Suzuki Coupling Reactions of (*E*)- and (*Z*)-Chloroenynes with Boronic Acids: A Versatile Access to Functionalized 1,3-EnynesAbdelatif Tikad,^[a] Abdallah Hamze,^[a] Olivier Provot,^[a] Jean-Daniel Brion^[a] and Mouâd Alami^{*[a]}**Keywords:** Chloroenynes / Suzuki Coupling / Functionalized 1,3-Enynes / Boronic Acids / Palladium

A stereoselective palladium-catalyzed cross-coupling reaction between chloroenynes **4** and boronic acids was successfully developed. This procedure is general and provides the desired functionalized enynes **1**

in high yields. The scope and limitations of this new reaction are described.

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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, or 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 has 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 (*path a*, Scheme 1). However, when enynes **1** bearing various R substituents at the double bond are needed, this method is less suitable since it requires the preparation of stereodefined vinyl halides **3** through lengthy procedures and is therefore time-consuming and economically inefficient. From the standpoint of flexibility, a method that employed 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 ($\geq 99.9\%$) by reaction of terminal alkynes **2** with commercially available (*E*)- or (*Z*)-1,2-dichloroethylene^[12] and, (ii) they are chemically stable and non-photosensitive. Additionally, we demonstrated that they are good partners in metal-catalyzed coupling reaction with organometallic reagents (*path b*, Scheme 1).^[13]

Among organometallic reagents used, we showed that Grignard compounds in the presence of a catalytic amount of PdCl₂(PPh₃)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), best routes consist on using iron^[13b-d] or manganese^[13e] salts catalysis. More recently, we reported a mild Pd-catalyzed procedure for the synthesis of **1** by coupling **4** with organozinc species, formed *in situ* by reaction of Grignard reagents with a catalytic amount of ZnCl₂.^[13f] However, if this procedure is appropriate to transfer efficiently alkyl, alkenyl, or aryl groups onto the enyne moiety, it is limited to non-functionalized Grignard reagents. To enlarge the scope of 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 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 Lemay's protocol^[15] using Pd₂(dba)₃/SPHOS as the catalyst system, K₃PO₄ as the base at room temperature. Under these conditions, the coupling gave enyne **1a** with retention of the *E*-double bond configuration, but with lower conversion and overall yield (20%, 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 one day (entry 2). Under the same conditions, replacing the

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

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

Entry	[Pd] / Ligand (mol%)	Solvent	Base (equiv.)	T (°C)	Time (h)	Conv. (%) ^[b]	Yield ^[c] (%)
1	Pd ₂ (dba) ₃ (5)/SPHOS (20)	THF	K ₃ PO ₄ (2)	25	3	24	20
2	Pd ₂ (dba) ₃ (5)/SPHOS (20)	THF	K ₃ PO ₄ (2)	70	24	53	-
3	Pd(PPh ₃) ₄ (5)	THF	K ₃ PO ₄ (2)	70	24	49	-
4	Pd(PPh ₃) ₄ (5)	Toluene	K ₂ CO ₃ (2)	100	24	76	-
5	Pd(PPh₃)₄ (5)	Toluene/EtOH (2:1)	K₂CO₃ (2)	100	1	100	94
6	Pd(OAc) ₂ (5)/PPh ₃ (10)	Toluene/EtOH (2:1)	K ₂ CO ₃ (2)	100	1.5	100	88

[a] All reaction were performed with 1 equiv. of **4a** and 1.2 equiv. of 4-MeOC₆H₄B(OH)₂. [b] Conversion was determined by ¹H NMR analysis. [c] Yields were given for isolated products.

catalyst system Pd₂(dba)₃/SPHOS by Pd(PPh₃)₄ resulted in a similar conversion (49%, 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 K₂CO₃/toluene at 100 °C led to **1a** with a better conversion (76%, entry 4). When adding EtOH as a co-solvent,^[16] we were pleased to observe total conversion of **4a** and **1a** was stereospecifically formed with an excellent yield (94%, entry 5). A similar result was obtained when replacing the previous catalytic system by Pd(OAc)₂/PPh₃ (88%, 1.5 h, 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 substrates chloroenyne and boronic acids 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 a good yield and with a total retention of the (*Z*)-configuration (entry 2, 76%). Non-substituted chloroenyne **4c** as well as **4d** bearing in the ortho position an electron-withdrawing group were also successfully transformed into their corresponding enynes **1c** and **1d**, respectively, in good yields (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 arylboronic acids. Switching the methoxyl substituent

