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PAPER

Synthesis of functionalized unsymmetrical 1,3-butadiene-3-yne derivatives from β-halo styrene derivatives and their application in the synthesis of trisubstituted pyridines†

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An approach for the synthesis of functionalized unsymmetrical 1,3-butadiene-3-yne derivatives is reported starting from β-halo styrene and phenyl acetylene derivatives in the presence of PdCl$_2$ and CuI catalysts. Functional groups such as aldehyde, cyano and ester groups are well tolerated and afford the desired functionalized dienynes. Further, these 1,3-buta-diene-3-yne derivatives are utilized for the synthesis of novel trisubstituted pyridine derivatives.

Introduction

Enynes are the predominant structures in modern organic chemistry since their derivatives are important intermediates in the synthesis of highly substituted aromatic rings and are found in various pharmaceutical drugs.[1] 1,3- and 1,4-disubstituted enynes are also interesting derivatives of enynes, which exist in various polymers[2] and biologically active molecules.[3] Owing to their applications, various methods for the synthesis of 1,3- and 1,4-disubstituted enynes are well known in the literature. A literature survey on the synthesis of 1,3-butadiene-5-yne derivatives revealed various reports with Ni,[4] Pd[5] and lanthanide[6] and actinide[7] catalysts being well documented for the trimerization of silyl alkynes and terminal alkynes. On the other hand, limited reports are available for the synthesis of 1,3-butadiene-3-yne derivatives, which are also 1,3-enynes. For instance, Wu *et al.* synthesized various symmetrical 1,3-diaryl-2-arylethynyl-1,3-butadienes by the Pd-catalyzed trimerization of arylalkynes.[8] Later, Oro *et al.* reported the synthesis of 1,3-diaryl/alkyl-2-trimethylsilylethynyl-1,3-butadienes by cross-trimerization of terminal alkynes with trimethylsilylacetylene through C–H activation using rhodium(ɪ)–pyridine-N-heterocyclic carbene catalyst.[9] Both the reported methods have certain limitations such as low yields and limited scope.

As a result, an efficient method for the synthesis of unsymmetrical 1,3-butadiene-3-yne derivatives is highly desirable and also to the best of our knowledge, very few reports exists in the

literature for the synthesis of functionalized dienynes. Herein, we report the synthesis of functionalized unsymmetrical 1,3-butadiene-3-yne derivatives from β-halo styrene derivatives. While our work is under progress, Swamy and coworkers reported the synthesis of norbornadienes/norbornenes starting from alkynyldienols in the presence of Au catalyst.[10] The starting material alkynyldienol is obtained from Sonogashira cross-coupling of 3-bromoenals to terminal alkynes followed by alkyne addition and reduction. Although they prepared dienynal derivative, further studies are not carried out on the role of the functional group during the alkyne addition step to enynal derivative.

Results and discussion

As a part of our interest in developing fascinating methodologies[11] for the synthesis of variety of heterocyclic compounds, we planned to carry out Sonogashira coupling between β-bromo cinnamaldehyde and phenyl acetylene under standard reaction conditions in the presence of CuI/Pd(PPh$_3$)$_2$Cl$_2$ bicatalytic system in acetonitrile solvent at room temperature for one hour. Under this reaction condition, unknown product **4** is observed in trace amounts along with the expected enynal product **3** (entry 1, Table 1). From ^{1}H and ^{13}C-NMR studies, X-ray crystallography studies[12] the structure of **4** is confirmed. We realized that the dienynal derivative **4** is formed by the addition of one more alkyne moiety to enynal derivative **3**. In order to improve the yield of dienynal **4**, we screened the reaction further. There is substantial increase in the yield of dienynal **4**, when we used excess of phenyl acetylene (entry 2, Table 1). Next, the yield of the desired product was slightly improved when the reaction temperature increased to 50 °C (entry 3, Table 1). Further, we added triphenyl phosphine as ligand to improve the yield of the

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Table 1 Optimization studies
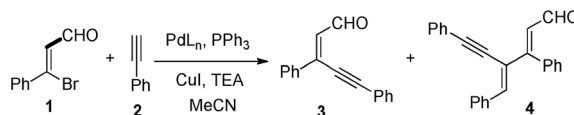
Entry[a]	Pd catalyst (mmol)	CuI (mmol)	2 (mmol)	T (°C)	Time (h)	Yield (%)[b]	
						3	4
1	PdCl$_2$(PPh$_3$)$_2$ (0.1)	0.1	1.2	rt	1	66	Trace
2	PdCl$_2$(PPh$_3$)$_2$ (0.05)	0.1	2.5	rt	2	Trace	70
3	PdCl$_2$(PPh$_3$)$_2$ (0.05)	0.1	2.5	50	1.5	—	74
4	PdCl$_2$(PPh$_3$)$_2$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	1.5	—	76
5	PdCl$_2$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	1.5	Trace	80
6	PdCl$_2$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	2	Trace	92
7	PdCl$_2$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	3	Trace	89
8	PdCl$_2$ (0.05)/PPh$_3$ (0.1)	0.1	3.0	50	2	Trace	70
9	PdCl$_2$ (0.05)/PPh$_3$ (0.1)	0.1	4.0	50	2	Trace	78
10	Pd(PPh$_3$)$_4$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	24	35	—
11	Pd(OAc)$_2$ (0.05)	0.1	2.5	50	0.25	—	85
12	Pd(OAc)$_2$ (0.05)/PPh$_3$ (0.1)	0.1	2.5	50	0.25	—	80
13	Pd(OAc)$_2$ (0.1)	0.1	2.5	50	2	—	—
14[c]	Pd(OAc)$_2$ (0.05)	0.1	2.5	50	2	Trace	88

[a] All the reactions are carried out in 1 mmol scale using 5.6 equiv. of TEA in the acetonitrile solvent (3.0 mL). [b] NMR yields. [c] Dioxane was used as solvent.

