

Rhodium-catalyzed carbonylative arylation of alkynes with arylboronic acids: an efficient and straightforward method in the synthesis of 5-aryl-2(5*H*)-furanones†

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5-Aryl-2(5*H*)-furanones can be synthesized by the Rh-catalyzed reactions of arylboronic acids with internal alkynes under a CO atmosphere.

Since Hayashi *et al.* reported the first Rh-catalyzed addition of aryl- and alkenylboronic acids to α,β -unsaturated ketones,¹ the Rh-catalyzed addition of organoboron reagents to various unsaturated systems has become increasingly popular as a method of constructing C–C bonds. Organoboron reagents readily undergo transmetalation with Rh to form arylrhodium(I) species that are capable of inducing the nucleophilic arylation of various electrophilic sites.^{1,2} It was also shown recently that the Rh-catalyzed reaction of arylboronic acids with terminal α,β -unsaturated ketones in a CO atmosphere yielded 1,4-diketones.³

In this paper, we present another example of the Rh-catalyzed reaction of arylboronic acids: a reaction of arylboronic acids with alkynes under a CO atmosphere to yield 2(5*H*)-furanones (2-butenolides).

Carbonylation of a phenylboronic acid and diphenyl acetylene mixture (in the ratio 3 : 1) in the presence of [RhCl(COD)]₂ (3% Rh) in dioxane solvent under 20 atm CO pressure at 120 °C for 16 h yielded 3,4,5-triphenylfuran-2(5*H*)-one (**3a**) as the major product, in addition to small amounts of 2,3-diphenyl-1*H*-inden-1-one (**4a**), 2,3-dihydro-2,3-diphenylinden-1-one (**5a**), and the *Z*- and *E*-stereoisomers of 1,2,3-triphenylprop-2-ene-1-one (**6a**) carbonylation products (Scheme 1) (Table 1, entry 1).‡

A direct carbonylation product of phenylboronic acid, benzaldehyde, was also produced by the reaction in significant amounts (45 mol% on the basis of the initial phenylboronic acid quantity). Addition of PPh₃ ligand or NEt₃ base to the reaction medium significantly reduced the formation of **3a** product (Table 1, entries 2 and 3). The reaction was observed to proceed less selectively in a

dioxane–water (9 : 1) mixture (Table 1, entry 4). The presence of water increased the formation of **4a**, **5a** and **6a** products, while formation of **3a** was greatly reduced. Use of a pre-dried dioxane solvent (dried over the molecular sieve 4A) lessened the formation of benzaldehyde and **6a** to trace amounts (Table 1, entry 5). However, the presence of 1 g of the molecular sieve 4A in the reaction medium appeared to be detrimental to the efficiency and selectivity of the process (Table 1, entry 6).

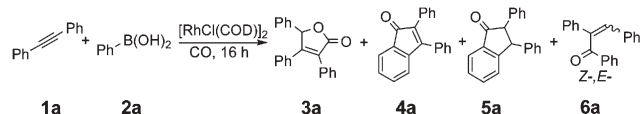
We postulate here a sequential insertion of CO–alkyne–CO leading to the formation of 2(5*H*)-furanones (Scheme 2): It is generally accepted that an arylrhodium(I) species (**A**) is formed by the transmetalation of Rh(I) compounds with organoborons.² The arylrhodium(I) could then insert into CO to give an arylrhodium(I) species (**B**), which then undergoes a 1,2-addition to the carbon–carbon triple bond. Insertion of the resulting β -aryloxy alkenylrhodium(I) complex (**C**) into CO, followed by a ring closure, could form a σ -furanoyl complex (**D**). Displacement of Rh from the cyclic complex by protonation leads to a 5-aryl-2(5*H*)-furanone molecule (**3**).⁴ The source of the proton should be mainly the arylboronic acid itself and its decomposition products.

The enhanced formation of benzaldehyde and other side products in moist dioxane could arise from a promoted hydrogen transfer in the form of H⁺ or from a water–gas shift reaction.

The optimum reaction temperature was determined to be 80 °C (Table 1, entries 7 and 8). The formation of by-products was greatly reduced at this temperature. However, no activity was observed at 60 °C in dioxane solvent. Decreasing the Rh concentration to 1 mol% on the basis of alkyne reduced the formation of **3a** (Table 1, entry 9).