from para to ortho position to the boronic acid does not affect the overall performance, nor the stereoselectivity of the reaction (compare entries 1 and 7). 1,3-Benzodioxyl and 2-naphthyl substituents were also successfully transferred onto the chloroenyne **4a** (entries 8 and 9). We were pleased to observe that functionalized boronic acids substituted with an electron-withdrawing group (Cl, CH₃CO, CHO, NO₂) have been coupled in good yields and with reasonable reaction times (entries 10-13). The use of heteroaromatic- or alkenyl-boronic acid (entries 14 and 15) was also effective, giving rise to enynes **1n** and **1o**, respectively, demonstrating the general character of the presented method to transfer Csp² substituents. In contrast under the same protocol, the coupling of *n*-butylboronic acid with **4a** failed and **1p**, resulting from the carbon-chlorine bond reduction, was isolated as the major product (entry 16). In order to improve this result, various combinations of Pd/ligand/additive mixtures were examined. Thus, the use of PdCl₂(dppf) or Pd(OAc)₂/dppf as catalytic systems also provided **1p** in 60-62% yields whereas, in the presence of CuI or Ag₂O 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 tetra-substituted double bond. To this end, β-chloro-α,β-unsaturated ester **4g** was coupled with 4-methoxyphenyl boronic acid under the above conditions to successfully give the desired enyne product **1q** in a good 77 % yield (scheme 2).

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

Entry	Substrat	RB(OH) ₂	Time (h)	Product	Yield (%) ^[b]	<i>E/Z</i> ^[c]
1	4a	MeO-C ₆ H ₄ -B(OH) ₂	1	1a	94	100/0
2	4b	MeO-C ₆ H ₄ -B(OH) ₂	3	1b	76	0/100
3	4c	MeO-C ₆ H ₄ -B(OH) ₂	1	1c	79	100/0
4	4d	MeO-C ₆ H ₄ -B(OH) ₂	2	1d	83	3/97
5	4e	MeO-C ₆ H ₄ -B(OH) ₂	3	1e	81	100/0
6	4f	MeO-C ₆ H ₄ -B(OH) ₂	5	1f	83	0/100
7	4a	MeO-C ₆ H ₄ -B(OH) ₂	2	1g	85	98/2
8	4a	MeO-C ₆ H ₄ -B(OH) ₂	2	1h	88	98/2
9	4a	MeO-C ₆ H ₄ -B(OH) ₂	2	1i	81	97/3
10	4a	Cl-C ₆ H ₄ -B(OH) ₂	1	1j	86	100/0
11	4a	H ₃ COC-C ₆ H ₄ -B(OH) ₂	4	1k	84	97/3
12	4a	OHC-C ₆ H ₄ -B(OH) ₂	5	1l	71	91/9
13	4a	O ₂ N-C ₆ H ₄ -B(OH) ₂	4	1m	71	95/5
14	4a	Thiophene-2-yl-B(OH) ₂	2	1n	93	100/0
15	4a	CH ₃ (CH ₂) ₄ -B(OH) ₂	3	1o	78	95/5 ^[d]
16	4a	CH ₃ (CH ₂) ₄ -B(OH) ₂	2	1p	52	-

[a] The reactions were performed with 1 equiv. of **4**, 1.2 equiv of RB(OH)₂, 5 mol% of Pd(PPh₃)₄, K₂CO₃ (2 equiv), in toluene/EtOH (2:1) at 100 °C. [b] Yields were given for isolated products. [c] Stereoisomeric purities were determined by ¹H NMR analysis on the crude product. [d] (3*E*, 5*E*)/(3*Z*, 5*E*) ratio.

