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Suzuki Coupling Reactions of (*E*)- and (*Z*)-Chloroenynes with Boronic Acids: Versatile Access to Functionalized 1,3-Enynes

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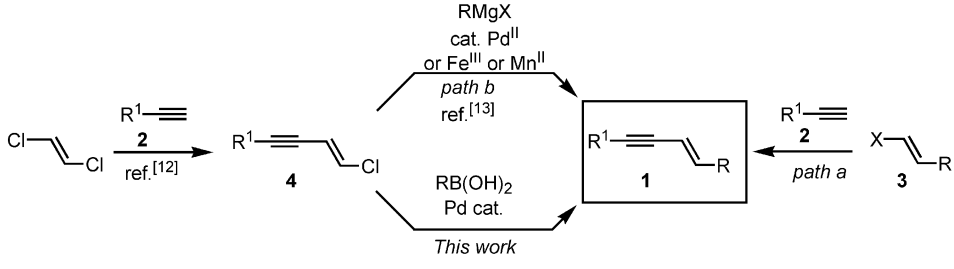
A stereoselective, palladium-catalyzed, cross-coupling reaction between chloroenynes **4** and boronic acids was successfully developed. This procedure is general and provides desired functionalized enynes **1** in high yields. The scope and limitations of this new reaction are described.

Introduction

The 1,3-enyne moiety is an important unit found in many compounds of biological interest,[1] including, hachijodine G,[2] a cytotoxic sponge alkaloid, terbinafine,[3] an antifungal agent used currently for the treatment of skin mycoses, and neocarzinostatin,[4] an effective antitumor antibiotic. Recently, a novel class of potent antitubulin agents containing this unit was reported by Lo[5] and our group.[6] 1,3-Enynes have also found increasing application in organic synthesis. Typically, they are valuable precursors for polysubstituted benzenes,[7] conjugated dienes,[8] and polyenes.[9] For these reasons, the design and synthesis of compounds containing an enyne moiety have received considerable attention in organic synthesis and have been extensively studied. Among various methods developed to synthesize 1,3-enynes **1**, the Pd–Cu-catalyzed Sonogashira coupling reaction between terminal alkynes **2** and vinyl halides **3** (I[10] or Br,[10a] Cl[11]) is undoubtedly the most prevalent route to such unsaturated compounds (Scheme 1, path a). However, when enynes **1** bearing various R substituents at the double bond are needed, this method is less suitable, because it requires the preparation of stereodefined vinyl halides **3** through lengthy procedures. Therefore, this method is time consuming and economically inefficient. From the standpoint of flexibility, a method that employs a common starting material as a precursor would have an obvious advantage. In recent years, we showed that the use (*E*)- or (*Z*)-chloroenynes **4** as synthetic intermediates presented several advantages: (i) They are easily accessible in high stereoisomeric purity (≥99.9%) by reaction of terminal alkynes **2** with commercially available (*E*)- or (*Z*)-1,2 dichloroethylene.[12] (ii) They are chemically stable and nonphotosensitive. Additionally, we demonstrated that they are good partners in metal-catalyzed coupling reactions with organometallic reagents (Scheme 1, path b).[13]

Among the organometallic reagents used, we showed that Grignard compounds in the presence of a catalytic amount of $PdCl_2(PPh_3)_2$[13a] reacted rapidly and cleanly with **4** to efficiently introduce aryl and alkenyl substituents, whereas to successfully transfer alkyl substituents containing β-hydrogen(s), the best routes involved the use of



Scheme 1. Synthetic strategies to target enynes **1**.

iron[13b–13d] or manganese[13e] salts as catalysts. More recently, we reported a mild Pd-catalyzed procedure for the synthesis of **1** by coupling **4** with organozincate species, formed in situ by reaction of Grignard reagents with a cata-

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lytic amount of $ZnCl_2$.[13f] However, if this procedure is appropriate to transfer efficiently alkyl, alkenyl, or aryl groups onto the enyne moiety, it is limited to nonfunctionalized Grignard reagents. To enlarge the scope of the application of chloroenynes chemistry to the synthesis of complex molecules, it was interesting to be able to couple functionalized boronic acid reagents to introduce functionalities from both substrate and reagent. Over the past few years, in particular, there has been an increased availability of boronic acids and esters.[14] Organoboron reagents exhibit greater functional group compatibility than organozinc or Grignard reagents. Moreover, the innocuous nature of boronic acids, which are generally nontoxic and thermally air- and moisture-stable, is a practical advantage of the Suzuki reaction relative to other coupling processes. To the best of our knowledge, except the coupling reaction of boronic acids with activated β-chloro-α,β-unsaturated esters reported by Lemay,[15] the coupling of these mild organometallic species with chloroenynes appears unprecedented. Therefore, we turned our attention to investigate the reactivity of various commercially available boronic acids towards (*E*)- and (*Z*)-chloroenynes **4** in the presence of palladium catalysts. The results of this study are now reported.

