JOC Article

Phosphine-Free Palladium Catalyzed Mizoroki−Heck Reaction Using Hydrazone as a Ligand

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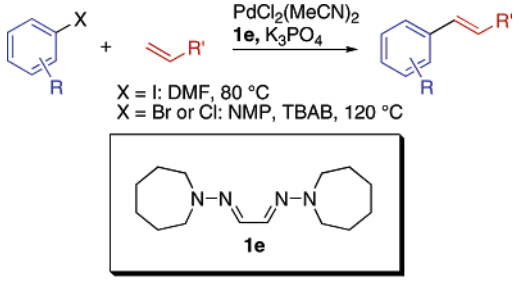

Glyoxal bishydrazones **1** and pyridyl-hydrazone **2b** were prepared and examined as a ligand for the Mizoroki−Heck cross-coupling reaction of aryl halides and olefin. We found that $PdCl_2(MeCN)_2$/hydrazone ligand **1e** was a phosphine-free efficient catalyst system for a variety of substrates to produce the Mizoroki−Heck coupling products in good yields.

Introduction

The palladium catalyzed C−C coupling reactions have been recognized as powerful tools in multiple organic transformations. One of the most important C−C coupling reactions is the Mizoroki−Heck reaction,[1,2] such as the arylation or vinylation of olefins by aryl or vinyl halides. The reaction has been applied to many areas, including natural product[3] and fine chemicals syntheses.[4] Palladium−phosphine complexes have been employed as an effective catalyst in controlling the reactivity and selectivity in the Mizoroki−Heck reaction. The main role of tertiary monophosphine ligands is to stabilize the palladium(0) as the PdL_4 species, which can enter the catalytic cycle and consequently prevent the formation of inactive palladium black. Important examples of the use of phosphines are found in the work of Fu,[5] Beller,[6] and Hartwig[7] who have made use of sterically demanding, electron-rich tertiary phosphines as catalyst modifiers in the Mizoroki−Heck reactions. The ligand properties in these cases make possible the activation of the less reactive aryl bromides and aryl chlorides, as well as palladacycle formed by the reaction of $Pd(OAc)_2$ and tris(*o*-tolyl)phosphine, which represents a very active catalyst for aryl bromides and activated aryl chlorides.[8] However, their phosphine or palladium complexes are often air-sensitive. On the other hand, nucleophilic *N*-heterocyclic carbenes (NHC), the imidazol-2-ylidenes, have

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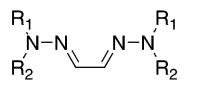
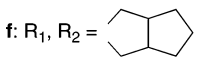
attracted extensive attention because of their similar electronic and steric properties to basic phosphines. NHC ligands have been employed efficiently for the Mizoroki−Heck reaction.[9] Alternatively, a noncarbene type nitrogen-containing ligand for palladium-catalytic systems was less explored. A palladacycle type imine[10] or oxime[11] catalyst for the Mizoroki−Heck reaction has been reported. Furthermore, recently diimine type ligands containing the 1,4-diaza-1,3-butadiene skeleton[12] and pyridylimine[13] have also been used as ligands for this reaction. We previously reported the Suzuki−Miyaura cross-coupling reaction using glyoxal bis(*N*-methyl-*N*-phenylhydrazone) (**1a**) and 2-pyridinecarboxaldehyde *N*-methyl-*N*-phenylhydrazone (**2a**) as ligands of the catalyst precursor.[14] We now wish to report the use of a modified phosphine-free hydrazone ligand such as **1e** for Mizoroki−Heck cross-coupling reactions.

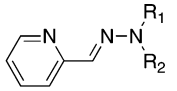


1

a: R_1 = Ph, R_2 = Me
b: R_1 = R_2 = Me
c: R_1, R_2 = -$(CH_2)_4$-
d: R_1, R_2 = -$(CH_2)_5$-
e: R_1, R_2 = -$(CH_2)_6$-



