), 2.71 (dd, *J* = 14.3, 0.8 Hz, 1H), 2.77 (dd, *J* = 14.1, 1.5 Hz, 1H), 3.13 (dq, *J* = 17.1, 2.1 Hz, 1H), 3.50 (s, 3H), 3.61 (d, *J* = 17.1 Hz, 1H), 3.68 (s, 3H), 3.82 (s, 3H), 6.12 (dd, *J* = 2.4, 1.5 Hz, 1H), 6.33–6.39 (m, 1H), 6.47–6.55 (m, 1H), 6.86–6.95 (m, 1H), 6.96–7.09 (m, 5H); ^{13}C NMR: δ = 23.7, 40.4, 52.8, 52.9, 53.0, 54.8, 57.4, 82.0, 112.66, 112.71, 119.8, 125.3, 125.9, 127.2, 128.7, 134.5, 141.4, 143.2, 146.4, 158.7, 171.7, 172.6; HRMS (FAB): *m/z* calcd for $C_{24}H_{26}O_6$: 410.1729 $[M]^+$; found 410.1728.

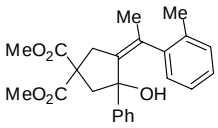
1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(3-chlorophenyl)ethylidene]-cyclopentane (3af)



IR (neat): 3505, 2958, 1735, 1593, 1436, 1068 cm^{-1}; ^1H NMR: δ = 1.96 (br s, 3H), 2.69 (s, 1H), 2.70 (d, *J* = 14.1 Hz, 1H), 2.77 (dd, *J* = 14.6, 1.7 Hz, 1H), 3.14 (dq, *J* = 17.3, 2.0 Hz, 1H), 3.60 (d, *J* = 17.4 Hz, 1H), 3.74 (s, 3H), 3.84 (s, 3H), 6.59–6.64 (m, 2H), 6.81–6.92 (m, 2H), 6.95–7.06 (m,

5H); ^{13}C NMR: δ = 23.5, 40.4, 53.0, 53.1, 53.4, 57.5, 81.9, 125.1, 125.9, 126.1, 127.2, 128.2, 128.5, 133.1, 133.7, 142.4, 143.5, 145.3, 171.7, 173.1; HRMS (FAB): *m/z* calcd for $C_{23}H_{23}ClO_5$: 414.1234 $[M]^+$; found 414.1234.

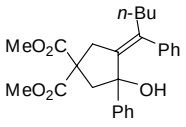
1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-(2-methylphenyl)ethylidene]-cyclopentane (3ag)



A mixture of atropisomers (56:44)

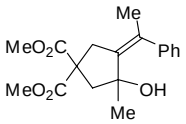
IR (nujol): 3530, 1736, 1458, 1238, 1203, 1063 cm^{-1}; ^{1}H NMR: δ = 1.59 (s, 1.680H), 1.90 (br s, 1.680H), 1.94 (br s, 1.320H), 2.19 (s, 0.440H), 2.24 (s, 1.320H), 2.52 (s, 0.560H), 2.68–2.86 (m, 2H), 3.03 (dq, *J* = 16.8, 2.1 Hz, 0.560H), 3.12 (dq, *J* = 16.4, 2.0 Hz, 0.440H), 3.57–3.74 (m, 1H), 3.66 (s, 1.320H), 3.78 (s, 1.680H), 3.80 (s, 1.320H), 3.84 (s, 1.680H), 6.01 (dd, *J* = 7.5, 1.2 Hz, 0.440H), 6.51 (t, *J* = 7.7 Hz, 0.440H), 6.55–6.62 (m, 0.560H), 6.83–7.16 (m, 7.560H); ^{13}C NMR: δ = 19.2, 19.4, 22.4, 22.9, 40.2, 40.6, 52.6, 52.8, 52.9, 53.0, 57.4, 57.6, 81.5, 81.8, 124.6, 124.7, 124.99, 125.05, 125.6, 126.2, 126.4, 126.8 127.0, 127.5, 128.2, 128.3, 129.5, 129.8, 133.7, 134.4, 134.8, 135.0, 140.5, 140.8, 140.9, 141.8, 144.5, 147.7, 171.5, 172.0, 172.3, 172.7; HRMS (FAB): calcd for $C_{24}H_{25}O_5$: 393.1702 $[M–H]^+$; found 393.1701.

1,1-Dimethoxycarbonyl-3-hydroxy-3-phenyl-4-[(*Z*)-1-phenylpentylidene]cyclopentane (3ba)



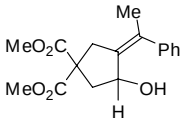
IR (neat): 3570, 2955, 1732, 1447, 1255, 1067 cm^{-1}; ^{1}H NMR: δ = 0.87 (t, *J* = 6.8 Hz, 3H), 1.18–1.44 (m, 4H), 2.14–2.41 (m, 3H), 2.69 (d, *J* = 14.1 Hz, 1H), 2.75 (d, *J* = 14.4 Hz, 1H), 3.08 (d, *J* = 16.5 Hz, 1H), 3.63–3.73 (m, 4H), 3.82 (s, 3H), 6.53–6.61 (m, 2H), 6.86–7.07 (m, 8H); ^{13}C NMR: δ = 14.0, 22.6, 29.3, 37.1, 40.1, 52.85, 52.90, 57.6, 81.9, 125.0, 125.8, 125.9, 127.2, 127.4, 128.3, 139.7, 140.4, 142.0, 146.6, 171.8, 172.4; HRMS (FAB): *m/z* calcd for $C_{26}H_{30}O_5$: 422.2093 $[M]^+$; found 422.2092.

1,1-Dimethoxycarbonyl-3-hydroxy-3-methyl-4-[(*Z*)-1-phenylethylidene]cyclopentane (3ca)



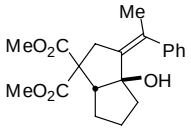
IR (neat): 3520, 2955, 1732, 1435, 1258, 1071 cm^{-1}; ^1H NMR: δ = 0.88 (s, 3H), 1.95 (t, *J* = 1.5 Hz, 3H), 2.16 (br s, 1H), 2.33 (d, *J* = 13.8 Hz, 1H), 2.54 (dd, *J* = 14.0, 2.0 Hz, 1H), 2.95 (dq, *J* = 17.4, 1.7 Hz, 1H), 4.40 (d, *J* = 17.3 Hz, 1H), 3.76 (s, 3H), 3.79 (s, 3H), 7.15–7.35 (m, 5H); ^{13}C NMR: δ = 24.1, 27.3, 39.7, 50.5, 52.8, 52.9, 56.5, 78.1, 126.7, 128.0, 128.2, 133.2, 139.0, 142.9, 172.1, 173.1; HRMS (FAB): *m/z* calcd for $C_{18}H_{21}O_4$: 301.1440 $[M–OH]^+$; found 301.1440.

1,1-Dimethoxycarbonyl-3-hydroxy-4-[(*Z*)-1-phenylethylidene]cyclopentane (3da)



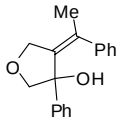
IR (neat): 3526, 2953, 1732, 1435, 1257, 1082 cm^{-1}; ^1H NMR: δ = 1.96 (d, *J* = 4.2 Hz, 1H), 2.02 (br s, 3H), 2.37 (dd, *J* = 14.1, 5.1 Hz, 1H), 2.47 (d, *J* = 14.1 Hz, 1H), 2.92 (dq, *J* = 17.7, 1.5 Hz, 1H), 3.39 (d, *J* = 17.7 Hz, 1H), 3.76 (s, 3H), 3.79 (s, 3H), 4.45–4.53 (m, 1H), 7.21–7.37 (m, 5H); ^{13}C NMR: δ = 21.6, 37.5, 43.0, 52.9, 53.0, 58.3, 72.2, 126.9, 127.5, 128.2, 134.1, 138.0, 142.5, 172.2, 173.3; HRMS (FAB): *m/z* calcd for $C_{17}H_{20}O_5$: 304.1311 $[M]^+$; found 304.1304.

(1*S,5*R**)-4,4-Dimethoxycarbonyl-1-hydroxy-2-[(*Z*)-1-phenyliedene]bicyclo[3.3.0]octane (3ea)**



IR (nujol): 3544, 1755, 1728, 1458, 1281, 1071 cm^{-1}; ^1H NMR: δ = 1.07–1.25 (m, 1H), 1.46–1.67 (m, 4H), 1.73–1.87 (m, 1H), 1.96 (br s, 3H), 2.83–2.93 (m, 1H), 3.05 (d, *J* = 17.4 Hz, 1H), 3.23 (s, 1H), 3.25 (dq, *J* = 17.3, 2.0 Hz, 1H), 3.74 (s, 3H), 3.80 (s, 3H), 7.16–7.39 (m, 5H); ^{13}C NMR: δ = 23.7, 25.4, 29.4, 38.3, 41.9, 52.4, 53.1, 59.2, 59.6, 88.8, 126.4, 127.6, 128.2, 133.3, 139.8, 143.2, 170.6, 174.3; HRMS (FAB): *m/z* calcd for $C_{20}H_{24}O_5$: 344.1624 $[M]^+$; found 344.1621.

3-Phenyl-4-[(*Z*)-1-phenylethylidene]tetrahydrofuran-3-ol (3fa)

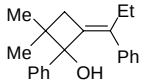


IR (nujol): 3436, 1493, 1204, 1100, 1038 cm^{-1}; ^1H NMR: δ = 1.97 (br s, 3H), 2.36 (br s, 1H), 3.85 (d, *J* = 9.0 Hz, 1H), 4.00 (d, *J* = 9.3 Hz, 1H), 4.74 (d, *J* = 13.5 Hz, 1H), 4.89 (d, *J* = 13.5 Hz, 1H), 6.79–6.87 (m, 2H), 6.96–7.22 (m, 8H); ^{13}C NMR: δ = 22.7, 72.5, 81.1, 83.7, 125.2, 126.4, 126.7, 127.55, 127.60, 127.8, 131.5, 140.7, 141.0, 144.0; HRMS (FAB): *m/z* calcd for $C_{18}H_{18}O_2$: 266.1307 $[M]^+$; found 266.1307.

*General procedure for arylative cyclization of 4-alkyn-1-ones **4**:*

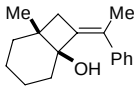
To an oven-dried, Ar-purged flask was added $[Rh(OH)(cod)]_2$ (2.58 mg, 6.25 μmol, 5 mol% of Rh), arylboronic acid **2** (1.25 mmol, 5.0 equiv), and 1,4-dioxane (1.25 mL). A solution of substrate **4** (0.25 mmol, 1.0 equiv) in 1,4-dioxane (1.25 mL) and H_2O (25 μL) was added to the reaction mixture at room temperature. After complete consumption of substrate was observed, water was added. The aqueous layer was extracted with ethyl acetate three times. The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product **5**.

2,2-Dimethyl-1-phenyl-4-[(*Z*)-1-phenylpropylidene]cyclobutan-1-ol (5aa)



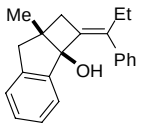
IR (neat): 3580, 2964, 1599, 1493, 1447, 1071 cm^{-1}; ^1H NMR: δ = 0.59 (s, 3H), 1.04 (t, *J* = 7.5 Hz, 3H), 1.23 (s, 3H), 1.85 (s, 1H), 2.31–2.55 (m, 4H), 7.06–7.17 (m, 5H), 7.22–7.29 (m, 1H), 7.30–7.38 (m, 2H), 7.40–7.46 (m, 2H); ^{13}C NMR: δ = 13.4, 24.1, 25.4, 26.4, 39.4, 41.5, 83.7, 126.6, 126.7, 127.6, 127.9, 128.1, 137.1, 139.2, 139.9, 144.7; HRMS (EI): *m/z* calcd for $C_{21}H_{24}O$: 292.1827 $[M]^+$; found 292.1833.

(1*R,6*S**)-1-Hydroxy-6-methyl-8-[(*Z*)-1-phenylethyliedene]bicyclo[4.2.0]octane (5ba)**



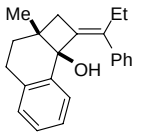
IR (nujol): 3561, 3474, 2926, 1069 cm^{-1}; ^1H NMR: δ = 1.04 (s, 3H), 1.20–1.66 (m, 7H), 1.81–1.88 (m, 2H), 1.91 (br s, 3H), 2.07 (d, *J* = 14.1 Hz, 1H), 2.40 (d, *J* = 14.4 Hz, 1H), 7.18–7.25 (m, 1H), 7.26–7.36 (m, 4H); ^{13}C NMR: δ = 19.3, 21.0, 21.7, 23.4, 33.0, 35.5, 36.3, 39.1, 77.7, 126.6, 127.5, 127.8, 127.9, 141.5, 142.0; HRMS (EI): *m/z* calcd for $C_{17}H_{22}O$: 242.1671 $[M]^+$; found 242.1670.

(2a*R,7a*S**)-7a-Methyl-2-[(*Z*)-1-phenylpropylidene]-1,2,7,7a-tetrahydrocyclobuta[*a*]inden-2a-ol (5ca)**



IR (nujol): 3467, 2961, 1601, 1456, 1144, 1069 cm^{-1}; ^1H NMR: δ = 0.86 (t, *J* = 7.5 Hz, 3H), 1.31 (s, 3H), 2.02 (s, 1H), 2.14–2.24 (m, 3H), 2.48 (d, *J* = 15.3 Hz, 1H), 2.92 (d, *J* = 16.5 Hz, 1H), 2.99 (d, *J* = 16.5 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 7.10–7.25 (m, 3H), 7.30–7.46 (m, 5H); ^{13}C NMR: δ = 12.6, 19.3, 27.3, 38.1, 45.0, 45.3, 89.0, 125.2, 125.3, 126.9, 127.0, 128.0, 128.2, 128.7, 136.5, 139.0, 140.5, 142.8, 145.5; HRMS (EI): *m/z* calcd for $C_{21}H_{22}O$: 290.1671 $[M]^+$; found 290.1670.

(2a*S,8b*R**)-2a-Methyl-1-[(*Z*)-1-phenylpropylidene]-2,2a,3,4-tetrahydro-*1H*-cyclobuta[*a*]-naphthalen-8b-ol (5da)**



IR (neat): 3443, 2963, 1601, 1456, 1175, 1107 cm^{-1}; ^1H NMR: δ = 0.84 (t, *J* = 7.7 Hz, 3H), 1.30 (s, 3H), 1.36 (td, *J* = 13.3, 4.6 Hz, 1H), 1.80 (ddd, *J* = 13.2, 4.4, 2.9 Hz, 1H), 2.02–2.26 (m, 3H), 2.43 (d, *J* = 15.6 Hz, 1H), 2.54 (d, *J* = 15.6 Hz, 1H), 2.70 (ddd, *J* = 15.6, 4.5, 2.7 Hz, 1H), 2.82 (ddd, *J* = 15.5, 13.1, 4.4 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.77–6.86 (m, 1H), 6.90–6.98 (m, 2H), 6.98–7.03 (m, 2H), 7.15–7.22 (m, 3H); ^{13}C NMR: δ = 12.4, 23.4, 27.4, 27.5, 32.1, 35.0, 40.7, 77.8, 125.5, 125.9, 126.4, 126.5, 127.2, 127.5, 128.7, 137.0, 138.6, 139.1, 139.7, 139.8; HRMS (EI): *m/z* calcd for $C_{22}H_{24}O$: 304.1827 $[M]^+$; found 304.1828.

