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Rhodium-Catalyzed Cyclization Reaction of 1,6-Enynes with Arylboronic Acids through β-Hydride Elimination/Hydrorhodation Sequence

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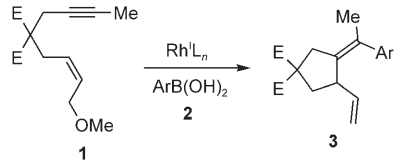
Abstract: Methoxy-substituted 1,6-enynes react with arylboronic acids in the presence of a rhodium(I) complex to give arylated cyclization products. This occurs by a multi-step mechanism consisting of rhodium/boron transmetalation, intermolecular carborhodation, intramolecular carborhodation, β-hydride elimination, hydrorhodation, and β-oxygen elimination. A shift of the position of a carbon–carbon double bond is observed, suggesting that the β-hydride elimination/hydrorhodation process is repeatedly taking place.

Keywords: boron · catalysis · cyclization · elimination · rhodium

Introduction

A wide range of organoboronic acids and esters are increasingly commercially available, promoting their use in organic synthesis.[1] While being fairly stable towards 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] We have previously described the rhodium-catalyzed cyclization reactions of 1,6-enynes with arylboronic acids,[4] wherein a catalytically active methoxorhodium(I) species is regenerated through β-methoxy elimination [Eq. (1)[5] and Eq. (2)]. The methoxo ligands on rhodium are sufficiently nucleophilic to coordinate to the boronic compound, facilitating transmetalation between rhodium and boron.

Continuing our studies on other 1,6-enyne compounds, we found that a cyclization reaction proceeded by a different pathway to give an unexpected cyclic product **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. We report herein the synthesis of arylated cyclic compounds by a new cyclization reaction of 1,6-enynes with arylboronic acids catalyzed by a rhodium(I) complex.



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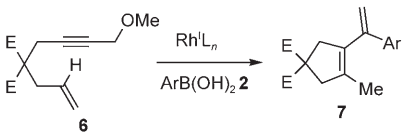

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Results and Discussion

Initially, we examined several rhodium catalysts (5 mol% 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 inefficiently catalyzed the reaction, the use of $[RhCl(binap)]_2$ or $[RhCl(cod)]_2$, together

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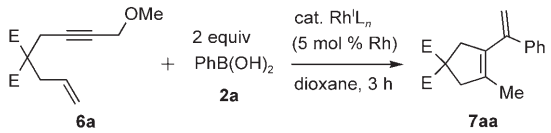
Table 1. Reaction of **6a** with **2a** in the presence of rhodium catalysts.[a]



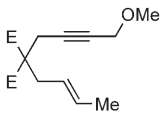
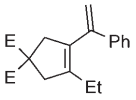
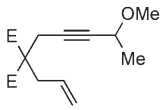
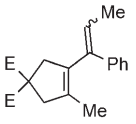
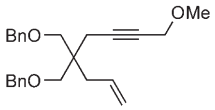
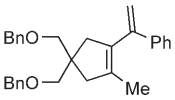
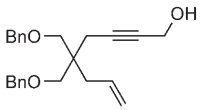
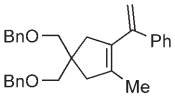
Entry	$Rh^{I}L_n$	Temp. [°C]	Base (0.6 equiv)	Yield [%][b]
1	$[RhCl(PPh_3)_3]$	80	KOH	14
2	$[RhCl(binap)]_2$	80	KOH	56
3	$[RhCl(cod)]_2$	80	KOH	44
4	$[RhCl(nbd)]_2$	80	KOH	66
5	$[RhCl(nbd)]_2$	50	KOH	65
6	$[Rh(OMe)(nbd)]_2$	50	–	72

[a] Reaction conditions: **6** (0.2 mmol), **2** (0.4 mmol), $Rh^{I}L_n$ (5 mol % Rh) in dioxane (2.0 mL) for 3 h under argon unless otherwise noted. [b] Yields of isolated product. E = methoxycarbonyl. binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, cod = cycloocta-1,5-diene. nbd = norbornadiene.

with KOH gave the arylative cyclization product **7aa** in 56 and 44% yields, respectively (entries 1–3, Table 1). Unlike the case of substrate **4** [Eq. (2)], no formation of vinylcyclopropane substructure was observed. Rhodium(I)–norbornadiene complexes gave better yields (entries 4–6, Table 1), 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.

