

# Ruthenium- and Rhodium-Catalyzed Direct Carbonylation of the Ortho C–H Bond in the Benzene Ring of *N*-Arylpyrazoles

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The direct carbonylation of C–H bonds in the benzene ring of *N*-phenylpyrazoles via catalysis by ruthenium or rhodium complexes is described. The reaction of *N*-phenylpyrazoles with carbon monoxide and ethylene in the presence of Ru<sub>3</sub>(CO)<sub>12</sub> or Rh<sub>4</sub>(CO)<sub>12</sub> resulted in the site-selective carbonylation of the ortho C–H bonds in the benzene ring to give the corresponding ethyl ketones. A variety of functional groups on the benzene ring can be tolerated. *N*-Phenylpyrazoles have higher reactivities than would be expected, based on the p*K*<sub>a</sub> values of the conjugate acid of pyrazole. The choice of solvent for this reaction is significant, and *N*, *N*-dimethylacetamide (DMA) gives the best result.

## Introduction

The direct functionalization of C–H bonds represents one of the most useful synthetic strategies in organic synthesis, since transforming C–H bonds into C–X bonds (X = Br, I, OTf, etc.) prior to the formation of C–C bonds is not necessary.<sup>1</sup> Among the several reported transformations, the transition-metal-catalyzed carbonylation of C–H bonds provides an effective and attractive method for the introduction of a carbonyl moiety into molecules. Hong and Yamazaki reported that propiophenone is obtained by the reaction of benzene with CO and ethylene in the presence of Rh<sub>4</sub>(CO)<sub>12</sub>, although it was a minor product.<sup>2</sup> The Pd- and/or Cu-catalyzed carboxylation of arenes and alkanes in trifluoroacetic acid, leading to the corresponding carboxylic acids, was reported by Fujiwara.<sup>3</sup> Eisenberg developed the Ir-,<sup>4</sup> Rh-,<sup>5</sup> or Ru<sup>6</sup>-catalyzed photoirradiated carbonylation of benzene. Tanaka achieved a more efficient carbonylation of benzene or hexane into the benzaldehyde or heptanal, respectively,

by irradiation in the presence of RhCl(CO)(PMe)<sub>2</sub> as a catalyst.<sup>7</sup> Similar photoirradiated transformations have been reported by several groups.<sup>8</sup> In 1992, Moore reported on the ruthenium-catalyzed acylation of pyridines, utilizing carbon monoxide and alkenes, in which a highly effective and site-selective carbonylation was achieved.<sup>9</sup> We also have reported a series on catalytic carbonylation reactions at C–H bonds utilizing chelation assistance.<sup>10,11</sup> The chelation-assisted carbonylation reactions at sp<sup>2</sup> C–H bonds thus reported can be classified into four types, depending on the position where the carbonylation takes place (Chart 1).<sup>9–11</sup>

In all cases, the presence of an sp<sup>2</sup> nitrogen atom as a directing group is essential for the carbonylation to proceed. Directing groups, such as a pyridine ring, an oxazoline ring, and an imino group, were found to function as a directing group for the carbonylation of the benzene ring ((iii) in Chart 1). In this paper we wish to

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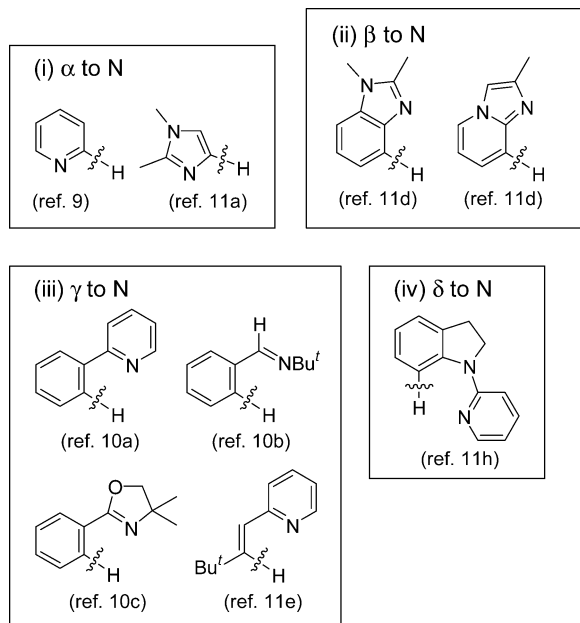
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(10) For our papers on direct carbonylation at C–H bonds in the benzene ring catalyzed by Ru<sub>3</sub>(CO)<sub>12</sub>, see: (a) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604. (b) Fukuyama, T.; Chatani, N.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 5647. (c) Ie, Y.; Chatani, N.; Ogo, T.; Marshall, D. R.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **2000**, *65*, 1475.

**CHART 1. Site-Selective Direct Carbonylation at  $sp^2$  C–H Bonds**

report that a pyrazole ring also functions as a directing group in the direct carbonylation at a C–H bond in the benzene ring.<sup>12,13</sup> We also report here that  $Ru_3(CO)_{12}$  catalyzes the direct carbonylation at a C–H bond in the benzene ring.