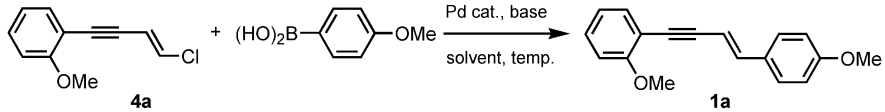
Results and Discussion

At first, we studied the coupling of (*E*)-chloroenyne **4a** with 4-methoxyphenylboronic acid as model substrates to establish the best reaction conditions (Table 1). Initially, this coupling was evaluated according to the protocol of Lemay[15] using $Pd_2(dba)_3$/SPHOS [SPHOS = 2-(dicyclohexylphosphanyl)-2′,6′-dimethoxybiphenyl] as the catalyst system and K_3PO_4 as the base at room temperature. Under these conditions, the coupling gave enyne **1a** with retention of the *E*-double bond configuration, but with low conversion and overall yield (20%; Table 1, Entry 1). It is noteworthy that a significant amount of starting material was recovered unchanged, as judged by ^1H NMR analysis. Increasing the temperature to 70 °C improved the conversion of **4a** to 53% after 1 d (Table 1, Entry 2). Under the same conditions, replacing the catalyst system $Pd_2(dba)_3$/SPHOS by $Pd(PPh_3)_4$ resulted in a similar conversion (49%; Table 1, Entry 3).

As a proper combination of base and solvent is very important for the success of the reaction, we then examined the influence of these parameters. After a series of assays (not shown in Table 1), we found that the combination involving K_2CO_3/toluene at 100 °C led to **1a** with a better conversion (76%; Table 1, Entry 4). When adding EtOH as a cosolvent,[16] we were pleased to observe total conversion of **4a**, and **1a** was stereospecifically formed with an excellent yield (94%; Table 1, Entry 5). A similar result was obtained when replacing the previous catalytic system by $Pd(OAc)_2/PPh_3$ (88%, 1.5 h; Table 1, Entry 6).

Having optimized the reaction parameters, the scope of the reaction was examined with a variety of functionalized boronic acids and (*E*)- or (*Z*)-chloroenynes **4**. The results presented in Table 2 show that chloroenyne and boronic acid substrates have been used successfully, and in all cases, the coupling process is highly stereoselective. Performing the reaction with **4b** resulted in the formation of enyne **1b** in good yield and with total retention of the (*Z*) configuration (76%; Table 2, Entry 2). Nonsubstituted chloroenyne **4c** as well as **4d** bearing an electron-withdrawing group in the *ortho* position were also successfully transformed into their corresponding enynes **1c** and **1d**, respectively, in good yields (Table 2, Entries 3 and 4). The results reported in Entries 5 and 6 also indicate that both (*E*)- and (*Z*)-aliphatic chloroenynes **4e** and **4f** provided the required coupling enynes in good yields and with excellent stereoselectivities. We then turned our attention to the scope of the arylboronic acids. Switching the methoxy substituent from the *para* to the *ortho* position to the boronic acid does not affect the overall performance or the stereoselectivity of the reaction (Table 2, compare Entries 1 and 7). 1,3-Benzodioxyl and 2-naphthyl substituents were also successfully transferred onto chloroenyne **4a** (Table 2, Entries 8 and 9). We were pleased to observe that functionalized boronic acids substituted with an electron-withdrawing group (Cl, CH_3CO, CHO, NO_2) were coupled in good yields and with reasonable reaction times (Table 2, Entries 10–13). The use of heteroaromatic- or alkenylboronic acid (Table 2, Entries 14 and 15) was also effective, giving rise to enyne **1n** or **1o**, respectively, demonstrating the general character of the presented method to transfer Csp^2 substituents. In contrast,

Table 1. Pd-catalyzed Suzuki coupling between **4a** and 4-methoxyphenylboronic acid.[a]

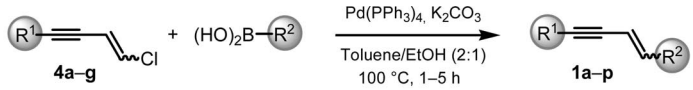


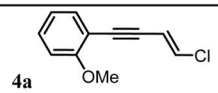
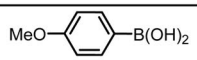
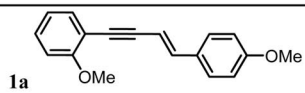
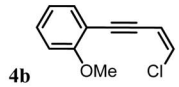
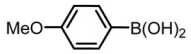
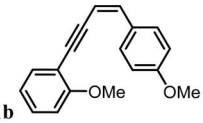
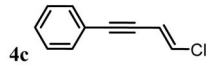
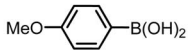
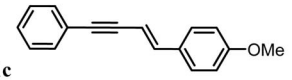
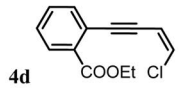
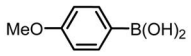
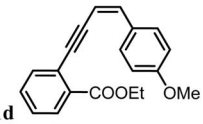
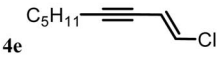
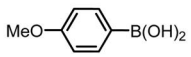
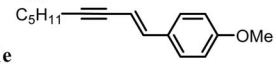
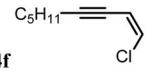
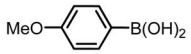
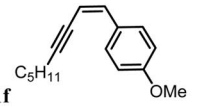
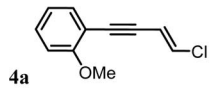
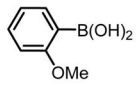
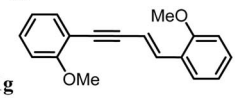
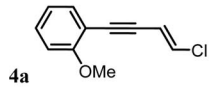
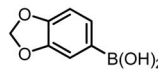
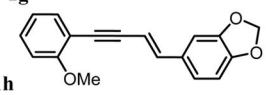
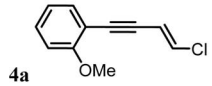
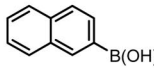
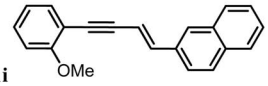
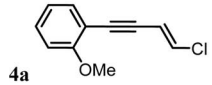
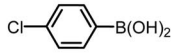
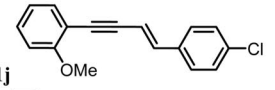
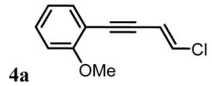
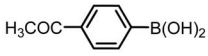
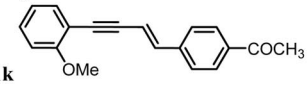
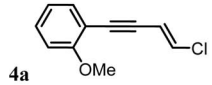
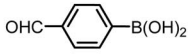
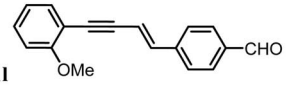
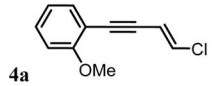
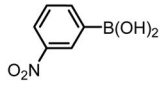
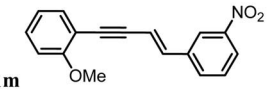
4a **1a**

