Communication

Bipyridine-Modulated Palladium-catalyzed Oxidative Heck-type Reactions of Arylboronic Acids with Olefins

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We have demonstrated that 4,4′-dimethyl 2,2′-bipyridine as ligand for Pd(II) catalysts was very efficient for oxidative Heck-type coupling reaction of arylboronic acids with olefins in DMA or CH_3CN under atm air at 80 °C. The presence of chelated bipyridine ligand isindispensable to achieve high reaction yields and to suppress the formation of biphenyl as homocoupled byproduct.

Keywords: Bipyridine-modulated; 4,4′-Dimethyl 2,2′-bipyridine; Pd(II) catalysts; Oxidative Heck-type coupling reaction; Arylboronic acids; Olefins.

INTRODUCTION

The transition metal-catalyzed cross-coupling reaction of organoboronic acid and olefins, known as the oxidative Heck reactions,[1] is now growing rapidly as one of the alternative tools for constructing C-C bonds, mainly because boronic acids are stable, low toxic, and commercially available.[2] Palladium-catalyzed oxidative Heck reactions[3] have been extensively investigated by several research groups including Larhed.'s in which a typical oxidative Heck experiments was investigated in acetonitrile using. p-Tolylboronic acid n-butyl acrylate N-methylmorpholine (NMM) as base, ligand and 2% $Pd(OAc)_2$ as the palladium source.[1d] They found phenanthroline-class ligand, especially 2,9-dimthyl-1,10-phenanthroline (dmphen) ligand provided high yields with good control over the regiochemistry and stereochemistry under open-air and at room temperature.[1d] Other nitrogen-containing ligands such as momodentate pyridine was ineffective, and both 2,2′-bipyridine and 6,6′-dimethyl-2,2′-bipyridine gave modest production with Pd black formation for the latter. Generally nitrogen-containing ligands, known to facilitate the reoxidation of Pd(0) and stabilize Pd(II) complex thus formed, are very cheap, air and moisture stable compared to their phosphine counterparts.[4] Nitrogen-containing ligands have been found most successful when the reaction is run under oxygen.[1] Although the mechanistic aspect of the reaction is not well-elucidated yet, based on the standpoint of better understanding and control of oxidative Heck reactions and their synthetic applications, it is intriguing to promote bipyridine ligands for oxidative Heck reactions since bipyridine ligands required are either commercially-available or synthetically accessible. Herein we reported that 4,4′-dimethyl-2,2′-bipyridine **1c** was screened as the most superior ligand for for Pd(II) catalysts, it was very efficient for oxidative Heck-type coupling reaction of arylboronic acids with olefins in DMA or CH_3CN under atm air at 80 °C in high yields and without biphenyl as homo-coupled byproduct.

RESULTS AND DISCUSSION

As illustrated in Table 1, several commercially available pyridine (**1a**) and bipyridine derivatives (**1b-1k**, except **1f** and **1j** were prepared) were screened as potential ligands, using a model cross-coupling reaction 1.0 mmol of butyl acrylate and 2.0 mmol of phenylboronic acid in the presence of 2 mol% of $Pd(OAc)_2$, 2.4 mol% of ligand and 2.0 mmol of N-methylmorpholine (NMM) in 5.0 mL of DMA at 80 °C in atm air. Ligand was found to be a crucial factor in determining the yields of product **3a** and biphenyl, a homocoupled byproduct. Without ligand, only 2% of **3a** was produced with 18% of biphenyl isolated as the major product (entry 1). Pyridine, a monodentate nitrogen ligand did not work either. Among bidentate nitrogen ligands, 4,4′-dimethyl-2,2′-bipyridine **1c** proved to be the most superior one to give **3a** in 96% yields, while 6,6′-dimethyl-2,2′-bipyridine **1i** gave considerably lower yields of 38%

