Ortho-Selective Allylation of 2-Pyridylarenes with Allyl Acetates Catalyzed by Ruthenium Complexes

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The ortho-position of 2-pyridylarenes is selectively allylated with allyl acetates in the presence of a ruthenium(II)−phosphine complex. In the case of aromatic-substituted allyl acetates, such as cinnamyl acetate, linear allylated compounds were the predominant products. However, the reaction with linear aliphatic allyl acetates afforded a mixture of linear and branched products, whereas reactions with branched aliphatic allyl acetates afforded linear products preferentially. From these results, the reaction mechanism is proposed to involve the formation of σ-allyl- and π-allylruthenium intermediates and ortho-ruthenation of the 2-pyridylarenes via the σ-allylruthenium intermediate directed by coordination of the 2-pyridyl group to the ruthenium center.

Introduction

Direct functionalization of aromatic C−H bonds catalyzed by transition metal complexes has attracted much attention in terms of synthetic and atom efficiency.[1] Particularly, functional group-directed aromatic C−H bond activation and C−C bond formation is a powerful method to introduce carbon functional groups to the ortho-position of an aromatic ring. This has proven extremely effective in reactions involving the ortho-selective addition of aromatic C−H bonds to carbon−carbon multiple bonds, such as alkenes[2] and alkynes,[3] the ortho-carbonylation of aromatic rings with carbon monoxide,[4] and the direct coupling of aromatic C−H bonds with aryl halides[5] or arylmetal reagents.[6] Our research has been focused on transition metal-catalyzed regioselective direct coupling reactions of aromatic compounds using substrates containing coordinating functional groups, such as pyridyl, imino, hydroxy, and oxazolinyl groups.[7]

As a carbon functional group, the allyl group is very useful and attractive because it can be easily converted to a variety of functional groups. Allylation of aromatic compounds with allylic compounds, such as allyl alcohols and allyl halides, is usually performed by Friedel−Crafts type electrophilic substitution using Lewis acids.[8] There have been only a few reports on transition metal-catalyzed allylation reactions of aromatic compounds using allyl esters or alcohols, in which palladium complexes,[9] molybdenum or tungsten complexes,[10] and diruthenium complexes[11] were used as the catalysts. Our research

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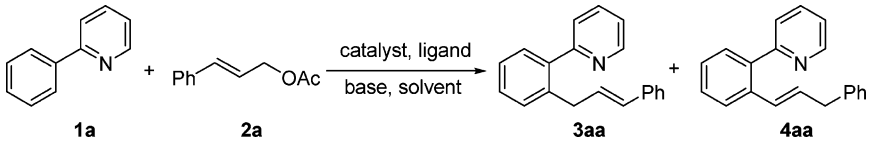
Table 1. Transition Metal-Catalyzed Ortho-Allylation of 2-Phenylpyridine (1a)[a]

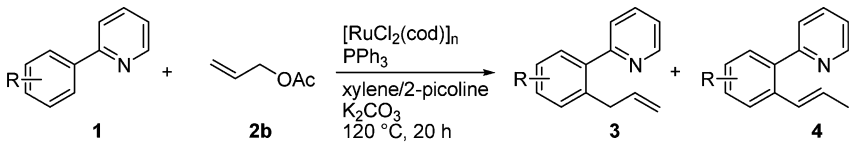


1a **2a** **3aa** **4aa**

entry	catalyst	base	solvent	temp (°C)/time (h)	total yield (%)[b]	ratio (**3**:**4**)[c]
1	$RuCl_2(PPh_3)_3$	K_2CO_3	1,4-dioxane	100/20	49	60:40
2	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	1,4-dioxane	100/20	55	60:40
3	$PdCl_2(PPh_3)_2$	K_2CO_3	1,4-dioxane	100/20	0	
4	$RhCl(PPh_3)_3$	K_2CO_3	1,4-dioxane	100/20	0	
5	$[RuCl_2(cod)]_n$·2*n*PCy_3	K_2CO_3	1,4-dioxane	100/20	17	60:40
6	$[RuCl_2(cod)]_n$·2*n*PBu^t_3	K_2CO_3	1,4-dioxane	100/20	0	
7	$[RuCl_2(cod)]_n$·*n*dppp	K_2CO_3	1,4-dioxane	100/20	0	
8	$[RuCl_2(cod)]_n$·*n*dppf	K_2CO_3	1,4-dioxane	100/20	0	
9	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_3PO_4	1,4-dioxane	100/20	35	60:40
10	$[RuCl_2(cod)]_n$·2*n*PPh_3	Cs_2CO_3	1,4-dioxane	100/20	35	60:40
11	$[RuCl_2(cod)]_n$·2*n*PPh_3	CsF	1,4-dioxane	100/20	51	60:40
12	$[RuCl_2(cod)]_n$·2*n*PPh_3	Et_3N	1,4-dioxane	100/20	0	
13	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	DMF	120/20	39	60:40
14	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	diglime	120/20	0	
15	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	toluene	100/20	40	60:40
16	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	xylene	120/20	66	60:40
17	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	2-phenylpyridine (**1a**)	120/20	93[d]	60:40
18	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	pyridine	120/20	0	
19	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	2-picoline	120/20	70	80:20
20	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	2,6-lutidine	120/20	66	80:20
21	$[RuCl_2(cod)]_n$·2*n*PPh_3	K_2CO_3	xylene−2-picoline (10:1)	120/20	79	80:20
22	$[RuCl_2(cod)]_n$·2*n*PPh_3	none	xylene−2-picoline (10:1)	120/20	0	