Entry	Pd cat. (mol-%)/ligand (mol-%)	Solvent	Base (equiv.)	*T* [°C]	Time [h]	Conv. [%][b]	Yield [%][c]
1	$Pd_2(dba)_3$ (5)/SPHOS (20)	THF	K_3PO_4 (2)	25	3	24	20
2	$Pd_2(dba)_3$ (5)/SPHOS (20)	THF	K_3PO_4 (2)	70	24	53	–
3	$Pd(PPh_3)_4$ (5)	THF	K_3PO_4 (2)	70	24	49	–
4	$Pd(PPh_3)_4$ (5)	toluene	K_2CO_3 (2)	100	24	76	–
5	$Pd(PPh_3)_4$ (5)	toluene/EtOH (2:1)	K_2CO_3 (2)	100	1	100	94
6	$Pd(OAc)_2$ (5)/PPh_3 (10)	toluene/EtOH (2:1)	K_2CO_3 (2)	100	1.5	100	88

[a] All reactions were performed with 1 equiv. of **4a** and 1.2 equiv. of 4-$MeOC_6H_4B(OH)_2$. [b] Conversion was determined by ^1H NMR analysis. [c] Yields were given for isolated products.

Table 2. Reactivity of chloroenynes **4** with various functionalized boronic acids under palladium catalysis.[a]

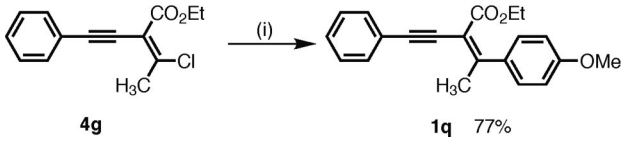


Entry	Substrate	$RB(OH)_2$	Time [h]	Product	Yield [%][b]	*E*/*Z*[c]
1	 **4a**		1	 **1a**	94	100:0
2	 **4b**		3	 **1b**	76	0:100
3	 **4c**		1	 **1c**	79	100:0
4	 **4d**		2	 **1d**	83	3:97
5	 **4e**		3	 **1e**	81	100:0
6	 **4f**		5	 **1f**	83	0:100
7	 **4a**		2	 **1g**	85	98:2
8	 **4a**		2	 **1h**	88	98:2
9	 **4a**		2	 **1i**	81	97:3
10	 **4a**		1	 **1j**	86	100:0
11	 **4a**		4	 **1k**	84	97:3
12	 **4a**		5	 **1l**	71	91:9
13	 **4a**		4	 **1m**	71	95:5
14	**4a**		2	**1n**	93	100:0
15	**4a**		3	**1o**	78	95:5[d]
16	**4a**		2	**1p**	52	–

[a] The reactions were performed with 1 equiv. of **4**, 1.2 equiv. of $RB(OH)_2$, 5 mol-% of $Pd(PPh_3)_4$, K_2CO_3 (2 equiv.), in toluene/EtOH (2:1) at 100 °C. [b] Yields are given for isolated products. [c] Stereoisomeric purities were determined by ^1H NMR analysis of the crude product. [d] (3*E*,5*E*)/(3*Z*,5*E*) ratio.

under the same protocol, the coupling of *n*-butylboronic acid with **4a** failed and **1p** resulting from carbon–chlorine bond reduction was isolated as the major product (Table 2, Entry 16). To improve this result, various combinations of Pd/ligand/additive mixtures were examined. Thus, the use of $PdCl_2$(dppf) or $Pd(OAc)_2$/dppf [dppf = 1,1′-bis(diphenylphosphanyl)ferrocene] as catalytic systems also provided **1p** in 60–62% yield, whereas in the presence of CuI or Ag_2O, which may facilitate the transmetalation step, no reaction occurred and **4a** was recovered unchanged (data not shown).

Finally, we extended the scope of our protocol to achieve the coupling of a boronic acid with a chloroenyne having a functionalized tetrasubstituted double bond. To this end, β-chloro-α,β-unsaturated ester **4g** was coupled with 4-methoxyphenylboronic acid under the above conditions to successfully give desired enyne product **1q** in a good 77% yield (Scheme 2).



Scheme 2. Synthesis of **1q**. Reagents and conditions: (*i*) 4-methoxyphenylboronic acid (1.2 equiv.) $Pd(PPh_3)_4$ (5 mol-%), K_2CO_3 (2 equiv.), toluene/EtOH (2:1), 100 °C, 1 h.

Conclusions

In summary, we developed an efficient and general catalytic system for the cross-coupling reaction of a wide range of (*Z*)- or (*E*)-chloroenynes and arylboronic acids. The process is stereoselective and provides good access to a series of functionalized 1,3-enynes in good to excellent yields. Moreover, the reaction tolerates several functional groups on both coupling partners. Further developments will be disclosed in due course.