## Results and Discussions


**$Ru_3(CO)_{12}$ -Catalyzed Reaction of *N*-Arylpyrazoles with CO and Alkenes.** We have already reported on a number of  $Ru_3(CO)_{12}$ -catalyzed site-selective carbonylation reactions (Chart 1).<sup>10–12</sup> In the cases of carbonylation at C–H bonds  $\alpha$  and  $\beta$  relative to the  $sp^2$  nitrogen ((i) and (ii) in Chart 1),<sup>11a,d,f</sup> the reactivity of these substrates corresponds to the  $pK_a$  values of the conjugate acid of the substrates. For example, a correlation between the  $pK_a$  values of the conjugate acid of substrates and the yields of carbonylation products on carbonylation  $\alpha$  to the  $sp^2$  nitrogen in five-membered heterocycles is shown in Table 1. The higher the  $pK_a$  values, the higher are the product yields. These results indicate that the ability of a nitrogen atom to coordinate to ruthenium is significant and  $pK_a$  values represent potentially good criteria for predicting the direct carbonylation.

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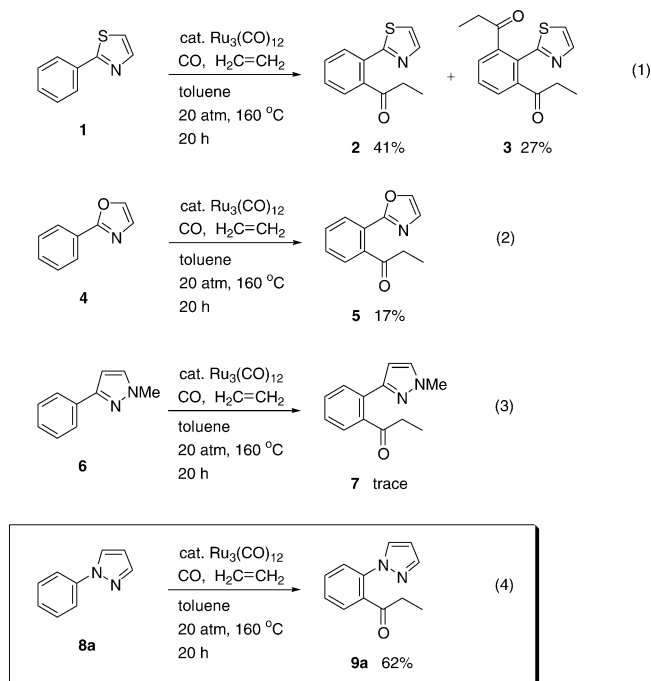
**TABLE 1. Correlation between  $pK_a$  Values of the Conjugate Acid of Substrates and Product Yields on the Carbonylation at  $\alpha$  C–H Bond  $\alpha$  To Nitrogen Atoms**

heterocycle	+ CO	+ 	$Ru_3(CO)_{12}$ 0.04 mmol		carbonylated product
1 mmol	20 atm	4 mmol	toluene 3 mL 160 °C, 20 h		

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$pK_a$	7.85		3.37		2.91		2.09		-2.97
yield	88%		8%		5%		trace		0%

On the basis of this consideration, a similar trend was anticipated, i.e., that the reactivity of benzene derivatives would be in the order 2-phenylthiazole (**1**) (3.37)<sup>14</sup> > 2-phenyloxazole (**4**) (2.91)<sup>15</sup> > 1-methyl-3-phenyl-1*H*-pyrazole (**6**), 1-phenyl-1*H*-pyrazole (**8a**) (2.0)<sup>16</sup> for the carbonylation at C–H bonds in a benzene ring utilizing the five-membered heterocycles as directing groups. In fact, when these substrates were employed under the identical reaction conditions (20 atm of CO, 160 °C in toluene), the product yields were arranged in order of the  $pK_a$  values, as shown in eqs 1–3. However, it was found that the reaction of *N*-phenylpyrazole **8a** unexpectedly proceeded smoothly to give the corresponding product **9a**,<sup>17</sup> as shown in eq 4, although its C-phenyl isomer **6** was a poor substrate.



Thus, the reaction of **8a** (2 mmol) with CO (20 atm) and ethylene (7 atm) in toluene (6 mL) in the presence

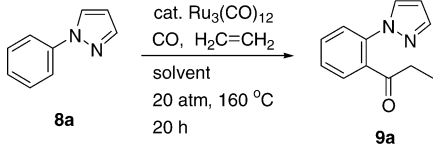
(14) The  $pK_a$  value is that of the conjugate acid of 2-ethylthiazole.

(15) The  $pK_a$  value is that of the conjugate acid of 2,4-dimethyl-oxazole. Brown, D. J.; Ghosh, P. B. *J. Chem. Soc. B* **1969**, 270.

(16) The  $pK_a$  value is that of the conjugate acid of 1-methylpyrazole. Reedijk, J. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Ed.; Pergamon Press: Oxford, UK, 1987; Vol. 2, p 73.

(17) All compounds were characterized by NMR, IR, and mass spectral data. For new compounds, elemental analyses or high-resolution mass were measured. For full characterization of new compounds, see the Supporting Information.