[a] Reactions were carried out using 0.5 mmol of **1a**, 0.6 mmol of **2a**, 0.025 mmol (based on metal) of catalyst, and 1.0 mmol of base in 1 mL of solvent under N_2. [b] Determined by GLC based on **1a** using internal standard. [c] Determined by GLC. [d] Yield based on **2a**.

Table 2. Ruthenium-Catalyzed Ortho-Allylation of 2-Arylpyridines (1)[a]



1 **2b** **3** **4**

entry	2-arylpyridine **1**	products	ratio	total yield (%)
1	(**1a**)	(**3ab**) (**4ab**)	85:15	86
2	(**1b**)		-	0
3	(**1c**)	(**3cb**) (**4cb**)	73:27	67
4	(**1d**)	(**3db**) (**3db'**)	71:29	30
5	(**1e**)	(**3eb**) (**4eb**)	88:12	92

[a] Reactions were carried out using 0.5 mmol of **1**, 0.6 mmol of **2b**, 0.025 mmol (based on metal) of $[RuCl_2(cod)]_n$, 0.05 mmol of PPh_3, and 1.0 mmol of K_2CO_3 in 1 mL of xylene−2-picoline (10:1) at 120 °C for 20 h under N_2.

group has also reported the allylation of electron-rich arenes using allyl tosylates catalyzed by rhodium or iridium complexes.[12] However, regioisomers of the allylated products were produced in these reactions when substituted benzenes were used as substrates. During the course of our study, we have found that pyridylarenes are selectively allylated at their ortho-position with allyl acetates catalyzed by ruthenium−phosphine complexes.

Results and Discussion

Initially, 2-phenylpyridine (**1a**) was reacted with 1.2 equiv of cinnamyl acetate (**2a**) in the presence of 5 mol % of $RuCl_2(PPh_3)_3$ and K_2CO_3 in 1,4-dioxane at 100 °C for 20 h, which

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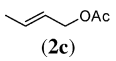
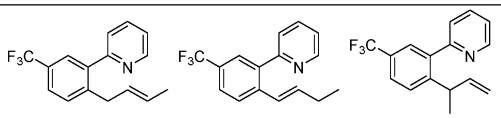
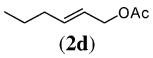
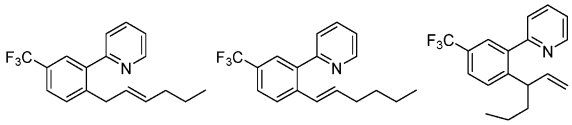
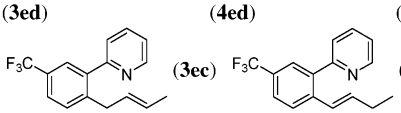
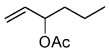
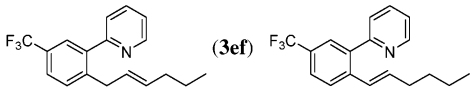
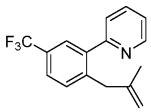
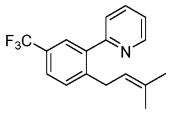
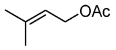
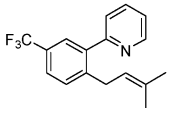
Table 3. Ruthenium-Catalyzed Ortho-Allylation of 2-(3′-Trifluoromethyl)phenylpyridine (1e) with Allyl Acetates (2)[a]

entry	allyl acetate **2**	products	ratio	total yield (%)
1	 (**2c**)	 (**3ec**) (**4ec**) (**5ec**)	46:12:42	67
2	 (**2d**)	 (**3ed**) (**4ed**) (**5ed**)	40:15:45	87
3	 (**2e**)	 (**3ec**) (**4ec**)	82:18	90
4	 (**2f**)	 (**3ef**) (**4ef**)	80:20	88
5	 (**2g**)	 (**3eg**)	-	74
6	 (**2h**)	 (**3eh**)	-	82
7	 (**2i**)	 (**3eh**)		trace

