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Palladium-catalyzed acylation and/or homo-coupling of aryl- and alkyl-acetylenes

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ABSTRACT

Allyl or benzyl halides, through a Pd(0)-catalyzed reaction and under CO pressure, generate acyl-palladium/halides that, in the presence of a base and an aryl- and alkyl-acetylene, undergo nucleophilic acyl substitution giving conjugated acetylenic ketones. Diynes, resulting from alkyne/alkyne homo-coupling, were instead the main products in reactions performed without allyl or benzyl halides. Moreover, dimerization, trimerization, and cyclotrimerization reactions of acetylenes were observed in reaction carried out even without base.

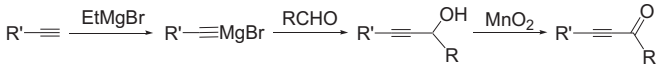
1. Introduction

Alkyne derivatives, such as diynes and conjugated acetylenic ketones, are very interesting molecules in organic chemistry.

In particular diynes are a class of compounds that have an important role in the synthesis of natural products, polymer chemistry, supramolecular chemistry, and materials science because they can be converted into various structural entities.[1–4] In the past years, several groups have developed homo-coupling reactions of alkynes using various catalytic systems. An oxidative alkyne/alkyne homo-coupling reaction is one of the most widely used procedures for the synthesis of symmetrical diyne derivatives. Stoichiometric amounts of copper salts[5] or copper salts in catalytic amounts with appropriate nitrogen bases in the presence of molecular oxygen[6] have typically been used for the oxidative alkyne/alkyne homo-coupling reactions. Oishi and co-workers showed that supported copper hydroxide on titanium oxide, $Cu(OH)_x/TiO_2$, acted as an efficient heterogeneous catalyst for the oxidative alkyne/alkyne homo-coupling.[7] Recently, a catalytic system, which used $Fe(acac)_3$ and a trace quantity of $Cu(acac)_2$ as the co-catalyst and air as the oxidant for the homo-coupling of terminal alkynes, has been developed.[8] This catalytic system could also apply to the cross-coupling reaction of two different terminal alkynes.[8]

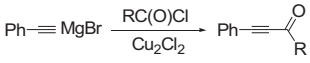
Furthermore, a single example was reported where palladium, in the form of a palladium/iminophosphine complex, was found to catalyze the homo-coupling reaction of alkynylstannanes using allyl acetate as an oxidant.[9]

The synthesis of acetylenic compounds, such as conjugated acetylenic ketones has been rarely reported in the literature. A general method, involving the alkylation of aldehydes with ethynyl magnesium bromides and oxidation of propargylic alcohols to conjugated ketones was used as shown in the Scheme 1.[10]



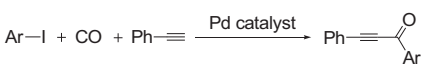
Scheme 1. Alkylation of aldehydes with ethynyl magnesium bromides and oxidation of the corresponding propargylic alcohols.

A direct ketone synthesis method through a nucleophilic substitution on the acyl chloride from ethynyl magnesium bromide in the presence of Cu_2Cl_2 was also described (Scheme 2).[11]



Scheme 2. Nucleophilic substitution on acyl chloride from ethynyl magnesium bromide.

Alternatively, an acylation of terminal alkynes with acyl chlorides, under copper and solvent-free conditions, using polystyrene-supported palladium(0) complex,[12] or a palladium-catalyzed carbonylative coupling of aryl iodides and phenylacetylene using a mutiphase microflow system was re1ported (Scheme 3).[13]



Scheme 3. Palladium-catalyzed carbonylative coupling of aryl iodides and phenylacetylene.

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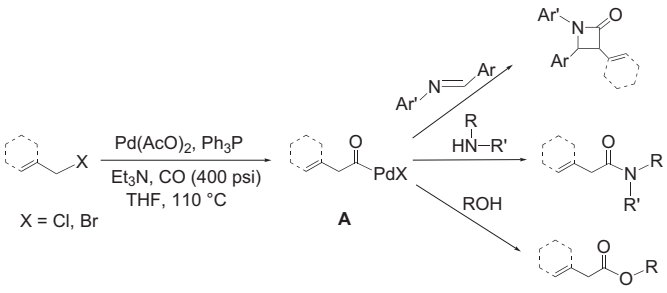
Recently, we have carried out several reactions involving palladium catalysis. A series of different allyl or benzyl halides, through a Pd(0)-catalyzed reaction and under CO pressure, generate an acyl-palladium/halide intermediate (**A**). This last one has led to the synthesis of many differently substituted and functinalized β-lactams in the presence of imines,[14] or amides in the presence of primary or secondary amines.[15] Moreover, esters can be prepared from alcohols and phenols using the same catalytic system (Scheme 4).[16]



Scheme 4. Acyl-palladium/halide in the synthesis of β-lactams, amides and esters.

