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Rhodium-catalysed arylative annulation of 1,4-enynes with arylboronic acids

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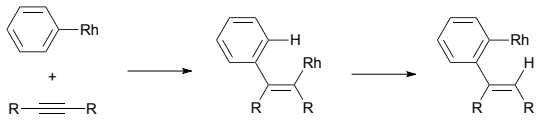
The rhodium(I)-catalysed arylative annulation of 1,4-enynes with arylboronic acids was investigated. The reaction was found to proceed via an addition–1,4-rhodium migration–addition sequence, affording the corresponding 1,1-disubstituted 3-(arylmethylene)indanes.

Rhodium-catalysed cyclisation and annulation reactions using arylboron compounds have proven to be highly useful and broadly applicable methods for obtaining a wide range of cyclic compounds.[1] Intramolecular activation of a neighbouring C–H bond can proceed via a 1,4-rhodium migration,[2,3,4] and is sometimes observed in rhodium(I)-catalysed arylation reactions. This migration allows for the regeneration of arylrhodium(I) species from (*Z*)-arylalkenylrhodium(I) intermediates, which are formed from the addition of an arylrhodium(I) species to an alkyne. This offers a novel strategic approach for the formation of carbon frameworks which are otherwise difficult to prepare (Scheme 1).

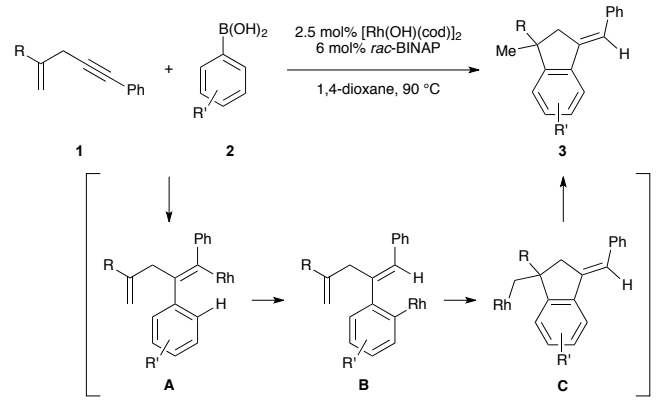


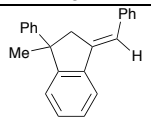
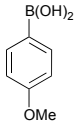
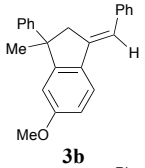
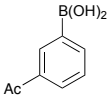
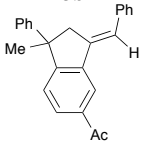
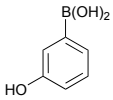
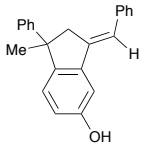
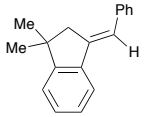
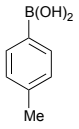
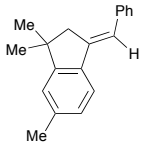
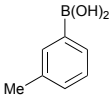
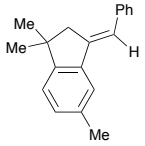
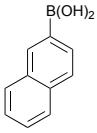
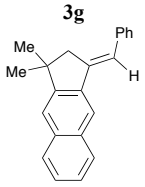
Scheme 1 Rhodium(I) catalysed arylation of an alkyne and regeneration of arylrhodium(I) species via a 1,4-rhodium migration

Further exploration of the utility of this process will greatly benefit the development of new cyclisation and annulation reactions. Our recent success with the rhodium(I)-catalysed spirocyclisation reaction involving 1,4-rhodium migration[3] led us to examine the rhodium(I)-catalysed arylation of 1,4-enynes,[5] with the intent to promote an annulation reaction encompassing the aforesaid migration. Gratifyingly, the rhodium(I)-catalysed arylation of 1,4-enynes resulted in an annulation reaction, forming 3-(arylmethylene)indanes via 1,4-rhodium migration.