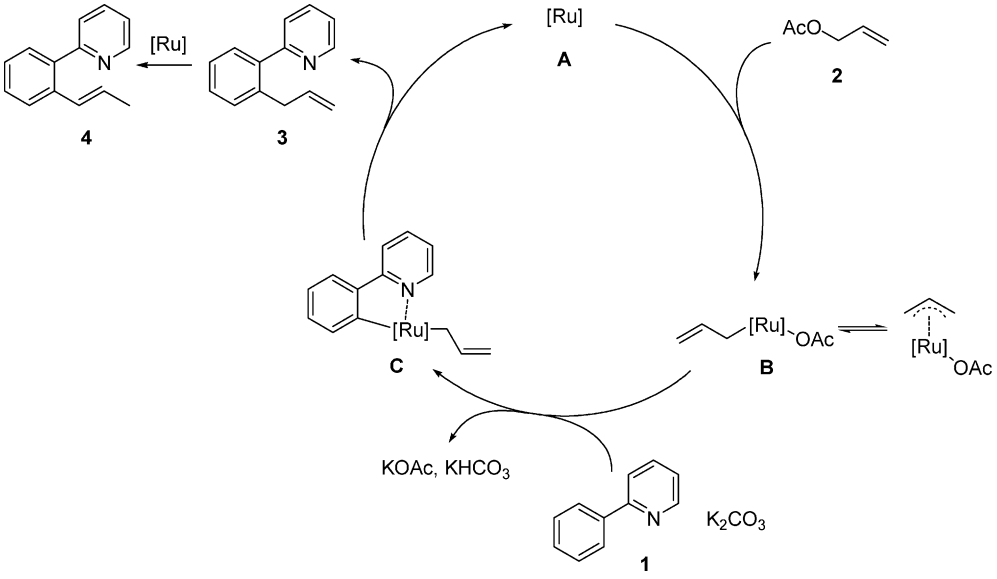
[a] Reactions were carried out using 0.5 mmol of **1e**, 0.6 mmol of **2**, 0.025 mmol (based on metal) of $[RuCl_2(cod)]_n$, 0.05 mmol of PPh_3, and 1.0 mmol of K_2CO_3 in 1 mL of xylene−2-picoline (10:1) at 120 °C for 20 h under N_2.

afforded the product **3aa** together with the isomer **4aa**, in which the olefinic moiety had isomerized, in 49% total yield and a ratio of 60:40 (Table 1, entry 1). When $[RuCl_2(cod)]_n$ with 2 equiv of PPh_3 (to Ru) was used as a catalyst precursor, the yield improved to 55% (entry 2). However, a palladium complex and a rhodium complex with PPh_3 did not show catalytic activity (entries 3 and 4). Combinations of $[RuCl_2(cod)]_n$ with trialkylphosphines, such as PCy_3 and PBu^t_3, and bidentate phosphines, such as dppp and dppf, showed little or no activity (entries 5−8). Inorganic bases, especially K_2CO_3, were suitable for this reaction (entries 2, 9−11); however, organic bases, such as triethylamine, were not good for this reaction (entry 12). Among the solvents examined, 1,4-dioxane and xylene gave good results, and the reaction in xylene at 120 °C afforded the products in 66% total yield (entries 2, 13−16). When the reaction was carried out using **1a** as the solvent, the products were obtained in a high yield of 93% based on **2a** (entry 17). However, the use of a large excess of substrate is very inefficient. Thus, pyridine derivatives were examined as possible solvents. Although pyridine completely inhibited the reaction, when 2-picoline was used as the solvent, the products were obtained in 70% yield and an improved **3aa**:**4aa** ratio of 80:20 (entries 18−20). Finally, a combination of xylene and 2-picoline (10:1) was found to be the best solvent system, and products **3aa** and **4aa** were afforded in 79% yield and a ratio of 80:20 (entry 21). Although 2-picoline should act as a base, the reaction in the absence of K_2CO_3 did not afford the product (entry 22), which was in agreement with the results for entry 12.

Using the optimized reaction conditions, reactions of various 2-arylpyridines with allyl acetates were examined. The reaction of 2-phenylpyridine (**1a**) with allyl acetate (**2b**) afforded **3ab** together with the isomer **4ab** in an 85:15 ratio and 85% total yield (Table 2 entry 1). Substrates having a methyl group at the ortho- (2′-) position of the benzene ring, e.g., **1b**, did not undergo allylation with **2b**. In this case, steric hindrance between the methyl group and the pyridine ring prevented ruthenation on the opposite side of the ortho-position (6′-position). Substrate **1c**, which has a methyl group at the 3′-position, on the other hand, underwent the allylation with **2b**, affording **3cb**, in which the coupling occurred at the less crowded 6′-position, and its isomer **4cb** in a 73:27 ratio and 67% total yield (entry 3). The reaction between **1d**, which has a methoxy group at the 3′-position, with **2b** gave products **3db** and **3db′**, which are allylated at the 2′- and 6′-positions, respectively, in a ratio of 71:29 and a lower yield of 30% (entry 4). It appears that the methoxy group had a directing effect in the ruthenation reaction but lowered the yield. In this case, formation of the olefin isomerized product **4** was not observed. We believe that the coordination of the methoxy group to the ruthenium catalyst lowers the catalytic activity for the olefin isomerization as well as the allylation reaction. The reaction between **1e**, which has a trifluromethyl substituent at the 3′-position, and **2b** gave products **3eb** and **4eb** in a good yield (92%) and a ratio of 88:12 (entry 5).

