Tetrahedron 66 (2010) 1188–1195

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Palladium/Imidazolium salt as a versatile catalyst for sequential coupling reactions of aryl dihalides to unsymmetrically substituted arenes

Xiaoming Zhang [a], Weilong Xie [a], Wanzhi Chen [a,b,*]

[a] Department of Chemistry, Zhejiang University, Xixi Campus, Hangzhou 310028, PR China
[b] State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjing, PR China

ARTICLE INFO

Article history:
Received 13 November 2009
Received in revised form 13 December 2009
Accepted 21 December 2009
Available online 28 December 2009

Keywords:
Palladium
Imidazolium
Double coupling
Dihaloarene

ABSTRACT

A simple method for one-pot sequential Heck/Suzuki coupling reactions of a range of substituted aryl dihalides has been described. The $Pd(OAc)_2$/imidazolium system catalyzed double coupling reactions proceed without isolation of the intermediates giving unsymmetrically polysubstituted biphenyls in good to excellent yields. Further couplings of the resultant products bearing additional C–Cl bonds with substituted arylboronic acids or amines lead to unsymmetrical terphenyls and aminobiphenyl derivatives.

1. Introduction

Palladium-catalyzed cross-coupling involving aryl halides with olefins, organomagnesium, organoboron, or organosilicon reagents etc., is an important protocol for the construction of carbon–carbon bonds. Such coupling reactions have found versatile applications in pharmaceutical, fungicide, and material industries.[1] Combination of two or more coupling reactions into a single vessel using a single catalyst is of practical importance for the manufacture of valuable structures, because it generates less waste and also obviates the tedious separation and purification of the intermediate products. A successful one-pot sequential reaction requires that the catalyst is highly efficient and chemoselective toward the first coupling reaction and maintains its catalytic activity in the subsequent coupling reaction. Therefore, only a few successful examples have been reported so far.[2] For example, the sequential double Hiyama process could be realized by the use of the dienylsilanol bearing a benzyldimethylsilyl or 2-thienyldimethylsilyl unit at one end with overall excellent yields of the unsymmetrical 1,4-diaryl-1,3-butadienes.[2a] Recently, a one-pot, simultaneous Suzuki–Miyaura cross-coupling of two different arylboronic acids with symmetrical aryl dibromides and heterocyclic dibromides substrates giving the unsymmetrical disubstituted tri(hetero)aryl derivatives has been reported.[2b] A novel strategy for the synthesis of multisubstituted olefins using 2-pyridyldimethyl(vinyl)silane as a versatile platform was described. The sequential integration of Heck coupling and Hiyama coupling afforded multisubstituted olefins, which are regioselective and stereoselective.[2d] A catalytic one-pot triarylation on the C=C core of vinylboronate pinacol ester has been described to give extended π-systems based on a multisubstituted olefin structure very rapidly.[2e]

N-Heterocyclic carbenes (NHCs) have been playing more and more important role in C–C and C–N formation reactions.[3] Either structurally characterized metal–NHC complexes[4] or metal/imidazolium salts systems[5] can be used. In this context, we have recently reported the one-pot sequential double couplings of aryl dihalides by using a well defined Pd–NHC complex, [Pd(3-(2,4-dimethyl-1,8-naphthyrid-7-yl)-1-picolylimidazolylidene)$_2$]$(PF_6)_2$, as a catalyst.[6] However, the special catalyst has to be pre-prepared, and the substrates are limited to 3- and 4-bromoiodobenzene. As an extension of our studies on the organometallic chemistry of functionalized NHCs,[7] here we report a one-pot sequential Heck/Suzuki coupling protocol, which is applicable to a wide range of substituted aryl dialyzes to give unsymmetrical substituted arenes and terphenyls using a Pd/imidazolium catalytic system.

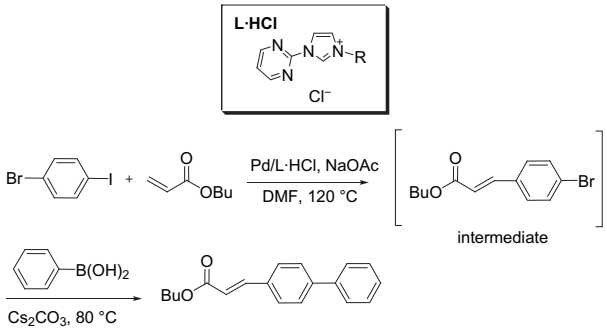
2. Results and discussion

As shown in Scheme 1, the one-pot sequential Heck/Suzuki reaction was conducted in a stepwise way starting from 4-bromoiodobenzene in order to introduce two different groups. Initially, we examined the efficiency of $Pd(OAc)_2$/IPr·HCl (IPr=1,3-bis(2,6-diisopropylphenyl)imidazolylidene) and $Pd(OAc)_2$/IMes·HCl

* Corresponding author. Tel./fax: +86 571 8827 3314.
E-mail address: chenwzz@zju.edu.cn (W. Chen).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.12.043

(Imes=1,3-bis(2,4,6-trimethylphenyl)imidazolylidene) systems, which have proven to be excellent catalysts in various coupling reactions.[8] We found that the chemoselectivity is high and the yield of the mono-coupled product of Heck reaction is nearly quantitative. However, both catalysts could not accomplish the Suzuki coupling reaction due to generation of palladium black in the course of the Heck coupling. Addition of catalytic amount of pyridine or PPh_3 could efficiently prohibit the generation of palladium black, however, the Suzuki coupling reaction still did not occur and only *n*-butyl 4-bromophenylacrylate could be obtained.



Scheme 1. Sequential Heck/Suzuki reactions.

In our previous studies, we have shown that NHCs bearing one or two heteroarene groups can efficiently increase the stability of palladium catalysts.[7a–c] Therefore, we turned our study to functionalized NHCs containing additional *N*-donors. We were pleased to find that a series of imidazolium salts, L1·HCl–L6·HCl, combining pyrimidine functional group and carbene ligand moiety (Chart 1) are quite suitable for the one-pot double coupling reactions. The detail of their catalytic behavior is given in Table 1. These ligands could efficiently prohibit the generation of palladium black in the Heck coupling reaction when heated at 120 °C in DMF. Furthermore, these $Pd(OAc)_2$/imidazolium systems show excellent catalytic activities in Heck coupling process and can also maintain their activities in the subsequent Suzuki coupling reaction. After completion of the Heck transformation at 120 °C and cooling the mixture to room temperature, $PhB(OH)_2$ and Cs_2CO_3 were directly added to the reaction vessel without isolation of the intermediate. The Suzuki coupling was performed 80 °C. The procedure gave the desired double coupling products in different yields with the ligands listed in Chart 1.

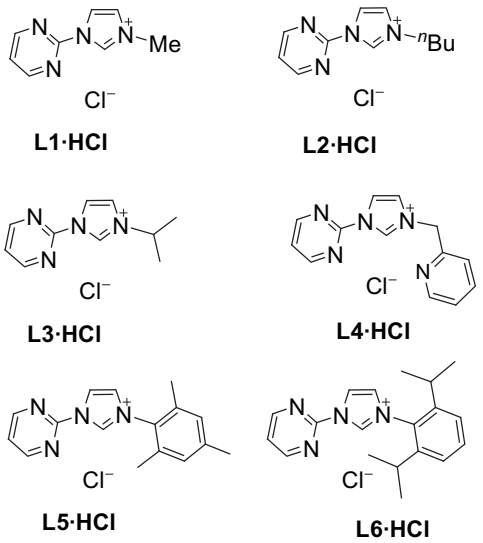


Chart 1. Schematic illustration of the imidazolium salts.