Experimental Section

General Comments: All glassware was oven-dried at 140 °C and all reactions were conducted under a nitrogen atmosphere. Solvents were dried by standard methods and distilled before use. Piperidine and *n*-butylamine were dried and distilled from potassium hydroxide prior to use. $Pd(PPh_3)_4$ was prepared following a literature procedure.[17] The compounds were all identified by usual physical methods, that is, ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, MS, and elemental analysis. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with a Bruker Avance 300. ^{1}H chemical shifts are reported in ppm from the peak of residual chloroform (δ = 7.27 ppm). The following abbreviations are used: m (multiplet), s (singlet), d (doublet), t (triplet) dd (doublet of doublets). ^{13}C chemical shifts are reported in ppm from the central peak of deuteriochloroform (δ = 77.14 ppm). IR spectra were measured with a Bruker Vector 22 spectrophotometer as neat samples. Elemental analyses were performed with a Perkin–Elmer 240 analyzer. Mass spectra were obtained by using a Bruker Esquire electrospray ionization apparatus. Analytical TLC was performed on Merck precoated silica gel 60F plates. Merck silica gel 60 (230-400 mesh) was used for column chromatography. Chloroenynes **4c**,[18] **4e**,[19] **4f**,[19] and **4g**[15] were prepared according to literature procedures.

Synthesis of (*Z*)-Chloroenynes 4b and 4d: To a solution of $PdCl_2(PPh_3)_2$ (702 mg, 1 mmol), (*Z*)-1,2-dichloroethylene (3.88 g, 40 mmol), *n*-butylamine (2.92 g, 40 mmol), and 1-alkyne (20 mmol) in ethyl ether (50 mL) was added CuI (380 mg, 2 mmol) at 0 °C (exothermic reaction). The stirred reaction was kept at room temperature for a night and treated with saturated NH_4Cl solution (25 mL). The aqueous layer was extracted with ethyl ether (3 × 20 mL), and the combined organic layer was washed successively with aqueous HCl (0.2 M, 15 mL), $NaHCO_3$ (10 mL), and H_2O (2 × 25 mL), dried with $MgSO_4$, and concentrated under vacuum. Purification by flash chromatography afforded the expected (*Z*)-chloroenynes.

(*Z*)-4-Chloro-1-(2-methoxyphenyl)but-3-en-1-yne (4b): Yellow oil (3.11 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, CH_3), 6.14 (d, J = 7.4 Hz, 1 H, H_{vinyl}), 6.42 (d, J = 7.4 Hz, 1 H, H_{vinyl}), 6.89 (d, J = 8.2 Hz, 1 H, H_{arom}), 6.93 (dd, J = 0.8, 7.5 Hz, 1 H, H_{arom}), 7.29–7.34 (m, 1 H, H_{arom}), 7.47 (dd, J = 7.5, 1.7 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 87.5 (C_q), 94.0 (C_q), 110.9 (CH), 112.1 (C_q), 112.6 (CH), 120.7 (CH), 128.0 (CH), 130.4 (CH), 133.9 (CH), 160.1 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2201, 1578, 1489, 1433, 1264, 1119 cm^{-1}. MS (APCI+): m/z = 193.0 [M + H]$^+$. $C_{11}H_9ClO$ (192.64): calcd. C 68.58, H 4.71; found C 68.40, H 4.61.

(*Z*)-1-(2-Ethoxycarbonylphenyl)-4-chlorobut-3-en-1-yne (4d): Yellow oil (2.85 g, 61%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 (t, J = 7.1 Hz, 3 H, CH_3), 4.39 (q, J = 7.1 Hz, 2 H, CH_2), 6.15 (d, J = 7.4 Hz, 1 H, H_{vinyl}), 6.46 (d, J = 7.4 Hz, 1 H, H_{vinyl}), 7.36–7.41 (m, 1 H, H_{arom}), 7.44–7.49 (m, 1 H, H_{arom}), 7.61 (d, J = 7.6 Hz, 1 H, H_{arom}), 7.95 (d, J = 7.8 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (CH_3), 27.0 (CH_2), 88.1 (C_q), 96.2 (C_q), 112.4 (CH), 123.1 (C_q), 128.5 (CH), 128.8 (CH), 130.4 (CH), 131.7 (CH), 132.2 (C_q), 134.7 (CH), 166.2 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1709, 1598, 1482, 1366, 1249, 1130, 1080 cm^{-1}. MS (APCI+): m/z = 235.0 [M + H]$^+$. $C_{13}H_{11}ClO_2$ (234.68): calcd. C 66.53, H 4.72; found C 66.35, H 4.52.

(*E*)-4-Chloro-1-(2-methoxyphenyl)but-3-en-1-yne (4a): The same procedure was used as that described for the (*Z*)-chloroenynes, except that piperidine was used as a base instead of *n*-butylamine and (*E*)-1,2-dichloroethylene instead of (*Z*)-1,2-dichloroethylene. Yellow oil (3.04 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, CH_3), 6.20 (d, J = 13.6 Hz, 1 H, H_{vinyl}), 6.63 (d, J = 13.6 Hz, 1 H, H_{vinyl}), 6.88 (d, J = 8.1 Hz, 1 H, H_{arom}), 6.92 (dd, J = 0.8, 7.5 Hz, 1 H, H_{arom}), 7.27–7.33 (m, 1 H, H_{arom}), 7.39 (dd, J = 1.6, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8 (CH_3), 88.4 (2 C_q), 110.7 (CH), 111.8 (C_q), 114.2 (CH), 120.6 (CH), 129.9 (CH), 130.3 (CH), 133.6 (CH), 159.9 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1598, 1489, 1435, 1243, 1119, 1022 cm^{-1}. MS (APCI+): m/z = 193.0 [M + H]$^+$. $C_{11}H_9ClO$ (192.64): calcd. C 68.58, H 4.71; found C 68.45, H 4.60.