The results of the reactions of **1e** with various allyl acetates are shown in Table 3. In the case of crotyl acetate (**2c**), **5ec**, of which the allylic moiety is branched, was also afforded in almost the same yield as the linear isomer **3ec** (entry 1). This result strongly suggests that a π-allylruthenium intermediate forms during the reaction. Similarly, the reaction between **1e** and 2-hexenyl acetate (**2d**) afforded **3ed**, **4ed**, and **5ed** in a ratio of 40:15:45 and 87% total yield (entry 2). On the other hand, the

Scheme 1. A Possible Reaction Pathway



reaction with branched allyl acetates, such as 3-buten-2-yl acetate (**2c**), afforded only linear products, **3ec** and its isomer **4ec**, in a ratio of 82:18 and 90% total yield (entry 3). The reaction with 1-hexen-3-yl acetate (**2f**) produced similar results (entry 4). The reaction with 2-methyl-2-butenyl acetate (**2g**) afforded product **3eg** in 74% yield, and isomerization of the double bond did not occur (entry 5). As in the case of **2e** and **2f** (entries 3 and 4), the reaction with the tertiary allyl acetate **2h** occurred at the γ-position, affording **3eh** as the sole product in 82% yield, whereas the reaction of γ-disubstituted primary allyl acetate **2i** was sluggish, affording only a trace amount of the product **3eh**.

The following three steps are believed to be involved in the catalytic pathway: (i) oxidative addition of the allyl acetate to the ruthenium complex to afford a σ-allylruthenium intermediate, (ii) isomerization of the σ-allylruthenium intermediate via a π-allylruthenium complex, and (iii) ortho-ruthenation of the aromatic ring, which is directed by coordination of the pyridine nitrogen to the ruthenium atom. A possible reaction pathway is shown in Scheme 1. Oxidative addition of **2** to ruthenium

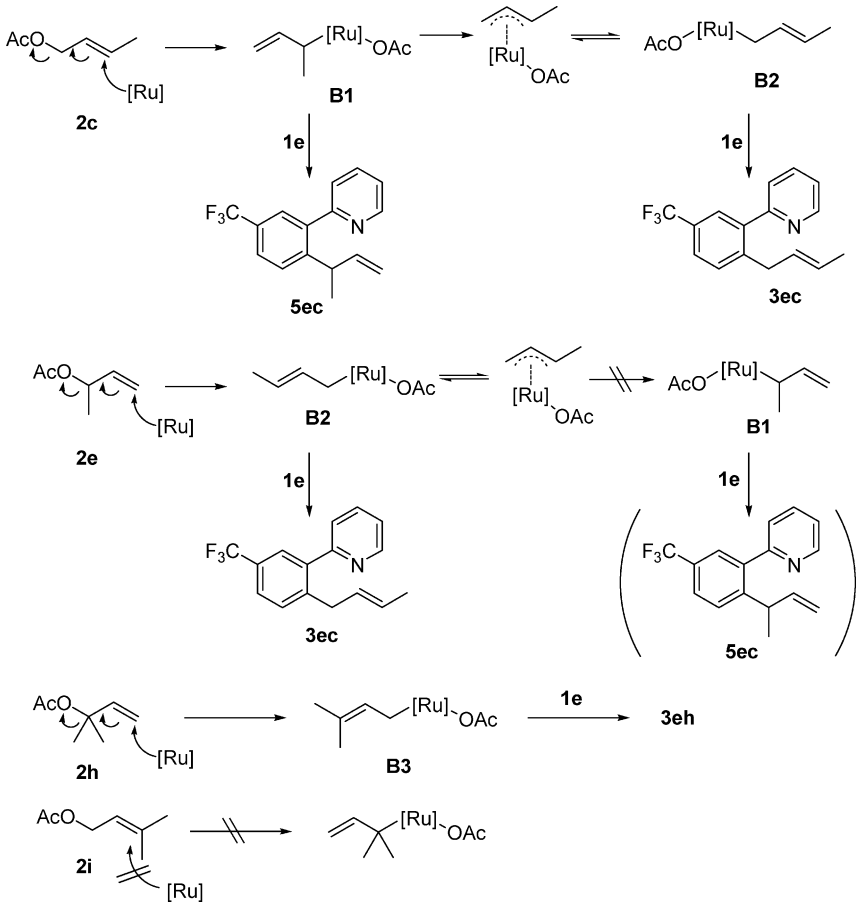


Figure 1. Isomerization of the Allylruthenium Intermediates.

complex **A** generates the σ-allylruthenium intermediate **B**. Ortho-ruthenation of **1** by **B** with the elimination of AcOH gives the corresponding ruthenacycle **C**. Product **3** is then formed through reductive elimination from **C**, with the simultaneous regeneration of **A**. On the other hand, an alternative pathway involves the ortho-ruthenation of the substrate **1** by the complex **A** followed by the oxidative addition of **2** to give the ruthenacycle **C**. This pathway cannot be totally ruled out.