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Chapter 4

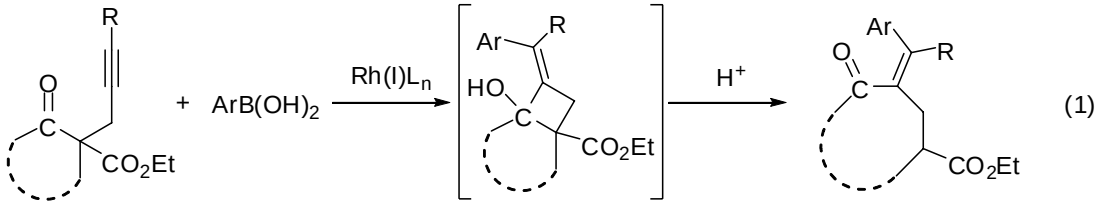
Acyl 1,3-Migration in Rhodium-Catalyzed Reactions of Acetylenic β-Ketoesters with Arylboronic Acids

Abstract

An intermediate organorhodium(I) formed in the rhodium(I)-catalyzed reaction of acetylenic β-ketoesters with arylboronic acids underwent intramolecular nucleophilic addition to the ketonic carbonyl group in a 4-*exo*-trig mode. The ensuing ring-opening reaction of the resultant cyclobutanols accomplished 1,3-acyl migration, which led to the development of a novel two-carbon ring-expansion reaction.

Introduction

Cyclization/ring-opening sequence is a useful strategy for the synthesis of various organic molecules. Four-membered carbocycles, in particular, are quite attractive as an intermediate in such process because the ring-opening step is facilitated by the release of ring strain. A photochemical [2+2] cycloaddition is frequently used in construction of the requisite cyclobutane skeleton and a lot of successful applications to natural product synthesis have been reported.[1] On the other hand, it is an alternative approach to generate cyclobutanol deravatives by way of intramolecular carbonyl addition.[2] In the previous chapter, the author showed the rhodium(I)-catalyzed reaction of 4-alkyn-1-ones with arylboronic acids, which proceeded at room temperature to form cyclobutanol derivatives via 4-*exo*-trig cyclization despite accompanying the development of ring strain.[3] Thus, he envisioned that an equivalent cyclization of β-ketoesters possessing an alkynyl chain at the α-position would be feasible, if rhodium(I)-catalyzed addition reaction[4] was employed. The putative cyclobutanols derivatives had a suitable framework for the ring-opening process through retro-aldol reaction [Eq. (1)].

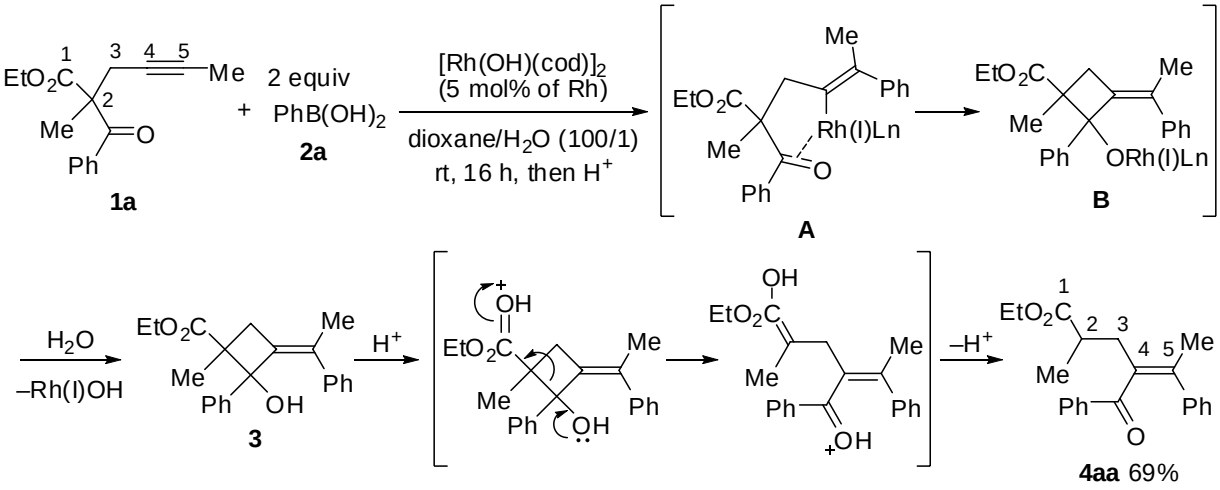


(1)

Described in this chapter is that a new acyl 1,3-migration reaction is initiated by rhodium(I)-catalyzed addition reaction.

Results and discussions

The desired 4-alkyn-1-one substructure was incorporated into the model substrate **1a**, which was readily synthesized by the alkylation reaction of a β-ketoester with 1-bromobut-2-yne. The 4-alkyn-1-one **1a** was treated with phenylboronic acid (**2a**, 2.0 equiv) in the presence of $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (100/1) at room temperature under an argon atmosphere. The substrate **1a** was consumed in 16 h, and subsequent chromatographic isolation on silica gel afforded not the cyclobutanol derivative **3**, but rather α,β-unsaturated ketone **4aa** in 69% yield (Scheme 1).



Scheme 1. Rhodium(I)-catalyzed reaction of **1a** with phenylboronic acid

The following mechanism explains the production of **4aa**. A phenylrhodium(I) species is initially generated by transmetalation of hydroxorhodium(I) with **2a**, which then undergoes *cis* 1,2-addition onto the carbon–carbon triple bond[5] in a regioselective manner directed by the carbonyl group.[6] The author proposes that the resulting alkenylrhodium(I) intermediate **A** undergoes intramolecular nucleophilic addition to the benzoyl group[7] in a 4-*exo* mode despite the development of ring strain. As a result, the four-membered ring carbocycle **B** is furnished in a form of a rhodium(I) alkoxide. Hydrolysis produces the cyclobutanol **3** with regeneration of the catalytically active hydroxorhodium(I). Cleavage of the cyclobutane ring through a retro-aldol reaction is promoted by the acidic nature of silica gel during purification,[8] to afford acyl 1,3-migration product **4aa**. During the transformation of **1a** to **4aa**, a phenyl group was introduced on the 5-carbon of **1a** and the resulting alkenylrhodium intermediate facilitated migration of the benzoyl group from the 2-carbon onto the 4-carbon.[9] This acyl 1,3-migration reaction was generally applicable to a variety of combinations of acetylenic β-keto esters **1** and arylboronic acids **2** (Table 1). Both electron-rich and -deficient arylboronic acids were suitably reactive (entries 1–4). *o*-Tolylboronic acid, however, failed in the acyl 1,3-migration reaction probably due to steric reasons.[10] Methyl ketone **1c** also underwent acetyl 1,3-migration (entry 6). The reaction of trimethylsilyl substituted alkyne **1d** suffered from lower regioselectivity of the initial 1,2-addition to give the product **3ad** in only 25% yield (entry 7).[11] Acetylenic β-keto ester **1e** without an α-substituent failed to undergo the cyclization reaction, probably because of the presence of a stable enol tautomer.

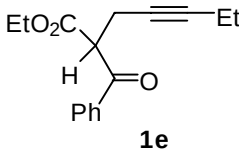
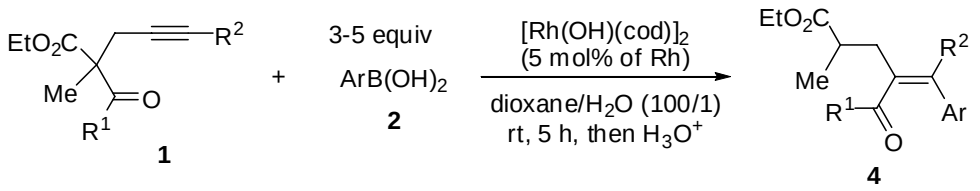


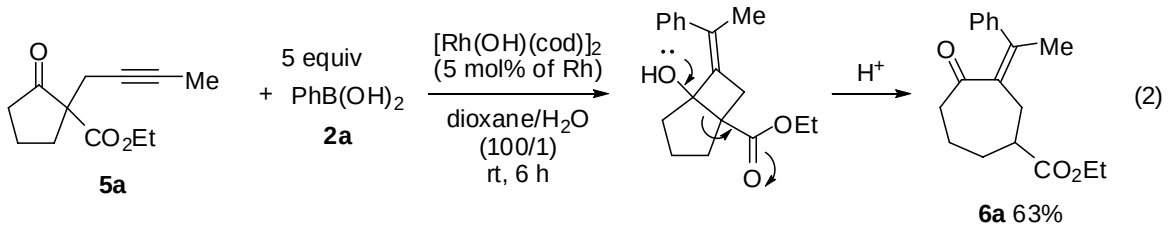
Table 1. Rhodium(I)-catalyzed acyl 1,3-migration in the reaction of **1** with **2**. [a]



entry	**1**	R^1	R^2	**2**	Ar	**4**	yield (%) [b]
1	**1a**	Ph	Me	**2b**	4-F-C_6H_4	**4ab**	63
2	**1a**	Ph	Me	**2c**	4-Me-C_6H_4	**4ac**	75
3	**1a**	Ph	Me	**2d**	3-Cl-C_6H_4	**4ad**	66
4	**1a**	Ph	Me	**2e**	3-MeO-C_6H_4	**4ae**	77
5	**1b**	Ph	Et	**2a**	Ph	**4ba**	92
6	**1c**	Me	Et	**2a**	Ph	**4ca**	67
7	**1d**	Ph	TMS	**2a**	Ph	**4da**	25

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.6-1.0 mmol), $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (2.0 mL/20 μL); then treatment with aqueous NH_4Cl.
[b] Yields of isolated products.

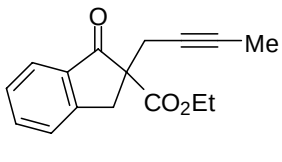
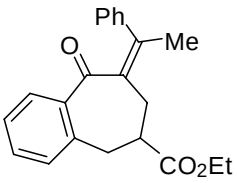
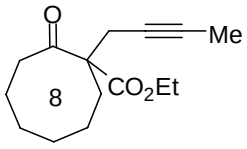
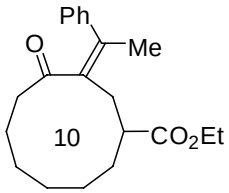
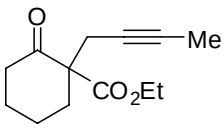
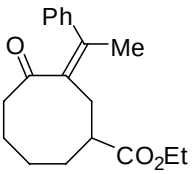
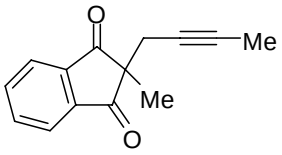
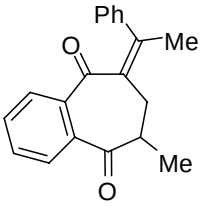
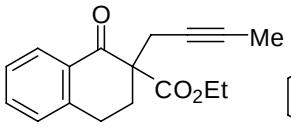
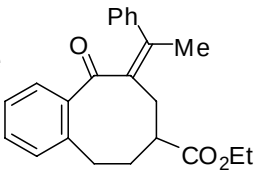
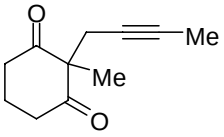
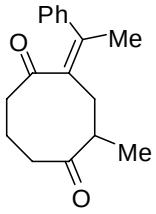
Next, the author envisioned that, if a β-keto ester moiety was installed in a cyclic skeleton, an analogous acyl 1,3-migration process would expand the ring by two carbons to serve as a synthetic method of medium-sized ring carbocyclic skeletons. Thus, he prepared the cyclopentanone substrate **5a** by the reaction of 2-(ethoxycarbonyl)cyclopentanone with 1-bromobut-2-yne. The cyclic substrate **5a** was reacted with **2a** in the presence of $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (100/1) at room temperature for 6 h under an argon atmosphere, and the resulting reaction mixture was successively treated with aq. NH_4Cl for 24 h to promote the retro-aldol process. As expected, the cycloheptanone **6a** was produced in 63% yield through phenyl addition and ring expansion [Eq. (2)].



(2)

As listed in Table 2, the catalytic ring-expansion process worked well with substrates of five-, six-, and eight-membered ring structures to give the corresponding seven, eight, and ten-membered ring products in yields ranging from 49% to 66%.[12] Cyclic 1,3-diketones **5f** and **5g** also underwent analogous ring-expansion reaction. The ring-opening of intermediate cyclobutanols formed from substrates **5c**, **5d**, and **5f** under the weakly acidic conditions proceeded more slowly than that of **5a**, and thus required longer time for completion.

Table 2. Rhodium(I)-catalyzed two-carbon-atom ring expansion of **5** with **2a**. [a]

entry	substrate **5**	product **6** / yield(%) [b]	entry	substrate **5**	product **6** / yield(%) [b]
1	 **5b**	 **6b** / 51	4	 **5e**	 **6e** / 54 [c]
2	 **5c**	 **6c** / 49	5	 **5f**	 **6f** / 57
3	 **5d**	 **6d** / 58	6	 **5g**	 **6g** / 66

[a] Reacttion condition: **5** (0.2 mmol), **2a** (1.0 mmol), $[Rh(OH)(cod)]_2$ (5 mol% of Rh) in dioxane/H_2O (2.0 mL /20 μL), room temperature; then treatment with aqueous NH_4Cl. [b] Yields of isolated products. [c] 100 °C.

Conclusion

A new rhodium(I)-catalyzed acyl 1,3-migration reaction of acetylenic β-keto esters has been developed, in which an intermediate organorhodium(I) species undergoes intramolecular nucleophilic addition to a ketonic carbonyl group in a 4-*exo* mode, and then the cyclobutane cleavage through a retro-aldol reaction follows. On the basis of this new 1,3-migration reaction, carbocyclic compounds of medium-sized rings that were otherwise difficult to form were constructed in a simple operation from readily available substrates.

Experimental Section

General

All rhodium(I)-catalyzed reactions were carried out with standard Schlenk technique under an argon atmosphere. Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300.07 Hz and ^{13}C at 75.46 Hz) spectrometer. NMR data were obtained in $CDCl_3$ otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm. Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.00 ppm. High resolution mass spectra were recorded on a JOEL JMS-SX102A spectrometer. IR spectra were recorded on a Shimadzu FTIR-8100 spectrometer.

Materials

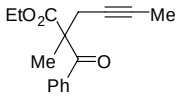
Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $[Rh(OH)(cod)]_2$ was prepared according to the reported procedure.[13] 1,4-Dioxane was distilled over sodium-benzophenone ketyl prior to use.

Starting Materials:

Acyclic acetylenic β-ketoesters **1a**-**d** were prepared by alkylation of α-methyl-β-ketoesters with the corresponding propargyl bromide (NaH, in THF). Cyclic derivatives **5a**-**e**, 1,3-diketones **5f**, **5g** were also synthesized by analogous methods from the β-ketoesters and 2-methyl-1,3-diketones, respectively. In case of **5b**, **5d** and **5e**, the commercially available cycloalkanones were

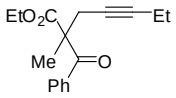
transformed into the requisite β-ketoesters by the reaction with diethyl carbonate in the presence of NaH in a toluene solution. 2-Methylindan-1,3-dione was prepared from dimethyl phthalate and pentan-3-one according to the literature.[14]

Ethyl 2-benzoyl-2-methylhex-4-ynoate (1a)



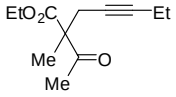
IR (neat): 2984, 1738, 1686, 1449, 1244, 1100 cm^{-1}; ^1H NMR: δ = 1.09 (t, *J* = 7.2 Hz, 3H), 1.64 (s, 3H), 1.74 (t, *J* = 2.6 Hz, 3H), 2.77–2.93 (m, 2H), 4.06–4.23 (m, 2H), 7.36–7.46 (m, 2H), 7.48–7.56 (m, 1H), 7.79–7.86 (m, 2H); ^{13}C NMR: δ = 3.5, 13.8, 21.1, 27.3, 57.0, 61.6, 73.7, 79.2, 128.4, 132.7, 135.4, 172.9, 196.5; HRMS (CI): *m/z* calcd for $C_{16}H_{19}O_3$: 259.1334 $[M+H]^+$; found 259.1335.