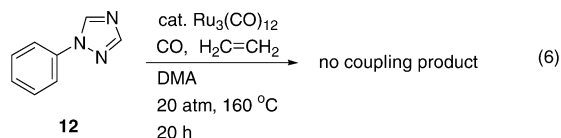
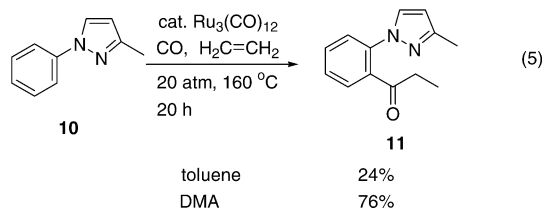
TABLE 2. Effect of Solvents<sup>a</sup>

		
solvent	yield <sup>b</sup> (%)	recovery of <b>8a</b> <sup>b</sup> (%)
toluene	62	20
THF	55	28
1,4-dioxane	48	20
CH <sub>3</sub> CN	42	45
<i>N</i> -methylpyrrolidinone (NMP)	74	16
1,3-dimethyl-2-imidazolidinone (DMI)	76	14
<i>N,N</i> -dimethylformamide (DMF)	75	18
<b><i>N,N</i>-dimethylacetamide (DMA)</b>	<b>94</b>	<b>1</b>

<sup>a</sup> Reaction conditions: *N*-phenylpyrazole **8a** (2 mmol), ethylene (7 atm), CO (20 atm), Ru<sub>3</sub>(CO)<sub>12</sub> (0.05 mmol) in a solvent (6 mL) at 160 °C for 20 h. <sup>b</sup> Isolated yields based on **8a**.

of Ru<sub>3</sub>(CO)<sub>12</sub> (0.05 mmol) at 160 °C for 20 h gave 1-[2-(1*H*-pyrazolyl)phenyl]-1-propanone (**9a**) in 62% yield, along with 20% of unreacted starting material **8a**. Carbonylation did not take place at a C–H bond on the pyrazole ring, although such a reaction has already been reported by us.<sup>11f</sup> Lowering the CO pressure to 10 atm decreased the product yield to 45%. The use of additives, such as PPh<sub>3</sub>, PBu<sub>3</sub>, P(OPh)<sub>3</sub>, P(OEt)<sub>3</sub>, and NEt<sub>3</sub>, had little effect. A brief solvent survey, as shown in Table 2, indicated that amide solvents gave good results and *N,N*-dimethylacetamide (DMA) was the best among the solvents examined.

The substitution of a methyl group at the ring carbon adjacent to the sp<sup>2</sup> nitrogen, as in **10**, resulted in a decreased yield, due to steric hindrance around the sp<sup>2</sup> nitrogen, again suggesting the importance of the coordination of an sp<sup>2</sup> nitrogen to ruthenium (eq 5). The

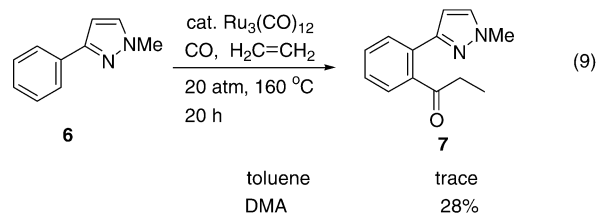
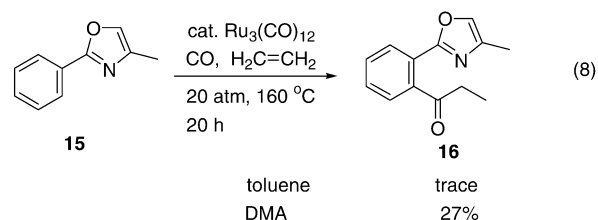
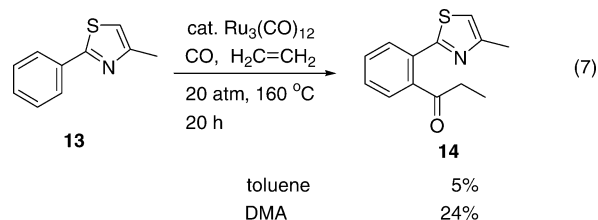


dramatic effect of DMA on the efficiency of the reaction was again observed and the yield of **11** was increased to 76%. A 1,2,4-triazole ring had no effect on the carbonylation reaction for two reasons. One is that the p*K*<sub>a</sub> value of the 1,2,4-triazole ring is too low (1.7)<sup>18</sup> for the carbonylation to proceed. The other is that the most basic nitrogen atom, which would be expected to coordinate to Ru, is located at the 4-position in the 1,2,4-triazole ring. In other words, the coordination site is far removed from the ortho C–H bond, which may react. These results

(18) The p*K*<sub>a</sub> value is that of the conjugate acid of 1-methyl-1,2,4-triazole. Kroeger, C. F.; Freiberg, W. *Chimia* **1967**, *21*, 161.

