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Facile and controllable synthesis of multiply substituted benzenes via a formal [3+3] cycloaddition approach

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ABSTRACT

A facile direct [3+3] approach for the conversion of α,β-unsaturated carbonyls to multi-substituted benzenes using allylic phosphonium ylide reagents has been developed. The substituents and their positions on the benzene ring are controllable and predictable by the choice of an appropriate combination of α,β-unsaturated carbonyl compounds and ylides.

1. Introduction

Multiply substituted benzenes are important building blocks in organic synthesis, and also the key structures of many natural products, bioactive molecules, and functional materials.[1] Modification of benzenes and ring synthesis are the two major approaches accessing multi-substituted benzene derivatives. Conventionally, aromatic substitution and coupling are widely employed methods to modify benzenes, but they require the pre-introduction of positioning or directing groups to achieve a precise installation.[2] Although a number of methods, such as transition metal-catalyzed [2+2+2] and [4+2] approaches have been reported for the construction of substituted benzenes, the control of both the substituents and their positions on the benzene ring at will remains quite a challenging task.[3–7] In the past decade, we focused on the development of ylide-initiated Michael addition-cyclization reactions (YIMACs) and their relevant synthetic applications.[8,9] Very recently, we found that the reactions of α,β-unsaturated ketones with crotonate-derived phosphonium ylides can yield multi-substituted benzenes efficiently in a formal [3+3][10] cycloaddition manner. Remarkably, the substituents and their positions on the benzene ring can be well controlled by the choice of enone and ylide components. In this communication, we wish to report the preliminary results.

2. Results and discussion

During the course of the reaction optimization of enone **1a** with phosphonium salt **2a** in our previous study,[11] when DBU was employed as the base and air was introduced, besides the anticipated cyclohexadiene compound **4a**, cycloaromatization product **3a** was also obtained in 23% yield, which was supposed to form via a conjugate addition/intramolecular Wittig reaction/aromatization reaction sequence (Table 1, entry 1). We thus envisioned that this tandem reaction might be a potential facile approach for the construction of multi-substituted benzenes from α,β-unsaturated carbonyl compounds. To improve the yield of benzene product **3a**, we first examined the effect of solvent and base. As shown in Table 1, toluene, 1,2-dichloroethane (DCE), *t*-BuOH, and THF afforded high total yields of **3a** and **4a**, but the aerial oxidation of cyclohexadiene was sluggish (entries 1–4), giving low **3a**/**4a** ratios. In contrast, acetone and ethyl acetate gave better ratios, but the total yields were only moderate (entries 5–6). To our delight, acetonitrile was found to be fairly efficient for this transformation, affording **3a** in 86% isolated yield, and no cyclohexadiene was detected by ^{1}H NMR analysis (entry 7). Consequently, acetonitrile was employed as the solvent for the investigation of base effect. Organic bases like DABCO, DMAP, and DIPEA gave poor **3a**-selectivity (entries 8–10). Inorganic bases, such as NaOH and *t*-BuOK were inefficient in this reaction (entries 11–12). K_2CO_3 provided a moderate selectivity for **3a** over **4a** (entry 13), whereas Cs_2CO_3 furnished complete conversion of cyclohexadiene to benzene derivative, yet the yield of **3a** was lower in comparison with DBU (entry 7 vs 14).[12] Moreover, reaction at 60 °C proved to be critical, as either elevating or

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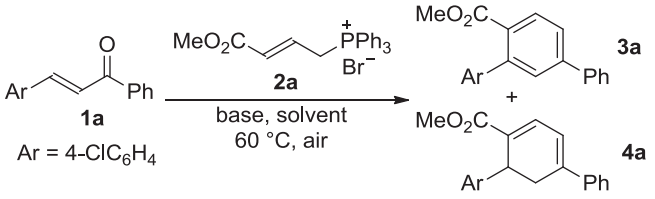
Table 1
Solvent and base effect on the reaction of enone **1a** with phosphonium salt **2a**



Entry[a]	Base	Solvent	Yield [%] **3a**+**4a**[b]	**3a**/**4a**[c]	Yield [%] **3a**[b]
1	DBU	Toluene	88	26/74	23
2	DBU	DCE	92	7/93	14
3	DBU	*t*-BuOH	95	19/81	18
4	DBU	THF	84	35/65	48
5	DBU	Acetone	67	49/51	33
6	DBU	EtOAc	60	38/62	42
7	DBU	CH_3CN	86	>99/1	86
8	DABCO	CH_3CN	72	9/91	11
9	DMAP	CH_3CN	88	7/93	27
10	DIPEA	CH_3CN	96	1/99	12
11	*t*-BuOK	CH_3CN	<5	—	<5
12	NaOH	CH_3CN	16	69/31	11
13	K_2CO_3	CH_3CN	86	45/55	39
14	Cs_2CO_3	CH_3CN	74	>99/1	74
15[d]	DBU	CH_3CN	77	>99/1	77
16[e]	DBU	CH_3CN	70	>99/1	70
17[f]	DBU	CH_3CN	86	>99/1	86

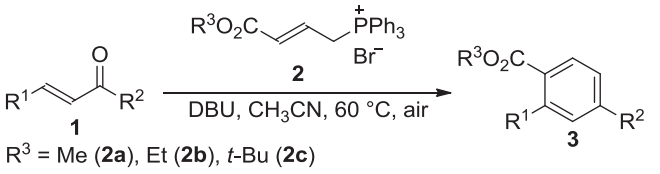
[a] Scale: 0.25 mmol, **1a**/**2a**/base=1/1.8/3.4, 48 h.
[b] Isolated yield.
[c] Determined by ^1H NMR.
[d] At 80 °C.
[e] At 40 °C.
[f] **1a**/**2a**/base=1/1.4/3.4.

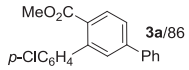
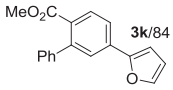
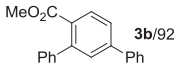
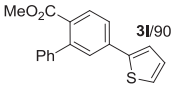
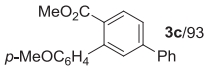
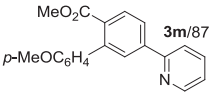
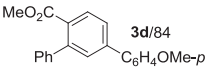
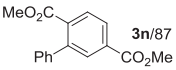
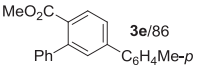
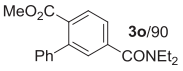
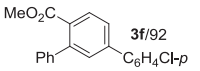
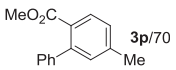
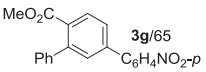
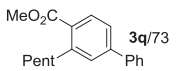
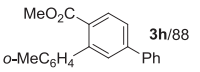
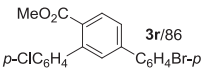
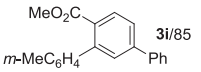
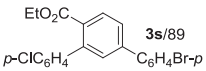
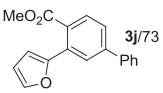
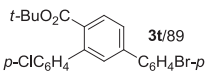
lowering the temperature decreased the yield (entry 7 vs 15, 16). The loading of the phosphonium salt **2a** can be further reduced to 1.4 equiv without loss in yield (entry 17).[13]

Having established the optimal reaction conditions, we next examined a series of aryl and alkyl substituted α,β-unsaturated ketones. As revealed in Table 2, the reaction proceeded well with a broad range of chalcone-type substrates, regardless of the electronic nature (entries 1–7) of the aryl group and the position of the substituents (entries 8–9), providing the corresponding 2,4-diaryl substituted benzoate products **3a**–**i** in high yields (entries 1–9). Furyl, thiophenyl, and pyridyl all were well tolerated in this reaction, which may provide potential application for materials science (entries 10–13).[1d] Functionalities like ester, amide can also be introduced into the multi-substituted benzene products by using the corresponding β,γ-unsaturated α-keto ester or amide (entries 14–15). Moreover, alkyl substituted α,β-unsaturated ketones are also suitable substrates (entries 16–17). On the other hand, variation on the ester group of the phosphonium **2** did not affect the results (entries 18–20). It is worth noting that this [3+3] annulation reaction could be a direct and useful method for the transformation of an enone linker in a molecule to a benzene ring as exemplified by chalcone (see the scheme in Table 2).

To further examine the generality of this [3+3] approach, α,β-unsaturated aldehyde, α-substituted α,β-unsaturated ketones, as well as 3-substituted crotonate-derived phosphonium salts were tested under the standard conditions. As shown in Table 3, all these substrates worked quite well, delivering the corresponding di-, tetra-, and penta-substituted benzenes in good to high yields. Cinnamaldehyde reacted with phosphonium salt **2a** giving di-substituted benzene **5a** (entry 1). Reactions of α-substituted α,β-unsaturated ketones with phosphonium **2a** afforded 1,2,3,4-tetra-substituted benzenes (**6a**–**c**) in good yields (entries 2–4). Accordingly, 1,2,4,6-tetra-substituted benzenes (**6d**–**g**) can also be prepared through the reactions of α,β-unsaturated carbonyl compounds with α-substituted phosphonium salts **2d**–**f** (entries 5–8). Notably, 1,2,3,4,6-penta-substituted benzenes **7a**–**d** are

Table 2
Syntheses of tri-substituted benzene derivatives[a]



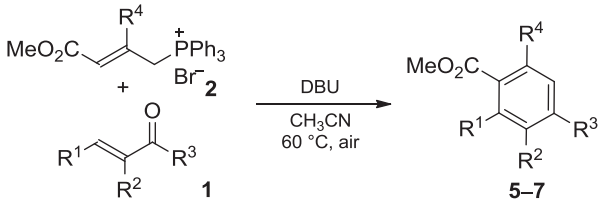
Entry	Product/yield (%)[b]	Entry	Product/yield (%)[b]
1	 **3a**/86	11	 **3k**/84
2	 **3b**/92	12	 **3l**/90
3	 **3c**/93	13	 **3m**/87
4	 **3d**/84	14	 **3n**/87
5	 **3e**/86	15	 **3o**/90
6	 **3f**/92	16[d]	 **3p**/70
7[c]	 **3g**/65	17[d,e]	 **3q**/73
8	 **3h**/88	18	 **3r**/86
9	 **3i**/85	19	 **3s**/89
10	 **3j**/73	20	 **3t**/89

[a] Scale: 0.25 mmol, **1**/**2**/DBU=1/1.4–1.8/3.4, 48 h.
[b] Isolated yield.
[c] 24 h.
[d] 72 h.
[e] Pure ylide was used.[14]

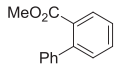
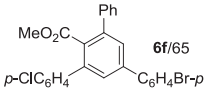
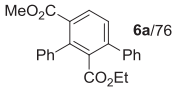
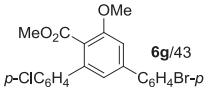
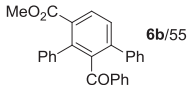
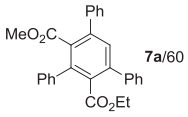
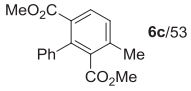
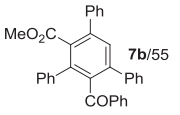
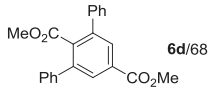
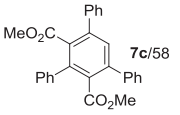
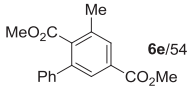
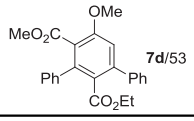
also accessible using this method (entries 9–12). Therefore, the [3+3] annulation reactions of α,β-unsaturated carbonyl compounds with crotonate-derived phosphonium ylides can provide a variety of di-, tri-, tetra-, and penta-substituted benzenes, and notably the substituents and their positions on the benzene ring can be controlled by the selection of an appropriate combination of the substituted enones with ylides.