2,5-Diphenylpent-1-en-4-yne (**1a**) was selected as the initial substrate for the rhodium(I)-catalysed arylation with phenylboronic acid (**2a**). The reaction of **1a** and **2a** (3 equiv. to **1a**) was performed in 1,4-dioxane at 90 °C in the presence of 2.5 mol% $[Rh(OH)(cod)]_2$[6]; however, this resulted in no conversion. In contrast, the use of *rac*-BINAP[6] as the ligand afforded (*E*)-3-benzylidene-1-methyl-1-phenylindane (**3a**) in 77% isolated yield (Table 1, entry 1).[7,8,9,10] The product **3a** was obtained through arylative annulation involving (i) regioselective addition of an aryl rhodium species to an alkyne moiety, generating (*Z*)-arylalkenylrhodium(I) species **A**; (ii) a 1,4-rhodium migration giving arylrhodium(I) species **B**; (iii) intramolecular addition to the pendant alkene moiety, generating indanylmethylrhodium(I) **C**; and (iv) protonation. The reaction of **1a** with substituted phenylboronic acids **2b–d** also gave the corresponding annulation products **3b–d** in 59–73% yields (entries 2–4). When *meta*-substituted phenylboronic acids **2c** and **2d** were used, the 1,4-rhodium migration occurred at the more sterically accessible site on the aromatic ring, resulting in the formation of a single product (entries 3 and 4). Under identical conditions, the arylative annulation of 5-phenyl-2-methylpent-1-en-4-yne (**1b**) with **1a** produced dimethylindane **3e** in low yield due to undesirable intermolecular reactions (entry 5). Further optimisation of the reaction conditions increased the yield of **3e** to 67% when 1.5 equiv. of Et_3N was added (entry 6). Arylboronic acids **2d–f** coupled with enyne **1b**, under the optimised conditions employing Et_3N, afforded the corresponding indanes **3f–h** (entries 7–9). Single isomers **3g** and **3h** were obtained in the reactions with **2e** and **2f**, respectively (entries 8 and 9).[11]

Table 1 Arylative annulation of 1,4-enynes[a]



Entry	**1** (R)	**2**	**3**	Yield[b] (%)
1	**1a** (Ph)	 **2a**	 **3a**	77
2	**1a**	 **2b**	 **3b**	73
3	**1a**	 **2c**	 **3c**	71
4	**1a**	 **2d**	 **3d**	59
5	**1b** (Me)	**2a**	 **3e**	43
6[c]	**1b**	**2a**	**3e**	67
7[c]	**1b**	 **2d**	 **3f**	66
8[c]	**1b**	 **2e**	 **3g**	48
9[c]	**1b**	 **2f**	 **3h**	68

[a] Reaction conditions: 1,4-Enyne **1** (0.10 mmol), arylboronic acid **2** (0.30 mmol), $[Rh(OH)(cod)]_2$ (2.5 μmol, 5 mol% Rh), *rac*-BINAP (6.0 μmol), 1,4-dioxane (1.0 mL), 90 °C, 2–4 h. [b] Isolated yield. [c] Et_3N (0.15 mmol) was added.

The substrate scope of the annulation reaction was further investigated by coupling various 1,4-enynes **1c**–**k** with boronic acid **2a** (Table 2). The reaction of 5-phenyl-2-methylpent-1-en-4-ynes **1c**–**e** bearing substituents on the phenyl ring provided the corresponding 3-(arylmethylene)indanes **3i**–**k** in 67–69% yields (entries 1–3). Arylative annulation was applied to 2,5-diarylpent-1-en-4-ynes **1f**–**h**, affording indanes **3l**–**n** (entries 4–6). Ester and siloxy-substituted 1,4-enynes (**1f** and **1g**) also participated in the annulation reaction (entries 7 and 8). As well, alkenyl(alkynyl)silane **1h** was converted into 2-silaindane **3n** (entry 9). However, the

reactions using 5-phenylpent-1-en-4-yne and 1,1-dimethyl-5-phenylpent-1-en-4-yne led to complex mixtures.[12]

Table 2 Arylative annulation of various 1,4-enynes **1**[a]

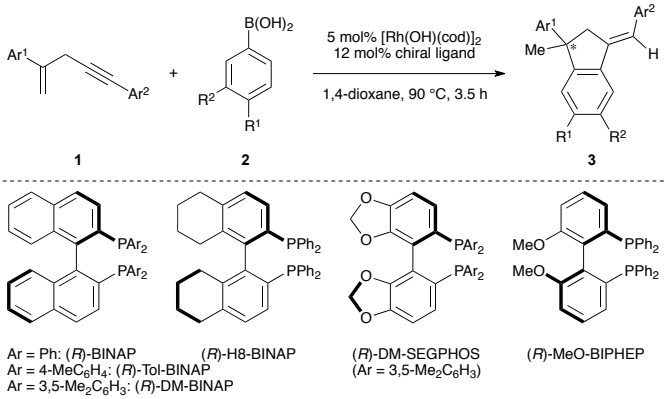
Entry	1	2	3	Yield[b] (%)
1	**1c** (Ar = 4-MeC_6H_4)	**2a**	**3i**	68
2	**1d** (Ar = 2-MeC_6H_4)	**2a**	**3j**	67
3	**1e** (Ar = 4-$MeOC_6H_4$)	**2a**	**3k**	69
4[c,d]	**1f**	**2b**	**3l**	72[e]
5[c,d]	**1g**	**2a**	**3m**	70[e]
6[c,d]	**1h**	**2b**	**3n**	66[e]
7[d]	**1i**	**2a**	**3o**	51
8	**1j**	**2a**	**3p**	50
9	**1k**	**2a**	**3q**	49

