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Rh(I)-Catalyzed CO Gas-Free Carbonylative Cyclization Reactions of Alkynes with 2-Bromophenylboronic Acids Using Formaldehyde

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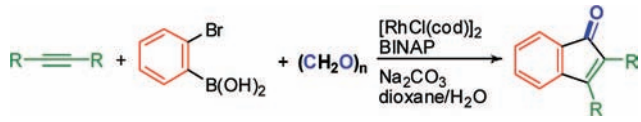
ABSTRACT



The rhodium(I)-catalyzed reaction of alkynes with 2-bromophenylboronic acids in the presence of paraformaldehyde resulted in a CO gas-free carbonylative cyclization, yielding indenone derivatives. $[RhCl(BINAP)]_2$ and $[RhCl(cod)]_2$ were responsible for the decarbonylation of formaldehyde and the subsequent carbonylation of alkynes with 2-haloboronic acids, respectively, leading to efficient whole carbonylation. Sterically bulky and electron-withdrawing groups on unsymmetrically substituted alkynes favored the α-position of indenones.

Transition-metal-catalyzed carbonylation has become an essential, powerful tool for the synthesis of a wide variety of carbonyl compounds.[1] Recent considerable efforts have focused on its experimental simplification and on the development of novel carbonylative transformations. Consequently, gaseous carbon monoxide has been replaced by much easier handling organic and inorganic carbonyl compounds in various carbonylation reactions, as follows: hydrocarbonylation (hydroesterification, hydroamidation, and hydrocarboxylation) of alkenes and alkynes;[2,3] hydroformylation of alkenes;[2] alkoxy-, amino-, and hydroxycarbonylation of aromatic and alkenyl halides;[2,4] the Pauson−Khand reaction;[2,5] hydrocyclocarbonylation of alkynes;[2,6] and carbonylative ring-expansion of spiropentanes.[7] In this paper, we describe a new utilization of the CO gas-free protocol consisting of decarbonylation of formaldehyde and sequential carbonylation;[2,4n,5b,6,7] thus, a rhodium(I)-catalyzed carbonylative cyclization reaction of alkynes with 2-haloboronic acids in the presence of formaldehyde results in carbonylative cyclization to afford indenones.[8,9]

Our previous work showed that phosphine-free rhodium complexes, such as $[RhCl(cod)]_2$ and $[RhCl(CO)_2]_2$, show catalytic activity for the carbonylation reaction using carbon monoxide, while rhodium−phosphine complexes, such as

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(1) (a) Kollár, L. *Modern Carbonylation Methods*; Wiley-VCH: Weinheim, 2008. (b) Beller, M. *Catalytic Carbonylation Reaction*; Springer-Verlag: Berlin, 2006. (c) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991.

(2) For a review, see: Morimoto, T.; Kakiuchi, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 5580–5588.

(3) Kobayashi, Y.; Kamisaki, H.; Yanada, K.; Yanada, R.; Takemoto, Y. *Tetrahedron Lett.* **2005**, *46*, 7549–7552 (intramolecular hydroamidation of yne−formamides).

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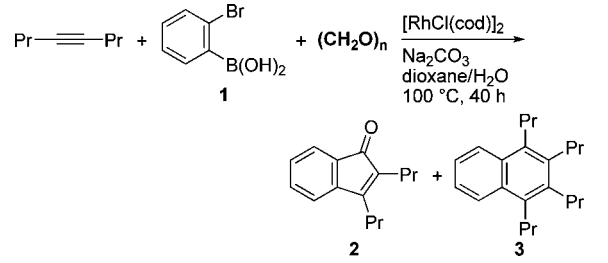
$RhCl(PPh_3)_3$ and $RhH(CO)(PPh_3)_3$, are catalytically ineffective.[8] This was a significant finding for our study, because it is generally recognized that rhodium−phosphine complexes more efficiently catalyze the decarbonylation of aldehydes.[10] The key to solving this question was to control the amount of added phosphine ligand so that rhodium complexes both with and without phosphine ligands, which should be responsible for decarbonylation and carbonylation, respectively, could coexist in one catalyst system.