Possible pathways accounting for the distribution of linear and branched products in the reactions of substituted allyl acetates are shown in Figure 1. In the case of **2c**, an S_N2'-like attack of ruthenium complex affords the secondary σ-allylruthenium intermediate **B1**. **B1** directly reacts with **1e** to give **5ec**; however, a substantial amount of **B1** isomerizes to the more stable primary σ-allylruthenium intermediate **B2**, which reacts with **1e** to give **3ec**. Thus, nearly the same amount of **5ec** and **3ec** was afforded in the reaction with **2c** (Table 3, entry 1). On the other hand, reaction with the secondary allyl acetate **2e** afforded the primary σ-allylruthenium intermediate **B2** in the same manner. Only a small amount of **B2** isomerized to **B1**, because it is unstable; thus, only **3ec** (with a small amount of **4ec**) was formed in this case (Table 3, entry 3). Similarly, reaction with **2h** gives the primary σ-allylruthenium intermediate **B3**, which further reacts to afford product **3eh** (Table 3, entry 6). In the case of **2i**, the two methyl groups prevent S_N2'-like attack of the ruthenium complex, so that the reaction did not proceed (Table 3, entry 7).

Conclusion

The ruthenium-catalyzed allylation of 2-pyridylarenes with allyl acetates is described. The reaction proceeds regioselectively at the ortho-position of the aromatic ring. The reaction mechanism is proposed to involve the formation of σ-allyl- and π-allylruthenium intermediates and ortho-ruthenation of the 2-pyridylarenes via the σ-allylruthenium intermediate, which is directed by coordination of the 2-pyridyl group to the ruthenium center.

Experimental Section

General Procedures. Infrared (IR) spectra were recorded on a JASCO FT/IR-350 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a Bruker DPX-400 or DRX-500 spectrometer. All reactions were performed in Schlenk tubes under a N_2 atmosphere. Arylpyridines were prepared by coupling reaction of 2-bromopyridine (30 mmol) with corresponding aryl Grignard reagents (36 mmol) using 1 mol % of $NiCl_2$(dppe) in Et_2O (60 mL) under reflux for 3 h.[13] $[RuCl_2(cod)]_n$ (available from Aldrich) was prepared as described in the literature.[14] Xylene was dried over CaH_2 and stored under N_2. K_2CO_3 was dried at 250 °C under reduced pressure and stored under N_2. Flash chromatographies were performed using spherical silica gel (40−100 μm, Kanto Chemical). Elemental analyses were performed by the Microanalytical Laboratory of the Institute of Multidisciplinary Research for Advanced Materials, Tohoku University.

Allylation of 2-Phenylpyridine (1a) with Cinnamyl Acetate (2a). A mixture of **1a** (77.6 mg, 0.50 mmol), **2a** (105.7 mg, 0.60 mmol), K_2CO_3 (138.6 mg, 1.0 mmol), PPh_3 (13.1 mg, 0.05 mmol), $[RuCl_2(cod)]_n$ (7.0 mg, 0.025 mmol of Ru), and 2-picoline (0.1 mL) in xylene (1 mL) was stirred at 120 °C for 20 h. The reaction mixture was diluted with 30 mL of Et_2O, and the precipitated solid was filtered off. After the solvent was removed in vacuo, the residue was purified by silica gel flash chromatography (hexane−EtOAc, 2:1) to give an 80:20 mixture of the products **3aa** and **4aa** (107.2 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (1H, ddd, J = 4.9, 1.8, 1.0 Hz), 7.70 (1H, dt, J = 7.7, 1.8 Hz), 7.40−7.16 (11H, m), 6.23−6.11 (2H, m), 3.65 (2H, d, J = 5.3 Hz). Peaks for **4aa**: 6.53 (1H, d, J = 15.6 Hz), 3.48 (2H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 149.1, 140.4, 137.8, 137.5, 136.1, 130.7, 130.0, 129.4, 128.5, 128.4, 128.3, 126.8, 126.3, 125.9, 124.1, 121.7, 36.5. IR (neat): 3056, 3024, 2909, 1724, 1646, 1585, 1563, 1492, 1466, 1443, 1425, 1293, 1150, 1058, 1024, 967, 795, 752, 694 cm^{-1}. Anal. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.31; N, 5.16. Found: C, 88.29; H, 6.46; N, 4.94. All reactions in Tables 2 and 3 were performed using the same procedure.

Mixture of 3ab and 4ab (85:15). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (1H, ddd, J = 4.8, 1.8, 1.0 Hz), 7.71 (1H, dt, J = 7.7, 1.8 Hz), 7.39 (1H, dt, J = 7.7, 1.0 Hz), 7.35−7.29 (4H, m), 7.23 (1H, ddd, J = 7.7, 4.8, 1.0 Hz), 5.87 (1H, ddt, J = 17.0, 10.1, 6.5 Hz), 4.95 (1H, dq, J = 10.1, 1.7 Hz), 4.89 (1H, dq, J = 17.0, 1.7 Hz), 3.49 (2H, dt, J = 6.5, 1.7 Hz). Peaks for **4ab**: 6.47 (1H, dq, J = 15.6, 1.5 Hz), 6.19 (1H, dq, J = 15.6, 6.6 Hz), 1.79 (3H, dd, J = 6.6, 1.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 149.0, 140.3, 137.5, 136.0, 129.9, 129.7, 128.3, 126.7, 126.2, 124.8, 121.6, 115.4, 37.3. IR (neat): 3059, 3007, 2975, 2911, 1637, 1585, 1563, 1466, 1425, 1294, 1150, 1091, 1023, 992, 913, 794, 752 cm^{-1}. Anal. Calcd for $C_{14}H_{13}N$: C, 86.12; H, 6.71; N, 7.17. Found: C, 86.01; H, 6.84; N, 7.02.

