Communication

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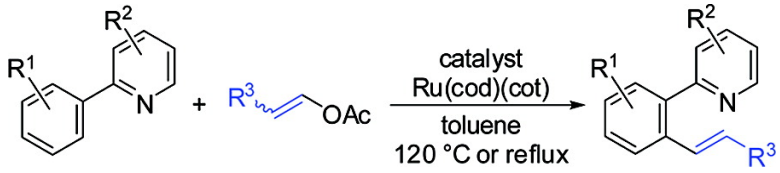

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The Ru(cod)(cot)-Catalyzed Alkenylation of Aromatic C−H Bonds with Alkenyl Acetates

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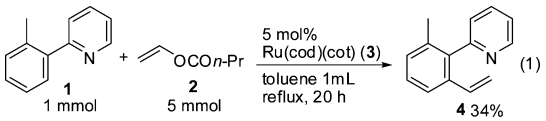
Transition metal-catalyzed regioselective carbon−carbon bond formations via carbon−hydrogen bond cleavage have recently become useful, reliable protocols in modern organic synthesis.[1] To date, a variety of reactions with respect to the catalytic conversion of C−H bonds to C−C bonds have been developed by us[2] and others.[1] Among these earlier studies, coupling reactions involving aryl−aryl and aryl−alkenyl bond formation are intriguing because these reactions afford π-conjugated aromatic compounds, which may be useful in organic electronic and optical devices.[3] In the previous studies, C−H/alkyne,[4] C−H/organohalide[5] and C−H/organometal,[6] and dehydrogenative couplings of a C−H bond with an alkene[7] and with an aromatic compound[8] have been developed for constructing aryl−aryl and aryl−alkenyl bonds. Particularly, chelation-assisted C−H bond cleavage at ortho positions of directing groups such as pyridyl, carbonyl, and imino groups has been recognized as one of the most powerful strategies applicable to regioselective C−H bond functionalization.[9] In this communication, we report a new method for producing π-conjugated aromatic compounds by the ruthenium-catalyzed alkenylation of an aromatic C−H bond in arylpyridines and related compounds with alkenyl esters. This reaction provides a new halogen-free protocol that can be used in the synthesis of π-conjugated aromatic compounds.

To evaluate the alkenylation of 2-(2-tolyl)pyridine (**1**) using vinyl butylate (**2**), Ru(cod)(cot) (**3**) (cod = 1,5-cyclooctadiene, cot = 1,3,5-cyclooctatriene) was used as a catalyst because interesting reactivities of vinyl acetate such as oxidative addition of the C−O bond to **3** have been reported by Komiya.[10] When **1** was reacted with **2** in refluxing toluene for 20 h in the presence of **3** as a catalyst, ortho vinylation product **4** was obtained in 34% yield (eq 1). After screening a series of solvents, dioxane (37% yield) and NMP (34% yield) were found to be good solvents, but other solvents such as DMF and CH_3CN and neat conditions were less effective for this reaction.



The use of vinyl acetate, in place of **2**, improved the yield slightly (44% yield). The addition of a base such as NEt_3, 2,6-lutidine, DABCO, K_2CO_3, Cs_2CO_3, and $KOBu^t$ resulted in no improvement in yield. After further optimization of the reaction conditions,[11,12] we adopted 5 mol % Ru(cod)(cot) (**3**), aromatic compound (1 mmol), and alkenyl acetate (3−5 equiv) in toluene (1.5 mL) at 120 °C as the standard reaction conditions.

The reaction was examined using a variety of alkenyl acetates (Table 1). The reaction of **1** with 1-propenyl acetate (**5**), which was used as a 40:60 mixture of *E*- and *Z*-isomers, gave the corresponding *E*-isomer as a major product (*E*/*Z* = 91/9) in 82% isolated yield (entry 1). Increasing the steric bulk of the β-substituent led to an increase in stereoselectivity (entries 1−4). The reaction using styryl acetate **11** provided *E*-isomer **12** as the sole product in 98% yield. In the case of 2-methyl-1-propenyl acetate **13**, the corresponding product **14** was obtained in 21% yield, and the starting material was recovered in 69% yield (entry 5). Screening of the suitable conditions for the reaction of **13** revealed that the use of tri-2-furylphosphine (**17**)[13] as an additive and higher catalyst loading (10 mol %) improves the catalytic activity (entry 6). The reaction using 1-cyclohexenyl acetate **15** provided the corresponding alkenylation product **16** in 75% yield.