desired product (entry 4, Table 1). However, there was no marked improvement in yield of the product was observed in this reaction. Then, we replaced Pd(PPh$_3$)$_2$Cl$_2$ with simple palladium catalyst such as palladium chloride and triphenyl phosphine, to our surprise, the reaction produced good yield of the desired product after 1.5 h (entry 5, Table 1). Further, we observed dramatic improvement in the yield of the desired product when reaction time extends to 2 h, (entry 6, Table 1). Moreover, further extending the reaction showed negative impact on the reaction (entry 7, Table 1). No improvement in the yield of dienynal derivative was observed with further additional amounts of phenylacetylene (entries 8–9, Table 1). Dienynal derivative **4** is not observed, when reaction carried out in the presence of Pd(PPh$_3$)$_4$ (entry 10, Table 1). Next we screened the reaction with palladium acetate as catalyst. Dienynal derivative formed in 85%, when β-bromo styrene reacts with phenyl acetylene in the presence of Pd(OAc)$_2$ (entry 11, Table 1). As the result with Pd(OAc)$_2$ was encouraging, we screened the reaction in various conditions with Pd(OAc)$_2$ (entries 12–14, Table 1). It was found that the reaction produced better yield in dioxane solvent in the presence of palladium acetate. Moreover, from optimization studies, it is observed that an excellent yield of the desired product **4** is obtained in 92% with 1 equiv. of β-bromo cinnamaldehyde, 2.5 equiv. of phenyl acetylene in the presence of PdCl$_2$ (0.05 mmol), PPh$_3$ (0.1 mmol), CuI (0.1 mmol) in acetonitrile solvent for 2 h at 50 °C.
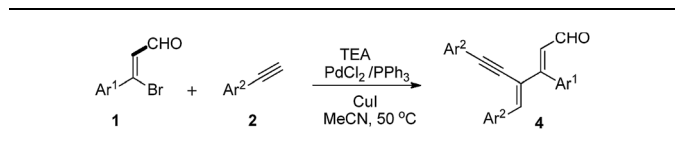
Having the optimized conditions in hand, we check the feasibility of the reaction with various substrates on both the reacting partners. The substrate scope of (Z)-3-bromo-3-arylacrylaldehyde derivatives with various aryl acetylenes in the presence of PdCl$_2$ (0.05 mmol), PPh$_3$ (0.1 mmol), and CuI

(0.1 mmol), TEA (5.6 mmol) afforded the desired dienynal products in good to excellent yields as shown in Table 2. By fixing phenyl acetylene as one of the reacting partner, the scope of the other reacting partner (Z)-3-bromo-3-arylacrylaldehyde derivatives is examined. Electron donating substituents such as Me and OMe on the phenyl ring of (Z)-3-bromo-3-arylacrylaldehyde derivatives furnished the desired dienynal derivatives in good to excellent yields (Table 2, entries 2, 3). On the other hand, good to moderate yields of the dienyal derivatives are observed with electron withdrawing substituents like 4-Br, 3-Br and 4-Cl, 3-NO$_2$ (Table 2, entries 4 to 7). To our delight, 1- and 2-naphthyl acrylaldehyde derivatives also afforded the desired dienyal derivatives in good yields (Table 2, entries 8 to 9). Good yields of the dienynal derivatives are obtained when disubstituted electron donating derivatives such as dimethyl, dimethoxy are subjected to optimized reaction conditions (Table 2, entries 10 to 14). Subsequently, we explored the substrate scope of 2 by fixing (Z)-3-bromo-3-phenylacrylaldehyde as one of the reacting partners. 4-Me, 4-isobutyl phenyl acetylenes furnished corresponding dienyal derivatives in moderate yields under the optimized reaction conditions (Table 2, entries 15 and 16). However, when the reaction was carried out with ortho and meta substituted phenyl acetylenes, desired dienynal derivatives were not observed (Table 2, entries 17 and 18).

To expand scope of our methodology, we turned our attention towards other functional group such as cyano group instead of aldehyde. We prepared 3-chloro-3-phenylacrylonitrile and subjected to the optimized reaction conditions with phenyl acetylene. To our delight, the corresponding dienyne derivative **6** is isolated in 71% yield as a separable mixture of E and Z

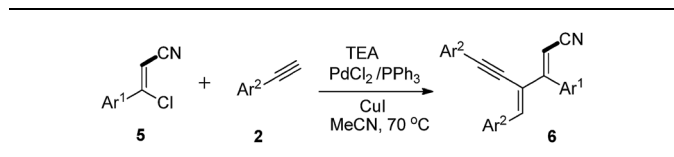**Table 2** Scope of the reaction with respect to 3-bromo-3-phenylacrylal derivatives

Entry[a]	Ar^1	Ar^2	Time (h)	Product	Yield[b] (%) 4
1	C$_6$H$_5$	C$_6$H$_5$	2	**4a**	90
2	4-MeC$_6$H$_4$	C$_6$H$_5$	2	**4b**	80
3	4-OMeC$_6$H$_4$	C$_6$H$_5$	2	**4c**	75
4	4-BrC$_6$H$_4$	C$_6$H$_5$	2	**4d**	70
5	3-BrC$_6$H$_4$	C$_6$H$_5$	2	**4e**	68
6	4-ClC$_6$H$_4$	C$_6$H$_5$	2	**4f**	73
7	3-NO$_2$C$_6$H$_4$	C$_6$H$_5$	2	**4g**	54
8	1-C$_{10}$H$_{17}$	C$_6$H$_5$	2	**4h**	70
9	2-C$_{10}$H$_{17}$	C$_6$H$_5$	2	**4i**	68
10	2,4-(CH$_3$)$_2$C$_6$H$_3$	C$_6$H$_5$	2	**4j**	71
11	2,5-(CH$_3$)$_2$C$_6$H$_3$	C$_6$H$_5$	2	**4k**	81
12	3,4-(CH$_3$)$_2$C$_6$H$_3$	C$_6$H$_5$	2	**4l**	62
13	3,4-(OCH$_3$)$_2$C$_6$H$_3$	C$_6$H$_5$	2	**4m**	71
14	4-isobutylC$_6$H$_4$	C$_6$H$_5$	2	**4n**	68
15	C$_6$H$_5$	4-MeIC$_6$H$_4$	2	**4p**	74
16	C$_6$H$_5$	4-isobutylC$_6$H$_4$	2.5	**4p**	65
17[c]	C$_6$H$_5$	2-NO$_2$C$_6$H$_4$	10	**4o**	—
18[c]	C$_6$H$_5$	3-ClC$_6$H$_4$	10	**4q**	—

[a] Reaction conditions: **1** (1 mmol), **2** (2.5 equiv.), TEA (5.6 equiv.), PdCl$_2$ (5 mol%), PPh$_3$ (10 mol%), CuI (10 mol%) and MeCN (3.0 mL) at 50 °C. [b] Isolated yields. [c] Formation of dienyne product was not observed.