With the aim of increasing the potential use of the acyl-palladium/halide intermediate **A**, we have considered the possibility of generating it in the presence of terminal alkynes, such as phenylacetylene and the results of this investigation are reported herein.

2. Results and discussion

Phenylacetylene, allyl chloride, $Pd(AcO)_2$, Ph_3P, and Et_3N were dissolved in THF and placed in an autoclave under CO pressure. The reaction mixture was heated at 100 °C for about 6 h. After this time, GC analysis showed the formation of a new product in 41% total yield. Purification by chromatography on silica gel of the crude mixture afforded the acylation product **1a**, *E*-1-phenylhex-4-en-1-yn-3-one, in which the unsaturation was in the more stable position conjugated to the carbonyl group. The homo-coupling product of phenylacetylene, **2a**, was found too. The yield and the product distribution are reported in Table 1 (entry 1). Interestingly, a better transformation yield (94%) and the same ratio (**1a**/**2a** 70:30) were observed with longer reaction times (Table 1, entry 2).

The same trend was found in a similar reaction carried out on phenylacetylene and 3-chloro-2-methylpropene as the halide; after a 36 h period, 5-methyl-1-phenyl-hex-4-en-1-yn-3-one (**1b**) and 1,4-diphenyl-1,3-butadiyne (**2a**) were obtained in 90% total yield (Table 1, entry 3).

In the reaction with allyl chloride, *p*-methoxyphenylacetylene, *p*-cyanophenylacetylene, 1,4-diethynylbenzene, treated under the same conditions, led to the acetylenic ketones with *E* configuration, **1d**, **1f**, **1h**, and trace amounts of the homo-coupling products **2b**, **2c**, and **2d**, respectively (Table 1, entries 5, 7, and 9).

The reactions of terminal alkynes with benzyl chloride proceeded with lower yields than those ones with allyl chloride. Phenylacetylene, *p*-methoxyphenylacetylene, *p*-cyanophenylacetylene, and 1,4-diethynylbenzene, after a reaction time of 20–36 h, were transformed into their corresponding diynes **2a**, **2b**, **2c**, **2d** and into conjugated acetylenic ketones **1c**, **1e**, **1g**, and **1i**, respectively, in only 60–65% total yield (Table 1, entries 4, 6, 8, and 10).

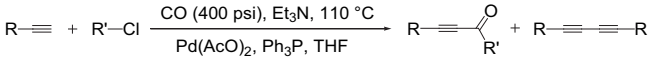
Moreover, we verified that the aforementioned alkynes behaved similarly with allyl and benzyl bromide and, in the absence of significant differences, we considered it unnecessary to report this data.

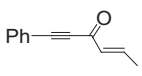
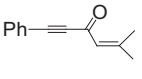
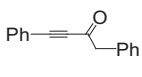
Aliphatic halides (Table 1, entry 11) and picolyl chlorides (Table 1, entries 12 and 13) instead did not lead to acylated compounds, and therefore diyne **2a** was the only product of the reactions. Probably the palladium acyl chloride intermediate is not formed from aliphatic and picolyl halides due to lack of unsaturation in the alpha position, as in the first case, or because of the coordinating effect of pyridine nitrogen, as in the second case.

Furthermore, the alkyl acetylenes reacted with the benzyl chloride under the same reaction conditions. When hex-1-yne and but-1-yne are reacted with benzyl chloride in the same reaction conditions, they form, in 36 h, only the acetylenic ketone **1l** or **1m** with a transformation yield of 30–32%, respectively. Not even traces of the diyne have been observed (Table 1, entries 14 and 15). Probably the decreased acidity of alkyl acetylenic hydrogen respect to aryl acetylenic one could cause the low observed reactivity in alkyne/alkyne homo-coupling.

However the same reactions, performed in a more polar solvent (CH_3CN) and with a stronger base than Et_3N, such as NaOH, led to an almost complete disappearance of the starting alkyne giving 1-phenyl-oct-3-yn-2-one **1l** (yield=55%) and 1-phenyl-hex-3-yn-2-one **1m** (yield=45%), respectively (Table 1, entries 16 and 17). Under these conditions, small quantities of homo-coupling products

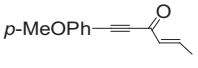
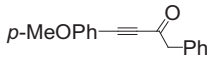
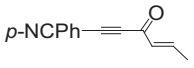
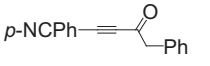
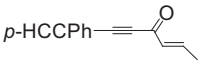
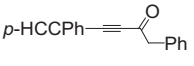
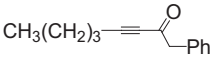
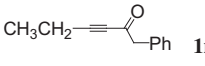
Table 1
Acetylenic ketones and diynes synthesis



