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Rhodium-Catalyzed Tandem Conjugate Addition−Mannich Cyclization Reaction: Straightforward Access to Fully Substituted Tetrahydroquinolines

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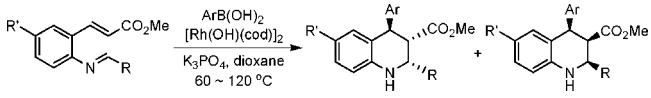
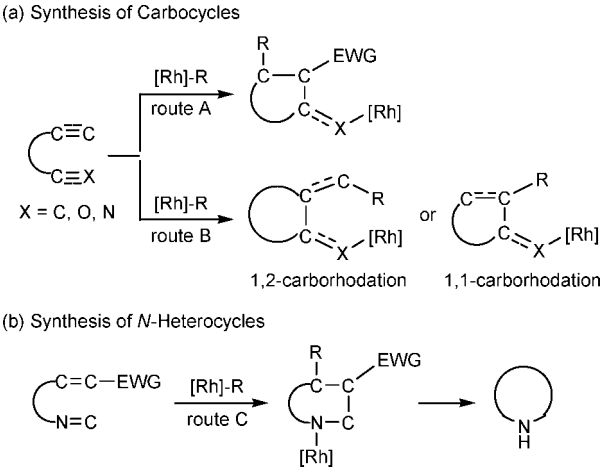


A new Rh(I)-catalyzed tandem conjugate addition−Mannich cyclization reaction of imine-substituted electron-deficient alkenes with arylboronic acids has been developed to afford 2,3,4-trisubstituted 1,2,3,4-tetrahydroquinolines. This is the first example involving imine group as a secondary electrophile in Rh(I)-catalyzed tandem reactions.

Transition-metal-catalyzed tandem C−C bond formations are powerful methods for the synthesis of structurally complex molecules from relatively simple starting materials in a convergent way.[1] Molecules that have two or more different unsaturated bonds are particularly interesting substrates for the tandem annulation involving multiple C−C bond formations with a single catalyst in one operation, allowing the construction of a variety of cyclic compounds. The more reactive functional group provides the entry point for the addition of a carbon nucleophile by way of initial intermolecular carbometalation, which triggers the second carbometalation on the less reactive functionality in an intramolecular way to construct a cyclic skeleton.

Recently, several examples of Rh(I)-catalyzed tandem annulations with organoboron reagents have been demonstrated in which the tandem cyclization was triggered by conjugate addition to α,β-unsaturated carbonyl compounds or 1,2-addition across the alkynes.[1e,2–4] An organorhodium(I) intermediate generated via carborhodation onto the alkene or alkyne moiety added to the intramolecular carbonyl, [2a–c] cyano,[2d,e] alkyne,[2g] and alkene[2g–m] groups, providing five- or six-membered carbocycles via a sequential second carborhodation (Scheme 1, routes A and B). Although several Rh(I)-catalyzed tandem reactions have been described, the process involving an imine group as a second electrophile has not yet been explored.[5] Since both α,β-unsaturated carbonyl compounds[1e,6] and imines[6c,7] are good acceptors of organorhodium(I) species, we envisioned that electron-deficient alkenes bearing imine moiety placed at an appropriate position are interesting bifunctional substrates with regard to the possibility of a tandem cyclization reaction, which could afford *N*-heterocycles such as tetrahydroquinolines (Scheme 1, route C). Tetrahydroquinoline derivatives constitute an important class possessing a wide range of biological activities and multiple applications and are found in a variety of natural

SCHEME 1. Rhodium(I)-Catalyzed Tandem Annulations



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(1) For reviews, see: (a) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. (b) Negishi, E.; Copéret, C.; Ma, S.; Liou, S. Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365. (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (d) Grigg, R.; Sridharan, V. *J. Organomet. Chem.* **1999**, *576*, 65. (e) Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217. For recent examples, see: (f) Agapiou, K.; Cauble, D. F.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 4528. (g) Subburaj, K.; Montgomery, J. *J. Am. Chem. Soc.* **2003**, *125*, 11210. (h) Guo, H.-C.; Ma, J.-A. *Angew. Chem., Int. Ed.* **2006**, *45*, 354.