The reaction was more efficient for the formation of **3a** when performed in dry toluene and the formation of other side products were minimized (Table 1, entry 10). Compared to dioxane, the smaller moisture content of toluene and its water immiscible nature is probably a significant factor in the diminution of the side reactions. The reaction also proceeded successfully in the case of a lower Rh concentration of 1% (Table 1, entry 11). Furthermore, the catalyst loading could also be lowered to 0.3% Rh with only a small sacrifice in the product formation (Table 1, entry 12). In contrast to the reaction in dioxane, performing the reaction at 60 °C afforded a moderate **3a** yield (Table 1, entry 13). The method does not require large excesses of boronic acids, since the reaction was also remarkably effective at a phenylboronic acid : diphenyl acetylene ratio of 1.2 (Table 1, entry 14).

The synthesis of furan-2(5*H*)-ones (2-butenolides) are of great interest since some derivatives of these compounds occur naturally and possess significant biological activity.⁵ Numerous transition



Scheme 1 Rhodium(I)-catalyzed carbonylative addition of phenylboronic acid to diphenylacetylene.

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† Electronic supplementary information (ESI) available: Description and NMR spectra of samples.

Table 1 Rhodium(I)-catalyzed reaction of phenylboronic acid and diphenyl acetylene under CO pressure^a

Entry	Solvent	Rh (%)	2a : 1a	T/°C	Conversion (%)	3a (%) ^b	4a(%) ^b	5a(%) ^b	6a(%) ^b
1	Dioxane	3	3	120	>99	70	5	15	11
2	Dioxane ^c	3	3	120	>99	44	15	15	<1
3	Dioxane ^d	3	3	120	>99	39	7	7	<1
4	Dioxane-H ₂ O (9 : 1)	3	3	120	>99	39	11	24	20
5	Dioxane ^e	3	3	120	>99	74	4	9	<1
6	Dioxane ^{e,f}	3	3	120	>99	43	9	16	<1
7	Dioxane ^e	3	3	100	>99	80	2	5	<1
8	Dioxane ^e	3	3	80	>99	86	2	3	1
9	Dioxane ^e	1	3	80	88	63	2	4	1
10	Toluene ^e	3	3	80	>99	90	<1	<1	<1
11	Toluene ^e	1	3	80	>99	85	1	<1	<1
12	Toluene ^e	0.3	3	80	95	81	2	1	<1
13	Toluene ^e	1	3	60	63	43	<1	<1	<1
14	Toluene ^e	1	1.2	80	>99	89 (78)	2	1	<1

^a Reaction conditions: 1 mmol **1a**, 10 mL solvent, 20 atm CO, 16 h. ^b GC yield, isolated yield is given within parentheses. ^c In the presence of 0.06 equiv. PPh₃. ^d In the presence of 2 mmol NEt₃. ^e Dried over molecular sieve 4A. ^f In the presence of 1 g of molecular sieve 4A.

metal-catalyzed methods have been exploited for the synthesis of multi-functional lactones. These methods usually involve carbonylative or non-carbonylative cyclization of unsaturated reagents functionalized by hydroxyl or carboxyl groups and the cyclo-carbonylation of acetylenes.⁶ The former methods usually suffer from the scarcity of the starting organic reagents, which require complicated synthetic routes. In contrast, alkynes are more readily available reagents.

