ORGANOMETALLICS

Volume 16, Number 20, September 30, 1997

Communications

Rhodium-Catalyzed Conjugate Addition of Aryl- or 1-Alkenylboronic Acids to Enones

Masaaki Sakai, Hiroyuki Hayashi, and Norio Miyaura*

Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060, Japan

Received June 16, 1997[⊗]

Summary: The rhodium(I)-catalyzed conjugate addition of aryl- or 1-alkenylboronic acids to enones was carried out in high yields at 50 °C in an aqueous solvent. A combination of (acac)Rh(CO)$_2$ and dppb was recognized to be highly effective for the addition to acyclic and cyclic enones.

The conjugated addition of organometallic reagents to enones is a powerful tool for appending organic residues to cyclic and acyclic substrates. Although organocopper complexes have been widely used,[1] other related reactions induced by transition metals have provided additional applications and extensions of this protocol. Ni(acac)$_2$ or PdCl$_2$ catalyzes the conjugate addition of organozinc,[2] -zirconium,[3] -aluminum,[4] -mercury compounds[5] to enones. The addition of terminal alkynes to α,β-unsaturated ketones and esters with RhCl(PMe$_3$)$_3$[6a] or H$_2$Ru(PBu$_3$)$_4$[6b,c] and the Michael addition of activated nitriles or esters with ruthenium(II)[7a] or rhodium(I)[7b] complexes have been extensively studied. The corresponding reactions or organoboron compounds have not yet been well developed, but the addition of NaBPh$_4$ or arylboronic acids to enones with Pd(OAc)$_2$ in the presence of NaOAc or SbCl$_3$ was

Table 1. Addition of Phenylboronic Acid to MVK or 2-Octen-3-one[a]

			yield/%[b]	
entry	ligand (equivs)	solvent	MVK	2-octen-3-one
1	PBu$_3$ (3)	DMF/H$_2$O	93	
2	PPh$_3$ (3)	DMF/H$_2$O	83	0
3	AsPh$_3$	DMF/H$_2$O		0
4	TFP[c] (3)	DMF/H$_2$O	94	12
5	dppe[d] (1)	DMF/H$_2$O	70	0
6	dppp[e] (1)	DMF/H$_2$O	97	19
7	dppb[e] (1)	DMF/H$_2$O	99	28
8	dppb[e] (1)	DMF	91	
9	dppb[e] (1)	toluene/H$_2$O		34
10	dppb[e] (1)	cyclohexane/H$_2$O		61
11	dppb[e] (1)	MeOH/H$_2$O		96
12	dppb[e] (1)	MeOH		0

[a] All reactions were carried out at 50 °C for 16 h using PhB(OH)$_2$ (1.3 mmol), methyl vinyl ketone (MVK) or 2-octen-3-one (1.0 mmol), (acac)Rh(CO)$_2$ (0.03 mmol), and an additional ligand (0.03 or 0.09 mmol) in aqueous solvent (6/1, 7 mL). [b] GC yields based on the enones. [c] Trifurylphosphine. [d] 1,2-Bis(diphenylphosphino)ethane. [e] 1,3-Bis(diphenylphosphino)propane. [f] 1,4-Bis(diphenylphosphino)butane.

[⊗] Abstract published in *Advance ACS Abstracts*, September 1, 1997.

(1) (a) Posner, G. H. *Org. React.* **1972**, *19*, 1. (b) Lipshutz, B. H. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: New York, 1994; pp 283−382.

(2) Greene, A. E.; Lansard, J.-P.; Luche, J.-L.; Petrier, C. *J. Org. Chem.* **1984**, *49*, 931. Petrier, C.; Barbosa, J. C. S.; Dupuy, C.; Luche, J.-L. *J. Org. Chem.* **1985**, *50*, 5761. Soai, K.; Hayasaka, T.; Ugajin, S. *J. Chem. Soc., Chem. Commun.* **1989**, 516. Bolm, C. *Tetrahedron: Asymmetry* **1991**, *2*, 701.

(3) (a) Loots, M. J.; Schwartz, J. *J. Am. Chem. Soc.* **1977**, *99*, 8045. (b) Dayrit, F. M.; Gladkowski, D. E.; Schwartz, J. *Ibid.* **1980**, *102*, 3976.

(4) Ashby, E. C.; Heinsohn, G. *J. Org. Chem.* **1974**, *39*, 3297. Hansen, R. T.; Carr, D. B.; Schwartz, J. *J. Am. Chem. Soc.* **1978**, *100*, 2244.