Interestingly, when an additional carbon–carbon double bond is present in the α,β-unsaturated ketone substrates (**8a** and **9a**, Scheme 1), apart from the desired alkenylated benzene derivatives **10a** and **12a**, the corresponding double bond-saturated compounds **11a** and **13a** were also observed as a major product under the standard reaction conditions. These results may suggest the existence of another aromatization approach via proton transfer, which would compete with the aromatization via the aerial oxidation and lead to product **11a** and **13a**. Thus, an inert reaction atmosphere and catalytic amount of base should suppress the aerial oxidation and favor the proton

Table 3
Syntheses of multi-substituted benzene derivatives[a]

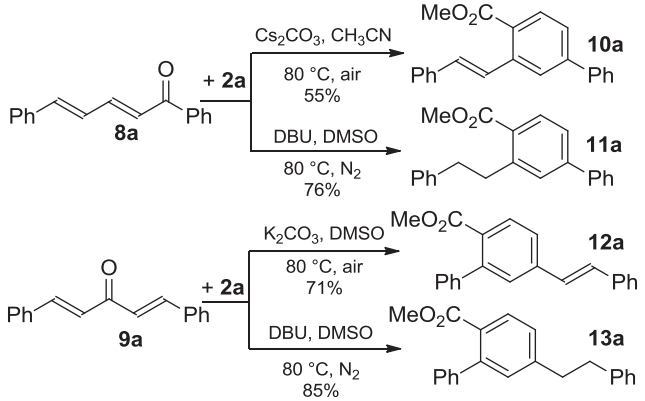


R^4 = H (**2a**), Ph (**2d**), Me (**2e**), OMe (**2f**)

Entry	Product/yield (%)[b]	Entry	Product/yield (%)[b]
1[c]	 **5a**/53	7[d]	 **6f**/65
2	 **6a**/76	8	 **6g**/43
3	 **6b**/55	9[d]	 **7a**/60
4	 **6c**/53	10[d]	 **7b**/55
5[d]	 **6d**/68	11	 **7c**/58
6[d]	 **6e**/54	12	 **7d**/53

[a] Scale: 0.25 mmol, **1**/**2**/DBU=1/1.4–1.8/3.4, 48 h.
[b] Isolated yield.
[c] At −20 °C.
[d] **1**/**2**/DBU=1/2.0/5.2.

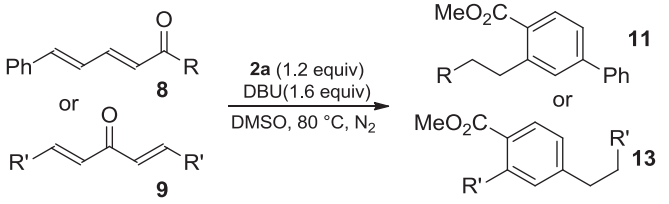
transfer path. Fortunately, through the careful choice of base, solvent, and reaction atmosphere, both the alkenylated benzene derivatives and phenylethyl substituted benzene derivatives can be obtained separately in good yields (Scheme 1). To our knowledge, the transformation of dienone substrates like **8a** and **9a** to alkylated benzenes like **11a** and **13a** has not been reported before.

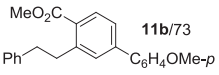
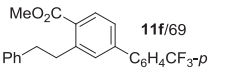
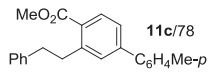
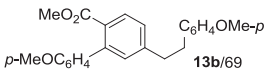
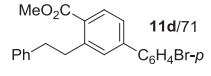
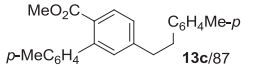
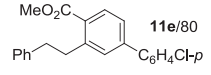
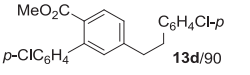


Scheme 1. Reaction of dienone substrates.

To examine the generality of the [3+3] process involving the proton-transfer-promoted aromatization, more cinnamylideneacetophenone and bisarylideneacetone substrates were prepared and subjected to the optimized reaction conditions (N_2 atmosphere and DBU as the base). As revealed in Table 4, the reactions proceeded smoothly under the inert atmosphere, and various electron-donating groups (e.g., −OMe, −Me) and electron-withdrawing groups (e.g., −Br, −Cl, $-CF_3$) were well tolerated, providing *ortho* (**11a**–**f**) and *para* (**13a**–**d**) alkylated benzoate in good to high yields (Scheme 1 and Table 4).

Table 4
Syntheses of ethidened benzene derivatives[a]



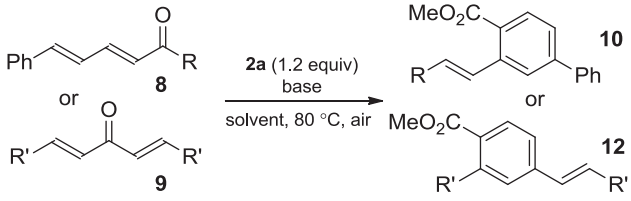
Entry	Product/yield (%)[b]	Entry	Product/yield (%)[b]
1	 **11b**/73	5	 **11f**/69
2	 **11c**/78	6[c]	 **13b**/69
3	 **11d**/71	7	 **13c**/87
4	 **11e**/80	8	 **13d**/90

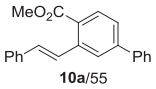
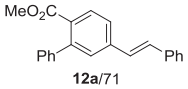
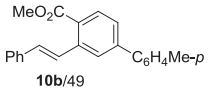
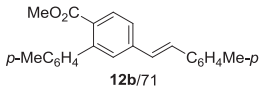
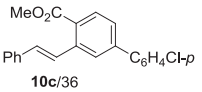
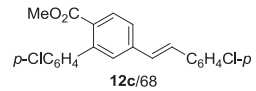
[a] Scale: 0.3 mmol, **8**/**2a**/DBU=1/1.2/1.4, **9**/**2a**/DBU=1/1.2/1.6, 48 h.
[b] Isolated yield.
[c] 72 h.

As aforementioned, the α,β-unsaturated ketone substrates **8** and **9**, which have two double bonds conjugating with the ketone prevailed the proton-transfer-promoted aromatization. In light of DBU favoring the proton-transfer-promoted aromatization process (Table 1), we conceived that weaker bases like Cs_2CO_3 might favor the oxidative aromatization process to afford alkenylated benzene derivatives **10** and **12**. Thus further optimization of reaction conditions was performed. As shown in Table 5, the reactions proceeded well in air, and electron-donating group (−Me) and electron-withdrawing groups (−Cl) were well tolerated except for product **10c**, which accompanied with product **11e** in similar yields.

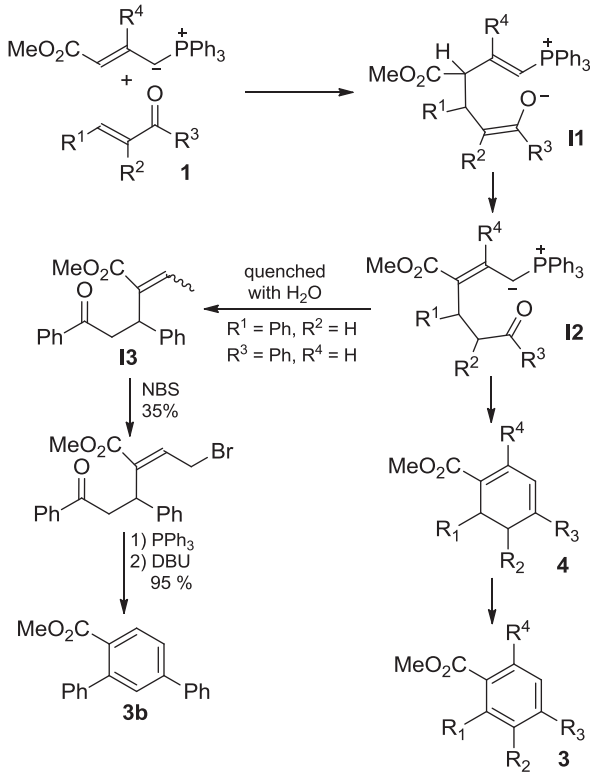
A tandem reaction sequence as outlined in Scheme 2 was proposed to explain the product formation. Nucleophilic attack of ylide to α,β-unsaturated ketone initiates the [3+3] reaction sequence, giving adduct **I1**, which is later converted to ylide **I2** via proton transfer. Intermediate **I2** then undergo an intramolecular Wittig reaction and the subsequent aerial oxidation, giving the desired multi-substituted benzene derivatives **3**. In fact, **I2** (R^1, R^3=Ph, R^2, R^4=H) can be intercepted by quenching the reaction in the early stage with water to give compound **I3**, which was subsequently brominated and then converted to its phosphonium salt. Subsequent treatment with DBU under the standard reaction conditions delivered compound **3b** in 95% yield, identical to the result obtained directly with chalcone **1b** (entry 2, Table 2). The interception of intermediate **I2** and its transformation to **3b** with high yield well confirmed the proposed mechanism.