Table 1
Sequential Heck/Suzuki reaction of 4-bromoiodobenzene with different Pd/L systems[a]

Entry	Ligand	Pd/L ratio	Time of Heck reaction (h)	Yield[b] (%)	Time of Suzuki reaction (h)	Yield[c] (%)
1	L1	1/2	1.5	92/6	5	24
2	L2	1/2	1.5	92/6	5	28
3	L3	1/2	1.5	94/5	5	35
4	L4	1/2	1.5	92/6	5	25
5	L5	1/2	1.5	96/4	2	92
6[d]	L5	1/2	1.5	95/5	2	90
7	L5	1/1	1.5	93/6	2	86
8	L6	1/2	1.5	93/6	2	87
9	L6	1/1	1.5	94/5	2	85

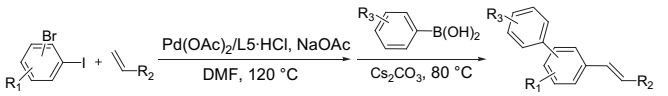
[a] Reaction conditions: Heck conditions. 4-bromoiodobenzene 1.0 mmol, *n*-butyl acrylate 1.05 mmol, NaOAc 1.2 mmol, $Pd(OAc)_2$ 1.0 mol %, L·HCl 2.0 mol %, DMF 5 mL, 120 °C. Suzuki conditions: $PhB(OH)_2$ 1.5 mmol, Cs_2CO_3 1.2 mmol, 80 °C.
[b] GC yield of mono-/double Heck coupling product.
[c] Overall yields of double coupling product.
[d] $Pd_2(dba)_3$ 0.5 mol % was used.

We found that all these $Pd(OAc)_2$/L·HCl catalytic systems are very active in the Heck reaction. The Heck coupling could be completed within 1.5 h at 120 °C regardless of which ligand was employed. The reaction is highly chemoselective giving 4-bromophenylacrylate ester in 92–96% yields. The double Heck coupling product, 1,4-phenylenediacrylate ester, was obtained in not more than 5% yield as determined by GC analysis. However, the catalytic activities the Pd/imidazolium systems differ from each other in the Suzuki coupling reaction. The Heck coupling is nearly quantitative for all ligands, and thus the overall yield depends on the Suzuki coupling. The carbene ligand with a bulky substituted group is much more active (Table 1, entries 5–9) than those carbene ligands with small substituted groups (Table 1, entries 1–4). Among these ligands, the pyrimidine functionalized imidazolium salts bearing bulky 2,4,6-trimethylphenyl and 2,6-diisopropylphenyl are most active in this sequential reaction. The employment of $Pd_2(dba)_3$ and $Pd(OAc)_2$ as palladium sources did not show any significant difference (Table 1, entry 6). Therefore, $Pd(OAc)_2$ was used for detailed investigation. The Pd/L ratio of 2 gave better overall yields and thus two equivalents of ligands were used for further study. With respect to bases, NaOAc and Cs_2CO_3 have been previously found to be most suitable for Heck and Suzuki coupling, respectively.[6]

After screening of the catalysts and the optimization of the reaction conditions, we continued our investigation of the Heck/Suzuki sequential couplings. We tried to extend the one-pot protocol to double coupling of other aryl dihalide derivatives with various phenylboronic acids. As shown in Table 2, the coupling of 4-bromoiodobenzene (**1a**) with *n*-butyl acrylate and subsequent phenylboronic acid affording **2a** in 85% yield (Table 2, entry 1). When 4-chlorophenylboronic acid was employed as a coupling partner, the C–Cl bond is inert under these conditions, and thus **2b** and **2c** bearing additional chloride could be obtained in 67% and 73% yields, respectively (Table 2, entries 2 and 3). These products offer opportunity for the construction of more complex structures through further coupling reaction.

We next examined the reactivities of the substituted aryl dihalides in order to understand the influence of substitutents. When electron-deficient substrate, 2-fluoro-4-bromoiodobenzene (**1c**), was employed as the reactant, the Heck reaction requires 3 h to achieve a complete conversion. The chemoselectivity is also very good, and the mono-coupled product could be obtained in more than 90% as determined by GC chromatography. The Suzuki reactions could complete within another 3 h at 80 °C. All the electron-rich and electron-deficient phenylboronic acid could give good yields of biphenylacrylate esters (Table 2, entries 4–6). It is

Table 2
One-pot sequential Heck/Suzuki reactions of aryl dihalides and substituted aryl dihalides[a]



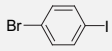
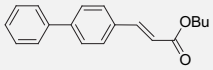
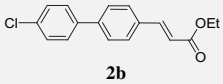
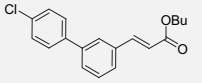
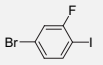
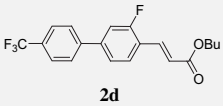
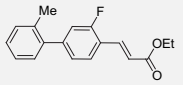
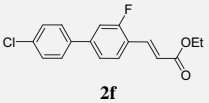
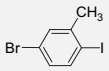
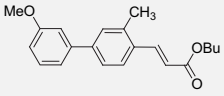
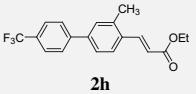
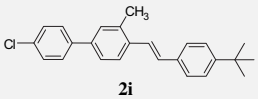
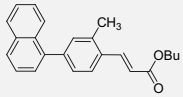
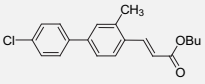
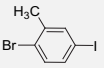
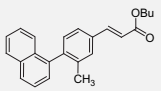
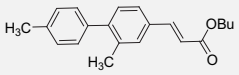
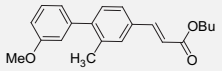
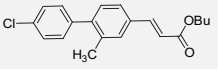
Entry	Substrate	R_2	R_3	Product	Yield (%)[b]
1	 **1a**	^{n}BuOCO	H	 **2a**	85
2	**1a**	EtOCO	4-Cl	 **2b**	67
3	 **1b**	^{n}BuOCO	4-Cl	 **2c**	73
4	 **1c**	^{n}BuOCO	4-CF_3	 **2d**	81
5	**1c**	EtOCO	2-Me	 **2e**	78
6	**1c**	EtOCO	4-Cl	 **2f**	75
7	 **1d**	^{n}BuOCO	3-MeO	 **2g**	88
8	**1d**	EtOCO	4-CF_3	 **2h**	71
9	**1d**	^{t}butyl phenyl	4-Cl	 **2i**	51[c]
10	**1d**	^{n}BuOCO		 **2j**	65
11	**1d**	^{n}BuOCO	4-Cl	 **2k**	62
12	 **1e**	^{n}BuOCO		 **2l**	63

Table 2 (*continued*)

Entry	Substrate	R_2	R_3	Product	Yield (%)[b]
13	**1e**	^{n}BuOCO	4-Me	 **2m**	72
14	**1e**	^{n}BuOCO	3-MeO	 **2n**	75
15	**1e**	^{n}BuOCO	4-Cl	 **2o**	66

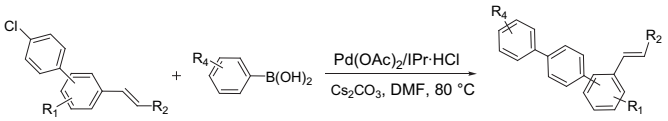
[a] Reaction conditions: ary halide 1.0 mmol, olefin 1.05 mmol, NaOAc 1.2 mmol, $Pd(OAc)_2$ 1.0 mol %, L5·HCl 2.0 mol %, DMF 5 mL, 120 °C. After 2 h, arylboronic acid 1.5 mmol, and Cs_2CO_3 1.2 mmol were added and heated to 80 °C.
[b] Isolated yield.
[c] The (*Z*)-isomer was not isolated.