Ethyl 2-benzoyl-2-methylhept-4-ynoate (1b)



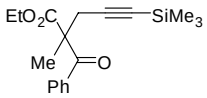
IR (neat): 2979, 1738, 1683, 1449, 1244, 1100 cm^{-1}; ^1H NMR: δ = 1.07 (t, *J* = 7.5 Hz, 3H), 1.10 (t, *J* = 7.2 Hz, 3H), 1.64 (s, 3H), 2.12 (qt, *J* = 7.4, 2.4 Hz, 2H), 2.79–2.94 (m, 2H), 4.06–4.23 (m, 2H), 7.37–7.46 (m, 2H), 7.48–7.56 (m, 1H), 7.79–7.87 (m, 2H); ^{13}C NMR: δ = 12.3, 13.8, 14.1, 21.0, 27.2, 57.0, 61.5, 73.9, 85.3, 128.4, 132.7, 135.4, 172.8, 196.4; HRMS (CI): *m/z* calcd for $C_{17}H_{21}O_3$: 273.1491 $[M+H]^+$; found 273.1490.

Ethyl 2-acetyl-2-methylhept-4-ynoate (1c)



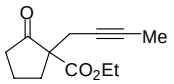
IR (neat): 2983, 1742, 1717, 1237, 1192, 1107 cm^{-1}; ^1H NMR: δ = 1.08 (t, *J* = 7.5 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.45 (s, 3H), 2.12 (qt, *J* = 7.5, 2.4 Hz, 2H), 2.18 (s, 3H), 2.61–2.76 (m, 2H), 4.12–4.29 (m, 2H); ^{13}C NMR: δ = 12.3, 14.0, 14.1, 19.1, 25.3, 26.1, 59.2, 61.5, 74.1, 84.9, 171.7, 204.1; HRMS (CI): *m/z* calcd for $C_{12}H_{19}O_3$: 211.1334 $[M+H]^+$; found 211.1337.

Ethyl 2-benzoyl-2-methyl-5-trimethylsilylpent-4-ynoate (1d)



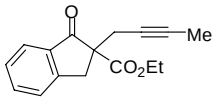
IR (neat): 2960, 1740, 1686, 1250, 1194, 1100 cm^{-1}; ^{1}H NMR: δ = 0.12 (s, 9H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.66 (s, 3H), 2.88 (d, *J* = 17.4 Hz, 1H), 2.96 (d, *J* = 17.1 Hz, 1H), 4.06–4.25 (m, 2H), 7.37–7.45 (m, 2H), 7.49–7.56 (m, 1H), 7.79–7.86 (m, 2H); ^{13}C NMR: δ = 0.0, 13.9, 21.1, 28.3, 57.0, 61.7, 88.5, 101.7, 128.4, 132.7, 135.4, 172.4, 196.2; HRMS (CI): *m/z* calcd for $C_{18}H_{25}O_3Si$: 317.1573 $[M+H]^+$; found 317.1573.

Ethyl 1-(but-2-ynyl)-2-oxocyclopentane-1-carboxylate (5a)



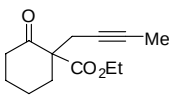
IR (neat): 2980, 1751, 1727, 1229, 1157 cm^{-1}; ^{1}H NMR: δ = 1.24 (t, *J* = 7.1 Hz, 3H), 1.74 (t, *J* = 2.3 Hz, 3H), 1.94–2.13 (m, 2H), 2.19–2.35 (m, 2H), 2.39–2.53 (m, 2H), 2.65 (q, *J* = 2.6 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR: δ = 3.5, 14.1, 19.8, 23.6, 32.6, 38.4, 59.1, 61.6, 74.4, 78.0, 170.6, 214.2; HRMS (CI): calcd for $C_{12}H_{17}O_3$: 209.1178 $[M+H]^+$; found 209.1175.

Ethyl 2-(but-2-ynyl)-1-oxoindane-2-carboxylate (5b)



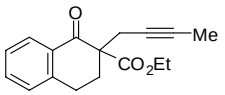
IR (nujol): 1730, 1705, 1605, 1285, 1254, 1188 cm^{-1}; ^{1}H NMR: δ = 1.19 (t, *J* = 7.1 Hz, 3H), 1.56 (t, *J* = 2.6 Hz, 3H), 2.77 (dq, *J* = 16.5, 2.5 Hz, 1H), 2.93 (dq, *J* = 16.6, 2.5 Hz, 1H), 3.36 (d, *J* = 17.4 Hz, 1H), 3.68 (d, *J* = 17.4 Hz, 1H), 4.07–4.23 (m, 2H), 7.35–7.43 (m, 1H), 7.48–7.53 (m, 1H), 7.56–7.67 (m, 1H), 7.77 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR: δ = 3.3, 14.0, 24.5, 36.8, 59.6, 61.8, 73.9, 77.9, 124.7, 126.2, 127.6, 135.2, 135.3, 153.5, 170.2, 201.5; HRMS (CI): *m/z* calcd for $C_{16}H_{17}O_3$: 257.1178 $[M+H]^+$; found 257.1180.

Ethyl 1-(but-2-ynyl)-2-oxocyclohexane-1-carboxylate (5c)



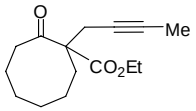
IR (neat): 2945, 1717, 1443, 1192, 1092, 1022 cm^{-1}; ^{1}H NMR: δ = 1.26 (t, *J* = 7.2 Hz, 3H), 1.52–1.85 (m, 4H), 1.75 (t, *J* = 2.7 Hz, 3H), 1.95–2.09 (m, 1H), 2.35–2.53 (m, 3H), 2.60–2.75 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR: δ = 3.6, 14.1, 22.4, 25.1, 27.4, 35.4, 40.9, 60.3, 61.5, 74.0, 78.7, 170.6, 206.4; HRMS (EI): *m/z* calcd for $C_{13}H_{18}O_3$: 222.1256 $[M]^+$; found 222.1257.

Ethyl 2-(but-2-ynyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (5d)



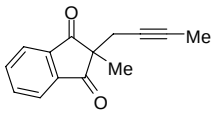
IR (neat): 2980, 1732, 1690, 1601, 1455, 1238 cm^{-1}; ^{1}H NMR: δ = 1.16 (t, *J* = 7.2 Hz, 3H), 1.73 (t, *J* = 2.6 Hz, 3H), 2.43 (ddd, *J* = 13.7, 10.7, 4.9 Hz, 1H), 2.62 (dt, *J* = 13.7, 4.8 Hz, 1H), 2.84 (q, *J* = 2.5 Hz, 2H), 2.96 (dt, *J* = 17.4, 5.0 Hz, 1H), 3.15 (ddd, *J* = 17.4, 10.8, 4.8 Hz, 1H), 4.15 (q, *J* = 7.0 Hz, 2H), 7.19–7.26 (m, 1H), 7.27–7.35 (m 1H), 7.48 (td, *J* = 7.5, 1.5 Hz, 1H), 8.05 (dd, *J* = 8.0, 1.4 Hz, 1H); ^{13}C NMR: δ = 3.6, 14.0, 24.6, 25.9, 30.6, 57.0, 61.5, 74.2, 78.6, 126.7, 128.1, 128.7, 131.8, 133.5, 143.3, 170.9, 194.1; HRMS (EI): *m/z* calcd for $C_{17}H_{18}O_3$: 270.1256 $[M]^+$; found 270.1255.

Ethyl 1-(but-2-ynyl)-2-oxocyclooctane-1-carboxylate (5e)



IR (neat): 2930, 1736, 1707, 1466, 1204 cm^{-1}; ^{1}H NMR: δ = 0.82–0.99 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.27–1.93 (m, 7H), 1.75 (t, *J* = 2.7 Hz, 3H), 2.16–2.29 (m, 2H), 2.42 (dq, *J* = 17.2, 2.5 Hz, 1H), 2.49–2.63 (m, 1H), 2.78 (td, *J* = 12.0, 3.7 Hz, 1H), 2.92–3.03 (m, 1H), 4.12–4.24 (m, 2H); ^{13}C NMR: δ = 3.5, 14.0, .21.3, 23.1, 24.3, 25.5, 27.8, 29.3, 38.3, 61.5, 62.5, 74.4, 78.2, 170.4, 211.1; HRMS (EI): *m/z* calcd for $C_{15}H_{22}O_3$: 250.1569 $[M]^+$; found 250.1569.

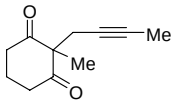
2-(But-2-ynyl)-2-methylindane-1,3-dione (5f)



IR (nujol): 1744, 1713, 1597, 1455, 1264, 1184 cm^{-1}; ^{1}H NMR: δ = 1.26 (s, 3H), 1.41 (t, *J* = 2.4 Hz, 3H), 2.60 (q, *J* = 2.5 Hz, 2H), 7.82–7.89 (m, 2H), 7.96–8.04 (m, 2H); ^{13}C NMR: δ = 3.1, 18.7, 24.8, 53.3, 73.5, 79.0, 123.3, 135.7, 141.5, 203.1; HRMS (EI): *m/z* calcd for $C_{14}H_{12}O_2$: 212.0837 $[M]^+$;

found 212.0842.

2-(But-2-ynyl)-2-methyl-cyclohexane-1,3-dione (5g)

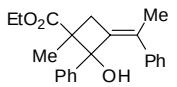


IR (nujol): 1725, 1700, 1325, 1208, 1100, 1028 cm^{-1}; ^{1}H NMR: δ = 1.26 (s, 3H), 1.69–1.73 (m, 3H), 1.87–2.08 (m, 2H), 2.55–2.60 (m, 2H), 2.65–2.73 (m, 4H); ^{13}C NMR: δ = 3.4, 17.2, 21.3, 26.0, 38.3, 64.1, 74.6, 78.3, 209.4; HRMS (EI) *m/z* calcd for $C_{11}H_{14}O_2$: 178.0994 $[M]^+$; found 178.0990.

General procedure for the rhodium-catalyzed acyl 1,3-migration reaction:

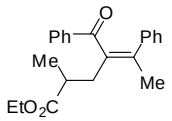
To an oven-dried, Ar-purged flask was added $[Rh(OH)(cod)]_2$ (2.28 mg, 5 μmol, 5 mol% of Rh), arylboronic acid **2** (2.0–5.0 equiv), and 1,4-dioxane (1 mL). A solution of substrate **1** or **5** (0.20 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL) and H_2O (20 μL) was added to the reaction mixture at room temperature. After complete consumption of the substrate was observed, the reaction was quenched with aq. NH_4Cl. Then, the resulting solution was stirred at room temperature overnight. The aqueous layer was extracted with ethyl acetate three times. The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product **4** or **6**. The ring-opening of **5c**, **5d**, and **5f** required 3 weeks for completion.

Ethyl 2-hydroxy-1-methyl-2-phenyl-3-[(*Z*)-1-phenylethylidene]cyclobutane-1-carboxylate (3) (This compound is unstable. Only ^{1}H NMR data are shown here.)

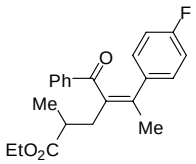


^{1}H NMR: δ = 0.89 (t, *J* = 7.1 Hz, 3H), 1.48 (s, 3H), 2.09 (br s, 3H), 2.19 (s, 1H), 2.42 (dq, *J* = 15.8, 1.1 Hz, 1H), 3.36 (dq, *J* = 15.6, 1.5 Hz, 1H), 3.49–3.70 (m, 2H), 7.12–7.63 (m, 10H).

Ethyl (*Z*)-4-benzoyl-2-methyl-5-phenylhex-4-enoate (4aa)



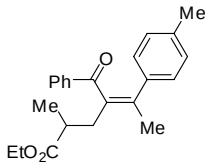
IR (neat): 2980, 1732, 1651, 1449, 1246, 1183 cm^{-1}; ^1H NMR: δ = 1.21 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 2.26 (s, 3H), 2.59–2.77 (m, 2H), 2.92–3.05 (m, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 6.91–7.06 (m, 5H), 7.10–7.18 (m, 2H), 7.22–7.29 (m, 1H), 7.57–7.63 (m, 2H); ^{13}C NMR: δ = 14.2, 17.7, 20.9, 35.6, 38.9, 60.4, 127.3, 127.7, 127.8, 128.2, 129.2, 132.1, 135.2, 137.5, 141.3, 142.6, 176.1, 200.6; HRMS (CI): *m/z* calcd for $C_{22}H_{25}O_3$: 337.1804 $[M+H]^+$; found 337.1804.



Ethyl (*Z*)-4-benzoyl-2-methyl-5-(4-fluorophenyl)hex-4-enoate (4ab)

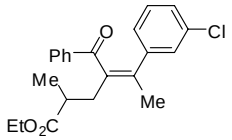
IR (neat): 2980, 1732, 1651, 1509, 1227, 1183 cm^{-1}; ^1H NMR: δ = 1.20 (t, *J* = 7.2 Hz, 3H), 1.24 (d, *J* = 6.6 Hz, 3H), 2.23 (s, 3H), 2.57–2.75 (m, 2H), 2.90–3.03 (m, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 6.65–6,74 (m, 2H), 6.95–7.03 (m, 2H), 7.13–7.21 (m, 2H), 7.26–7.34 (m, 1H), 7.56–7.62 (m, 2H); ^{13}C NMR: δ = 14.1, 17.7, 20.9, 35.5, 38.8, 60.4, 114.7 (d, *J* = 20.9 Hz), 127.8, 129.1, 129.9 (d, *J* = 8.1 Hz), 132.3, 135.6, 137.2, 138.5 (d, *J* = 3.5 Hz), 140.0, 161.7 (d, *J* = 247.1 Hz), 176.0, 200.5; HRMS (CI): *m/z* calcd for $C_{22}H_{24}FO_3$: 355.1709 $[M+H]^+$; found 355.1708.

Ethyl (*Z*)-4-benzoyl-2-methyl-5-(4-methylphenyl)hex-4-enoate (4ac)



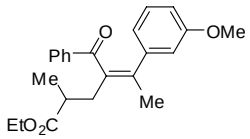
IR (neat): 2980, 1732, 1653, 1449, 1248, 1183 cm^{-1}; ^1H NMR: δ = 1.20 (t, *J* = 7.1 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3H), 2.12 (s, 3H), 2.23 (s, 3H), 2.57–2.75 (m, 2H), 2.91–3.03 (m, 1H), 4.05 (q, *J* = 7.0 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 6.88–6.96 (m, 2H), 7.12–7.20 (m, 2H) 7.23–7.32 (m, 1H), 7.58–7.64 (m, 2H); ^{13}C NMR: δ = 14.1, 17.6, 20.9, 21.0, 35.6, 38.8, 60.4, 127.6, 128.1, 128.5, 129.2, 132.0, 134.7, 137.0, 137.4, 139.6, 141.3, 176.1, 200.8; HRMS (CI): *m/z* calcd for $C_{23}H_{27}O_3$: 351.1960 $[M+H]^+$; found 351.1959.

Ethyl (*Z*)-4-benzoyl-2-methyl-5-(3-chlorophenyl)hex-4-enoate (4ad)



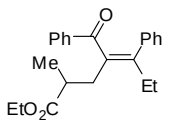
IR (neat): 2980, 1732, 1653, 1449, 1242, 1183 cm^{-1}; ^1H NMR: δ = 1.18–1.27 (m, 6H), 2.23 (s, 3H), 2.58–2.76 (m, 2H), 2.92–3.03 (m, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 6.86–6.94 (m, 3H), 6.99–7.03 (m, 1H), 7.14–7.22 (m, 2H), 7.25–7.34 (m, 1H), 7.54–7.62 (m, 2H); ^{13}C NMR: δ = 14.1, 17.7, 20.7, 35.5, 38.7, 60.5, 126.4, 127.3, 127.8, 128.2, 129.0, 129.1, 132.3, 133.6, 136.3, 137.2, 139.7, 144.2, 175.9, 200.2; HRMS (CI): *m/z* calcd for $C_{22}H_{24}ClO_3$: 371.1414 $[M+H]^+$; found 371.1412.