Entry	RCCH	R′Cl	Time (h)	Total yield[a] (%)	Products distribution[b] (%)	
					1	**2**
1	PhCCH		6	41	 **1a** (69)	PhCC–CCPh **2a** (31)
2			36	94	**1a** (70)	**2a** (30)
3			36	90	 **1b** (83)	**2a** (17)
4		$PhCH_2Cl$	36	65	 **1c** (59)	**2a** (41)

(*continued on next page*)

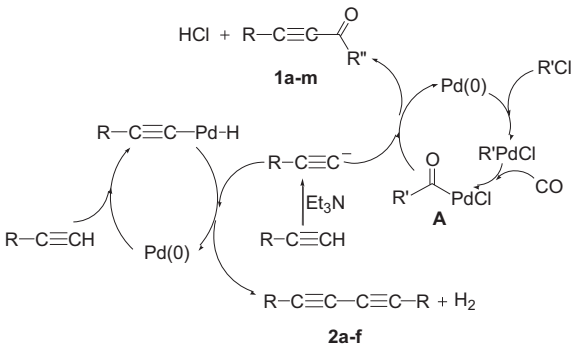
Table 1 (*continued*)

Entry	RCCH	R′Cl	Time (h)	Total yield[a] (%)	Products distribution[b] (%)	
					1	**2**
5	*p*-MeOPhCCH		36	85	 **1d** (98)	MeOPhCC–CCPhOMe **2b** (2)
6		$PhCH_2Cl$	36	60	 **1e** (90)	**2b** (10)
7	*p*-NCPhCCH		36	80	 **1f** (99)	NCPhCC–CCPhCN **2c** (1)
8		$PhCH_2Cl$	36	63	 **1g** (85)	**2c** (15)
9	*p*-HCCPhCCH		20	88	 **1h** (95)	HCCPhCC–CCPhCCH **2d** (5)
10		$PhCH_2Cl$	20	60	 **1i** (80)	**2d** (20)
11	PhCCH	CH_3CH_2Cl	14	99	—	**2a** (100)
12		2-$PyCH_2Cl$	14	99	—	**2a** (100)
13		4-$PyCH_2Cl$	14	99	—	**2a** (100)
14	$CH_3(CH_2)_3CCH$	$PhCH_2Cl$	36	30	 **1l** (100)	—
15	CH_3CH_2CCH	$PhCH_2Cl$	36	32	 **1m** (100)	—
16[c]	$CH_3(CH_2)_3CCH$	$PhCH_2Cl$	10	95	**1l** (55)	$CH_3(CH_2)_3CC–CC(CH_2)_3CH_3$ **2e** (5)
17[c]	CH_3CH_2CCH	$PhCH_2Cl$	10	95	**1m** (45)	$CH_3CH_2CC–CCCH_2CH_3$ **2f** (5)

[a] Yield measured by GC analysis on the basis of the converted starting acetylene.
[b] Product distribution measured by GC analysis or isolation of the product.
[c] Reaction conditions: CH_3CN as solvent and NaOH as base. Benzyl alcohol, 1-phenylhept-2-yne and phenylacetic acid were identified in the mixture, too.

2e and **2f** together with other compounds resulting from nucleophilic substitution of OH^- on the benzyl chloride, such as benzyl alcohol, 1-phenylhept-2-yne, and phenylacetic acid were identified in the mixture, too.

According to our results, two possible mechanisms for Pd-catalyzed acylation and homo-coupling reaction of terminal acetylenes were proposed (Scheme 5).



Scheme 5. Suggested mechanism for acetylenic ketones and diynes synthesis.

With the aid of the base (Et_3N), terminal acetylene could lead to the formation of acetylide anion. The next reaction with the palladium acyl chloride intermediate (**A**) would release the conjugated acetylenic ketone (**1a**–**m**) and generate Pd(0).

Acetylide anion could also react with a second Pd-activated molecule of alkyne to afford the homo-coupling product (**2a**–**f**).

According to the suggested mechanism, carbon monoxide, allyl and/or benzyl chloride seems unnecessary for the alkyne/alkyne homo-coupling reaction. For this reason, we have performed different reactions without them. The results of this investigation are summarized in Table 2.

