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Rhodium-catalyzed coupling reaction of 2-vinylpyridines with 1,5-hexadiene: effects of phosphine ligands

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Abstract

The coupling reaction of 2-isopropenylpyridine with 1,5-hexadiene via C–H bond activation gave different products depending on the ligands: triphenylphosphine as a ligand led to the cyclized products and trimethylphosphite to the Markovnikov addition product. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: coupling reaction; C–H bond activation; rhodium catalyst.

Recently, the formation of C–C bond by C–H bond activation and insertion of unsaturated substrates has become a useful method for use in synthetic chemistry. The alkylation with alkenes and alkynes via C–H bond activation has been reported by us[1] and other groups.[2–8] During the course of our studies of alkylation by rhodium metal catalysts, we have found the very interesting results in which the coupling reaction of 2-isopropenylpyridine **1a** with 1,5-hexadiene **2** gave different products depending on the ligands. Here we report the preliminary results of the coupling reaction of **1** with **2** via C–H bond activation in the presence of a rhodium catalyst as shown in Scheme 1.

Substrate **1a** reacted with 1.5 equiv. of **2** in the presence of $RhCl(PPh_3)_3$ (10 mol%) in toluene at 130°C for 20 h to give the 5-membered ring compounds **3** and **4** in 75% isolated yield along with small amounts of the linear product **5** (**3**:**4**:**5**=69:28:3). Doubly intermolecular-alkylated product **6**, containing 2-isopropenylpyridyl moiety introduced in both terminal alkenes of **2**, was also isolated in 20% yield. Neither 6- nor 7-membered ring products were detected in this reaction. The alkylated product **3** may be formed by intermolecular coupling, *E*–*Z* isomerization[1e] and then intramolecular coupling,[2d,g,h] taking place successively. In order to reduce the undesired product **6**, excess (2 equiv. and 5 equiv.) of **2** was used, but the reaction could not be improved.

Toluene as a solvent gave better results than THF. Another hexadiene such as 1,4-hexadiene gave **3** as the major product under the same reaction conditions but the ratio of the linear product **5** was higher than

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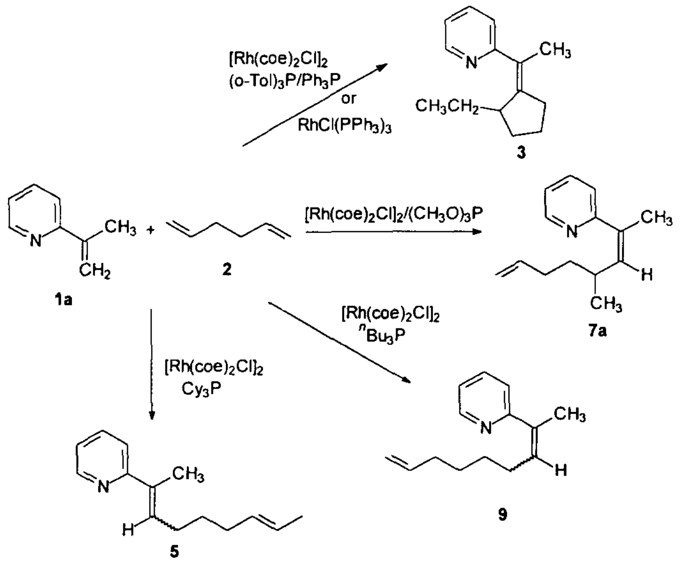
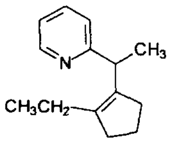


Scheme 1.

that of **2**. It was found that **4** was formed by the isomerization of *exo* double bond to *endo* double bond of the cyclic product **3** under both thermal and rhodium-catalyzed conditions.

A mixture of 5 mol% of chlorobis(cyclooctene)rhodium(I) dimer [Rh(coe)$_2$Cl]$_2$, 20 mol% of PPh$_3$ and 20 mol% of (*o*-tolyl)$_3$P also gave similar results (72%, **3**:**4**:**5**=73:25:2; 19% **6**).