First, we pursued a rhodium species generated from the reaction of $[RhCl(cod)]_2$ with BINAP, the amount of which was not to cover all of a given rhodium center. The ^{31}P NMR-experimental treatment of $[RhCl(cod)]_2$ with BINAP ($[RhCl(cod)]_2$/BINAP = 2.5:1) in CD_2Cl_2 at room temperature resulted in complete consumption of the BINAP to give $[RhCl(BINAP)]_2$ as the sole rhodium complex having a BINAP ligand.[11] Furthermore, ^{103}Rh NMR analysis revealed the existence of two kinds of rhodium species, which can be assigned to $[RhCl(cod)]_2$ and $[RhCl(BINAP)]_2$. These results encouraged us to verify the synergism between decarbonylation formaldehyde by $[RhCl(BINAP)]_2$ and carbonylative cyclization of alkynes with 2-haloarylboronic acids by $[RhCl(cod)]_2$.

Under the catalyst consisting of $[RhCl(cod)]_2$ and BINAP in a molar ratio of 2.5:1, we examined the reaction of 4-octyne with 2-bromophenylboronic acid in the presence of paraformaldehyde instead of carbon monoxide (Table 1,

Table 1. Effect of BINAP in the Reaction of 4-Octyne with **1** and Paraformaldehyde[a]



entry	BINAP (mol %)	yield of **2**[b] (%)	yield of **3**[b] (%)
1		41	9
2	1	75	4
3	2	47	3
4	5	32	trace
5[c]	1	83	4

[a] Reaction conditions: 4-octyne (1 mmol), **1** (1.5 mmol), paraformaldehyde (5 mmol), $[RhCl(cod)]_2$ (0.025 mmol), BINAP, Na_2CO_3 (2 mmol) in dioxane/H_2O (100/1, 2 mL) at 100 °C for 40 h. [b] Isolated yield. [c] 3 mmol of **1** was used for 30 h.

entry 2). The reaction proceeded efficiently to afford the desired indenone **2** in 75% yield, along with 4% of naphthalene derivative **3**. The addition of up to 5 mol % of BINAP led to the formation of **2** in much lower yields (entries 1 and 4). From these results, we postulated that $[RhCl(BINAP)]_2$ and $[RhCl(cod)]_2$ are involved mainly in the decarbonylation and carbonylative cyclization processes, respectively, as we expected. Among other phosphines tested, BIPHEP was almost as effective as BINAP: BIPHEP (71%), dppe (68%), dppp (58%), dppb (62%), dppf (55%), and $2PPh_3$ (53%). Use of 3 equiv of 2-bromophenylboronic acid increased the yield of **2** to as high as 83% in even a shorter reaction time (30 h) (entry 5). Under these conditions, pentafluorobenzaldehyde and *trans*-cinnamaldehyde did not work better than paraformaldehyde (28% and 13% yields).[12] The standard conditions established thus constituted 2.5 mol % of $[RhCl(cod)]_2$, 1 mol % of BINAP, 3 equiv of 2-bromophenylboronic acid, and 2 equiv of Na_2CO_3, in dioxane/H_2O (100/1) at 100 °C for 30 h.

A proposed reaction pathway for the present reaction is shown in Scheme 1.[8] First, addition of BINAP, the amount