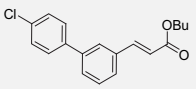
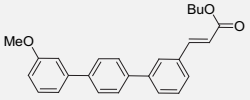
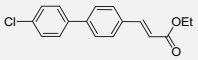
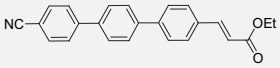
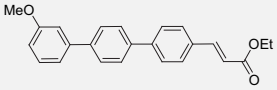
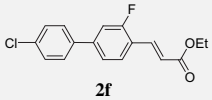
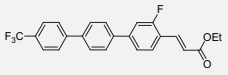
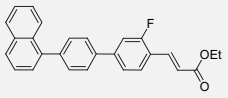
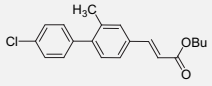
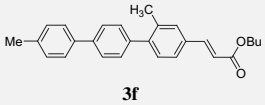
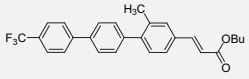
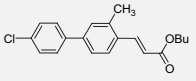
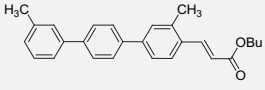
also found that the steric hindrance has little influence on the reactions.

Although 2-methyl-4-bromoiodobenzene (**1d**) has a methyl group neighboring to iodide, this reactant is quite reactive in the Heck coupling reaction. The olefination reactions with various alkenes could be completed within 1 h giving mono-coupled product in 94% yields. The Heck coupling of 2-methyl-4-bromoiodobenzene is even more facile than those of unsubstituted bromoiodobenzene. It seems that the observation is opposite to the commonly recognized fact that the electron-deficient halobenzene has higher reactivity in carbon–carbon formation reactions. Further Suzuki couplings with substituted phenylboronic acids also proceeded smoothly giving the double coupled products in 62–88% isolated yields (Table 2, entries 7, 8, 10, and 11). However, when *tert*-butylstyrene was used, the desired product has a poor solubility in petroleum ether and ethyl acetate causing some trouble in isolation, and the total yield is comparatively low (Table 2, entry 9). For 3-methyl-4-bromoiodobenzene containing a methyl group adjacent to the bromide, the Heck coupling reaction is as reactive as 2-methyl-4-bromoiodobenzene affording mono-coupled product in 94% yield. Further Suzuki coupling with the substituted phenylboronic acids gave biphenylarylate esters in good yields (Table 2, entries 12–15). Even in the case of sterically hindered 1-naphthalenylboronic acid, the overall yield is also good (Table 2, entry 12).

Terphenyls are a class of important compounds, which are frequently found in nature,[9] predominantly as *p*-terphenyl derivatives. Synthetic terphenyls are known to possess biological activities including potent immunosuppressant, neuroprotective, antithrombotic, anticoagulant, and cytotoxic activities.[10] In addition, terphenyls and polyphenyls are also important structural elements in liquid crystals and fluorescent compounds.[11] We are able to prepare polysubstituted terphenyls via further coupling of the coupling products bearing C–Cl bonds. Actually, the third step Suzuki coupling reaction could be easily performed in one-flask by simply adding another substituted arylboronic acid and $Pd(OAc)_2$/IPr·HCl after the second Suzuki coupling without isolation of chlorobiphenylacrylate ester. However, the resultant products are complicated and the overall isolated yields of desired terphenyls are not satisfactory. Therefore, the preparation of substituted terphenyls from the isolated intermediate products bearing additional C–Cl bond is needed. As shown in Table 3, starting from the isolated chlorobiphenylacrylate esters various substituted terphenyls could be obtained via Suzuki coupling reactions with additional substituted phenylboronic acids by using $Pd(OAc)_2$/IPr·HCl as a catalyst in DMF at 80 °C. These

Table 3
Preparation of terphenyl alkenes[a]



Entry	Substrate	R_4	Product	Yield[b] (%)
1	 **2c**	3-MeO	 **3a**	88
2	 **2b**	4-CN	 **3b**	63
3	**2b**	3-MeO	 **3c**	81
4	 **2f**	4-CF_3	 **3d**	80
5	**2f**		 **3e**	78
6	 **2k**	4-Me	 **3f**	79
7	**2k**	4-CF_3	 **3g**	83
8	 **2o**	3-Me	 **3h**	85

[a] Reaction conditions: chlorobiphenylacrylate ester 0.5 mmol, arylboronic acid 0.75 mmol, Cs_2CO_3 1.0 mmol, $Pd(OAc)_2$ 2.0 mol %, IPr·HCl 4.0 mol %, DMF 5 mL, 80 °C, 3 h.
[b] Isolated yield.

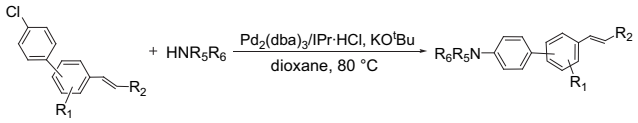
reactions could be completed within 3 h and are also tolerant to many functional groups. The terphenyls with different substituents could be obtained in ca. 80% isolated yields (Table 3, entries 1 to 8).

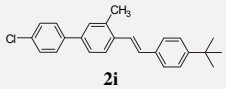
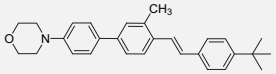
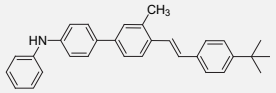
Through C–N coupling of the obtained chlorobiphenyl derivatives we were also able to prepare aminobiphenyl derivatives. Such nitrogen-containing moiety represents an important motif in natural products and pharmaceutical and medicinal compounds,[12] as well as in polymers and materials.[13] The amination of substituted chlorobiphenyls could also be simply conducted by using $Pd_2(dba)_3$/IPr·HCl as catalyst in dioxane. As shown in Table 4, (*E*)-4-(4′-(4-*tert*-butylstyryl)-3′-methylbiphenyl-4-yl)morpholine (**4a**) and (*E*)-4′-(4-*tert*-butylstyryl)-3′-methyl-*N*-phenylbiphenyl-4-amine (**4b**) could be obtained in 81% and 72% yields, respectively.

3. Conclusions

In summary, we described a convenient one-pot sequential approach to prepare unsymmetrically substituted arenes by using a Pd/imidazolium salt system. Two different carbon–carbon formation reactions can be achieved in one pot by using a simple catalyst. Pyrimidine group play important role in stabilizing the catalyst and preventing the formation of palladium black. This protocol is convenient and efficient for various combinations of dihaloarene, olefin, and arylboronic acid. In addition, the biphenyl products bearing chloride could be further converted to polysubstituted terphenyls and aminobiphenyls via additional C–C and C–N coupling reactions.