Table 5
Syntheses of alkenylated benzene derivatives[a]



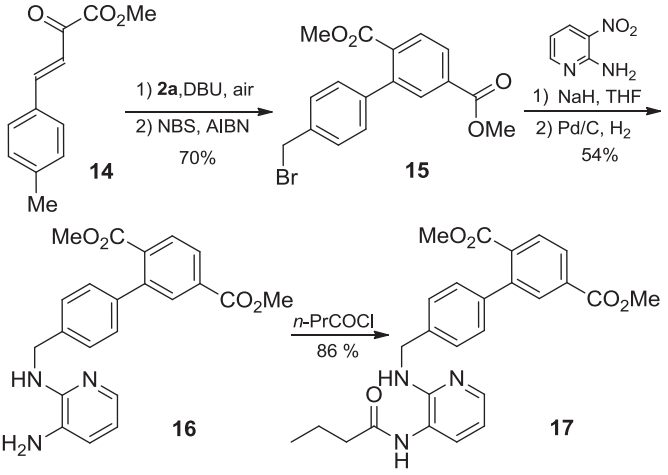
Entry[a]	Product/yield (%) [b]	Entry[c]	Product/yield (%)
1	 **10a**/55	4	 **12a**/71
2	 **10b**/49	5[e]	 **12b**/71
3[d]	 **10c**/36	6	 **12c**/68

[a] Scale: 0.3 mmol, **8**/**2a**/Cs_2CO_3=1/1.2/2.4, CH_3CN, 24 h.
[b] Isolated yield.
[c] Scale: 0.3 mmol, **9**/**2a**/K_2CO_3=1/1.2/1.6, DMSO, 48 h.
[d] **11e** was isolated in 28% yield.
[e] 72 h.



Scheme 2. A proposed mechanism and the interception of reaction intermediates.

The potential synthetic application of the present reaction was demonstrated in a short synthesis of **17**, a potent bradykinin receptor β1 antagonist.[15] As described in Scheme 3, **15** was obtained through the [3+3] annulation of enone **14** with phosphonium salt **2a** under the standard reaction conditions followed by bromination with NBS/AIBN. Subsequent amination, hydrogenation, and acylation gave the target molecule **17** in 32.7% yield over five steps.



Scheme 3. Synthesis of a bradykinin receptor β1 antagonist.

3. Conclusion

A facile and controllable [3+3] approach for the synthesis of di-, tri-, tetra-, and, pent-substituted benzene derivatives has been developed. A broad range of α,β-unsaturated carbonyl compounds can be efficiently converted to multi-substituted benzenes through the reaction with crotonate-derived phosphonium ylides. Both the substituents and their positions on the benzene ring can be easily controlled by choosing appropriate combination of the starting materials. Widespread presence of α,β-unsaturated carbonyl moiety, readily accessible ylide reagents, and the straightforward transformation make this [3+3] approach potentially useful in organic synthesis and materials science. A rational mechanism is proposed and a key intermediate is intercepted. Relevant synthetic applications of the current method are in progress.

4. Experimental section

4.1. General information and materials

All reactions were carried out under dry nitrogen atmosphere. Acetonitrile was purified according to standard methods unless otherwise noted. The phosphonium salt **2**, enone **1** were prepared according to literature procedures.[16] NMR spectra were recorded on a Varian Mercury-300 or a Varian Mercury-400 nuclear magnetic resonance spectrometer. Chemical shifts are reported in parts per million (ppm) down field from TMS, using residual $CDCl_3$ as an internal standard. The data is being reported as (s=singlet, d=doublet, t=triplet, m=multiplet or unresolved, br=broad signal, coupling constant(s) in Hertz, integration).

4.2. Typical procedure for the synthesis of multi-substituted benzenes

A mixture of unsaturated ketone **1a** (60.7 mg, 0.25 mmol) and phosphonium salt **2a** (198.6 mg, 0.45 mmol) in CH_3CN (2 mL) was stirred for 5 min. Then DBU (127 μL) in CH_3CN (0.5 mL) was added. The reaction mixture was stirred at 60 °C for 6 h and then air was introduced with a balloon for another 42 h. After the reaction was completed, the reaction mixture was filtered through a short silica gel column and washed with DCM. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (PE/EtOAc, 60/1) to afford **3a** as a colorless oil (69.3 mg, 86% yield).

*4.2.1. Methyl 4″-chloro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3a**).* Colorless oil. Yield: 63.5 mg (86%). ^1H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, *J*=8.1 Hz, 1H), 7.64–7.60 (m, 3H), 7.53–7.52 (m, 1H), 7.45–7.36 (m,

5H), 7.27 (m, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.2, 144.3, 142.1, 139.9, 139.5, 133.4, 130.8, 129.7, 129.4, 128.9, 128.2, 128.1, 127.2, 126.0, 51.9; IR (KBr) ν/cm^{-1}: 3030 (w), 2949 (w), 2341 (w), 1726 (s), 1603 (m), 1477 (m), 1433 (m), 1289 (s), 1257 (s), 1100 (m), 1089 (m), 1009 (w), 832 (m), 759 (m); LRMS (EI): *m*/*z* (% relative intensity): 322 (M$^+$, 84.65), 291 (100); HRMS (EI): calcd for $C_{20}H_{15}O_2Cl$: 322.0761, found: 322.0759.

*4.2.2. Methyl [1,1′:3′,1″-terphenyl]-4′-carboxylate (**3b**).* White solid. Yield: 67.5 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J*=8.0 Hz, 1H), 7.64–7.60 (m, 4H), 7.46–7.35 (m, 8H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.8, 144.1, 143.2, 141.4, 139.8, 130.6, 129.5, 129.3, 128.9, 128.3, 128.1, 128.0, 127.3, 127.2, 125.7, 51.9; IR (KBr, ν/cm^{-1}): 2924 (s), 1716 (s), 1599 (m), 1477 (m), 1443 (m), 1287 (m), 1250 (m), 1099 (m), 839 (w), 755 (m), 697 (m); LRMS (EI): *m*/*z* (% relative intensity): 288 (M$^+$, 65.86), 257 (100); HRMS (EI): calcd for $C_{20}H_{16}O_2$: 288.1150, found: 288.1154.

*4.2.3. Methyl 4″-methoxy-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3c**).* Pale oil. Yield: 72.8 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J*=8.0 Hz, 1H), 7.64–7.58 (m, 4H), 7.47–7.38 (m, 3H), 7.30 (d, *J*=8.8 Hz, 2H), 6.97–6.94 (m, 2H), 3.86 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.0, 159.0, 144.0, 142.8, 139.9, 133.7, 130.5, 129.6, 129.5, 129.3, 128.9, 128.0, 127.3, 125.4, 113.5, 55.2, 52.0; IR (KBr) ν/cm^{-1}: 2951 (s), 2924 (s), 2851 (m), 1720 (s), 1605 (m), 1514 (m), 1432 (m), 1379 (w), 1287 (m), 1246 (m), 1096 (m), 1028 (m), 832 (m), 758 (m), 697 (m); LRMS (EI): *m*/*z* (% relative intensity): 318 (M$^+$,100), 287 (70.21); HRMS (EI): calcd for $C_{21}H_{18}O_3$: 318.1256, found: 318.1251.

*4.2.4. Methyl 4-methoxy-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3d**).* White solid. Yield: 67.0 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J*=8.0 Hz, 1H), 7.60–7.55 (m, 4H), 7.42–7.35 (m, 5H), 6.99 (d, *J*=8.8 Hz, 2H), 3.85 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.7, 159.8, 143.7, 143.3, 141.5, 132.1, 130.6, 129.0, 128.5, 128.3, 128.0, 127.2, 125.1, 114.3, 55.3, 51.8; IR (KBr) ν/cm^{-1}: 2923 (s), 1723 (s), 1602 (s), 1517 (m), 1431 (m), 1287 (s), 1249 (s), 1179 (m), 1099 (m), 827 (m), 760 (m), 692 (m); LRMS (EI): *m*/*z* (% relative intensity): 318 (M$^+$, 100), 278 (63.14); HRMS (EI): calcd for $C_{21}H_{18}O_3$: 318.1256, found: 318.1252.

*4.2.5. Methyl 4-methyl-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3e**).* White solid. Yield: 64.8 mg (86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J*=8.0 Hz, 1H), 7.61 (dd, *J*=8.0, 1.6 Hz, 1H), 7.58 (d, *J*=1.6 Hz, 1H), 7.54–7.52 (m, 2H), 7.43–7.34 (m, 5H), 7.25 (d, *J*=8.0 Hz, 2H), 3.65 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.7, 144.0, 143.2, 141.5, 138.0, 136.8, 130.6, 129.6, 129.3, 128.9, 128.3, 128.0, 127.2, 127.1, 125.5, 51.9, 21.1; IR (KBr, ν/cm^{-1}): 2923 (s), 2851 (m), 1728 (s), 1716 (s), 1456 (m), 1434 (m), 1288 (m), 1251 (m), 1102 (m), 810 (w), 762 (m), 700 (m); LRMS (EI): *m*/*z* (% relative intensity): 302 (M$^+$, 92.62), 271 (100); HRMS (EI): calcd for $C_{21}H_{18}O_2$: 302.1307, found: 302.1304.

*4.2.6. Methyl 4-chloro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3f**).* Colorless oil. Yield: 74.3 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J*=8.0 Hz, 1H), 7.59–7.54 (m, 4H), 7.44–7.33 (m, 7H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.6, 143.4, 142.8, 141.2, 138.2, 134.3, 130.6, 129.6, 129.3, 129.1, 128.5, 128.3, 128.0, 127.4, 125.5, 51.9; IR (KBr, ν/cm^{-1}): 3028 (w), 2949 (w), 1721 (s), 1603 (m), 1495 (w), 1478 (m), 1433 (m), 1381 (m), 1285 (s), 1251 (s), 1189 (w), 1093 (s), 1045 (m), 1008 (m), 822 (s), 785 (m), 763 (s), 733 (m), 699 (s); LRMS (EI): *m*/*z* (% relative intensity): 291 (100), 322 (M$^+$,90.90); HRMS (EI): calcd for $C_{20}H_{15}O_2Cl$: 322.0761, found: 322.0757.

*4.2.7. Methyl 4-nitro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3g**).* White solid. Yield: 55.1 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J*=9.2 Hz, 2H), 7.97 (d, *J*=8.4 Hz, 1H), 7.80 (d, *J*=8.4 Hz, 2H), 7.67 (dd, *J*=8.0, 1.6 Hz, 1H), 7.62 (d, *J*=1.6 Hz, 1H), 7.44–7.35 (m, 5H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.4, 147.5, 146.1, 143.5, 141.5, 140.7, 130.9, 130.8, 129.8, 128.2(4), 128.1(7), 128.1, 127.6, 126.0, 124.2, 52.1; IR (KBr, ν/cm^{-1}): 2923 (s), 2852 (m), 1725 (s), 1596 (m), 1517 (s), 1433 (m), 1292 (m), 1254 (m), 1104 (m), 836 (m), 752 (m), 699 (m); LRMS (EI): *m*/*z* (% relative intensity): 333 (M$^+$,74.61), 302 (100); HRMS (EI): calcd for $C_{20}H_{15}NO_4$: 333.1001, found: 333.0997.