(2) For examples of Rh(I)-catalyzed tandem cyclization reactions, see: (a) Cauble, D. F.; Gipson, J. D.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 1110. (b) Bocknack, B. M.; Wang, L.-C.; Krische, M. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5421. (c) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (d) Miura, T.; Murakami, M. *Org. Lett.* **2005**, *7*, 3339. (e) Miura, T.; Harumashi, T.; Murakami, M. *Org. Lett.* **2007**, *9*, 741. (f) Miura, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2007**, *9*, 5075. (g) Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094. (h) Lautens, M.; Mancuso, J. *Org. Lett.* **2002**, *4*, 2105. (i) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478. (j) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607. (k) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909. (l) Chen, Y.; Lee, C. *J. Am. Chem. Soc.* **2006**, *128*, 15598. (m) Navarro, C.; Csákÿ, A. G., *Org. Lett.* **2008**, *10*, 217.

(3) For examples of Rh(I)-catalyzed tandem noncyclization reactions, see: (a) Yoshida, K.; Ogasawara, M.; Hayashi, T. *J. Am. Chem. Soc.* **2002**, *124*, 10984. (b) Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. J. *Organomet. Chem.* **2002**, *648*, 297. (c) Kurahash, T.; Shinokubo, H.; Osuka, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 6336.

(4) Examples of similar reactions using other transition metals. Nickel catalysis: (a) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1364. (b) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2004**, *43*, 3941. (c) Jayanth, T. T.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5921. Ir catalysis: (d) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 7506. Pd catalysis: (e) Nishikata, T.; Kobayashi, Y.; Kobayashi, K.; Yamamoto, Y.; Miyaura, N. *Synlett* **2007**, 3055. (f) Tsukamoto, H.; Kondo, Y. *Org. Lett.* **2007**, *9*, 4227. (g) Tsukamoto, H.; Ueno, T.; Kondo, Y. *Org. Lett.* **2007**, *9*, 3033. (h) Tsukamoto, H.; Matsumoto, T.; Kondo, Y. *J. Am. Chem. Soc.* **2008**, *130*, 388, and references therein.

(5) Tandem reactions using imine as a secondary electrophile. Nickel catalysis: ref 4a,b. Pd catalysis: ref 4g.

(6) (a) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229. (b) Hayashi, T. *Synlett* **2001**, 879. (c) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (d) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (e) Hayashi, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 13.

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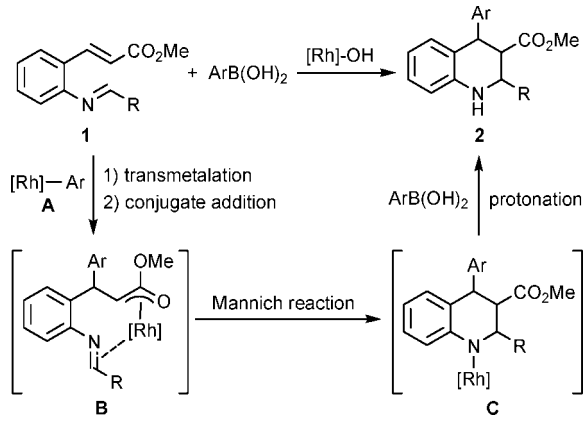
SCHEME 2. Rh(I)-Catalyzed Tandem Conjugate Addition−Mannich Cyclization Reaction of Imine-Substituted α,β-Unsaturated Ester with Arylboronic Acids

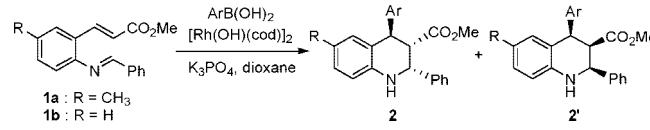


products and pharmaceuticals that exhibit potent and varied biological activities.[8]