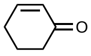
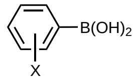
(5) Cacchi, S.; Palmieri, G. *J. Organomet. Chem.* **1985**, *282*, C3.

(6) (a) Nikishin, G. I.; Kovalev, I. P. *Tetrahedron Lett.* **1990**, *31*, 7063. (b) Mitsudo, T.; Nakagawa, Y.; Watanabe, K.; Hori, Y.; Misawa, H.; Watanabe, H.; Watanabe, Y. *J. Org. Chem.* **1985**, *50*, 565. (c) Trost, B. M. *Angew. Chem.* **1995**, *107*, 285.

(7) (a) Murahashi, S.-I.; Naota, T.; Taki, H.; Mizuno, M.; Takaya, H.; Komiya, S.; Mizuno, Y.; Oyasato, N.; Hiraoka, M.; Hirano, M.; Fukuoka, A. *J. Am. Chem. Soc.* **1995**, *117*, 12436. (b) Sawamura, M.; Sudoh, M.; Ito, Y. *Ibid.* **1996**, *118*, 3309.

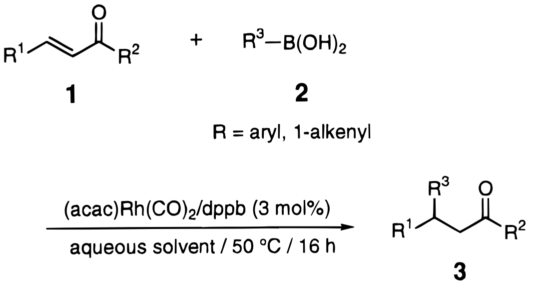
S0276-7333(97)00511-6 CCC: $14.00 © 1997 American Chemical Society

Table 2. Rhodium-Catalyzed Conjugate Addition of Arylboronic Acids (Eq 1)[a]

entry	arylboronic acid	X	enone	yield/%[b]		
				A[c]	B[d]	C[e]
1	$PhB(OH)_2$		$CH_2=CHCOCH_3$	82 (99)	(90)	(99)
2			$CH_3CH=CHCOC_4H_9$	28	60, 74[f]	96[f]
3			$CH_3CH=CHCOPh$		75[f]	
4			$PhCH=CHCOCH_3$		43[f]	99[f]
5			$PhCH=CHCOPh$		58[f]	86[f]
6				trace	52[f]	trace
7		4-Br	$CH_2=CHCOCH_3$	90		
8		$4\text{-}CH_3O$	$CH_2=CHCOCH_3$	84	82	86
9		$2\text{-}CH_3O$	$CH_2=CHCOCH_3$	68	81	84
10		$4\text{-}CH_3CO$	$CH_2=CHCOCH_3$	94		
11		$2,4,6\text{-}(CH_3)_3$	$CH_2=CHCOCH_3$	(44) (80)[f]		(9)[f]
12	$PhB(OH)_2$		$CH_2=CHCHO$	(56)	(43)	(59)

[a] The experimental procedure is given in the text.[11] [b] Isolated yields are based on the enones, and GC yields are given in parentheses. [c] DMF/H_2O (6/1). [d] Cyclohexane/H_2O (6/1). [e] $MeOH/H_2O$ (6/1). [f] Two equivalents of $ArB(OH)_2$ was used.

recently reported by Uemura and co-workers.[8] The reaction was proposed to proceed through the oxidative addition of the C−B bond to the Pd(0) species; however, another probable process, the transmetalation to transition metals, may allow a similar catalytic transformation by the use of organoboronic acids. The efficiency of the transmetalation from boron to palladium was previously demonstrated in the cross-coupling reaction of organoboron compounds with organic electrophiles.[9] Now, we report the 1,4-addition reaction of organoboronic acids to enones catalyzed by a $(acac)Rh(CO)_2$/dppb complex (dppb 1,4-bis(diphenylphosphino)butane), which may involve the B−Rh transmetalation as the key step (eq 1).