Table 3 Scope of the reaction with respect to 3-chloro-3-phenylacrylonitrile

Entry[a]	Ar^1	Ar^2	Time (h)	6 E/Z	Yield[b] (%)	E/Z ratio[c]
1	C$_6$H$_5$	C$_6$H$_5$	12	**6a/6'a**	71	1:2
2	4-CH$_3$C$_6$H$_4$	C$_6$H$_5$	12	**6b/6'b**	69	3:7
3	2-CH$_3$C$_6$H$_4$	C$_6$H$_5$	12	**6c**	38	1:0
4	4-OCH$_3$C$_6$H$_4$	C$_6$H$_5$	12	**6d/6'd**	68	1:2:3
5	4-ClC$_6$H$_4$	C$_6$H$_5$	12	**6e/6'e**	53	1:5
6	1-C$_{10}$H$_7$	C$_6$H$_5$	12	**6'f**	41	0:1
7	2-C$_{10}$H$_7$	C$_6$H$_5$	12	**6g/6'g**	66	5:4
8	C$_6$H$_5$	4-CH$_3$C$_6$H$_4$	14	**6h/6'h**	55	3:5
9	C$_6$H$_5$	4-ClC$_6$H$_4$	14	**6i/6'i**	49	2:5

[a] Reaction conditions: **5** (1 mmol), **2** (2.5 equiv.), TEA (5.6 equiv.), PdCl$_2$ (5 mol%), PPh$_3$ (10 mol%), CuI (10 mol%) and MeCN (3.0 mL) at 70 °C. [b] Isolated yields. [c] Ratio of E/Z calculated based on crude ^{1}H NMR spectra.

isomers (**6/6'**) at 70 °C (Table 3, entry 1). The structures of these dienyne E and Z isomers are further confirmed from X-ray crystallography studies.[12] Electron donating groups such as 4-Me, 2-Me, 4-OMe on the phenyl ring of 3-chloro-3-arylacrylonitrile afforded mixture of dienynes with 69%, 38% and 68% respectively (Table 3, entries 2 to 4). Interestingly in the case of 2-methyl substituted acrylonitrile derivative exclusive formation of E-isomer takes place. On the other hand, in the presence of electron withdrawing group such as Cl, desired dienyne isomers obtained in 53% yield (Table 3, entry 5). To investigate the further scope of the reaction, we treated 1-naphthyl-3-chloroacrylonitrile or 2-naphthyl-3-chloroacrylonitrile with phenyl acetylene to afford corresponding dienyne derivatives in 41% and 66% yield respectively (Table 3, entries 6 and 7). In the case of 1-naphthyl group, only Z isomer is formed. Furthermore, reaction of 3-chloro-3-phenylacrylonitrile with 4-Me and 4-Cl substituted phenyl acetylenes afford the desired dienyne derivatives in 55 and 49% yields respectively (Table 3, entries 8 and 9).

The scope of the present protocol is further elaborated with the ester functional group by examining with methyl 3-chloro-3-phenylacrylate under the optimized reaction conditions. To our delight, methyl 3-chloro-3-phenylacrylate **7** reacts with phenyl acetylene in the presence of PdCl$_2$, PPh$_3$, and CuI, TEA in CH$_3$CN solvent at 60 °C afforded the desired dienyne derivative

8 in 76% yield. From ^{1}H and ^{13}C-NMR studies, X-ray crystallography studies[12] the structure of **8** is confirmed. To investigate the role of functional group in the present protocol, we prepared chloro stilbene derivative **9** and treated with phenyl acetylene under the optimized reaction conditions. To our surprise desired dienyne derivative is not observed which confirms the vital role of functional group i.e., CHO, CN, COOEt in β-halo styrene derivative in affording the desired 1,3-butadiene-3-yne derivatives as shown in Scheme 1.
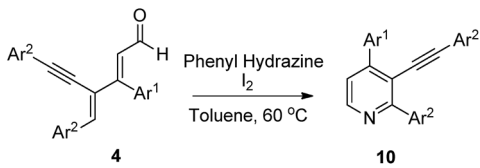
In order to enhance the synthetic utility of the current protocol, novel 2,3,5-trisubstituted pyridine derivatives are prepared from dienal derivatives **4** and phenyl hydrazine in the presence of iodine as shown in Table 4. Trisubstituted pyridine derivatives are also obtained when the reaction carried with glycine methyl ester and NH$_4$Cl albeit in low yield under similar conditions. Reaction of dienynal **4a** with phenyl hydrazine in the presence of iodine in DCM at rt, furnished the dienyne hydrazine intermediate. However, when we replaced DCM with toluene and enhanced the temperature to 60 °C, to our delight trisubstituted pyridine is obtained in 66% yield (Table 4, entry
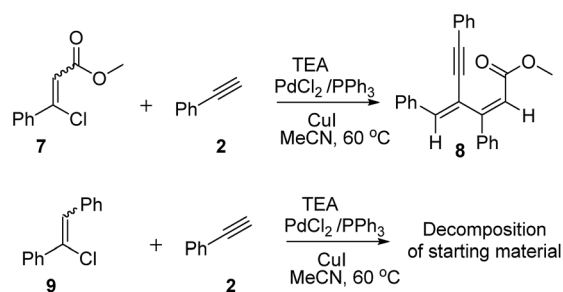
Scheme 1 Scope with methyl 3-chloro-3-phenylacrylate.

Table 4 Synthesis of trisubstituted pyridine derivatives

Entry[a]	Ar[1]	Ar[2]	Time (h)	Product	Yield[b] (%)
1	C_6H_5	C_6H_5	9	**10a**	66
2	4-OMeC_6H_4	C_6H_5	9	**10b**	68
3	4-ClC_6H_4	C_6H_5	10	**10c**	62
4	3-NO_2C_6H_4	C_6H_5	11	**10d**	58
5	1-C_10H_17	C_6H_5	10	**10e**	46
6	2-C_10H_17	C_6H_5	10	**10f**	53
7	4-MeC_6H_4	C_6H_5	15	**10g**	58
8	3,4-(MeO)_2C_6H_3	C_6H_5	16	**10h**	50
9	C_6H_5	4-MeC_6H_4	20	**10i**	56

[a] Reaction conditions: **4** (0.5 mmol), phenyl hydrazine (0.75 mmol), I_2 (0.15 mmol), toluene (4.0 mL) at 60 °C. [b] Isolated yields.

1). The structure of **10a** is further confirmed from X-ray crystallography studies.[12]

Both electron donating and withdrawing substituents afford the desired trisubstituted pyridine derivatives in moderate to good yield. For instance, with methoxy and methyl substituents desired trisubstituted pyridine derivative is isolated in moderate yields (Table 4, entries 2, 7–9). Electron withdrawing groups such as chloro and nitro substituents afford the pyridine derivative in 62% and 58% yield respectively (Table 4, entry 3 and 4). However, 46% and 53% yields of pyridine derivatives were obtained successively in the case of 1-naphthyl and 2-naphthyl derivatives (Table 4, entries 5 and 6).