The scope of the reaction was examined by using various combinations of 1,6-enynes **6** and arylboronic acids **2** under 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, Table 2). A vicinally disubstituted (*E*)-**6b** participated in the rhodium-catalyzed cyclization to afford **7ba** in 55% yield (entry 6, Table 2).[7]

Table 2. Rh^{I}-catalyzed reaction of 1,6-enynes **6** with arylboronic acids **2**.[a]

Entry	Substrate	$ArB(OH)_2$	Product	Yield [%][b]
1	**6a**	**2b** 4-Me-C_6H_4	**7ab**	67
2	**6a**	**2c** 3-Me-C_6H_4	**7ac**	66
3	**6a**	**2d** 2-Me-C_6H_4	**7ad**	65
4	**6a**	**2e** 3-Br-C_6H_4	**7ae**	71
5	**6a**	**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**	**2a** Ph	 **7da**	66[f]
9	 **6e**	**2a** Ph	 **7da**	54[d]

[a] Reaction conditions: **6** (0.2 mmol), **2** (0.4 mmol), $[Rh(OMe)(nbd)]_2$ (5 μmol, 5 mol % Rh) in dioxane (2.0 mL) at 50°C for 3–5 h under argon unless otherwise noted. [b] Yields of isolated product. [c] 80°C. [d] **2a** (0.8 mmol), $[Rh(OMe)(nbd)]_2$ (10 μmol, 10 mol % Rh). [e] *E*/*Z* = 57:43. [f] RT. E = methoxycarbonyl. Bn = benzyl.

A mixture of *E* and *Z* isomers was produced from substrate **6c** (entry 7, Table 2). The cyclization reaction also occurred with substrate **6e** having a free hydroxy group at the propargylic position (entry 9, Table 2). The reaction of 1,6-enynes bearing sulfonamide and ether tethers hardly occurred, giving the corresponding cyclized products in low yield (ca. 5%).

We propose that the reaction proceeds through the pathway outlined in Scheme 1.[8] The arylrhodium species **A**, generated by transmetalation of an arylboronic acid with a rhodium(I) complex,[9] adds regioselectively across the carbon–carbon triple bond of **6** to afford alkenylrhodium(I) species **B**.[10] Then, intramolecular carborhodation occurs onto the pendent carbon–carbon double bond in a 5-*exo*-trig mode to give a (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,[11] 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.[12] The methoxo ligand on rhodium is sufficiently nucleophilic to coordinate to the arylboronic acid, facilitating the next transmetalation between rhodium and boron.[13]

Abstract in Japanese:

ロジウム触媒存在下、メトキシ基をもつ1,6-エンインにアリールボロン酸を作用させると、アリール基を含む環状化合物が得られた。ロジウムとアリールボロン酸の金属交換により生成したアリールロジウム種がアルキンに付加してアルケニルロジウム中間体を与え、ついで分子内のアルケンに付加して環状骨格を構築し、さらにβ水素脱離／ヒドロロデーション過程を経て、β酸素脱離が起こったと考えられる。