Ethyl (*Z*)-4-benzoyl-2-methyl-5-(3-methoxyphenyl)hex-4-enoate (4ae)



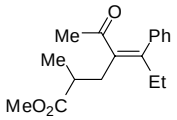
IR (neat): 2980, 1730, 1656, 1578, 1221, 1179 cm^{-1}; ^1H NMR: δ = 1.21 (t, *J* = 7.2 Hz, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 2.24 (s, 3H), 2.58–2.71 (m, 2H), 2.92–3.03 (m, 1H), 3.63 (s, 3H), 4.06 (q, *J* = 7.1 Hz, 2H), 6.50 (ddd, *J* = 8.2, 2.8, 1.0 Hz, 1H), 6.54–6.58 (m, 1H), 6.63 (ddd, *J* = 7.8, 1.5, 0.9 Hz, 1H), 6.92 (t, *J* = 7.8 Hz, 1H), 7.13–7.21 (m, 2H), 7.24–7.32 (m, 1H), 7.58–7.64 (m, 2H); ^{13}C NMR: δ = 14.1, 17.6, 20.7, 35.5, 38.8, 55.1, 60.4, 113.2, 113.6, 120.8, 127.6, 128.9, 129.0, 132.1, 135.2, 137.3, 141.0, 143.8, 158.8, 176.0, 200.6; HRMS (CI): *m/z* calcd for $C_{23}H_{27}O_4$: 367.1909 $[M+H]^+$; found 367.1910.

Ethyl (*Z*)-4-benzoyl-2-methyl-5-phenylhept-4-enoate (4ba)



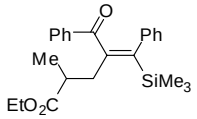
IR (neat): 2977, 1732, 1651, 1449, 1238, 1183 cm^{-1}; ^1H NMR: δ = 0.94 (t, *J* = 7.5 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 2.49–2.66 (m, 2H), 2.67–2.82 (m, 2H), 3.00 (dd, *J* = 14.1, 7.8 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 6.90–7.04 (m, 5H), 7.10–7.19 (m, 2H), 7.21–7.30 (m, 1H), 7.56–7.63 (m, 2H); ^{13}C NMR: δ = 12.7, 14.1, 17.7, 27.2, 34.7, 38.8, 60.4, 127.2, 127.6, 127.7, 128.9, 129.1, 132.0, 134.5, 137.6, 140.8, 147.3, 176.0, 200.6; HRMS (CI): *m/z* calcd for $C_{23}H_{27}O_3$: 351.1960 $[M+H]^+$; found 351.1959.

Ethyl (*Z*)-4-acetyl-2-methyl-5-phenylhept-4-enoate (4ca)



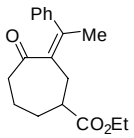
IR (neat): 2979, 1732, 1676, 1352, 1177, 1121 cm^{-1}; ^1H NMR: δ = 0.87 (t, *J* = 7.7 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.58 (s, 3H), 2.36–2.69 (m, 4H), 2.78 (dd, *J* = 13.7, 8.6 Hz, 1H), 4.08–4.19 (m, 2H), 7.09–7.15 (m, 2H), 7.28–7.34 (m, 3H); ^{13}C NMR: δ = 12.5, 14.3, 17.2, 27.9, 31.3, 34.2, 38.8, 60.4, 128.0, 128.4, 128.5, 138.0, 141.4, 148.0, 176.0, 207.3; HRMS (EI): *m/z* calcd for $C_{18}H_{24}O_3$: 288.1725 $[M]^+$; found 288.1723.

Ethyl (*E*)-4-benzoyl-2-methyl-5-phenyl-5-trimethylsilylpent-4-enoate (4da)



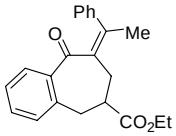
IR (neat): 2980, 1732, 1664, 1449, 1250, 1183 cm^{-1}; ^1H NMR: δ = 0.20 (s, 9H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.26 (d, *J* = 6.9 Hz, 3H), 2.49–2.63 (m, 1H), 2.79 (dd, *J* = 14.1, 7.5 Hz, 1H), 3.07 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.97–4.08 (m, 2H), 6.72–6.79 (m, 2H), 6.84–7.00 (m, 3H), 7.19–7.28 (m, 2H), 7.32–7.39 (m, 1H), 7.61–7.67 (m, 2H); ^{13}C NMR: δ = 0.7, 14.1, 17.7, 37.4, 38.3, 60.4, 125.6, 127.4, 127.9, 128.2, 129.1, 132.5, 136.6, 142.1, 145.6, 149.6, 175.7, 200.0; HRMS (CI): *m/z* calcd for $C_{24}H_{31}O_3Si$: 395.2042 $[M+H]^+$; found 395.2044.

Ethyl 4-oxo-3-[(*Z*)-1-phenylethylidene]cycloheptane-1-carboxylate (6a)



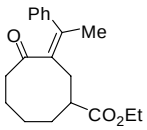
IR (nujol): 1725, 1648, 1289, 1161, 1102, 1028 cm^{-1}; ^1H NMR: δ = 1.29 (t, *J* = 7.1 Hz, 3H), 1.63–1.86 (m, 2H), 1.92–2.09 (m, 1H), 2.10 (s, 3H), 2.16–2.52 (m, 4H), 2.54–2.67 (m, 1H), 2.97 (d, *J* = 14.7 Hz, 1H), 4.18 (q, *J* = 6.9 Hz, 2H), 7.05–7.12 (m, 2H), 7.18–7.33 (m, 3H); ^{13}C NMR: δ = 14.2, 20.8, 22.5, 31.5, 32.6, 42.8, 45.3, 60.7, 126.97, 127.03, 128.1, 137.2, 140.0, 142.9, 174.8, 208.6; HRMS (EI): *m/z* calcd for $C_{18}H_{22}O_3$: 286.1569 $[M]^+$; found 286.1569.

Ethyl 9-oxo-8-[(*Z*)-1-phenylethylidene]-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-6-carboxylate (6b)



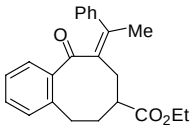
IR (nujol): 1732, 1663, 1595, 1186, 1159 cm^{-1}; ^1H NMR: δ = 1.30 (t, *J* = 7.2 Hz, 3H), 2.22 (s, 3H), 2.65 (dd, *J* = 14.7, 8.4 Hz, 1H), 2.95 (dd, *J* = 14.6, 7.4 Hz, 1H), 3.08–3.19 (m, 1H), 3.27–3.42 (m, 2H), 4.10–4.27 (m, 2H), 7.10–7.17 (m, 2H), 7.23–7.35 (m, 5H), 7.45 (td, *J* = 7.5, 1.5 Hz, 1H), 7.81 (dd, *J* = 7.8, 1.5 Hz, 1H); ^{13}C NMR: δ = 14.3, 22.5, 28.6, 33.9, 41.9, 60.9, 127.1, 127.4, 128.2, 129.7, 130.7, 132.7, 134.5, 137.4, 137.8, 143.7, 147.2, 173.8, 195.7; HRMS (EI): *m/z* calcd for $C_{22}H_{22}O_3$: 334.1569 $[M]^+$; found 334.1567.

Ethyl 4-oxo-3-[(*Z*)-1-phenylethylidene]cyclooctane-1-carboxylate (6c)



IR (neat): 2938, 1732, 1684, 1443, 1179, 1028 cm^{-1}; ^1H NMR: δ = 1.27 (t, *J* = 7.2 Hz, 3H), 1.35–1.89 (m, 7H), 1.92–2.06 (m, 1H), 2.15 (s, 3H), 2.34–2.48 (m, 1H), 2.53–2.67 (m, 1H), 2.93 (dd, *J* = 13.8, 3.3 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 7.11–7.19 (m, 2H), 7.21–7.33 (m, 3H); ^{13}C NMR: δ = 14.3, 19.9, 24.4, 27.2, 29.7, 35.1, 43.1, 43.3, 60.6, 127.6, 127.7, 128.4, 135.8, 137.6, 142.5, 175.5, 215.4; HRMS (EI): *m/z* calcd for $C_{19}H_{24}O_3$: 300.1725 $[M]^+$; found 300.1723.

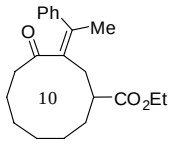
Ethyl 5,6,7,8,9,10-hexahydro-10-oxo-9-[(*Z*)-1-phenylethylidene]benzo[8]annulene-7-carboxylate (6d)



IR (neat): 2936, 1732, 1653, 1445, 1240, 1184 cm^{-1}; ^1H NMR: δ = 1.22 (t, *J* = 7.2 Hz, 3H), 2.00 (ddt, *J* = 13.7, 11.9, 4.6 Hz, 1H), 2.09–2.18 (m, 1H), 2.18–2.23 (m, 3H), 2.66 (tdd, *J* = 12.0, 4.1, 2.9 Hz, 1H), 2.80 (dd, *J* = 14.9, 12.2 Hz, 1H), 2.89–2.99 (m, 1H), 3.02 (dt, *J* = 14.4, 4.4 Hz, 1H), 3.65 (ddd, *J* = 14.3, 11.9, 4.0 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 6.96–7.05 (m, 2H), 7.08–7.23 (m, 5H),

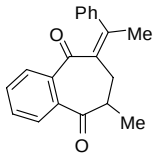
7.40 (td, *J* = 7.4, 1.5 Hz, 1H), 7.69 (dd, *J* = 7.7, 1.4 Hz, 1H); ^{13}C NMR: δ = 14.2, 21.0, 31.8, 32.0, 32.1, 40.8, 60.7, 126.8, 126.9, 127.2, 128.0, 129.3, 131.3, 133.1, 136.2, 138.0, 138.9, 140.9, 142.7, 175.0, 199.8; HRMS (EI): *m/z* Calcd for $C_{23}H_{24}O_3$: 348.1725 $[M]^+$; found 348.1725.

Ethyl 4-oxo-3-[(*Z*)-1-phenylethylidene]cyclodecane-1-carboxylate (6e)



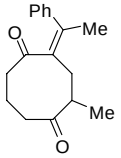
IR (neat): 2934, 1732, 1667, 1445, 1177, 1034 cm^{-1}; ^{1}H NMR: δ = 1.15–1.85 (m, 12H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.16 (s, 3H), 2.60–2.78 (m, 2H), 2.82–2.96 (m, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 7.11–7.20 (m, 2H), 7.26–7.35 (m, 3H); ^{13}C NMR: δ = 14.3, 21.7, 22.6, 24.5, 26.6, 30.1, 31,9, 42.4, 43.4, 60.5, 128.1, 128.4, 140.8 142.2, 143.2, 176.1, 212.6; HRMS (EI): *m/z* calcd for $C_{21}H_{28}O_3$: 328.2038 $[M]^+$; found 328.2039.

5,9-Dioxo-6-methyl-8-[(*Z*)-1-phenylethylidene]-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene (6f)



IR (neat) 2975, 1682, 1592, 1443, 1375, 1240 cm^{-1}; ^{1}H NMR: δ = 1.31 (d, *J* = 6.6 Hz, 3H), 2.11 (s, 3H), 2.48 (dd, *J* = 14.9, 11.6 Hz, 1H), 2.88 (ddq, *J* = 15.3, 5.4, 0.9 Hz, 1H), 3.15–3.30 (m, 1H), 6.91–6.98 (m, 2H), 7.17–7.25 (m, 3H), 7.51–7.66 (m, 3H), 7.68–7.72 (m, 1H); ^{13}C NMR: δ = 17.2, 21.5, 32.1, 45.8, 127.2, 128.1, 128.3, 128.4, 131.9, 132.3, 136.0, 137.8, 138.2, 142.4, 143.4, 197.0, 205.3; HRMS (EI): *m/z* calcd for $C_{20}H_{18}O_2$: 290.1307 $[M]^+$; found 290.1306.

2-Methyl-4-[(*Z*)-1-phenylethylidene]cyclooctane-1,5-dione (6g)



IR (nujol): 1700, 1671, 1306, 1125, 1073 cm^{-1}; ^{1}H NMR: δ = 1.12 (d, *J* = 6.3 Hz, 3H), 1.84–2.01 (m, 4H), 2.16 (s, 3H), 2.22–2.35 (m, 1H), 2.41–2.58 (m, 2H), 2.71 (dd, *J* = 13.4, 4.7 Hz, 1H), 2.93–3.07 (m, 1H), 7.12–7.19 (m, 2H), 7.25–7.33 (m, 3H); ^{13}C NMR: δ = 16.8, 19.8, 22.7, 38.4,

43.46, 43.51, 44.7, 127.7, 128.0, 128.5, 137.3, 138.1, 142.0, 213.0, 216.3; HRMS (EI): *m/z* calcd for $C_{17}H_{20}O_2$: 256.1463 $[M]^+$; found 256.1464.

References and notes

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2. For examples of intramolecular carbonyl addition/ring-opening: a) C.-J. Li, D.-L. Chen, Y.-Q. Lu, J. X. Haberman, J. T. Mague, *J. Am. Chem. Soc.* **1996**, *118*, 4216–4217; b) A. E. Imai, Y. Sato, M. Nishida, M. Mori, *J. Am. Chem. Soc.* **1999**, *121*, 1217–1225. For an intermolecular reaction using benzyne derevatives: c) U. K. Tambar, B. M. Stoltz, *J. Am. Chem. Soc.* **2005**, *127*, 5340–5341. A review: d) P. M. Wovkulich in *Comprehensive Organic Synthesis*, *Vol. 1* (Eds. B. M. Trost and I. Fleming), Pergamon, Oxford, **1991**, pp. 892–897.
3. a) J. E. Baldwin in *Comprehensive Organic Synthesis*, *Vol. 5* (Eds. B. M. Trost and I. Fleming), Pergamon, Oxford, **1991**, pp. 63–84; b) M. T. Crimmins in *Comprehensive Organic Synthesis*, *Vol. 5* (Eds. B. M. Trost and I. Fleming), Pergamon, Oxford, **1991**, pp. 123–150.
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5. For 1,2-addition of arylrhodium(I) onto an internal alkyne: a) T. Hayashi, K. Inoue, N. Taniguchi, M. Ogasawara, *J. Am. Chem. Soc.* **2001**, *123*, 9918–9919; b) M. Lautens, M. Yoshida, *Org. Lett.* **2002**, *4*, 123–125.
6. An analogous 1,2-addition reaction onto dimethyl 2-(but-2-ynyl)-2-methylmalonate possessing a methoxycarbonyl group in place of a benzoyl group in **1a** proceeded much more slowly: T. Miura, M. Shimada, M. Murakami, *J. Am. Chem. Soc.* **2005**, *127*, 1094–1095.
7. For intramolecular addition of an organorhodium(I) to a ketonic carbonyl group: a) A. Takezawa, K. Yamaguchi, T. Ohmura, Y. Yamamoto, N. Miyaura, *Synlett* **2002**, 1733–1735; b) D. F. Cauble, J. D. Gipson, M. J. Krische, *J. Am. Chem. Soc.* **2003**, *125*, 1110–1111; c) R. Shintani, K. Okamoto, Y. Otomaru, K. Ueyama, T. Hayashi, *J. Am. Chem. Soc.* **2005**, *127*, 54–55; d) T. Matsuda, M. Makino, M. Murakami, *Angew. Chem. Int. Ed.* **2005**, *44*, 4608–4611.

8. When the ^{1}H NMR spectra of the crude reaction mixture was measured prior to chromatographic purification, we observed ca. 50% of **3** and ca. 20% of **4aa**.
9. For examples of photochemical 1,3-acyl migration of β,γ-unsaturated cyclic ketones: a) H. Suginome, M. Takemura, N. Shimoyama, K. Orito, *J. Chem. Soc. Perkin Trans. 1*. **1991**, 2721–2723; b) J. Shin, W. Fenical, *J. Org. Chem.* **1991**, *56*, 1227–1233.
10. Although *o*-tolylboronic acid underwent 1,2-addition to the carbon–carbon triple bond, the resultant alkenylrhodium(I) intermediate was not reactive enough to add the benzoyl group.
11. A 1,2-adduct formed by addition of a phenylrhodium species with the opposite regiochemistry was obtained in 47%.
12. Other by-products included simple 1,2-adducts onto the carbon–carbon triple bond as the major one.
13. R. Uson, L. A. Oro, J. A. Cabeza, *Inorg. Synth.* **1985**, *23*, 126–130.
14. W. A. Mosher, R. W. Soeder, *J. Org. Chem.* **1971**, *36*, 1561–1563.