The proposed mechanism for the formation of pyridine derivatives is shown in Fig. 1. In the presence of iodine, dienyl derivative **4** reacts with phenyl hydrazine to form hydrazone intermediate. This hydrazone intermediate will undergo electrocyclic reaction followed by the elimination of aniline affords the desired pyridine derivative **10**. To the best of our knowledge no reports are available in the literature in which phenyl hydrazine acts as nitrogen source for the synthesis of pyridine derivatives.
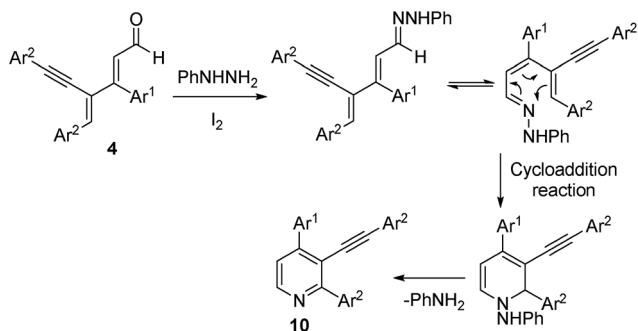

Fig. 1 A plausible mechanism for the formation of pyridine derivative.

Experimental section

General information

Reagents and solvents were purchased from various commercial sources and were used directly without any further purification. Column chromatography was performed with 63–200 mesh silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (d) using chloroform as internal standards and coupling constants are expressed in Hertz. Melting points were recorded using an electro thermal capillary melting point apparatus and are uncorrected.

General procedure for the synthesis of (*E*)-4-((*E*)-benzylidene)-3,6-diphenylhex-2-en-5-ynal derivatives (4a–4o)

Triethyl amine (567 mg, 5.6 equiv.), palladium chloride (9 mg, 5 mol%), triphenyl phosphine (26 mg, 10 mol%), copper iodide (20 mg, 10 mol%) and phenyl acetylene (255 mg, 2.5 equiv.) were added successively to a stirred solution of (*Z*)-3-bromo-3-phenylacrylaldehyde (210 mg, 1.0 mmol) in acetonitrile under nitrogen atmosphere. The reaction mixture was heated to 50 °C and monitored by TLC. After completion of the reaction, the resulting reaction mixture was cooled to room temperature and solvent was removed under reduced pressure. Now add ethyl acetate and filtered through celite pad to remove metal catalysts. Later organic layer was washed with brine and dried over $MgSO_4$. The resulting crude compound was purified by flash column chromatography (eluent: petroleum ether/ethyl acetate) 20 : 1 on silica gel to afford desired product.

General procedure for the synthesis of (*E*)-4-((*E*)-benzylidene)-3,6-diphenylhex-2-en-5-ynenitrile derivatives (6a–6j)

Triethyl amine (567 mg, 5.6 equiv.), palladium chloride (9 mg, 5 mol%), triphenyl phosphine (26 mg, 10 mol%), copper iodide (20 mg, 10 mol%) and phenyl acetylene (255 mg, 2.5 equiv.) were added successively to a stirred solution of 3-chloro-3-phenylacrylnitrile (164 mg, 1.0 mmol) in acetonitrile under nitrogen atmosphere. The reaction mixture was heated to 70 °C and monitored by TLC. After completion of the reaction, the resulting reaction mixture was cooled to room temperature and solvent was removed under reduced pressure. Now add ethyl acetate and filtered through celite pad to remove metal catalysts. Later organic layer was washed with brine. The organic layer was separated; dried over anhydrous $MgSO_4$ and filtered the dried organic layer, then concentrated it to obtain the crude product. The resulting crude compound was purified by flash column chromatography (eluent: petroleum ether/ethyl acetate) 20 : 1 on silica gel to afford desired product.

Procedure for the synthesis of methyl (*E*)-4-((*E*)-benzylidene)-3,6-diphenylhex-2-en-5-ynoate (8)

Triethyl amine (567 mg, 5.6 equiv.), palladium chloride (9 mg, 5 mol%), triphenyl phosphine (26 mg, 10 mol%), copper iodide (20 mg, 10 mol%) and phenyl acetylene (255 mg, 2.5 equiv.) were added successively to a stirred solution of methyl 3-chloro-

3-phenylacrylate (197 mg, 1.0 mmol) in acetonitrile under nitrogen atmosphere. The reaction mixture was heated to 60 °C and monitored by TLC. After completion of the reaction, the resulting reaction mixture was cooled to room temperature and solvent was removed under reduced pressure. Now add ethyl acetate and filtered through celite pad to remove metal catalysts. Later organic layer was washed with brine. The organic layer was separated; dried over anhydrous $MgSO_4$ and filtered the dried organic layer, then concentrated it to obtain the crude product. The resulting crude compound was purified by flash column chromatography (eluent : petroleum ether/ethyl acetate) 20 : 1 on silica gel to afford desired product.

General procedure for the synthesis of 2,4-diphenyl-3-(phenylethynyl)pyridine derivatives (10a–10f)

Phenyl hydrazine (162 mg, 1.5 mmol.), and iodine (76 mg, 0.3 mmol) were added successively to a stirred solution of (E)-4-((E)-benzylidene)-3,6-diphenylhex-2-en-5-ynal (334 mg, 1.0 mmol) in toluene. The reaction mixture was heated to 60 °C and monitored by TLC. After completion of the reaction, the resulting reaction mixture was cooled to room temperature and treated with hypo solution to quench iodine. The organic layer was extracted with ethyl acetate, washed with brine. The organic layer was separated; dried over anhydrous $MgSO_4$ and filtered the dried organic layer, then concentrated it to obtain the crude product. The resulting crude compound was purified by flash column chromatography (eluent : petroleum ether/ethyl acetate) 10 : 1 on silica gel to afford desired product.

Spectral data of compounds

(E)-4-((E)-benzylidene)-3,6-diphenylhex-2-en-5-ynal (4a). Yellow solid, mp: 162–162 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.52 (d, J = 8.2 Hz, 1H), 7.91–7.89 (m, 2H), 7.57–7.55 (m, 2H), 7.50–7.48 (m, 3H), 7.40–7.34 (m, 8H), 6.96 (d, J = 8.2 Hz, 1H), 6.75 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.2, 160.8, 143.7, 135.6, 135.1, 131.8, 130.5, 130.3, 130.1, 129.4, 129.3, 129.2, 128.8, 128.7, 128.6, 122.9, 122.8, 99.3, 85.8; HRMS (EI) m/z calcd for $C_{25}H_{18}O$ (M$^+$): 334.1358, found 334.1358.