Table 4
Amination of the substituted biphenyl chlorides[a]



Entry	Substrate	Amine	Product	Yield[b] (%)
1	 **2i**	Morph-oline	 **4a**	81
2	**2i**	$PhNH_2$	 **4b**	72

[a] Reaction conditions. biphenyl chlorides, 0.5 mmol, amines 1.0 mmol, KO^{t}Bu 1.0 mmol, $Pd_2(dba)_3$ 1.0 mol %, IPr·HCl 4.0 mol %, dioxane 5 mL, 80 °C, 6 h.
[b] Isolated yield.

4. Experimental

4.1. General

All the chemicals were obtained from commercial suppliers and used without further purification. L·HCl salts were prepared according to the known procedure.[7g] Elemental analyses were performed on a Flash EA1112 instrument. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance-400 (400 MHz) spectrometer. Chemical shifts (δ) are expressed in part per million downfield to TMS at δ=0 ppm and coupling constants (J) are expressed in hertz. HRMS data were acquired with a FT-ICR mass spectrometer. Column chromatography was performed using silica gel (60 Å 200–300 mesh).

4.2. Typical procedure for one-pot Heck/Suzuki sequence reaction

To 5 mL of degassed DMF in a Schlenk tube were subsequently added 4-bromoiodobenzene (283 mg, 1.0 mmol), *n*-butyl acrylate (134 mg, 1.05 mmol), NaOAc (100 mg, 1.2 mmol), $Pd(OAc)_2$ (2.2 mg, 1.0 mmol %), and L5·HCl (6.0 mg, 2.0 mmol %). The solution was heated to 120 °C under an atmosphere of N_2 for 1.5 h. The reaction mixture was then allowed to cool to room temperature and phenylboronic acid (183 mg, 1.5 mmol), Cs_2CO_3 (400 mg, 1.2 mmol) were added and heated to 80 °C for another 3 h. The reaction mixture was added to 20 mL of water and extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was washed with water (2×20 mL), dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give the desired product.

4.2.1. (E)-Butyl 3-(biphenyl-4-yl)acrylate (Table 2, Entry 1, ***2a****).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J=16.0,=C*H*COOBu, 1H), 7.57–7.62 (m, C_6H_4+*o*-C_6H_5, 6H), 7.44 (t, J=8.0, *m*-C_6H_5, 2H), 7.36 (t, J=8.0, *p*-C_6H_5, 1H), 6.46 (d, J=16.0, –C*H*=CHCOOBu, 1H), 4.21 (t, J=6.4, CH_2, 2H), 1.66–1.73 (m, CH_2, 2H), 1.39–1.48 (m, CH_2, 2H), 0.97 (t, J=8.0, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 144.0, 142.9, 140.1, 133.4, 128.8, 128.5, 127.8, 127.5, 127.0, 118.1, 64.4, 30.7, 19.1, 13.7. EIMS *m*/*z* 280 [M]$^+$.

4.2.2. (E)-Ethyl 3-(4′-chlorobiphenyl-4-yl)acrylate (Table 2, Entry 2, ***2b****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J=16.0, =C*H*COOEt, 1H), 7.58 (d, J=8.4, C_6H_4, 4H), 7.52 (d, J=8.0, C_6H_4, 2H), 7.41 (d, J=8.0, C_6H_4, 2H), 6.47 (d, J=16.0, C*H*=CHCOOEt, 1H), 4.25–4.30 (m, CH_2, 2H), 1.35 (t, J=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 143.8, 141.6, 138.5, 133.9, 133.7, 129.0, 128.6, 128.1, 127.3, 118.3, 60.5, 14.3. HRMS (ESI) *m*/*e* calcd (M$^+$+Na) 309.0653, found 309.0655.

4.2.3. (E)-Butyl 3-(4′-chlorobiphenyl-3-yl)acrylate (Table 2, Entry 3, ***2c****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$). δ 7.73 (d, J=16.0, =C*H*COOBu, 1H), 7.68 (s, aromatic, 1H), 7.50–7.57 (m, aromatic 4H), 7.41–7.48 (m, aromatic 3H), 6.50 (d, J=16.0, C*H*=CHCOOBu, 1H), 4.23 (t, J=6.4, CH_2, 2H), 1.65–1.74 (m, CH_2, 2H), 1.42–1.48 (m, CH_2, 2H), 0.97 (t, J=8.0, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 144.0, 140.5, 138.6, 134.9, 133.6, 129.2, 128.8, 128.6, 128.2, 126.9, 126.4, 118.6, 64.3, 30.5, 19.0, 13.6. Anal. calcd (%) for $C_{19}H_{19}O_2Cl$. C, 72.49; H, 6.08. Found. C, 72.13; H, 6.13. EIMS *m*/*z* 314 [M]$^+$.

4.2.4. (E)-Butyl 3-(3-fluoro-4′-(trifluoromethyl)biphenyl-4-yl)acrylate (Table 2, Entry 4, ***2d****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J=16.0,=C*H*COOBu, 1H), 7.72–7.67 (m, $C_6H_4(CF_3)$, 4H), 7.63 (t, J=8.0, C_6H_3F, 1H), 7.41 (d, J=8.0, C_6H_3F, 1H), 7.35 (d, J_{HF}=12.0, C_6H_3F, 1H), 6.59 (d, J=16.0, C*H*=CHCOOBu, 1H), 4.23 (t, J=6.4, CH_2, 2H), 1.72–1.67 (m, CH_2, 2H), 1.48–1.42 (m, CH_2, 2H), 0.97 (t, J=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 162.7, 160.2, 143.1, 143.0, 142.3, 136.4, 136.3, 129.6, 129.5, 127.2, 125.9, 125.9, 125.8, 123.1, 123.0, 122.2, 122.1, 121.2, 121.1, 114.8, 114.6, 64.6, 30.7, 19.1, 13.6. HRMS (ESI) m/e calcd (M$^+$+Na) 389.1141, found 389.1135.

4.2.5. (E)-Ethyl 3-(3-fluoro-2′-methylbiphenyl-4-yl)acrylate (Table 2, Entry 5, ***2e****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J=16.0,=C*H*COOBu, 1H), 7.55 (t, J=8.0, 1H), 7.20–7.28 (m, aromatic, 4H), 7.12 (d, J=8.0, aromatic, 1H), 7.08 (d, J_{HF}=12.0, C_6H_3F, 1H), 6.57 (d, J=16.0, C*H*=CHCOOBu, 1H), 4.29 (m, CH_2, 2H), 2.29 (s, $C_6H_4(CH_3)$, 3H), 1.35 (t, J=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 162.2, 159.7, 146.0, 145.9, 139.9, 137.0, 136.9, 135.1, 130.6, 129.4, 128.7, 128.6, 128.0, 126.0, 125.5, 125.4, 121.0, 120.9, 120.7, 120.6, 117.0, 116.8, 60.6, 20.3, 14.3. HRMS (ESI) *m*/*e* calcd (M$^+$+Na) 307.1105, found 307.1105.