Chapter 5

Stereoselective Synthesis of α-Allenols by Rhodium-Catalyzed Reaction of Alkynyl Oxiranes with Arylboronic Acids

Abstract

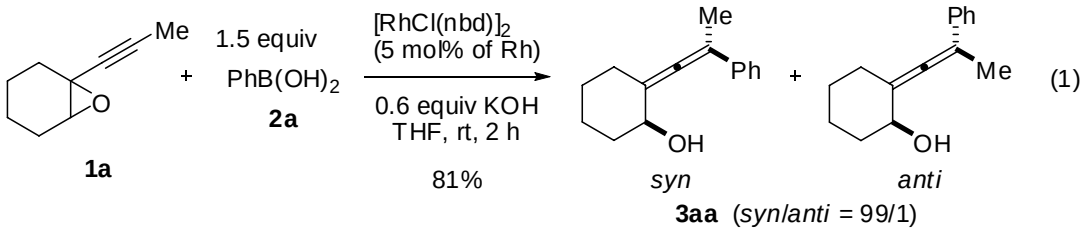
Alkynyl oxiranes were transformed into *syn*-configured α-allenols in good yields by the rhodium(I)-catalyzed reaction with arylboronic acids. An initial addition of arylboronic acids onto the alkyne moiety produced the alkenylrhodium(I) intermediate, which underwent stereoselective β-oxygen elimination in a *syn* fashion. Protonolysis of the resulting alkoxorhodium(I) afforded the product and a catalytically active rhodium(I) species.

Introduction

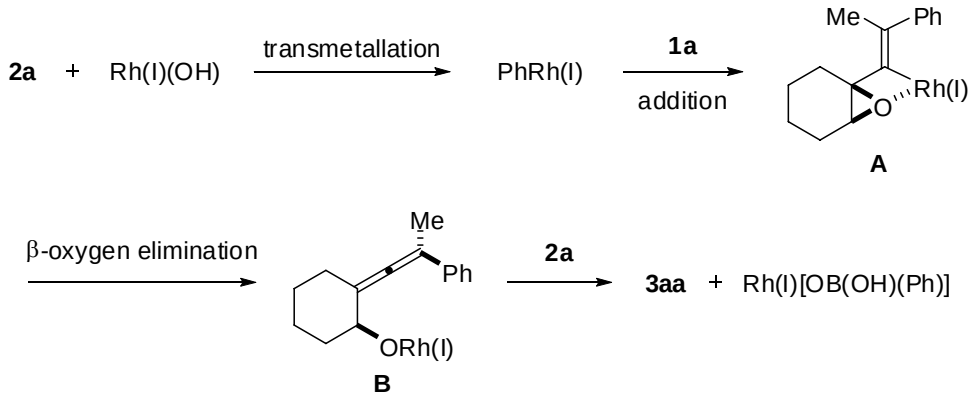
Allenes constitute an important class of building blocks possessing axial chirality as well as unique reactivities.[1] The S_N2'-type substitution of propargylic alcohol derivatives with organometallic reagents is one of the most reliable procedures for the stereoselective preparation of substituted allenes.[2] The author's laboratory previously reported the rhodium-catalyzed substitution reaction of propargylic acetates with phenylboronic acid, wherein the resulting alkenylrhodium(I) intermediate underwent β-oxygen elimination to afford a trisubstituted allene.[3] He conceived of the use of alkynyl oxiranes as acceptors for arylboronic acids in the rhodium(I)-catalyzed reaction, owing to the considerable interest in the resulting α-allenols as building blocks for the construction of oxygenated heterocycles of biological and pharmacological relevance.[4] It has known that the synthesis of α-allenols from alkynyl oxiranes and organometallic reagents was catalyzed or mediated by several transition metals. Organocopper and organocuprate reagents preferentially afford *anti*-configured α-allenols in most cases[5] with very few exceptions.[6] Palladium-catalyzed reactions with organostannanes[7] and organoborons[8] also give the corresponding *anti* substitution product. On the other hand, *syn*-configured α-allenols were selectively produced by the iron-catalyzed reaction of alkynyl oxiranes with Grignard reagents.[9] Chapter 5 describes the rhodium-catalyzed reaction of alkynyl oxiranes with arylboronic acids to yield α-allenols.

Results and discussions

Alkynyl oxirane **1a** was treated with phenylboronic acid (**2a**, 1.5 equiv) in the presence of $[RhCl(nbd)]_2$ (5 mol% of Rh) and KOH (0.6 equiv) in THF (0.1 M) at room temperature. The reaction was completed in 2 h, and an extractive workup followed by chromatographic isolation afforded the α-allenol **3aa** in 81% yield with excellent diastereoselectivity (*syn*/*anti* = 99/1)[10] [Eq (1)]. The highly stereoselective formation of the *syn*-configured α-allenol is beneficial among other S_N2'-type reactions of alkynyl oxiranes with organometallic reagents.[11] The iron-catalyzed reaction of **1a** with PhMgBr, unfortunately, exhibited only moderate diastereoselectivity (*syn*/*anti* = 66/34).[9]



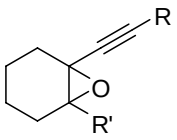
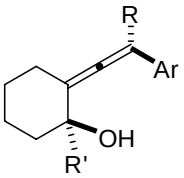
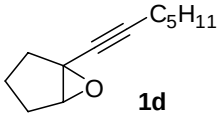
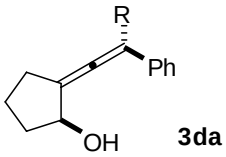
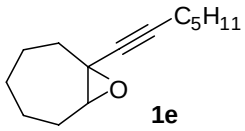
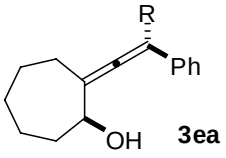
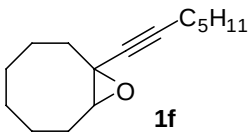
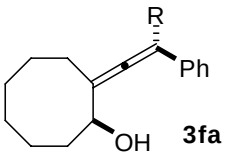
The mechanism shown in Scheme 1 explains the stereoselective production of **3aa**. Initially, a phenylrhodium(I) species is generated by transmetalation of hydroxorhodium(I) with **2a**.[12] Then, *cis* 1,2-addition of the phenylrhodium(I) species to **1a** takes place to afford the alkenylrhodium(I) intermediate **A**. Noteworthy was that addition of the phenylrhodium(I) species across the carbon–carbon triple bond of the epoxy-substituted alkyne, which otherwise required heating over 80 °C,[13] occurred at room temperature. Precoordination of the oxygen atom of the oxirane ring to rhodium is assumed to contribute to the high stereoselectivity as well as high reactivity, as with the case of the iron-catalyzed reaction.[9] Subsequent β-oxygen elimination occurs in a *syn* mode to open the oxirane ring.[14] The resulting rhodium(I) alkoxide **B** reacts with **2a** to release the product **3aa** along with a rhodium(I) boronate.[15]



Scheme 1. Mechanism explaining the stereoselective formation of the *syn*-configured α-allenol

Other examples of the stereoselective synthesis of α-allenols **3** from various combinations of alkynyl oxiranes **1** and arylboronic acids **2** are listed in Table 1. The catalytic process worked well with a sterically and electronically diverse array of arylboronic acids **2b**–**2h**, as well as heteroarylboronic acid **2i**, to give *syn*-configured α-allenols **3ab**–**3ai** with stereoselectivities higher than 96:4, except in the case of the sterically hindered *o*-tolylboronic acid (entries 1–8).[16] It is worth pointing out that the reaction conditions tolerate various functional groups including a formyl group, which is incompatible with Grignard reagents.

Table 1. Rhodium(I)-catalyzed *syn*-selective synthesis of α-allenols from alkynyl oxiranes using arylboronic acids. [a]

entry	substrate	$ArB(OH)_2$	major product	yield (%) [b]	*syn*/*anti* [c]
					
1	**1a** R=Me R'=H	**2b** 4-F-C_6H_4	**3ab**	76	98/2
2	**1a**	**2c** 4-Br-C_6H_4	**3ac**	86	99/1
3	**1a**	**2d** 4-Me-C_6H_4	**3ad**	77	98/2
4	**1a**	**2e** 3-MeO-C_6H_4	**3ae**	80	99/1
5	**1a**	**2f** 3-Cl-C_6H_4	**3af**	74	99/1
6	**1a**	**2g** 3-CHO-C_6H_4	**3ag**	72	96/4
7	**1a**	**2h** 2-Me-C_6H_4	**3ah**	83	83/17
8	**1a**	**2i** 2-thienyl	**3ai**	75	97/3
9	(*R*,*R*)-**1a** (82% ee)	**2a** Ph	(R,S_a)-**3aa** (82% ee)	84	99/1
10	**1b** R=C_5H_{11} R'=H	**2a** Ph	**3ba**	74	97/3
11	**1c** R=C_5H_{11} R'=Me	**2a** Ph	**3ca**	65	99/1
12	 **1d**	**2a** Ph	 **3da**	82	97/3
13	 **1e**	**2a** Ph	 **3ea**	83	99/1
14	 **1f**	**2a** Ph	 **3fa**	83	99/1

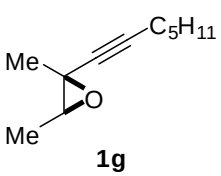
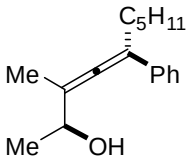
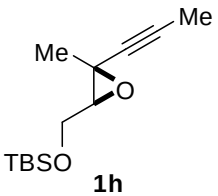
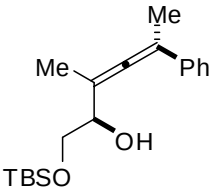
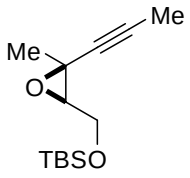
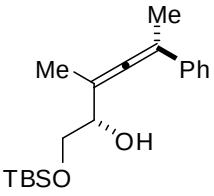
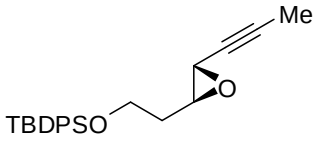
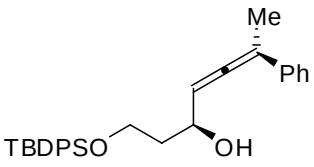
[a] Reaction condition: **1** (0.4 mmol), **2** (0.6 mmol), KOH (0.2-0.3 mmol), $[RhCl(nbd)]_2$ (10 μmol, 5 mol% of Rh) in THF, room temperature, 3-16 h. [b] Yields of isolated products. [c] Relative stereochemistry was assigned by comparison with authentic *anti* isomer prepared by literature procedures [5g, 8] and the ratio was determined by HPLC analysis of the isolated mixture of the α-allenols or the corresponding acetates.

Substrate **1c** having a tetrasubstituted oxirane also gave the tertiary alcohol **3ca** stereoselectively (entry 11). Substrates **1d**–**1f** with five-, seven-, and eight-membered-ring structures gave the products **3da**–**3fa** stereoselectively in high yield (entries 12–14). When enantiomerically enriched

1a[17] was used, the enantiomeric purity of the product **3aa** was exactly identical to that of the starting oxirane (entry 9).[18]

The result of acyclic substrates was shown in Table 2. Trisubstituted oxirane **1g** reacted with **2a** to afford *syn*-configured α-allenol **3ga** with high selectivity (entry 1). Siloxy-substituted oxiranes **1h** and **1i** gave the corresponding products **3ha** and **3ia** in 86% and 77% yields, respectively (entries 2 and 3). The diastereoselectivity of **1h** which had a *trans*-configured alkyne moiety to the siloxymethyl substituent was higher than that of **1i**. Preservation of enantiomeric purity was also observed in the case of acyclic substrate **1j**[19] (entry 4).

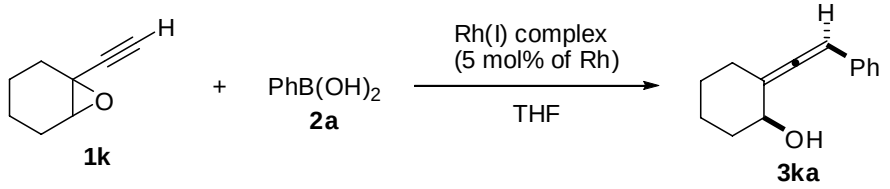
Table 2. Rhodium(I)-catalyzed *syn*-selective synthesis of α-allenols from acyclic alkynyl oxiranes and phenylboronic acid (**2a**). [a]

entry	substrate	major product		yield (%) [b]	*syn*/*anti* [c]
1	 **1g**		**3ga**	85	99/1
2	 **1h**		**3ha**	86	98/2
3	 **1i**		**3ia**	77	77/23
4	 (*S*,*S*)-**1j** (80% ee)	 (*S*,R_a)-**3ja** (80% ee)		61	94/6

[a] Reaction condition: **1** (0.3 mmol), **2** (0.45 mmol), KOH (0.2 mmol), $[RhCl(nbd)]_2$ (7.5 μmol, 5 mol% of Rh) in THF, room temperature, 3 h. [b] Yields of isolated products. [c] Relative stereochemistry was assigned by comparison with an authentic *anti* isomer prepared by the literature procedures[5g,8] and the ratio wes determined by HPLC analysis of the isolated mixture of the α-allenols.

The reaction of **1k** having a terminal alkyne moiety was examined (Table 3). Under the same condition as internal system, the desired **3ka** was obtained in only 19% yield with a moderate selectivity (entry 1). Changing the catalyst to $[Rh(OH)(cod)]_2$ gave a slightly better result (entry 2). The reaction temperature affected both yield and selectivity (entry 3) and finally, the reduced equivalent of **2a** brought the best result (entry 4).

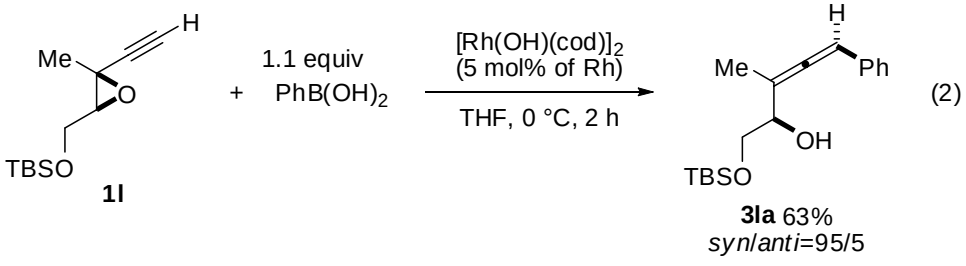
Table 3. Rhodium(I)-catalyzed reaction of terminal alkyne **1k** with phenylboronic acid [a]

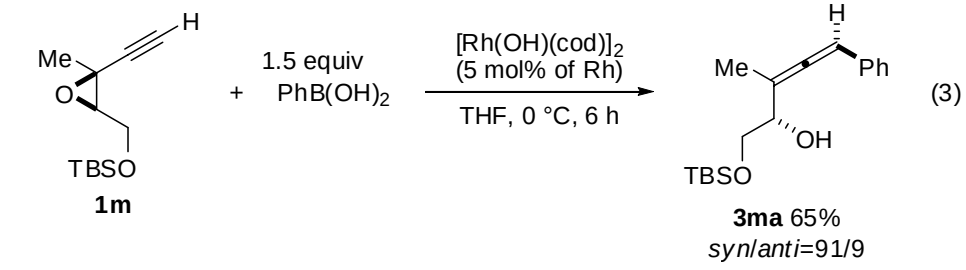


entry	**2a** (equiv)	Rh(I) complex	time (h)	temp (°C)	yield (%) [b]	*syn*/*anti* [c]
1	1.5	$[RhCl(nbd)]_2$ / 0.6 eq KOH	4	rt	19	83/17
2	1.5	$[Rh(OH)(cod)]_2$	4	rt	27	85/15
3	1.5	$[Rh(OH)(cod)]_2$	3.5	0	50	94/6
4	1.1	$[Rh(OH)(cod)]_2$	1.5	0	71	97/3

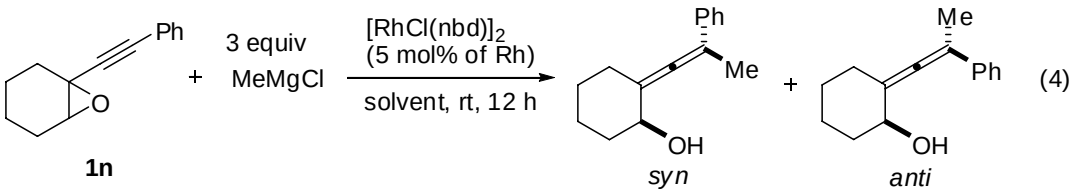
[a] Reaction condition: **1k** (0.4 mmol), **2a**, Rh(I) complex (10 μmol, 5 mol% of Rh) in THF. [b] Yields of isolated products. [c] Relative stereochemistry was assigned by comparison with an authentic *anti* isomer prepared by literature procedures[8] and the ratio were determined by HPLC analysis of the isolated mixture of the α-allenols.