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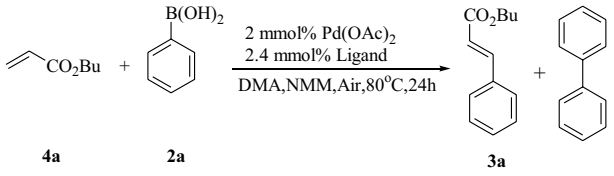
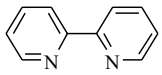
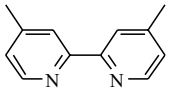
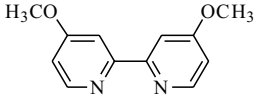
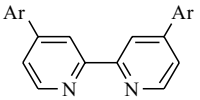
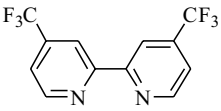
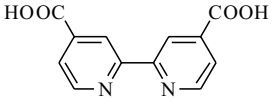
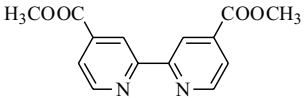
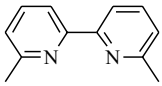
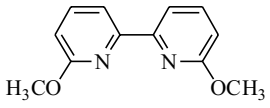
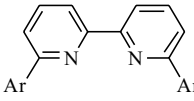
Table 1. Ligand screenig on oxidative arylation of *n*-butyl acrylate with phenylboronic acid[a]



4a **2a** **3a**

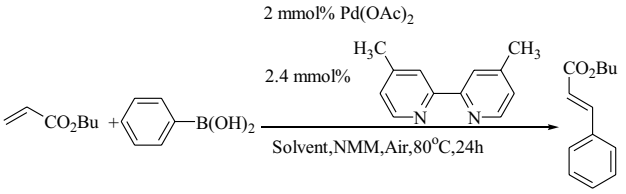
Entry		Ligand	Yield (%)[b]	Yield of biphenyl (%)[b]
1		No L	2	18
2	**1a**		1	1
3	**1b**		51	1
4	**1c**		96 6[c] 85[d]	1 0[c] 1[d]
5	**1d**		88	1
6	**1e**		75	1
7	**1f**		11	1
8	**1g**		51	3
9	**1h**		51	2
10	**1i**		38 39[c]	7 20[c]
11	**1j**		11	1
12	**1k**		11	1

[a] Reaction conditions: 1.0 mmol of olefin, 2.0 mmol of boronic acid, 2 mol% of $Pd(OAc)_2$, 2.4 mol% of ligand, 2.0 mmol of NMM, 5.0 mL of DMA.
[b] Isolated yield.
[c] Performed at rt, 5.0 mL of CH_3CN.
[d] 4.5 mmol% Ligand.

and significant amount of biphenyl as homocoupled byproduct due to the steric hindrance of dimethyl at 6,6′-position of bipyridyl (entry 10). Stronger electron-donating methoxy group, at 4,4′-position, did not improve but resulted in lower reaction yields (entry 5) and at 6,6′-position, gave very low yield of 11% (entry 11). Even lower reaction yields of 51% were obtained with electron-withdrawing groups –COOH (entry 8), -COOMe (entry 9) and poor yield of 11% with the strongest electron-withdrawing group $–CF_3$ (entry 7). Slight electron-withdrawing phenyl group, at 4,4′-position, gave moderate yield of 75% (entry 6), but poor yield of 11% at 6,6′-position (entry 12). When increasing ligand **1c** from 2.4 mol% to 4.5 mol%, it resulted in a yield decrease of **3a** by 11%. From our observation, it may suggest that dimethyl group at 4,4′-position (**1c**) of bipyridyl will give a tight bidentate-Pd coordination bonding which afforded a stable Pd complex with higher catalytic activity. However, dimethoxyl group at 4,4′-positoin (**1d**) of bipyridyl will give a stronger bonding to inhibit the catalytic activity of Pd complex. It is also clear that weaker coordination bonding between N-Pd-N will lead to low reaction efficacy as electron-withdrawng groups were attached at 4,4′-positoin (**1d**) of bipyridyl. Generally, steric hindrance imposed by substituents at 6,6′-position of bipyridyl will destabilize the Pd complex and lower the catalytic activity. The presence of chelated bipyridine ligand is indispensable to achieve high reaction yields and to suppress the formation of biphenyl as homocoupled byproduct.