Scheme 2. Synthesis of **1q**. Reagents and conditions: (i) 4-methoxyphenylboronic acid (1.2 equiv.) Pd(PPh₃)₄ (5 mol%), K₂CO₃ (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 between a wide range of (*Z*)- or (*E*)-chloroenynes and arylboronic acids. The process is stereoselective and provides a 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 glasswares were 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(PPh₃)₄ was prepared following literature procedure.^[17] The compounds were all identified by usual physical methods, i.e. ¹H-NMR, ¹³C-NMR, IR, MS and elemental analysis. ¹H and ¹³C NMR spectra were measured in CDCl₃ with a Bruker Avance 300. ¹H chemical shifts are reported in ppm from the peak of residual chloroform (7.27 ppm) and coupling constants *J* were measured in Hz. The following abbreviation are use: m (multiplet), s (singlet), d (doublet), t (triplet) dd (doublet of doublet). ¹³C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). IR spectra were measured on a Bruker Vector 22 spectrophotometer (neat, cm⁻¹). Elemental analyses were performed with a Perkin-Elmer 240 analyser. Mass spectra were obtained 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*) or (*E*)-chloroenynes **4b and **4d**:** To a solution of PdCl₂(PPh₃)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 diethylether (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 NH₄Cl solution (25 mL). The aqueous layer was extracted with diethylether (3 x 20 mL), the combined organic layers were washed successively with aqueous HCl (0.2 M, 15 mL), NaHCO₃ (10 mL) and H₂O (2 x 25 mL), dried over MgSO₄ 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.90 (s, 3H, CH₃), 6.14 (d, *J* = 7.4 Hz, 1H, *H*_{vinyl}), 6.42 (d, *J* = 7.4 Hz, 1H, *H*_{vinyl}), 6.89 (d, *J* = 8.2 Hz, 1H, *H*_{arom}), 6.93 (dd, *J* = 0.8, 7.5 Hz, 1H, *H*_{arom}), 7.29-7.34 (m, 1H, *H*_{arom}), 7.47 (dd, *J* = 7.5, 1.7 Hz, 1H, *H*_{arom}). ¹³C NMR (CDCl₃,

75MHz): δ = 56.0 (CH₃), 87.5 (Cq), 94.0 (Cq), 110.9 (CH), 112.1 (Cq), 112.6 (CH), 120.7 (CH), 128.0 (CH), 130.4 (CH), 133.9 (CH), 160.1 (Cq). IR (neat, ν_{max}/cm⁻¹): 2201, 1578, 1489, 1433, 1264, 1119. MS (APCI+) *m/z* 193.0 (M+H)⁺. C₁₁H₉ClO (192.64) : calc. C, 68.58; H, 4.71; found C, 68.40; H, 4.61.

(*Z*)-1-(2-Carboethoxyphenyl)-4-chlorobut-3-en-1-yne (4d**):** (2.85 g, 61%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 1.39 (t, *J* = 7.1 Hz, 3H, CH₃), 4.39 (q, *J* = 7.1 Hz, 2H, CH₂), 6.15 (d, *J* = 7.4 Hz, 1H, *H*_{vinyl}), 6.46 (d, *J* = 7.4 Hz, 1H, *H*_{vinyl}), 7.36-7.41 (m, 1H, *H*_{arom}), 7.44-7.49 (m, 1H, *H*_{arom}), 7.61 (d, *J* = 7.6 Hz, 1H, *H*_{arom}), 7.95 (d, *J* = 7.8 Hz, 1H, *H*_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 14.3 (CH₃), 27.0 (CH₂), 88.1 (Cq), 96.2 (Cq), 112.4 (CH), 123.1(Cq), 128.5 (CH), 128.8 (CH), 130.4 (CH), 131.7 (CH), 132.2 (Cq), 134.7 (CH), 166.2 (Cq). IR (neat, ν_{max}/cm⁻¹): 1709, 1598, 1482, 1366, 1249, 1130, 1080. MS (APCI+) *m/z* 235.0 (M+H)⁺. C₁₃H₁₁ClO₂ (234.68) : calc. C, 66.53; H, 4.72; found C, 66.35; H, 4.52.