*4.2.8. Methyl 3″-methyl-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3h**).* Colorless oil. Yield: 68.6 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J*=8.4 Hz, 1H), 7.66–7.62 (m, 3H), 7.48 (d, *J*=1.6 Hz, 1H), 7.45–7.42 (m, 2H), 7.38–7.36 (m, 1H), 7.28–7.22 (m, 3H), 7.13 (d, *J*=7.6 Hz, 1H), 3.63 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.5, 144.2, 143.6, 141.5, 139.6, 135.3, 130.7, 129.5, 129.4, 128.9, 128.7, 128.4, 128.1, 127.3, 127.2, 125.6, 125.2, 51.8, 20.1; IR (KBr, ν/cm^{-1}): 2950 (w), 1714 (s), 1599 (m), 1285 (s), 1254 (s), 1142 (m), 1094 (s), 845 (m), 755 (s), 696 (m); LRMS (EI): *m*/*z* (% relative intensity): 302 (M$^+$,55), 271 (100); HRMS (EI): calcd for $C_{21}H_{18}O_2$: 302.1307, found: 302.1304.

*4.2.9. Methyl 2″-methyl-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3i**).* Yellow oil. Yield: 64.3 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.88 (m, 1H), 7.63–7.59 (m, 4H), 7.43 (t, *J*=7.2 Hz, 2H), 7.36 (t, *J*=7.2 Hz, 1H), 7.29 (t, *J*=7.6 Hz, 1H), 7.18–7.14 (m, 3H), 3.66 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.9, 144.0, 143.2, 141.2, 139.8, 137.6, 130.4, 129.5, 129.3, 129.0, 128.9, 128.0, 127.9, 127.2, 125.6, 125.5, 51.9, 21.4; IR (KBr, ν/cm^{-1}): 2947 (w), 1715 (s), 1601 (m), 1432 (m), 1286 (s), 1250 (s), 1100 (s), 1050 (w), 786 (m), 756 (s), 698 (s); LRMS (EI): *m*/*z* (% relative intensity): 302 (M$^+$,85), 271 (100); HRMS (EI): calcd for $C_{21}H_{18}O_2$: 302.1307, found: 302.1311.

*4.2.10. Methyl 3-(furan-2-yl)-[1,1′-biphenyl]-4-carboxylate (**3j**).* White solid. Yield: 51.7 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J*=2.0 Hz, 1H), 7.76 (dd, *J*=8.0, 0.8 Hz, 1H), 7.64–7.61 (m, 2H), 7.56 (dd, *J*=8.0, 1.6 Hz, 1H), 7.512–7.506 (m, 1H), 7.49–7.44 (m, 2H), 7.41–7.37 (m, 1H), 6.63–6.62 (m, 1H), 6.51–6.49 (m, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.2, 152.4, 143.9, 142.8. 139.7, 130.5, 130.0, 128.9, 128.6, 128.1, 127.2, 127.0, 126.2, 111.5, 108.2, 52.3; IR (KBr) ν/cm^{-1}: 2954 (s), 2853 (s), 1775(w), 1718 (s), 1594 (w), 1459 (m), 1372 (m), 1289 (s), 759 (m); LRMS (EI): *m*/*z* (% relative intensity): 278 (M$^+$, 100); HRMS (EI): calcd for $C_{18}H_{14}O_3$: 278.0943, found: 278.0948.

*4.2.11. Methyl 5-(furan-2-yl)-[1,1′-biphenyl]-2-carboxylate(**3k**).* Yellow oil. Yield: 58.7 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J*=8.0 Hz, 1H), 7.70–7.66 (m, 2H), 7.50 (d, *J*=1.2 Hz, 1H), 7.42–7.33 (m, 5H), 6.76 (d, *J*=2.8 Hz, 1H), 6.49 (dd, *J*=3.2, 2.0 Hz, 1H), 3. 64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.4, 152.7, 143.4, 143.0, 141.3, 133.4, 130.7, 128.8, 128.2, 128.0, 127.3, 125.9, 122.1, 111.9, 107.1, 51.9; IR (neat, ν/cm^{-1}): 2950 (w), 1715 (s), 1609 (m), 1433 (m), 1287 (s), 1251 (s), 1099 (s), 1010 (m), 761 (m), 738 (m), 699 (s); LRMS (EI): *m*/*z* (% relative intensity): 278 (M$^+$, 100); HRMS (EI): calcd for $C_{18}H_{14}O_3$: 278.0943, found: 278.0942.

*4.2.12. Methyl 5-(thiophen-2-yl)-[1,1′-biphenyl]-2-carboxylate (**3l**).* Yellow oil. Yield: 66.7 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J*=8.0 Hz, 1H), 7.65–7.60 (m, 2H), 7.42–7.33 (m, 7H), 7.11–7.09 (m, 1H), 3. 46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.4, 143.6, 142.8, 141.2, 137.2, 130.8, 129.0, 128.3, 128.0, 127.4, 126.2, 124.4, 124.2, 51.9; IR (neat, ν/cm^{-1}): 3027 (w), 2947 (w), 1724 (s), 1600 (m), 1483 (w), 1432 (m), 1286 (s), 1252 (s), 1098 (s), 825 (m), 762 (m), 697 (s); LRMS (EI): *m*/*z* (% relative intensity): 294 (M$^+$, 100); HRMS (EI): calcd for $C_{18}H_{14}O_2S$: 294.0715, found: 294.0717.

*4.2.13. Methyl 4′-methoxy-5-(pyridin-2-yl)-[1,1′-biphenyl]-2-carboxylate (**3m**).* White solid. Yield: 58.7 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72–8.71 (m, 1H), 8.02–8.00 (m, 2H), 7.92 (d,

J=8.8 Hz, 1H), 7.79–7.77 (m, 2H), 7.33–7.26 (m, 3H), 6.95 (dd, J=6.8, 2.0 Hz, 2H), 3. 86 (s, 3H), 3. 70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.0, 159.0, 156.2, 149.8, 142.7, 141.9, 136.9, 133.6, 130.8, 130.4, 129.5, 129.3, 125.1, 122.8, 121.0, 113.5, 55.3, 52.0; IR (neat, ν/cm^{-1}): 2950 (w), 1719 (s), 1609 (m), 1585 (m), 1516 (s), 1433 (m), 1287 (s), 1246 (s), 1178 (m), 1102 (m), 834 (m), 773 (s), 742 (m); LRMS (EI): m/z (% relative intensity): 319 (M^+, 100); HRMS (EI): calcd for $C_{20}H_{17}NO_3$: 319.1208, found: 319.1211.

*4.2.14. Dimethyl [1,1′-biphenyl]-2,5-dicarboxylate (**3n**).* Colorless oil. Yield: 61.6 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–8.05 (m, 2H), 7.85 (d, J=8.8 Hz, 2H), 7.42–7.32 (m, 5H), 3.94 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.6, 166.2, 142.4, 140.2, 134.8, 132.4, 131.7, 129.7, 128.2(2), 128.2(1), 128.1, 127.7, 52.4, 52.2; IR (KBr, ν/cm^{-1}): 3016 (w), 2970 (m), 2950 (w), 1737 (s), 1434 (m), 1366 (m), 1289 (w), 1232 (s), 1115 (m), 751 (m), 700 (m); LRMS (EI): m/z (% relative intensity): 270 (M^+, 64.28), 239 (100); HRMS (EI): calcd for $C_{16}H_{14}O_4$: 270.0892, found: 270.0891.

*4.2.15. Methyl 5-(diethylcarbamoyl)-[1,1′-biphenyl]-2-carboxylate (**3o**).* White solid. Yield: 69.8 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J=8.0 Hz, 1H), 7.41–7.31 (m, 7H), 3.64 (s, 3H), 3.56 (q, J=6.0 Hz, 2H), 3.27 (q, J=6.8 Hz, 2H), 1.26 (br s, 3H), 1.13 (br s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 170.0, 168.5, 142.7, 140.4, 140.0, 131.3, 130.0, 128.4, 128.2, 128.1, 127.5, 124.8, 52.0, 43.2, 39.3, 14.2, 12.8; IR (KBr, ν/cm^{-1}): 2963 (w), 1732 (s), 1633 (s), 1434 (m), 1283 (m), 1247 (m), 1109 (m), 954 (w), 821 (m), 696 (m); LRMS (EI): m/z (% relative intensity): 310 (M^+, 77.32), 239 (100); HRMS (EI): calcd for $C_{19}H_{21}NO_3$: 311.1521, found: 311.1526.

*4.2.16. Methyl 5-methyl-[1,1′-biphenyl]-2-carboxylate (**3p**).* Colorless oil. Yield: 55.5 mg (70%) and trace cyclohexadiene. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J=7.6 Hz, 1H), 7.38–7.28 (m, 5H), 7.24–7.17 (m, 2H), 3.61 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.9, 142.8, 141.7, 141.6, 131.6, 130.1, 128.3, 127.9, 127.8, 127.7, 127.0, 51.7, 21.4; IR (KBr, ν/cm^{-1}): 3026 (w), 2970 (w), 2949 (w), 1737 (s), 1434 (m), 1366 (m), 1286 (w), 1229 (m), 1217 (m), 966 (w), 763 (m), 699 (m); LRMS (EI): m/z (% relative intensity): 226 (M^+, 60.29), 195 (100); HRMS (EI): calcd for $C_{15}H_{14}O_2$: 226.0994, found: 226.0996.

*4.2.17. Methyl 3-pentyl-[1,1′-biphenyl]-4-carboxylate (**3q**).* White solid. Yield: 53 mg (73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J=5.7 Hz, 1H), 7.62 (d, J=5.7 Hz, 2H), 7.49–7.33 (m, 5H), 3.91 (s, 3H), 3.02 (t, J=4.8 Hz, 2H), 1.66–1.62 (m, 2H), 1.40–1.30 (m, 4H), 0.93–0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.0, 145.5, 144.5, 140.2, 131.3, 129.7, 128.8, 128.1, 127.9, 127.2, 124.3, 51.9, 34.7, 32.0, 31.6, 22.6, 14.1; IR (neat, ν/cm^{-1}): 2952 (w), 2925 (w), 1720 (s), 1607 (m), 1457 (m), 1433 (m), 1278 (m), 1247 (s), 1190 (m), 1150 (m), 1098 (s), 1081 (s), 756 (s), 696 (s); LRMS (EI): m/z (% relative intensity): 251 (100), 282 (M^+, 69.2); HRMS (EI): calcd for $C_{19}H_{22}O_2$: 282.1620, found: 282.1622.