To optimize the reaction condition, solvents were found to have profound effect on palladium catalytic activity (Table 2). Attempts on optimization with respect to solvent showed that the reaction proceeded best in DMA (96%), Other aprotic polar solvents such as acetonitrile, DMF and DMSO, except NMP, proved to be effective also with no more than 90% yields. The nopolar solvents such as dioxane and toluene gave lower yields. Notably, both electronic effect and steric effect were pronounced for substituted arylboronic acids. Generally, electron-donating arylboronic acids with MeO- or Me- at 4-position (entry 2 and entry 3) gave significantly higher yields than those of electron-withdrawing arylboronic acids with Me(C=O)- or CF_3- at 4-position (entry 5 and entry 7) and NO_2- at 3-position (entry 10). Steric hindrance was found to decrease significantly the reaction yields at 2-position (entry 4 and entry 9). But unsubstituted arylboronic acid (entry 1) af-

Table 2. Solvent effect on oxidative arylation of *n*-butyl acrylate with phenylboronic acid[a]



Entry	Solvent	Yield (%)[b]
1	CH_3CN	90
2	DMF	91
3	DMA	96
4	DMSO	92
5	NMP	63
6	Dioxane	61
7	Toluene	61

[a] Reaction conditions: 1.0 mmol of olefin, 2.0 mmol of boronic acid, 2.0 mmol of NMM, 5.0 mL of solvent.
[b] Isolated yield.

forded the highest yields than the substituted ones. Unexpectedly, electron-releasing 4-butyl diminished while electron-withdrawing 4-fluoro enhanced the reaction yields.

In a typical reaction mechanism proposed for Heck-type coupling reaction, aryl group is transferred to bipyridine palladium(II) intermediate to form an aryl palladium complex (Scheme I). Presumably, the reactivity of bipyridine aryl-Pd complex is determined by a resultant electronic balance on π-donating and π-accepting ability of substituent on aryl ring. Electron-donating group will increase π-donating ability, meanwhile decrease its π-accepting ability of aryl ring, and reverse are the electron-withdrawing groups.

The open vessel procedure employing 6,6′-dimethyl-2,2′-bipyridine **1i** was thereafter applied directly to a range of olefins (**4a**-**f**), utilizing phenylboronic acid (**2a**) as the arylating agent (Table 4). Both electron-poor and electron-rich olefins were coupled in moderate to good yields.