[a] Reaction conditions: 1,4-Enyne **1** (0.10 mmol), arylboronic acid **2** (0.30 mmol), $[Rh(OH)(cod)]_2$ (2.5 μmol, 5 mol% Rh), *rac*-BINAP (6.0 μmol), 1,4-dioxane (1.0 mL), Et_3N (1.5 mmol), 90 °C, 2–4.5 h. [b] Isolated yield. [c] The reaction was performed with $[Rh(OH)(cod)]_2$ (5.0 μmol) and *rac*-BINAP (12.0 μmol). [d] The reaction was performed without adding Et_3N. [e] Yields with 5 mol% Rh catalyst: **3l** (60%); **3m** (57%); **3n** (49%).

The asymmetric induction occurring at the intramolecular addition step was then investigated. This was accomplished by employing optically active diphosphine ligands, thereby constructing chiral all-carbon quaternary centres at the benzylic position (Table 3).

The reaction of **1a** and **2a** employing (*R*)-BINAP as the ligand afforded indane **3a** in 70% yield, with an enantiomeric excess (ee) of 76% (entry 1). Screening of other chiral diphosphine ligands considered in this study revealed that MeO-BIPHEP displayed the highest enantioselectivity (entries 2–6).[13] With (*R*)-MeO-BIPHEP as the ligand of choice,[14] the asymmetric annulation of enyne **1a** with arylboronic acids **2b–d** gave the corresponding products **3b–d** in good yields with over 87% ee (entries 7–9). 2,5-Diaryl 1,4-enynes **1f–h** cyclised with either **2a** or **2b** to afford indanes **3l–n** with enantioselectivities ranging from 84% to 90% ee (entries 10–12).

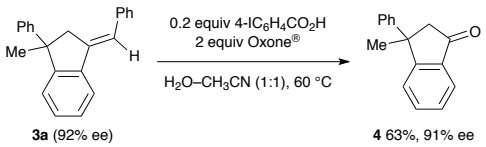
Table 3 Asymmetric arylative anulation[a]



Entry	1	2	Ligand	3	Yield[b] (%)	ee[c] (%)
1[d]	**1a**	**2a**	(*R*)-BINAP	**3a**	70	76
2[d]	**1a**	**2a**	(*R*)-Tol-BINAP	**3a**	76	75
3[d]	**1a**	**2a**	(*R*)-DM-BINAP	**3a**	57	42
4[d]	**1a**	**2a**	(*R*)-H8-BINAP	**3a**	51	82
5[d]	**1a**	**2a**	(*R*)-DM-SEGPHOS	**3a**	58	81
6	**1a**	**2a**	(*R*)-MeO-BIPHEP	**3a**	72	92
7	**1a**	**2b**	(*R*)-MeO-BIPHEP	**3b**	72	87
8	**1a**	**2c**	(*R*)-MeO-BIPHEP	**3c**	70	91
9	**1a**	**2d**	(*R*)-MeO-BIPHEP	**3d**	61	89
10	**1f**	**2b**	(*R*)-MeO-BIPHEP	**3l**	75	84
11	**1g**	**2a**	(*R*)-MeO-BIPHEP	**3m**	64	90
12	**1h**	**2b**	(*R*)-MeO-BIPHEP	**3n**	70	86

[a] Reaction conditions: 1,4-Enyne **1** (0.10 mmol), arylboronic acid **2** (0.30 mmol), $[Rh(OH)(cod)]_2$ (5.0 μmol, 10 mol% Rh), chiral ligand (12.0 μmol), 1,4-dioxane (1.0 mL), 90 °C, 3.5 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The reaction was performed with 2.5 mol% $[Rh(OH)(cod)]_2$ and 6 mol% diphosphine ligand.

Alkylideneindanes **3** obtained by the annulation can be derivatised into more useful structures. For example, oxidative cleavage of **3a** (92% ee) with an in situ generated iodonium ion with Oxone® delivered 3-methyl-3-phenylindanone **4** in 63% yield and 91% ee (eqn (1)).[15]



(1)

In summary, we have developed a rhodium(I)-catalysed annulation reaction of 1,4-enynes with arylboronic acids, utilizing a 1,4-rhodium migration as a means for regenerating arylrhodium(I) species. Various substituted indane products were obtained in good yields through this reaction. By using a rhodium(I)–chiral diphosphine catalyst, a chiral all-carbon

quaternary centre at the benzylic position was constructed with an enantioselectivity of up to 92% ee.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures and characterisation data for new compounds. See DOI: 10.1039/c000000x/

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3 T. Matsuda, Y. Suda and A. Takahashi, *Chem. Commun.*, 2012, **48**, 2988.