Synthesis of (*E*)-chloroenynes **4a**

(*E*)-4-Chloro-1-(2-methoxyphenyl)but-3-en-1-yne (4a**):** the same procedure was used as described for (*Z*)-chloroenynes, except that piperidine was used as a base instead of *n*-butylamine. (3.04 g, 79%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 3.88 (s, 3H, CH₃), 6.20 (d, *J* = 13.6 Hz, 1H, *H*_{vinyl}), 6.63 (d, *J* = 13.6 Hz, 1H, *H*_{vinyl}), 6.88 (d, *J* = 8.1 Hz, 1H, *H*_{arom}), 6.92 (dd, *J* = 0.8, 7.5 Hz, 1H, *H*_{arom}), 7.27-7.33 (m, 1H, *H*_{arom}), 7.39 (dd, 1H, *J* = 1.6, 7.5 Hz, *H*_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 55.8 (CH₃), 88.4 (2Cq), 110.7 (CH), 111.8 (Cq), 114.2 (CH), 120.6 (CH), 129.9 (CH), 130.3 (CH), 133.6 (CH), 159.9 (Cq). IR (neat, ν_{max}/cm⁻¹): 1598, 1489, 1435, 1243, 1119, 1022. (M+H)⁺. MS (APCI+) *m/z* 193.0 (M+H)⁺. C₁₁H₉ClO (192.64) : calc. 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 (4mL) and EtOH (2 mL), were successively added the desired boronic acid (1.2 mmol), K₂CO₃ (2 mmol) and Pd(PPh₃)₄ (0.05 mmol). The reaction 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 10 mL of water were added. After extraction with CH₂Cl₂ (3 x 10 mL), the combined organic layers were dried over MgSO₄ 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**):** (248 mg, 94%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 3.72 (s, 3H, CH₃), 3.81 (s, 3H, CH₃), 6.22 (d, *J* = 16.2 Hz, 1H, *H*_{vinyl}), 6.76-6.80 (m, 3H, *H*_{arom}), 6.84 (d, *J* = 7.5 Hz, 1H, *H*_{arom}), 6.92 (d, *J* = 16.2 Hz, 1H, *H*_{vinyl}), 7.16-7.21 (m, 1H, *H*_{arom}), 7.27 (d, *J* = 8.8 Hz, 2H, *H*_{arom}), 7.35 (dd, *J* = 1.6, 7.5 Hz, 1H, *H*_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 55.4 (CH₃), 55.9 (CH₃), 87.4 (Cq), 93.4 (Cq), 106.2 (CH), 110.7 (CH), 112.9 (Cq), 114.3 (2CH), 120.6 (CH), 127.7 (2CH), 129.5 (Cq), 129.6 (CH), 133.5 (CH), 140.7 (CH), 159.9 (Cq), 160.1 (Cq). IR (neat, ν_{max}/cm⁻¹): 2933, 1601, 1492, 1434, 1245, 1174, 1019. MS (APCI+) *m/z* 265.0 (M+H)⁺. C₁₈H₁₆O₂ (264.32) : calc. 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**):** (201 mg, 76%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 3.84 (s, 3H, CH₃), 3.95 (s, 3H, CH₃), 5.86 (d, *J* = 11.9 Hz, 1H, *H*_{vinyl}), 6.62 (d, 1H, *J* = 11.9 Hz, *H*_{vinyl}), 6.90-6.93 (m, 3H, *H*_{arom}), 6.96 (dd, 1H, *J* = 1.0, 7.5 Hz, *H*_{arom}), 7.31 (ddd, *J* = 1.7, 7.5, 8.3 Hz, 1H, *H*_{arom}), 7.45 (dd, *J* = 1.7, 7.5 Hz 1H, *H*_{arom}), 8.03 (d, *J* = 8.7 Hz, 2H, *H*_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 55.4 (CH₃), 56.0 (CH₃), 92.3 (Cq), 92.9 (Cq), 105.2 (CH), 110.7 (CH), 113.0 (Cq), 113.7 (2CH), 120.7 (CH), 129.8 (CH), 129.9 (Cq), 130.5 (2CH), 133.3 (CH), 137.8 (CH), 159.8 (Cq), 160.2 (Cq). IR

(neat, $\nu_{\max}/\text{cm}^{-1}$): 1603, 1509, 1461, 1253, 1172, 1115, 1024. MS (APCI+) m/z 265.0 (M+H)⁺. C₁₈H₁₆O₂ (264.32) : calc. C, 81.79; H, 6.10; found C, 81.74; H, 6.05.

(E)-4-(4-Methoxyphenyl)-1-phenylbut-3-en-1-yne (1c): (185 mg, 79%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 3.83 (s, 3H, CH₃), 6.25 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.88 (d, J = 8.7 Hz, 2H, H_{arom}), 7.00 (d, J = 16.2, 1H, H_{vinyl}), 7.31-7.33 (m, 3H, H_{arom}), 7.37 (d, J = 8.7 Hz, 2H, H_{arom}), 7.45-7.48 (m, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 55.5 (CH₃), 89.39 (Cq), 91.1 (Cq), 105.8 (CH), 114.3 (2CH), 123.7 (Cq), 127.8 (2CH), 128.1 (CH), 128.4 (2CH), 129.3 (Cq), 131.6 (2CH), 141.0 (CH), 160.2 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1023, 1175, 1251, 1441, 1487, 1509, 1601. MS (APCI+) m/z 235.0 (M+H)⁺. C₁₇H₁₄O (234.29) : calc. C, 87.15; H, 6.02; found C, 87.01; H, 5.93.