(2E,4E)-4-benzylidene-6-phenyl-3-(p-tolyl)hex-2-en-5-ynal (4b). Yellow solid, mp: 112–113 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.43 (d, J = 8.1 Hz, 1H), 7.90–7.88 (m, 2H), 7.55–7.53 (m, 2H), 7.38–7.31 (m, 6H), 7.27–7.21 (m, 4H), 6.91 (d, J = 8.0 Hz, 1H), 6.77 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.3, 161.0, 143.5, 139.3, 135.7, 132.0, 131.8, 130.5, 130.2, 130.0, 129.3, 129.2, 128.7, 128.6, 123.1, 122.8, 99.2, 86.0, 21.5; HRMS (EI) m/z calcd for $C_{26}H_{20}O$ (M$^+$): 348.1514, found 348.1514.

(2E,4E)-4-benzylidene-3-(4-methoxyphenyl)-6-phenylhex-2-en-5-ynal (4c). Yellow solid, mp: 165–166 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.47 (d, J = 8.0 Hz, 1H), 7.94–7.92 (m, 2H), 7.58–7.56 (m, 2H), 7.40–7.28 (m, 8H), 7.03–7.00 (m, 2H), 6.94 (d, J = 8.0 Hz, 1H), 6.83 (s, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.3, 160.7, 160.5, 143.5, 135.7, 132.0, 131.7, 130.2, 129.9, 129.3, 129.1, 128.7, 128.6, 127.0, 123.1, 122.8, 114.1, 99.2, 86.1, 55.53; HRMS (EI) m/z calcd for $C_{26}H_{20}O_2$ (M$^+$): 364.1463, found 364.1463.

(2E,4E)-4-benzylidene-3-(4-bromophenyl)-6-phenylhex-2-en-5-ynal (4d). Yellow solid, mp: 148–149 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.43 (d, J = 8.2 Hz, 1H), 7.93–7.91 (m, 2H), 7.65–7.63 (m, 2H), 7.57–7.54 (m, 2H), 7.41–7.34 (m, 6H), 7.26–7.23 (m, 2H), 6.95 (d, J = 8.1 Hz, 1H), 6.71 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 193.5, 159.3, 143.6, 135.4, 133.9, 132.0, 131.9, 131.8, 130.2, 129.6, 129.3, 128.8, 128.6, 123.7, 122.6, 122.5, 99.5, 85.5; HRMS (EI) m/z calcd for $C_{25}H_{17}BrO$ (M$^+$): 412.0463, found 412.0463.

(E)-4-((E)-Benzylidene)-3-(3-bromophenyl)-6-phenylhex-2-en-5-ynal (4e). Yellow solid, mp: 109–110 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.44 (d, J = 8.0 Hz, 1H), 7.93–7.91 (m, 2H), 7.64 (dt, J = 5.2 Hz, J = 1.5 Hz, 1H), 7.58–7.54 (m, 3H), 7.41–7.36 (m, 7H), 7.32–7.30 (m, 1H), 6.95 (d, J = 8.1 Hz, 1H), 6.71 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 193.3, 158.7, 143.5, 136.9, 135.2, 133.1, 132.9, 132.2, 131.6, 130.1, 130.0, 129.5, 129.1, 128.9, 128.6, 128.5, 128.2, 122.7, 122.4, 122.3, 99.3, 85.2; HRMS (ESI) m/z calcd for $C_{25}H_{18}OBr$ (M + H)$^+$: 413.0541, found 413.0541.

(2E,4E)-4-Benzylidene-3-(4-chlorophenyl)-6-phenylhex-2-en-5-ynal (4f). Yellow solid, mp: 147–148 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.44 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 6.8 Hz, 2H), 7.57–7.55 (m, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.41–7.34 (m, 6H), 7.31 (d, J = 8.2 Hz, 2H), 6.96 (d, J = 8.1 Hz, 1H), 6.72 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 193.5, 159.4, 143.6, 135.5, 135.4, 133.5, 131.8, 131.7, 130.3, 130.2, 129.7, 129.3, 129.0, 128.8, 128.6, 122.7, 122.6, 99.5, 85.6; HRMS (EI) m/z calcd for $C_{25}H_{17}ClO$ (M$^+$): 368.0968, found 368.0968.

(2E,4E)-4-Benzylidene-3-(3-nitrophenyl)-6-phenylhex-2-en-5-ynal (4g). Yellow solid, mp: 178–179 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.40 (d, J = 8.1 Hz, 1H), 8.39–8.37 (m, 1H), 8.27 (s, 1H), 7.91–7.89 (m, 2H), 7.73–7.71 (m, 2H), 7.57–7.55 (m, 2H), 7.42–7.37 (m, 6H), 7.02 (d, J = 8.1 Hz, 1H), 6.61 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 192.5, 157.7, 148.5, 143.7, 136.9, 136.3, 135.2, 131.8, 130.5, 130.3, 130.2, 129.9, 129.4, 128.8, 128.7, 125.1, 124.3, 122.4, 122.3, 99.9, 85.1; HRMS (EI) m/z calcd for $C_{25}H_{17}NO_3$ (M$^+$): 379.1208, found 379.1208.

(2E,4E)-4-Benzylidene-3-(naphthalen-1-yl)-6-phenylhex-2-en-5-ynal (4h). Yellow solid, mp: 167–168 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.10 (d, J = 8.1 Hz, 1H), 7.83–7.76 (m, 2H), 7.67–7.64 (m, 3H), 7.48–7.31 (m, 9H), 7.25–7.14 (m, 3H), 7.06 (d, J = 7.8 Hz, 1H), 6.46 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 197.3, 160.1, 143.3, 135.5, 133.6, 132.5, 131.8, 130.6, 130.2, 130.0, 129.6, 129.2, 128.8, 128.6, 128.5, 128.4, 127.4, 126.7, 125.9, 125.2, 122.8, 122.5, 99.4, 85.6; HRMS (EI) m/z calcd for $C_{29}H_{20}O$ (M$^+$): 384.1514, found 384.1514.

(2E,4E)-4-Benzylidene-3-(naphthalen-2-yl)-6-phenylhex-2-en-5-ynal (4i). Yellow solid, mp: 196–197 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.47 (d, J = 8.2 Hz, 1H), 7.98–7.91 (m, 6H), 7.89–7.60 (m, 4H), 7.47 (dd, J = 8.4, 1.3 Hz, 1H), 7.42–7.35 (m, 6H), 7.07 (d, J = 8.1 Hz, 1H), 6.79 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.2, 160.8, 143.9, 135.6, 133.5, 132.9, 132.5, 131.8, 130.3, 130.2, 130.1, 129.9, 129.2, 128.8, 128.6, 128.4, 128.1, 127.6, 127.3, 127.2, 122.9, 122.8, 99.3, 85.9; HRMS (EI) m/z calcd for $C_{29}H_{20}O$ (M$^+$): 384.1514, found 384.1514.