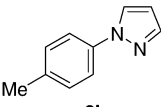
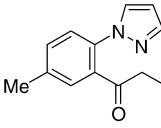
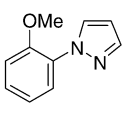
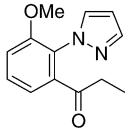
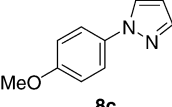
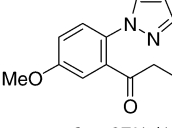
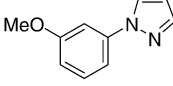
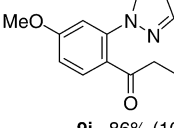
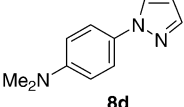
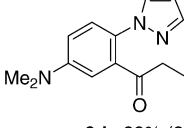
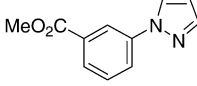
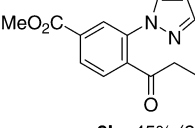
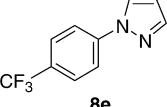
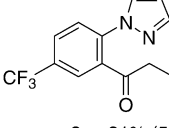
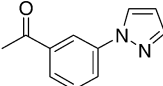
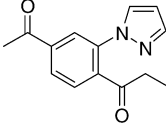
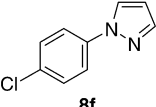
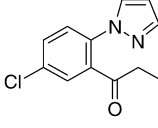
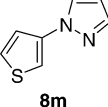
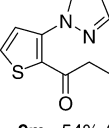
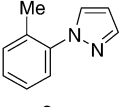
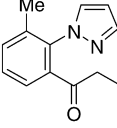
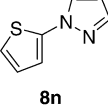
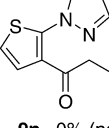
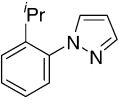
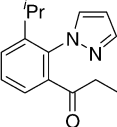
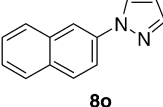
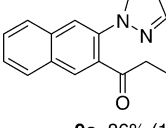
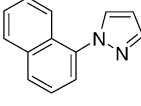
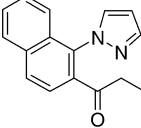
suggest that coordination of the nitrogen to ruthenium is an important step in this reaction.

When reactions of **13**, **15**, and **6** with CO and ethylene were carried out, a dramatic effect of DMA was again observed, in all cases tested (eqs 7–9), although the efficiency was not great because of steric bulkiness around the sp<sup>2</sup> nitrogen.



Among substrates examined, *N*-phenylpyrazole (**8a**) was found to a superior substrate. The results of the reactions of substituted *N*-arylpayrazoles are shown in Table 3. In all cases, the starting materials were not completely consumed, even when the reaction was carried out for extended reaction times or with higher catalyst loading. It has already been noted that the coordination ability of a directing group and the electronic nature of a substituent on the phenyl ring has a significant effect on the ratio of monocarbonylation product to dicarbonylation product.<sup>10a</sup> The reaction of *N*-phenylpyrazoles bearing an electron-donating group proceeded smoothly, irrespective of the substitution position. On the other hand, the substitution of an electron-withdrawing group on the benzene ring, as in **8e** and **8f**, led to a low conversion, even when longer reaction times were used. These results provide convincing evidence that in contrast to arylpyridines,<sup>10a</sup> dicarbonylation does not take place in the reaction of *N*-arylpayrazoles because the first carbonylation results in an electron-withdrawing keto group being introduced on the aromatic ring. The substitution of a methyl group at the ortho position, as in **8g**, also gives a lower product yield. In contrast to the case of the methyl group, a methoxy group in **8i** had no influence on the yield. The reason why the *o*-methyl group retarded the desired carbonylation is probably that cleavage of the benzylic C–H bond took place, along with cleavage of the ortho C–H bond.<sup>19</sup> The reaction of meta-substituted substrates **8j–l** resulted in site-selective

**TABLE 3. The Ru<sub>3</sub>(CO)<sub>12</sub>-Catalyzed Carbonylation at C–H Bonds in *N*-Arylpyrazoles<sup>a</sup>**

pyrazole	product <sup>b</sup>	pyrazole	product <sup>b</sup>
	 <b>9b</b> 87% (nd) <sup>c</sup>		 <b>9i</b> 94% (5%)
	 <b>9c</b> 87% (12%)		 <b>9j</b> 86% (10%)
	 <b>9d</b> 89% (3%)		 <b>9k</b> 45% (27%)
	 <b>9e</b> 31% (50%) 40% (49%) <sup>d</sup>		 <b>9l</b> 25% (47%)
	 <b>9f</b> 37% (45%)		 <b>9m</b> 54% (42%)
	 <b>9g</b> 30% (65%) 45% (47%) <sup>d</sup>		 <b>9n</b> 0% (nd) <sup>c</sup>
	 <b>9h</b> trace (nd) <sup>c</sup>		 <b>9o</b> 86% (13%)
			 <b>9p</b> trace (nd) <sup>c</sup>

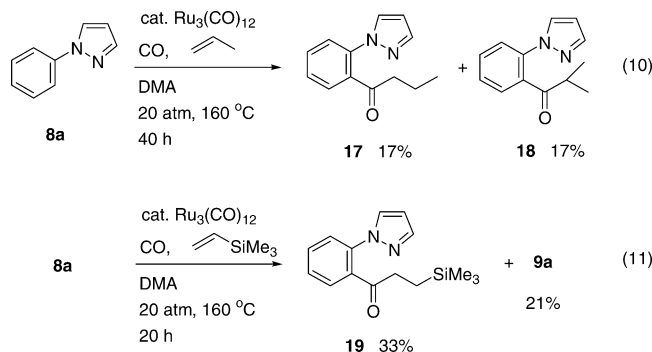
<sup>a</sup> Reaction conditions: *N*-arylpyrazole (2 mmol), ethylene (7 atm), CO (20 atm), Ru<sub>3</sub>(CO)<sub>12</sub> (0.05 mmol) in DMA (6 mL) at 160 °C for 20 h. <sup>b</sup> Isolated yields based on *N*-arylpyrazole. The numbers in parentheses are the recovered yield of *N*-arylpyrazole. <sup>c</sup> Not determined. <sup>d</sup> 160 °C.

carbonylation. Thus, the carbonylation occurred exclusively at the less hindered C–H bond. While the 2-naphthyl substrate **8o** gave the expected ketone **9o** in high yield, the 1-naphthyl substrate **8p** gave no carbonylation product, probably because of the steric repulsion of the peri-hydrogen at the 8-position.