When acyclic substrates **1l** and **1m** were examined, the α-allenols formed with stereoselectivities higher than 90:10 [Eqs. (2) and (3)].





Next, the author explored nucleophiles other than arylboronic acids, and found that MeMgCl reacted analogously.[20] For example, treatment of substrate **1j** (1.0 equiv) with MeMgCl (3.0 equiv) in the presence of $[RhCl(nbd)]_2$ (5 mol% of Rh) for 12 h at room temperature afforded the desired methylated α-allenol **3aa'** [Eq (4)]. However, the *syn* selectivity was lower than that observed with arylboronic acids.



(4)

THF	74% (*syn*/*anti* = 68/32)
THF, 3.3 equiv TMEDA	86% (*syn*/*anti* = 57/43)
dioxane	65% (*syn*/*anti* = 77/23)

Conclusion

The author has developed rhodium-catalyzed reactions which permits the construction of *syn*-configured α-allenols from alkynyl oxiranes and arylboronic acids. Precoordination of the oxygen atom of the oxirane ring to rhodium is assumed to contribute to the high stereoselectivity as well as high reactivity. It is noteworthy that optically active α-allenols are produced from the enantiomerically enriched substrates without any loss of the enatiomeric excess. Occurring with a high level of diastereoselectivity under mild conditions, the reaction will become a good supplement to the well-studied copper-catalyzed reactions.

Experimental Section

General

All rhodium(I)-catalyzed reactions were carried out with standard Schlenk techniques under an inert atmosphere. Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300.07 MHz and ^{13}C at 75.46 MHz)

spectrometer. All NMR data were obtained in $CDCl_3$. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm. Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.00 ppm. High resolution mass spectra were recorded on a JOEL JMS-SX102A spectrometer.

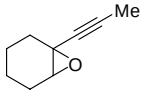
Materials

Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $[RhCl(nbd)]_2$[21] and $[Rh(OH)(cod)]_2$[22] were prepared according to the reported procedure, respectively. 1,4-Dioxane was distilled over sodium-benzophenone ketyl prior to use. THF was dried and deoxygenized using an alumina/catalyst column system (Glass Contour Co.).

Starting Materials:

Alkynyl oxiranes **1a-f**, **1k-m** were prepared from the corresponding 1,3-enynes by oxidation with *m*-chloroperbenzoic acid in a CH_2Cl_2 solution.[6a] Tetrasubstituted oxirane **1c** was prepared from 1-(hept-1-ynyl)-2-methylcyclohex-1-ene which was synthesized by Sonogashira coupling reaction of alkenyl triflate[23] with 1-heptyne (cat. $Pd(PPh_3)_4$, cat. CuI, in pyrrolidine)[24]. Acylic oxirane **1g** was prepared from 3-chlorobutan-2-one and 1-heptyne by the reported procedure.[25] Methylation of **1l** and **1m** (MeOTf, LHMDS in THF) gave **1h**, **1i**, respectively. Enantiomerically enriched oxiranes (*R*,*R*)-**1a**[17] and (*S*,*S*)-**1j**[19] were synthesized according to the literatures, respectively.

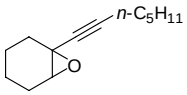
1-(Prop-1-ynyl)-7-oxabicyclo[4.1.0]heptane (1a) [17]



$[\alpha]_D^{22.6}$ = +13.1 (*c* = 1.00, $CHCl_3$, 82% ee); IR (neat): 2940, 2861, 2253, 1435, 1227 cm^{-1}; ^1H NMR: δ = 1.13–1.47 (m, 4H), 1.83 (s, 3H), 1.86–1.92 (m, 2H), 1.96 (ddd, *J* = 15.1, 7.7, 5.6 Hz, 1H), 2.12 (dt, *J* = 15.1, 5.8 Hz, 1H), 3.29 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR: δ = 3.5, 18.9, 19.4, 24.1, 29.9, 50.4, 59.9, 78.3, 79.7; HRMS (CI): *m/z* calcd for $C_9H_{12}O$: 136.0888 $[M]^+$; found 136.0887.

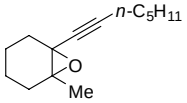
[HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 98/2, flow rate = 0.6 mL/min, λ = 210 nm): t_1 = 8.5 min (*minor*), t_2 = 10.1 min (*major*).]

1-(Hept-1-ynyl)-7-oxabicyclo[4.1.0]heptane (1b)



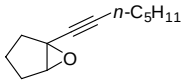
IR (neat): 2936, 2861, 2242, 1435, 1221 cm^{-1}; ^{1}H NMR: δ = 0.89 (t, *J* = 6.8 Hz, 3H), 1.14–1.57 (m, 10H), 1.85–2.02 (m, 3H), 2.07–2.17 (m, 1H), 2.18 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR: δ = 13.9, 18.6, 18.9, 19.4, 22.1, 24.1, 28.1, 30.0, 30.9, 50.5, 60.0, 80.5, 82.9; HRMS (CI): *m/z* calcd for $C_{13}H_{20}O$:192.1514 $[M]^{+}$; found 192.1512.

1-(hept-1-ynyl)-6-methyl-7-oxabicyclo[4.1.0]heptane (1c)



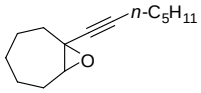
IR (neat): 2936, 2863, 2240, 1435, 1213, 1115 cm^{-1}; ^{1}H NMR: δ = 0.88 (t, *J* = 7.1 Hz, 3H), 1.18–1.55 (m, 10H), 1.43 (s, 3H), 1.63–1.76 (m, 1H), 1.82–2.03 (m, 2H), 2.05–2.19 (m, 1H), 2.20 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR: δ = 14.0, 18.7, 20.05, 20.10, 22.1, 22.2, 28.3, 30.1, 30.97, 31.00, 56.7, 63.3, 79.5, 85.0; HRMS (CI): *m/z* calcd for $C_{14}H_{22}O$: 206.1671 $[M]^{+}$; found 206.1674.

1-(Hept-1-ynyl)-6-oxabicyclo[3.1.0]hexane (1d)



IR (neat): 2932, 2244, 1468, 1402, 1296 cm^{-1}; ^{1}H NMR: δ = 0.89 (t, *J* = 6.9 Hz, 3H), 1.23–1.78 (m, 9H), 1.78 (ddd, *J* = 13.8, 10.4, 8.3 Hz, 1H), 1.98 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.13 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.21 (t, *J* = 7.2 Hz, 2H), 3.59 (s, 1H); ^{13}C NMR: δ = 13.9, 18.8, 19.1, 22.1, 27.5, 28.1, 31.0, 32.0, 56.2, 65.0, 76.4, 85.3; HRMS (CI): *m/z* calcd for $C_{12}H_{18}O$: 178.1358 $[M]^{+}$; found 178.1355.

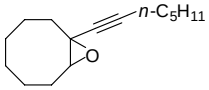
1-(Hept-1-ynyl)-8-oxabicyclo[5.1.0]octane (1e)



IR (neat): 2930, 2857, 2244, 1464, 1250 cm^{-1}; ^{1}H NMR: δ = 0.89 (t, *J* = 6.9 Hz, 3H), 1.23–1.63 (m, 12H), 1.67–1.81 (m, 1H), 1.87–2.07 (m, 2H), 2.08–2.20 (m, 1H), 2.17 (t, *J* = 7.1 Hz, 2H), 3.22 (dd, *J* = 6.9, 3.6 Hz, 1H); ^{13}C NMR: δ = 13.9, 18.6, 22.1, 24.2, 24.7, 28.2, 29.1, 31.0, 31.1, 34.8, 54.4,

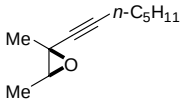
63.4, 81.3, 82.2; HRMS (CI): *m/z* calcd for $C_{14}H_{22}O$: 206.1671 $[M]^+$; found 206.1677.

1-(Hept-1-ynyl)-9-oxabicyclo[6.1.0]nonane (1f)



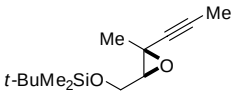
IR (neat): 2930, 2859, 2242, 1470, 1267 cm^{-1}; ^1H NMR: δ = 0.89 (t, *J* = 6.8 Hz, 3H), 1.15–1.80 (m, 16H), 2.08–2.20 (m, 2H), 2.19 (t, *J* = 7.1 Hz, 2H), 3.03 (dd, *J* = 10.2, 4.2 Hz, 1H); ^{13}C NMR: δ = 13.9, 18.6, 22.1, 25.2, 25.8, 26.0, 26.4, 27.1, 28.2, 30.8, 30.9, 54.0, 63.6, 79.6, 83.4; HRMS (CI): calcd for $C_{15}H_{24}O$: 220.1827 $[M]^+$; found 220.1824.

(2*R,3*R**)-2-(hept-1-ynyl)-2,3-dimethyloxirane (1g)**



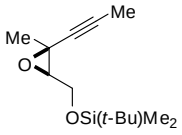
IR (neat): 2934, 2242, 1458, 1383, 1260, 1075 cm^{-1}; ^1H NMR: δ = 0.89 (t, *J* = 6.9 Hz, 3H), 1.23–1.40 (m, 4H), 1.29 (d, *J* = 5.7 Hz, 3H), 1.43–1.55 (m, 2H), 1.46 (s, 3H), 2.17 (t, *J* = 7.2 Hz, 2H), 3.20 (q, *J* = 5.5 Hz, 1H); ^{13}C NMR: δ = 13.5, 13.8, 18.4, 18.5, 22.1, 28.1, 30.9, 50.9, 60.4, 80.8, 82.4; HRMS (CI): *m/z* calcd for $C_{11}H_{18}O$: 166.1358 $[M]^+$; found 166.1351.

(2*R,3*R**)-3-(*tert*-Butyldimethylsilyloxy)-2-methyl-2-prop-1-ynyloxirane (1h)**



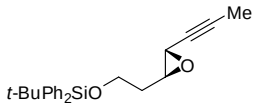
IR (neat): 2930, 2247, 1474, 1258, 1090 cm^{-1}; ^1H NMR: δ = 0.08 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.47 (s, 3H), 1.83 (s, 3H), 3.25 (t, *J* = 5.4 Hz, 1H), 3.72 (d, *J* = 5.7 Hz, 2H); ^{13}C NMR: δ = –5.3, –5.2, 3.6, 18.3, 18.9, 25.8, 51.0, 61.5, 64.3, 78.5, 79.5; HRMS (FAB): *m/z* calcd for $C_{13}H_{25}O_2Si$: 241.1624 $[M+H]^+$; found 241.1621.

(2*R,3*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methyl-2-prop-1-ynyloxirane (1i)**



IR (neat): 2930, 2245, 1474, 1256, 1092 cm^{-1}; ^1H NMR: δ = 0.10 (s, 6H), 0.91 (s, 9H), 1.53 (s, 3H), 1.84 (s, 3H), 2.98 (t, *J* = 5.1 Hz, 1H), 3.80 (dd, *J* = 11.4, 5.1 Hz, 1H), 3.86 (dd, *J* = 11.4, 5.4 Hz, 1H); ^{13}C NMR: δ = –5.23, –5.16, 3.6, 18.4, 23.6, 25.9, 52.3, 63.1, 64.4, 76.5, 81.1; HRMS (FAB): *m/z* calcd for $C_{13}H_{25}O_2Si$: 241.1624 $[M+H]^+$; found 241.1627.

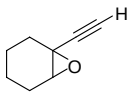
(2*S*,3*S*)-2-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-3-prop-1-ynyloxirane (1j)[19]



$[\alpha]_D^{23.2}$ = –3.3 (*c* = 1.22, $CHCl_3$, 80% ee); ^1H NMR: δ = 1.06 (s, 9H), 1.76 (q, *J* = 6.0 Hz, 2H), 1.86 (d, *J* = 1.8 Hz, 3H), 3.13–3.16 (m, 1H), 3.23 (td, *J* = 5.7, 2.1 Hz, 1H), 3.73–3.84 (m, 2H), 7.35–7.47 (m, 6H), 7.64–7.71 (m, 4H)

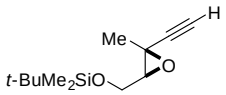
[HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 99/1, flow rate = 0.6 mL/min, λ = 254 nm): t_1 = 12.7 min (*minor*), t_2 = 13.9 min (*major*).]

1-(Ethynyl)-7-oxabicyclo[4.1.0]heptane (1k)



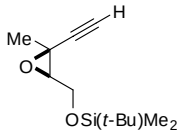
IR (neat): 3291, 2944, 2865, 2120, 1435, 1190 cm^{-1}; ^1H NMR: δ = 1.15–1.48 (m, 4H), 1.87–1.94 (m, 2H), 2.00 (ddd, *J* = 15.1, 7.4, 5.8 Hz, 1H), 2.15 (dt, *J* = 15.2, 6.1 Hz, 1H), 2.31 (s, 1H), 3.35 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR: δ = 18.7, 19.2, 23.9, 29.3, 49.7, 59.6, 70.1, 84.1; HRMS (CI): *m/z* calcd for $C_8H_{10}O$: 122.0732 $[M]^+$; found 122.0729.

(2*R,3*R**)-(*tert*-Butyldimethylsilyloxy)-2-ethynyl-2-methyloxirane (1l)**



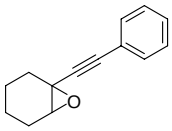
IR (neat): 3310, 2930, 1474, 1258, 1089 cm^{-1}; ^1H NMR: δ = 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.52 (s, 3H), 2.31 (s, 1H), 3.31 (t, *J* = 5.3 Hz, 1H), 3.73 (d, *J* = 5.1 Hz, 2H); ^{13}C NMR: δ = –5.3, –5.2, 18.28, 18.33, 25.8, 50.3, 61.3, 64.0, 70.2, 83.9; HRMS (FAB): *m/z* calcd for $C_{12}H_{23}O_2Si$: 227.1467 $[M+H]^+$; found 227.1470.