Scheme I Proposed mechanism for Heck-type oxidative arylation of olefins

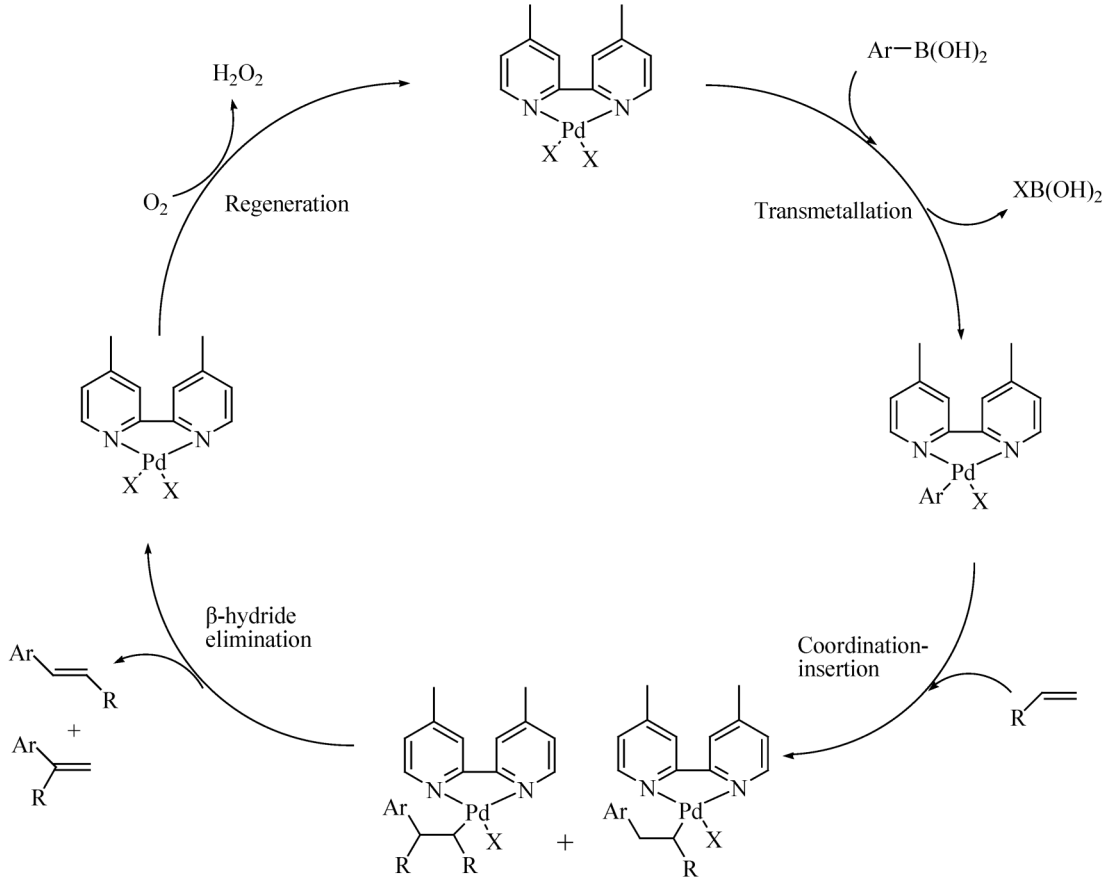
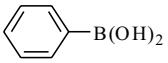
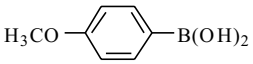
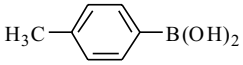
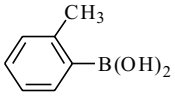
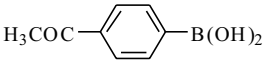
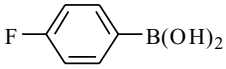
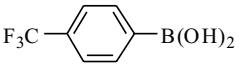
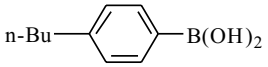
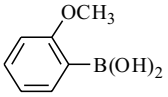
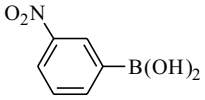


Table 3. Oxidative arylation of *n*-butyl acrylate with diverse arylboronic acid[a]

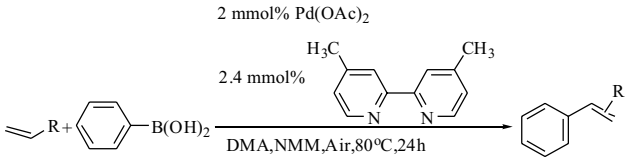
Entry		Boronic acid	Products & Yield (%)[b]
1	**2a**		**3a**, 96[c]
2	**2b**		**3b**, 90[c]
3	**2c**		**3c**, 86
4	**2d**		**3d**, 32[c]
5	**2e**		**3e**, 68
6	**2f**		**3f**, 84
7	**2g**		**3g**, 35[c]
8	**2h**		**3h**, 33
9	**2i**		**3i**, 29
10	**2j**		**3j**, 24

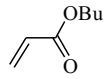
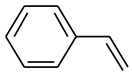
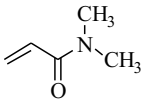
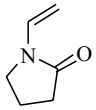
[a] Reaction conditions: 1.0 mmol of olefin, 2.0 mmol of boronic acid, 2.0 mmol of NMM, 5.0 mL of DMA.
[b] Isolated yield.
[c] Determined by NMR, α/β = 1/99.

The high reactivity of both electron-poor **4a** and **4c** produced excellent yields (93% and 88%) after 24 h at 80 °C (entry 1 and entry 3, Table 4) with high regioselectivity (99%) at β-position. The electron-rich olefin (**4d**) gave lower yield (68%) with high regioselectivity at α-position. Surprisingly styrene (**4b**) only afforded low yield (36%) in DMA and high yield (93%) in acetonitrile with slightly lower regioselectivity.

