4564 *J. Org. Chem.* **1997,** *62,* 4564−4565

Rhodium-Catalyzed Coupling Reaction of Salicyl Aldehydes with Alkynes via Cleavage of the Aldehyde C−H Bond

Ken Kokubo, Kenji Matsumasa,
Masahiro Miura,* and Masakatsu Nomura

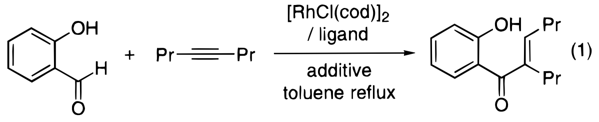
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

Received May 29, 1997

The activation of C−H bonds in organic compounds by transition-metal complexes is currently one of the most significant subjects in both organic and organometallic chemistry. An effective strategy to regioselectively activate a C−H bond in a given molecule has been known to introduce a functional group having ligating ability at an appropriate position of it.[1] Recently, a number of *catalytic* coupling reactions of aromatic or vinylic compounds bearing carbonyl- or nitrogen-containing groups with alkenes and/or alkynes involving such a C−H bond activation mode as the key step have been developed, especially by using ruthenium and rhodium complexes.[2,3] The reaction of acylarenes has also been minutely described by Murai et al.[2b,c]

Meanwhile, we have recently reported that salicyl aldehydes smoothly react with aryl iodides in the presence of a palladium catalyst and a base to give 2-aroylphenols, demonstrating that the phenolic function can act as a good anchor for the catalytic intermolecular C−C coupling via cleavage of the aldehyde C−H bond.[4] It was expected that, if vinyl halides could be used in place of aryl iodides, 2-alkenoylphenols could also be obtained in one step: The phenolic compounds are valuable precursors of chromanones and chromones,[5,6] whose skeletons are widely found in naturally occurring compounds, and a number of them exhibit interesting biological activities.[5] However, the reaction using vinyl halides was less efficient. One of the other possible routes to prepare 2-alkenoylphenols using salicyl aldehydes via the C−H cleavage is their coupling with alkynes, which may be regarded as a hydroacylation reaction.[7,8] We report herein our new findings that the latter route can be realized with high efficiency by using a rhodium-based catalyst system.

The reaction of salicyl aldehyde (**1a**) with 4-octyne (**2a**) was first examined in the presence of $[RhCl(cod)]_2$ and a variety of ligands in toluene (5 mL) under nitrogen (monitored by GLC), the relative amount of **1a**, **2a**, $[RhCl(cod)]_2$ being 2:2:0.01 (in mmol) (eq 1). It was found that, by using dppf (0.02 mmol) as ligand and refluxing the solvent for 24 h, the expected product, (*E*)-1-(2-hydroxyphenyl)-2-propyl-2-hexen-1-one (**3**), was produced in an almost quantitative yield, no isomer being accompanied.[9] Addition of an inorganic carbonate, Na_2CO_3 (0.1 mmol), was also found to significantly enhance the rate of the reaction, so that it was completed within 0.5 h, while a tertiary amine, NEt(*i*-Pr)$_2$, which is effective for the rhodium-catalyzed hydroacylation of alkenes with acid anhydrides and molecular hydrogen,[10] showed no meaningful effect. Although other bidentate phosphine ligands, dppe, dppp, and dppb, as well as monodentate ones, PPh_3 and tricyclohexylphosphine, could be used in place of dppf, they were much less effective.[9]



(1)

1a **2a** **3**

ligand	additive	time / h	% yield
dppf	none	0.5	5
dppf	none	24	99
dppf	Na_2CO_3	0.5	100
dppp	Na_2CO_3	21	52
PPh_3	Na_2CO_3	20	33

The reaction of **1a** with **2a** using the catalyst system of $[RhCl(cod)]_2$/dppf/Na_2CO_3 could also be completed in refluxing benzene in a period of 2.5 h (eq 2); product **3** (99%) also was cleanly isolated by means of flash chro-

---

[1] For reviews, see: (a) Newkome, G. R.; Puckett, W. E.; Gupta, V. K.; Kiefer, G. E. *Chem. Rev.* **1986**, *86*, 451. (b) Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403.

[2] Carbonyl-directed catalytic reactions: (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* (*London*) **1993**, *366*, 529. (b) Murai, S. *J. Synth. Org. Chem. Jpn.* **1994**, *54*, 992. (c) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62. (d) Kakiuchi, F.; Tanaka, Y.; Sato, T.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 679. (e) Kakiuchi, F.; Yamamoto, Y.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 681. (f) Sonoda, M.; Kakiuchi, F.; Kamatani, A.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 109. (g) Trost, B. M.; Imi, K. Davies, I. W. *J. Am. Chem. Soc.* **1995**, *117*, 5371.