(2*R,3*S**)-(*tert*-Butyldimethylsilyloxy)-2-ethynyl-2-methyloxirane (1m)**



IR (neat): 3310, 2930, 1474, 1258, 1094 cm^{-1}; ^1H NMR: δ = 0.095 (s, 3H), 0.100 (s, 3H), 0.91 (s, 9H), 1.57 (s, 3H), 2.37 (s, 1H), 3.03 (t, *J* = 5.1 Hz, 1H), 3.80 (dd, *J* = 11.9, 5.3 Hz, 1H), 3.90 (dd, *J* = 11.9, 5.0 Hz, 1H); ^{13}C NMR: δ = –5.23, –5.16, 18.3, 23.0, 25.9, 51.4, 63.0, 64.2, 72.8, 81.1; HRMS (FAB): *m/z* calcd for $C_{12}H_{23}O_2Si$: 227.1467 $[M+H]^+$; found 227.1462.

1-(Phenylethynyl)-7-oxabicyclo[4.1.0]heptane (1n)

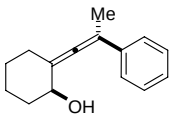


IR (nujol): 2926, 2230, 1487, 1443, 1348, 1177 cm^{-1}; ^1H NMR: δ = 1.18–1.54 (m, 4H), 1.91–2.01 (m, 2H), 2.10 (ddd, *J* = 15.1, 7.4, 5.5 Hz, 1H), 2.24 (dt, *J* = 15.1, 5.9 Hz, 1H), 3.44 (t, *J* = 2.1 Hz, 1H), 7.24–7.34 (m, 3H), 7.39–7.46 (m, 2H); ^{13}C NMR: δ = 18.9, 19.5, 24.2, 29.8, 50.7, 60.4, 82.0, 89.6, 122.3, 128.2, 128.4, 131.8; HRMS (CI): *m/z* calcd for $C_{14}H_{14}O$: 198.1045 $[M]^+$; found 198.1044.

General procedure for the rhodium-catalyzed α-allenol synthesis with $ArB(OH)_2$:

To an oven-dried, argon-purged flask was added $[RhCl(nbd)]_2$ (0.01 mmol, 5 mol% of Rh), **2** (0.6 mmol, 1.5 equiv), KOH (0.2–0.3 mmol, 0.5–0.75 equiv), THF (2.0 mL), and a solution of **1** (0.4 mmol, 1.0 equiv) in THF (2.0 mL). The reaction mixture was stirred at room temperature for 3–16 h, and quenched with water (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography to give **3**.

(1*S)-2-[(*R**)-2-Phenylprop-1-enylidene]cyclohexanol (3aa)**

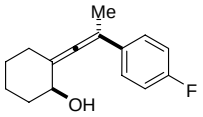


$[\alpha]_D^{23.6}$ = +50.9 (*c* = 1.03, $CHCl_3$, Table 1, Entry 9); IR (neat): 3412, 2932, 1954, 1493, 1445, 1075 cm^{-1}; ^1H NMR: δ = 1.38–1.57 (m, 3H), 1.73–1.99 (m, 3H), 2.01–2.28 (m, 2H), 2.14 (s, 3H), 2.44–2.56 (m, 1H), 4.00–4.17 (m, 1H), 7.18–7.25 (m, 1H), 7.29–7.38 (m, 2H), 7.41–7.48 (m, 2H); ^{13}C NMR: δ = 17.5, 24.0, 27.2, 30.2, 36.8, 69.5, 104.9, 110.2, 125.5, 126.7, 128.3, 137.5, 194.5; HRMS (CI): calcd for $C_{15}H_{18}O$: 214.1358 $[M]^+$; found 214.1355.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 20.7 min (*syn*), t_2 = 22.0 min (*anti*).]

[HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 99.3/0.7, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 38.6 min (*syn, minor*), t_2 = 42.7 min (*anti*), t_3 = 46.7 min (*anti*), t_4 = 54.6 min (*syn, major*).]

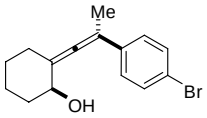
(1*S)-2-[(*R**)-2-(4-Fluorophenyl)prop-1-enylidene]cyclohexanol (3ab)**



IR (neat): 3418, 2934, 1954, 1507, 1231, 1159 cm^{-1}; ^1H NMR: δ = 1.38–1.56 (m, 3H), 1.74–1.95 (m, 3H), 2.01–2.26 (m, 2H), 2.12 (s, 3H), 2.43–2.53 (m, 1H), 3.98–4.17 (m, 1H), 6.95–7.05 (m, 2H), 7.32–7.42 (m, 2H); ^{13}C NMR: δ = 17.7, 24.0, 27.2, 30.2, 36.8, 69.5, 104.0, 110.4, 115.1 (d, *J* = 21.9 Hz), 127.0 (d, *J* = 8.1 Hz), 133.6 (d, *J* = 3.5 Hz), 161.8 (d, *J* = 244.4 Hz), 194.4; HRMS (CI): *m/z* calcd for $C_{15}H_{17}FO$: 232.1263 $[M]^+$; found 232.1263.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 22.5 min (*syn*), t_2 = 24.1 min (*anti*).]

(1*S)-2-[(*R**)-2-(4-Bromophenyl)prop-1-enylidene]cyclohexanol (3ac)**

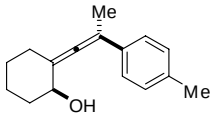


IR (nujol): 3296, 1952, 1487, 1445, 1140, 1078 cm^{-1}; ^1H NMR: δ = 1.36–1.56 (m, 3H), 1.73–1.96 (m, 3H), 2.01–2.25 (m, 2H), 2.10 (s, 3H), 2.43–2.53 (m, 1H), 3.98–4.17 (m, 1H), 7.23–7.32 (m, 2H), 7.38–7.47 (m, 2H); ^{13}C NMR: δ = 17.5, 23.9, 27.2, 30.1, 36.7, 69.5, 103.9, 110.6, 120.5, 127.1,

131.3, 136.7, 194.8; HRMS (CI): *m/z* calcd for $C_{15}H_{17}BrO$: 292.0463 $[M]^+$; found 292.0469.

To assay a stereoisomeric purity, **3ac** was converted to **3aa**. To a solution of **3ac** in THF was added *s*-BuLi (10 equiv) at –78 °C. The reaction was stirred for 1.5 h at –78 °C, and quenched with aqueous NH_4Cl to afford **3aa** in 85% yield.

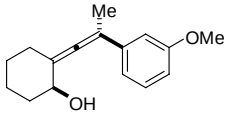
(1*S)-2-[(*R**)-2-(4-Methylphenyl)prop-1-enylidene]cyclohexanol (3ad)**



IR (nujol): 3258, 1952, 1510, 1443, 1140, 1082 cm^{-1}; ^1H NMR: δ = 1.38–1.56 (m, 3H), 1.73–1.98 (m, 3H), 2.00–2.26 (m, 2H), 2.13 (s, 3H), 2.35 (s, 3H), 2.44–2.54 (m, 1H), 3.97–4.19 (m, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR: δ = 17.6, 21.0, 24.0, 27.2, 30.3, 36.9, 69.5, 104.9, 110.1, 125.5, 129.0, 134.6, 136.4, 194.1; HRMS (CI): *m/z* calcd for $C_{16}H_{20}O$: 228.1514 $[M]^+$; found 228.1518.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 16.8 min (*syn*), t_2 = 18.3 min (*anti*).]

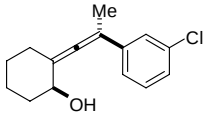
(1*S)-2-[(*R**)-2-(3-Methoxyphenyl)prop-1-enylidene]cyclohexanol (3ae)**



IR (neat): 3429, 2934, 1954, 1601, 1287, 1048 cm^{-1}; ^1H NMR: δ = 1.38–1.56 (m, 3H), 1.73–1.98 (m, 3H), 2.02–2.27 (m, 2H), 2.13 (s, 3H), 2.45–2.56 (m, 1H), 3.81 (s, 3H), 4.01–4.15 (m, 1H), 6.73–6.80 (m, 1H), 6.96–7.06 (m, 2H), 7.24 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR: δ = 17.5, 24.0, 27.3, 30.2, 37.0, 55.1, 69.5, 104.8, 110.3, 111.3, 112.2, 118.1, 129.2, 139.1, 159.6, 194.7; HRMS (CI): *m/z* Calcd for $C_{16}H_{20}O_2$: 244.1463 $[M]^+$; found 244.1453.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): The corresponding acetate was analyzed, t_1 = 9.7 min (*anti*), t_2 = 10.6 min (*syn*).]

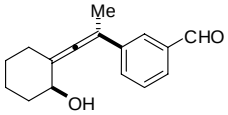
(1*S)-2-[(*R**)-2-(3-Chlorophenyl)prop-1-enylidene]cyclohexanol (3af)**



IR (neat): 3405, 2934, 1954, 1593, 1445, 1078 cm^{-1}; ^1H NMR: δ = 1.38–1.61 (m, 3H), 1.73–1.97 (m, 3H), 2.01–2.26 (m, 2H), 2.11 (s, 3H), 2.43–2.54 (m, 1H), 4.03–4.16 (m, 1H), 7.14–7.33 (m, 3H), 7.35–7.40 (m, 1H); ^{13}C NMR: δ = 17.5, 23.9, 27.2, 30.1, 36.8, 69.6, 103.7, 110.8, 123.7, 125.6, 126.6, 129.4, 134.3, 139.8, 195.1; HRMS (CI): *m/z* calcd for $C_{15}H_{17}ClO$: 248.0968 $[M]^+$; found 248.0957.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 23.6 min (*syn*), t_2 = 25.3 min (*anti*).]

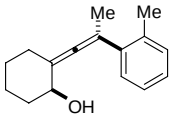
(1*S)-2-[(*R**)-2-(3-Formylphenyl)prop-1-enylidene]cyclohexanol (3ag)**



IR (nujol): 3395, 2722, 1950, 1700, 1688, 1163 cm^{-1}; ^1H NMR: δ = 1.39–1.59 (m, 3H), 1.74–2.00 (m, 3H), 2.03–2.25 (m, 2H), 2.17 (s, 3H), 2.45–2.55 (m, 1H), 4.07–4.17 (m, 1H), 7.43–7.50 (m, 1H), 7.697 (d, *J* = 8.1 Hz, 1H), 7.702 (d, *J* = 7.8 Hz, 1H), 7.86–7.91 (m, 1H), 10.00 (s, 1H); ^{13}C NMR: δ = 17.5, 23.8, 27.2, 30.0, 36.6, 69.5, 103.5, 110.9, 126.2, 128.1, 128.8, 131.6, 136.4, 138.9, 192.3, 195.5; HRMS (CI): *m/z* Calcd for $C_{16}H_{18}O_2$: 242.1307 $[M]^+$; found 242.1305.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.8/0.2, flow rate = 0.6 mL/min, λ = 220 nm): The corresponding acetate was analyzed, t_1 = 29.8 min (*syn*), t_2 = 32.4 min (*anti*).]

(1*S)-2-[(*R**)-2-(2-Methylphenyl)prop-1-enylidene]cyclohexanol (3ah)**

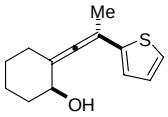


IR (neat): 3420, 2932, 1956, 1487, 1445, 1076 cm^{-1}; ^1H NMR: diasteromixture (*syn*/*anti* = 83/17) δ = 1.32–1.53 (m, 3H), 1.63–1.93 (m, 3H), 1.97–2.17 (m, 2H), 2.10 (s, 2.49H), 2.12 (s, 0.51H), 2.38 (s, 0.51H), 2.41 (s, 2.49H), 2.43–2.54 (m, 1H), 3.96–4.07 (m, 0.17H), 4.00–4.17 (m, 0.83H), 7.11–7.29 (m, 4H); ^{13}C NMR: *syn* δ = 21.0, 21.4, 23.5, 26.4, 29.8, 35.6, 69.3, 103.5, 106.3, 125.8, 126.6, 127.5, 130.5, 135.4, 138.4, 195.0; *anti* δ = 20.9, 21.8, 23.6, 26.6, 29.8, 35.8, 69.2, 103.8, 106.7, 125.8, 126.8, 127.6, 130.6, 135.5, 138.4, 194.9; HRMS (CI): *m/z* Calcd for $C_{16}H_{20}O$: 228.1514 $[M]^+$; found 228.1514.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220

nm): t_1 = 18.1 min (*syn*), t_2 = 19.0 min (*anti*).]

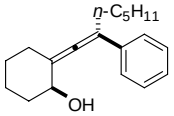
(1*S)-2-[(*R**)-2-(Thiophen-2-yl)prop-1-enylidene]cyclohexanol (3ai)**



IR (neat): 3420, 2932, 1447, 1240, 1076 cm^{-1}; ^1H NMR: δ = 1.37–1.60 (m, 3H), 1.72–1.95 (m, 3H), 1.98–2.25 (m, 2H), 2.13 (s, 3H), 2.43–2.55 (m, 1H), 3.92–4.15 (m, 1H), 6.91 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.96 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.14 (dd, *J* = 5.1, 1.2 Hz, 1H); ^{13}C NMR: δ = 18.1, 24.2, 27.1, 30.6, 37.0, 69.8, 100.9, 111.2, 122.9, 124.2, 127.5, 143.7, 193.7; HRMS (CI): *m/z* Calcd for $C_{13}H_{16}OS$: 220.0922 $[M]^+$; found 220.0922.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 18.2 min (*syn*), t_2 = 21.6 min (*anti*).]

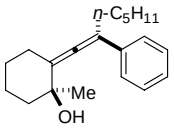
(1*S)-2-[(*R**)-2-Phenylhept-1-enylidene]cyclohexanol (3ba)**



IR (neat): 3279, 2930, 1952, 1597, 1495, 1455 cm^{-1}; ^1H NMR: δ = 0.91 (t, *J* = 7.1 Hz, 3H), 1.24–1.64 (m, 9H), 1.71–1.97 (m, 3H), 2.04–2.23 (m, 2H), 2.40–2.56 (m, 3H), 4.03–4.18 (m, 1H), 7.16–7.24 (m, 1H), 7.27–7.36 (m, 2H), 7.39–7.46 (m, 2H); ^{13}C NMR: δ = 14.1, 22.6, 23.8, 27.2, 27.8, 30.0, 30.3, 31.6, 36.7, 69.5, 110.2, 111.3, 125.9, 126.7, 128.3, 137.4, 194.5; HRMS (CI): calcd for *m/z* $C_{19}H_{26}O$: 270.1984 $[M]^+$; found 270.1986.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.9/0.1, flow rate = 0.6 mL/min, λ = 220 nm): The corresponding acetate was analyzed, t_1 = 13.0 min (*syn*), t_2 = 14.0 min (*anti*).]

(*S)-1-Methyl-2-[(*R**)-2-phenylhept-1-enylidene]cyclohexanol (3ca)**

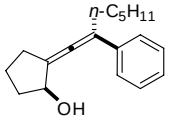


IR (neat): 3418, 2930, 1948, 1493, 1451, 1169 cm^{-1}; ^1H NMR: δ = 0.91 (t, *J*= 7.1 Hz, 3H), 1.27–1.89 (m, 13H), 1.38 (s, 3H), 2.23 (ddd, *J*= 13.5, 7.1 4.7 Hz, 1H), 2.38–2.47 (m, 2H), 2.48 (ddd,

J= 13.8, 7.4, 4.2 Hz, 1H), 7.15–7.24 (m, 1H), 7.27–7.36 (m, 2H), 7.39–7.46 (m, 2H); ^{13}C NMR: δ = 14.1, 22.7, 22.9, 27.3, 27.7, 27.9, 29.0, 30.0, 31.7, 41.4, 70.9, 108.1, 113.4, 125.7, 126.4, 128.3, 137.6, 195.8; HRMS (CI): *m/z* calcd for $C_{20}H_{28}O$: 284.2140 $[M]^+$; found 284.2145.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 11.7 min (*anti*), t_2 = 16.4 min (*syn*).]

