COMMUNICATION

ChemComm
www.rsc.org/chemcomm

An unprecedented rhodium-catalysed self-conjugate reduction, cross-coupling tandem reaction of cinnamaldehydes with arylboronic acids

Zhiyong Wang, Gang Zou* and Jie Tang

Department of Chemistry, East China Normal University, 3663 North Zhongshan Road, Shanghai, 200062, P. R. China. E-mail: gzou@chem.ecnu.edu.cn; Fax: 86-21-62232100; Tel: 86-21-62232764

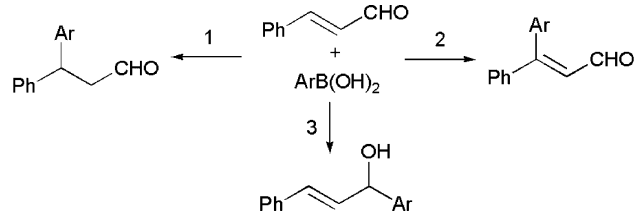
Received (in Cambridge, UK) 2nd February 2004, Accepted 17th March 2004
First published as an Advance Article on the web 14th April 2004

A novel rhodium-catalysed self-conjugate reduction, cross-coupling tandem reaction of cinnamaldehydes with arylboronic acids through a three-membered metallocyclopropanone intermediate is disclosed.

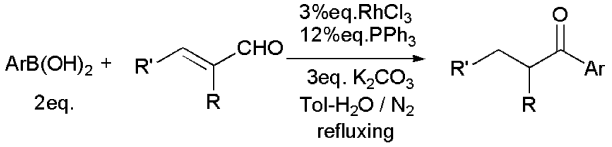
Arylboronic acids have recently attracted much attention as an air-stable and non-toxic alternative to traditional organometallic nucleophiles, such as organic magnesium (ArMgX), copper (Ar_2CuLi) and tin ($ArSnBu_3$) compounds, in organic and inorganic transformations, especially in transition-metal mediated C–C bond forming processes.[1–9] Rhodium has proven to be versatile for the transformation of organoboronic acids. Both coupling-type and addition-type reactions of arylboronic acids with multiple bonds in olefins, alkynes and carbonyls could be effected using rhodium-based catalysts with high selectivity. Based on knowledge from the literature, there are three possible patterns for the reaction of arylboronic acids with α,β-unsaturated aldehydes such as cinnamaldehyde: conjugate addition (1,4-addition), carbonyl addition (1,2-addition) and Heck-type coupling (Scheme 1).

It is reported that the 1,2- and 1,4-reactions of arylboronic acids with cinnamaldehyde could be switched by tuning rhodium catalysts.[10] We have recently reported a sterically sensitive rhodium–phosphine biphasic system that catalysed Heck-type reaction of arylboronic acids with α,β-unsaturated esters and nitriles under aqueous conditions.[11] As a part of our continuing exploration of catalysis with the biphasic system, we investigated the possibility of switching the Heck-type coupling to 1,2-addition of arylboronic acids to α,β-unsaturated aldehydes. Unexpectedly, we uncovered a novel self-conjugate reduction, cross-coupling tandem reaction of arylboronic acids with cinnamaldehyde and analogues.

Considering the steric hindrance of cinnamaldehyde, we had originally expected a 1,2-carbonyl addition reaction with phenylboronic acid to occur using our sterically dependent biphasic catalysis system. However, reaction of 1.0 equivalent phenylboronic acid with cinnamaldehyde catalysed by 3 mol% $RhCl_3$–12 mol% PPh_3 in an aqueous/toluene biphasic system at reflux in the presence of excess K_2CO_3 gave only a trace of the expected alcohol and Heck-type coupling products. Instead, a novel conjugate reduction, cross-coupling tandem reaction occurred to produce β-phenylpropiophenone as the major product (54% by GC-MS and 40% isolated yield). The isolated yield of β-phenylpropiophenone could be increased to 59% (72% by GC-MS) using 2.0 equivalent phenylboronic acid (Scheme 2).† To the best of our knowledge, there is no literature reporting this kind of tandem reaction pattern for α,β-unsaturated aldehydes.



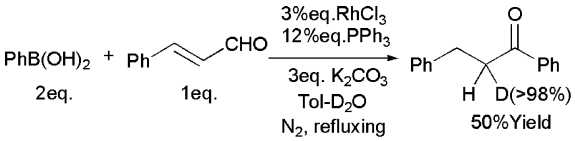
Scheme 1 Possible reaction patterns for $PhB(OH)_2$ with cinnamaldehyde catalysed by rhodium-based catalysts.