(1)

A mixture of $Rh(acac)(CO)_2$ (3 mol %), a phosphine ligand, an enone (1 equiv), and phenylboronic acid (1.3 equiv) in aqueous solvent was stirred for 16 h at 50 °C (Table 1). Various phosphine ligands gave good results for methyl vinyl ketone (MVK), giving a quantitative yield of 4-phenyl-2-butanone as the sole product, but the reaction with less reactive 2-octen-4-one revealed the order of dppb > dppp > TFP > dppe, PPh_3, and $AsPh_3$ suggesting that the reaction is accelerated upon the increase of the P−Rh−P angles.[10] Other rhodium(I) complexes such as $[Rh(cod)_2]BF_4$/dppb (99%), $[Rh(CO)(PPh_3)_2]ClO_4$ (95%), (acac)Rh(cod)/dppb (99%), $RhCl(PPh_3)_3$ (16%), and $RhCl(CO)(PPh_3)_2$ (35%) were also effective for MVK. The solvent also affects the rate of addition. Aqueous DMF can be used for methyl vinyl ketone, but less polar solvents such as cyclohexane afforded a higher yield for 2-octen-4-one (entry 10). However, a combination of methanol and water was finally recognized to be a highly efficient system, having a wide generality for various enones (entry 11 and Table 2). Although the effect of added water has not yet been elucidated, the yields decreased in the absence of water (entries 8 and 12). The addition of a base, such as NaOH, NaOAc, and Et_3N, or the addition of $SbCl_3$ unexpectedly retarded the reaction, which is in sharp contrast to the palladium-catalyzed cross-coupling reaction[9] of organoboronic acids and the conjugate addition[8] with palladium(II) acetate.

The representative results obtained by the three procedures using $Rh(acac)(CO)_2$/dppb in aqueous solvents at 50 °C are compared in Table 2.[11] The addition to MVK worked well in aqueous DMF (procedure A), but aqueous MeOH (procedure C) was apparently advantageous for a wide range of enones and arylboronic acids (entries 2−12). Aqueous cyclohexane (procedure C) exceptionally gave the best result in the reaction with 2-cyclohexenone (entry 6). Various arylboronic acids having *ortho*- and *para*-substituents smoothly underwent the addition to methyl vinyl ketone (MVK) (entries 1 and 7−11). There is no appreciable difference in the yields between electron-withdrawing and -donating groups, but the *ortho*-substituents strongly retarded the addition (entries 9 and 11). For such reactions of sterically hindered arylboronic acids, the use of excess amounts (2 equiv) of arylboronic acids was advantageous to achieve high yields, because prolonging the reaction time did not improve the yields due to the competitive hydrolytic deboronation of arylboronic acids with water (entries 2 and 11). The reduction potential

---

(8) Cho, C. S.; Motofusa, S.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 883.

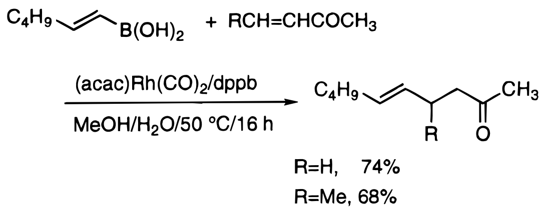
(9) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(10) The bond angle affects the rate of CO insertion into the C−Pd bond, see: Dekker, G. P. C.; Elsevier, C. J.; Vrieze, K. *Organometallics* **1992**, *11*, 1598.

(11) The following procedure for the synthesis of 2-phenyloctan-4-one is reprensentative. Methanol (6 mL) was added to a flask charged with $Rh(acac)(CO)_2$ (0.03 mmol), dppb (0.03 mmol), and PhB(OH) (2.0 mmol) and flushed with nitrogen. After being stirred for 15 min at room temperature, water (1 mL) and 2-octen-3-one (1 mmol) were added, and the resulting mixture was then stirred at 50 °C for 16 h. The product was extracted with benzene, washed with brine, and dried over $MgSO_4$. Chromatography over silica gel with hexane/AcOEt (10/1) gave a colorless oil (96%): IR (neat) 1710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16−7.31 (m, 5H), 3.31 (ddq, 1H, $J = 6.6$, 6.8, and 7.8 Hz), 2.72 (dd, 1H, $J = 6.6$ and 16.1 Hz), 2.62 (dd, 1H, $J = 7.8$ and 16.1 Hz), 2.30 (8 lines, 2H, $J = 7.3$ Hz), 1.48 (tt, 2H, $J = 7.3$ and 7.3 Hz), 1.25 (d, 3H, $J = 6.8$ Hz), 1.23 (tq, 2H, $J = 7.3$ and 7.3 Hz), 0.86 (t, 3H, $J = 7.3$ Hz); MS *m/e* 105 (100), 119 (8), 129 (3), 147 (18), 162 (7), 189 (16), 204 (22, M^+). HRMS for $C_{14}H_{20}O$: 204.1507. Found: 204.1500.