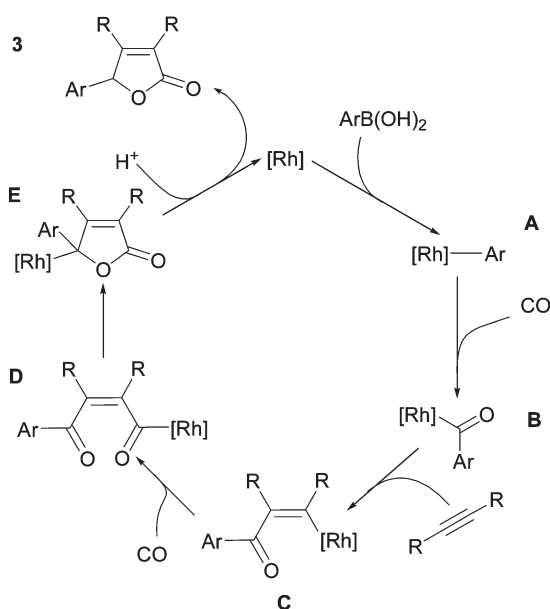
There are only a few reports on the carbonylative synthesis of 5-aryl-substituted furanones in the literature. The Pd(II)-catalyzed cyclocarbonylation of 3-aryl-1-propynes and iodoarenes or acyl chlorides, in the presence of Pd(OAc)₂ (5 mol%), PPh₃ ligand and Et₃N base under ~20–80 atm CO pressure, led to fair-to-good yields of *E*-3-arylbutenolides.⁷ The Rh-catalyzed cyclohydrocarbonylation of α -keto alkynes^{4c} and Ru-catalyzed cyclocarbonylation of allenyl alcohols⁸ yielded related multi-functional lactones. Negishi *et al.* employed two carbonylative methods in the synthesis of 5-arylated furanones.⁹ Good yields were obtained

via carbonylation of *Z*- β -iodoenones in the presence of PdCl₂(PPh₃)₂ catalyst and Et₃N base at 100–140 °C, whereas a more direct method, the Pd-catalyzed carbonylative addition of aryl iodides to internal alkynes, proceeded less effectively, giving fair-to-moderate yields.

Our methodology was well applicable to *para*-substituted arylboronic acids (Table 2, entries 2–5) under the optimized conditions given above. Electron rich arylboronic acids were sufficiently reactive with diphenyl acetylene (Table 2, entries 2 and 3). Modest furanone product was recovered with an electron deficient arylboronic acid, 4-(trifluoromethyl)phenylboronic acid, at a Rh concentration of 1% (Table 2, entry 4), probably due to its poor ability to insert carbon monoxide. However, a higher yield for the corresponding furanone product succeeded at a Rh concentration of 3% (Table 2, entry 5).

ortho-Tolylboronic acid failed in the carbonylative addition to diphenyl acetylene, probably owing to steric reasons. The alkyne conversion was about 50% with *ortho*-tolylboronic acid, and the reaction yielded 1-methyl-2-((*E*)-1,2-diphenylvinyl)benzene as the primary arylation product. It seems that although arylrhodium(I) species are capable of insertion into alkynes, the *ortho*-substituted arylrhodium(I) intermediate was not reactive enough for the 1,2-addition to the carbon–carbon triple bond.

As an alkyl-substituted acetylene, 4-octyne also displayed high activity, providing a high furanone yield (Table 2, entry 6).



Scheme 2 Proposed mechanism for the carbonylative addition of boronic acids to alkynes.

Table 2 Rhodium(I)-catalyzed reaction of arylboronic acid and alkynes under CO pressure

Entry	R ₁	R ₂	Isolated yield (%)
1	Ph	H	78 (3a)
2	Ph	CH ₃	77 (3b)
3	Ph	OCH ₃	82 (3c)
4	Ph	CF ₃	40, 47 (3d)
5	Ph	CF ₃	93 ^a (3e)
6	n-C ₃ H ₇	H	80 (3e)

^a With 3 mol% Rh, GC yield.

However, the method was unsuccessful with a terminal alkyne, phenyl acetylene, even though no acetylene substrate could be recovered at the end of the reaction. Here, the propensity of the terminal alkyne to undergo polymerization might have disfavored the carbonylation pathway.

In summary, the methodology established in this study proposes a relatively mild and simple way for the synthesis of 5-aryl substituted 2(5*H*)-furanones (2-butenolides). The application of the process to a variety of alkyne and organoboron reagents for the selective formation of other products, given in Scheme 1, and for other unsaturated systems, is under way to expand the scope of the methodology.

Notes and references

‡ Representative conditions for the synthesis of **3a** (conditions of Table 1, entry 14): A mixture of alkyne (1 mmol), arylboronic acid (1 mmol), [RhCl(COD)]₂ (0.005 mmol, 1 mol% Rh) and 10 mL toluene (pre-dried) was added into a 50 mL stainless steel autoclave with a glass insert tube. The sealed autoclave was then evacuated and purged twice successively with 10 atm CO. Subsequently, the reactor was pressurized to 20 atm with CO and the mixture stirred magnetically in a pre-heated oil bath. After cooling, the reaction mixture was recovered with ethyl acetate and extracted with a brine solution. The products were analyzed by GC and GC-MS and isolated by column chromatography.