4 For analogous 1,3- and 1,5-rhodium migrations, see: (*a*) Y. Shimamoto, T. Yano and M. Murakami, *J. Am. Chem. Soc.*, 2013, **135**, 19103; (*b*) J. Zhang, P. Zhao, J.-F. Liu, A. Ugrinov, A. F. X. Pillai and Z.-M. Sun, *J. Am. Chem. Soc.*, 2013, **135**, 17270; (*c*) C. M. So, S. Kume, T. Hayashi, *J. Am. Chem. Soc.*, 2013, **135**, 10990; (*d*) M. Tobisu, J. Hasegawa, Y. Kita, H. Kinuta and N. Chatani, *Chem. Commun.*, 2012, **48**, 11437.

5 For rhodium-catalysed arylation reactions of 1,5- and 1,6-enynes, see: (*a*) R. Shintani, K. Okamoto, Y. Otomaru, K. Ueyama and T. Hayashi, *J. Am. Chem. Soc.*, 2005, **127**, 54; (*b*) T. Miura, M. Shimada and M. Murakami, *J. Am. Chem. Soc.*, 2005, **127**, 1094; (*c*) R. Shintani, A. Tsurusaki, K. Okamoto and T. Hayashi, *Angew. Chem., Int. Ed.*, 2005, **44**, 3909; (*d*) T. Miura, M. Shimada and M. Murakami, *Chem. Asian J.*, 2006, **1**, 868; (*e*) M. Shimada, T. Harumashi, T. Miura and M. Murakami, *Chem. Asian J.*, 2008, **3**, 1035. (*f*) X. Fang, C. Li and X. Tong, *Chem. Commun.*, 2009, 5311. (*g*) R. Shintani, S. Isobe, M. Takeda and T. Hayashi, *Angew. Chem., Int. Ed.*, 2010, **49**, 3795; (*h*) J. Keilitz, S. G. Newman and M. Lautens, *Org. Lett.*, 2013, **15**, 1148.

6 Abbreviations: COD = cycloocta-1,5-diene; BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

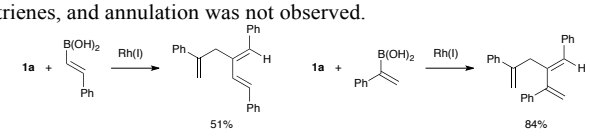
7 For selected recent examples of transition-metal-catalysed cyclisation and annulation reactions giving 1-alkylideneindanes, see: (*a*) A. B. Machotta, B. F. Straub and M. Oestreich, *J. Am. Chem. Soc.*, 2007, **129**, 13455; (*b*) L.-N. Guo, X.-H. Duan, J. Hu, H.-P. Bi, X.-Y. Liu and Y.-M. Liang, *Eur. J. Org. Chem.*, 2008, 1418; (*c*) E. Marchal, J.-F. Cupif, P. Uriac and P. van de Weghe, *Tetrahedron Lett.*, 2008, **49**, 3713; (*d*) X. Wang, L. Liu, W. Chang and J. Li, *Eur. J. Org. Chem.*, 2010, 5391; (*e*) N. Chernyak, S. I. Gorelsky and V. Gevorgyan, *Angew. Chem., Int. Ed.*, 2011, **50**, 2342; (*f*) P. Xing, Z.-g. Huang, Y. Jin and B. Jiang, *Tetrahedron Lett.*, 2013, **54**, 699; (*g*) E. R. Fruchey, B. M. Monks, A. M. Patterson and S. P. Cook, *Org. Lett.*, 2013, **15**, 4362; (*h*) D. N. Tran, and N. Cramer, *Angew. Chem., Int. Ed.*, 2013, **52**, 10630.

8 The reaction with 1.2 equiv. of $PhB(OH)_2$ failed to achieve complete conversion of **1a**.

9 The following results were obtained with other ligands: PPh_3 (complex mixture); P(*t*-Bu)$_3$ (complex mixture); 1,4-bis(diphenylphosphino)butane (51%); 2,2′-bis(diphenylphosphino)-1,1′-biphenyl (75%).

10 The reactions performed in THF and in MeOH led to the formation of complex mixtures of products.

11 The use of alkenylboronic acids instead of arylboronic acids gave trienes, and annulation was not observed.



12 2-Phenylpent-1-en-4-yne (a terminal alkyne) and 2,6-diphenylhex-1-en-5-yne (the one-carbon longer homolog of **1a**) also gave complex mixtures of products.

13 Because of the formation of inseparable byproducts, the selectivity of the reaction with SEGPHOS and C3-TunePhos could not be determined.

14 The catalyst with MeO-BIPHEP showed diminished activity (required 10 mol% Rh to achieve full conversion) when compared to those with other diphosphine ligands.

15 P. P. Thottumkara and T. K. Vinod, *Org. Lett.*, 2010, **12**, 5640.