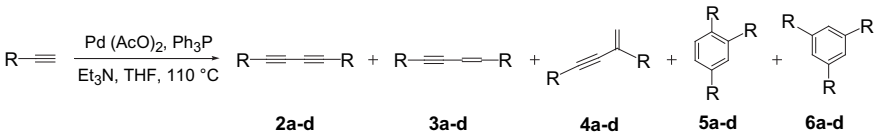
In particular, a solution of phenylacetylene, $Pd(AcO)_2$, PPh_3, and Et_3N in THF heated at 110 °C, after a 6 h period, provided 1,4-diphenyl-1,3-butadiyne **2a**, as shown in Scheme 5, together with other products derived from dimerization (**3a**, **4a**) and asymmetrical and symmetrical cyclotrimerization (**5a**, **6a**), Table 2, entry 1.

Even *p*-methoxyphenylacetylene behaved similarly. The homo-coupling, dimerization and cyclotrimerization products, **2b**, **3b**, **4b**, **5b**, and **6b** were formed, respectively, under the same conditions (Table 2, entry 2).

Hex-1-yne produced different results affording only dimeric enynes **3d**, **4d** and cyclotrimers **5d**, **6d**. No homo-coupling product was observed in this reaction, probably due to a lower acidity of the acetylenic proton (Table 2, entry 4). Several new approaches to the rhodium catalyzed dimerization[17] and cobalt catalyzed cyclotrimerization of alkynes have been reported recently.[18]

The importance of the acetylide anion formation to obtain the diyne was put in evidence carrying out the same reactions

Table 2
1,3-Diynes, 1,3-enynes, and tri-substituted benzenes synthesis



Entry	RCCH	Time (h)	Total yield[a] (%)	Products distribution[a] (%)				
				2	**3**	**4**	**5**	**6**
1	PhCCH	6	95	**2a** (55)	**3a** (35)	**4a** (2)	**5a** (5)	**6a** (3)
2	*p*-MeOPhCCH	6	90	**2b** (48)	**3b** (35)	**4b** (6)	**5b** (8)	**6b** (3)
3	*p*-HCCPhCCH	6	98	Mixture of polymers and traces of **2c**–**6c** identified only by GC–MS[c]				
4	$CH_3(CH_2)_3CCH$	15	40	—	**3d** (40)	**4d** (30)	**5d** (15)	**6d** (15)
5[b]	PhCCH	6	90	—	**3a** (55)	**4a** (8)	**5a** (28)	**6a** (9)
6[b]	*p*-MeOPhCCH	6	79	—	**3b** (55)	**4b** (10)	**5b** (25)	**6b** (10)
7[b]	*p*-HCCPhCCH	6	98	Mixture of polymers and traces of **2c**–**6c** identified only by GC–MS[c]				

[a] Yield and product distribution measured by GC analysis.
[b] Reactions performed without Et_3N.
[c] The mixture of polymers observed is due to the dimerization and trimerization of the starting materials on both sides of the molecules.

described above without Et_3N. In all these cases, the homo-coupling product was not found (Table 2, entries 5 and 6).

Analyzing the collected data we hypothesize that the activated complex R–CC–Pd–H can be added to a second molecule of acetylene generating the enynes **3a**–**d** and **4a**–**d**. These last ones, through the catalysis of palladium, can further add a third molecule of alkyne generating the two possible tri-substituted benzenes **5a**–**d** and **6a**–**d**, asymmetrical and symmetrical, respectively. In addition, trace amounts of liner trimers were detected by GC–MS analysis of the reaction mixture.

Finally, a distinctive trend was found in similar reactions carried out on 1,4-diethynylbenzene with two acetylenic groups. Dimerization and subsequent trimerization on both sides of the molecule resulted in a mixture of high molecular weight polymers, both in the presence (Table 2, entry 3) and absence of Et_3N (Table 2, entry 7). These polymers are currently analyzed in terms of structure and their properties will be evaluated.

3. Conclusions

In conclusion, we have discovered a simple and efficient method for transforming terminal acetylenes into conjugated acetylenic ketones, 1,3-diynes, 1,3-enynes, asymmetrical, and symmetrical tri-substituted benzenes. The ability to modulate the formation of the various unsaturated compounds, depending on the reaction conditions, makes this synthetic methodology employable for a number of applications involving polymer chemistry, supramolecular chemistry and materials science.