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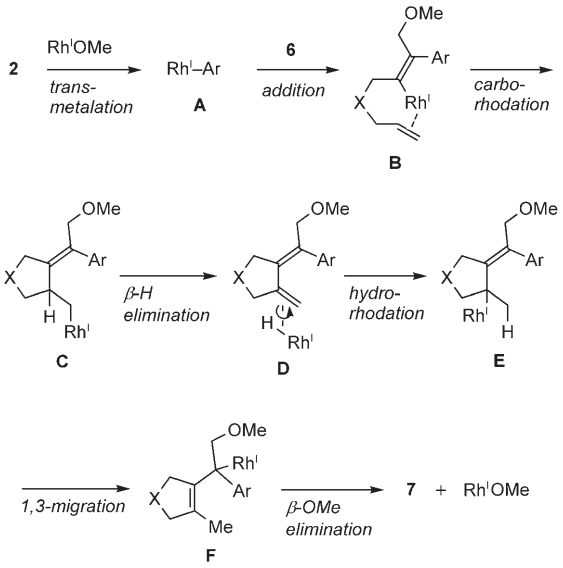
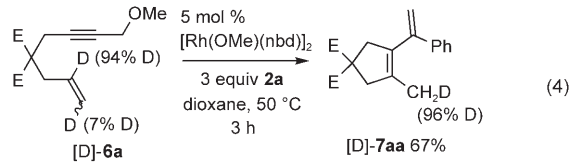


Scheme 1. Proposed mechanism for the formation of **7** from **6**.

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

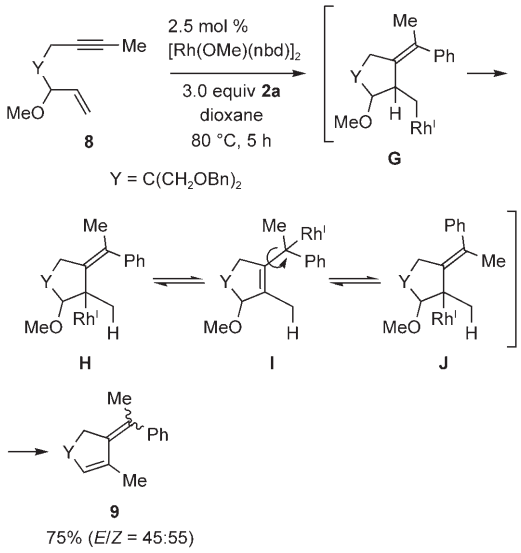


(4)

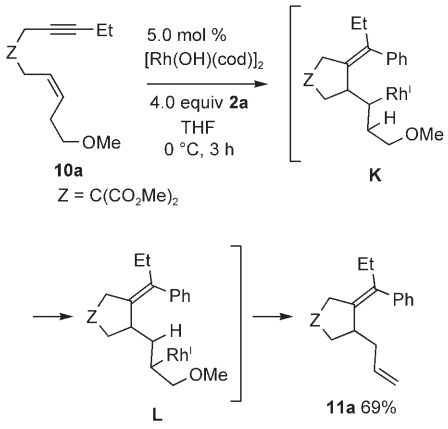
Variants of the cyclization reaction involving the successive β-hydride elimination/hydrorhodation process were found when analogous 1,6-enynes having a methoxy group at different positions were used. The reaction of 1,6-enyne **8** having a methoxy group at the inner allylic position reacted with **2a**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

We also studied the reaction of 1,6-enyne **10a** with a methoxy group at the homo-allylic position. An analogous arylative cyclization reaction proceeded to afford an 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).[14]

In the case of substrate **10b** with 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)].[15] The product **11b** was accompanied by a certain amount (ca. 30%) of several regioisomers having a carbon–carbon

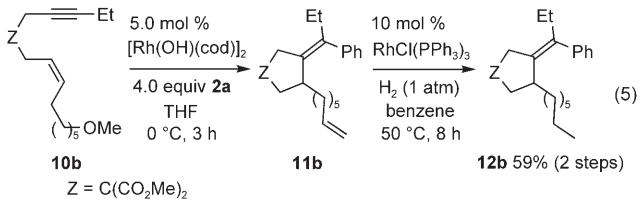


Scheme 2.



Scheme 3.

double bond at inner positions. Therefore, to estimate the efficiency of the cyclization reaction, the crude **11b** was subjected to a hydrogenation reaction.



(5)

Conclusions

We have developed new cyclization reactions of methoxy-substituted 1,6-enynes with arylboronic acids catalyzed by a rhodium(I) complex. The reaction proceeds through a multistep sequence consisting of rhodium/boron transmetalation,

intermolecular carborhodation, intramolecular carborhodation, β-hydride elimination, hydrorhodation, and β-oxygen elimination.