f: R_1, R_2 =



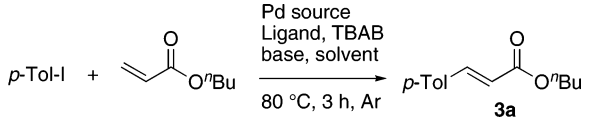
2

a: R_1 = Ph, R_2 = Me
b: R_1, R_2 = -$(CH_2)_6$-

Results and Discussion

Optimization of Reaction Conditions. Glyoxal bishydrazones **1** and 2-pyridinecarboxaldehyde hydrazone **2b** were prepared from glyoxal or 2-pyridinecarboxaldehyde with various commercially available hydrazines in methanol. Using phosphine-free air-stable hydrazone ligands **1** and **2b**, we applied the coupling of 4-iodotoluene and *n*-butyl acrylate in the presence of 2 mol % $PdCl_2(MeCN)_2$ and 10 mol % tetra-*n*-butylammonium bromide (TBAB) as the reagent for activation and stabilization of palladium(0) species[12] under an argon atmosphere at 80 °C to determine the optimum reaction conditions (Table 1). In the presence of glyoxal bis(*N*-methyl-*N*-phenylhydrazone) (**1a**), which was the effective ligand for the Suzuki−Miyaura reaction,[14] Mizoroki−Heck cross-coupling product **3a** was obtained in moderate yield (entry 1). The effect of ligands in this reaction was investigated (entries 1−7). Although bicyclic-type bishydrazone ligand **1f** and a pyridine-type ligand with a 7-membered-ring, such as **2b**, were also effective ligands for the Mizoroki−Heck reaction, the use of **1e** as a ligand led to higher yield for this reaction (entry 5 vs entries 6 and 7). Using K_3PO_4 as a base without the presence of TBAB, the reaction gave good yield of the desired product (entry 11 vs entries 5, 8−10, and 12). In this condition, several commonly used solvents were tested (entries 11 and 13−16). The nonpolar solvent toluene was not effective (entry 13), and polar solvents, such as DMAc and DMF, were preferred for this reaction (entries 11 and 16). Other palladium sources including $Pd(OAc)_2$ proved to be less effective in this reaction (entries 17−21). We found the following optimized conditions: using the $PdCl_2(MeCN)_2$/hydrazone **1e** system, the reaction proceeded with 97% in DMF with K_3PO_4 at 80 °C for 3 h under an argon atmosphere (entry 16). The molecular structure of the palladium complex derived from ligand **1a** had previously been determined by single-crystal X-ray diffraction (Figure 1).[14] This palladium atom bound to two nitrogen atoms and one carbon atom on ligand **1a**.

TABLE 1. Optimization of Reaction Conditions on Mizoroki−Heck Reaction of 4-Iodotoluene with *n*-Butyl Acrylate[a]



3a

entry	ligand	base	TBAB (mol %)	solvent	Pd source	yield (%)[b]
1	**1a**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	41
2	**1b**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	45
3	**1c**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	38
4	**1d**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	50
5	**1e**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	89
6	**1f**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	77
7	**2b**	NaOAc	10	DMAc	$PdCl_2(MeCN)_2$	79
8	**1e**	NaOAc		DMAc	$PdCl_2(MeCN)_2$	52
9	**1e**	Cs_2CO_3		DMAc	$PdCl_2(MeCN)_2$	42
10	**1e**	KO^{t}Bu		DMAc	$PdCl_2(MeCN)_2$	77
11	**1e**	K_3PO_4		DMAc	$PdCl_2(MeCN)_2$	93
12	**1e**	DIEA		DMAc	$PdCl_2(MeCN)_2$	90
13	**1e**	K_3PO_4		PhMe	$PdCl_2(MeCN)_2$	1
14	**1e**	K_3PO_4		MeCN	$PdCl_2(MeCN)_2$	17
15	**1e**	K_3PO_4		DMSO	$PdCl_2(MeCN)_2$	52
16	**1e**	**K_3PO_4**		**DMF**	**$PdCl_2(MeCN)_2$**	**97**
17	**1e**	K_3PO_4		DMF	$PdCl_2(PhCN)_2$	77
18	**1e**	K_3PO_4		DMF	$PdCl_2$	42
19	**1e**	K_3PO_4		DMF	$Pd(OAc)_2$	85
20	**1e**	K_3PO_4		DMF	$PdCl_2$(cod)	35
21	**1e**	K_3PO_4		DMF	$Pd(dba)_2$	45

[a] Reaction conditions: 4-iodotoluene (1 mmol), *n*-butyl acrylate (3 mmol), base (1.4 mmol), solvent (4 mL), Pd source (0.02 mmol), ligand **1** (0.02 mmol), 3 h. [b] Isolated yields.

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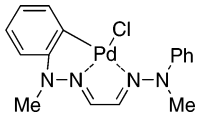

FIGURE 1. Palladium Complex from Ligand **1a**.