4. Experimental section

4.1. General

Triethylamine, palladium(II) acetate, triphenylphosphine, phenylacetylene, *p*-methoxyphenylacetylene, *p*-cyanophenylacetylene, and 1,4-diethynylbenzene, hex-1-yne, but-1-yne, allyl chloride and bromide, benzyl chloride and bromide, 3-chloro-2-methylpropene, chloroethane, 2-chloromethylpyridine, 4-chloromethylpyridine, acetonitrile, and NaOH were of commercial grade (Aldrich) and used without further purification. THF was purified by distillation from sodium before use. Petroleum ether refers to the 40–60 °C boiling fraction. The ^1H and the ^{13}C NMR spectra were recorded with a Bruker Avance 400 apparatus (400.13 and 100.62 MHz, for ^1H and ^{13}C, respectively) with $CDCl_3$ as the solvent and TMS as an internal standard (δ=7.26 ppm for ^1H spectra; δ=77.0 ppm for ^{13}C spectra). The IR spectra were recorded with an FT-IR spectrophotometer Digilab Scimitar Series FTS 2000. GC–MS analyses were performed with an Agilent Technologies 6850 series II gas chromatograph (5% phenyl-polymethylsiloxane capillary column, 30 m, 0.25 mm i.d.), equipped with a 5973 Network mass-selective detector operating at 70 eV. The electrospray ionization [HRMS (ESI)] experiments were carried out in a hybrid QqTOF mass spectrometer (PE SCIEX–QSTAR) equipped with an ion-spray ionization source. MS (+) spectra were acquired by direct infusion (5 μL min^{-1}) of a solution containing the appropriate sample (10 pmol μL^{-1}) dissolved in a solution 0.1% acetic acid, methanol/water (50:50) at the optimum ion voltage of 4800 V. The nitrogen gas flow was set at 30 psi (pounds per square inch) and the potentials of the orifice, the focusing ring and the skimmer were kept at 30, 50 and 25 V relative to ground, respectively. Melting points were determined with an Electrothermal melting point apparatus and are uncorrected. TLC was performed on Merck silica gel plates with F-254 indicator; viewing was by UV light (254 nm). Column chromatographies were performed on silica gel (63–200 mm) using petroleum ether/diethyl ether (Et_2O) mixture as eluent. All reactions involving air-sensitive reagents were performed under an atmosphere of nitrogen in oven-dried glassware by using syringe/septum cap techniques.

4.2. General procedure for the palladium-catalyzed acylation and homo-coupling reaction of terminal alkynes

A solution of terminal alkyne (1.0 mmol), aliphatic or aryl halide (1.5 mmol), $Pd(AcO)_2$ (4 mg, 0.02 mmol), PPh_3 (21 mg, 0.08 mmol), and Et_3N (202 mg, 2.0 mmol) in THF (15 mL) was placed in a 45 mL autoclave. The autoclave was purged, pressurized (400 psi CO) and then heated at 110 °C, under magnetic stirring, for 6–36 h. After this time, the solution was cooled to room temperature and the solvent was removed under reduced pressure to give a crude material. The crude mixture was then purified by chromatography on silica gel (petroleum ether/Et_2O 90:10) to afford, for each reaction shown in Table 1, the conjugated acetylenic ketone **1a**–**m** and the corresponding diyne of the terminal alkyne **2a**–**f** as pure compounds. The compounds **1c**, **2a**, **2e**, and **2f** are commercially available. The compounds **1a**,[19] **1l**,[20] **1m**,[21] **2b**,[22] **2c**,[23] and **2d**,[24] are known and their characterization data resulted in agreement with those reported in literature. The

acetylenic ketones **1b**, and **1d–i** are unknown and their full characterization is reported below.

*4.2.1. E-1-Phenylhex-4-en-1-yn-3-one (**1a**).* Known product, the following characterization data are in agreement with those reported in the literature.[19] Yield: 49 mg (29%), yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.54; ^1H NMR (400.13 MHz, $CDCl_3$): δ=2.02 (3H, dd, J=1.6, 6.9 Hz, CH_3), 6.26 (1H, dq, J=1.6, 15.6 Hz, =CH–C=O), 7.28 (1H, dq, J=6.9, 15.6 Hz, =CH–CH_3), 7.39 (2H, t, J=7.3 Hz, Ph), 7.45 (1H, t, J=7.2 Hz, Ph), 7.59 (2H, d, J=7.1 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=18.5, 86.1, 91.0, 120.1, 128.6, 130.5, 132.8, 133.9, 149.5, 178.3 ppm; FTIR ($CHCl_3$): 3012, 2960, 2854, 2210 (triple bond), 1648 (C=O), 1621, 1310, 1190 cm^{-1}; GC–MS (70 eV): m/z (%)=170 (38) $[M]^+$, 155 (9), 141 (58), 129 (100); HRMS (ESI): calcd for $C_{12}H_{11}O$: (171.0810) $[M+H]^+$; found: (171.0811).