(4) For recent papers on use of $Mo(CO)_6$, see: (a) Wu, X.; Mahalingam, A. K.; Wan, Y.; Alterman, M. *Tetrahedron Lett.* **2004**, *45*, 4635–4638. (b) Herrero, M. A.; Wannberg, J.; Larhed, M. *Synlett* **2004**, 2335–2338. (c) Wannberg, J.; Dallinger, D.; Kappe, C. O.; Larhed, M. *J. Comb. Chem.* **2005**, *7*, 574–583. (d) Wannberg, J.; Kaiser, N.-F. K.; Vrang, L.; Samuelsson, B.; Larhed, M.; Hallberg, A. *J. Comb. Chem.* **2005**, *7*, 611–617. (e) Wu, X.; Rönn, R.; Gossas, T.; Larhed, M. *J. Org. Chem.* **2005**, *70*, 3094–3098. (f) Wu, X.; Larhed, M. *Org. Lett.* **2005**, *7*, 3327–3329. (g) Wu, X.; Ekegren, J. K.; Larhed, M. *Organometallics* **2006**, *25*, 1434–1439. (h) Wu, X.; Wannberg, J.; Larhed, M. *Tetrahedron* **2006**, *62*, 4665–4670. (i) Gold, H.; Ax, A.; Vrang, L.; Samuelsson, B.; Karlén, A.; Hallberg, A.; Larhed, M. *Tetrahedron* **2006**, *62*, 4671–4675. (j) Wannberg, J.; Sabnis, Y. A.; Vrang, L.; Samuelsson, B.; Karlén, A.; Hallberg, A.; Larhed, M. *Bioorg. Med. Chem.* **2006**, *14*, 5303–5315. (k) Letavic, M. A.; Ly, K. S. *Tetrahedron Lett.* **2007**, *48*, 2339–2343. For recent papers on the use of DMF, see: (l) Ju, J.; Jeong, M.; Moon, J.; Jung, H. M.; Lee, S. *Org. Lett.* **2007**, *9*, 4615–4618. (m) Tambade, P. J.; Patil, Y. P.; Bhanushali, M. J.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 2221–2224. For a recent paper on the use of aldehydes, see: (n) Morimoto, T.; Fujioka, M.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Organomet. Chem.* **2007**, *692*, 625–634. For a recent paper on the use of acetic formic anhydride, see: (o) Berger, P.; Bessmernykh, A.; Caille, J.-C.; Mignonac, S. *Synthesis* **2006**, 3106–3110. For a recent paper on the use of a carbamoylsilane, see: (p) Cunico, R. F.; Pandey, R. K. *J. Org. Chem.* **2005**, *70*, 9048–9050.

(5) For recent papers on the use of aldehydes, see: (a) Jeong, N.; Kim, D. H.; Choi, J. H. *Chem. Commun.* **2004**, 1134–1135. (b) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Tetrahedron Lett.* **2004**, *45*, 9163–9166. (c) Kwong, F. Y.; Li, Y. M.; Lam, W. H.; Qiu, L.; Lee, H. W.; Yeung, C. H.; Chan, K. S.; Chan, A. S. C. *Chem.—Eur. J.* **2005**, *11*, 3872–3880. (d) Shibata, T.; Toshida, N.; Yamasaki, M.; Maekawa, S.; Takagi, K. *Tetrahedron* **2005**, *61*, 9974–9979. (e) Kwong, F. Y.; Lee, H. W.; Qiu, L.; Lam, W. H.; Li, Y.-M.; Kwong, H. L.; Chan, A. S. C. *Adv. Synth. Catal.* **2005**, *347*, 1750–1754. (f) Kwong, F. Y.; Lee, H. W.; Lam, W. H.; Qiu, L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2006**, *17*, 1238–1252. For a recent paper on the use of formates, see: (g) Lee, H. W.; Chan, A. S. C.; Kwong, F. Y. *Chem. Commun.* **2007**, 2633–2635.

(6) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Chem. Commun.* **2005**, 3295–3297 (use of formaldehyde).

(7) Matsuda, T.; Tsuboi, T.; Murakami, M. *J. Am. Chem. Soc.* **2007**, *129*, 12596–12597 (use of formaldehyde).

(8) Harada, Y.; Nakanishi, J.; Fujihara, H.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2007**, *129*, 5766–5771.