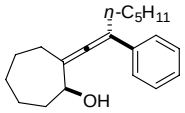
(1*S)-2-[(*R**)-2-Phenylhept-1-enylidene]cyclopentanol (3da)**



IR (nujol): 3366, 1946, 1593, 1493, 1453, 1034 cm^{-1}; ^{1}H NMR: δ = 0.90 (t, *J* = 7.1 Hz, 3H), 1.25–2.06 (m, 11H), 2.37–2.51 (m, 3H), 2.62–2.76 (m, 1H), 4.64–4.78 (m, 1H), 7.15–7.23 (m, 1H), 7.26–7.35 (m, 2H), 7.39–7.46 (m, 2H); ^{13}C NMR: δ = 14.1, 22.6, 23.2, 27.6, 29.1, 30.1, 31.6, 35.9, 75.4, 109.3, 111.6, 125.8, 126.6, 128.4, 137.2, 198.0; HRMS (CI): *m/z* calcd for $C_{18}H_{24}O$: 256.1827 $[M]^+$; found 256.1829.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 15.7 min (*anti*), t_2 = 19.1 min (*syn*).]

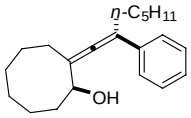
(1*S)-2-[(*R**)-2-Phenylhept-1-enylidene]cycloheptanol (3ea)**



IR (neat): 3407, 2928, 1943, 1597, 1495, 1455 cm^{-1}; ^{1}H NMR: δ = 0.91 (t, *J* = 7.1 Hz, 3H), 1.25–1.89 (m, 14H), 2.00–2.14 (m, 1H), 2.25 (ddd, *J* = 13.9, 8.1, 3.0 Hz, 1H), 2.35–2.51 (m, 3H), 4.31–4.49 (m, 1H), 7.16–7.24 (m, 1H), 7.27–7.36 (m, 2H), 7.40–7.47 (m, 2H); ^{13}C NMR: δ = 14.1, 22.6, 23.8, 27.8, 29.0, 29.5, 29.6, 30.3, 31.7, 36.9, 72.3, 108.8, 112.9, 125.8, 126.6, 128.3, 137.3, 200.3; HRMS (CI): *m/z* calcd for $C_{20}H_{28}O$: 284.2140 $[M]^+$; found 284.2143.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.93/0.07, flow rate = 0.6 mL/min, λ = 220 nm): The corresponding acetate was analyzed, t_1 = 20.0 min (*syn*), t_2 = 21.1 min (*anti*).]

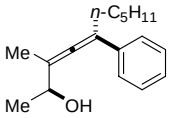
(1*S)-2-[(*R**)-2-Phenylhept-1-enylidene]cyclooctanol (3fa)**



IR (neat): 3393, 2928, 1943, 1493, 1449, 1028 cm^{-1}; ^1H NMR: δ = 0.90 (t, *J*= 6.9 Hz, 3H), 1.24–1.90 (m, 16H), 1.91–2.03 (m, 1H), 2.25 (ddd, *J*= 13.8, 7.2, 4.2 Hz, 1H), 2.37 (ddd, *J*= 13.4, 8.3, 4.7 Hz, 1H), 2.42–2.51 (m, 2H), 4.16–4.36 (m, 1H), 7.16–7.24 (m, 1H), 7.28–7.35 (m, 2H), 7.38–7.44 (m, 2H); ^{13}C NMR: δ = 14.1, 22.5, 22.9, 25.5, 25.9, 27.9, 28.1, 29.3, 30.6, 31.7, 32.7, 72.7, 108.6, 111.7, 126.1, 126.6, 128.3, 137.4, 201.2; HRMS (CI): *m/z* calcd for $C_{21}H_{30}O$: 298.2297 $[M]^+$; found 298.2290.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.9/0.1, flow rate = 0.6 mL/min, λ = 220 nm): The corresponding acetate was analyzed, t_1 = 15.0 min (*syn*), t_2 = 16.2 min (*anti*).]

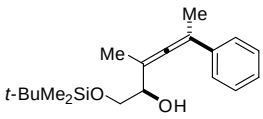
(2*S,4*R**)-3-Methyl-5-phenyldec-3,4-dien-2-ol (3ga)**



IR (neat): 3385, 2928, 1948, 1448, 1370, 1073 cm^{-1}; ^1H NMR: δ = 0.91 (t, *J* = 7.2 Hz, 3H), 1.27–1.44 (m, 4H), 1.37 (d, *J* = 6.3 Hz, 3H), 1.45–1.68 (m, 3H), 1.84 (s, 3H), 2.39–2.48 (m, 2H), 4.24–4.36 (m, 1H), 7.16–7.23 (m, 1H), 7.27–7.34 (m, 2H), 7.35–7.41 (m, 2H); ^{13}C NMR: δ = 14.1, 14.9, 22.2, 22.6, 27.8, 30.2, 31.6, 69.1, 107.6, 108.3, 125.9, 126.5, 128.3, 137.3, 199.1; HRMS (CI): *m/z* calcd for $C_{17}H_{24}O$: 244.1827 $[M]^+$; found 244.1825.

[HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 99.3/0.7, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 26.0 min (*anti*), t_2 = 30.7 min (*anti*), t_3 = 33.3 min (*syn*), t_4 = 41.5 min (*syn*).]

(2*R,4*R**)-1-(*tert*-Butyldimethylsilyloxy)-3-methyl-5-phenylhex-3,4-dien-2-ol (3ha)**

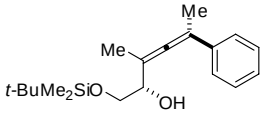


IR (neat): 3446, 2928, 1952, 1472, 1256, 1117 cm^{-1}; ^1H NMR: δ = 0.075 (s, 3H), 0.084 (s, 3H), 0.91 (s, 9H), 1.84 (s, 3H), 2.10 (s, 3H), 2.52 (d, *J* = 4.8 Hz, 1H), 3.66 (dd, *J* = 10.2, 6.3 Hz, 1H), 3.76 (dd, *J* = 10.1, 3.8 Hz, 1H), 4.15–4.22 (m, 1H), 7.16–7.23 (m, 1H), 7.27–7.35 (m, 2H), 7.37–7.43 (m, 2H); ^{13}C NMR: δ = –5.34, –5.31, 15.4, 17.2, 18.4, 25.9, 65.9, 72.8, 101.9, 102.3, 125.7, 126.5,

128.2, 137.4, 200.8; HRMS (FAB): *m/z* calcd for $C_{19}H_{30}O_2Si$: 318.2015 $[M]^+$; found 318.2009.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 16.2 min (*anti*), t_2 = 17.5 min (*syn*).]

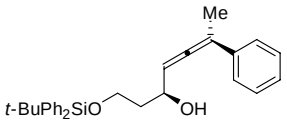
(2*S,4*R**)-1-(*tert*-Butyldimethylsilyloxy)-3-methyl-5-phenylhex-3,4-dien-2-ol (3ia)**



IR (neat): 3447, 2928, 1952, 1472, 1254, 1117 cm^{-1}; ^1H NMR: δ = 0.066 (s, 3H), 0.073 (s, 3H), 0.90 (s, 9H), 1.83 (s, 3H), 2.10 (s, 3H), 2.54 (d, *J* = 4.8 Hz, 1H), 3.64 (dd, *J* = 10.1, 6.8 Hz, 1H), 3.76 (dd, *J* = 10.1, 4.1 Hz, 1H), 4.16–4.22 (m, 1H), 7.16–7.23 (m, 1H), 7.27–7.34 (m, 2H), 7.37–7.43 (m, 2H); ^{13}C NMR: δ = –5.4, 15.4, 17.2, 18.3, 25.9, 66.0, 73.0, 101.7, 102.1, 125.6, 126.5, 128.2, 137.4, 201.0; HRMS (FAB): *m/z* calcd for $C_{19}H_{30}O_2Si$: 318.2015 $[M]^+$; found 318.2015.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 16.2 min (*syn*), t_2 = 17.5 min (*anti*).]

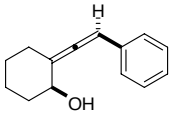
(3*S*,5*R*)-1-(*tert*-Butyldiphenylsilyloxy)-6-phenylhept-4,5-dien-3-ol (3ja)



$[\alpha]_D^{22.7}$ = –77.4 (*c* = 1.10, $CHCl_3$, Table 1, Entry 17); IR (neat): 3428, 2930, 1950, 1472, 1428, 1111 cm^{-1}; ^1H NMR: δ = 1.06 (s, 9H), 1.90 (q, *J* = 5.7 Hz, 2H), 2.10 (d, *J* = 2.7 Hz, 3H), 3.13 (d, *J* = 4.2 Hz, 1H), 3.82–3.99 (m, 2H), 4.55–4.64 (m, 1H), 5.60–5.67 (m, 1H), 7.18–7.24 (m, 1H), 7.27–7.35 (m, 2H), 7.36–7.48 (m, 8H), 7.66–7.71 (m, 4H); ^{13}C NMR: δ = 17.1, 19.1, 26.8, 38.9, 62.4, 69.3, 97.5, 103.1, 125.6, 126.7, 127.7, 128.3, 129.7, 133.0, 133.1, 135.47, 135.50, 136.6, 202.4; HRMS (CI): *m/z* Calcd for $C_{29}H_{34}O_2Si$; 442.2328 $[M]^+$; found 442.2313.

[HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH = 97/3, flow rate = 0.6 mL/min, λ = 254 nm): t_1 = 12.8 min (*anti*), t_2 = 20.9 min (*syn*), t_3 = 24.1 min (*anti*), t_4 = 32.7 min (*syn*).]

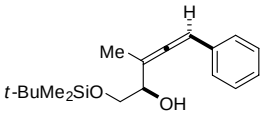
(1*S)-2-[(*R**)-2-phenylethenylidene]cyclohexanol (3ka)**



IR (neat): 3402, 2934, 1954, 1497, 1447, 1075 cm^{-1}; ^1H NMR: δ = 1.39–1.60 (m, 3H), 1.73–1.99 (m, 3H), 2.02–2.27 (m, 2H), 2.47–2.58 (m, 1H), 4.03–4.17 (m, 1H), 6.35 (td, *J* = 3.6, 0.6 Hz, 1H), 7.16–7.34 (m, 5H); ^{13}C NMR: δ = 23.9, 27.2, 30.0, 36.8, 69.4, 98.4, 112.3, 126.6, 127.0, 128.6, 134.8, 196.2; HRMS (CI): *m/z* calcd for $C_{14}H_{16}O$: 200.1201 $[M]^+$; found 200.1206.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 25.1 min (*syn*), t_2 = 26.5 min (*anti*).]

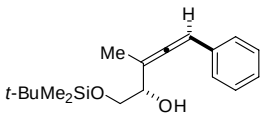
(2*R,4*R**)-1-(*tert*-Butyldimethylsilyloxy)-3-methyl-5-phenylpent-3,4-dien-2-ol (3la)**



IR (neat): 3449, 2928, 1954, 1464, 1256, 1115 cm^{-1}; ^1H NMR: δ = 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.86 (d, *J* = 3.0 Hz, 3H), 2.58 (d, *J* = 5.1 Hz, 1H), 3.67 (dd, *J* = 10.1, 6.5 Hz, 1H), 3.78 (dd, *J* = 10.2, 3.6 Hz, 1H), 4.15–4.23 (m, 1H), 6.23 (quint, *J* = 2.9 Hz, 1H), 7.15–7.24 (m, 1H), 7.26–7.31 (m, 4H); ^{13}C NMR: δ = –5.34, –5.31, 15.5, 18.3, 25.9, 65.7, 72.4, 96.4, 104.1, 126.7, 126.8, 128.5, 134.7, 201.9; HRMS (FAB): *m/z* calcd for $C_{18}H_{28}O_2Si$: 304.1859 $[M]^+$; found 304.1859.

[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): t_1 = 21.1 min (*anti*), t_2 = 240 min (*syn*).]

(2*S,4*R**)-1-(*tert*-Butyldimethylsilyloxy)-3-methyl-5-phenylpent-3,4-dien-2-ol (3ma)**



IR (neat): 3436, 2928, 1954, 1464, 1256, 1115 cm^{-1}; ^1H NMR: δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 1.86 (d, *J* = 3.0 Hz, 3H), 2.61 (d, *J* = 4.5 Hz, 1H), 3.65 (dd, *J* = 10.1, 6.8 Hz, 1H), 3.78 (dd, *J* = 10.2, 3.9 Hz, 1H), 4.17–4.26 (m, 1H), 6.17–6.22 (m, 1H), 7.15–7.23 (m, 1H), 7.25–7.32 (m, 4H); ^{13}C NMR: δ = –5.4, 15.3, 18.3, 25.9, 65.8, 72.6, 96.0, 103.9, 126.7, 126.8, 128.5, 134.7, 202.1; HRMS (FAB): *m/z* calcd for $C_{18}H_{29}O_2Si$: 305.1937 $[M+H]^+$; found 305.1927.

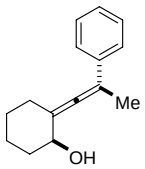
[HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220

nm): t_1 = 21.1 min (*syn*), t_2 = 240 min (*anti*).]

Typical procedure for the rhodium-catalyzed α-allenol synthesis with MeMgCl:

In a N_2-purged glovebox, to an oven-dried screw-capped vial was added $[RhCl(nbd)]_2$ (2.9 mg, 6.3 μmol), a solution of **1i** (48.7 mg, 0.25 mmol) in THF (2.4 mL), and a solution of MeMgCl (3.0 M in THF, 0.25 mL, 0.75 mmol). The reaction mixture was stirred at room temperature for 12 h, and quenched with 2N HCl (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give **3aa'** (38.8 mg, 74%, *syn*/*anti* = 68/32).

(1*R)-2-[(*R**)-2-Phenylprop-1-enylidene]cyclohexanol (3aa')**



IR (nujol): 3191, 1952, 1597, 1493, 1447, 1076 cm^{-1}; ^1H NMR: δ = 1.38–1.57 (m, 3H), 1.71–1.95 (m, 3H), 2.05–2.21 (m, 2H), 2.15 (s, 3H), 2.43–2.54 (m, 1H), 4.10–4.22 (m, 1H), 7.17–7.25 (m, 1H), 7.28–7.36 (m, 2H), 7.37–7.43 (m, 2H); ^{13}C NMR: δ = 18.0, 23.6, 27.0, 29.8, 36.2, 69.3, 104.6, 109.8, 125.7, 126.7, 128.3, 137.6, 194.9; HRMS (CI): *m/z* calcd for $C_{15}H_{18}O$: 214.1358 $[M]^+$ found 214.1355.

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List of Publications

Chapter 1. Rhodium-Catalyzed Cyclization of 1,6-Enynes Triggered by Addition of Arylboronic Acids
T. Miura, M. Shimada, M. Murakami
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Rhodium-Catalyzed Cascade Reaction of 1,6-Enynes Involving Addition, Cyclization, and β-Oxygen Elimination
T. Miura, M. Shimada, M. Murakami
Chem. Asian J. **2006**, *1*, 868–877.

Chapter 2. Rhodium-Catalyzed Cyclization of 1,6-Enynes with Arylboronic Acids through β-Hydride Elimination/Hydrorhodation Sequence
M. Shimada, T. Harumashi, T. Miura, M. Murakami
Submitted

Chapter 3. Rhodium-Catalyzed Addition-Cyclization Reactions of 5-Yn-1-ones with Arylboronic Acids
T. Miura, M. Shimada, M. Murakami
Synlett **2005**, 667–669.

Rhodium-catalyzed arylative cyclization of alkynones induced by addition of arylboronic acids
T. Miura, M. Shimada, M. Murakami
Tetrahedron **2007**, *63*, 6131–6140.

Chapter 4. Acyl 1,3-Migration in Rhodium-Catalyzed Reactions of Acetylenic β-Ketoesters with Aryl Boronic Acids: Application to Two-Carbon-Atom Ring Expansions
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Chapter 5. Stereoselective Synthesis of α-Allenols by Rhodium-Catalyzed Reaction of Alkynyl Oxiranes with Arylboronic Acids
T. Miura, M. Shimada, S.-Y. Ku, T. Tamai, M. Murakami
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