*4.2.2. 5-Methyl-1-phenylhex-4-en-1-yn-3-one (**1b**).* Yield: 138 mg (75%), pale yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.52; ^1H NMR (400.13 MHz, $CDCl_3$): δ=1.96 (3H, s, CH_3), 2.27 (3H, s, CH_3), 6.27 (1H, s, =CH), 7.36 (2H, t, J=7.1 Hz, Ph), 7.42 (1H, t, J=7.1 Hz, Ph), 7.56 (2H, d, J=7.1 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=21.1, 27.8, 89.0, 90.3, 120.4, 126.1, 128.5, 130.3, 132.8, 158.0, 176.4 ppm; FTIR ($CHCl_3$): 3014, 2927, 2860, 2208 (triple bond), 1645 (C=O), 1604, 1269, 1221, 1120, 1048 cm^{-1}; GC–MS (70 eV): m/z (%)=184 (40) $[M]^+$, 179 (6), 102 (20), 129 (100); HRMS (ESI): calcd for $C_{13}H_{13}O$: (185.0967) $[M+H]^+$; found: (188.0966).

*4.2.3. 1,4-Diphenylbut-3-yn-2-one (**1c**).* Product commercially available. Yield: 84 mg (38%), yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.56; ^1H NMR (400.13 MHz, $CDCl_3$): δ=3.94 (2H, s, CH_2), 7.29–7.46 (10H, m, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=52.2, 87.7, 92.9, 119.8, 127.4, 128.1, 128.6, 128.7, 129.8, 130.8, 133.1, 185.2 ppm; FTIR ($CHCl_3$): 3034, 2929, 2859, 2204 (triple bond), 1702 (C=O), 1666 cm^{-1}; GC–MS (70 eV): m/z (%)=220 (12) $[M]^+$, 192 (20), 129 (100), 91 (15); HRMS (ESI): calcd for $C_{16}H_{13}O$: (221.0966) $[M+H]^+$; found: (221.0967).

*4.2.4. E-1-(4-Methoxyphenyl)hex-4-en-1-yn-3-one (**1d**).* Yield: 166 mg (83%), yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.55; ^1H NMR (400.13 MHz, $CDCl_3$): δ=2.02 (3H, dd, J=1.5, 6.9 Hz, =$CHCH_3$), 3.85 (3H, s, OCH_3), 6.26 (1H, dq, J=1.5, 15.6 Hz, COCH), 6.90 (2H, d, J=8.9 Hz, Ph), 7.27 (1H, dq, J=6.9, 15.6 Hz, =$CHCH_3$), 7.56 (2H, d, J=8.9 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=18.1, 55.4, 85.5, 92.5, 113.7, 114.3, 131.2, 134.9, 150.0, 160.0, 172.0 ppm; FTIR ($CHCl_3$): 3009, 2927, 2855, 2210 (triple bond), 1650 (C=O), 1455 cm^{-1}; GC–MS (70 eV): m/z (%)=200 (68) $[M]^+$, 185 (17), 172 (21), 159 (100), 132 (48); HRMS (ESI): calcd for $C_{13}H_{13}O_2$: (201.0916) $[M+H]^+$; found: (201.0914).

*4.2.5. 4-(4-Methoxyphenyl)-1-phenylbut-3-yn-2-one (**1e**).* Yield: 108 mg (54%), pale yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.57; ^1H NMR (400.13 MHz, $CDCl_3$): δ=3.80 (3H, s, OCH_3), 3.90 (2H, s, CH_2), 6.90 (2H, d, J=8.9 Hz, Ph), 7.20–7.56 (7H, m, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=48.1, 56.0, 86.8, 90.6, 114.1, 114.8, 127.1, 129.1, 129.3, 133.1, 135.2, 159.8, 181.0 ppm; FTIR ($CHCl_3$): 3030, 2926, 2860, 2208 (triple bond), 1650 (C=O) cm^{-1}; GC–MS (70 eV): m/z (%)=250 (13) $[M]^+$, 222 (15), 159 (100), 91 (20); HRMS (ESI): calcd for $C_{17}H_{15}O_2$: (251.1073) $[M+H]^+$; found: (251.1076).

*4.2.6. E-4-(3-Oxohex-4-en-1-ynyl)benzonitrile (**1f**).* Yield: 154 mg (79%), yellow solid, mp 127–128 °C (petroleum ether). R_f (petroleum ether/Et_2O 90:10): 0.49; ^1H NMR (400.13 MHz, $CDCl_3$): δ=2.04 (3H, d, J=6.9 Hz, =$CHCH_3$), 6.28 (1H, d, J=15.7 Hz, COCH), 7.30 (1H, dq, J=6.9, 15,7 Hz, =$CHCH_3$), 7.69 (4H, s, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=18.6, 87.8, 88.8, 113.8, 117.9, 125.1, 132.2, 133.1, 133.7, 150.4, 177.6 ppm; FTIR ($CHCl_3$): 3030, 2926, 2856, 2225 (triple bond), 1655 (C=O) cm^{-1}; GC–MS (70 eV): m/z (%)=195 (45) $[M]^+$, 166 (70), 154 (100), 140 (30), 127 (40); HRMS (ESI): calcd for $C_{13}H_{10}NO$: (196.0763) $[M+H]^+$; found: (196.0765).