While *tert*-butylethylene failed to react,<sup>13</sup> the reaction with propylene or vinylsilane, in place of ethylene, afforded the corresponding ketones (eqs 10 and 11). The reaction of **8a** with propylene gave a 1:1 mixture of normal and branched isomers **17** and **18** (eq 10). When trimethylvinylsilane was used as the alkene, the expected

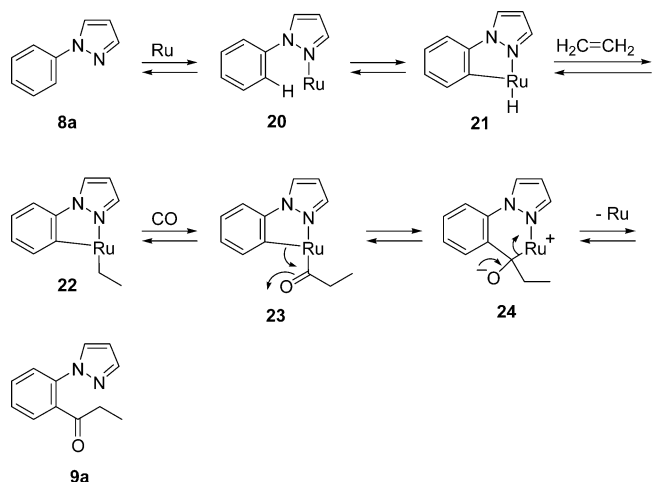


ketone **19** was obtained as the major product, along with protodesilylated ketone **9a** in 21% yield (eq 11).<sup>20</sup> The lack of reactivity of  $\alpha$ -olefins other than ethylene limits the scope of the reaction.



A proposed mechanism for this reaction is shown in Scheme 1. The coordination of the  $\text{sp}^2$  nitrogen in **8a** to

### SCHEME 1. A Proposed Mechanism



ruthenium gives **20**. The site-selective cleavage of the ortho C–H bond takes place to give a hydride complex **21**, in which ethylene and CO are inserted to give an acyl complex **23**. The C–C bond formation step proceeds via the attack of the ortho carbon in **23** to the keto-carbon, leading to the tetrahedral intermediate **24**.<sup>21</sup> We specu-

(19) We recently found the transformation of C–H bonds to the C–Si bond by the Ru-catalyzed reaction of **8g** with a hydrosilane at the benzylic position. Kakiuchi, F.; Igi, K.; Matsumoto, M.; Hayamizu, T.; Chatani, N.; Murai, S. *Chem. Lett.* **2002**, 396. In the case of the carbonylation of **8g**, the cleavage of the benzylic C–H bonds did not lead to the formation of carbonylation product, although we do not know the reason.

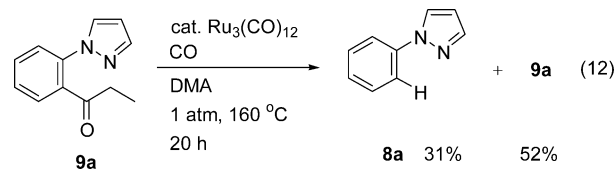
(20) The mechanism of the formation of **9a** is not clear. We have already obtained similar results, see ref 10a,c. There are two possible mechanisms for the formation of a protodesilylated product. One involves the formation of **9a** by the reaction of **8a** with CO and ethylene, which is formed, along with disilylethylene, from two molecules of vinylsilane via a Ru-catalyzed metathesis of vinylsilanes. For a paper on the ruthenium-catalyzed conversion of vinylsilane to ethylene and disilylethylene, see: Seki, Y.; Takeshita, K.; Kawamoto, K. *J. Organomet. Chem.* **1989**, 369, 117. An alternative mechanism involves the hydrolysis of  $\alpha$ -silyl ketone, a regioisomer of **19**.

(21) The mechanisms of carbon–heteroatom bond-forming reductive elimination of amines, ethers, and sulfides have recently been studied by Hartwig and Buchwald independently. The proposed mechanisms are stepwise mechanisms, which involve the inner-sphere attack of one ligand at the  $\pi$ -bond of the other ligand. Hartwig, J. F. *Acc. Chem. Res.* **1998**, 31, 852. Widenhofer, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, 120, 6504.

late that reductive elimination leading to the product is the rate-determining step. As the electron-donating nature of the nitrogen in the pyrazole ring attached to the benzene ring enhances the nucleophilicity of the ortho carbon atom,<sup>22</sup> the step (**23**  $\rightarrow$  **24**) is accelerated. This might be a reason why the pyrazole ring functions as a more superior directing group than anticipated from its lower  $\text{p}K_a$  value.