Mixture of 3cb and 4cb (73:27). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.68−8.67 (1H, m), 7.71−7.69 (1H, m), 7.39−7.38 (1H, m), 7.23−7.16 (4H, m), 5.88 (1H, ddt, J = 17.0, 10.2, 6.6 Hz), 4.95 (1H, dq, J = 10.2, 1.6 Hz), 4.88 (1H, dq, J = 17.0, 1.6 Hz), 3.44 (2H, dt, J = 6.6, 1.6 Hz), 2.36 (3H, s). Peaks for **4cb**: 6.43 (1H, dq, J = 15.6, 1.6 Hz), 6.14 (1H, dq, J = 15.6, 6.6 Hz), 2.43 (3H, s), 1.80 (3H, dd, J = 6.6, 1.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.8, 149.1, 140.1, 137.7, 135.9, 135.7, 130.4, 129.9, 128.5, 126.1, 124.8, 121.5, 115.2, 36.9, 20.8. IR (neat): 3010, 2974, 2916, 1636, 1586, 1563, 1466, 1428, 1149, 1091, 1040, 993, 911, 793, 749 cm^{-1}. Anal. Calcd for $C_{15}H_{15}N$: C, 86.08; H, 7.22; N, 6.69. Found: C, 86.07; H, 7.31; N, 6.53.

Mixture of 3db and 3db′ (71:29). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (1H, ddd, J = 4.8, 1.8, 0.9 Hz), 7.72 (1H, dt, J = 7.7, 1.8 Hz), 7.40 (1H, dt, J = 7.7, 0.9 Hz), 7.24 (1H, ddd, J = 7.7, 4.8, 0.9 Hz), 7.21 (1H, d, J = 8.4 Hz), 6.95 (1H, d, J = 2.8 Hz), 6.91 (1H, dd, J = 8.4, 2.8 Hz), 5.85 (1H, ddt, J = 17.0, 10.1, 6.4 Hz), 4.94 (1H, dq, J = 10.1, 1.5 Hz), 4.86 (1H, dq, J = 17.0, 1.5 Hz), 3.82 (3H, s), 3.41 (2H, dt, J = 6.4, 1.5 Hz). Peaks for **3db′**: 5.92 (1H, ddt, J = 17.1, 10.1, 6.0 Hz), 4.89 (1H, dq, J = 10.1, 1.6 Hz), 4.77 (1H, dq, J = 17.1, 1.6 Hz), 3.86 (3H, s), 3.43 (2H, dt, J = 6.0, 1.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.6, 157.8, 149.1, 141.3, 137.9, 136.0, 131.1, 126.9, 124.0, 122.1, 121.7, 115.2, 114.7, 55.3, 36.5. IR (neat): 3073, 3001, 2936, 2833, 1636, 1608, 1584, 1563, 1500, 1467, 1428, 1297, 1221, 1178, 1036, 993, 912, 824, 796, 774, 749 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.73; H, 6.82; N, 6.12.

Mixture of 3eb and 4eb (88:12). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (1H, ddd, J = 4.8, 1.8, 1.0 Hz), 7.77 (1H, dt, J = 7.7, 1.8 Hz), 7.67 (1H, d, J = 1.4 Hz), 7.60 (1H, dd, J = 8.0, 1.4 Hz), 7.44 (1H, d, J = 8.0 Hz), 7.41 (1H, dt, J = 7.7, 1.0 Hz), 7.29 (1H, ddd, J = 7.7, 4.8, 1.0 Hz), 5.86 (1H, ddt, J = 17.0, 10.1, 6.5 Hz), 5.01 (1H, dq, J = 10.1, 1.6 Hz), 4.91 (1H, dq, J = 17.0, 1.6 Hz), 3.54 (2H, dt, J = 6.5, 1.6 Hz). Peaks for **4eb**: 6.49 (1H, dq, J = 15.7, 1.5 Hz), 6.30 (1H, dq, J = 15.7, 6.6 Hz), 1.85 (3H, dd, J = 6.6, 1.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 149.4, 141.9, 140.9, 136.5, 130.5, 128.7 (q, J_{C-F} = 32.0 Hz), 126.8 (q, J_{C-F} = 3.8 Hz), 125.0 (q, J_{C-F} = 3.8 Hz), 124.8, 124.2 (q, J_{C-F} = 270.5 Hz), 124.1, 122.2, 116.4, 37.2. IR (neat): 3078, 3008, 2980, 2916, 1639, 1617, 1587, 1567, 1470, 1411, 1337, 1261, 1167, 1125, 1078, 1037, 993,

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909, 835, 794, 749 cm^{-1}. Anal. Calcd for $C_{15}H_{12}F_3N$: C, 68.44; H, 4.59; N, 5.32. Found: C, 68.63; H, 4.77; N, 5.25.