Experimental Section

General

All 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. All NMR data were obtained in $CDCl_3$ unless 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 77.0 ppm. High-resolution mass spectra were recorded on a JEOL JMS-SX102 A 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).

Synthesis

6a: To a suspension of NaH (77 mg, 3.2 mmol) in THF (15 mL) was added dropwise a solution of dimethyl 2-allylmalonate (446 mg, 2.6 mmol) in THF (5 mL) at 0 °C. After 30 min, a solution of 1-bromo-4-methoxybut-2-yne[16] (634 mg, 3.9 mmol) in THF (5 mL) was added at 0 °C. The reaction mixture was stirred at room temperature for 28 h, and then quenched with addition of H_2O (20 mL). The resulting aqueous phase was extracted with ethyl acetate (3×20 mL). The combined organic phase was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate = 9:1) to afford **6a** (550 mg, 2.2 mmol, 83%). IR (neat): $\tilde{\nu}$ = 2955, 2244, 1740, 1642, 1437 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{13}H_{18}O_5$: 254.1154 $[M]^+$; found: 254.1160.

[D]-**6a**: Compound [D]-**6a** was prepared from dimethyl 2-(4-methoxybut-2-enyl)malonate[17] and 2-deuterioprop-2-enyl methanesulfonate, prepared from 2-deuterioprop-2-en-1-ol,[18] under the reported reaction conditions.[19] ^{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 ppm (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 ppm; HRMS (FAB): m/z calcd for $C_{13}H_{18}O_5D$: 256.1295 $[M+H]^+$; found: 256.1293.

(*E*)-**6b**: Compound (*E*)-**6b** was prepared from (*E*)-dimethyl 2-crotylmalonate[20] and 1-bromo-4-methoxybut-2-yne[16] according to a similar procedure as **6a** in 46% yield. IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{14}H_{21}O_5$: 269.1389 $[M+H]^+$; found: 269.1389.

6c: Compound **6c** was prepared from dimethyl 2-allylmalonate and 1-bromo-4-methoxy-4-methylbut-2-yne according to a similar procedure as **6a** in 82% yield. IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{14}H_{21}O_5$: 269.1389 $[M+H]^+$; found: 269.1386.

6d: To a solution of **6e** (1.09 g, 3.0 mmol) and 2,6-di*tert*-butyl-4-methylpyridine (1.85 g, 9.0 mmol) in CH_2Cl_2 (20 mL) was added MeOTf (1.47 g, 9.0 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 days, and then quenched with addition of sat. $NaHCO_3$ aq. (20 mL). The resulting aqueous solution was extracted with ethyl acetate (3× 20 mL). The combined organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 5:1) to afford **6d** (822 mg, 2.2 mmol, 72%). IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{25}H_{30}O_3$: 378.2195 $[M]^+$; found: 378.2200.

6e: Compound **6e** was prepared by homologation reaction of 4,4-bis(-benzyloxymethyl)hept-1-en-6-yne[21] with paraformaldehyde according to the method in the literature.[22] IR (neat): $\tilde{\nu}$ = 3420, 2863, 2222, 1638, 1455, 1366 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (EI): m/z calcd for $C_{24}H_{28}O_3$: 364.2038 $[M]^+$; found: 364.2035.

8: Diethyl 2-(but-2-ynyl)-2-(diethoxymethyl)malonate, prepared from diethyl 2-(diethoxymethyl)malonate[23] and 1-bromobut-2-yne, according to a similar procedure used for **6a**, was subjected to reduction ($LiAlH_4$ in Et_2O), benzylation (NaH, BnBr, cat. TBAI in THF/DMF (5:1)), and acidic hydrolysis (3 M HCl in THF). The resulting 2,2-bis(benzyloxymethyl)hex-4-ynal was reacted with vinylmagnesium bromide in a THF solution, followed by methylation under the same conditions as **6d** to afford the desired **8**. IR (neat): $\tilde{\nu}$ = 2919, 2245, 1638, 1455, 1366, 1092 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{25}H_{30}O_3$: 378.2195 $[M]^+$; found: 378.2199.