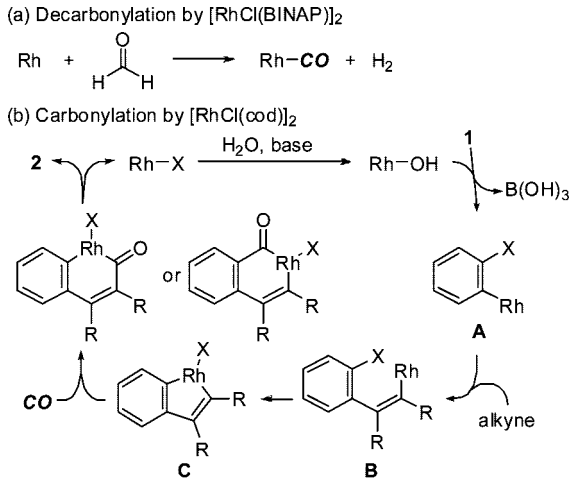
(9) Recently, Rh(I)-catalyzed carbonylation reactions of alkynes with phenylboronic acid leading to α,β-unsaturated γ-lactones were reported. See: (a) Aksin, Ö; Dege, N.; Artok, L.; Türkmen, H.; Çetinkaya, B. *Chem. Commun.* **2006**, 3187–3189. (b) Kuş, M.; Artok, Ö. A.; Ziyanak, F.; Artok, L. *Synlett* **2008**, 2587–2592.

(10) Kreis, M.; Palmelund, A; Bunch, L.; Madsen, R. *Adv. Synth. Catal.* **2006**, *348*, 2148–2154, and references therein.

(11) $[RhCl(BINAP)]_2$: ^{31}P NMR (CD_2Cl_2) δ 49.5 ppm (d, $J_{P\text{-}Rh}$ = 199 Hz). $[RhCl(cod)]_2$: ^{103}Rh NMR (CD_2Cl_2) δ 2438 ppm (s). The mixture of $[RhCl(cod)]_2$ (2.5 equiv) with BINAP (1 equiv): ^{31}P NMR (CD_2Cl_2) δ 49.5 ppm (d, $J_{P\text{-}Rh}$ = 199 Hz); 103Rh NMR (CD_2Cl_2) δ 1620 (t, $J_{Rh\text{-}P}$ = 199 Hz), 2438 ppm (s). For details, see the Supporting Information.

(12) For successful uses of other aldehydes on the CO gas-free carbonylations, see: (a) Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3806–3807. (b) Morimoto, T.; Fujioka, M.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *Chem. Lett.* **2003**, *32*, 154–155. (c) References 4n, 5a and 5c−f.

Scheme 1. Reaction Pathway

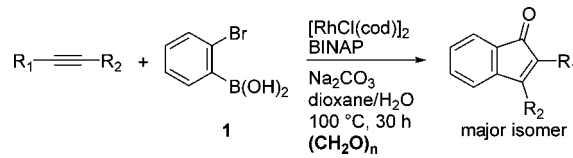


of which cannot cover all of the given rhodium metal, leads to the partial formation of $[RhCl(BINAP)]_2$, along with the intact $[RhCl(cod)]_2$. The former complex would mainly decarbonylate formaldehyde to yield the carbonyl moiety and hydrogen. On the other hand, the latter would predominantly catalyze the actual carbonylation step as shown in Scheme 1b. Thus, transmetalation of Rh−OH with 2-haloarylboronic acid **1** yields the arylrhodium(I) complex **A**. The addition, in a *cis*-manner, of complex **A** to an alkyne gives the vinylrhodium(I) complex **B**, in which the oxidative addition of the proximal C−Br bond to the rhodium center produces the rhodacycle **C**. The insertion of the carbonyl moiety abstracted from formaldehyde, followed by reductive elimination, affords indenone **2** with regeneration of the rhodium(I) catalyst.

Under the aforementioned optimized conditions, various alkynes having aryl, alkyl, ester, and silyl groups could be used to give the corresponding indenones in moderate to high yields, as shown in Table 2. Diphenylacetylene also worked well. For unsymmetrically substituted alkynes, the reaction proceeded generally in a regioselective manner, and either a sterically bulky group or an electron-withdrawing group on alkynes favored the α-position of indenones. The reaction of 1-phenyl-1-propyne proceeded regioselectively to afford mainly an indenone with a phenyl group located at the α-position (entry 2). The replacement of the methyl group with a bulkier butyl group led to a decrease in regioselectivity (entry 3). In the case of the reaction of trimethylsilylacetylene derivatives, an exclusive α-orientation of the silyl group was observed (entries 4 and 5). The above results show that the bulkier group selectively locates at the α−position of the carbonyl in the product. This tendency could be explained based on the rational consideration of Larock, who maintains that the high regioselectivity would probably depend on the steric hindrance present in the developing carbon−carbon bond.[13] The alkyne insertion to intermediate **A** occurs so as

(13) Zhang, D.; Liu, Z.; Yum, E. K.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 251–262.