of enones serves to estimate the addition rate of organocuprates[12] and perhaps the addition of other organometallics,[3b] but the reaction seemed to be more sensitive to the steric effect of the substituents than that of an electronic effect, presumably due to the steric hindrance at the steps of coordination and insertion to the enone (entries 1−5). The reaction under neutral conditions in the presence of water avoids the aldol condensation of substrates or products, thus allowing the conjugate addition to enals. The preliminary results for the addition of phenylboronic acid to acrolein gave a 59% yield of 3-phenylpropanal (entry 12).[13]

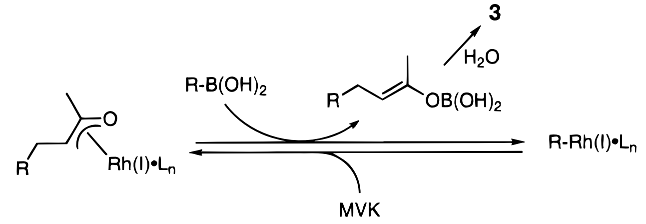
(*E*)-1-Hexenylboronic acids similarly participated in the rhodium-catalyzed conjugate addition to MVK giving (*E*)-5-decen-2-one in a 62% yield by procedure A, 74% yield by procedure B, and 74% yield by procedure C. The addition to 2-octen-4-one by procedure C resulted in a 68% yield, retaining its stereochemistry during the reaction (eq 2).



(2)

This research has been carried out based on the previous observations that the organic groups on the boron atom readily displace the RO−Pd(II)X bond (RO = acac, AcO, and MeO) under neutral conditions, whereas the halogen−metal complexes are quite inert to such transmetalation with organoboronic acids.[8] Work on the mechanistic details is in progress, but the present transformation may result from a catalytic cycle that involves the transmetalation between the rhodium(I) enolate[14] and arylboronic acid to give the arylrhodium(I) species[15] and the insertion of the enone into the Ar−Rh bond, as shown in Scheme 1.[16]

Scheme 1. Catalytic Cycle



The intermolecular transfer reactions of organoboron compounds such as the Grignard-type reaction are rare; however, several methods have been reported for the conjugate addition to enones.[17−19] The present rhodium-catalyzed reaction provides an additional method for the conjugate addition of aryl- and alkenylboronic acids to enones. Because of the simple experimental procedure under neutral conditions, the rhodium-catalyzed asymmetric addition will be the topic of further accounts from this laboratory.

OM9705113

---

[12] House, H. O.; Huber, L. E.; Umen, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 8471.

[13] The addition to other α,*β*-unsaturated aldehydes, nitriles, or esters is in progress; however, these reactions are very slow under the above reaction conditions.

[14] Slough, G. A.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 938.

[15] The reaction of $(PPh_3)_3RhCl$ with PhMgBr or *trans*-RhCl(CO)-$(PPh_3)_2$ with PhLi gives the corresponding phenylrhodium(I) complexes, see: Keim, W. *J. Organomet. Chem.* **1968**, *14*, 179. Hegedus, L. D.; Lo, S. M.; Bloss, D. E. *J. Am. Chem. Soc.* **1973**, *95*, 3040. However, the isolation and characterization of arylrhodium species need to be investigated further.

[16] The hydrolysis of the rhodium(I) enolate with water to give a hydroxorhodium species and its transmetalation with arylboronic acid is another probable process to give a phenylrhodium(I) intermediate, see: Grushin, V. V.; Kuznetsov, V. F.; Bensimon, C.; Alper, H. *Organometallics* **1995**, *14*, 3927.

[17] Suzuki, A.; Arase, A.; Matsumoto, H.; Itoh, M.; Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1967**, *89*, 5708.

[18] Fujishima, H.; Takada, E.; Hara, S.; Suzuki, A. *Chem. Lett.* **1992**, 695. Ishimura, S.; Hara, S.; Suzuki, A. *Synlett* **1996**, 993.

[19] Molander, G. A.; Shingaram, B.; Brown, H. C. *J. Org. Chem.* **1984**, *49*, 5024. Molander, G. A.; Brown, H. C. *Ibid.* **1977**, *42*, 3106.