General Procedure for Suzuki Cross-Coupling: To a mixture of chloroenyne (1 mmol) in toluene (4 mL) and EtOH (2 mL) was successively added the desired boronic acid (1.2 mmol), K_2CO_3 (2 mmol), and $Pd(PPh_3)_4$ (0.05 mmol). The reaction mixture was heated at 100 °C, under vigorous stirring and monitored by TLC until complete disappearance of starting material. The solvent was evaporated in vacuo and water (10 mL) was added. After extraction with CH_2Cl_2 (3 × 10 mL), the combined organic layer was dried with $MgSO_4$, and the solvent was removed under reduced pressure. The

crude material was purified by column chromatography to afford the expected 1,3-enyne **1**.

(*E*)-1-(2-Methoxyphenyl)-4-(4-methoxyphenyl)but-3-en-1-yne (1a): Yellow oil (248 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3 H, CH_3), 3.81 (s, 3 H, CH_3), 6.22 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.76–6.80 (m, 3 H, H_{arom}), 6.84 (d, J = 7.5 Hz, 1 H, H_{arom}), 6.92 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.16–7.21 (m, 1 H, H_{arom}), 7.27 (d, J = 8.8 Hz, 2 H, H_{arom}), 7.35 (dd, J = 1.6, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3), 55.9 (CH_3), 87.4 (C_q), 93.4 (C_q), 106.2 (CH), 110.7 (CH), 112.9 (C_q), 114.3 (2 CH), 120.6 (CH), 127.7 (2 CH), 129.5 (C_q), 129.6 (CH), 133.5 (CH), 140.7 (CH), 159.9 (C_q), 160.1 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2933, 1601, 1492, 1434, 1245, 1174, 1019 cm^{-1}. MS (APCI+): m/z = 265.0 [M + H]$^+$. $C_{18}H_{16}O_2$ (264.32): calcd. C 81.79, H 6.10; found C 81.74, H 6.00.

(*Z*)-1-(2-Methoxyphenyl)-4-(4-methoxyphenyl)but-3-en-1-yne (1b): Yellow oil (201 mg, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, CH_3), 3.95 (s, 3 H, CH_3), 5.86 (d, J = 11.9 Hz, 1 H, H_{vinyl}), 6.62 (d, J = 11.9 Hz, 1 H, H_{vinyl}), 6.90–6.93 (m, 3 H, H_{arom}), 6.96 (dd, J = 1.0, 7.5 Hz, 1 H, H_{arom}), 7.31 (ddd, J = 1.7, 7.5, 8.3 Hz, 1 H, H_{arom}), 7.45 (dd, J = 1.7, 7.5 Hz 1 H, H_{arom}), 8.03 (d, J = 8.7 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3), 56.0 (CH_3), 92.3 (C_q), 92.9 (C_q), 105.2 (CH), 110.7 (CH), 113.0 (C_q), 113.7 (2 CH), 120.7 (CH), 129.8 (CH), 129.9 (C_q), 130.5 (2 CH), 133.3 (CH), 137.8 (CH), 159.8 (C_q), 160.2 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1603, 1509, 1461, 1253, 1172, 1115, 1024 cm^{-1}. MS (APCI+): m/z = 265.0 [M + H]$^+$. $C_{18}H_{16}O_2$ (264.32): calcd. C 81.79, H 6.10; found C 81.74, H 6.05.

(*E*)-4-(4-Methoxyphenyl)-1-phenylbut-3-en-1-yne (1c): Yellow oil (185 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, CH_3), 6.25 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.88 (d, J = 8.7 Hz, 2 H, H_{arom}), 7.00 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.31–7.33 (m, 3 H, H_{arom}), 7.37 (d, J = 8.7 Hz, 2 H, H_{arom}), 7.45–7.48 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (CH_3), 89.39 (C_q), 91.1 (C_q), 105.8 (CH), 114.3 (2 CH), 123.7 (C_q), 127.8 (2 CH), 128.1 (CH), 128.4 (2 CH), 129.3 (C_q), 131.6 (2 CH), 141.0 (CH), 160.2 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1023, 1175, 1251, 1441, 1487, 1509, 1601 cm^{-1}. MS (APCI+): m/z = 235.0 [M + H]$^+$. $C_{17}H_{14}O$ (234.29): calcd. C 87.15, H 6.02; found C 87.01, H 5.93.

(*Z*)-1-(2-Ethoxycarbonylphenyl)-4-(4-methoxyphenyl)but-3-en-1-yne (1d): Yellow oil (254 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.1 Hz, 3 H, CH_3), 3.83 (s, 3 H, CH_3), 4.37 (q, J = 7.1 Hz, 2 H, CH_2), 5.87 (d, J = 11.9 Hz, 1 H, H_{vinyl}), 6.67 (d, J = 11.9 Hz, 1 H, H_{vinyl}), 6.91 (d, J = 8.8 Hz, 2 H, H_{arom}), 7.34–7.40 (m, 1 H, H_{arom}), 7.46–7.51 (m, 1 H, H_{arom}), 7.59 (dd, J = 1.2, 7.7 Hz, 1 H, H_{arom}), 7.94–7.99 (m, 3 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (CH_3), 55.4 (CH_3), 61.3 (CH_2), 93.6 (C_q), 94.3 (C_q), 105.0 (CH), 113.8 (2 CH), 124.1 (C_q), 127.9 (CH), 129.6 (C_q), 130.5 (3 CH), 131.7 (CH), 132.0 (C_q), 134.1 (CH), 138.8 (CH), 159.9 (C_q), 166.4 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1721, 1604, 1510, 1248, 1172, 1079, 1031 cm^{-1}. MS (APCI+): m/z = 307.0 [M + H]$^+$. $C_{20}H_{18}O_3$ (306.36): calcd. C 78.41, H 5.92; found C 78.35, H 5.87.