(2E,4E)-4-Benzylidene-3-(2,4-dimethylphenyl)-6-phenylhex-2-en-5-ynal (4j). Yellow liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H

(ppm): 9.35 (d, J = 8.2 Hz, 1H), 7.91–7.89 (m, 2H), 7.60–7.58 (m, 2H), 7.41–7.34 (m, 6H), 7.14–7.10 (m, 3H), 6.99 (d, J = 8.2 Hz, 1H), 6.66 (s, 1H), 2.41 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.4, 160.9, 142.4, 139.0, 136.6, 135.7, 131.8, 131.4, 131.3, 130.5, 130.3, 130.0, 129.4, 129.1, 128.7, 128.6, 126.8, 122.8, 122.2, 99.1, 85.6, 21.4, 19.7; HRMS (EI) m/z calcd for C$_{27}$H$_{22}$O (M$^+$): 362.1671, found 362.1671.

(2E,4E)-4-benzylidene-3-(2,5-dimethylphenyl)-6-phenylhex-2-en-5-ynal (4k). Yellow solid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.35 (d, J = 8.3 Hz, 1H), 7.91–7.89 (m, 2H), 7.60–7.58 (m, 2H), 7.41–7.31 (m, 6H), 7.22–7.17 (m, 2H), 7.03 (s, 1H), 6.98 (d, J = 8.2 Hz, 1H), 6.65 (s, 1H), 2.37 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.3, 160.9, 142.5, 135.7, 135.6, 134.3, 133.6, 131.8, 131.0, 130.4, 130.3, 130.0, 129.9, 129.2, 129.1, 128.7, 128.5, 122.8, 122.0, 99.1, 85.6, 21.1, 19.2; HRMS (EI) m/z calcd for C$_{27}$H$_{22}$O (M$^+$): 362.1671, found 362.1671.

(2E,4E)-4-Benzylidene-3-(3,4-dimethylphenyl)-6-phenylhex-2-en-5-ynal (4l). Yellow solid, mp: 143–144 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.40 (d, J = 8.1 Hz, 1H), 7.86–7.84 (m, 2H), 7.51–7.48 (m, 2H), 7.32–7.26 (m, 6H), 7.16 (d, J = 8.1 Hz, 1H), 7.05–7.01 (m, 2H), 6.87 (d, J = 8.1 Hz, 1H), 6.75 (s, 1H), 2.28 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.4, 161.1, 143.5, 137.9, 136.9, 135.7, 132.3, 131.7, 131.6, 130.2, 129.9, 129.7, 129.1, 129.0, 128.7, 128.5, 128.0, 123.0, 122.8, 99.1, 86.0, 19.9, 19.8; HRMS (EI) m/z calcd for C$_{27}$H$_{22}$O (M$^+$): 362.1671, found 362.1671.

(2E,4E)-4-benzylidene-3-(3,4-dimethoxyphenyl)-6-phenylhex-2-en-5-ynal (4m). Yellow solid, mp: 166–167 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.49 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 6.8 Hz, 2H), 7.57–7.55 (m, 2H), 7.40–7.35 (m, 6H), 6.98–6.90 (m, 3H), 6.86–6.84 (m, 2H), 3.97 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.2, 160.6, 150.0, 149.0, 143.4, 135.6, 131.7, 130.2, 130.0, 129.3, 129.1, 128.7, 128.6, 127.4, 123.7, 122.9, 122.8, 113.5, 111.1, 99.2, 86.0, 56.2, 56.1; HRMS (EI) m/z calcd for C$_{27}$H$_{22}$O$_3$ (M$^+$): 394.1569, found 394.1569.

(2E,4E)-4-benzylidene-3-(4-isobutylphenyl)-6-phenylhex-2-en-5-ynal (4n). Yellow solid, mp: 139–140 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.38 (d, J = 8.1 Hz, 1H), 7.84–7.82 (m, 2H), 7.50–7.47 (m, 2H), 7.31–7.28 (m, 6H), 7.25–7.16 (m, 3H), 6.87 (d, J = 8.1 Hz, 1H), 6.72 (m, 1H), 2.49 (d, J = 7.2 Hz, 2H), 1.90–1.84 (m, 1H), 0.87 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.3, 161.1, 143.5, 143.1, 135.6, 132.2, 131.7, 130.3, 130.2, 129.9, 129.3, 129.2, 129.1, 128.7, 128.5, 122.9, 122.8, 99.2, 85.9, 45.3, 30.3, 22.5; HRMS (EI) m/z calcd for C$_{29}$H$_{26}$O (M$^+$): 390.1984, found 390.1984.

(E)-4-((E)-4-Methylbenzylidene)-3-phenyl-6-(p-tolyl)hex-2-en-5-ynal (4o). Yellow solid, mp: 140 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 9.41 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.49–7.46 (m, 5H), 7.36–7.34 (m, 2H), 7.19 (dd, J = 8.0 Hz, J = 4.0 Hz, 4H), 6.94 (d, J = 8.1 Hz, 1H), 6.70 (s, 1H), 2.40 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.3, 161.2, 143.5, 140.5, 139.4, 135.2, 133.0, 131.7, 131.6, 130.5, 130.3, 129.9, 129.5, 129.3, 129.2, 129.1, 129.1, 128.6, 128.5, 122.0, 119.8, 99.5, 85.4, 21.8, 21.7; HRMS (ESI) m/z calcd for C$_{27}$H$_{23}$O (M + H)$^+$: 363.1749, found 363.1747.

(E)-4-((E)-4-Isobutylbenzylidene)-6-(4-isobutylphenyl)-3-phenyl hex-2-en-5-ynal (4p). Yellow thick liquid, ^{1}H NMR (400 MHz,

CDCl$_3$) δ_H (ppm): 9.41 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 8.1 Hz, 2H), 7.50–7.47 (m, 5H), 7.36–7.34 (m, 2H), 7.19–7.15 (m, 4H), 6.95 (d, J = 8.2 Hz, 1H), 6.71 (s, 1H), 2.52 (d, J = 7.2 Hz, 2H), 2.49 (d, J = 7.2 Hz, 2H), 1.94–1.84 (m, 2H), 0.94 (d, J = 6.6 Hz, 6H), 0.90 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 194.2, 161.3, 144.4, 143.5, 143.2, 135.2, 133.2, 131.5, 130.5, 130.2, 129.5, 129.4, 129.1, 129.0, 128.5, 121.9, 120.1, 99.7, 85.5, 45.6, 45.5, 30.3, 22.5; HRMS (EI) m/z calcd for C$_{33}$H$_{34}$O (M$^+$): 446.2610, found 446.2612.