4.2.6. (E)-Ethyl 3-(4′-chloro-3-fluorobiphenyl-4-yl)acrylate (Table 2, Entry 6, ***2f****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J=16.0, =C*H*COOBu, 1H), 7.58 (t, J=8.0, aromatic, 1H), 7.50 (d, J=8.0, aromatic, 2H), 7.41 (d, J=8.0, aromatic, 2H), 7.35 (d, J=8.0, aromatic, 1H), 7.29 (d, J_{HF}=12.0, C_6H_3F, 1H), 6.56 (d, J=16.0, C*H*=CHCOOBu, 1H), 4.28 (m, CH_2, 2H), 1.34 (t, J=7.2, CH_3, 3H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ 166.8, 162.9, 160.3, 143.5, 143.4, 137.4, 136.7, 136.6, 134.6, 129.6, 129.5, 129.2, 128.1, 122.8, 122.7, 121.7, 121.5, 120.9, 120.8, 114.5, 114.3, 60.6, 14.3. HRMS (ESI) *m*/*e* calcd (M^++Na) 327.0564, found 327.0559.

4.2.7. (E)-Butyl 3-(3′-methoxy-3-methylbiphenyl-4-yl)acrylate (Table 2, Entry 7, ***2g****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J*=16.0, =C*H*COOBu, 1H), 7.63 (d, *J*=8.0, aromatic, 1H), 7.43 (m, aromatic, 2H), 7.36 (t, *J*=8.0, aromatic, 1H), 7.18 (d, *J*=8.0, aromatic, 1H), 7.12 (m, aromatic, 1H), 6.91 (d, *J*=8.0, aromatic, 1H), 6.40 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.22 (t, *J*=6.4, 2H), 3.87 (s, OCH_3, 3H), 2.50 (s, $C_6H_3(CH_3)$, 3H), 1.74–1.67 (m, CH_2, 2H), 1.49–1.40 (m, CH_2, 2H), 0.97 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 159.9, 142.4, 141.7, 141.6, 138.0, 132.4, 129.8, 129.4, 126.8, 125.0, 119.4, 119.0, 113.0, 112.6, 64.4, 55.2, 30.7, 19.9, 19.1, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 347.1618, found 347.1616.

4.2.8. (E)-Ethyl 3-(3-methyl-4′-(trifluoromethyl)biphenyl-4-yl)acrylate (Table 2, Entry 8, ***2h****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J*=16.0, =C*H*COOBu, 1H), 7.69 (s, aromatic, 5H), 7.45 (s, aromatic, 2H), 6.42 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.28 (d, *J*=6.0, CH_2, 2H), 2.52 (s, $C_6H_3(CH_3)$, 3H), 1.36 (s, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$). δ 166.9, 143.7, 141.4, 140.9, 138.3, 133.2, 129.5, 127.2, 127.0, 125.7, 125.6, 125.5, 125.1, 119.6, 60.5, 19.9, 14.3. HRMS (ESI) *m*/*e* calcd (M^++Na) 357.1078, found 357.1073.

4.2.9. (E)-4-(4-tert-Butylstyryl)-4′-chloro-3-methylbiphenyl (Table 2, Entry 9, ***2i****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=8.0, aromatic, 1H), 7.53 (d, *J*=8.0, aromatic, 2H), 7.48 (d, aromatic, *J*=8.0, 2H), 7.41–7.38 (m, 6H), 7.30, 7.04 (both d, *J*=16.0, CH=CH, each 1H), 2.48 (s, $C_6H_3(CH_3)$, 3H), 1.34 (s, $C(CH_3)_3$, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 139.2, 138.7, 136.1, 135.9, 134.8, 133.2, 130.0, 128.8, 128.1, 126.3, 125.8, 125.6, 125.1, 124.7, 34.6, 31.2, 20.1. HRMS (ESI) *m*/*e* calcd (M^++Na) 383.1537, found 383.1542.

4.2.10. (E)-Butyl 3-(2-methyl-4-(naphthalen-1-yl)phenyl)acrylate (Table 2, Entry 10, ***2j****).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J*=16.0, =C*H*COOBu, 1H), 7.90 (d, *J*=8.4, aromatic, 2H), 7.86 (d, *J*=7.6, aromatic, 1H), 7.68 (d, *J*=8.4, aromatic, 1H), 7.54–7.41 (m, aromatic, 4H), 7.35 (m, aromatic, 2H), 6.46 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.24 (t, *J*=6.8, CH_2, 2H), 2.52 (s, $C_6H_3(CH_3)$, 3H), 1.76–1.70 (m, CH_2, 2H), 1.49–1.43 (m, CH_2, 2H), 0.99 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 142.5, 141.8, 139.3, 137.6, 133.7, 132.3, 132.2, 131.3, 128.3, 128.0, 127.8, 126.7, 126.2, 126.1, 125.8, 125.7, 125.3, 119.1, 64.4, 30.7, 19.9, 19.2, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 367.1674, found 367.1669.

4.2.11. (E)-Butyl 3-(4′-chloro-3-methylbiphenyl-4-yl)acrylate (Table 2, Entry 11, ***2k****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J*=16.0, =C*H*COOBu, 1H), 7.63 (d, *J*=8.8, aromatic, 1H), 7.52 (d, *J*=8.8, aromatic, 2H), 7.39–7.41 (m, aromatic, 4H), 6.41 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.27 (t, *J*=6.8, CH_2, 2H), 2.50 (s, $C_6H_3(CH_3)$, 3H), 1.74–1.67 (m, CH_2, 2H), 1.49–1.42 (m, CH_2, 2H), 0.98 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 141.5, 141.3, 138.6, 138.2, 133.7, 132.6, 129.2, 128.9, 128.1, 126.9, 124.8, 119.2, 64.4, 30.7, 19.9, 19.1, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 351.1128, found 351.1122.

4.2.12. (E)-Butyl 3-(3-methyl-4-(naphthalen-1-yl)phenyl)acrylate (Table 2, Entry 12, ***2l****).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86–7.92 (m, aromatic, 2H), 7.76 (d, *J*=16.0, =C*H*COOBu, 1H), 7.54–7.38 (m, aromatic, 6H), 7.26–7.32 (m, aromatic, 2H), 6.52 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.24 (t, *J*=6.8, CH_2, 2H), 2.04 (s, $C_6H_3(CH_3)$, 3H), 1.75–1.67 (m, CH_2, 2H), 1.51–1.41 (m, CH_2, 2H), 0.98 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 144.4, 142.4, 138.9, 137.5, 133.7, 133.4, 131.6, 130.9, 129.6, 128.2, 127.7, 126.4, 126.1, 125.8, 125.7, 125.3, 125.2, 118.0, 64.4, 30.7, 20.0, 19.2, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 367.1674, found 367.1669.

4.2.13. (E)-Butyl 3-(2,4′-dimethylbiphenyl-4-yl)acrylate (Table 2, Entry 13, ***2m****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J*=16.0, =C*H*COOBu, 1H), 7.39–7.42 (m, aromatic, 2H), 7.20–7.25 (m, aromatic, 5H), 6.46 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.22 (t, *J*=6.4, CH_2, 2H), 2.41 (s, $C_6H_3(CH_3)$, 3H), 2.29 (s, $C_6H_3(CH_3)$, 3H), 1.72–1.67 (m, CH_2, 2H), 1.48–1.42 (m, CH_2, 2H), 0.98 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 144.3, 143.9, 138.1, 136.8, 135.9, 133.1, 130.3, 130.1, 128.9, 128.8, 125.4, 117.8, 64.3, 30.7, 21.1, 20.5, 19.1, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 331.1674, found 331.1669.