The reaction is strongly affected by the electron density of the benzene ring. In fact, the presence of an electron-donating group on the benzene ring renders the substrate more reactive. Furthermore, the upfield shift (119.4 ppm) of the ortho carbon atom in the  $^{13}\text{C}$  NMR spectrum of *N*-phenylpyrazole (**8a**) indicates that the electron density of the ortho carbon is increased relative to that of unsubstituted benzene (128.5 ppm).<sup>22</sup> On the other hand, in the case of 2-phenylthiazole (**1**),<sup>23</sup> 2-phenyloxazole (**4**),<sup>24</sup> and 1-methyl-3-phenyl-1*H*-pyrazole (**6**),<sup>25</sup> the  $^{13}\text{C}$  NMR chemical shifts for the ortho carbon atoms are shifted slightly downfield to that of unsubstituted benzene, indicating that the heterocyclic rings function as electron-withdrawing groups. On the basis of the  $^{13}\text{C}$  NMR chemical shift (126.8 ppm) of the ortho carbon atom in 2-phenylpyridine, it would be expected to be less reactive. However, 2-phenylpyridine is a good substrate for the carbonylation of ortho C–H bonds.<sup>10a</sup> These results indicate that  $\text{p}K_a$  values represent a good indicator of reactivity. Thus, the  $\text{p}K_a$  value (5.19) of 2-phenylpyridine apparently indicates a high reactivity. Consequently,  $\text{p}K_a$  values are important factors when conjugation between an aromatic C=C bond and a C=N bond is present in a directing group. Electron density is also an important factor in the case of substrates, such as *N*-phenylpyrazole, in which the electron-donating nature of the nitrogen is attached directly to the benzene ring. A similar high reactivity was observed in the carbonylation of the C–H bond  $\delta$  to a nitrogen (see (iv) in Chart 1).<sup>11h</sup>

In most cases, the starting materials were not completely consumed even with higher catalyst loadings or longer reaction times. We therefore speculate that the backward reaction took place from ethyl ketones (carbonylated products) to starting materials, similar to the case of oxazolylphenyl ethyl ketone, reported by us.<sup>26</sup> On the basis of this assumption, the following experiments were conducted (eq 12).



This result indicates that a decarbonylation reaction from ethyl ketones to starting materials occurs, although

(22) Carrillo, J. R.; Cossío, F. P.; Díaz-Ortiz, A.; Gómez-Escalonilla, M. J.; de la Hoz, A.; Lecea, B.; Moreno, A.; Prieto, P. *Tetrahedron* **2001**, 57, 4179. See also: Carrillo, J. R.; Cossío, F. P.; Díaz-Ortiz, A.; Gómez-Escalonilla, M. J.; de la Hoz, A.; Lecea, B.; Moreno, A.; Prieto, P. *Tetrahedron* **2001**, 57, 4179.

(23) Steel, P. J.; Caygill, G. B. *J. Organomet. Chem.* **1987**, 327, 101.

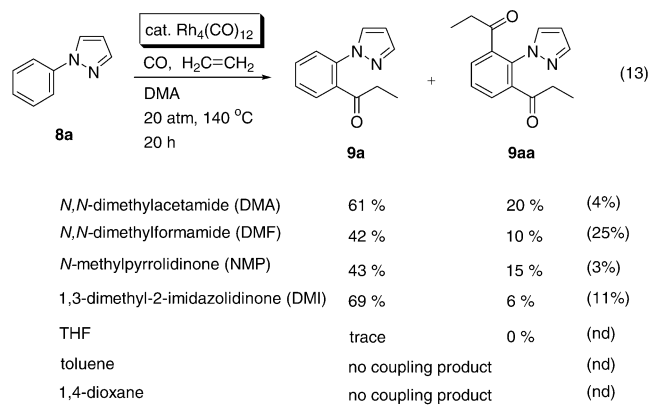
(24) Crowe, E.; Hossner, F.; Hughes, M. J. *Tetrahedron* **1995**, 51, 8889. Prager, R. H.; Smith, J. A.; Weber, B.; Williams, C. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2665.

(25) Pavlik, J. W.; Kebede, N. *J. Org. Chem.* **1997**, 62, 8325.

(26) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1999**, 121, 8645.

the efficiency is low. It is likely that this carbonylation resulted in *no* full conversion in many cases, due to the backward reaction. The mechanism controlling the backward reaction is the reverse of that for the carbonylation reaction and is initiated by a nucleophilic attack by ruthenium on the carbonyl carbon in the ethyl ketone to form the complex **24**. However, decarbonylation does not proceed efficiently compared with the case of pyridylphenyl ketones and oxazolylphenyl ketones because of the lower electrophilicity of the carbonyl carbon in **9a** compared to those of pyridylphenyl ketones and oxazolylphenyl ketones. Since the pyrazole  $\text{sp}^3$  nitrogen acts as an electron-donating group through the benzene ring, the electron density of the carbonyl carbon is increased.

**$\text{Rh}_4(\text{CO})_{12}$ -Catalyzed Reaction of *N*-Arylpyrazoles with CO and Alkenes.** In all chelation-assisted direct carbonylations at the ortho C–H bonds in a benzene ring reported thus far,  $\text{Ru}_3(\text{CO})_{12}$  was the only active catalyst.<sup>10</sup> However, it was found that carbonylation at C–H bonds in *N*-arylpyrazoles is also efficiently catalyzed by  $\text{Rh}_4(\text{CO})_{12}$  even at 140 °C, provided DMA is used as the solvent (eq 13). This is the first example of a rhodium-



The numbers in parenthesis are the recovered yield of **8a**.