- 1 M. Sakai, H. Hayashi and N. Miyaura, *Organometallics*, 1997, **16**, 4229.
- 2 For reviews, see: (a) K. Fagnou and M. Lautens, *Chem. Rev.*, 2003, **103**, 169; (b) T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829. For recent examples, see: (c) M. Sakai, M. Ueda and N. Miyaura, *Angew. Chem., Int. Ed.*, 1998, **37**, 3279; (d) K. Oguma, M. Miura, T. Satoh and

- M. Nomura, *J. Am. Chem. Soc.*, 2000, **122**, 10464; (e) C. G. Frost and K. J. Wadsworth, *Chem. Commun.*, 2001, 2316; (f) M. Lautens, A. Roy, K. Fukuoka, K. Fagnou and B. Martín-Matute, *J. Am. Chem. Soc.*, 2001, **123**, 5358; (g) T. Hayashi, K. Inoue, N. Taniguchi and M. Ogasawara, *J. Am. Chem. Soc.*, 2001, **123**, 9918; (h) K. Oguma, M. Miura, T. Satoh and M. Nomura, *J. Organomet. Chem.*, 2002, **648**, 297; (i) M. Lautens, C. Dockendorff, K. Fagnou and A. Malicki, *Org. Lett.*, 2002, **4**, 1311; (j) T. Matsuda, M. Makino and M. Murakami, *Org. Lett.*, 2004, **6**, 1257; (k) T. Miura, M. Shimada and M. Murakami, *Angew. Chem., Int. Ed.*, 2005, **44**, 7598; (l) K. Ueura, T. Satoh and M. Miura, *Org. Lett.*, 2005, **7**, 2229; (m) R. Shintani, A. Tsurusaki, K. Okamoto and T. Hayashi, *Angew. Chem., Int. Ed.*, 2005, **44**, 3909; (n) R. Shintani, W.-L. Duan, T. Nagano, A. Okada and T. Hayashi, *Angew. Chem., Int. Ed.*, 2005, **44**, 4614.
- 3 M. Sauthier, Y. Castanet and A. Mortreux, *Chem. Commun.*, 2004, 1520.
- 4 (a) T. Mise, P. Hong and H. Yamazaki, *J. Org. Chem.*, 1983, **48**, 238; (b) T. Joh, K. Doyama, K. Onitsuka, T. Shiohara and S. Takanashi, *Organometallics*, 1991, **10**, 2493; (c) B. G. Van den Hoven, B. El Ali and H. Alper, *J. Org. Chem.*, 2000, **65**, 4131.
- 5 (a) Y. S. Rao, *Chem. Rev.*, 1976, **76**, 625; (b) G. V. Rao and R. B. Cain, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2111; (c) S. Handa, *Tetrahedron: Asymmetry*, 1996, **7**, 7565; (d) S. V. Ley, L. R. Cox and G. Meek, *Chem. Rev.*, 1996, **96**, 423; (e) E. Negishi and M. Kotora, *Tetrahedron*, 1997, **53**, 6707; (f) *Comprehensive Natural Products Chemistry*, ed. D. H. R. Barton, K. Nakanishi and O. Meth-Cohn, Elsevier Science Ltd., Oxford, 1999, vol. **8**, pp. 378–385.
- 6 For reviews, see: (a) B. El Ali and H. Alper, *Synlett*, 2000, 161; (b) S. S. Vizer, K. B. Yerzhanov, A. A. Al Quntar and V. M. Dembitsky, *Tetrahedron*, 2004, **60**, 5499.
- 7 Y. Huang and H. Alper, *J. Org. Chem.*, 1991, **56**, 4534.
- 8 E. Yoneda, S.-W. Zhang, D.-Y. Zhou, K. Onitsuka and S. Takahashi, *J. Org. Chem.*, 2003, **68**, 8571.
- 9 C. Copéret, T. Sugihara, G. Wu, I. Shimoyama and E.-i. Negishi, *J. Am. Chem. Soc.*, 1995, **117**, 3422.