Mixture of 3ec and 4ec (82:18). ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (1H, ddd, J = 4.9, 1.8, 1.0 Hz), 7.76 (1H, dt, J = 7.7, 1.8 Hz), 7.65 (1H, d, J = 1.5 Hz), 7.59 (1H, dd, J = 8.0, 1.5 Hz), 7.43 (1H, d, J = 8.0 Hz), 7.40 (1H, dt, J = 7.7, 1.0 Hz), 7.28 (1H, ddd, J = 7.7, 4.9, 1.0 Hz), 5.46 (1H, dtq, J = 15.2, 6.4, 1.4 Hz), 5.32 (1H, dtq, J = 15.2, 6.4, 1.4 Hz), 3.45 (2H, dd, J = 6.4, 1.4 Hz), 1.60 (3H, dd, J = 6.4, 1.4 Hz). Peaks for **4ec**: 6.48 (1H, d, J = 15.8 Hz), 6.31 (1H, dt, J = 15.8, 6.4 Hz), 2.20 (2H, dq, J = 7.5, 6.4 Hz), 1.03 (3H, t, J = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 149.4, 142.9, 140.8, 136.6, 136.3, 130.4, 128.6 (q, J_{C-F} = 32.7 Hz), 126.6 (q, J_{C-F} = 3.8 Hz), 124.9 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 270.5 Hz), 124.1, 122.2, 119.6, 36.1, 17.8. IR (neat): 3023, 2965, 2918, 1617, 1587, 1410, 1337, 1262, 1167, 1125, 1078, 968, 906, 833, 793, 749 cm^{-1}. Anal. Calcd for $C_{16}H_{14}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.34; H, 5.28; N, 4.96.

5ec. ^1H NMR (500 MHz, $CDCl_3$): δ 8.71 (1H, ddd, J = 4.8, 1.8, 1.0 Hz), 7.77 (1H, dt, J = 7.7, 1.8 Hz), 7.65 (1H, d, J = 1.4 Hz), 7.59 (1H, dd, J = 8.0, 1.4 Hz), 7.43 (1H, d, J = 8.0 Hz), 7.40 (1H, dt, J = 7.7, 1.0 Hz), 7.30 (1H, ddd, J = 7.7, 4.8, 1.0 Hz), 5.98 (1H, ddd, J = 17.2, 10.4, 5.6 Hz), 5.03 (1H, dt, J = 10.4, 1.5 Hz), 4.91 (1H, dt, J = 17.2, 1.5 Hz), 3.85 (1H, dtq, J = 6.9, 5.6, 1.5 Hz), 1.30 (3H, d, J = 6.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 149.5, 147.3, 142.8, 140.6, 136.3, 130.4, 128.9 (q, J_{C-F} = 32.0 Hz), 126.7 (q, J_{C-F} = 3.8 Hz), 125.1 (q, J_{C-F} = 3.8 Hz), 124.3 (q, J_{C-F} = 270.0 Hz), 124.1, 122.2, 113.8, 38.1, 20.6. IR (neat): 3054, 2968, 2933, 1617, 1587, 1410, 1337, 1263, 1167, 1125, 1080, 969, 908, 836, 793, 749 cm^{-1}. Anal. Calcd for $C_{16}H_{14}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.31; H, 5.30; N, 4.93.

Mixture of 3ed and 4ed (80:20). ^1H NMR (500 MHz, $CDCl_3$): δ 8.71 (1H, ddd, J = 4.8, 1.7, 0.9 Hz), 7.76 (1H, dt, J = 7.6, 1.7 Hz), 7.65 (1H, d, J = 1.6 Hz), 7.59 (1H, dd, J = 8.0, 1.6 Hz), 7.43 (1H, d, J = 8.0 Hz), 7.41 (1H, dt, J = 7.6, 0.9 Hz), 7.29 (1H, ddd, J = 7.6, 4.8, 0.9 Hz), 5.43 (1H, dtt, J = 15.3, 6.6, 1.2 Hz), 5.29 (1H, dtt, J = 15.3, 6.6, 1.2 Hz), 3.47 (2H, dd, J = 6.6, 1.2 Hz), 1.92 (2H, dq, J = 6.6, 1.2 Hz), 1.29 (2H, sext, J = 7.4 Hz), 0.84 (3H, t, J = 7.4 Hz). Peaks for **4ed**: 6.46 (1H, d, J = 15.7 Hz), 6.26 (1H, dt, J = 15.7, 6.9 Hz), 2.17 (2H, q, J = 6.9 Hz), 1.42 (2H, tt, J = 7.5, 6.9 Hz), 1.34 (2H, sext, J = 7.5 Hz), 0.90 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.5, 149.4, 142.9, 140.8, 136.3, 136.0, 130.4, 128.4 (q, J_{C-F} = 32.5 Hz), 127.8, 126.7 (q, J_{C-F} = 3.8 Hz), 125.3, 124.9 (q, J_{C-F} = 3.8 Hz), 124.1 (q, J_{C-F} = 270.0 Hz), 122.2, 36.2, 34.5, 22.5, 13.6. IR (neat): 2959, 2929, 2871, 1617, 1587, 1566, 1467, 1410, 1337, 1262, 1167, 1126, 1078, 970, 907, 834, 792, 749 cm^{-1}. Anal. Calcd for $C_{18}H_{18}F_3N$: C, 70.80; H, 5.94; N, 4.59. Found: C, 70.79; H, 6.04; N, 4.33.