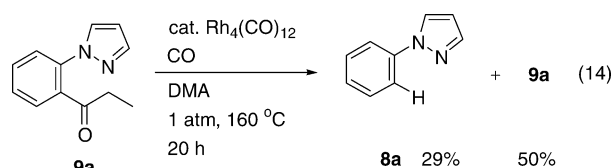
catalyzed direct carbonylation at C–H bonds  $\gamma$  to the  $\text{sp}^2$  nitrogen.<sup>27,28</sup> The addition of phosphines, such as  $\text{PPh}_3$ ,  $\text{PBu}_3$ , and  $\text{dppp}$ , inhibited the reaction. Dramatic solvent effects were also observed in the Rh-catalyzed carbonylation of *N*-arylpyrazoles. The use of common solvents, such as THF, toluene, and 1,4-dioxane, gave only small yields of product or none at all, but amide-based solvents, such as DMA, DMF, NMP, and DMI, allowed the reaction to proceed. Among the amide solvents, DMA was again the solvent of choice.

The results for the  $\text{Rh}_4(\text{CO})_{12}$ -catalyzed carbonylation at C–H bonds in *N*-arylpyrazoles are shown in Table 4. A characteristic feature is that the reaction was not affected by steric substitution, as shown by the ortho-substituted substrates **8g** and **8p**. The reaction of **8p** in the presence of  $\text{Ru}_3(\text{CO})_{12}$  led to no conversion (see Table 3), but  $\text{Rh}_4(\text{CO})_{12}$  gave **9p** in 70% yield. The reaction was significantly affected by the electronic nature of a substituent compared with the case of the  $\text{Ru}_3(\text{CO})_{12}$ -

catalyzed reaction. The introduction of an electron-withdrawing group in the benzene ring resulted in low product yields, as in **8e**, **8f**, and **8k**. In contrast, the reaction of substrates bearing an electron-donating group, such as **8c** and **8j**, gave a small amount of dicarbonylation products. Although the reason for this is not clear at present, the 3-thienyl substrate **8n**, which gave no coupling product in the case of  $\text{Ru}_3(\text{CO})_{12}$ , reacted to give the corresponding ketone **9n**, when Rh-catalyzed reaction conditions were employed.

Several other olefins were examined. It was, however, found that no other olefins, e.g. propylene, vinylsilane, and 1-hexene, are applicable to the Rh system. The scope of this reaction is less wider than that of the Ru system.

The decarbonylation reaction was also found to be catalyzed by  $\text{Rh}_4(\text{CO})_{12}$  (eq 14), indicating that the reversibility of carbonylation is similar to that for the ruthenium-catalyzed system.



The proposed mechanism of the Rh-catalyzed carbonylation of *N*-phenylpyrazoles is the same as that for the Ru system. The choice of solvent is also important and DMA was, again, the solvent of choice.

## Summary

We previously observed that the  $\text{pK}_a$  value of the conjugate acids of heterocycles (directing group) is an important factor in evaluating the efficiency of the carbonylation at C–H bonds. The higher the  $\text{pK}_a$ , the higher the overall reactivity. In this context, a pyrazole ring was predicted to be a less effective directing group. However, *N*-arylpyrazoles were found to be much more reactive than anticipated, based on their  $\text{pK}_a$  values. This is presumably due to the electron-rich system that accelerates the reductive elimination. It was found that, not only  $\text{pK}_a$  values of the directing groups, but electron density of benzene rings in the substrates as well are important factors in the chelation-assisted direct carbonylation of C–H bonds. In addition, it was found that rhodium complexes also have the ability to catalyze C–H/CO/olefin coupling. These are important aspects and suggest that a new type of carbonylation reactions at C–H bonds should be explored through the coordination of a directing group.

## Experimental Section

**Typical Procedure for the Ru-Catalyzed Carbonylation.** In a 50-mL stainless autoclave were placed  $\text{Ru}_3(\text{CO})_{12}$  (32 mg, 0.05 mmol), 1-phenylpyrazole (**8a**) (288 mg, 2 mmol), and DMA (6 mL). After the system was flushed with 10 atm of ethylene three times, it was pressurized with ethylene to 7 atm and then with carbon monoxide to an additional 20 atm. The autoclave was then immersed in an oil bath at 160 °C. After 20 h, it was removed from the oil bath and allowed to cool for ca. 1 h and the gases were then released. The contents were transferred to a separatory funnel with EtOAc. EtOAc (50 mL) and water (50 mL) were added and then the organic

(27) We have already developed Rh-catalyzed carbonylation reactions of the C–H bond at the olefinic C–H bond or the  $\text{sp}^3$  C–H bond, see ref 11b,c,e,g.

(28) In a pioneering study, Hong and Yamazaki reported on the Rh-catalyzed carbonylation of benzene, although the selectivity of products was quite low. See ref 2.

**TABLE 4.** The  $\text{Rh}_4(\text{CO})_{12}$ -Catalyzed Carbonylation at C–H Bonds in *N*-Arylpyrazoles<sup>a</sup>

pyrazole		product <sup>b</sup>		pyrazole		product <sup>b</sup>	
		50%				14% (69%)	
		4% (70%)				29% (59%)	
		14% (53%)				44%	
		33% (63%) 88% (0%) <sup>c</sup>				39% (36%)	
		99% (0%)				83% (10%)	
		62%				70% (15%) <sup>c,d</sup>	
		21% (9%)	17%				
		21% (0%)					

<sup>a</sup> Reaction conditions: *N*-arylpyrazole (2 mmol), ethylene (7 atm), CO (20 atm),  $\text{Rh}_4(\text{CO})_{12}$  (0.05 mmol) in DMA (3 mL) at 140 °C for 20 h. <sup>b</sup> Isolated yields based on *N*-arylpyrazole. The numbers in parentheses are the recovered yield of *N*-arylpyrazole. <sup>c</sup> 60 h. <sup>d</sup> 160 °C.

layer was separated, washed, with water (50 mL×2) and saturated brine (50 mL), and dried over anhydrous  $\text{MgSO}_4$ . After filtration and evaporation, the resulting residue was subjected to column chromatography on silica gel with hexane/EtOAc as the eluent to give 1-[2-(1*H*-pyrazolyl)phenyl]-1-propanone (**9a**) (377 mg, 94% yield) as a colorless oil. An analytical sample was obtained by bulb-to-bulb distillation.