1) Ar = Ph, R = H, R' = Ph, **59**%
2) Ar = Ph, R = H, R' = *p*-$CH_3OC_6H_4$, **48**%
3) Ar = Ph, R = H, R' = *p*-$NO_2C_6H_4$, 60%
4) Ar = Ph, R = Me, R' = Ph, 45%
5) Ar = *p*-$CH_3OC_6H_4$, R = H, R' = Ph, 44%
6) Ar = Ph, R = H, R' = 2-Furyl, 58%
7) Ar = Ph, R = Et, R =*p*-$NO_2C_6H_4$, 65%

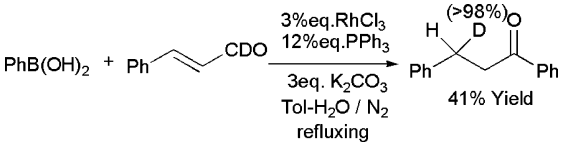
Scheme 2 Rh-catalysed self-conjugate reduction, cross-coupling tandem reaction of cinnamaldehydes with arylboronic acids.

This novel reaction pattern has been unmistakeably confirmed for substituted cinnamaldehydes such as 4-nitro (electron deficient) and 4-methoxy (electron-rich) cinnamaldehydes although acrolein and crotonaldehyde decomposed under the basic conditions. Water seemed to play an important role in the tandem process. Only traces of the desired products were detected when the reaction was conducted in pure THF or toluene. When the reaction was carried out in toluene–D_2O, one deuterium (> 98%) was incorporated into the product, β-phenylpropiophenone, at the α-position, supporting a hydrolysis of the Rh–C bond being involved in the process (eqn. 1).



(1)

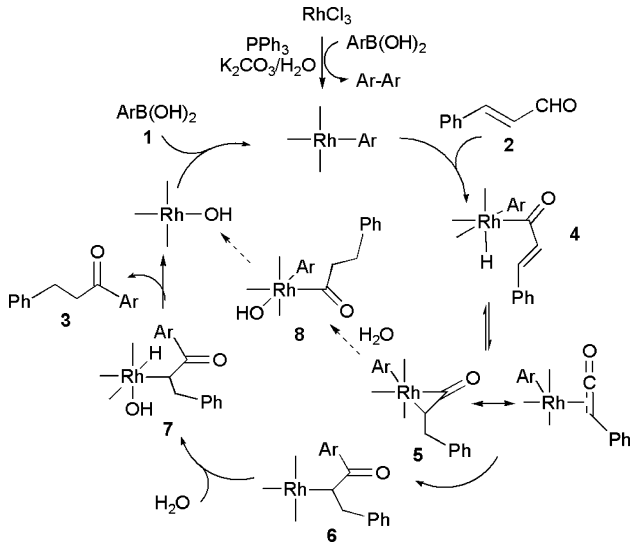
To gain further insight into the mechanism of this novel tandem process, 1-deuterated cinnamaldehyde was used to elucidate how the C=C bond of the α,β-unsaturated aldehydes was saturated while coupling with phenylboronic acid (eqn. 2). β-Deuterated (98%) β-phenylpropiophenone was isolated in 41% isolated yield with a 1 : 1 mole ratio of 1-deuterated cinnamaldehyde and phenylboronic acid, indicating that the C=C double bond of cinnamaldehyde was self-reduced by the proton from the aldehyde group.



(2)

Control experiments for the H/D exchange of cinnamaldehyde with toluene–D_2O catalysed by Wilkinson catalyst $(PPh_3)_3RhCl$ or the $RhCl_3$–PPh_3 biphasic system in the absence of phenylboronic acid showed no H/D exchange occurred in either case, implying that neither Rh^I–Cl nor Rh^I–OH species initiated the tandem process. Based on these experimental results, a plausible mechanism for this rhodium-catalysed self-conjugate reduction, cross-coupling tandem reaction of arylboronic acids **1** with cinnamaldehydes **2** is tentatively proposed (Scheme 3).[12]

DOI: 10.1039/b401511h



Scheme 3 A plausible mechanism for the novel self-conjugate reduction, cross-coupling of cinnamaldehyde with arylboronic acids.