10a: Compound **10a** was prepared from dimethyl 2-(5-methoxypent-2-enyl)malonate and 1-bromopent-2-yne according to a similar procedure as **6a** in 75% yield. IR (neat): $\tilde{\nu}$ = 2950, 1740, 1437, 1293, 1210 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{16}H_{25}O_5$: 297.1702 $[M+H]^+$; found: 297.1700.

10b: Compound **10b** was prepared from dimethyl 2-(9-methoxynon-2-enyl)malonate and 1-bromopent-2-yne according to a similar procedure used for **6a** in 75% yield. IR (neat): $\tilde{\nu}$ = 2932, 1740, 1437, 1293, 1211 cm^{-1}; ^{1}H 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 ppm (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 ppm; 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 (3×10 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**.

7aa: IR (neat): $\tilde{\nu}$ = 2955, 1732, 1599, 1435, 1260 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{18}H_{20}O_4$: 300.1362 $[M]^+$; found: m/z 300.1360.

[D]-**7aa**: ^{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 ppm (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 ppm; HRMS (EI): m/z calcd for $C_{18}H_{19}O_4D$: 301.1424 $[M]^+$; found: m/z 301.1421.

7ab: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found: 314.1519.

7ac: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found: 314.1518.

7ad: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found: 314.1513.

7ae: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{18}H_{19}O_4Br$: 378.0467 $[M]^+$; found: 378.0470.

7af: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{19}H_{22}O_5$: 330.1467 $[M]^+$; found: 330.1465.

7ba: IR (neat): $\tilde{\nu}$ = 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found: 314.1513.

7ca: A mixture of geometrical isomers (E/Z = 57:43). IR (neat, mixture): $\tilde{\nu}$ = 2953, 1738, 1435, 1260 cm^{-1}; ^{1}H 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 ppm (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 ppm (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 ppm; HRMS (CI, mixture): m/z calcd for $C_{19}H_{22}O_4$: 314.1518 $[M]^+$; found: 314.1520.

7ea: IR (neat): $\tilde{\nu}$ = 2851, 1948, 1808, 1599, 1495, 1453, 1362 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (CI): m/z calcd for $C_{30}H_{32}O_2$: 424.2402 $[M]^+$; found: 424.2395.

9: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 × 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). IR (neat, mixture): $\tilde{\nu}$ = 2853, 1734, 1597, 1455, 1362, 1115 cm^{-1}; ^{1}H 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 ppm (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 ppm (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 ppm; HRMS (CI, mixture): m/z calcd for $C_{30}H_{32}O_2$: 424.2402 $[M]^+$; found: 424.2404.

11: 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 × 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%). IR (neat): $\tilde{\nu}$ = 2955, 1738, 1640, 1435, 1258 cm^{-1}; ^{1}H 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 ppm (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 ppm; 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 using the freeze-pump-thaw method, and then dihydrogen gas was introduced. After stirring 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% (2 steps)). IR (neat): $\tilde{\nu}$ = 2928, 1738, 1435, 1256, 1171 cm^{-1}; ^{1}H 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 ppm (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 ppm; HRMS (EI): Calcd for $C_{25}H_{36}O_4$: 400.2614 $[M]^+$; found: 400.2616

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[13] For the superiority of alkoxo (or hydroxo) ligands to an acetoxy ligand, see Ref. [4d].

[14] The use of $[Rh(OMe)(nbd)]_2$ gave **11a** in a lower yield together with other by-products.

[15] For a rare example of a catalytic process involving sequential β-hydride elimination/hydrometalation followed by final β-heteroatom elimination, see: S. Ma, Z. Yu, *Angew. Chem.* **2003**, *115*, 1999; *Angew. Chem. Int. Ed.* **2003**, *42*, 1955.

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