Table 2. Rh(I)-Catalyzed Reaction of Alkynes with **1** and Paraformaldehyde[a]

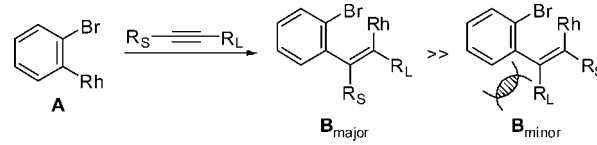


entry	R_1	R_2	yield[b] (%)
1	Ph	Ph	**4**, 78
2	Ph	Me	**5**, 80 (16:1)
3	Ph	Bu	**6**, 76 (6:1)
4[c]	Me_3Si	Me	**7**, 67
5	Me_3Si	Ph	**8**, 75
6[c]	COOMe	Ph	**9**, 73 (26:1)
7[c]	Me_3Si	COOEt	**10**, 44 (3:1)

[a] Reaction conditions: alkyne (1 mmol), **1** (3 mmol), paraformaldehyde (5 mmol), $[RhCl(cod)]_2$ (0.025 mmol), BINAP (0.01 mmol), Na_2CO_3 (2 mmol) in dioxane/H_2O (100/1, 2 mL) at 100 °C for 30 h. [b] Isolated yields. The numbers in parentheses are the ratios of regioisomers. [c] 1.5 mmol of **1** was used.

to lead to the least steric strain around the forming carbon−carbon bond, rather than to the longer carbon−rhodium bond (Scheme 2). For unsymmetrical alkynes with

Scheme 2



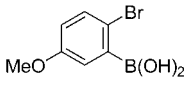
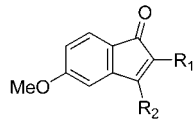
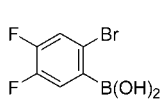
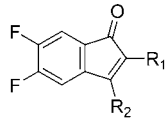
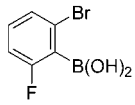
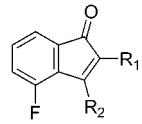
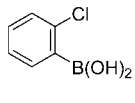
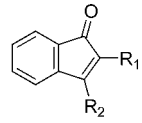
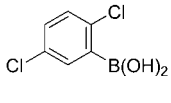
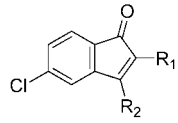
an ester group, the electronic factor is involved in the selectivity in the manner of a 1,4-addition. An ester group affects the regioselectivity more strongly than a phenyl group and locates at the α-position (entry 6), while the effect on α-selectivity is inferior to the steric effect of a silyl group (entry 7).

Thus, the strength of the effect of substituents on α-selectivity can be summarized as follows: $SiMe_3 > CO_2R \gg$ aryl > alkyl, which is consistent with that observed in the reaction using carbon monoxide.[8]

Substituents on the aromatic ring of boronic acid were tolerant to the carbonylation reaction (Table 3). The reaction of 4-octyne with 2-bromo-5-methoxyphenylboronic acid gave indenone **11**, where the carbonyl moiety was introduced into the Br-bound carbon. This implied that the product would not form via the [2 + 2 + 1] cycloaddition of the in situ generated benzyne, the alkyne, or the abstracted CO moi-

(14) (a) Retboll, M.; Edwards, A. J.; Rae, A. D.; Willis, A. C.; Bennett, M. A.; Wenger, E. *J. Am. Chem. Soc.* **2002**, *124*, 8348–8360. (b) Chatani, N.; Kamitani, A.; Oshita, M.; Fukumoto, Y.; Murai, S. *J. Am. Chem. Soc.* **2001**, *123*, 12686–12687. For a review, see: (c) Dyke, A. M.; Hester, A. J.; Lloyd-Jones, G. C. *Synthesis* **2006**, 4093–4112.