To date, Rh(I)-catalyzed tandem cyclization reactions using organoboron reagents have been reported in the context of synthesis of carbocyclic compounds.[9] In parallel with our efforts to develop a catalytic system for heterocyclic synthesis,[10] we were interested in developing a one-pot synthesis of *N*-heterocycles, tetrahydroquinolines, whereby a single catalytic system would invoke sequential C−C bond formations in an efficient manner. Herein we report a new Rh(I)-catalyzed tandem conjugate addition−Mannich cyclization reaction of imine-substituted electron-deficient alkenes with arylboronic acids. *This is the first example involving imine moiety as a secondary electrophile in Rh(I)-catalyzed tandem reactions.*

The success of a tandem cyclization triggered by the conjugate addition of an organorhodium(I) species (**A**) to an electron-deficient alkene could be achieved by choosing the adequate secondary functionality placed at an appropriate position in the molecule. The secondary functional group should not react faster than the electron-deficient alkene with the organorhodium(I) species in an intermolecular way but should be reactive enough to trap intramoleculary the (oxa-π-allyl)rhodium(I) intermediate (**B**) generated in the conjugate addition step (Scheme 2). In this regard, the combination of α,β-unsaturated ester and imine seems plausible. On the other hand, the Rh^I-catalyzed conjugate addition reactions of organoboronic acids to α,β-unsaturated carbonyl compounds are usually carried out in water-containing solvents. However, anhydrous solvents might be required both to minimize imine hydrolysis and to prevent Rh^I-enolate (**B**) from protonation in this tandem process.[11] The low reactivity and instability of imine moiety relative to other functional groups that were used in the related Rh^I-catalyzed tandem reactions could present significant challenges in this process.

TABLE 1. Rh(I)-Catalyzed Tandem Conjugate Addition−Mannich Cyclization Reactions of 1 with Various Arylboronic Acids[a]



entry	substrate	Ar	product	time (h)	yield (%)[b]	2:2'[c]
1	**1a**	Ph	**2a**	1	74	77:23
2[d]	**1b**	Ph	**2b**	12	86	63:37
3	**1a**	3-$MeOC_6H_4$	**2c**	1	73	77:23
4	**1a**	4-$MeOC_6H_4$	**2d**	1	72	71:29
5	**1b**	4-$MeOC_6H_4$	**2e**	1	75	83:17
6	**1a**	4-MeC_6H_4	**2f**	1	74	71:29
7	**1a**	4-HOC_6H_4	**2g**	1	74	77:23
8	**1a**	2-naphthyl	**2h**	1	70	83:17
9[d]	**1a**	4-FC_6H_4	**2i**	24	80	77:23
10	**1a**	4-ClC_6H_4	**2j**	1	67	91:9
11[e]	**1a**	4-BrC_6H_4	**2k**	48	51	63:37
12[e]	**1a**	3-$O_2NC_6H_4$	**2l**	48	55	83:17
13[e]	**1a**	4-$CH_3COC_6H_4$	**2m**	48	50	67:33

[a] The reaction was carried out with **1**, $ArB(OH)_2$ (2.5 equiv), $[Rh(OH)(cod)]_2$ (2 mol %, 4 mol % Rh), and K_3PO_4 (2 equiv) in 1,4-dioxane (0.1 M) at 80 °C, unless otherwise noted. [b] Isolated yields. [c] The ratio of two isomers was determined by ^1H NMR. [d] Performed at 60 °C. [e] Performed with 5 mol % $[Rh(OH)(cod)]_2$ (10 mol % Rh).

We focused our initial efforts on establishing optimal conditions for the Rh(I)-catalyzed tandem conjugate addition−Mannich cyclization reaction of **1a**, which was selected as the first substrate for screening of several solvents and bases. Gratifyingly, it was found that reaction between **1a** and phenylboronic acid in 1,4-dioxane for 1 h at 80 °C in the presence of $[Rh(OH)(cod)]_2$ (4 mol % Rh) and K_3PO_4 gave the desired 1,2,3,4-tetrahydroquinoline **2a** in 74% yield as an inseparable mixture of two diastereomers in a ratio of 77:23 favoring the *cis-trans* isomer, of which substituents on C-2 and C-3 and those on C-3 and C-4 are located in *cis* and *trans* configuration, respectively (Table 1, entry 1). The structure of the compound **2a** was determined by examination of ^1H NMR spectrum and NOE experiment. It should be noted that direct 1,2-addition of $PhB(OH)_2$ to the imine moiety was not observed.