(E)-4-((E)-Benzylidene)-3,6-diphenylhex-2-en-5-ynenitrile (6a). Colorless solid, mp: 110–112 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.89–7.87 (m, 2H), 7.57–7.50 (m, 5H), 7.43–7.35 (m, 8H), 6.73 (s, 1H), 6.31 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.7, 143.5, 135.5, 135.3, 131.7, 130.2, 130.1, 129.7, 129.4, 129.3, 128.9, 128.8, 128.6, 122.5, 121.0, 118.0, 99.4, 98.8, 85.4; HRMS (ESI) m/z calcd for C$_{25}$H$_{18}$N (M + H)$^+$: 332.1439, found 332.1440.

(Z)-4-((E)-Benzylidene)-3,6-diphenylhex-2-en-5-ynenitrile (6'a). Colorless solid, mp: 114–115 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.04 (d, J = 7.5 Hz, 2H), 7.54 (d, J = 7.0 Hz, 2H), 7.47–7.39 (m, 8H), 7.32–7.30 (m, 3H), 7.06 (s, 1H), 5.67 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.9, 142.3, 137.6, 135.4, 131.7, 130.6, 129.9, 129.8, 128.9, 128.8, 128.6, 128.5, 128.5, 122.9, 118.4, 117.2, 98.9, 95.7, 87.1; HRMS (ESI) m/z calcd for C$_{25}$H$_{18}$N (M + H)$^+$: 332.1439, found 332.1439.

(E)-4-((E)-Benzylidene)-6-phenyl-3-(p-tolyl)hex-2-en-5-ynenitrile (6b). Colorless solid, mp: 130–132 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.94 (d, J = 6.8 Hz, 2H), 7.60 (s, 2H), 7.46–7.36 (m, 10H), 6.83 (s, 1H), 6.32 (s, 1H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.7, 143.3, 139.7, 135.3, 132.5, 131.7, 130.1, 130.0, 129.6, 129.2, 128.8, 128.5, 122.5, 121.1, 118.1, 99.2, 98.3, 85.6, 21.5; HRMS (EI) m/z calcd for C$_{26}$H$_{20}$N (M$^+$ + H): 346.1596, found 346.1598.

(Z)-4-((E)-Benzylidene)-6-phenyl-3-(p-tolyl)hex-2-en-5-ynenitrile (6'b). Colorless solid, mp: 114–116 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.06 (d, J = 7.2 Hz, 2H), 7.47–7.39 (m, 7H), 7.35–7.32 (m, 3H), 7.28–7.24 (m, 2H), 7.06 (s, 1H), 5.67 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.8, 142.1, 141.0, 135.4, 134.6, 131.7, 129.8, 129.6, 128.9, 128.6, 128.5, 128.4, 123.0, 118.5, 117.4, 98.7, 94.8, 87.2, 21.6; HRMS (ESI) m/z calcd for C$_{26}$H$_{20}$N (M + H)$^+$: 346.1596, found 346.1595.

(E)-4-((E)-Benzylidene)-6-phenyl-3-(o-tolyl)hex-2-en-5-ynenitrile (6c). Yellow thick liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.94–7.92 (m, 2H), 7.66–7.64 (m, 2H), 7.49–7.47 (m, 3H), 7.45–7.37 (m, 6H), 7.27 (s, 1H), 6.63 (s, 1H), 6.48 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.5, 142.6, 136.0, 135.2, 135.0, 131.7, 130.7, 130.1, 130.1, 129.4, 129.3, 129.1, 128.8, 128.6, 128.5, 126.4, 122.4, 117.5, 99.6, 99.3, 84.9, 19.4; HRMS (ESI) m/z calcd for C$_{26}$H$_{20}$N (M + H)$^+$: 346.1596, found 346.1598.

(E)-4-((E)-Benzylidene)-3-(4-methoxyphenyl)-6-phenylhex-2-en-5-ynenitrile (6d). Pale yellow gummy liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.88–7.86 (m, 2H), 7.53–7.51 (m, 2H), 7.39–7.32 (m, 8H), 7.00–6.98 (m, 2H), 6.77 (s, 1H), 6.21 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.5, 160.7, 143.3, 135.3, 131.7, 130.9, 130.1, 130.0, 129.3, 128.8, 128.6, 127.5, 122.5, 121.2, 118.3, 114.3, 99.2, 97.9, 85.7, 55.4; HRMS (ESI) m/z calcd for C$_{26}$H$_{20}$NO (M + H)$^+$: 362.1545, found 362.1548.

(Z)-4-((E)-Benzylidene)-3-(4-methoxyphenyl)-6-phenylhex-2-en-5-ynenitrile (6′d). Pale brown solid, mp: 104–105 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.06 (d, J = 7.9 Hz, 2H), 7.51 (d, J = 8.7 Hz, 2H), 7.45–7.40 (m, 5H), 7.33–7.32 (m, 3H), 7.07 (s, 1H), 6.94 (d, J = 8.6 Hz, 2H), 5.62 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.7, 161.3, 141.9, 135.4, 131.6, 129.9, 129.8, 129.7, 129.5, 128.9, 128.6, 128.5, 122.9, 118.4, 117.6, 114.2, 98.5, 93.5, 87.2, 55.5; HRMS (ESI) m/z calcd for C$_{26}$H$_{20}$NO (M + H)$^+$: 362.1545, found 362.1547.

(E)-4-((E)-benzylidene)-3-(4-chlorophenyl)-6-phenylhex-2-en-5-ynenitrile (6e). Colorless solid, mp: 140–142 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.92–7.90 (m, 2H), 7.58–7.56 (m, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.44–7.35 (m, 8H), 6.71 (s, 1H), 6.31 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 160.5, 143.4, 135.9, 135.1, 133.9, 131.7, 130.7, 130.3, 130.2, 129.4, 129.3, 128.8, 128.7, 122.3, 120.7, 117.7, 99.6, 99.1, 85.2; HRMS (ESI) m/z calcd for C$_{25}$H$_{17}$ClNO (M + H)$^+$: 366.1050, found 366.1044.

(Z)-4-((E)-Benzylidene)-3-(4-chlorophenyl)-6-phenylhex-2-en-5-ynenitrile (6′e). Colorless solid, mp: 128–130 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.04–8.02 (m, 2H), 7.49–7.39 (m, 9H), 7.34–7.30 (m, 3H), 7.06 (s, 1H), 5.64 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 160.6, 142.5, 136.8, 135.9, 135.2, 131.7, 130.1, 129.8, 129.8, 129.2, 129.1, 128.7, 128.6, 122.7, 117.9, 117.0, 99.0, 96.0, 86.8; HRMS (ESI) m/z calcd for C$_{25}$H$_{17}$ClNO (M + H)$^+$: 366.1050, found 366.1049.