This coupling reaction can be applied to substrates with various aromatic compounds with substituents including polar functional groups. Selected examples are listed in Table 2. In the case of 2-phenylpyridine, double alkenylation product **18** was isolated in 93% yield after 72 h. The double alkenylation is considered to occur via a stepwise pathway, because the corresponding mono-alkenylation product was observed in the early stage of this reaction. Substituents on the aromatic ring affected both reactivity and product selectivity. A methyl group at the 3-position in the pyridine ring inhibits the second alkenylation due to steric repulsion between the methyl group and the introduced styryl group (**19**, 93% yield). When 2-methyl-6-(2-tolyl)pyridine was used, the yield of the coupling product (**20**) was decreased to 19% even after 60 h. This suggests that coordination of the pyridyl nitrogen to the ruthenium is important in attaining a high yield of the product. Carbon−carbon bond formation took place exclusively at the less congested ortho position (**21**−**22**). Both electron-donating (CH_3 and OCH_3) and -withdrawing (CF_3, CN, and Ac) groups are tolerated in this reaction (**21**−**26**). Although acetyl and nitrile groups can function[2b] as directing groups in the alkylation reaction of C−H bonds with olefins, in the present coupling reaction, the C−C bond formation took place exclusively at the ortho position of the pyridyl group. C−H bonds of pyrrole rings can also be efficiently cleaved under the reaction conditions, and in the case of *N*-(2-pyridyl)pyrrole, conjugate diarylethene-type compound **27** was obtained in 92% yield.

Heterocycles other than pyridine can also be used as directing groups for this coupling reaction (Table 3). Oxazolines, known synthetic intermediates and protecting groups, can promote the reaction as directing groups. When the reaction of tolyloxazoline was carried out in the absence of base, insoluble solids were precipitated during the reaction. The use of 2,6-lutidine as a base was effective for attaining a high yield of alkenylation product **28**.

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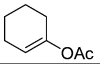
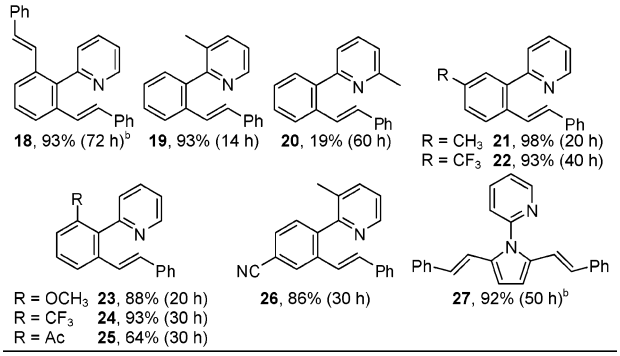
Table 1. Alkenylation of **1** with Alkenyl Acetate[a]

entry	alkenyl acetate	R^1	R^2	(*E*/*Z*)	time	product, yield[b] (*E*/*Z*)[c]
1	**5**	Me	H	(40/60)	40 h	**6**, 82% (91/9)
2	**7**	Et	H	(51/49)	40 h	**8**, 91% (92/8)
3	**9**	*n*-Bu	H	(59/41)	40 h	**10**, 83% (96/4)
4	**11**	Ph	H	(58/42)	15 h	**12**, 98% (100/0)
5	**13**	Me	Me		50 h	**14**, 21%[d,e]
6	**13**	Me	Me		50 h	**14**, 91%[f]
7	**15**				50 h	**16**, 75%

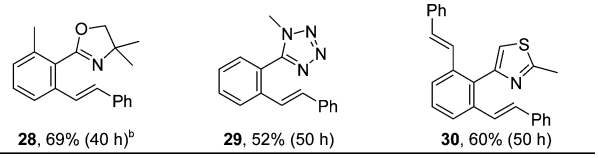
[a] Reaction conditions: **1** (1 mmol), alkenyl acetate (3 mmol), Ru(cod-)(cot) (**3**) (0.05 mmol), toluene (1.5 mL), 120 °C. [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopy. [d] **1** was recovered in 69% yield. [e] NMR yield. [f] Tri(2-furyl)phosphine **17** (0.1 mmol), **3** (0.1 mmol).