*4.2.7. 4-(3-Oxo-4-phenylbut-1-ynyl)benzonitrile (**1g**).* Yield: 132 mg (54%), light yellow solid with mp 80–81 °C (n-hexane). R_f (petroleum ether/Et_2O 90:10): 0.45; ^1H NMR (400.13 MHz, $CDCl_3$): δ=3.94 (2H, s, CH_2), 7.29–7.40 (5H, m, Ph), 7.51 (2H, d, J=8.3 Hz, Ph), 7.64 (2H, d, J=8.3 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=52.1, 89.3, 90.0, 114.1, 117.8, 124.6, 127.6, 128.8, 129.8, 132.2, 133.0, 133.3, 184.6 ppm; FTIR ($CHCl_3$): 3027, 2930, 2855, 2223 (triple bond), 1650 (C=O) cm^{-1}; GC–MS (70 eV): m/z (%)=245 (25) $[M]^+$, 217 (70), 203 (40), 154 (100), 91 (60); HRMS (ESI): calcd for $C_{17}H_{12}NO$: (246.0920) $[M+H]^+$; found: (246.0921).

*4.2.8. E-1-(4-Ethynylphenyl)hex-4-en-1-yn-3-one (**1h**).* Yield: 163 mg (84%), orange solid with mp 95–96 °C (n-hexane). R_f (petroleum ether/Et_2O 90:10): 0.46; ^1H NMR (400.13 MHz, $CDCl_3$): δ=2.03 (3H, dd, J=1.5, 6.9 Hz, =$CHCH_3$), 3.24 (1H, s, acetylenic H), 6.26 (1H, dq, J=1.5, 15.6 Hz, COCH), 7.27 (1H, dq, J=6.9, 15.6 Hz, =$CHCH_3$), 7.49 (2H, d, J=8.0 Hz, Ph), 7.54 (2H, d, J=8.0 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=18.5, 80.2, 82.7, 87.6, 89.9, 120.5, 124.3, 132.2, 132.6, 133.8, 149.6, 178.1 ppm; FTIR ($CHCl_3$): 3012, 2960, 2855, 2207 (triple bond), 1650 (C=O) cm^{-1}; GC–MS (70 eV): m/z (%)=194 (69) $[M]^+$, 165 (85), 153 (100), 139 (15), 126 (60); HRMS (ESI): calcd for $C_{14}H_{11}O$: (195.0811) $[M+H]^+$; found: (195.0810).

*4.2.9. 4-(4-Ethynylphenyl)-1-phenylbut-3-yn-2-one (**1i**).* Yield: 117 mg (48%), dark yellow solid with mp 62–63 °C (n-hexane). R_f (petroleum ether/Et_2O 90:10): 0.53; ^1H NMR (400.13 MHz, $CDCl_3$): δ=3.23 (1H, s, acetylenic H), 3.93 (2H, s, CH_2), 7.29–7.46 (9H, m, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=52.1, 80.4, 82.7, 89.0, 91.7, 120.1, 124.7, 127.4, 128.7, 129.8, 132.2, 132.8, 133.1, 184.9 ppm; FTIR ($CHCl_3$): 3034, 2929, 2860, 2200 (triple bond), 1665 (C=O) cm^{-1}; GC–MS (70 eV): m/z (%)=244 (45) $[M]^+$, 216 (55), 154 (71), 153 (100), 91 (35); HRMS (ESI): calcd for $C_{18}H_{13}O$: (245.0967) $[M+H]^+$; found: (245.0969).

*4.2.10. 1-Phenyloct-3-yn-2-one (**1l**).* Known product, the following characterization data are in agreement with those reported in the literature.[20] Yield: 104 mg (52%), yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.57; ^1H NMR (400.13 MHz, $CDCl_3$): δ=0.95 (3H, t, J=6.5 Hz, CH_3), 1.33–1.36 (2H, m, CH_3CH_2), 1.43–1.46 (2H, m, $CH_3CH_2CH_2$), 2.15 (2H, t, J=6.6 Hz, CH_2–CC), 3.65 (2H, s, CH_2Ph), 7.10–7.16 (5H, m, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=13.5, 18.1, 21.9, 29.1, 43.0, 79.1, 91.7, 127.3, 129.1, 130.0, 135.1, 178.2 ppm; FTIR ($CHCl_3$): 3020, 2927, 2860, 2210 (triple bond), 1655 (C=O), 1453 cm^{-1}; GC–MS (70 eV): m/z (%)=200 (65) $[M]^+$, 171 (20), 119 (21), 91 (100); HRMS (ESI): calcd for $C_{14}H_{17}O$: (201.1279) $[M+H]^+$; found: (201.1278).