*4.2.18. Methyl 4-bromo-4″-chloro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3r**).* White solid. Yield: 85.3 mg (86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J=8.1 Hz, 1H), 7.61–7.57 (m, 3H), 7.48 (d, J=8.4 Hz, 3H), 7.38 (d, J=8.4 Hz, 2H), 7.27 (d, J=8.4 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.2, 143.0, 142.3, 139.7, 138.4, 133.5, 132.1, 130.9, 129.7, 129.3, 129.2, 128.8, 128.2, 125.8, 122.6, 52.1; IR (KBr, ν/cm^{-1}): 2949 (w), 2924 (w), 2850 (m), 1726 (s), 1603 (m), 1477 (m), 1434 (m), 1286 (s), 1256 (s), 1102 (m), 821 (m), 784 (m); LRMS (EI): m/z (% relative intensity): 400 (M^+, 75.09), 402 (100); HRMS (EI): calcd for $C_{20}H_{14}O_2ClBr$: 399.9866, found: 399.9863.

*4.2.19. Ethyl 4-bromo-4″-chloro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3s**).* White solid. Yield: 92.3 mg (89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J=8.1 Hz, 1H), 7.61–7.57 (m, 3H), 7.49–7.46 (m, 3H), 7.38 (d, J=8.4 Hz, 2H), 7.27 (d, J=8.4 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.2, 143.0, 142.3, 139.7, 138.4, 133.5, 132.1, 130.9, 129.7, 129.3, 129.2, 128.8, 128.2, 125.8, 122.6, 52.1; IR (KBr, ν/cm^{-1}): 2949 (w), 2924 (w), 2850 (m), 1726 (s), 1603 (m), 1477 (m), 1434 (m), 1286 (s), 1256 (s), 1102 (m), 821 (m), 784 (m); LRMS (EI): m/z (% relative intensity): 400 (M^+, 75.09), 402 (100); HRMS (EI): calcd for $C_{20}H_{14}O_2ClBr$: 399.9866, found: 399.9863.

*4.2.20. tert-Butyl 4-bromo-4″-chloro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**3t**).* White solid, Yield: 98.3 mg (89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J=7.8 Hz, 1H), 7.61–7.56 (m, 3H), 7.49–7.46 (m, 3H), 7.38 (d, J=8.4 Hz, 2H), 7.27 (d, J=7.9 Hz, 2H), 4.14 (q, J=7.2 Hz, 2H), 1.08 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.8, 142.9, 142.2, 139.8, 138.5, 133.4, 132.1, 130.8, 129.8, 129.7, 129.1, 128.8, 128.2, 125.8, 122.6, 61.0, 13.8; IR (KBr, ν/cm^{-1}): 2956 (w), 2925 (w), 1716 (s), 1603 (m), 1476 (m), 1378 (m), 1285 (s), 1269 (m), 1102 (m), 1090 (m), 821 (m), 784 (m); LRMS (EI): m/z (% relative intensity): 416 (M^+, 32.04), 43 (100); HRMS (EI): calcd for $C_{21}H_{16}O_2ClBr$: 414.0022, found: 414.0021.

*4.2.21. Methyl [1,1′-biphenyl]-2-carboxylate (**5a**).* Yellow oil. Yield: 41.7 mg (53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (dq, J=8.0, 0.8 Hz, 1H), 7.52 (t, J=7.6 Hz, 1H), 7.42–7.30 (m, 7H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.1, 142.4, 141.3, 131.2, 130.8, 130.7, 129.7, 128.3, 128.0, 127.2, 127.1, 51.9; IR (KBr, ν/cm^{-1}): 2950 (s), 2925 (s), 2853 (m), 1723 (s), 1590 (w), 1476 (m), 1451 (m), 1430 (m), 1125 (s), 1089 (s), 1049 (s), 964 (w), 745 (m), 699 (m), 664 (m); LRMS (EI): m/z (% relative intensity): 212 (M^+, 67.32), 181 (100); HRMS (EI): calcd for $C_{14}H_{12}O_2$: 212.0837, found: 212.0831.

*4.2.22. 2′-Ethyl 4′-methyl [1,1′:3′,1″-terphenyl]-2′,4′-dicarboxylate (**6a**).* White solid. Yield: 68.5 mg (76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J=8.0 Hz, 1H), 7.45–7.35 (m, 9H), 7.29–7.25 (m, 2H), 3.74 (q, J=7.2 Hz, 2H), 3.59 (s, 3H), 0.75 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.1, 167.8, 142.7, 140.2, 139.5, 138.5, 135.3, 130.4, 130.3, 128.8, 128.7, 128.4, 128.3, 128.0, 127.5, 60.9, 52.0, 13.4; IR (KBr, ν/cm^{-1}): 2951 (m), 2924 (m), 2844 (m), 1731 (s), 1588 (m), 1444 (m), 1302 (m), 1227 (s), 1143 (m), 1095 (m), 759 (m), 699 (m); LRMS (EI): m/z (% relative intensity): 360 (M^+,38.66), 43 (100); HRMS (EI): calcd for $C_{23}H_{20}O_4$: 360.1362, found: 360.1359.

*4.2.23. Methyl 2′-benzoyl-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**6b**).* Colorless oil. Yield: 55.5 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J=7.6 Hz, 1H), 7.50 (d, J=8.4 Hz, 1H), 7.40–7.37 (d, J=8.4 Hz, 2H), 7.29–7.26 (m, 4H), 7.23–7.12 (m, 7H), 7.02 (br s, 1H), 6.89 (br s, 1H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 197.5, 168.2, 143.1, 140.3, 140.0, 139.2, 137.8 (4), 137.8 (2), 132.8, 130.9, 130.1, 129.1 (3), 129.1 (2), 129.1, 128.1, 127.9, 127.8, 127.3, 52.1; IR (neat, ν/cm^{-1}): 3059 (w), 2950 (w), 1729 (s), 1671 (s), 1583 (m), 1432 (m), 1299 (m), 1228 (s), 1161 (s), 941 (m), 757 (s), 734 (s), 698 (s); LRMS (EI): m/z (% relative intensity): 392 (M^+, 100); HRMS (EI): calcd for $C_{27}H_{20}O_3$: 392.1412, found: 392.1407.

*4.2.24. Dimethyl 3-methyl-[1,1′-biphenyl]-2,6-dicarboxylate (**6c**).* Colorless oil, Yield 35.8 mg (53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J=8.0 Hz, 1H), 7.38–7.32 (m, 3H), 7.28 (dd, J=8.0 Hz, 0.8 Hz, 1H), 7.22–7.20 (m, 2H), 3.56 (s, 3H), 3.47 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.2, 167.8, 140.1, 138.8, 138.5, 135.7, 130.6, 129.1, 128.9, 128.4, 127.6, 127.4, 51.9, 51.8, 19.8; IR (neat, ν/cm^{-1}): 2950 (w), 1725 (s), 1593 (w), 1432 (m), 1305 (m), 1258 (s), 1209 (s), 1144 (m), 997 (m), 795 (m), 700 (s); LRMS (EI): m/z (% relative intensity): 221 (93.53), 284 (M^+, 100); HRMS (EI): calcd for $C_{17}H_{16}O_4$: 284.1049, found: 284.1052.

*4.2.25. Dimethyl [1,1′:3′,1″-terphenyl]-2′,5′-dicarboxylate (**6d**).* White solid. Yield: 60.4 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07

(d, J=1.2 Hz 2H), 7.42 (s, 10H), 3.94 (s, 3H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.1, 166.2, 140.7, 139.5, 136.6, 130.9, 129.8, 128.4, 128.3, 127.9, 52.4, 51.9; IR (KBr, ν/cm^{-1}): 2951 (s), 2925, 1730 (s), 1460 (m), 1438 (m), 1342 (m), 1245 (s), 1124 (m), 1052 (m), 765 (m), 749 (m), 701 (m); LRMS (EI): m/z (% relative intensity): 346 (M^+, 96.91), 315 (100); calcd for $C_{22}H_{18}O_4$: 346.1205, found: 346.1201.

*4.2.26. Dimethyl 3-methyl-[1,1′-biphenyl]-2,5-dicarboxylate (**6e**).* White solid. Yield: 37.2 mg (54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 2H), 7.39–7.37 (m, 5H), 3.92 (s, 3H), 3.61 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.5, 166.4, 140.3, 139.8, 137.1, 135.8, 130.8, 129.9, 128.4, 128.3, 128.1, 127.7, 52.3, 52.0, 19.6; IR (KBr, ν/cm^{-1}): 2951 (s), 2923 (s), 2850 (m), 1726 (s), 1575 (w), 1437 (m), 1329 (m), 1268 (s), 1242 (s), 1123 (m), 1080 (m), 991 (w), 903 (w), 764 (m), 701 (m); LRMS (EI): m/z (% relative intensity): 284 (M^+, 86.64), 253 (100); HRMS (EI): calcd for $C_{17}H_{16}O_4$: 284.1049, found: 284.1046.

*4.2.27. Methyl 5′-(4-bromophenyl)-4-chloro-[1,1′:3′,1″-terphenyl]-2′-carboxylate (**6f**).* White solid, Yield: 79.3 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (m, 3H), 7.52–7.50 (m, 3H), 7.44–7.39 (m, 9H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.4, 141.3, 141.1, 140.1, 139.9, 138.7, 138.6, 133.9, 132.0, 131.9, 129.7, 128.8, 128.6, 128.4, 128.3, 127.8, 127.6, 127.1, 122.4, 51.9; IR (neat, ν/cm^{-1}): 2957 (m), 2924 (s), 2854 (m), 1729 (s), 1662 (w), 1603 (m), 1491 (s), 1406 (w), 1261 (s), 1213 (w), 1092 (s), 1008 (s), 892 (w), 810 (w), 770 (m), 730 (m), 701 (m); LRMS (EI): m/z (% relative intensity): 241 (100), 476 (M^+, 5.43); HRMS (EI): calcd for $C_{26}H_{18}O_2ClBr$: 476.0179, found: 476.0176.

*4.2.28. Methyl 4-bromo-4″-chloro-5′-methoxy-[1,1′:3′,1″-terphenyl]-4′-carboxylate (**6g**).* White solid. Yield: 46.0 mg (43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, J=8.4 Hz, 2H), 7.45 (d, J=8.4 Hz, 2H), 7.39–7.34 (m, 4H), 7.11 (d, J=7.2 Hz, 2H), 3.94 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.1, 157.0, 142.8, 140.5, 139.2, 138.3, 134.0, 132.0, 129.5, 128.8, 128.6, 122.4, 122.1, 120.6, 108.8, 56.2, 52.3; IR (neat, ν/cm^{-1}): 2949 (w), 2848 (w), 1729 (s), 1602 (m), 1578 (w), 1557 (m), 1494 (s), 1457 (m), 1381 (m), 1264 (s), 1227 (m), 1151 (m), 1103 (s), 1027 (m), 1011 (s), 820 (s), 715 (m); LRMS (EI): m/z (% relative intensity): 401 (93.08), 430 (M^+, 75.98); HRMS (EI): calcd for $C_{21}H_{16}O_3ClBr$: 429.9971, found: 429.9973.