In the case of the palladium complex from a 1,4-diaza-1,3-butadiene type diimine ligand,[12,15] the palladium atom is also bound to two nitrogen atoms on the diimine ligand. Although analysis of a single-crystal X-ray diffraction of the palladium complex prepared from $PdCl_2(MeCN)_2$/hydrazone **1e** was not successful, it probably has a similar coordination, such as N−Pd−N, with a couple of C═N moieties on the hydrazone.

Mizoroki−Heck Reaction of Aryl Iodide with Olefin. The effect of various aryl iodides in the Mizoroki−Heck reaction was investigated using *n*-butyl acrylate as an olefin (Table 2). Using 4-substituted aryl iodides led to good yields of the desired products (entries 1−7). Moreover, 3-substituted and 2-substituted aryl iodides and 1-iodonaphthalene also led to good yields (entries 8−10). We also investigated the effect of varying the olefins using 4-iodotoluene as the substrate (entries 11−13). Using methyl acrylate led to good yield of the Mizoroki−Heck reaction product (entry 11). Although the reaction of acrylonitrile occurred easily, the desired *E*-isomeric product was obtained in good yields accompanied by *Z*-isomers, according to ^{1}H NMR analysis (entry 12). The reaction of 4-iodotoluene with styrene was necessary to extend longer reaction times, such as to 24 h (entry 13).

Mizoroki−Heck Reaction of Aryl Bromide and Chloride with Olefin. We next tried the coupling of 4-bromotoluene and *n*-butyl acrylate (Table 3). Using similar conditions to the coupling of aryl iodide (entry 1) and 5 mol % Pd catalyst for 24 h (entry 2), the reaction did not proceed; however, this result was not surprising because the bis-coupling product and/or *n*-butyl 4-iodocinnamate were not detected by GC and ^{1}H NMR analysis in the reaction of 1-bromo-4-iodobenzene and *n*-butyl acrylate (see entry 4, Table 2). Consequently, we attempted to re-optimize the conditions for the coupling of 4-bromotoluene and *n*-butyl acrylate (Table 3). When NMP was used as a solvent instead of DMF, a small amount of the Mizoroki−Heck reaction product was obtained (entry 3). After increasing the reaction temperature to 120 °C and adding 40 mol % TBAB, the reaction produced a good yield of the desired product (entry 7).

Next, we investigated the effect of various aryl bromides in the Mizoroki−Heck reaction using *n*-butyl acrylate (entries 1−9, Table 4). Using 4-substituted aryl bromides led to good yields of the desired products (entries 1−5). Although a 2-substituted aryl bromide, such as 2-tolylbromide, led to a low yield (entry 6), the reaction of 1-bromonaphthalene produced a good yield of the corresponding product (entry 7). The reaction of 4-bromotoluene with methyl acrylate and styrene gave the corresponding products with moderate to good yields (entries 8 and 9). We also tried the coupling reaction using aryl chlorides with *n*-butyl acrylate (entries 10−16, Table 4). Unfortunately, there was almost no reaction of the neutral (entry 10) and unactivated aryl chlorides (entry 11). On the other hand, the corresponding products were obtained in good yields using activated (electron-deficient) aryl chlorides including the ortho-substituted chlorides (entries 12−16).