*4.2.11. 1-Phenylhex-3-yn-2-one (**1m**).* Known product, the following characterization data are in agreement with those reported in the literature.[21] Yield: 74 mg (43%), yellow oil. R_f (petroleum ether/Et_2O 90:10): 0.47; ^1H NMR (400.13 MHz, $CDCl_3$): δ=1.20 (3H, t, J=6.6 Hz, CH_3), 2.10 (2H, q, J=6.6 Hz, CH_3CH_2), 3.63 (2H, s, CH_2Ph), 7.10–7.15 (5H, m, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=11.5, 13.6, 43.5, 77.2, 91.5, 127.2, 129.0, 130.1, 135.2, 177.9 ppm; FTIR ($CHCl_3$): 3021, 2928, 2857, 2209 (triple bond), 1654 (C=O), 1453 cm^{-1}; GC–MS (70 eV): m/z (%)=172 (40) $[M]^+$, 143 (35), 119 (20), 91 (100); HRMS (ESI): calcd for $C_{12}H_{13}O$: (173.0966) $[M+H]^+$; found: (173.0964).

*4.2.12. 1,4-Diphenylbuta-1,3-diyne (**2a**).* Product commercially available. Yield: 200 mg (99%, Table 1, entry 11), white solid, mp 85–87 °C.

*4.2.13. 1,4-Bis(4-methoxyphenyl)buta-1,3-diyne (**2b**).* Known product, the following characterization data are in agreement with

those reported in the literature.[22] Yield: 16 mg (6%, Table 1, entry 6), yellow solid, mp 138–140 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ=3.83 (6 H, s, OCH_3), 6.88 (4H, d, J=8.6 Hz, Ph), 7.48 (4H, d, J=8.6 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=55.5, 73.2, 81.4, 114.2, 114.3, 134.3, 160.2 ppm; HRMS (ESI): calcd for $C_{18}H_{15}O_2$: (263.1072) $[M+H]^+$; found: (263.1070).

*4.2.14. 4,4′-(Buta-1,3-diyne-1,4diyl)dibenzonitrile (**2c**).* Known product, the following characterization data are in agreement with those reported in the literature.[23] Yield: 23 mg (9%, Table 1, entry 8), brown solid, mp 182–184 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ=7.48 (4H, d, J=8.6 Hz, Ph), 7.61 (4H, d, J=8.6 Hz, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=74.5, 76.8, 112.3, 115.6, 127.0, 131.7, 133.0 ppm; HRMS (ESI): calcd for $C_{18}H_9N_2$: (253.0765) $[M+H]^+$; found: (253.0766).

*4.2.15. 1,4-Bis(4-ethynylphenyl)buta-1,3-diyne (**2d**).* Known product, the following characterization data are in agreement with those reported in the literature.[24] Yield: 30 mg (12%, Table 1, entry 10), white solid, mp 148–151 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ=3.06 (2H, s, CCH), 7.40 (8H, s, Ph) ppm; ^{13}C NMR (100.62 MHz, $CDCl_3$): δ=77.1, 77.3, 84.1, 85.0, 122.2, 132.3 ppm; HRMS (ESI): calcd for $C_{20}H_{11}$: (251.0861) $[M+H]^+$; found: (251.0862).

*4.2.16. 4,6-Decadiyne (**2e**) and 3,5-octadiyne (**2f**).* Products commercially available; they were isolated in traces and identified only by GC–MS.

4.3. General procedure for the synthesis of 1,3-diynes, 1,3-enynes and tri-substituted benzenes

A solution of terminal alkyne (1.0 mmol), $Pd(AcO)_2$ (4 mg, 0.02 mmol), PPh_3 (21 mg, 0.08 mmol), and Et_3N (202 mg, 2.0 mmol) in THF (10 mL) was heated at reflux, under magnetic stirring for 6 h. The solution was cooled to room temperature and the solvent was removed under reduced pressure to give a crude material. The crude mixture was then purified by chromatography on silica gel (petroleum ether/Et_2O 95:5) to afford, as shown in Table 2, 1,4-dialkyl- and 1,4-diaryl-1,3-butadiynes **2a**–**c** together with dimerization products **3a**–**d** and **4a**–**d**, asymmetrical and symmetrical cyclotrimerisation products **5a**–**d** and **6a**–**d**. The compounds **3a**, and **6a**, are commercially available. The compounds **3b**,[25] **3d**,[26] **4a**,[27] **4b**,[28] **4d**,[29] **5a**, **6a**[30] **5b**, **6b**,[30b,31] and **5d**, **6d**[32] are known and their characterization data resulted in agreement with those reported in literature. Compounds **2c**–**6c** were isolated in traces and identified only by GC–MS.

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