A comparison is made in Table 5 on chelated bidentate 4,4′-dimethyl 2,2′-bipyridine and 2,9-dimethyl-1,10-phenanthroline as ligand in Heck-type reaction. 2,9-dimethyl-1,10-phenanthroline was reported as a superior ligand in which the reaction was performed at room temperature to give 81% yield and high regioselectivity in acetonitrile with butyl acrylate (entry 1), and 85% yield with styrene (entry 2). Importantly, 4,4′-dimethyl 2,2′-bipyridine performed better at higher temperature 80 °C to give 96% yield with butyl acrylate in DMA (entry 3), and 93% yield with styrene in acetonitrile (entry 4). Both reactions also afforded high regioselectivities.

Table 4. Oxidative arylation of different olefins with phenylboronic acid[a]

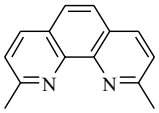
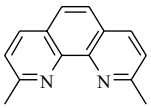
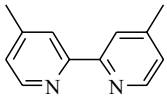
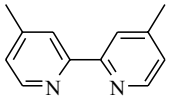
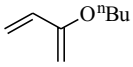
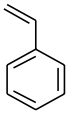
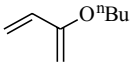
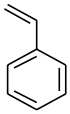


Entry		Olefin	Product & Yield (%)[b]	α/β[d]
1	**4a**		**3a**, 96	1/99
2	**4b**		**5b**, 36 **5b**, 93[c]	2/98 5/95
3	**4c**		**5c**, 88	1/99
4	**4d**		**5d**, 68	99/1

[a] Reaction conditions: 1.0 mmol of olefin, 2.0 mmol of boronic acid, 2.0 mmol of NMM, 5.0 mL of DMA.
[b] Isolated yield.
[c] Solvent is CH_3CN.
[d] Determined by NMR.

In conclusion, we have demonstrated that 4,4′-dimethyl 2,2′-bipyridine as ligand for Pd(II) catalysts was very efficient for oxidative Heck-type coupling reaction of arylboronic acids with olefins in DMA or CH_3CN under atm air at 80 °C. The presence of chelated bipyridine ligand is indispensable to achieve high reaction yields and to suppress the formation of biphenyl as homocoupled byproduct. The catalytic activity was found sensitive to both electronic and steric effect of substituents on the 2,2′-bipyridine. Electron-withdrawing groups and steric hindrance will retard the reaction, while the electron-donating groups will enhance it. However, too strong electron-donating group such as methoxy group will result in lower yield than moderate electron-donating group such as methyl group.

Table 5. Comparison of 4,4′-dimethyl 2,2′-bipyridine and 2,9-dimethyl-1,10-phenanthroline as ligand in Heck-type reaction

	Entry 1[1d]	Entry 2[1d]	Entry 3	Entry 4
Ligand				
Olefin				
Solvent	CH_3CN	CH_3CN	DMA	CH_3CN
Base	NMM	NMM	NMM	NMM
Temperature	RT	RT	80 °C	80 °C
Time	24 h	24 h	24 h	24 h
Yield	81%	85%	96%	93%
α/β	0/100	15/85	1/99	5/95

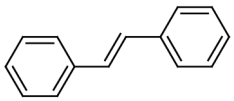
EXPERIMENTAL

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AVA-300 spectrometer with TMS as internal standard. All reagents were used directly as obtained commercially. All products are known.

Typical experimental procedure for the palladium-catalyzed Heck-type cross-coupling reaction

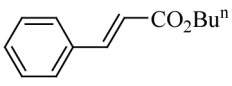
Under an atmosphere of air, a mixture of $Pd(OAc)_2$ (4.5 mg, 2.0 mmol%), bipyridine (2.4 mmol%), olefin (1.0 mmol), arylboronic acid (2.0 mmol), NMM (2.0 mmol) and DMA (5.0 mL) were charged to a 25 mL round-buttom flask and stirred at 80 °C for 24 h. After ordinary workup and being evaporated by rotary evaporator, the residue was purified by column chromatography to give the required cross-coupled derivative (hexane/ethyl acetate).

***Trans*-stilbene (5b)**[7]



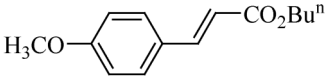
White solid, mp = 121-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.7 Hz, 4H, Ar), 7.38 (t, *J* = 7.4 Hz, 4H, Ar), 7.31-7.27 (m, 2H, Ar), 7.14 (s, 2H, ArC*H*C*H*Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.3, 128.7, 128.6, 127.6, 126.