5ed. ^1H NMR (500 MHz, $CDCl_3$): δ 8.72 (1H, ddd, J = 4.8, 1.8, 1.0 Hz), 7.75 (1H, dt, J = 7.7, 1.8 Hz), 7.63 (1H, s), 7.62 (1H, d, J = 8.0 Hz), 7.47 (1H, d, J = 8.0 Hz), 7.37 (1H, dt, J = 7.7, 1.0 Hz), 7.28 (1H, ddd, J = 7.7, 4.8, 1.0 Hz), 5.95 (1H, ddd, J = 17.2, 10.3, 7.2 Hz), 5.02 (1H, dt, J = 10.3, 1.3 Hz), 4.86 (1H, dt, J = 17.2, 1.3 Hz), 3.65 (1H, tq, J = 7.2, 1.3 Hz), 1.65 (2H, q, J = 7.2 Hz), 1.12 (2H, sext, J = 7.2 Hz), 0.73 (3H, t, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 149.4, 146.3, 141.6, 136.1, 136.0, 132.6, 127.8 (q, J_{C-F} = 32.0 Hz), 127.3, 126.6 (q, J_{C-F} = 3.8 Hz), 125.1, 124.9 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 270.5 Hz), 114.7, 44.0, 29.3, 20.3, 13.7. IR (neat): 2959, 2930, 2870, 1617, 1587, 1468, 1410, 1337, 1262, 1167, 1125, 1078, 970, 908, 835, 792, 749 cm^{-1}. Anal. Calcd for $C_{18}H_{18}F_3N$: C, 70.80; H, 5.94; N, 4.59. Found: C, 70.78; H, 6.08; N, 4.56.

3eg. ^1H NMR (500 MHz, $CDCl_3$): δ 8.70 (1H, ddd, J = 4.9, 1.8, 0.9 Hz), 7.75 (1H, dt, J = 7.7, 1.8 Hz), 7.69 (1H, d, J = 1.6 Hz), 7.59 (1H, dd, J = 8.0, 1.6 Hz), 7.42 (1H, d, J = 8.0 Hz), 7.41 (1H, dt, J = 7.7, 0.9 Hz), 7.28 (1H, ddd, J = 7.7, 4.9, 0.9 Hz), 4.76 (1H, s), 4.44 (1H, s), 3.48 (2H, s), 1.60 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 149.3, 144.2, 141.4, 141.2, 136.3, 130.9, 128.7 (q, J_{C-F} = 32.7 Hz), 126.8 (q, J_{C-F} = 3.8 Hz), 124.8 (q, J_{C-F} = 3.8 Hz), 124.1 (q, J_{C-F} = 270.6 Hz), 124.0, 122.2, 112.6, 41.0, 22.5. IR (neat): 3077, 2971, 2933, 1617, 1587, 1410, 1337, 1262, 1167, 1125, 1078, 896, 791, 749 cm^{-1}. Anal. Calcd for $C_{16}H_{17}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.50; H, 5.14; N, 4.99.

3eh. ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (1H, ddd, J = 4.9, 1.8, 1.0 Hz), 7.76 (1H, dt, J = 7.7, 1.8 Hz), 7.63 (1H, d, J = 1.5 Hz), 7.58 (1H, dd, J = 8.0, 1.5 Hz), 7.42 (1H, d, J = 8.0 Hz), 7.39 (1H, dt, J = 7.7, 1.0 Hz), 7.28 (1H, ddd, J = 7.7, 4.9, 1.0 Hz), 5.14 (1H, tsept, J = 7.2, 1.4 Hz), 3.46 (2H, d, J = 7.2 Hz), 1.66 (3H, d, J = 1.4 Hz), 1.52 (3H, d, J = 1.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 149.3, 143.8, 140.7, 136.3, 133.1, 130.0, 128.2 (q, J_{C-F} = 32.1 Hz), 126.6 (q, J_{C-F} = 3.8 Hz), 125.0 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 270.5 Hz), 124.1, 122.2, 122.1, 31.7, 25.5, 17.6. IR (neat): 3052, 2971, 2915, 1617, 1587, 1565, 1470, 1410, 1337, 1262, 1166, 1125, 1078, 1036, 906, 830, 795 cm^{-1}. Anal. Calcd for $C_{17}H_{16}F_3N$: C, 70.09; H, 5.54; N, 4.81. Found: C, 70.02; H, 5.70; N, 4.80.

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