With the establishment of these optimized conditions, we set out to explore the scope of this tandem process. As shown in Table 1, reaction of **1** with organoboronic acids took place smoothly with good yield to provide 2,3,4-trisubstituted 1,2,3,4-tetrahydroquinoline **2**. A wide range of arylboronic acids with electron-donating or -withdrawing substituents at various positions were found to be good nucleophiles in the reaction (Table 1, entries 1−13). Generally, electron-rich arylboronic acids

(7) For selected examples, see: (a) Wang, Z.-Q.; Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336. (b) Marelli, C.; Monti, C.; Gennari, C.; Piarulli, U. *Synlett* **2007**, 2213. (c) Duan, H.-F.; Jia, Y.-X.; Wang, L.-X.; Zhou, Q.-L. *Org. Lett.* **2006**, *8*, 2567. (d) Kuriyama, M.; Soeta, T.; Hao, X.; Chen, Q.; Tomioka, K. *J. Am. Chem. Soc.* **2004**, *126*, 8128. (e) Ueda, M.; Miyaura, N. *J. Organomet. Chem.* **2000**, *595*, 31.

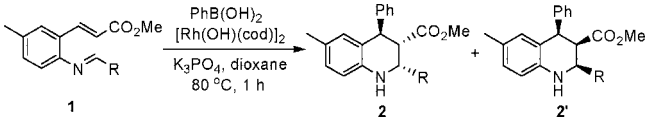
(8) (a) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *Tetrahedron* **1996**, *52*, 15031. (b) Steinhagen, H.; Corey, E. J. *Org. Lett.* **1999**, *1*, 823. (c) Dannhardt, G.; Gruchalla, M. V.; Kohl, B. K.; Parsons, C. G. *Arch. Pharm.* **2000**, *333*, 267. (d) Hoemann, M. Z.; Xie, R. L.; Ross, R. F.; Meyer, S.; Sidhu, A.; Cunny, G. D.; Hauske, J. R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 129. (e) Smith, H. C.; Cavanaugh, C. K.; Friz, J. L.; Thompson, C. S.; Saggers, J. A.; Michelotti, E. L.; Garcia, J.; Tice, C. M. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1943. (f) Theeraladanon, C.; Arisawa, M.; Nakagawa, M.; Nishida, A. *Tetrahedron: Asymmetry* **2005**, *16*, 827. (g) Liu, H. M.; Liu, F. W.; Zou, D. P.; Dai, G. F. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1821.

(9) There is one example for Rh(I)-catalyzed synthesis of 3-alkylideneoxindoles using isocyanates as a secondary electrophile; see ref 2f.

(10) (a) Pastine, S. J.; Youn, S. W.; Sames, D. *Org. Lett.* **2003**, *5*, 1055. (b) Pastine, S. J.; Youn, S. W.; Sames, D. *Tetrahedron* **2003**, *59*, 8859. (c) Youn, S. W.; Pastine, S. J.; Sames, D. *Org. Lett.* **2004**, *6*, 581. (d) Youn, S. W.; Eom, J. I. *Org. Lett.* **2005**, *7*, 3355. (e) Youn, S. W. *J. Org. Chem.* **2006**, *71*, 2521. (f) Youn, S. W. *Org. Prep. Proced. Int.* **2006**, *38*, 505. (g) Youn, S. W.; Eom, J. I. *J. Org. Chem.* **2006**, *71*, 6705. (h) Youn, S. W. *Synlett* **2007**, 3050.

(11) It was found that both water and protic acid such as H_3BO_3 were detrimental to the reaction presented herein (see Supporting Information). It has been reported that boric acid is presumed to facilitate the release of rhodium from the iminorhodium(I) intermediate by protonolysis in the Rh-catalyzed reaction of ethyl cyanoformate with arylboronic acids; see: Shimizu, H.; Murakami, M. *Chem. Commun.* **2007**, 2855.