4.2.14. (E)-Butyl 3-(3′-methoxy-2-methylbiphenyl-4-yl)acrylate (Table 2, Entry 14, ***2n****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J*=16.0, =C*H*COOBu, 1H), 7.41–7.44 (m, aromatic, 2H), 7.35 (t, *J*=8.0, aromatic, 1H), 7.28 (d, *J*=2.0, aromatic, 1H), 6.93–6.91 (m, aromatic, 2H), 6.86 (s, $C_6H_3(CH_3)$, 1H), 6.48 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.24 (t, *J*=6.4, CH_2, 2H), 3.85 (s, OCH_3, 3H), 2.31 (s, $C_6H_3(CH_3)$, 3H), 1.68–1.75 (m, CH_2, 2H), 1.42–1.51 (m, CH_2, 2H), 0.99 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 159.3, 144.2, 143.7, 142.4, 135.9, 133.4, 130.1, 130.0, 129.1, 125.3, 121.4, 117.9, 114.6, 112.5, 64.3, 55.2, 30.7, 20.4, 19.1, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 347.1618, found 347.1619.

4.2.15. (E)-Butyl 3-(4′-chloro-2-methylbiphenyl-4-yl)acrylate (Table 2, Entry 15, ***2o****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J*=16.0, =C*H*COOBu, 1H), 7.39–7.43 (m, aromatic, 4H), 7.31–7.26 (m, aromatic, 3H), 6.47 (d, *J*=16.4, C*H*=CHCOOBu, 1H), 4.21–4.24 (t, *J*=6.8, CH_2, 2H), 2.28 (s, $C_6H_3(CH_3)$, 3H), 1.67–1.74 (m, CH_2, 2H), 1.41–1.48 (m, CH_2, 2H), 0.98 (t, *J*=8.0, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 144.1, 142.6, 139.5, 135.9, 133.8, 133.2, 130.3, 130.2, 130.1, 128.4, 125.5, 118.3, 64.4, 30.8, 20.4, 19.2, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 351.1128, found 351.1124.

4.3. Typical procedure for Suzuki coupling of the substituted biphenyl chloride

To 5 mL of degassed DMF in a Schlenk tube were subsequently added (*E*)-butyl 3-(4′-chlorobiphenyl-3-yl)acrylate (157 mg, 0.5 mmol), 3-methoxyphenylboronic acid (114 mg, 0.75 mmol), Cs_2CO_3 (340 mg, 1.0 mmol), $Pd(OAc)_2$ (2.2 mg, 2.0 mmol %), and IPr·HCl (8.5 mg, 4.0 mmol %). The solution was heated to 80 °C under an atmosphere of N_2 for 3 h. The reaction mixture was added to 20 mL of water and extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was washed with water (2×20 mL), dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give the desired product.

4.3.1. (E)-Butyl 3-(3-methoxy-[1,1′;4′,1″]terphenyl-3″-yl)acrylate (Table 3, Entry 1, ***3a****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.78 (m, aromatic, 2H), 7.64–7.69 (m, aromatic+=C*H*COOBu, 5H), 7.53–7.45 (m, aromatic, 2H), 7.38 (t, *J*=8.0, aromatic, 1H), 7.23 (d, *J*=8.0, aromatic, 1H), 7.18 (s, $C_6H_3(OCH_3)$ 1H), 6.92 (d, *J*=8.0, 1H), 6.52 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.23 (t, *J*=6.4, CH_2, 2H), 3.88 (s, OCH_3, 3H), 1.67–1.72 (m, CH_2, 2H), 1.49–1.42 (m, CH_2, 2H), 0.97 (t, *J*=7.2 CH_3,, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 159.9, 144.4, 142.0, 141.3, 140.3, 139.3, 134.9, 129.8, 129.3, 128.8, 127.6, 127.4, 126.8, 126.7, 119.5, 118.6, 112.7, 64.4, 55.3, 30.7, 19.1, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 409.1774, found 409.1782.

4.3.2. (E)-Ethyl 3-(4-cyano-[1,1′;4′,1″]terphenyl-4″-yl)acrylate (Table 3, Entry 2, ***3b****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.64 (m, aromatic+=C*H*COOBu, 13H), 6.49 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.28 (m, *J*=5.6, CH_2, 2H), 1.35 (t, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 144.9, 143.8, 141.8, 140.4, 138.4, 133.8, 132.6, 128.6,

127.7, 127.6, 127.5, 127.4, 118.8, 118.4, 111.0, 60.5, 14.3. HRMS (ESI) *m*/*e* calcd (M^++Na) 376.1308, found 376.1311.

4.3.3. (E)-Ethyl 3-(3-methoxy-[1,1′;4′,1″]terphenyl-4″-yl)acrylate (Table 3, Entry 3, ***3c****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.60 (m, aromatic, 9H), 7.40–7.36 (m, aromatic, 1H), 7.25–7.22 (m, aromatic, 1H), 7.17 (s, $C_6H_3(OCH_3)$ 1H), 6.91 (d, *J*=6.0, aromatic, 1H), 6.48 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.26–4.31 (m, CH_2, 2H), 3.88 (s, OCH_3, 3H), 1.35 (t, *J*=6.8, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 160.0, 144.0, 142.4, 142.0, 140.6, 139.2, 133.6, 129.8, 128.6, 127.6, 127.4, 127.3, 119.5, 118.2, 112.8, 60.5, 55.3, 14.3. HRMS (ESI) *m*/*e* calcd (M^++Na) 381.1461, found 381.1476.

4.3.4. (E)-Ethyl 3-(4-trifluoromethyl-3″-fluoro-[1,1′;4′,1″]terphenyl-4″-yl)acrylate (Table 3, Entry 4, ***3d****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J*=16.0, =C*H*COOBu, 1H), 7.73–7.71 (m, aromatic, 8H), 7.63 (t, *J*=8.0, aromatic, 1H), 7.47–7.45 (m, aromatic, 1H), 7.41–7.38 (m, aromatic, 1H), 6.59 (d, *J*=16, C*H*=CHCOOBu, 1H), 4.32–4.27 (m, CH_2, 2H), 1.36 (t, *J*=7.6, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 162.9, 160.4, 144.0, 143.9, 143.8, 139.7, 138.7, 136.8, 129.6, 129.5, 127.8, 127.5, 127.3, 125.9 125.8, 125.7, 122.9, 121.6, 121.5, 120.8, 120.7, 114.5, 114.3, 60.7, 14.3. HRMS (ESI) *m*/*e* calcd (M^++Na) 437.1135, found 437.1153.

4.3.5. (E)-Ethyl 3-(3-fluoro-4′-(naphthalen-1-yl)biphenyl-4-yl)acrylate (Table 3, Entry 5, ***3e****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97–7.86 (m, aromatic, 4H), 7.73 (d, *J*=8.0, aromatic, 2H), 7.67–7.44 (m, aromatic, 9H), 6.61 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.34–4.28 (m, CH_2, 2H), 1.38 (t, *J*=7.6, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 162.9, 160.4, 144.5, 144.4, 140.9, 139.3, 137.7, 136.8, 136.7, 133.8, 131.4, 130.7, 129.5, 129.4, 128.3, 127.9, 126.9, 126.7, 126.1, 125.8, 125.7, 125.3, 122.8, 122.7, 121.3, 121.2, 120.6, 120.5, 114.5, 114.3, 60.6, 14.2. HRMS (ESI) *m*/*e* calcd (M^++Na) 419.1418, found 419.1431.