T*rans*-cinnamic acid *n*-butyl ester (3a)[7]



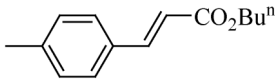
Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.2 Hz, 1H, ArC*H*), 7.52-7.48 (m, 2H, Ar), 7.37-7.34 (m, 3H, Ar), 6.43 (d, *J* = 15.9 Hz, 1H, C*H*CO_2Bu), 4.20 (t, *J* = 6.6 Hz, 2H, $CO_2CH_2CH_2$), 1.73-1.63 (m, 2H, $CO_2CH_2CH_2$), 1.47-1.39 (m, 2H, CH_2CH_3), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 144.4, 134.3, 130.0, 128.7, 127.9, 118.1, 64.2, 30.6, 19.0, 13.6.

4-Methoxy-*trans*-cinnamic acid *n*-butyl ester (3b)[7]



Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 15.9 Hz, 1H, ArC*H*), 7.42 (d, *J* = 8.8 Hz, 2H, Ar), 6.85 (d, *J* = 8.76 Hz, 2H, Ar), 6.27 (d, *J* = 15.9 Hz, 1H, C*H*CO_2Bu), 4.16 (t, *J* = 6.7 Hz, 2H, $CO_2CH_2CH_2$), 3.77 (s, 3H, ArOCH_3), 1.67-1.60 (m, 2H, $CO_2CH_2CH_2$), 1.42-1.36 (m, 2H, CH_2CH_3), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 161.2, 144.1, 129.5, 127.1, 115.7, 114.2, 64.1, 55.2, 30.7, 19.1, 13.6.

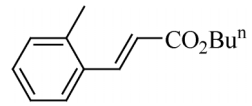
4-Methyl-*trans*-cinnamic acid *n*-butyl ester (3c)[7]



Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, *J* = 16.0 Hz, 1H, ArC*H*), 7.37 (d, *J* = 7.8 Hz, 2H, Ar), 7.13 (d, *J* = 7.8 Hz, 2H, Ar), 6.37 (d, *J* = 16.2 Hz, 1H, C*H*CO_2Bu), 4.18 (t, *J* = 6.6 Hz, 2H, $CO_2CH_2CH_2$), 2.32 (s, 3H, ArCH_3), 1.68-1.61 (m, 2H, $CO_2CH_2CH_2$), 1.45-1.38

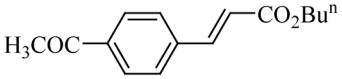
(m, 2H, CH_2CH$_3$), 0.95 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 166.9, 144.2, 140.2, 131.5, 129.3, 127.8, 116.9, 64.0, 30.6, 21.1, 19.0, 13.5.

2-Methyl-*trans*-cinnamic acid *n*-butyl ester (3d)[6]



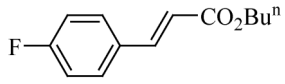
Pale yellow liquid; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.97 (d, J = 15.9 Hz, 1H, ArCH), 7.54-7.52 (m, 1H, Ar), 7.27-7.16 (m, 3H, Ar), 6.35 (d, J = 15.9 Hz, 1H, CHCO$_2$Bu), 4.21 (t, J = 6.7 Hz, 2H, CO$_2$CH_2CH$_2$), 2.42 (s, 3H, ArCH_3), 1.72-1.65 (m, 2H, CO$_2$CH$_2$CH_2), 1.48-1.39 (m, 2H, CH_2CH$_3$), 0.96 (t, J = 7.4 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.0, 142.1, 137.5, 133.3, 130.6, 129.8, 126.3, 126.2, 119.2, 64.3, 30.7, 19.6, 19.1, 13.6.