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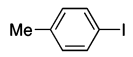
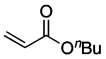
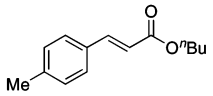
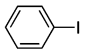
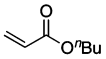
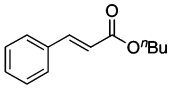
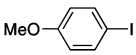
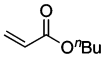
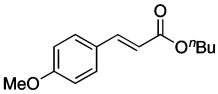
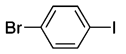
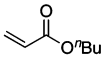
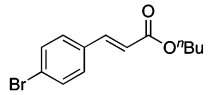
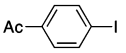
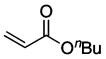
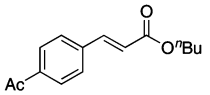
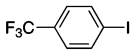
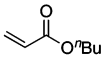
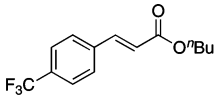
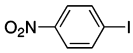
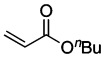
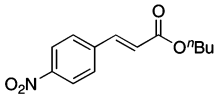
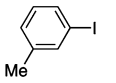
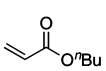
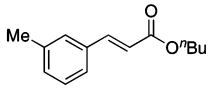
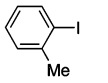
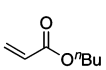
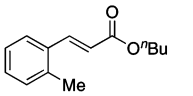
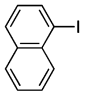
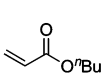
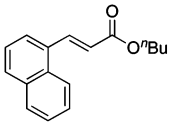
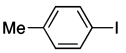
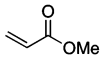
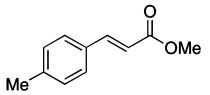
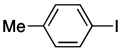
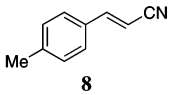
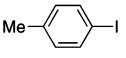
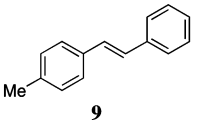
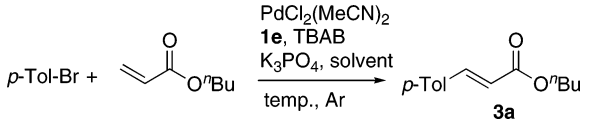
TABLE 2. Mizoroki−Heck Reaction of Aryl Iodide with Olefin[a]

entry	aryl iodide	olefin	time (h)	product	yield (%)[b]
1			3	 **3a**	97
2			3	 **3b**	93
3			6	 **3c**	91
4			6	 **3d**	99
5			3	 **3e**	92
6			6	 **3f**	97
7			9	 **3g**	93
8			6	 **4**	97
9			6	 **5**	78
10			6	 **6**	95
11			6	 **7**	92
12			6	 **8**	80[c]
13			24	 **9**	73

[a] Reaction conditions: aryl iodide (1 mmol), olefin (3 mmol), K_3PO_4 (1.4 mmol), DMF (4 mL), $PdCl_2(MeCN)_2$ (0.02 mmol), ligand **1e** (0.02 mmol). [b] Isolated yields. [c] *E*/*Z* = 3.7:1.

Mizoroki−Heck Reaction with Low Catalyst Loading. We investigated the low catalyst loading condition under the $PdCl_2(MeCN)_2$/hydrazone **1e** system (Scheme 1). The reaction of

TABLE 3. Optimization of Reaction Conditions on Mizoroki−Heck Reaction of 4-Bromotoluene with *n*-Butyl Acrylate[a]



entry	temp (°C)	TBAB (mol %)	solvent	yield (%)[b]
1[c]	80		DMF	0
2	80		DMF	0
3	80		NMP	17
4	120		NMP	38
5	120	5	NMP	50
6	120	20	NMP	79
7	120	40	NMP	89

[a] Reaction conditions: 4-bromotoluene (1 mmol), *n*-butyl acrylate (3 mmol), K_3PO_4 (1.4 mmol), solvent (4 mL), $PdCl_2(MeCN)_2$ (0.05 mmol), ligand **1f** (0.05 mmol), 24 h. [b] Isolated yields. [c] This reaction was carried out using 2 mol % of $PdCl_2(MeCN)_2$ for 3 h.

4-iodotoluene with *n*-butyl acrylate was carried out using 0.01 mol % Pd with 40 mol % TBAB in DMF at 130 °C. The reaction product was obtained quantitatively for 24 h. Using 0.0005 mol % Pd, the reaction also gave a good yield with a high turnover number (TON = 168000) and turnover frequency (TOF = 7000 h^{-1}).

Mizoroki−Heck Reaction at Room Temperature. We also investigated the coupling of 4-iodotoluene and *n*-butyl acrylate in the presence of 5 mol % $PdCl_2(MeCN)_2$/hydrazone **1e** at room temperature (Scheme 2). When the reaction was carried out in DMF, the corresponding product was obtained in moderate yield. However, when we used NMP as a solvent instead of DMF, the reaction gave a good yield of the desired product.