(*E*)-1-(4-Methoxyphenyl)non-1-en-3-yne (1e): Yellow oil (185 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.1 Hz, 3 H, CH_3), 1.31–1.46 (m, 4 H, 2 CH_2), 1.57 (m, 2 H, CH_2), 2.33–2.38 (m, 2 H, CH_2), 3.81 (s, 3 H, CH_3), 6.02 (dt, J = 2.2, 16.2 Hz, 1 H, H_{vinyl}), 6.79–6.86 (m, 3 H, H_{vinyl}, H_{arom}), 7.30 (d, J = 8.5 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 19.8 (CH_2), 22.4 (CH_2), 28.7 (CH_2), 31.3 (CH_2), 55.4 (CH_3), 80.0 (C_q), 92.3 (C_q), 106.6 (CH), 114.2 (2 CH), 127.4 (2 CH), 129.6 (C_q), 139.6 (CH), 159.9 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2928, 1605, 1510, 1463, 1246, 1174, 1033 cm^{-1}. MS (APCI+): m/z = 229.0 [M + H]$^+$. $C_{16}H_{20}O$ (228.33): calcd. C 84.16, H 8.83; found C 84.12, H 8.77.

(*Z*)-1-(4-Methoxyphenyl)non-1-en-3-yne (1f): Yellow oil (189 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, J = 7.1 Hz, 3 H, CH_3), 1.30–1.50 (m, 4 H, 2 CH_2), 1.56–1.67 (m, 2 H, CH_2), 2.41–2.47 (m, 2 H, CH_2), 3.83 (s, 3 H, CH_3), 5.58 (dt, J = 2.5, 11.9 Hz, 1 H, H_{vinyl}), 6.49 (d, J = 11.9 Hz, 1 H, H_{vinyl}), 6.87 (d, J = 8.8 Hz, 2 H, H_{arom}), 7.84 (d, J = 8.8 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.0 (CH_2), 22.4 (CH_2), 28.5 (CH_2), 31.3 (CH_2), 55.4 (CH_3), 79.5 (C_q), 97.3 (C_q), 105.9 (CH), 113.6 (2 CH), 129.9 (C_q), 130.0 (2 CH), 136.8 (CH), 159.5 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2931, 1605, 1510, 1463, 1304, 1254, 1175, 1033 cm^{-1}. MS (APCI+): m/z = 229.0 [M + H]$^+$. $C_{16}H_{20}O$ (228.33): calcd. C 84.16, H 8.83; found C 84.05, H 8.69.

(*E*)-1,4-Bis(2-methoxyphenyl)but-3-en-1-yne (1g): Yellow oil (224 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3 H, CH_3), 3.82 (s, 3 H, CH_3), 6.45 (d, J = 16.4 Hz, 1 H, H_{vinyl}), 6.78–6.87 (m, 4 H, H_{arom}), 7.15 (dd, J = 1.6, 7.2 Hz, 1 H, H_{arom}), 7.20 (dd, J = 1.7, 7.4 Hz, 1 H, H_{arom}), 7.28 (d, J = 16.4 Hz, 1 H, H_{vinyl}), 7.34–7.38 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.6 (CH_3), 55.9 (CH_3), 87.7 (C_q), 93.9 (C_q), 109.1 (CH), 110.7 (CH), 111.1 (CH), 112.9 (C_q), 120.6 (CH), 120.8 (CH), 125.6 (C_q), 126.9 (CH), 129.6 (2 CH), 133.6 (CH), 136.5 (CH), 157.1 (C_q), 159.9 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2933, 1593, 1485, 1434, 1241, 1119, 1024 cm^{-1}. MS (APCI+): m/z = 265.0 [M + H]$^+$. $C_{18}H_{16}O_2$ (264.32): calcd. C 81.79, H 6.10; found C 81.65, H 6.00.

(*E*)-1-(2-Methoxyphenyl)-4-(3,4-methylenedioxyphenyl)but-3-en-1-yne (1h): Yellow oil (245 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 5.98 (s, 2 H, CH_2), 6.27 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.78 (d, J = 8.0 Hz, 1 H, H_{arom}), 6.85–7.00 (m, 5 H, vinyl, arom.), 7.26–7.32 (m, 1 H, H_{arom}), 7.44 (dd, J = 1.7, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 87.8 (C_q), 93.2 (C_q), 101.4 (CH_2), 105.3 (CH), 106.7 (CH), 108.6 (CH), 110.7 (CH), 112.8 (C_q), 120.6 (CH), 121.8 (CH), 129.7 (CH), 131.2 (C_q), 133.6 (CH), 140.8 (CH), 148.2 (C_q), 148.3 (C_q), 159.9 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1591, 1488, 1237, 1117, 1025, 925, 790, 739 cm^{-1}. MS (APCI+): m/z = 279.0 [M + H]$^+$. $C_{18}H_{14}O_3$ (278.30): calcd. C 77.68, H 5.07; found C 77.54, H 5.00.