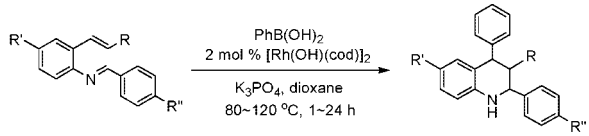
TABLE 2. Rh(I)-Catalyzed Tandem Annulations of Various Imine-Substituted α,β-Unsaturated Esters 1 with $PhB(OH)_2$[a]



entry	substrate	R	product	yield (%)[b]	2:2′[c]
1	**1c**	4-$MeOC_6H_4$	**2n**	83	83:17
2	**1d**	4-$O_2NC_6H_4$	**2o**	71	59:41
3	**1e**	2-BrC_6H_4	**2p**	45	50:50
4	**1f**	2-(6-methylpyridinyl)	**2q**	55	59:41
5	**1g**	2-(5-methylfuranyl)	**2r**	55	83:17
6	**1h**	cinnamyl	**2s**	45	100:0
7	**1i**	CO_2Et	**2t**	33	n.d.[d]

[a] The reaction was carried out with **1**, $PhB(OH)_2$ (2.5 equiv), $[Rh(OH)(cod)]_2$ (2 mol %, 4 mol % Rh), and K_3PO_4 (2 equiv) in 1,4-dioxane (0.1 M) at 80 °C for 1 h. [b] Isolated yields. [c] The ratio of two isomers was determined by ^1H NMR. [d] Not determined.

SCHEME 3. Rh(I)-Catalyzed Tandem Annulations of Imine-Substituted Various Alkenes 1 with $PhB(OH)_2$



1j : R=$CONMe_2$, R'=Me, R''=OMe
1k : R=CN, R'=H, R''=OMe
1l : R=Ph, R'=Me, R''=OMe
1m : R=H, R'=Me, R''=H

2u : R=$CONMe_2$, R'=Me, R''=OMe (64%)
2v : R=CN, R'=H, R''=OMe (34%)
2w : R=Ph, R'=Me, R''=OMe (no reaction)
2x : R=H, R'=Me, R''=H (no reaction)

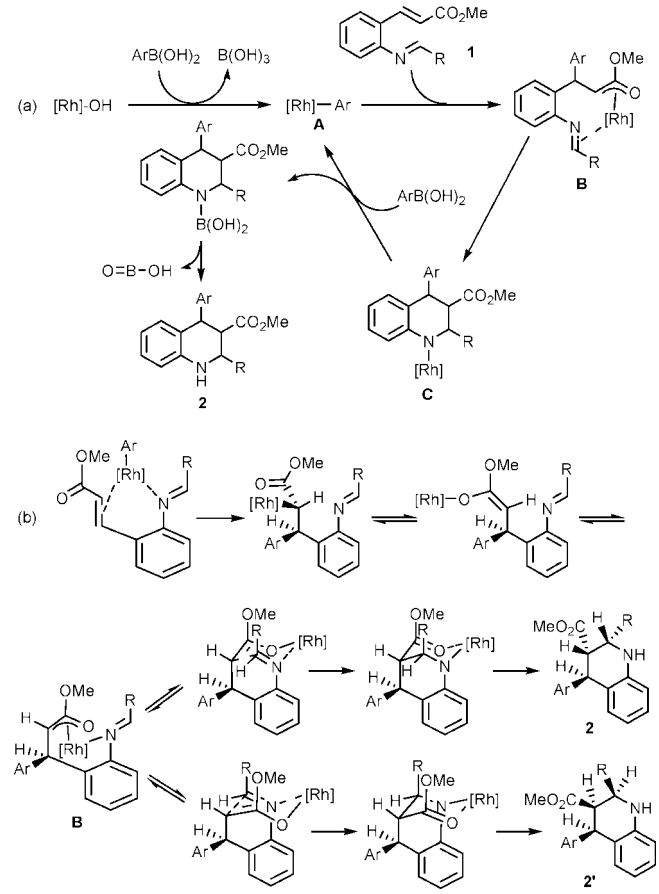
required shorter reaction time and gave higher yields than their electron-deficient counterparts, which required higher catalyst loadings. 2-Naphthylboronic acid also reacted with **1a** to give the corresponding tetrahydroquinoline **2h** (Table 1, entry 8). In contrast, these cyclization reactions failed with sterically hindered aryl- (*o*-$MeOC_6H_4$), heteroaryl- (2-thienyl, 2-furanyl), and alkenyl- (β-styryl, (*E*)-1-octenyl) boronic acids to give the corresponding products in 15−30% yields, probably due to steric and electronic reasons, respectively.