Conclusions

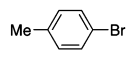
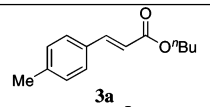
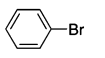
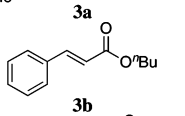
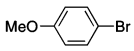
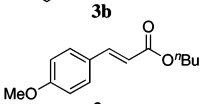
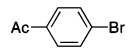
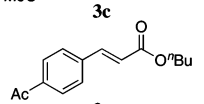
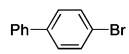
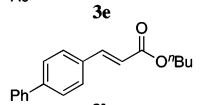
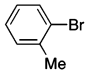
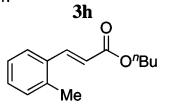
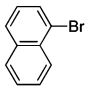
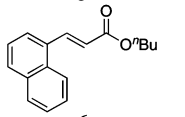
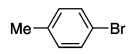
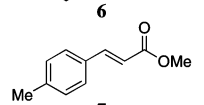
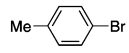
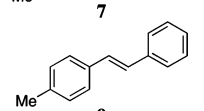
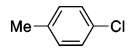
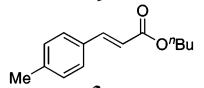
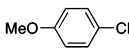
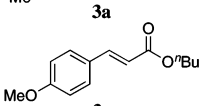
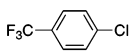
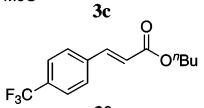
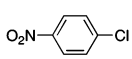
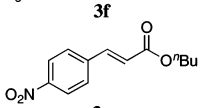
It can be concluded that the Mizoroki−Heck reaction of aryl halides and olefins can be performed under phosphine-free conditions, based on $PdCl_2(MeCN)_2$/hydrazone **1e**. Under the condition of low catalyst loading, ligand **1e** gave a high turnover number and turnover frequency. This palladium catalyst system shows the reactivity of the coupling reaction with 4-iodotoluene at room temperature and the reaction with electron-deficient aryl chlorides at 120 °C.

Experimental Section

Preparation of Glyoxal Bis(*N*-methyl-*N*-phenylhydrazone) (1a).[14] A mixture of *N*-methyl-*N*-phenylhydrazine (0.122 g, 1.0 mmol) in MeOH (1 mL) was added to 40 wt % of glyoxal in water (0.072 g, 0.5 mmol) at 0 °C. The mixture was stirred for 1 h at room temperature. The yellow solid precipitated and was collected by filtration, washed with water, and dried under reduced pressure. Recrystallization from hexane-chloroform gave **1a** as a yellow solid: 74% as a yellow solid; mp 209−210 °C. ^{1}H NMR ($CDCl_3$) δ: 3.39 (s, 6H), 6.89 (seq, J = 4.0 Hz, 2H), 7.31 (d, J = 4.2 Hz, 8H), 7.51 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 33.4, 115.3, 120.8, 129.0, 133.8, 147.6; EI-MS *m*/*z* (rel intensity): 266 (M^+, 71).

Typical Procedure for the Preparation of Ligands 1b−f. A mixture of hydrazine (1.0 mmol) in MeOH (1 mL) was added to 40 wt % of glyoxal in water (0.072 g, 0.5 mmol) at 0 °C. The mixture was stirred for 1 h at room temperature. The mixture was directly concentrated under reduced pressure. The

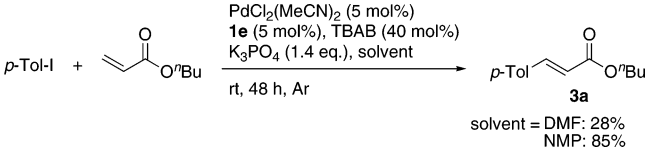
TABLE 4. Mizoroki−Heck Reaction of Aryl Bromide and Chloride with Olefin[a]

entry	aryl halide	olefin	time (h)	product	yield (%)[b]
1			24	 **3a**	89
2			24	 **3b**	77
3			24	 **3c**	52
4			24	 **3e**	69
5			24	 **3h**	94
6			24	 **5**	35
7			24	 **6**	93
8			24	 **7**	67
9			24	 **9**	30
10			48	 **3a**	trace
11			48	 **3c**	trace
12			24	 **3f**	44
13			24	 **3g**	69
14			24	**3i**	58
15			48	**10**	63
16			48	**11**	27

[a] Reaction conditions: aryl halide (1 mmol), olefin (3 mmol), K_3PO_4 (1.4 mmol), NMP (4 mL), $PdCl_2(MeCN)_2$ (0.05 mmol), ligand **1e** (0.05 mmol). [b] Isolated yields.

SCHEME 1. Low Catalyst Loading Mizoroki−Heck Reaction of 4-Iodotoluene with *n*-Butyl Acrylate

SCHEME 2. Mizoroki−Heck Reaction of 4-Iodotoluene with *n*-Butyl Acrylate at Room Temperature



residue was purified by silica gel chromatography (hexane/EtOAc = 4−1/1).