4-Acetyl-*trans*-cinnamic acid *n*-butyl ester (3e)[7]



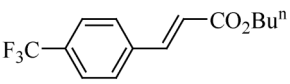
Pale yellow liquid; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.96 (d, J = 8.1 Hz, 1H, ArCH), 7.68 (d, J = 16.2 Hz, 2H, Ar), 7.60 (d, J = 8.4 Hz, 2H, Ar), 6.53 (d, J = 16.2 Hz, 1H, CHCO$_2$Bu), 4.22 (t, J = 6.6 Hz, 2H, CO$_2$CH_2CH$_2$), 2.61 (s, 3H, COCH_3), 1.75-1.65 (m, 2H, CO$_2$CH$_2$CH_2), 1.51-1.38 (m, 2H, CH_2CH$_3$), 0.97 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 197.1, 166.4, 142.8, 138.6, 137.8, 128.7, 128.0, 120.6, 64.5, 30.6, 26.5, 19.0, 13.6.

T*rans*-4-fluoro-cinnamic acid *n*-butyl ester (3f)[8]



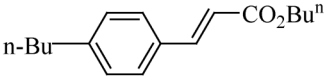
Pale yellow liquid; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.63 (d, J = 16.0 Hz, 1H, ArCH), 7.50 (dd, J = 8.6, 5.4 Hz, 2H, Ar), 7.05 (d, J = 8.6 Hz, 2H, Ar), 6.35 (d, J = 16.0 Hz, 1H, CHCO$_2$Bu), 4.20 (t, J = 6.7 Hz, 2H, CO$_2$CH_2CH$_2$), 1.71-1.63 (m, 2H, CO$_2$CH$_2$CH_2), 1.47-1.39 (m, 2H, CH_2CH$_3$), 0.96 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 166.0 (d, J = 103.3 Hz), 162.0, 143.0, 130.6, 129.7, 106.0 (d, J = 21.8 Hz), 64.3, 30.6, 19.0, 13.6.

4-Trifluormethyl-*trans*-cinnamic acid *n*-butyl ester (3g)[6]



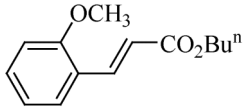
Colourless liquid; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.71 (d, J = 16.2 Hz, 1H, ArCH), 7.64 (d, J = 7.8 Hz, 2H, Ar), 7.59 (d, J = 7.8 Hz, 2H, Ar), 6.51 (d, J = 16.2 Hz, 1H, CHCO$_2$Bu), 4.23 (t, J = 6.6 Hz, 2H, CO$_2$CH_2CH$_2$), 1.73-1.65 (m, 2H, CO$_2$CH$_2$CH_2), 1.48-1.41 (m, 2H, CH_2CH$_3$), 0.97 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 166.3, 142.4, 137.7, 131.3, 127.9, 125.6, 121.8, 120.7, 64.5, 30.5, 19.0, 13.5.

4-Butyl-*trans*-cinnamic acid *n*-butyl ester (3h)[9]



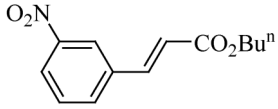
Pale yellow liquid; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.69 (d, J = 16.2 Hz, 1H, ArCH), 7.46 (d, J = 7.8 Hz, 2H, Ar), 7.20 (d, J =7.8 Hz, 2H, Ar), 6.43 (d, J = 16.2 Hz, 1H, CHCO$_2$Bu), 4.23 (t, J = 6.6 Hz, 2H, CO$_2$CH_2CH$_2$), 2.64 (t, 2H, ArCH_2), 1.74-1.60 (m, 4H, CO$_2$CH$_2$CH_2), 1.50-1.34 (m, 4H, CH_2CH$_3$), 0.97 (t, J = 7.5 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 167.1, 145.4, 144.4, 131.8, 128.8, 127.9, 117.0, 64.1, 35.4, 33.2, 30.7, 22.2, 19.1, 13.8, 13.6.

2-Methoxy-*trans*-cinnamic acid *n*-butyl ester (3i)[5]



Pale yellow liquid; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.99 (d, J = 16.2 Hz, 1H, ArCH), 7.51-7.48 (m, 1H, Ar), 7.35-7.30 (m, 1H, Ar), 6.97-6.88 (m, 2H, Ar), 6.53 (d, J = 15.9 Hz, 1H, CHCO$_2$Bu), 4.20 (t, J = 6.6 Hz, 2H, CO$_2$CH_2CH$_2$), 3.81 (s, 3H, ArOCH_3), 1.73-1.64 (m, 2H, CO$_2$CH$_2$CH_2), 1.47-1.39 (m, 2H, CH_2CH$_3$), 0.96 (t, J = 7.4 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 167.5, 158.2, 139.8, 131.3, 128.7, 123.3, 120.5, 118.6, 111.0, 64.1, 55.3, 30.7, 19.1, 13.6.