(*E*)-1-(2-Methoxyphenyl)-4-(2-naphthyl)but-3-en-1-yne (1i): Yellow oil (230 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, CH_3), 6.58 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.89–6.97 (m, 2 H, H_{arom}), 7.23 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.28–7.34 (m, 1 H, H_{arom}), 7.46–7.49 (m, 3 H, H_{arom}, H_{naph}), 7.62 (dd, J = 1.6, 8.6 Hz, 1 H, H_{naph}), 7.78–7.84 (m, 4 H, H_{naph}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 88.6 (C_q), 93.3 (C_q), 108.9 (CH), 110.7 (CH), 112.7 (C_q), 120.7 (CH), 122.9 (CH), 126.5 (CH), 126.6 (CH), 127.0 (CH), 127.8 (CH), 128.4 (CH), 128.6 (CH), 129.9 (CH), 133.6 (C_q), 133.7 (CH), 134.1 (2 C_q), 141.2 (CH), 160.0 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1589, 1490, 1462, 1433, 1270, 1118, 1025 cm^{-1}. MS (APCI+): m/z = 285.0 [M + H]$^+$. $C_{21}H_{16}O$ (284.35): calcd. C 88.70, H 5.67; found C 88.57, H 5.56.

(*E*)-4-(4-Chlorophenyl)-1-(2-methoxyphenyl)but-3-en-1-yne (1j): Yellow oil (230 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 6.42 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.88–6.96 (m, 2 H, H_{arom}), 7.00 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.27–7.36 (m, 5 H, H_{arom}), 7.43–7.46 (m, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 88.8 (C_q), 92.7 (C_q), 109.3 (CH), 110.7 (CH), 112.5 (C_q), 120.7 (CH), 127.6 (2 CH), 129.1 (2 CH), 130.0 (CH), 133.6 (CH), 134.3 (C_q), 135.1 (C_q), 139.7 (CH), 160.0 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1591, 1489, 1432, 1240, 1122, 1026 cm^{-1}. MS (APCI+): m/z = 269.0 [[M + H]$^+$ Cl^{35}], 271.0 [[M + H]$^+$ Cl^{37}]. $C_{17}H_{13}ClO$ (268.74): calcd. C 75.98, H, 4.88; found C 75.89, H, 5.01.

(*E*)-4-(4-Acetylphenyl)-1-(2-methoxyphenyl)but-3-en-1-yne (1k): Yellow oil (225 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59 (s, 3 H, CH_3), 3.91 (s, 3 H, CH_3), 6.56 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.88–6.96 (m, 2 H, H_{arom}), 7.06 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.28–7.34 (m, 1 H, H_{arom}), 7.44 (dd, J = 1.7, 7.7 Hz, 1 H, H_{arom}), 7.48 (d, J = 8.3 Hz, 2 H, H_{arom}), 7.91 (d, J = 8.3 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.7 (CH_3), 55.9 (CH_3), 90.1 (C_q), 92.7 (C_q), 110.8 (CH), 111.6 (CH), 112.4 (C_q), 120.7 (CH), 126.4 (2 CH), 129.0 (2 CH), 130.2 (CH), 133.7 (CH), 136.7 (C_q), 139.6 (CH), 141.1 (C_q), 160.1 (C_q), 197.4 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2195, 1676, 1598, 1490, 1357, 1256, 1180 cm^{-1}. MS (APCI+): m/z = 277.0 [M + H]$^+$. $C_{19}H_{16}O_2$ (276.33): calcd. C 82.58, H 5.84; found C 82.55, H 5.75.

(*E*)-4-(4-Formylphenyl)-1-(2-methoxyphenyl)but-3-en-1-yne (1l): Yellow oil (186 mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 6.60 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.89–6.96 (m, 2 H, H_{arom}), 7.07 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.29–7.35 (m, 1 H, H_{arom}), 7.45 (dd, J = 1.3, 7.5 Hz, 1 H, H_{arom}), 7.55 (d, J = 8.1 Hz, 2 H, H_{arom}), 7.84 (d, J = 8.1 Hz, 2 H, H_{arom}), 9.98 (s, 1 H, C*H*O) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 90.6 (C_q), 92.6 (C_q), 110.8 (CH), 112.3 (CH), 120.7 (CH), 126.8 (2 CH), 130.3 (3 CH), 133.7 (CH), 136.0 (C_q), 139.5 (CH), 142.4 (C_q), 160.1 (C_q), 191.1 (CH) ppm. IR (neat): $\tilde{\nu}$ = 1693, 1597, 1490, 1434, 1212, 1165, 1024 cm^{-1}. MS (APCI+): m/z = 263.0 [M + H]$^+$. $C_{18}H_{14}O_2$ (262.30): calcd. C 82.42, H 5.38; found C 82.41, H 5.32.

(*E*)-1-(2-Methoxyphenyl)-4-(3-nitrophenyl)but-3-en-1-yne (1m): Yellow oil (198 mg, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 6.58 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.89–6.96 (m, 2 H, H_{arom}), 7.07 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.29–7.35 (m, 1 H, H_{arom}), 7.45 (dd, J = 1.2, 7.6 Hz, 1 H, H_{arom}), 7.47–7.53 (m, 1 H, H_{arom}), 7.70 (d, J = 7.8 Hz, 1 H, H_{arom}), 8.09–8.13 (m, 1 H, H_{arom}), 8.25 (s, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.9 (CH_3), 90.3 (C_q), 92.0 (C_q), 110.8 (CH), 112.0 (CH), 112.2 (C_q), 120.7 (CH), 120.9 (CH), 122.9 (CH), 129.8 (CH), 130.3 (CH), 131.9 (CH), 133.7 (CH), 138.1 (CH), 138.3 (C_q), 148.8 (C_q), 160.1 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1601, 1529, 1422, 1330, 1238, 1117, 1022 cm^{-1}. MS (APCI+): m/z = 280.0 [M + H]$^+$. $C_{17}H_{13}NO_3$ (279.29): calcd. C 73.11, H 4.69, N 5.02; found C 73.07, H 4.65, N 4.81.