(Z)-1-(2-Carboethoxyphenyl)-4-(4-methoxyphenyl)but-3-en-1-yne (1d): (254 mg, 83%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 1.36 (t, J 7.1 Hz, 3H, CH₃), 3.83 (s, 3H, CH₃), 4.37 (q, J = 7.1 Hz, 2H, CH₂), 5.87 (d, J = 11.9 Hz, 1H, H_{vinyl}), 6.67 (d, J = 11.9 Hz, 1H, H_{vinyl}), 6.91 (d, J 8.8 Hz, 2H, H_{arom}), 7.34-7.40 (m, 1H, H_{arom}), 7.46-7.51 (m, 1H, H_{arom}), 7.59 (dd, J = 1.2, 7.7 Hz, 1H, H_{arom}), 7.94-7.99 (m, 3H, H_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 14.3 (CH₃), 55.4 (CH₃), 61.3 (CH₂), 93.6 (Cq), 94.3 (Cq), 105.0 (CH), 113.8 (2CH), 124.1 (Cq), 127.9 (CH), 129.6 (Cq), 130.5 (3CH), 131.7 (CH), 132.0 (Cq), 134.1 (CH), 138.8 (CH), 159.9 (Cq), 166.4 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1721, 1604, 1510, 1248, 1172, 1079, 1031. MS (APCI+) m/z 307.0 (M+H)⁺. C₂₀H₁₈O₃ (306.36) : calc. C, 78.41; H, 5.92; found C, 78.35; H, 5.87.

(E)-1-(4-Methoxyphenyl)non-1-en-3-yne (1e) : (185 mg, 81%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 0.91 (t, J = 7.1 Hz, 3H, CH₃), 1.31-1.46 (m, 4H, 2CH₂), 1.57 (m, 2H, CH₂), 2.33-2.38 (m, 2H, CH₂), 3.81 (s, 3H, CH₃), 6.02 (dt, 1H, J = 2.2, 16.2 Hz, H_{vinyl}), 6.79-6.86 (m, 3H, H_{vinyl} , H_{arom}), 7.30 (d, J = 8.5 Hz, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 14.1 (CH₃), 19.8 (CH₂), 22.4 (CH₂), 28.7 (CH₂), 31.3 (CH₂), 55.4 (CH₃), 80.0 (Cq), 92.3 (Cq), 106.6 (CH), 114.2 (2CH), 127.4 (2CH), 129.6 (Cq), 139.6 (CH), 159.9 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 2928, 1605, 1510, 1463, 1246, 1174, 1033. MS (APCI+) m/z 229.0 (M+H)⁺. C₁₆H₂₀O (228.33) : calc. C, 84.16; H, 8.83; found C, 84.12; H, 8.77.

(Z)-1-(4-Methoxyphenyl)non-1-en-3-yne (1f) : (189 mg, 83%). Yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 0.93 (t, J = 7.1 Hz, 3H, CH₃), 1.30-1.50 (m, 4H, 2CH₂), 1.56-1.67 (m, 2H, CH₂), 2.41-2.47 (m, 2H, CH₂), 3.83 (s, 3H, CH₃), 5.58 (dt, 1H, J 2.5, 11.9 Hz, H_{vinyl}), 6.49 (d, 1H, J = 11.9 Hz, H_{vinyl}), 6.87 (d, J = 8.8 Hz, 2H, H_{arom}), 7.84 (d, J = 8.8 Hz, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 14.2 (CH₃), 20.0 (CH₂), 22.4 (CH₂), 28.5 (CH₂), 31.3 (CH₂), 55.4 (CH₃), 79.5 (Cq), 97.3 (Cq), 105.9 (CH), 113.6 (2CH), 129.9 (Cq), 130.0 (2CH), 136.8 (CH), 159.5 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 2931, 1605, 1510, 1463, 1304, 1254, 1175, 1033. MS (APCI+) m/z 229.0 (M+H)⁺. C₁₆H₂₀O (228.33) : calc. C, 84.16; H, 8.83; found C, 84.05; H, 8.69.