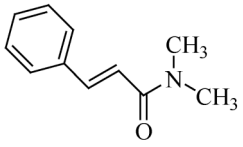
3-Nitro-*trans*-cinnamic acid *n*-butyl ester (3j)[10]



White solid, mp = 63-65 °C; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.21 (d, J = 16.2 Hz, 2H, Ar), 7.70 (d, J = 16.2 Hz, 1H, ArCH), 7.62 (d, J = 16.2 Hz, 2H, Ar), 6.57 (d, J = 15.9 Hz, 1H, CHCO$_2$Bu), 4.23 (t, J = 6.6 Hz, 2H, CO$_2$CH_2CH$_2$),

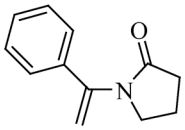
1.73-1.66 (m, 2H, $CO_2CH_2CH_2$), 1.49-1.41 (m, 2H, CH_2CH_3), 0.97 (t, J = 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.9, 148.4, 141.4, 136.0, 133.4, 129.7, 124.2, 122.2, 121.2, 64.5, 30.5, 19.0, 13.5.

(*E*)-*N*,*N*-dimethylcinnamamide (5c)[11]



Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, J = 15.5 Hz, 1H, ArC*H*), 7.54-7.51 (m, 2H, Ar), 7.39-7.36 (m, 3H, Ar), 6.89 (d, J = 15.5 Hz, 1H, COC*H*), 3.16 (s, 3H, CH_3), 3.06 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 142.3, 135.1, 129.4, 128.6, 127.6, 117.2, 37.3, 35.8.

***N*-(1-Phenylethenyl)-2-pyrrolidinone (5d)**[1d]

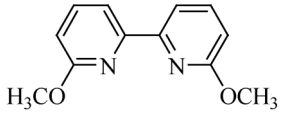


Colourless liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (m, 2H, Ar), 7.17 (m, 3H, Ar), 5.42 (s, 1H, CCH_2), 5.27 (s, 1H, CCH_2), 3.57 (dd, 2H, J = 7.0, J = 7.1 Hz), 2.53 (dd, 2H, J = 8.2, J = 7.9 Hz), 2.12-2.04 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 133.9, 130.5, 128.6, 127.6, 125.6, 49.7, 31.2, 20.5, 17.7.

Typical experimental procedure for the preparation of bipyridine[12]

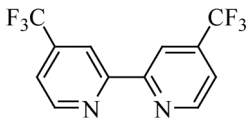
To a 25 mL round-buttomed flask, was charged a mixture of $Pd(OAc)_2$ (11.3 mg, 0.05 mmol), 6-substituted 2-bromopyridine (1 mmol), n-Bu_4NBr (161.2 mg, 0.5 mmol) and K_2CO_3 (138.2 mg, 1.0 mmol) in the cosolvent of isopropanol/DMF/H_2O (1.25/0.9/0.35) under N_2 at 115 °C for 48 hr. After ordinary workup and being evaporated by rotary evaporator, the residue was purified by column chromatography to give the required homo-coupled derivative (hexane/ethyl acetate).

6,6′-Dimethoxy-2,2′-bipyridine (1d)[13]



White solid, mp = 117-118 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, 2H, J = 7.5 Hz), 7.70 (t, 2H, J = 8.1 Hz), 6.78 (d, 2H, J = 8.3 Hz), 4.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 153.4, 139.1, 113.5, 110.8, 53.1.

4,4′-Di(trifluoromethyl)-2,2′-bypyridine (1f)[14]



Light yellow solid, mp = 78-80 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.88 (d, J = 5.1 Hz, 2H), 8.73 (s, 2H), 7.58 (d, J = 3.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 150.3, 139.6 (d, J = 34.1 Hz), 124.6, 119.9 (d, J = 3.0 Hz), 117.1 (d, J = 3.3 Hz).

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