Oxidative addition of the C–H of the aldehyde group from cinnamaldehyde **2** to the Rh^{I}–C_{Ar} species that is generated *in situ* by reduction of $RhCl_3$ with arylboronic acids initiates the tandem process, followed by an intramolecular insertion of the C=C bond to Rh–H of species **4**, affording a ketene complex/three-membered metallocyclopropanone intermediate **5**. One path to complete the self-conjugate reduction, cross-coupling tandem process involves a reductive elimination from the Rh^{III} **5** to release the strain of the metallocyclopropanone and generate a Rh^{I}–Csp^3 species **6**, which hydrolyses through oxidative addition of water to the Rh^{I} species **6** and reductive elimination from the resulting Rh^{III} **7**,[13] affording **3** and rhodium hydroxide Rh^{I}–OH that produces the initiating species Rh–Ar through a subsequent B to Rh transmetalation. The other one includes a direct hydrolysis of the metallocyclopropanone **5**, generating rhodium hydroxide **8** and reductive elimination from the hydroxide, completing the catalytic cycle after a B to Rh transmetalation. Although the latter could not be excluded, from an organometallic chemistry point of view the former path is preferred considering that Rh^{III}–Csp^3 is quite inert towards direct hydrolysis.

In conclusion, we have observed an unprecedented self-conjugate reduction, cross-coupling tandem reaction pattern between α,β-unsaturated arylaldehydes and arylboronic acids catalysed by the $RhCl_3/PPh_3$ system through a novel three-membered metallocyclopropanone intermediate. Optimisation of the procedure, investigation of the scope of the rhodium-catalysed tandem reaction and control of enantioselectivity with chiral phosphine ligands, such as BINAP, are in progress in our laboratory.

We thank Shanghai Science & Technology Council (02QA14016, 02JG05040) and NNSF, P. R. China (20242008) for financial support.

Notes and references

† General procedure for the rhodium-catalysed self-conjugate reduction, cross-coupling tandem reaction: To a suspension of phenylboronic acid (0.25 g, 2.0 mmol), $RhCl_3(H_2O)_x$ (40% Rh, 15 mg, 0.06 mmol) and PPh_3 (65 mg, 0.25 mmol) in toluene/water (15 mL/5 mL) was added cinnamaldehyde (130 μl, 1.0 mmol). The mixture was stirred at 100 °C (bath temperature) under nitrogen. The reaction progress was monitored by TLC until cinnamaldehyde was consumed (24–30 h). After cooling to room temperature, the organic phase was concentrated and purified by flash column chromatography to afford β-phenylpropiophenone (124 mg, 59% based on cinnamaldehyde). Selected spectroscopic data: NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm), ^{1}H: 7.90–8.00 (dd, J_1 = 8 Hz, J_2 = 1 Hz, 2H, Ph), 7.50–7.55 (m, 1H, Ph), 7.40–7.50 (m, 2H, Ph), 7.10–7.30 (m, 5H, Ph), 3.30 (t, J = 7 Hz, 2H, CH_2), 3.00 (t, J = 7 Hz, 2H, CH_2); ^{13}C: 199.0 (C=O), 141.0, 136.6, 132.8, 128.4, 128.3, 128.1, 127.8, 125.9, 40.1 (CH_2), 29.9 (CH_2), EI-MS, *m*/*z*: 210 (M^+, 35%), 105 (100), 77 (24).

Analytical data for α- and β-deuterated β-phenylpropiophenone: For α-deuterated β-phenylpropiophenone: NMR (300 MHz, $CDCl_3$, 25 °C), δ (ppm), ^{1}H: 7.90–8.00 (m, 2H, Ph), 7.50–7.60 (m, 1H, Ph), 7.40–7.50 (t, J = 8 Hz, 2H, Ph), 7.10–7.30 (m, 5H, Ph), 3.30 (d, J = 8 Hz, 2H, CH_2), 3.10 (m, 1H, CHD); ^{13}C: 199.1 (C=O), 141.2, 136.8, 132.9, 128.5, 128.4, 128.3, 127.9, 126.0, 39.9 (t, 75 Hz, CHD), 30.0 (CH_2), EI-MS, *m*/*z*: 211(M^+, 98%), 182 (100), 105 (100), 77 (99); HRMS (TOF-MS ES): Found: 234.1007, Calc. for $C_{15}H_{13}ODNa$: 234.1005. For β-deuterated β-phenylpropiophenone: NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm), ^{1}H: 7.90–7.95 (dd, J_1 = 8 Hz, J_2 = 1 Hz, 2H, Ph), 7.55–7.60 (m, 1H, Ph), 7.40–7.45 (t, J = 8 Hz, 2H, Ph), 7.10–7.30 (m, 5H, Ph), 3.30 (d, J = 8 Hz, 2H, CH_2), 3.05 (m, 1H, CHD); ^{13}C: 199.5 (C=O), 141.6, 137.2, 133.4, 128.9, 128.8, 128.7, 128.3, 126.4, 40.7 (CH_2), 30.1 (t, J_{C-D} = 80 Hz, CDH), EI-MS, *m*/*z*: 211 (M^+, 70%), 105 (100), 77 (50); HRMS (TOF-MS ES): Found: 234.1007, Calc. for $C_{15}H_{13}ODNa$: 234.1005.