*4.2.29. 2′-Ethyl 4′-methyl 5′-phenyl-[1,1′:3′,1″-terphenyl]-2′,4′-dicarboxylate (**7a**).* White solid, Yield: 66.8 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.34 (m, 16H), 3.78 (q, J=7.2 Hz, 2H), 3.29 (s, 3H), 0.76 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.8, 168.1, 140.8, 140.6, 139.6 (2), 139.6 (0), 138.3, 137.6, 133.2, 133.0, 130.3, 129.0, 128.4 (4), 128.4 (1), 128.3 (4), 128.3 (1), 127.9 (2), 127.9 (0), 127.8 (7), 127.8, 60.9, 51.7, 13.4; IR (neat, ν/cm^{-1}): 2924 (w), 1729 (s), 1587 (w), 1494 (m), 1444 (m), 1292 (m), 1243 (s), 1138 (m), 1106 (m), 1029 (w), 796 (m), 700 (s); LRMS (EI): m/z (% relative intensity): 359 (100), 436 (M^+, 86.49); HRMS (EI): calcd for $C_{29}H_{24}O_4$: 436.1675, found: 436.1674.

*4.2.30. Methyl 4′-benzoyl-5′-phenyl-[1,1′:3′,1″-terphenyl]-2′-carboxylate (**7b**).* White solid, Yield: 73.8 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.48 (m, 5H), 7.46–7.29 (m, 7H), 7.25–6.96 (m, 9H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 197.6, 169.0, 141.3, 140.5, 139.6, 139.2, 138.5, 138.1, 137.9, 137.1, 133.2, 132.8, 130.6, 129.3, 129.1, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 127.6, 51.8; IR (neat, ν/cm^{-1}): 3058 (w), 2948 (w), 1730 (s), 1671 (s), 1581 (m), 1446 (m), 1390 (m), 1241 (s), 1121 (s), 941 (m), 897 (m), 796 (w), 756 (s), 734 (s), 698 (s); LRMS (EI): m/z (% relative intensity): 105 (100), 468 (M^+, 92.88); HRMS (EI): calcd for $C_{33}H_{24}O_3$: 468.1725, found: 468.1729.

*4.2.31. Dimethyl 5′-methyl-[1,1′:3′,1″-terphenyl]-2′,4′-dicarboxylate (**7c**).* White solid, Yield 58% (average for twice). ^{1}H NMR (400 MHz, $CDCl_3$): 7.40–7.30 (m, 10H), 7.26 (s, 1H), 3.50 (s, 3H), 3.27 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.2, 168.9, 140.8, 139.8, 138.1, 138.0, 136.3, 133.5, 131.6, 130.6, 128.7, 128.3, 128.2, 127.8 (1), 127.8, 127.7, 51.8, 51.7, 19.7; IR (neat, ν/cm^{-1}): 3058 (w), 2949 (w), 1726 (s), 1591 (w), 1496 (w), 1436 (m), 1295 (m), 1248 (m), 1214 (s), 1162 (m), 1113 (m), 1092 (m), 954 (w), 737 (m), 700 (s); LRMS (EI): m/z (% relative intensity): 297 (100), 360 (M^+, 99.44); HRMS (EI): calcd for $C_{23}H_{20}O_4$: 360.1362, found: 360.1364.

*4.2.32. 2′-Ethyl 4′-methyl 5′-methoxy-[1,1′:3′,1″-terphenyl]-2′,4′-dicarboxylate (**7d**).* White solid. Yield: 52.6 mg (53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.33 (m, 10H), 6.92 (s, 1H), 3.91 (s, 3H), 3.72 (q, J=7.2 Hz, 2H), 3.53 (s, 3H), 0.71 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.1, 167.3, 156.1, 142.9, 140.2, 139.5, 137.4, 128.7, 128.3, 127.9, 127.8 (3), 127.7 (8), 126.9, 123.3, 111.4, 60.7, 56.1, 52.1, 13.3. IR (neat, ν/cm^{-1}): 3058 (w), 2949 (w), 1726 (s), 1587 (m), 1564 (m), 1497 (w), 1461 (w), 1345 (m), 1294 (m), 1243 (s), 1221 (s), 1174 (m), 1127 (m), 1075 (s), 979 (s), 922 (w), 859 (w), 755 (m), 735 (m), 700 (s); LRMS (EI): m/z (% relative intensity): 313 (69.54), 390 (M^+, 100); HRMS (EI): calcd for $C_{24}H_{22}O_5$: 390.1467, found: 390.1460.

*4.2.33. (E)-Methyl 3-styryl-[1,1′-biphenyl]-4-carboxylate (**10a**).* White solid. Yield: 47.9 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J=16.4 Hz, 1H), 8.00 (d, J=8.0 Hz, 1H), 7.89 (s, 1H), 7.56–7.50 (m, 5H), 7.36 (t, J=7.2 Hz, 2H), 7.28 (d, J=8.0 Hz, 3H), 7.06 (d, J=16.0 Hz, 1H), 3. 93 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.7, 144.9, 139.9, 138.1, 137.4, 137.0, 131.5, 131.3, 129.6, 128.6, 127.8, 127.7, 127.1, 126.9, 126.7, 125.6, 125.5, 52.1, 21.1; IR (neat, ν/cm^{-1}): 2948 (w), 1713 (s), 1599 (m), 1432 (m), 1256 (s), 1188 (m), 1083 (s), 961 (m), 814 (s), 780 (s), 749 (m), 692 (s); LRMS (EI): m/z (% relative intensity): 328 (M^+,100); HRMS (EI): calcd for $C_{23}H_{20}O_2$: 328.1463, found: 328.1460.

*4.2.34. (E)-Methyl 4′-methyl-3-styryl-[1,1′-biphenyl]-4-carboxylate (**10b**).* White solid. Yield: 47.9 mg (49%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J=16.4 Hz, 1H), 8.00 (d, J=8.0 Hz, 1H), 7.89 (s, 1H), 7.56–7.50 (m, 5H), 7.36 (t, J=7.2 Hz, 2H), 7.28 (d, J=8.0 Hz, 3H), 7.06 (d, J=16.0 Hz, 1H), 3. 93 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.7, 144.9, 139.9, 138.1, 137.4, 137.0, 131.5, 131.3, 129.6, 128.6, 127.8, 127.7, 127.1, 126.9, 126.7, 125.6, 125.5, 52.1, 21.1; IR (neat, ν/cm^{-1}): 2948 (w), 1713 (s), 1599 (m), 1432 (m), 1256 (s), 1188 (m), 1083 (s), 961 (m), 814 (s), 780 (s), 749 (m), 692 (s); LRMS (EI): m/z (% relative intensity): 328 (M^+,100); HRMS (EI): calcd for $C_{23}H_{20}O_2$: 328.1463, found: 328.1460.

*4.2.35. (E)-Methyl 4′-chloro-3-styryl-[1,1′-biphenyl]-4-carboxylate (**10c**).* Yellow oil. Yield: 37.9 mg (36%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J=16.0 Hz, 1H), 8.01 (d, J=8.0 Hz, 1H), 7.86 (d, J=2.0 Hz, 1H), 7.59–7.56(m, 4H), 7.48 (dd, J=8.4, 2.0 Hz, 1H), 7.46–7.43 (m, 2H), 7.37 (t, J=7.2 Hz, 2H), 7.30–7.26 (m, 1H), 7.06 (d, J=16.0 Hz, 1H), 3. 94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.5, 143.6, 140.0, 138.4, 137.2, 134.3, 131.8, 131.5, 129.1, 128.7, 128.5, 128.0, 127.4, 127.3, 126.9, 125.6, 125.5, 52.2; IR (neat, ν/cm^{-1}): 2924 (w), 1714 (s), 1600 (w), 1282 (s), 1241 (s), 1085 (s), 962 (m), 823 (s), 782 (s), 750 (m), 691 (m); LRMS (EI): m/z (% relative intensity): 348 (M^+,100); HRMS (EI): calcd for $C_{22}H_{17}ClO_2$: 348.0917, found: 348.0919.

*4.2.36. (E)-Methyl 5-styryl-[1,1′-biphenyl]-2-carboxylate (**12a**).* Yellow solid. Yield: 67.6 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J=8.0 Hz, 1H), 7.55–7.49 (m, 4H), 7.44–7.29 (m, 8H), 7.22 (d, J=16.4 Hz, 1H), 7.13 (d, J=16.4 Hz, 1H), 3. 64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.4, 143.2, 141.4, 140.2, 136.6, 131.1, 130.5, 129.1, 128.8, 128.7, 128.2, 128.1, 127.9, 127.2, 127.2, 126.7, 124.9, 51.8; IR (neat, ν/cm^{-1}): 2948 (w), 1715 (s), 1599 (w), 1432 (m), 1282 (s), 1189 (w), 1096 (m), 959 (m), 763 (s), 696 (s); LRMS (EI): m/z (%

relative intensity): 314 (M^+, 100); HRMS (EI): calcd for $C_{22}H_{18}O_2$: 314.1307, found: 314.1303.

*4.2.37. (E)-Methyl 4′-methyl-5-(4-methylstyryl)-[1,1′-biphenyl]-2-carboxylate (**12b**).* White solid. Yield: 63.2 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J=8.0 Hz, 1H), 7.50–7.46 (m, 2H), 7.40 (d, J=8.0 Hz, 2H), 7.25–7.15 (m, 7H), 7.06 (d, J=16.8 Hz, 1H), 3. 66 (s, 3H), 2.40 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.6, 143.3, 140.4, 138.5, 138.2, 136.9, 133.9, 131.0, 130.5, 129.4, 128.8, 128.7, 128.1, 126.6, 126.3, 124.7, 51.9, 21.3, 21.2; IR (neat, ν/cm^{-1}): 2947 (w), 1717 (s), 1597 (m), 1432 (m), 1280 (s), 1094 (m), 962 (m), 822 (s), 803 (s), 734 (m), 713 (m); LRMS (EI): m/z (% relative intensity): 342 (M^+,100); HRMS (EI): calcd for $C_{24}H_{22}O_2$: 342.1620, found: 342.1621.

*4.2.38. (E)-Methyl 4′-chloro-5-(4-chlorostyryl)-[1,1′-biphenyl]-2-carboxylate (**12c**).* White solid. Yield: 78.2 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J=8.4 Hz, 1H), 7.53 (dd, J=8.4, 2.0 Hz, 1H), 7.45–7.32 (m, 7H), 7.27–7.25 (m, 2H), 7.16 (d, J=16.4 Hz, 1H), 7.08 (d, J=16.4 Hz, 1H), 3. 68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.0, 142.3, 140.2, 139.8, 135.1, 133.9, 133.4, 130.9, 130.0, 129.6, 129.0 (2), 128.9 (6), 128.8, 128.2, 127.9, 127.7, 125.3, 52.0; IR (neat, ν/cm^{-1}): 2949 (w), 1717 (s), 1597 (w), 1489 (m), 1260 (s), 1012 (m), 831 (s), 809 (m), 735 (s); LRMS (EI): m/z (% relative intensity): 382 (M^+,100); HRMS (EI): calcd for $C_{22}H_{16}O_2Cl_2$: 382.0527, found: 382.0527.