We proceeded to examine the reaction with various imines (Table 2). Both electron-deficient and electron-rich aromatic imines as well as sterically hindered aromatic imine underwent tandem cyclization reaction to form the corresponding tetrahydroquinolines (Table 2, entries 1−3). Heteroaromatic imines (Table 2, entries 4 and 5), α,β-unsaturated imine (Table 2, entry 6), and glyoxylate imine (Table 2, entry 7) also proved to be suitable substrates, whereas aliphatic imines led to a complicated mixture and no reaction occurred with ketimine substrates.

Last, we explored the effects of substituents at the alkene moiety. Whereas the tandem annulations of α,β-unsaturated amide (**1j**) and nitrile (**1k**) afforded the corresponding cyclized products in moderate to good yields, phenyl-substituted (**1l**) and terminal alkenes (**1m**) were unsuccessful (Scheme 3).

A plausible mechanism for Rh-catalyzed tandem cyclization presented herein is outlined in Scheme 4 and is based on the related mechanisms established for the Rh-catalyzed tandem cyclizations triggered by conjugate addition with organoboronic acids.[2,12] Initially, an organorhodium(I) species (**A**) is generated by transmetalation of hydroxorhodium(I) with arylboronic acid. Then, conjugate addition of the arylrhodium(I) species (**A**) to substrate **1** occurs to afford the (oxa-π-allyl)rhodium(I) intermediate (**B**), which undergoes intramolecular nucleophilic addition to the pendant imine group, forming *N*-rhodium(I) species (**C**). The reaction was complete in the absence of proton source such as H_2O, which suggests that a proton source for this reaction could be the organoboronic acid.[2f,4c,13] Protonation of **C** with arylboronic acid releases the product **2** along with metaboric acid and **A** to promote the next catalytic cycle. Even though the dependence of stereochemical bias on the substrate structures is unclear and difficult to explain at this stage, the observed relative stereochemistry may be understood on the basis of a *Z*-enolate and a Zimmerman−Traxler-type transition state model (Scheme 4b).[2a,f,m,3a]

SCHEME 4. Proposed Mechanism for the Rh(I)-Catalyzed Tandem Conjugate Addition−Mannich Cyclization Reaction



In summary, we have developed a new Rh(I)-catalyzed tandem conjugate addition−Mannich cyclization reaction to afford 2,3,4-trisubstituted 1,2,3,4-tetrahydroquinolines. It is interesting that sequential C−C bond formations, conjugate addition and Mannich reaction, are catalyzed by a Rh complex in a single catalytic cycle. This process represents the first example in which an imine group can serve as a secondary electrophile that accepts the (oxa-π-allyl)rhodium(I) intermediate in an intramolecular way. Noteworthy is the fact that this process can tolerate various functional groups such as methoxy, free hydroxyl, halogen, ketone, nitro, alkene, ester, cyano, and amide groups. Moreover, the arylboronic acids act as a proton source as well as a carbon nucleophile. Future studies will focus on

(12) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.

(13) (a) Oh, C. H.; Jung, H. H.; Kim, K. S.; Kim, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 805. (b) Miura, T.; Shimada, M.; Ku, S.-Y.; Tamai, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 7101. (c) Zhao, P.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 1876.

the development of related catalytic tandem annulations and asymmetric variants.