(E)-1,4-di-(2-Methoxyphenyl)but-3-en-1-yne (1g): Yellow oil. (224 mg, 85%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.77 (s, 3H, CH₃), 3.82 (s, 3H, CH₃), 6.45 (d, J = 16.4 Hz, 1H, H_{vinyl}), 6.78-6.87 (m, 4H, H_{arom}), 7.15 (dd, J = 1.6, 7.2 Hz, 1H, H_{arom}), 7.20 (dd, J = 1.7, 7.4 Hz, 1H, H_{arom}), 7.28 (d, J = 16.4 Hz, 1H, H_{vinyl}), 7.34-7.38 (m, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75MHz): δ = 55.6 (CH₃), 55.9 (CH₃), 87.7 (Cq), 93.9 (Cq), 109.1 (CH), 110.7 (CH), 111.1 (CH), 112.9 (Cq), 120.6 (CH), 120.8 (CH), 125.6 (Cq), 126.9 (CH), 129.6 (2CH), 133.6 (CH), 136.5 (CH), 157.1 (Cq), 159.9 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 2933, 1593, 1485, 1434, 1241, 1119, 1024. MS (APCI+) m/z 265.0 (M+H)⁺. C₁₈H₁₆O₂ (264.32) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.91 (s, 3H, CH₃), 5.98 (s, 2H, CH₂), 6.27 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.78 (d, J = 8.0 Hz, 1H, H_{arom}), 6.85-7.00 (m, 5H, vinyl, arom), 7.26-7.32 (m, 1H, H_{arom}), 7.44 (dd, J = 1.7, 7.5 Hz, 1H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ = 56.0 (CH₃), 87.8 (Cq), 93.2 (Cq), 101.4 (CH₂), 105.3 (CH), 106.7 (CH), 108.6 (CH), 110.7 (CH), 112.8 (Cq), 120.6 (CH), 121.8 (CH), 129.7 (CH), 131.2 (Cq), 133.6 (CH), 140.8 (CH), 148.2 (Cq), 148.3 (Cq), 159.9 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1591, 1488, 1237, 1117, 1025, 925, 790, 739. MS (APCI+) m/z 279.0 (M+H)⁺. C₁₈H₁₄O₃ (278.30) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.93 (s, 3H, CH₃), 6.58 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.89-6.97 (m, 2H, H_{arom}), 7.23 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.28-7.34 (m, 1H, H_{arom}), 7.46-7.49 (m, 3H, H_{arom} , H_{naph}), 7.62 (dd, J = 1.6, 8.6 Hz, 1H, H_{naph}), 7.78-7.84 (m, 4H, H_{naph}). ¹³C NMR (CDCl₃, 75 MHz): δ = 56.0 (CH₃), 88.6 (Cq), 93.3 (Cq), 108.9 (CH), 110.7 (CH), 112.7 (Cq), 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 (Cq), 133.7 (CH), 134.1 (2Cq), 141.2 (CH), 160.0 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1589, 1490, 1462, 1433, 1270, 1118, 1025. MS (APCI+) m/z 285.0 (M+H)⁺. C₂₁H₁₆O (284.35) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.91 (s, 3H, CH₃), 6.42 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.88-6.96 (m, 2H, H_{arom}), 7.00 (d, J 16.2 Hz, 1H, H_{vinyl}), 7.27-7.36 (m, 5H, H_{arom}), 7.43-7.46 (m, 1H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ = 56.0 (CH₃), 88.8 (Cq), 92.7 (Cq), 109.3 (CH), 110.7 (CH), 112.5 (Cq), 120.7 (CH), 127.6 (2CH), 129.1 (2CH), 130.0 (CH), 133.6 (CH), 134.3 (Cq), 135.1 (Cq), 139.7 (CH), 160.0 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1591, 1489, 1432, 1240, 1122, 1026. MS (APCI+) m/z 269.0 [(M+H)⁺ Cl³⁵], 271.0 [(M+H)⁺ Cl³⁷]. C₁₇H₁₃ClO (268.74) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 2.59 (s, 3H, CH₃), 3.91 (s, 3H, CH₃), 6.56 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.88-6.96 (m, 2H, H_{arom}), 7.06 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.28-7.34 (m, 1H, H_{arom}), 7.44 (dd, J = 1.7, 7.7 Hz, 1H, H_{arom}), 7.48 (d, J = 8.3 Hz, 2H, H_{arom}), 7.91 (d, J = 8.3 Hz, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ = 26.7 (CH₃), 55.9 (CH₃), 90.1 (Cq), 92.7 (Cq), 110.8 (CH), 111.6 (CH), 112.4 (Cq), 120.7 (CH), 126.4 (2CH), 129.0 (2CH), 130.2 (CH), 133.7 (CH), 136.7 (Cq), 139.6 (CH), 141.1 (Cq), 160.1 (Cq), 197.4 (Cq). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 2195, 1676, 1598, 1490, 1357, 1256, 1180. MS (APCI+) m/z 277.0 (M+H)⁺. C₁₉H₁₆O₂ (276.33) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.91 (s, 3H, CH₃), 6.60 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.89-6.96 (m, 2H, H_{arom}), 7.07 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.29-7.35 (m, 1H, H_{arom}), 7.45 (dd, J = 1.3, 7.5 Hz, 1H, H_{arom}), 7.55 (d, J = 8.1 Hz, 2H, H_{arom}), 7.84 (d, J = 8.1 Hz, 2H, H_{arom}), 9.98 (s, 1H, CHO). ¹³C NMR (CDCl₃, 75 MHz): δ = 56.0 (CH₃), 90.6 (Cq), 92.6 (Cq), 110.8 (CH), 112.3 (CH), 120.7 (CH), 126.8 (2CH), 130.3 (3CH), 133.7 (CH), 136.0 (Cq), 139.5 (CH), 142.4 (Cq), 160.1 (Cq), 191.1 (CH). IR (neat, $\nu_{\max}/\text{cm}^{-1}$): 1693, 1597, 1490, 1434, 1212, 1165, 1024. MS (APCI+) m/z 263.0 (M+H)⁺. C₁₈H₁₄O₂ (262.30) : calc. 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%). ¹H NMR (CDCl₃, 300 MHz): δ = 3.91 (s, 3H, CH₃), 6.58 (d, J = 16.2 Hz, 1H, H_{vinyl}), 6.89-6.96 (m, 2H, H_{arom}), 7.07 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.29-7.35 (m, 1H, H_{arom}), 7.45 (dd, J =