(*E*)-1-(2-Methoxyphenyl)-4-(3-thienyl)but-3-en-1-yne (1n): Yellow oil (223 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 6.29 (d, J = 16.1 Hz, 1 H, H_{vinyl}), 6.88–6.95 (m, 2 H, H_{arom}), 7.06 (d, J = 16.1 Hz, 1 H, H_{vinyl}), 7.25–7.32 (m, 4 H, H_{arom}), 7.44 (dd, J = 1.7, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (CH_3), 88.1 (C_q), 93.0 (C_q), 108.4 (CH), 110.7 (CH), 112.8 (C_q), 120.6 (CH), 123.6 (CH), 124.6 (CH), 126.6 (CH), 129.8 (CH), 133.6 (CH), 135.1 (CH), 139.5 (C_q), 159.9 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1591, 1489, 1433, 1272, 1238, 1161, 1118 cm^{-1}. MS (APCI+): m/z = 241.0 [M + H]$^+$. $C_{15}H_{12}OS$ (240.32): calcd. C 74.97, H 5.03; found C 74.80, H 4.85.

(*E*)-1-(2-Methoxyphenyl)non-3,5-dien-1-yne (1o): Yellow oil (176 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.3 Hz, 3 H, CH_3), 1.44 (m, J = 7.3 Hz, 2 H, CH_2), 2.07–2.14 (m, 2 H, CH_2), 3.88 (s, 3 H, CH_3), 5.74–5.87 (m, 2 H, H_{vinyl}), 6.14 (dd, J = 10.3, 14.9 Hz, 1 H, H_{vinyl}), 6.68 (dd, J = 10.8, 15.4 Hz, 1 H, H_{vinyl}), 6.86 (d, J = 7.6 Hz, 1 H, H_{arom}), 6.91 (dd, J = 0.9, 7.5 Hz, 1 H, H_{arom}), 7.23–7.29 (m, 1 H, H_{arom}), 7.38 (dd, J = 1.6, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 22.4 (CH_2), 35.0 (CH_2), 55.9 (CH_3), 87.6 (C_q), 93.4 (C_q), 109.2 (CH), 110.7 (CH), 112.9 (C_q), 120.6 (CH), 129.6 (CH), 130.2 (CH), 133.5 (CH), 138.0 (CH), 142.2 (CH), 159.8 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 2958, 2192, 1679, 1593, 1491, 1434, 1267, 1119 cm^{-1}. MS (APCI+): m/z = 227.0 [M + H]$^+$. $C_{16}H_{18}O$ (226.31): calcd. C 84.91, H 8.02; found C 84.65, H 7.74.

1-(2-Methoxyphenyl)but-3-en-1-yne (1p): Yellow oil (82 mg, 52%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, CH_3), 5.53 (dd, J = 2.1, 11.1 Hz, 1 H, H_{vinyl}), 5.75 (dd, J = 2.1, 17.5 Hz, 1 H, H_{vinyl}), 6.08 (dd, J = 11.1, 17.5 Hz, 1 H,H_{vinyl}), 6.86–6.93 (m, 2 H, H_{arom}), 7.26–7.32 (m, 1 H, H_{arom}), 7.42 (dd, J = 1.6, 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.9 (CH_3), 86.4 (C_q), 92.3 (C_q), 110.7 (CH), 112.4 (C_q), 117.6 (CH), 120.6 (CH), 126.8 (CH_2), 129.9 (CH), 133.7 (CH), 160.0 (C_q) ppm. IR (neat): $\tilde{\nu}$ = 1595, 1491, 1434, 1263, 1181, 1119, 1021 cm^{-1}. MS (APCI+): m/z = 159.0 [M + H]$^+$. $C_{11}H_{10}O$ (158.20): calcd. C 83.51, H 6.37; found C 83.30, H 6.15.

(*Z*)-Ethyl 3-(4-methoxyphenyl)-2-(phenylethynyl)but-2-enoate (1q): Yellow oil (150 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, J = 7.1 Hz, 3 H, CH_3), 2.44 (s, 3 H, CH_3), 3.82 (s, 3 H, CH_3), 4.07 (q, J = 7.1 Hz, 2 H, CH_2), 6.87 (d, J = 8.6 Hz, 2 H, H_{arom}), 7.19 (d, J = 8.6 Hz, 2 H, H_{arom}), 7.32–7.34 (m, 3 H, H_{Ph}), 7.49–7.52 (m, 2 H, H_{Ph}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 24.4 (CH_3), 55.4 (CH_3), 61.2 (CH_2), 86.0 (C_q), 95.9 (C_q), 113.7 (2 CH), 123.4 (C_q), 128.5 (5CH), 131.6 (2 CH), 133.7 (C_q), 154.6 (C_q), 159.8 (C_q), 166.5 (C_q). ppm. IR (neat): $\tilde{\nu}$ = 1719, 1605, 1510, 1324, 1248, 1178, 1109, 1031, 832 cm^{-1}. MS (APCI+): m/z = 321.0 [M + H]$^+$. $C_{21}H_{20}O_3$ (320.38): calcd. C 78.73, H 6.29; found C 78.51, H 6.10.

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