[3] Nitrogen-directed catalytic reactions: (a) Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888. (b) Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2201. (c) Aulwurm, U. R.; Melchinger, J. U.; Kisch, H. *Organometallics* **1995**, *14*, 3385. (d) Kakiuchi, F.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 111. (e) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 493.

[4] Satoh, T.; Itaya, T.; Miura, M.; Nomura, M. *Chem. Lett.* **1996**, 823.

[5] For example: (a) Coffey, S. *Rodd's Chemistry of Carbon Compounds*, 2nd Ed.; Elsevier: Amsterdam, 1977; Vol. IV, Part E. (b) Katritzky, A.; Rees, C. W. In *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., Mckillop, A., Eds.; Pergamon Press: Oxford, 1984; Vol. 3, pp 573−883.

[6] (a) Kasahara, A.; Izumi, T.; Ooshima, M. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2526. (b) Cullen, W. P.; Donnelly, D. M. X.; Keenan, A. K.; Keenan, P. J.; Ramdas, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1671. (c) Furlong, J. J. P.; Nudelman, N. S. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1213.

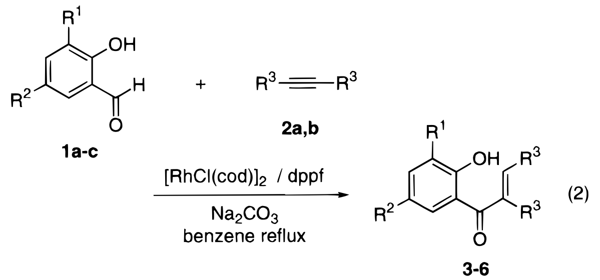
[7] While Rh-catalyzed hydroacylation of alkenes with aldehydes has been well studied, only the intermolecular cases have generally been efficient,[8] and the reaction with alkynes[7j,8e] has been little known: (a) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, *13*, 1287. (b) Larock, R. C.; Oertle, K.; Potter, G. F. *J. Am. Chem. Soc.* **1980**, *102*, 190. (c) Vora, K. P.; Lochow, C. F.; Miller, R. G. *J. Organomet. Chem.* **1980**, *192*, 257. (d) Okano, T.; Kobayashi, T.; Konishi, H.; Kiji, J. *Tetrahedron Lett.* **1982**, *23*, 4967. (e) Rode, E.; Davis, M. E.; Hanson, B. E. *J. Chem. Soc., Chem. Commun.* **1985**, 716. (f) Marder, T. B.; Roe, D. C.; Milstein, D. *Organometallics* **1988**, *7*, 1451. (g) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 946. (h) Wu, X.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron Lett.* **1992**, *33*, 6331. (i) Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821. (j) Lee, H.; Jun, C.-H. *Bull. Korean Chem. Soc.* **1995**, *16*, 1135; *Chem. Abstr.* **1996**, *124*, 202420b.

[8] Rh-catalyzed reaction of aldimines with alkenes: (a) Suggs, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 489. (b) Jun, C.-H.; Lee, H.; Hong, J.-B. *J. Org. Chem.* **1997**, *62*, 1200. Ru-catalyzed hydroacylation of alkenes: (c) Isnard, P.; Denise, B.; Sneeden, R. P. A.; Congnion, J. M.; Durual, P. *J. Organomet. Chem.* **1982**, *240*, 285. (d) Kondo, T.; Akazome, M.; Tsuji, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286. Ni-catalyzed hydroacylation of alkynes: (e) Tsuda, T.; Kiyoi, T.; Saegusa, T. *J. Org. Chem.* **1990**, *55*, 2554. Very recently, efficient Co-catalyzed hydroacylation of alkenes has also been reported: (f) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1997**, *119*, 3165.

[9] Abbreviations: dppf = 1,1′-bis(diphenylphosphino)ferrocene, dppe = 1,2-bis(diphenylphosphino)ethane, dppp = 1,3-bis(diphenylphosphino)propane, dppb = 1,4-bis(diphenylphosphino)butane.

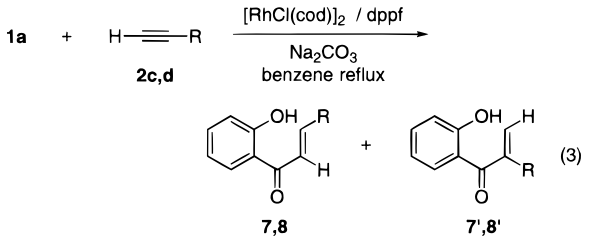
[10] Kokubo, K.; Miura, M.; Nomura, M. *Organometallics* **1995**, *14*, 4521.