1.2, 7.6 Hz, 1H, H_{arom}), 7.47-7.53 (m, 1H, H_{arom}), 7.70 (d, $J = 7.8$ Hz, 1H, H_{arom}), 8.09-8.13 (m, 1H, H_{arom}), 8.25 (s, 1H, H_{arom}). ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 55.9$ (CH_3), 90.3 (Cq), 92.0 (Cq), 110.8 (CH), 112.0 (CH), 112.2 (Cq), 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 (Cq), 148.8 (Cq), 160.1 (Cq). IR (neat, $\nu_{\text{max}}/\text{cm}^{-1}$): 1601, 1529, 1422, 1330, 1238, 1117, 1022. MS (APCI+) m/z 280.0 ($\text{M}+\text{H}^+$). $\text{C}_{17}\text{H}_{13}\text{NO}_3$ (279.29) : calc. 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%). ^1H NMR (CDCl_3 , 300 MHz): $\delta = 3.91$ (s, 3H, CH_3), 6.29 (d, $J = 16.1$ Hz, 1H, H_{vinyl}), 6.88-6.95 (m, 2H, H_{arom}), 7.06 (d, $J = 16.1$ Hz, 1H, H_{vinyl}), 7.25-7.32 (m, 4H, H_{arom}), 7.44 (dd, $J = 1.7$, 7.5 Hz, 1H, H_{arom}). ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 56.0$ (CH_3), 88.1 (Cq), 93.0 (Cq), 108.4 (CH), 110.7 (CH), 112.8 (Cq), 120.6 (CH), 123.6 (CH), 124.6 (CH), 126.6 (CH), 129.8 (CH), 133.6 (CH), 135.1 (CH), 139.5 (Cq), 159.9 (Cq). IR (neat, $\nu_{\text{max}}/\text{cm}^{-1}$): 1591, 1489, 1433, 1272, 1238, 1161, 1118. MS (APCI+) m/z 241.0 ($\text{M}+\text{H}^+$). $\text{C}_{15}\text{H}_{12}\text{OS}$ (240.32) : calc. 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%). ^1H NMR (CDCl_3 , 300 MHz): $\delta = 0.91$ (t, $J = 7.3$ Hz, 3H, CH_3), 1.44 (m, $J = 7.3$ Hz, 2H, CH_2), 2.07-2.14 (m, 2H, CH_2), 3.88 (s, 3H, CH_3), 5.74-5.87 (m, 2H, H_{vinyl}), 6.14 (dd, $J = 10.3$, 14.9 Hz, 1H, H_{vinyl}), 6.68 (dd, $J = 10.8$, 15.4 Hz, 1H, H_{vinyl}), 6.86 (d, $J = 7.6$ Hz, 1H, H_{arom}), 6.91 (dd, 1H, $J = 0.9$, 7.5 Hz, H_{arom}), 7.23-7.29 (m, 1H, H_{arom}), 7.38 (dd, $J = 1.6$, 7.5 Hz, 1H, H_{arom}). ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 13.8$ (CH_3), 22.4 (CH_2), 35.0 (CH_2), 55.9 (CH_3), 87.6 (Cq), 93.4 (Cq), 109.2 (CH), 110.7 (CH), 112.9 (Cq), 120.6 (CH), 129.6 (CH), 130.2 (CH), 133.5 (CH), 138.0 (CH), 142.2 (CH), 159.8 (Cq). IR (neat, $\nu_{\text{max}}/\text{cm}^{-1}$): 2958, 2192, 1679, 1593, 1491, 1434, 1267, 1119. MS (APCI+) m/z 227.0 ($\text{M}+\text{H}^+$). $\text{C}_{16}\text{H}_{18}\text{O}$ (226.31) : calc. 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%). ^1H NMR (CDCl_3 , 300 MHz): $\delta = 3.89$ (s, 3H, CH_3), 5.53 (dd, 1H, $J = 2.1$, 11.1, H_{vinyl}), 5.75 (dd, $J = 2.1$, 17.5 Hz, 1H, H_{vinyl}), 6.08 (dd, $J = 11.1$, 17.5 Hz, 1H, H_{vinyl}), 6.86-6.93 (m, 2H, H_{arom}), 7.26-7.32 (m, 1H, H_{arom}), 7.42 (dd, $J = 1.6$, 7.5 Hz, 1H, H_{arom}). ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 55.9$ (CH_3), 86.4 (Cq), 92.3 (Cq), 110.7 (CH), 112.4 (Cq), 117.6 (CH), 120.6 (CH), 126.8 (CH_2), 129.9 (CH), 133.7 (CH), 160.0 (Cq). IR (neat, $\nu_{\text{max}}/\text{cm}^{-1}$): 1595, 1491, 1434, 1263, 1181, 1119, 1021. MS (APCI+) m/z 159.0 ($\text{M}+\text{H}^+$). $\text{C}_{11}\text{H}_{10}\text{O}$ (158.20) : calc. 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%). ^1H NMR (CDCl_3 , 300 MHz): δ 1.09 (t, 3H, $J = 7.1$ Hz, CH_3), 2.44 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 4.07 (q, 2H, $J = 7.1$ Hz, CH_2), 6.87 (d, 2H, $J = 8.6$ Hz, H_{arom}), 7.19 (d, 2H, $J = 8.6$ Hz, H_{arom}), 7.32-7.34 (m, 3H, H_{Ph}), 7.49-7.52 (m, 2H, H_{Ph}). ^{13}C NMR (CDCl_3 , 75 MHz): δ 14.0 (CH_3), 24.4 (CH_3), 55.4 (CH_3), 61.2 (CH_2), 86.0 (Cq), 95.9 (Cq), 113.7 (2CH), 123.4 (Cq), 128.5 (5CH), 131.6 (2CH), 133.7 (Cq), 154.6 (Cq), 159.8 (Cq), 166.5 (Cq). IR (neat, $\nu_{\text{max}}/\text{cm}^{-1}$): 1719, 1605, 1510, 1324, 1248, 1178, 1109, 1031, 832. MS (APCI+) m/z 321.0 ($\text{M}+\text{H}^+$). $\text{C}_{21}\text{H}_{20}\text{O}_3$ (320.38) : calc. C, 78.73; H, 6.29; found C, 78.51; H, 6.10.

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