Substrate **1a** reacted with **2** in the presence of [Rh(coe)$_2$Cl]$_2$ (5 mol%) and trimethylphosphite (6 equiv. based on Rh) in toluene to give the Markovnikov addition product **7a** in 53% isolated yield; **1a** was recovered in 22% (run 1 in Table 1). Most cases of this type of alkylation gave the anti-Markovnikov addition product exclusively,[1a–f] but interestingly, this catalytic system exclusively gave the Markovnikov addition product. In order to understand the effect of amounts of P(OMe)$_3$, 4 equiv. and 5 equiv. respectively, of it to Rh were applied to this reaction. The former showed that the total isolated yield enhanced to 87%, but *E*-isomer of **7a** and **8a** formed (run 3 in Table 1). The latter gave the enhancement of yield (77%) and the high ratio of **7a** (run 2). The above results led to us to decide that 5 equiv. of P(OMe)$_3$ is applied to various substrates.



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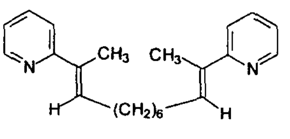

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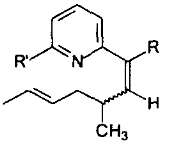

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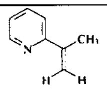
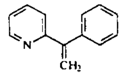
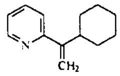
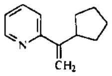
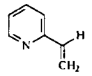
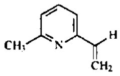
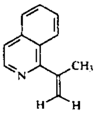
The results of these reactions are listed in Table 1. Substrates **1b**–**1d** (R=Ph, cyclohexyl and cyclopentyl), like **1a**, worked well (runs 4–6). But, substrates **1e** and **1f** reacted sluggishly to give **7e** and **7f** in 15% yields, respectively (runs 7, 8), because of their low reactivity.[1e] Isoquinolinyl substrate **1g** also worked well under the same reaction conditions (run 9). β-Substituted 2-vinylpridine and 3-methyl-2-phenylpyridine did not work, maybe due to steric congestion. Other alkenes such as 1,4-pentadiene, 1,7-octadiene and 1-hexene gave no coupling products under this catalytic system; **1a** was recovered.[9]

When used tri-*n*-butylphosphine as a ligand, the coupling reaction of **1a** with **2** gave a mixture of *Z*- and *E*-isomers of **9** (*Z*:*E*=88:12) in 56% isolated yield together with *Z*-isomer of **6** (13%); 23% of **1a** was recovered. Use of tricyclohexylphosphine (Cy$_3$P) gave **5** as a major product (61%, *E*:*Z*=74:26; 14%

Table 1
The results of coupling reaction of **1a**–**g** with **2** by [Rh(coe)$_2$Cl]$_2$/(MeO)$_3$P[a]

Entry	Substrate	[Rh(coe)$_2$Cl]$_2$/ (McO)$_3$P	Isolated yield (%)	Ratio of Products[b]	
				7 :	**8**
1	 **1a**	6	53[c]	R = Me, **7a** 100 ($Z:E$ = 100 : 0)	R = Me 0
2		5	77	R = Me, **7a** 92 ($Z:E$ = 95 : 5)	8
3		4	87	R = Me, **7a** 45 ($Z:E$ = 62 : 38)	55
4	 **1b**	5	66[d]	R = Ph, **7b** 100 ($Z:E$ = 97 : 3)	R = Ph 0
5	 **1c**	5	83	R = C_6H_{11}, **7c** 85 ($Z:E$ =100 : 0)	R = C_6H_{11} 15
6	 **1d**	5	80	R = C_5H_9, **7d** 93 ($Z:E$ = 100 : 0)	R =C_5H_9 7
7	 **1e**	5	15[e]	R = H, **7e** 100 ($Z:E$ = 93 : 7)	R = H 0
8	 **1f**	5	15[e]	R = H, **7f** 100 ($Z:E$ = 100 : 0)	R = H 0
9	 **1g**	5	86	R = CH_3, **7g** 69 ($Z:E$ = 100 : 0)	R = CH_3 31

[a] Substrate : [Rh(coe)$_2$Cl]$_2$: 1,5-hexadiene = 1 : 0.05 : 1.5, 140 °C, 20 h, toluene (4.5cm^3), [b] ratio of isomers was determined by ^{1}H NMR, [c] 22% of the starting material was recovered, [d] 18% of the starting material was recovered. [e] starting material was remained in the reaction mixture.

6). However, Me$_3$P, Ph$_2$P(CH$_2$)$_3$PPh$_2$ and (PhO)$_3$P were inactive. Further detailed investigations of these efforts are currently underway in our laboratory.

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9. These experiments were carried out to obtain information for the mechanistic aspect. These results imply that 5-membered ring rhodium intermediate formed from 1,5-hexadiene is stable in catalytic cycle.