**Typical Procedure for the Rh-Catalyzed Carbonylation.** In a 50-mL stainless autoclave were placed  $\text{Rh}_4(\text{CO})_{12}$  (37 mg, 0.05 mmol), 1-phenylpyrazole (**8a**) (288 mg, 2 mmol), and DMA (3 mL). After the system was flushed with 10 atm of ethylene three times, it was pressurized with ethylene to 7 atm and then with carbon monoxide to an additional 20 atm. The autoclave was then immersed in an oil bath at 140 °C. After 20 h, it was removed from the oil bath and allowed to cool for ca. 1 h and the gases were then released. The contents were transferred to a round-bottomed flask with EtOAc, and the volatiles were removed by evaporation. The resulting residue was subjected to column chromatography on silica gel with hexane/Et<sub>2</sub>O as the eluent to give 1-[2-(1*H*-pyrazolyl)phenyl]-1-propanone (**9a**) (244 mg, 61% yield) as a colorless oil and 1-[3-(1-propionyl)-2-(1*H*-pyrazolyl)phenyl]-1-propanone (**9aa**) (102 mg, 20% yield) as a colorless oil. Analytical samples were obtained by bulb-to-bulb distillation.

**1-[2-(1*H*-Pyrazolyl)-3-methylphenyl]-1-propanone (**9g**).** Colorless oil; bp 110 °C (1 mmHg);  $R_f$  0.57 (hexane/EtOAc = 1/1); <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0.93 (t,  $J$  = 7.36 Hz, 3H), 2.09 (q,  $J$  = 7.3 Hz, 2H), 2.15 (s, 3H), 6.46 (dd,  $J$  = 2.3, 2.0 Hz, 1H), 7.37–7.42 (c, 3H), 7.51 (d,  $J$  = 2.3 Hz, 1H), 7.72 (d,  $J$  = 2.0 Hz, 1H);

<sup>13</sup>C NMR ( $\text{CDCl}_3$ )  $\delta$  8.3, 17.6, 34.7, 106.8, 125.6, 128.8, 131.9, 133.0, 135.9, 136.7, 138.9, 140.5, 204.6; IR (neat) 3476 w, 3120 w, 2984 m, 2940 m, 1694 s, 1588 m, 1516 s, 1478 s, 1414 m, 1394 s, 1352 m, 1320 m, 1290 s, 1190 m, 1172 m, 1124 w, 1088 m, 1044 m, 1022 m, 972 m, 940 s, 868 w; MS,  $m/z$  (rel intensity, %) 214 ( $\text{M}^+$ , 0), 186 (19), 185 (100). Anal. Calcd for  $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}$ : C, 72.87; H, 6.59; N, 13.07. Found: C, 72.97; H, 6.80; N, 13.03.

**1-[1-(1*H*-Pyrazolyl)-2-naphthalenyl]-1-propanone (**9p**).** Colorless oil; bp 150 °C (1 mmHg);  $R_f$  0.51 (hexane/EtOAc = 2/1); <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0.99 (t,  $J$  = 7.3 Hz, 3H), 2.14 (q,  $J$  = 7.3 Hz, 2H), 6.58 (dd,  $J$  = 2.0, 1.3 Hz, 1H), 7.49–7.65 (c, 3H), 7.63 (d,  $J$  = 8.6 Hz, 1H), 7.70 (d,  $J$  = 2.0 Hz, 1H), 7.86 (d,  $J$  = 1.3 Hz, 1H), 7.93 (d,  $J$  = 7.6 Hz, 1H), 7.98 (d,  $J$  = 8.6 Hz, 1H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ )  $\delta$  8.4, 34.9, 107.3, 123.8, 124.1, 127.8, 127.9, 128.0, 129.5, 130.0, 133.3, 134.7, 134.9, 135.2, 141.1, 204.7; IR (neat) 3860 w, 3548 w, 3376 w, 3112 m, 2988 m, 2944 w, 2884 w, 2560 w, 2456 w, 1984 w, 1948 w, 1826 w, 1792 w, 1752 w, 1696 s, 1626 m, 1600 w, 1572 m, 1512 m, 1466 m, 1430 s, 1402 s, 1328 m, 1350 m, 1306 m, 1266 w, 1222 m, 1188 m, 1164 w, 1134 w, 1088 m, 1054 m, 1034 w, 992 w, 964 m, 924 m, 896 w, 860 m; MS,  $m/z$  (rel intensity, %) 250 ( $\text{M}^+$ , 2), 222 (23), 221 (100), 166 (12). Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$ : C, 76.78; H, 5.64; N, 11.19. Found: C, 76.70; H, 5.55; N, 11.16.

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versity, for assistance in obtaining MS, HRMS, and elemental analyses.

**Supporting Information Available:** Full experimental details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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