1 For a review of Pd-catalysed Suzuki coupling: N. Miyaura and A. Suzuki, *Chem. Rev*., 1995, **95**, 2457. For a recent example see: R. B. Bedford, S. L. Hazelwood, P. N. Horton and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans*., 2003, 4164.

2 For Rh-catalysed C–C bond forming reactions: K. Fagnou and M. Lautens, *Chem. Rev*., 2003, **103**, 169.

3 For Heck-type reaction of arylboronic acids, Ru-catalysed see: E. J. Farrington, J. M. Brown, C. F. J. Barnard and E. Rowsell, *Angew. Chem., Int. Ed*., 2002, **41**, 169. For Ir-catalysed see: T. Koike, X. Du, T. Sanada, Y. Danda and A. Mori, *Angew. Chem., Int. Ed*., 2003, **42**, 89. For Pd-catalysed see: C. S. Cho and S. Uemura, *J. Organomet. Chem.*, 1994, **465**, 85.

4 For Rh-catalysed addition to alkynes: M. Lautens and M. Yoshida, *J. Org. Chem.*, 2003, **68**, 762 and to alkenes: M. Murakami and H. Igawa, *Chem. Commun.*, 2002, 390. For Pd-catalysed coupling with alkynes: G. Zou, J. Zhu and J. Tang, *Tetrahedron Lett.*, 2003, **44**, 8709; addition to alkynes: C. H. Oh, H. H. Jung, K. S. Kim and N. Kim, *Angew. Chem., Int. Ed*., 2003, **42**, 805; and to allene: C. H. Oh, T. W. Ahn and R. Reddy V., *Chem. Commun.*, 2003, 2622.

5 For Rh-catalysed 1,2-addition to aldehydes: A. Fürstner and H. Krause, *Adv. Synth. Catal.*, 2001, **343**, 343 and to aldimines: M. Ueda and N. Miyaura, *J. Organomet. Chem.*, 2002, **595**, 31.

6 For Rh-catalysed 1,4-addition: M. Sakai, H. Hayashi and N. Miyaura, *Organometallics*, 1997, **16**, 4229; R. Itooka, Y. Iguchi and N. Miyaura, *J. Org. Chem.*, 2003, **68**, 6000. For Pd-catalysed 1,4-addition: T. Nishikata, Y. Yamamoto and N. Miyaura, *Angew. Chem., Int. Ed.*, 2003, **42**, 2768.

7 For coupling with anhydrides and acid chlorides: Rh-catalysed, C. G. Frost and K. J. Wadsworth, *Chem. Commun.*, 2001, 2316; Pd-catalysed, L. J. Gooβen and K. Ghosh, *Chem. Commun.*, 2001, 2084; L. J. Gooβen and K. Ghosh, *Angew. Chem., Int. Ed.*, 2001, **40**, 3458; Y. Urawa and K. Ogura, *Tetrahedron Lett.*, 2003, **44**, 271.

8 For recent examples using arylboronic acids as nucleophile without metal catalyst: S. C. Cole, M. P. Coles and P. B. Hitchcock, *J. Chem. Soc., Dalton Trans*., 2003, 3663.

9 For asymmetric 1,4-conjugate addition: T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829; M. Kuriyama, K. Nagai, K. Yamada, Y. Miwa, T. Taga and K. Tomioka, *J. Am. Chem. Soc.*, 2002, **124**, 8932.

10 M. Ueda and N. Miyaura, *J. Org. Chem.*, 2000, **65**, 4450.

11 G. Zou, Z. Wang, J. Zhu and J. Tang, *Chem. Commun.*, 2003, 2438.

12 An alternative mechanism involving an addition of arylboronic acid to the aldehyde group, followed by Rh-catalysed 1,3-allylic hydride transfer cannot be completely excluded at present.

13 T. Yoshida, T. Okano, Y. Ueda and S. Otsuka, *J. Am. Chem. Soc.*, 1981, **103**, 3411.