S0022-3263(97)00945-6 CCC: $14.00

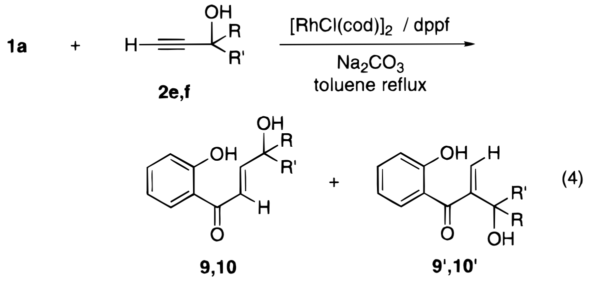


		time / h	% yield
$R^1 = R^2 = H$ (**1a**)	R^3 = Pr (**2a**)	2.5	99 (**3**)
R^1 = OMe, R^2 = H (**1b**)	R^3 = Pr (**2a**)	0.5	99 (**4**)
R^1 = H, R^2 = Cl (**1c**)	R^3 = Pr (**2a**)	4	98 (**5**)
$R^1 = R^2 = H$ (**1a**)	R^3 = Ph (**2b**)	7	94 (**6**)

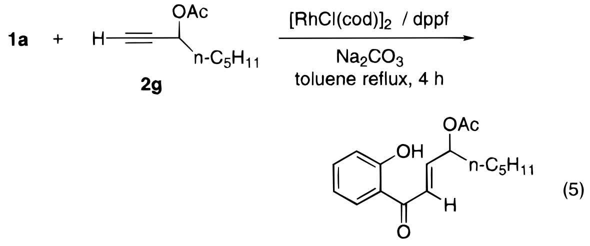
matography on silica gel. Similarly, 3-methoxy- and 5-chlorosalicyl aldehydes **1b** and **1c** quantitatively reacted with **2a** to give the corresponding alkenoylphenols **4** and **5**, respectively. Note that the reaction using 20 mmol of each of **1b** and **2a** in refluxing toluene quantitatively proceeded within 2 h, the turnover rate being approximately estimated to be as high as 500 h^{-1}. The reaction of **1a** with 1,2-diphenylacetylene (**2b**) also gave product **6**. In contrast to other catalytic C−H/alkyne coupling reactions,[2e,g,3c] terminal alkynes, 1-octyne (**2c**) and 1-phenylacetylene (**2d**), could smoothly react with **1a**, giving pairs of regioisomers **7**/**7′** and **8**/**8′** in comparable amounts (eq 3). Styrene, however, did not react with **1a**. Good regioselectivities were observed in the reactions with propargyl alcohols **2e** and **2f** (eq 4). The regioisomers of **7**−**10** and **7′**−**10′** could be also separated by column chromatography on silica gel. The reaction of **1a** with 3-acetoxy-1-octyne (**2g**) predominantly afforded compound **11** along with minor amounts of some unidentified products (eq 5).



	time / h	% yield	
R = n-C_6H_{13} (**2c**)	2	99	(**7**/**7'** = 45:55)
R = Ph (**2d**)	4	93	(**8**/**8'** = 34:66)



	time / h	% yield	
R = R' = Me (**2e**)	5.5	75	(**9**/**9'** = 83:17)
R, R' = -$(CH_2)_5$- (**2f**)	4	86	(**10**/**10'** = 85:15)



11, 70 %

The present reaction may involve initial coordination of **1** to a chlororhodium(I) species complexed by dppf to form a 2-formylphenolate complex accompanied by liberation of HCl and then oxidative addition of the aldehyde C−H bond to the metal center to give an (aroylhydrido)rhodium(III) as the key steps.[4,11,12] It should be noted that 4-hydroxybenzaldehyde and 2-methoxybenzaldehyde as well as benzaldehyde itself could not be used in place of **1a**, supporting the above consideration that coordination of the phenolic oxygen to the metal center plays a significant role. It was confirmed that addition of AgOTf or $AgClO_4$ in place of Na_2CO_3 to the reaction of **1a** with **2a**, which may generate a cationic rhodium(I) species, could not enhance the reaction. Thus, the insoluble solid base seems to effectively remove initially formed HCl, which could be a poison for the catalysis. The origin of high efficiency of dppf as ligand, however, is not definitive at the present stage.

In summary, we have shown that salicyl aldehydes can readily react with alkynes accompanied by cleavage of the aldehyde C−H bond in the presence of a catalytic amount of a rhodium(I) complex to produce synthetically useful 2-alkenoylphenols.

Acknowledgment. This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

Supporting Information Available: Typical experimental procedure and characterization data of the new compounds **3**−**5**, **7**, **9**−**11**, and **8′**−**10′** (3 pages).

JO9709458

---

(11) Stoichiometric cyclometalation of salicyl aldehydes with Pd, Pt, and Ni is known: (a) Bryndza, H. E.; Tam, W. *Chem. Rev.* **1988**, *88*, 1163. (b) Klein, H.-F.; Bickelhaupt, A.; Lemke, M.; Sun, H.; Brand, A.; Jung, T.; Röhr, C.; Flörke, U.; Haupt, H.-J. *Organometallics* **1997**, *16*, 668.

(12) Rhodium-catalyzed reaction of aroyl chlorides with alkynes that may involve alkyne insertion to arylchlorhodium(III) species: Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941.