Table 2. Generality of Arylpyridines[a]



[a] Reaction conditions: aryl pyridines (1 mmol), **11** (3 mmol), **3** (0.05 mmol), toluene (1.5 mL), reflux, isolated yield. [b] **11** (5 mmol).

Table 3. Directing Groups Other than Pyridyl Groups[a]



[a] Reaction conditions: *N*-heterocycle (1 mmol), **11** (3 mmol), **3** (0.05 mmol), toluene (1.5 mL), reflux, isolated yield. [b] 2,6-lutidine (2 mmol) was used as an additive.

Tetrazoles and thiazoles can also function as a directing group (**29**, **30**).

Preliminary studies of the reaction mechanism by ^{1}H NMR spectroscopy showed that reaction of **3** with **1** (3 equiv) and **2** (1 equiv) at 120 °C for 3 h afforded signals assignable to an ortho-ruthenated tolylpyridine complex,[14] while reactions of **3** with **1** resulted only in isomerization of **3** to Ru(cyclooctadienyl)$_2$. These results suggest that both alkenyl acetate and arylpyridine are essential to accomplish the efficient C−H bond cleavage by ruthenium.[15,16]

In summary, we describe a new method for the direct functionalization of aromatic C−H bonds with alkenyl acetates to give π-conjugated aromatic compounds under halogen-free reaction conditions. This coupling reaction can be applied to a variety of aromatic compounds having sp^2 nitrogen directing groups. Carbon−carbon bond formation took place regioselectively at the ortho position. We are currently focusing our attention on efforts to uncover the mechanistic details of this coupling reaction and on application of the reaction for efficient syntheses of compounds that are useful for organic electronic and/or optical devices.

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Supporting Information Available: Experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Several other transition metal complexes such as $Ru_3(CO)_{12}$, $[RhCl(coe)_2]_2$, $[RhCl(coe)_2]_2/PCy_3$, $RuH_2(CO)(PPh_3)_3$, $Ru(CO)_3(PPh_3)_2$, $RuHCl(CO)(PPh_3)_3$, $RuH(OAc)(CO)(PPh_3)_2$, $[RuCl_2(C_6H_6)]_2/PPh_3$, $RhCl(PPh_3)_3$, and $Pd(OAc)_2/PPh_3$ were also screened, but no improvement of the yields was observed (0−21% yields).

(12) After the discovery of the reaction conditions for Table 1, entry 6, we examined vinylation of **1** with alkenyl acetates in the presence of trifurylphosphine. However, these attempts only resulted in lower yields.

(13) The reason for the beneficial effect of **17** remains elusive at present, but the use of **17** has frequently been reported to be advantageous in transition metal-mediated organic reactions; Andersen, N. G.; Keay, B. A. *Chem. Rev.* **2001**, *101*, 997−1030.

(14) The observed pattern of new signals on the ^{1}H NMR spectrum was similar to those of some reported ortho-ruthenated phenylpyridine complexes; Matthes, J.; Grundemann, S.; Toner, A.; Guari, Y.; Donnadieu, B.; Spandl, J.; Sabo-Etienne, S.; Clot, E.; Limbach, H.-H.; Chaudret, B. *Organometallics* **2004**, *23*, 1424−1433.

(15) See Supporting Information for further details on mechanistic studies.

(16) Very recently, Oi et al. reported that the $[RuCl_2(cod)]_n/PPh_3$-catalyzed reaction of arylpyridines with allyl acetates gave a mixture of ortho allylation and alkenylation products. We believe the mechanism of this reaction is different from our reaction described here due to much lower catalytic activity of our reaction under Oi's reaction conditions. See Supporting Information for further details: Oi, S.; Tanaka, Y.; Inoue, Y. *Organometallics* **2006**, *25*, 4773−4778.

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