Table 3. Rh(I)-Catalyzed Reaction of Alkynes with 2-Bromoarylboronic Acids and Paraformaldehyde[a]

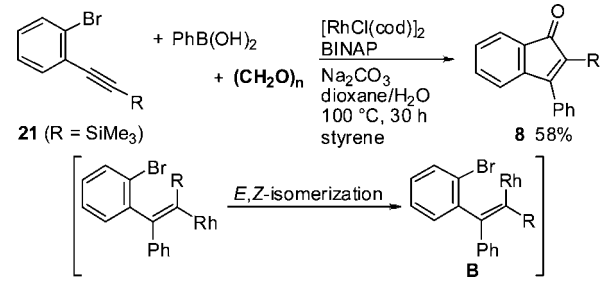
boronic acid	R_1—≡—R_2	product[b]
		
	R_1 = Pr R_2 = Pr	**11** 71%
	R_1 = $SiMe_3$ R_2 = Me	**12** 64%
	R_1 = $SiMe_3$ R_2 = Ph	**13** 51%
		
	R_1 = Pr R_2 = Pr	**14** 62%
	R_1 = $SiMe_3$ R_2 = Me	**15** 67%
	R_1 = $SiMe_3$ R_2 = Ph	**16** 50%
		
	R_1 = Pr R_2 = Pr	**17** 44%
	R_1 = $SiMe_3$ R_2 = Me	**18** 69%
	R_1 = $SiMe_3$ R_2 = Ph	**19** 36%
		
	R_1 = Pr R_2 = Pr	**2** 37%
		
	R_1 = Pr R_2 = Pr	**20** 35%

[a] Reaction conditions: alkyne (1 mmol), 2-bromoarylboronic acid (3 mmol), paraformaldehyde (5 mmol), $[RhCl(cod)]_2$ (0.025 mmol), BINAP (0.01 mmol), Na_2CO_3 (2 mmol) in dioxane/H_2O (100/1, 2 mL) at 100 °C for 30 h. [b] Isolated yields. All products were obtained as a single regioisomer.

ety.[14] For reactions of silylacetylenes having methyl and phenyl groups, the corresponding indenones **12** and **13** were obtained as sole products, respectively. Other substituted 2-bromophenylboronic acids also could be used for the present carbonylation reaction, being converted into indenones **14**−**19**. Replacement of 2-bromophenylboronic acid with 2-chloro analogues also gave indenones **2** and **20**, although in lower yields, along with ca. 5% yields of styrene derivatives as byproducts. The latter was formed by protonation of the generated vinylrhodium species, related to complex **B**, probably due to the poorer reactivity of the C−Cl bond.

Finally, we investigated application of the CO gas-free method using formaldehyde in the reaction of 2-bromoarylacetylenes with nonhalogenated arylboronic acid, in which intermediate **B** could be generated by the insertion of the alkyne to arylrhodium followed by *E*,*Z*-isomerization (Scheme 3). Indeed, the reaction of 2-bromophenyl(trimethylsilyl)acetylene (**21**) with phenylboronic acid gave indenone **8** in 58% yield, albeit requiring the additional use of 2 equiv of styrene as the additive. A butyl and phenyl analogue to **21** did not give the corresponding indenones, and complex mixtures were obtained.

Scheme 3. Reaction of 2-Bromophenyl(trimethylsilyl)acetylene (**21**) with Phenylboronic Acid and Paraformaldehyde



In conclusion, we have reported that the CO gas-free protocol utilizing the decarbonylation of formaldehyde with a rhodium(I) catalyst is applicable to the carbonylative cyclization reaction of alkynes with 2-haloarylboronic acids leading to indenones. The addition of BINAP, the amount of which must not cover all the given $[RhCl(cod)]_2$, leads to the partial formation of $[RhCl(BINAP)]_2$ and intact $[RhCl(cod)]_2$. These are mainly involved in the decarbonylation, and subsequent carbonylation, of formaldehyde, respectively, leading to efficient carbonylation. The reaction proceeded generally in a regioselective manner, and sterically bulky and electron-withdrawing groups favored the α-position of the indenones.

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Supporting Information Available: Experimental details and copies of ^1H, ^{13}C, ^{31}P, and ^{103}Rh NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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