Glyoxal Bis(*N, N*-dimethylhydrazone) (1b).[16] Yield 81% as an orange liquid. ^{1}H NMR ($CDCl_3$) δ: 2.89 (s, 12H), 7.12 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 42.8, 134.6; EI-MS *m*/*z* (rel intensity): 142 (M^+, 45)

***N,N′*-(1,2-Ethanediylidene)bis-1-pyrrolidinamine (1c).** Yield 30% as a orange solid; mp 125−127 °C. IR(KBr): 1541 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.92 (q, J = 6.7 Hz, 8H), 3.25 (t, J = 6.7 Hz, 8H), 7.05 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 23.4, 50.9, 134.5. EI-MS *m*/*z* (rel intensity): 194 (M^+, 48). HRMS (FAB-MS): *m*/*z* calcd for $C_{10}H_{18}N_4$+H, 195.1610; found, 195.1615.

***N,N′*-(1,2-Ethanediylidene)bis-1-piperidinamine (1d).** Yield 93% as a white solid; mp 73−77 °C. IR(KBr): 1559 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.51 (q, J = 5.7 Hz, 4H), 1.71 (q, J = 5.7 Hz, 8H), 3.08 (t, J = 5.6 Hz, 8H), 7.37 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 24.4, 25.4, 52.4, 136.5. EI-MS *m*/*z* (rel intensity): 222 (M^+, 41). HRMS (FAB-MS): *m*/*z* calcd for $C_{12}H_{22}N_4$+H, 223.1923; found, 223.1922.

***N,N′*-(1,2-Ethanediylidene)bishexahydro-1*H*-azepin-1-amine (1e).** Yield 80% as a white solid; mp 101−103 °C. IR(KBr): 1544 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.55 (q, J = 2.9 Hz, 8H), 1.53−1.58 (m, 8H), 3.41 (t, J = 5.7 Hz, 8H), 7.03 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 27.5, 28.3, 53.3, 130.3. EI-MS *m*/*z* (rel intensity): 250 (M^+, 43). HRMS (FAB-MS): *m*/*z* calcd for $C_{12}H_{26}N_4$+H, 251.2240; found, 251.2236.

***N,N′*-(1,2-Ethanediylidene)bisoctahydrocyclopenta[*c*]pyrrole-1-amine (1f).** Yield 64% as a white solid; mp 83−84 °C. IR(KBr): 1543 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.42−1.55 (m, 6H), 1.57−1.64 (m, 2H), 1.67−1.86 (m, 4H), 2.60−2.71 (m, 4H), 2.93 (dd, J = 3.5 and 9.7 Hz, 4H), 3.30 (dd, J = 8.0 and 9.5 Hz, 4H), 7.08 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 26.4, 33.8, 40.8, 58.6, 137.3. EI-MS *m*/*z* (rel intensity): 274 (M^+, 19). HRMS (FAB-MS): *m*/*z* calcd for $C_{16}H_{26}N_4$+H, 251.2240; found, 275.2211.

Preparation of *N*-(2-Pyridinylmethylene)hexahydro-1*H*-azepin-1-amine (2b). A mixture of 1-aminohomopiperidine (1.375 g, 12.0 mmol) in MeOH (4 mL) was added to 2-pyridinecarboxaldehyde (1.071 g, 10.0 mmol) at 0 °C. The mixture was stirred for 24 h at room temperature. The mixture was directly concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 1/1): 1.685 g, 8.3 mmol, 83% as a orange liquid. IR(KBr): 1551 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.49−1.68 (m, 4H), 1.77 (m, 4H), 3.56 (t, J = 4.6 Hz, 4H), 6.85−7.10 (m, 1H), 7.18 (s, 1H), 7.55 (t, J = 7.7 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 8.45 (d, J = 4.9 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 27.5, 28.5, 53.5, 118.1, 120.4, 126.2, 135.8, 148.9, 156.8. EI-MS *m*/*z* (rel intensity): 203 (M^+, 36). HRMS (FAB-MS): *m*/*z* calcd for $C_{12}H_{18}N_3$+H, 204.1501; found, 204.1507.