4.3. Procedure for the syntheses of 11 and 13

General procedure: A mixture of **8a** (70.3 mg, 0.3 mmol) and **1a** (172.2 mg, 0.36 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere for 5 min at room temperature. Then DBU (0.065 mL, 0.45 mmol), followed by DMSO (1 mL), was added and the resulting mixture was heated to 80 °C in N_2 atmosphere. After the reaction was complete, the mixture was filtered through a thin layer (30 mm) of silica gel (100–200 mesh) and washed with DCM. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (PE/EtOAc=60/1) to afford **11a** (72.1 mg, 76%).

*4.3.1. Methyl 3-phenethyl-[1,1′-biphenyl]-4-carboxylate (**11a**).* Colorless oil. Yield: 72.2 mg (76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, J=8.4 Hz, 1H), 7.54–7.22 (m, 12H), 3.91 (s, 3H), 3.36–3.30 (m, 2H), 2.98–2.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.6, 144.5, 144.2, 141.9, 139.9, 131.4, 130.0, 128.8, 128.6, 128.3, 128.0, 127.9, 127.2, 125.8, 124.6, 51.9, 38.1, 37.1; IR (neat, ν/cm^{-1}): 2950 (w), 1706 (s), 1602 (m), 1436 (m), 1285 (m), 1249 (s), 1046 (s), 757 (s), 696 (s); LRMS (EI): m/z (% relative intensity): 316 (M^+, 53); HRMS (EI): calcd for $C_{22}H_{20}O_2$: 316.1463, found: 316.1465.

*4.3.2. Methyl 4′-methoxy-3-phenethyl-[1,1′-biphenyl]-4-carboxylate (**11b**).* White solid. Yield: 75.3 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J=8.0 Hz, 1H), 7.48 (dd, J=6.8, 2.0 Hz, 2H), 7.43 (dd, J=8.0, 2.0 Hz, 1H), 7.33–7.20 (m, 6H), 6.97 (dd, J=8.8, 2.0 Hz, 2H), 3.91 (s, 3H), 3.84 (s, 3H), 3.34–3.30 (m, 2H), 2.97–2.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.7, 159.7, 144.2 (4), 144.1 (7), 142.0, 132.4, 131.5, 129.5, 128.6, 128.2 (9), 128.2 (7), 127.2, 125.8, 124.1, 114.3, 55.3, 51.9, 38.1, 37.1; IR (neat, ν/cm^{-1}): 2948 (w), 1714 (s), 1603 (w), 1433 (w), 1278 (m), 1246 (s), 1085 (m), 827 (m), 783 (m), 749 (w), 699 (m); LRMS (EI): m/z (% relative intensity): 346 (M^+, 100); HRMS (EI): calcd for $C_{23}H_{22}O_3$: 346.1569, found: 346.1565.

*4.3.3. Methyl 4′-methyl-3-phenethyl-[1,1′-biphenyl]-4-carboxylate (**11c**).* White solid. Yield: 78.1 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J=8.0 Hz, 1H), 7.47–7.43 (m, 3H), 7. 36 (d, J=1.6 Hz, 1H), 7.31–7.20 (m, 7H), 3.91 (s, 3H), 3.34–3.30 (m, 2H), 2.97–2.93 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.7, 144.5, 144.2, 142.0, 137.9, 137.1, 131.5, 129.8, 129.5, 128.6, 128.3, 127.6, 127.0, 125.8, 124.4, 51.9, 38.1, 37.1, 21.1; IR (neat, ν/cm^{-1}): 2948 (w), 1716 (s), 1604 (w), 1433 (m), 1248 (s), 1189 (w), 1084 (s), 815 (s), 781 (s), 748 (w), 699 (s); LRMS (EI): m/z (% relative intensity): 91 (100), 330 (M^+, 69); HRMS (EI): calcd for $C_{23}H_{22}O_2$: 330.1620, found: 330.1618.

*4.3.4. Methyl 4′-bromo-3-phenethyl-[1,1′-biphenyl]-4-carboxylate (**11d**).* White solid. Yield: 84.4 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J=8.0 Hz, 1H), 7.55–7.53 (m, 2H), 7.40 (dd, J=8.0, 2.0 Hz, 1H), 7.37–7.35 (m, 2H), 7.30–7.26 (m, 3H), 7.22–7.19 (m, 3H), 3.91 (s, 3H), 3.34–3.30 (m, 2H), 2.96–2.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.5, 144.3, 143.2, 141.7, 138.8, 131.9, 131.5, 129.8, 128.7, 128.6, 128.29, 128.26, 125.9, 124.4, 122.3, 52.0, 38.0, 37.0; IR (neat, ν/cm^{-1}): 2932 (w), 1716 (s), 1604 (w), 1433 (w), 1282 (s), 1249 (m), 1084 (m), 1008 (m), 820 (s), 782 (s), 749 (m), 699 (s); LRMS (EI): m/z (% relative intensity): 91 (100), 394 (M^+, 30), 396 (M^+, 30); HRMS (EI): calcd for $C_{22}H_{19}O_2Br$: 394.0568, found: 394.0570.

*4.3.5. Methyl 4′-chloro-3-phenethyl-[1,1′-biphenyl]-4-carboxylate (**11e**).* White solid. Yield: 80% for the yields of two experiments on average. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J=8.4 Hz, 1H), 7.45–7.38 (m, 5H), 7.31–7.27 (m, 3H), 7.23–7.20 (m, 3H), 3.92 (s, 3H), 3.34–3.30 (m, 2H), 2.96–2.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.5, 144.3, 143.2, 141.8, 138.3, 134.1, 131.5, 129.9, 129.0, 128.6, 128.4, 128.3, 128.2, 125.9, 124.5, 52.0, 38.1, 37.0; IR (neat, ν/cm^{-1}): 2951 (w), 1716 (s), 1604 (w), 1433 (w), 1247 (s), 1088 (s), 823 (m), 782 (m), 753 (w), 699 (m); LRMS (EI): m/z (% relative intensity): 350 (M^+, 36); HRMS (EI): calcd for $C_{22}H_{19}O_2Cl$: 350.1074, found: 350.1078.

*4.3.6. Methyl 3-phenethyl-4′-(trifluoromethyl)-[1,1′-biphenyl]-4-carboxylate (**11f**).* Yellow oil. Yield: 79.6 mg (69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J=8.4 Hz, 1H), 7. 68 (d, J=8.4 Hz, 2H), 7. 59 (d, J=8.4 Hz, 2H), 7. 45 (dd, J=8.4, 2.0 Hz, 1H), 7.31–7.27 (m, 3H), 7.23–7.21 (m, 3H), 3.93 (s, 3H), 3.36–3.32 (m, 2H), 2.98–2.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 167.5, 144.3, 142.9, 141.7, 131.6, 130.3, 128.9, 128.7, 128.3 (4), 128.3 (3), 127.5 (3), 127.5 (1), 125.9, 125.7 (4), 125.7 (1), 124.8, 52.0, 38.0, 37.0; IR (neat, ν/cm^{-1}): 2951 (w), 1718 (s), 1606 (w), 1324 (s), 1250 (m), 1164 (m), 1122 (s), 1085 (s), 832 (m), 784 (m), 747 (w), 699 (m); LRMS (EI): m/z (% relative intensity): 91 (100), 384 (M^+, 19); HRMS (EI): calcd for $C_{23}H_{19}O_2F_3$: 384.1337, found: 384.1339.

*4.3.7. Methyl 5-phenethyl-[1,1′-biphenyl]-2-carboxylate (**13a**).* Yellow oil. Yield: 79.6 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J=8.4 Hz, 1H), 7.39–7.35 (m, 3H), 7.30–7.26 (m, 4H), 7.21–7. 14 (m, 5H), 3.62 (s, 3H), 3.00–3.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.9, 145.4, 142.8, 141.5, 141.1, 131.0, 130.1, 128.4 (4), 128.3 (9), 128.3, 128.2, 127.9, 127.3, 127.1, 126.1, 51.8, 37.7, 37.5; IR (neat, ν/cm^{-1}): 2947 (w), 1716 (s), 1603 (w), 1432 (m), 1281 (s), 1249 (m), 1095 (m), 762 (w), 697 (s); LRMS (EI): m/z (% relative intensity): 36 (M^+, 100); HRMS (EI): calcd for $C_{22}H_{20}O_2$: 316.1475, found: 316.1463.

*4.3.8. Methyl 4′-methoxy-5-(4-methoxyphenethyl)-[1,1′-biphenyl]-2-carboxylate (**13b**).* White solid. Yield: 77.8 mg (69%, 3 days). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J=8.0 Hz, 1H), 7.20 (dd, J=6.8, 1.6 Hz, 2H), 7.15 (d, J=8.4 Hz, 1H), 7.11 (d, J=1.2 Hz, 1H), 7.06 (d, J=8.4 Hz, 2H), 6.92 (d, J=8.8 Hz, 2H), 6.82 (d, J=8.4 Hz, 2H), 3. 83 (s, 3H), 3. 77 (s, 3H), 3. 65 (s, 3H), 2.95–2.83 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 169.1, 158.8, 157.9, 145.4, 142.2, 133.8, 133.2, 131.1, 130.0, 129.4, 129.3, 128.1, 126.9, 113.7, 113.4, 55.2, 51.8, 37.9, 36.5; IR (neat, ν/cm^{-1}): 2928 (w), 1717 (m), 1607 (m), 1511 (m), 1241 (s), 1176 (m), 1029 (s), 831 (m), 715 (m); LRMS (EI): m/z (%

relative intensity): 376 (M^+, 29.3), 121 (100); HRMS (EI): calcd for $C_{24}H_{24}O_4$: 376.1675, found: 376.1674.

*4.3.9. Methyl 4′-methyl-5-(4-methylphenethyl)-[1,1′-biphenyl]-2-carboxylate (**13c**).* Yellow oil. Yield: 89.7 mg (87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ7.75 (d, J=7.8 Hz, 1H), 7.18–7.06 (m, 10H), 3. 65 (s, 3H), 2.94–2.90 (m, 4H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.9, 145.4, 142.7, 138.5, 138.1, 136.7, 135.4, 131.1, 130.0, 129.0, 128.6, 128.3, 128.2, 128.1, 127.0, 51.7, 37.8, 37.0, 21.1, 20.9; IR (neat, ν/cm^{-1}): 2922 (w), 1717 (s), 1604 (m), 1432 (m), 1278 (s), 1248 (s), 1092 (m), 822 (s), 783 (s), 750 (m); LRMS (EI): m/z (% relative intensity): 105 (100), 344 (M^+, 25); HRMS (EI): calcd for $C_{24}H_{24}O_2$: 344.1776, found: 344.1775.