Experimental Section

General Procedure for Rh(I)-Catalyzed Tandem Conjugate Addition−Mannich Cyclization Reaction of Imine-Substituted Electron-Deficient Alkenes 1 with Arylboronic Acids. To a solution of the substrate **1** (0.15 mmol) in 1,4-dioxane (0.1 M) were added $[Rh(OH)(cod)]_2$ (2 mol %, 4 mol % Rh, 0.003 mmol), K_3PO_4 (2 equiv, 0.3 mmol), and boronic acid (2.5 equiv, 0.375 mmol). The resulting mixture was stirred at the reported temperature for 1−48 h. After the reaction was completed, the reaction mixture was quenched with distilled water, extracted with CH_2Cl_2 (three times), washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane = 1:2−1:10) to give the corresponding product **2**.

Data for 2a. Signals corresponding to the major isomer: δ_H ($CDCl_3$, 400 MHz) 2.14 (s, 3H), 3.35 (dd, J = 4.1, 7.2 Hz, 1H), 3.42 (s, 3H), 4.30 (d, J = 7.2 Hz, 1H), 4.71 (d, J = 4.1 Hz, 1H), 6.55 (s, 1H), 6.60 (d, J = 7.9 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 7.16−7.42 (m, 10H). δ_C ($CDCl_3$, 100 MHz) 20.5, 42.6, 51.2, 52.0, 54.6, 114.1, 121.8, 126.3, 126.5, 126.6, 126.9, 127.7, 127.9, 128.2, 128.3, 128.6, 129.3, 130.8, 141.4, 141.7, 144.9, 171.7. Representative signals corresponding to the minor isomer: δ_H ($CDCl_3$, 400 MHz) 2.14 (s, 3H), 3.13 (s, 3H), 3.24 (dd, J = 3.2, 6.0 Hz, 1H), 4.66 (d, J = 5.8 Hz, 1H), 4.87 (d, J = 3.1 Hz, 1H), 6.63 (d, J = 8.2 Hz, 1H), 6.66 (s, 1H), 6.90 (d, J = 7.8 Hz, 1H), 7.16−7.42 (m, 10H). δ_C ($CDCl_3$, 100 MHz) 20.5, 47.4, 50.6, 53.0, 58.6, 114.5, 114.8, 121.8, 125.2, 126.1, 127.0, 127.1, 128.1, 128.4, 128.5, 128.9, 129.5, 129.8, 140.8, 141.2, 142.5, 169.8. υ_{max} (NaCl, cm^{-1}) 3384, 3025, 2921, 2852, 2351, 1735, 1617, 1508, 1454, 1360, 1264, 1219, 1165, 1088, 1029, 811, 752, 701. HREIMS m/z 357.1728 $(M)^+$, calcd for $C_{24}H_{23}NO_2$ 357.1729.

Data for 2b. Signals corresponding to the major isomer: δ_H ($CDCl_3$, 400 MHz) 3.41 (dd, J = 4.4, 7.9 Hz, 1H), 3.43 (s, 3H), 4.32 (d, J = 7.9 Hz, 1H), 4.76 (d, J = 4.4 Hz, 1H), 6.62−7.44 (m, 14H). δ_C ($CDCl_3$, 100 MHz) 42.2, 51.2, 51.7, 54.7, 113.8, 117.7, 122.0, 126.3, 126.6, 127.4, 127.8, 128.3, 128.6, 129.3, 130.5, 141.5, 143.6, 144.5, 171.5. Representative signals corresponding to the minor isomer: δ_H ($CDCl_3$, 400 MHz) 3.14 (s, 3H), 3.26 (dd, J = 3.3, 5.9 Hz, 1H), 4.69 (d, J = 6.1 Hz, 1H), 4.92 (d, J = 3.5 Hz, 1H), 6.62−7.44 (m, 14H). δ_C ($CDCl_3$, 100 MHz) 47.3, 50.6, 52.8, 58.4, 114.5, 117.6, 121.6, 126.4, 126.5, 127.0, 127.2, 128.1, 128.4, 128.9, 129.5, 140.6, 141.0, 144.9, 169.8. υ_{max} (NaCl, cm^{-1}) 3392, 3028, 2951, 2855, 2356, 1735, 1605, 1490, 1454, 1434, 1366, 1267, 1162, 1117, 1077, 1029, 802, 750, 701. HREIMS m/z 343.1570 $(M)^+$, calcd for $C_{23}H_{21}NO_2$ 343.1572.

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Supporting Information Available: Full experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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