Mizoroki−Heck Reaction of Aryl Iodide with Olefin (Table 2). Under an atmosphere of argon, $PdCl_2(MeCN)_2$ (5.2 mg, 0.02 mmol) was added to ligand **1e** (5.0 mg, 0.02 mmol) in MeCN (1 mL). The mixture was stirred overnight at room temperature. After the mixture was concentrated under reduced pressure, the palladium complex was directly used in the next step. Under an atmosphere of argon, olefin (3 mmol) was added to the mixture of aryl iodide (1 mmol), K_3PO_4 (0.298 g, 1.4 mmol) and palladium complex (0.02 mmol) in *N*,*N*-dimethylformamide (DMF) (4 mL) at room temperature. The mixture was stirred at 80 °C and monitored by TLC. After 3−24 h, the mixture was diluted with ether and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 250−10/1).

Mizoroki−Heck Reaction of Aryl Bromide or Chloride with Olefin (Table 4). Under an atmosphere of argon, olefin (3 mmol) was added to the mixture of aryl bromide or chloride (1 mmol), K_3PO_4 (0.298 g, 1.4 mmol), TBAB (0.130 g, 0.4 mmol), and palladium complex (0.05 mmol) in *N*-methylpyrrolidone (NMP) (4 mL) at room temperature. The mixture was stirred at 120 °C. After 24 or 48 h, the mixture was diluted with ether and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 250−10/1).

(*E*)-3-([1,1′-Biphenyl]-4-yl)acrylic Acid *n*-Butyl Ester (3h). A white solid; mp 43−48 °C. IR(KBr): 1711 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 0.97 (t, J = 7.4 Hz, 3H), 1.44 (sextet, J = 7.4 Hz, 2H), 1.63−1.76 (m, 2H), 4.22 (t, J = 6.7 Hz, 2H), 6.47 (d, J = 16.0 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.52−7.63 (m, 6H), 7.71 (d, J = 16.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 14.2, 19.7, 31.2, 64.9, 118.5, 127.4, 127.9, 128.2, 129.0, 129.3, 133.8, 140.5, 143.4, 144.5, 167.5. EI-MS *m*/*z* (rel intensity): 280 (M^+, 33). HRMS (FAB-MS): *m*/*z* calcd for $C_{19}H_{20}O_2$+H, 281.1542; found, 281.1533.

(*E*)-3-(2′-Tolyl)acrylic Acid *n*-Butyl Ester (5). A pale yellow liquid; IR(KBr): 1714 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 0.97 (t, J = 7.4 Hz, 3H), 1.44 (sextet, J = 7.5 Hz, 2H), 1.65−1.75 (m, 2H), 2.44 (s, 3H), 4.22 (t, J = 6.7 Hz, 2H), 6.36 (d, J = 15.9 Hz, 1H), 7.14−7.32 (m, 3H), 7.51−7.61 (m, 1H), 7.98 (d, J = 15.9 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 11.8, 17.3, 17.9, 28.8, 62.5, 117.4, 124.4, 124.5, 128.0, 128.8, 131.5, 135.7, 140.3, 165.2. EI-MS *m*/*z* (rel intensity): 218 (M^+, 24). HRMS (FAB-MS): *m*/*z* calcd for $C_{14}H_{18}O_2$+H, 219.1385; found, 219.1367.

(*E*)-3-(2′-Cyanophenyl)acrylic Acid *n*-Butyl Ester (11). A pale yellow liquid. IR(KBr): 1714 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 0.97 (t, J = 7.3 Hz, 3H), 1.45 (sextet, J = 7.4 Hz, 2H), 1.66−1.76 (m, 2H), 4.24 (t, J = 6.7 Hz, 2H), 6.62 (d, J = 16.0 Hz, 1H), 7.48 (dt, J = 1.2 and 7.6 Hz, 1H), 7.63 (dt, J = 1.2 and 7.6 Hz, 1H), 7.73 (dt, J = 0.8 and 7.7 Hz, 2H), 7.97 (d, J = 16.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 14.1, 19.6, 31.1, 65.3, 113.1, 117.5, 123.6, 127.4, 130.4, 133.4, 133.9, 137.8, 139.7, 166.3. EI-MS *m*/*z* (rel intensity): 230 (M^+, 20). HRMS (FAB-MS): *m*/*z* calcd for $C_{14}H_{16}O_2N$, 230.1181; found, 230.1165.

(16) Ehlers, J.; Dieck, T. *Z. Allg. J. Chem.* **1988**, *560*, 80.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all compounds and X-ray crystallographic file (CIF) for **1e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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