4.3.6. (E)-Butyl 3-(4-methyl-2″-methyl-[1,1′;4′,1″]terphenyl-4″-yl)-acrylate (Table 3, Entry 6, ***3f****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J*=16.0, =C*H*COOBu, 1H), 7.63 (d, *J*=8.0, aromatic, 2H), 7.54 (d, *J*=8.0, aromatic, 2H), 7.45–7.42 (m, aromatic, 2H), 7.38 (d, *J*=8.0, aromatic, 2H), 7.31–7.25 (m, aromatic, 3H), 6.47 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.22 (t, *J*=8.0, CH_2, 2H), 2.41 (s, $C_6H_3(CH_3)$, 3H), 2.35 (s, $C_6H_3(CH_3)$, 3H), 1.74–1.67 (m, CH_2, 2H), 1.50–1.41 (m, CH_2, 2H), 0.98 (t, *J*=8.0, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 144.3, 143.6, 140.0, 139.8, 137.8, 137.2, 136.0, 133.4, 130.4, 130.2, 129.5, 129.4, 126.9, 126.7, 125.5, 118.0, 64.4, 30.8, 21.1, 20.6, 19.2, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 407.1982, found 407.1990.

4.3.7. (E)-Butyl 3-(4-trifluoromethyl-2″-methyl-[1,1′;4′,1″]terphenyl-4″-yl)acrylate (Table 3, Entry 7, ***3g****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65–7.76 (m, aromatic+=C*H*COOBu, 7H), 7.44 (t, *J*=8.0, aromatic, 4H), 7.29 (d, *J*=8.0, aromatic, 1H), 6.48 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.23 (t, *J*=8.0, CH_2, 2H), 2.35 (s, $C_6H_3(CH_3)$, 3H), 1.67–1.74 (m, CH_2, 2H), 1.43–1.50 (m, CH_2, 2H), 0.98 (t, *J*=8.0, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 167.1, 144.3, 144.2, 143.6, 143.1, 141.0, 139.9, 139.7, 138.5, 137.7, 137.2, 136.0, 135.9, 133.6, 133.4, 130.4, 130.3, 130.2, 130.1, 129.6, 129.5, 129.3, 127.3, 127.0, 126.8, 126.6, 125.8, 125.7, 125.5, 125.4, 118.2, 118.0, 64.4, 64.3, 30.7, 21.1, 20.5, 20.4, 19.2, 13.7. HRMS (ESI) *m*/*e* calcd (M^++Na) 461.1699, found 461.1706.

4.3.8. (E)-Butyl 3-(3-methyl-3″-methyl-[1,1′;4′,1″]terphenyl-4″-yl)-acrylate (Table 3, Entry 8, ***3h****).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J*=16.0, =C*H*COOBu, 1H), 7.67–7.64 (m, aromatic, 5H), 7.50–7.43 (m, aromatic, 4H), 7.35 (t, *J*=7.6, aromatic, 1H), 7.18 (d, *J*=7.6, aromatic, 1H), 6.42 (d, *J*=16.0, C*H*=CHCOOBu, 1H), 4.24 (t, *J*=6.8, CH_2, 2H), 2.52 (s, $C_6H_3(CH_3)$, 3H), 2.44 (s, $C_6H_3(CH_3)$ 3H), 1.75–1.68 (m, CH_2, 2H), 1.50–1.41 (m, CH_2, 2H), 0.98 (t, *J*=7.2, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 142.2, 141.7, 140.7, 140.5, 139.0, 138.4, 138.1, 132.4, 129.3, 128.7, 128.2, 127.8, 127.5, 127.3, 126.9, 124.9, 124.1, 119.0, 64.4, 30.7, 21.5, 20.0, 19.2, 13.8. HRMS (ESI) *m*/*e* calcd (M^++Na) 407.1982, found 407.1985.

4.4. Typical procedure for amination of the substituted biphenyl chloride

To 5 mL of degassed dioxane in a Schlenk tube were subsequently added (*E*)-4-(4-*tert*-butylstyryl)-4′-chloro-3-methylbiphenyl (130 mg, 0.5 mmol), morpholine (65 mg, 0.75 mmol), K^tOBu (112 mg, 1.0 mmol), $Pd_2(dba)_3$ (8.0 mg, 2.0 mmol %), and IPr·HCl (8.5 mg, 4.0 mmol %). The solution was heated to 80 °C under an atmosphere of N_2 for 6 h. The reaction mixture was added to 20 mL of water and extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was washed with water (2×20 mL), dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate/petroleum ether mixed solvent to give the desired product.

4.4.1. (E)-4-(4′-(4-tert-Butylstyryl)-3′-methylbiphenyl-4-yl)morpholine (Table 4, Entry 1, ***4a****).* Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J*=8.0, aromatic, 1H), 7.55 (d, *J*=8.0, aromatic, 2H), 7.48 (d, *J*=8.0, aromatic, 2H), 7.42–7.39 (m, aromatic, 4H), 7.32, 7.02 (both d, *J*=16.0, CH=CH, each 1H), 6.98 (d, *J*=8.0, 2H), 3.89 (t, *J*=4.8, OCH_2CH_2N, 2H), 3.21 (t, *J*=4.8, OCH_2CH_2N, 2H), 2.48 (s, $C_6H_3(CH_3)$, 3H), 1.34 (s, $C(CH_3)_3$, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 136.1, 135.4, 134.9, 129.7, 129.4, 128.5, 128.2, 127.9, 126.2, 125.7, 125.6, 125.2, 125.0, 124.6, 124.4, 72.7, 65.7, 34.4, 30.7, 19.6. HRMS (ESI) *m*/*e* calcd (M^++H) 412.2635, found 412.2643.

4.4.2. (E)-4′-(4-tert-Butylstyryl)-3′-methyl-N-phenylbiphenyl-4-amine (Table 4, Entry 2, ***4b****).* Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=8.0, aromatic, 1H), 7.54 (d, *J*=8.0, aromatic, 2H), 7.49 (d, *J*=8.0, aromatic, 2H), 7.44–7.40 (m, aromatic+CH=CH, 4H), 7.35–7.27 (m, aromatic, 3H), 7.13 (t, *J*=7.2, aromatic, 4H), 7.04 (d, *J*=16.0, CH=CH, 1H), 6.97 (d, *J*=8.0, aromatic, 1H), 5.79 (s, NH, 1H), 2.50 (s, $C_6H_3(CH_3)$, 3H), 1.36 (s, CH_3, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7, 142.9, 142.5, 139.7, 136.0, 135.0, 134.9, 133.3, 129.4, 129.3, 128.4, 127.7, 126.2, 125.7, 125.6, 125.4, 124.2, 121.2, 118.0, 117.8, 34.6, 31.2, 20.0. HRMS (ESI) *m*/*e* calcd (M^++Na) 418.2529, found 418.2542.

Acknowledgements

We are grateful to the support of the NSF of China (gs1) (20872129 and J0830413), and Zhejiang University K.P. Chao's High Technology Development Foundation for financial support.

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2009.12.043.