*4.3.10. Methyl 4′-chloro-5-(4-chlorophenethyl)-[1,1′-biphenyl]-2-carboxylate (**13d**).* White solid. Yield: 103.7 mg (90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, J=8.1 Hz, 1H), 7.35 (d, J=8.4 Hz, 2H), 7.24–7.16 (m, 5H), 7.04 (d, J=8.7 Hz, 3H), 3.65 (s, 3H), 2.98–2.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 168.3, 145.1, 141.7, 139.9, 139.3, 133.2, 131.8, 131.0, 130.4, 129.8, 129.6, 128.4, 128.1, 128.0, 127.6, 51.8, 37.4, 36.7; IR (neat, ν/cm^{-1}): 2961 (w), 1720 (s), 1604 (w), 1433 (w), 1259 (s), 1087 (s), 1013 (s), 799 (s), 736 (w), 709 (w); LRMS (EI): m/z (% relative intensity): 125 (100), 384 (M^+, 36); HRMS (EI): calcd for $C_{22}H_{18}O_2Cl_2$: 384.0684, found: 384.0683.

4.4. Synthesis of bradykinin receptor β1 antagonists (17)

To a solution of **16**[13] (170.5 mg, 0.43 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added butanoyl chloride (50 μL, 0.48 mmol) and *N*,*N*-diisopropylethylamine (90 μL, 0.51 mmol). The resulting solution was stirred for 2 h at room temperature, and partitioned between ethyl acetate and water and extracted with ethyl acetate. The organic layer extract was concentrated under vacuum. Purification was achieved by flash chromatography (PE/EtOAc=2/1) to afford **17** (173.5 mg, 86%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04–8.00 (m, 3H), 7.82 (d, J=7.5 Hz, 1H), 7.74 (br s, 1H) 7.46 (d, J=7.8 Hz, 1H), 7.34 (d, J=7.7 Hz, 2H), 7.23 (d, J=7.8 Hz, 2H), 6.59 (dd, J=6.6, 5.1 Hz, 1H), 5.20 (br s, 1H), 4.63 (d, J=5.1 Hz, 2H), 3.93 (s, 3H), 3.67 (s, 3H), 2.26 (t, J=7.5 Hz, 2H), 1.67 (q, J=7.5 Hz, 2H), 0.93 (t, J=7.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ 172.8, 168.5, 166.1, 152.4, 144.5, 142.1, 139.1, 138.7, 134.4, 132.6, 132.4, 131.7, 129.7, 128.3, 128.0, 127.4, 118.9, 112.8, 52.4, 52.3, 45.1, 38.5, 19.0, 13.6; IR (neat, ν/cm^{-1}): 3310 (w), 2962 (w), 2874 (w), 1725 (s), 1657 (m), 1586 (w), 1507 (m), 1458 (w), 1418 (m), 1289 (s), 1241 (s), 1115 (m), 1040 (w), 811 (w), 756 (m), 739 (m), 704 (w); LRMS (EI): m/z (% relative intensity): 390 (48.5), 460 (M^+, 100); calcd for $C_{26}H_{27}N_3O_5$: 461.1951, found: 461.1955.

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Supplementary data

Reaction optimization, procedures, data and copies of ^{1}H and ^{13}C NMR spectra for all new compounds. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.10.028.

References and notes

1. (a) Astruc, D. *Modern Arene Chemistry*; Wiley-VCH: Weinheim, Germany, 2002; (b) Nicolaou, K. C.; Boddy, C. N. C.; Bräse, S.; Winssinger, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 2096–2152; (c) Liu, J.-K. *Chem. Rev.* **2006**, *106*, 2209–2223; (d) Xiao, L.-X.; Chen, Z.-J.; Qu, B.; Luo, J.-X.; Kong, S.; Gong, Q.-H. *Adv. Mater.* **2011**, *23*, 926–952.
2. (a) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, NY, 1992, Chapter 11, pp 501–568; (b) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879–933; (c) Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 3–4; (d) *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, NY, 1998; (e) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731–1770.
3. For reviews on the syntheses of substituted benzenes, see: (a) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, pp 741–770; (b) Bonnemann, H.; Brijoux, W. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 171–197; (c) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901–2915; (d) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085–1094.
4. For selected examples on the synthesis of benzene derivatives through [2+2+2] cycloaddition, see: (a) Tsuji, H.; Yamagata, K. I.; Fujimoto, T.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 7792–7793; (b) Galan, B. R.; Rovis, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 2830–2834; (c) Qiu, Z.-Z.; Xie, Z.-W. *Angew. Chem., Int. Ed.* **2009**, *48*, 5729–5732; (d) Kuninobu, Y.; Nishi, M.; Kawata, A.; Takata, H.; Hanatani, Y.; Yudha, S. S.; Iwai, A.; Takai, K. *J. Org. Chem.* **2010**, *75*, 334–341.
5. For selected examples on the synthesis of benzene derivatives through RCM reaction, see: (a) Donohoe, T. J.; Orr, A. J.; Bingham, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2664–2670; (b) Van Otterlo, W. A. L.; Koning, C. B. *Chem. Rev.* **2009**, *109*, 3743–3782; (c) Yoshida, K.; Shida, H.; Takahashi, H.; Yanagisawa, A. *Chem.—Eur. J.* **2011**, *17*, 344–349.
6. For selected examples on the synthesis of benzene derivatives through intramolecular tandem reaction, see: (a) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436–7437; (b) Blond, G.; Bour, C.; Salem, B.; Suffert, J. *Org. Lett.* **2008**, *10*, 1075–1078.
7. For selected recent other methods on the synthesis of benzenes, see: (a) Neumann, H.; Von Wangelin, A. J.; Klaus, S.; Strubing, D.; Gordes, D.; Beller, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4503–4507; (b) Takahashi, T.; Liu, Y.-H.; Iesato, A.; Chaki, S.; Nakajima, K.; Kanno, K.-I. *J. Am. Chem. Soc.* **2005**, *127*, 11928–11929; (c) Serra, S.; Fuganti, C.; Brenna, E. *Chem.—Eur. J.* **2007**, *13*, 6782–6791; (d) Quiclet-Sire, B.; Revol, G.; Zard, S. Z. *Org. Lett.* **2009**, *11*, 2832–2835; (e) Li, C.-K.; Zeng, Y.; Zhang, H.; Feng, J.-J.; Zhang, Y.; Wang, J.-B. *Angew. Chem., Int. Ed.* **2010**, *49*, 6413–6417; (f) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 6169–6173; (g) Li, G.-J.; Liu, Y.-H. *J. Org. Chem.* **2010**, *75*, 2903–2909.
8. (a) Sun, X.-L.; Tang, Y. *Acc. Chem. Res.* **2008**, *41*, 937–948; (b) Tang, Y.; Ye, S.; Sun, X.-L. *Synlett* **2005**, 2720–2730; (c) Deng, X.-M.; Cai, P.; Ye, S.; Sun, X.-L.; Liao, W.-W.; Li, K.; Tang, Y.; Wu, Y.-D.; Dai, L.-X. *J. Am. Chem. Soc.* **2006**, *128*, 9730–9740; (d) Ye, L.-W.; Sun, X.-L.; Zhu, C.-Y.; Tang, Y. *Org. Lett.* **2006**, *8*, 3853–3856; (e) Ye, L.-W.; Sun, X.-L.; Wang, Q.-G.; Tang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 5951–5954; (f) Wang, Q.-G.; Deng, X.-M.; Zhu, B.-H.; Ye, L.-W.; Sun, X.-L.; Li, C.-Y.; Zhu, C.-Y.; Shen, Q.; Tang, Y. *J. Am. Chem. Soc.* **2008**, *130*, 5408–5409; (g) Zhu, C.-Y.; Cao, X.-Y.; Zhu, B.-H.; Deng, C.; Sun, X.-L.; Wang, B.-Q.; Shen, Q.; Tang, Y. *Chem.—Eur. J.* **2009**, *15*, 11465–11468.
9. For selected reviews on YIMAC reactions, see: (a) Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. *Chem. Rev.* **1997**, *97*, 2341–2372; (b) Aggarwal, V. K.; Winn, C. L. *Acc. Chem. Res.* **2004**, *37*, 611–620; (c) Gaunt, M. J.; Johansson, C. C. *Chem. Rev.* **2007**, *107*, 5596–5605; (d) McGarrigle, E. M.; Myers, E. L.; Illa, O.; Shaw, M. A.; Riches, S. L.; Aggarwal, V. K. *Chem. Rev.* **2007**, *107*, 5841–5883.
10. [3+3] approaches to benzene derivatives (phenols): (a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534–3538; (b) Feist, H.; Langer, P. *Synthesis* **2007**, 327–347 (review); (c) Izawa, Y.; Pun, D.; Stahl, S. S. *Science* **2011**, *333*, 209–213.
11. (a) Ye, L.-W.; Han, X.; Sun, X.-L.; Tang, Y. *Tetrahedron* **2008**, *64*, 8149–8154; (b) Ye, L.-W.; Wang, S.-B.; Wang, Q.-G.; Sun, X.-L.; Tang, Y.; Zhou, Y.-G. *Chem. Commun.* **2009**, 3092–3094.
12. DBU can assist the aerial oxidation of cylcohexadiene to benzene, see the Supplementary data.
13. For details, see the Supplementary data.
14. 2a reacted with sodium hydroxide to generate the corresponding ylide. The ylide was recrystallized and then reacted with 1q to provide 3q. For details see the Supplementary data.
15. Kuduk, S.D.; Bock, M.G.; Feng, D.-M.; Wai, M.-C. U.S. Pat. Appl. 2004034064, 2004.
16. (a) Wattanasin, S.; Murphy, W. S. *Synthesis* **1980**, 647–650; (b) Baeckstrom, P.; Jacobsson, U.; Norin, T.; Unelius, C. R. *Tetrahedron* **1988**, *44*, 2541–2548; (c) Ishino, Y.; Mihara, M.; Nishihama, S.; Nishiguchi, I. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2669–2672; (d) Graden, H.; Hallberg, J.; Kann, N.; Olsson, T. *J. Comb. Chem.* **2004**, *6*, 783–788; (e) Sun, B.-F.; Hong, R.; Kang, Y.-B.; Li, D. *J. Am. Chem. Soc.* **2009**, *131*, 10384–10385.