References and notes

1. (a) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: Chichester, UK, 1995; (b) Díez-González, S.; Nolan, S. P. *Top. Organomet. Chem.* **2007**, *21*, 47; (c) Schils, D.; Stappers, F.; Solberghe, G.; Heck, R.; Coppens, M.; Heuvel, D. V.; Donck, P. V.; Callewaert, T.; Meeussen, F.; Bie, E. D.; Eersels, K.; Schouteden, E. *Org. Process Res. Dev.* **2008**, *12*, 530; (d) Zapf, A.; Beller, M. *Chem. Commun.* **2005**, 431; (e) Jensen, T.; Pedersen, H.; Bang-Andersen, B.; Madsen, R.; Jørgensen, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 888; (f) Huang, Z.; Negishi, E. *J. Am. Chem. Soc.* **2007**, *129*, 14788.
2. (a) Denmark, S. E.; Tymonko, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 8004; (b) Beaumard, F.; Dauban, P.; Dodd, R. H. *Org. Lett.* **2009**, *11*, 1801; (c) Wu, T. Y. H.; Schultz, P. G.; Ding, S. *Org. Lett.* **2003**, *5*, 3587; (d) Itami, K.; Nokami, T.;

Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 11577; (e) Itami, K.; Tonogaki, K.; Ohashi, Y.; Yoshida, J. *Org. Lett.* **2004**, *6*, 4093.
3. (a) Marion, N.; Nolan, S. P. *Acc. Chem. Res.* **2008**, *41*, 1440; (b) Würtz, S.; Glorius, F. *Acc. Chem. Res.* **2008**, *41*, 1523; (c) He, M.; Beahm, B. J.; Bode, J. W. *Org. Lett.* **2008**, *10*, 3817; (d) Wang, W.; Zhang, T.; Shi, M. *Organometallics* **2009**, *28*, 2640; (e) Hartmann, C. E.; Nolan, S. P.; Cazin, C. S. J. *Organometallics* **2009**, *28*, 2915; (f) Lebeuf, R.; Hirano, K.; Glorius, F. *Org. Lett.* **2008**, *10*, 4243; (g) Hadei, N.; Assen, E.; Kantchev, B.; O'Brien, C. J.; Organ, M. G. *Org. Lett.* **2005**, *7*, 3805.
4. (a) Trindade, A. F.; Gois, P. M. P.; Veiros, L. F.; André, V.; Duarte, M. T.; Afonso, C. A. M.; Caddick, S.; Cloke, F. G. N. *J. Org. Chem.* **2008**, *73*, 4076; (b) Viciu, M. S.; Kelly, R. A.; Stevens, E. D.; Naud, F.; Studer, M.; Nolan, S. P. *Org. Lett.* **2003**, *5*, 1479; (c) Jarusiewicz, J.; Choe, Y.; Yoo, K. S.; Park, C. P.; Jung, K. W. *J. Org. Chem.* **2009**, *74*, 2873; (d) Schaub, T.; Fischer, P.; Steffen, A.; Braun, T.; Radius, U.; Mix, A. *J. Am. Chem. Soc.* **2008**, *130*, 9304; (f) Matsubara, K.; Ueno, K.; Koga, Y.; Hara, K. *J. Org. Chem.* **2007**, *72*, 5069.
5. (a) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 418; (b) Matsumoto, Y.; Yamada, K.; Tomioka, K. *J. Org. Chem.* **2008**, *73*, 4578; (c) Stauffer, S. R.; Lee, S.; Stambuli, J. P.; Hauck, S. I.; Hartwig, J. F. *Org. Lett.* **2000**, *2*, 1423; (d) Grasa, G. A.; Nolan, S. P. *Org. Lett.* **2001**, *3*, 119; (e) Struble, J. R.; Kaeobamrung, J.; Bode, J. W. *Org. Lett.* **2008**, *10*, 957; (f) Altenhoff, G.; Goddard, R.; Lehmann, C. W.; Glorius, F. *J. Am. Chem. Soc.* **2004**, *126*, 15195; (g) Lee, K.; M. Brown, K.; Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 7182.
6. Zhang, X.; Liu, A.; Chen, W. *Org. Lett.* **2008**, *10*, 3849.
7. (a) Zhang, X.; Xi, Z.; Liu, A.; Chen, W. *Organometallics* **2008**, *27*, 4401; (b) Ye, J.; Zhang, X.; Chen, W.; Shimada, S. *Organometallics* **2008**, *27*, 4166; (c) Ye, J.; ChenWang, W. D. *Dalton Trans.* **2008**, 4015; (d) Xi, Z.; Zhang, X.; Chen, W.; Fu, S.; Wang, D. *Organometallics* **2007**, *26*, 6636; (e) Xi, Z.; Liu, B.; Chen, W. *J. Org. Chem.* **2008**, *73*, 3954; (f) Xi, Z.; Zhou, Y.; Chen, W. *J. Org. Chem.* **2008**, *73*, 8497; (g) Zhou, Y.; Xi, Z.; Chen, W. *Organometallics* **2008**, *27*, 5911; (h) Liu, B.; Xia, Q.; Chen, W. *Angew. Chem., Int. Ed.* **2009**, *48*, 5513.
8. (a) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804; (b) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866; (c) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889; (d) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029; (e) Viciu, M. S.; Kissling, R. M.; Stevens, E. D.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 2229; (f) Lebel, H.; Janes, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046; (g) Zhang, X.; Liu, B.; Xie, W.; Chen, W. *Organometallics* **2009**, *28*, 1336.
9. Liu, J. K. *Chem. Rev.* **2006**, *106*, 2209.
10. (a) Roberti, M.; Pizzirani, D.; Recanatini, M.; Simoni, D.; Grimaudo, S.; Di Cristina, A.; Abbadessa, V.; Gebbia, N.; Tolomeo, M. *J. Med. Chem.* **2006**, *49*, 3012; (b) Ichimura, K. *Chem. Rev.* **2000**, *100*, 1847; (c) Zhang, C.; Ondeyka, J. G.; Herath, K. B.; Guan, Z.; Collado, J.; Pelaez, F.; Leavitt, P. S.; Gurnett, A.; Nare, B.; Liberator, P.; Singh, S. B. *J. Nat. Prod.* **2006**, *69*, 710; (d) Yin, H.; Lee, G.-I.; Sedey, K. A.; Kutzki, O.; Park, H. S.; Orner, B. P.; Ernst, J. T.; Wang, H.-G.; Sebti, S. M.; Hamilton, A. D. *J. Am. Chem. Soc.* **2005**, *127*, 10191.
11. (a) Chen, B.; Baumeister, U.; Pelzl, G.; Das, M. K.; Zeng, X.; Ungar, G.; Tschierske, C. *J. Am. Chem. Soc.* **2005**, *127*, 16578; (b) Shimizu, M.; Nagao, I.; Tomioka, Y.; Hiyama, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 8096; (c) Kiryanov, A. A.; Sampson, P.; Seed, A. J. *J. Mater. Chem.* **2001**, *11*, 3068; (d) Shibata, T.; Tsuchikama, K. *Chem. Commun.* **2005**, 6017; (e) Murphy, A. R.; Fréchet, J. M. J. *Chem. Rev.* **2007**, *107*, 1066.
12. (a) Peat, A. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 1028; (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127; (e) Koike, K.; Jia, Z.; Nikaido, T.; Liu, Y.; Zhao, Y.; Guo, D. *Org. Lett.* **1999**, *1*, 197.
13. (a) Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 11695; (c) Persson, J. C.; Jannasch, P. *Chem. Mater.* **2003**, *15*, 3044.