(E)-4-((E)-Benzylidene)-3-(naphthalen-1-yl)-6-phenylhex-2-en-5-ynenitrile (6′f). Colorless solid, mp: 95–96 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.07–8.05 (m, 3H), 7.90–7.86 (m, 3H), 7.62–7.51 (m, 3H), 7.47–7.37 (m, 5H), 7.33–7.27 (m, 3H), 7.09 (s, 1H), 5.81 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.8, 142.5, 135.4, 134.8, 134.3, 133.1, 131.7, 130.0, 128.9, 128.9, 128.8, 128.6, 128.5, 127.9, 127.6, 127.0, 125.2, 122.9, 118.4, 117.3, 98.9, 96.0, 87.1; HRMS (ESI) m/z calcd for C$_{29}$H$_{20}$N (M + H)$^+$: 382.1596, found 382.1596.

(E)-4-((E)-Benzylidene)-3-(naphthalen-2-yl)-6-phenylhex-2-en-5-ynenitrile (6g). Colorless solid, mp: 170–172 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.00–7.87 (m, 6H), 7.63–7.56 (m, 4H), 7.50–7.34 (m, 7H), 6.76 (s, 1H), 6.41 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.6, 143.7, 135.2, 133.7, 133.2, 132.9, 130.1, 130.1, 129.4, 129.2, 128.8, 128.7, 128.6, 128.6, 128.0, 127.3, 126.9, 126.5, 122.4, 121.0, 118.0, 99.4, 99.1, 85.5. HRMS (ESI) m/z calcd for C$_{29}$H$_{20}$N (M + H)$^+$: 382.1596, found 382.1598.

(Z)-4-((E)-Benzylidene)-3-(naphthalen-2-yl)-6-phenylhex-2-en-5-ynenitrile (6′g). Colorless solid, mp: 103–105 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.08–8.05 (m, 3H), 7.91–7.87 (m, 3H), 7.62–7.52 (m, 3H), 7.48–7.39 (m, 5H), 7.31–7.25 (m, 3H), 7.10 (s, 1H), 5.81 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.8, 142.4, 135.4, 134.8, 134.2, 133.1, 131.7, 129.9, 129.8, 128.9, 128.9, 128.8, 128.6, 128.5, 127.9, 127.6, 127.0, 125.2, 122.9, 118.4, 117.3, 98.9, 96.0, 87.1; HRMS (ESI) m/z calcd for C$_{29}$H$_{20}$N (M + H)$^+$: 382.1596, found 382.1596.

(E)-4-((E)-4-Methylbenzylidene)-3-phenyl-6-(p-tolyl)hex-2-en-5-ynenitrile (6h). Colorless Solid, mp: 195–196 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.79 (d, J = 8.2 Hz, 2H), 7.51–7.44 (m, 5H), 7.39–7.37 (m, 2H), 7.20 (dd, J = 8.0 Hz, J = 10.0 Hz, 4H), 6.66 (s, 1H), 6.27 (s, 1H), 2.41 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100

MHz, CDCl$_3$) δ_C (ppm): 162.0, 143.3, 140.6, 139.6, 135.7, 132.7, 131.6, 130.2, 129.6, 129.4, 128.9, 120.1, 119.5, 118.2, 99.7, 98.3, 85.1, 21.8, 21.7 HRMS (ESI) m/z calcd for C$_{27}$H$_{22}$N (M + H)$^+$: 360.1752, found 360.1753.

(Z)-4-((E)-4-Methylbenzylidene)-3-phenyl-6-(p-tolyl)hex-2-en-5-ynenitrile (6'h). Yellow liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.92 (d, J = 8.2 Hz, 2H), 7.50–7.47 (m, 2H), 7.43–7.35 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 6.98 (s, 1H), 5.58 (s, 1H), 2.37 (s, 3H), 2.31 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 162.0, 142.0, 140.1, 139.0, 137.7, 132.7, 131.4, 130.4, 129.7, 129.3, 129.2, 128.7, 128.5, 119.9, 117.4, 117.3, 99.1, 95.3, 86.7, 21.6; HRMS (ESI) m/z calcd for C$_{27}$H$_{22}$N (M + H)$^+$: 360.1752, found 360.1754.

(E)-4-((E)-4-Chlorobenzylidene)-6-(4-chlorophenyl)-3-phenylhex-2-en-5-ynenitrile (6i). Colorless solid, mp: 175–176 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.78–7.76 (m, 2H), 7.52–7.50 (m, 3H), 7.47–7.44 (m, 2H), 7.41–7.33 (m, 6H), 6.67 (s, 1H), 6.24 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.3, 142.2, 136.0, 135.8, 135.2, 133.7, 132.9, 131.3, 129.9, 129.3, 129.0, 128.9, 121.4, 120.7, 117.7, 99.2, 98.6, 86.0; HRMS (EI) m/z calcd for C$_{25}$H$_{15}$NCl$_2$ (M$^+$): 399.0582, found 399.0582.

(Z)-4-((E)-4-Chlorobenzylidene)-6-(4-chlorophenyl)-3-phenylhex-2-en-5-ynenitrile (6'i). Colorless solid, mp: 150–151 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 7.92 (d, J = 8.5 Hz, 2H), 7.51–7.38 (m, 7H), 7.32–7.27 (m, 4H), 7.00 (s, 1H), 5.67 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.4, 141.2, 137.4, 135.8, 135.3, 133.7, 132.9, 130.9, 130.7, 129.0, 128.9, 128.9, 128.5, 121.1, 118.8, 117.1, 98.2, 96.1, 87.6; HRMS (ESI) m/z calcd for C$_{25}$H$_{15}$NCl$_2$ (M + H)$^+$: 400.0660, found 400.0655.

Methyl (Z)-4-((E)-benzylidene)-3,6-diphenylhex-2-en-5-ynoate (8). Colorless solid, mp: 101–102 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.01 (d, J = 7.6 Hz, 2H), 7.64–7.61 (m, 2H), 7.45–7.35 (m, 8H), 7.31–7.30 (m, 3H), 6.75 (s, 1H), 6.29 (s, 1H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 166.6, 154.7, 139.4, 139.2, 136.1, 131.6, 129.7, 129.3, 129.0, 128.7, 128.6, 128.5, 128.4, 128.4, 123.4, 119.3, 118.1, 96.4, 88.5, 51.7; HRMS (EI) m/z calcd for C$_{26}$H$_{20}$O$_2$ (M$^+$): 364.1463, found 364.1463.

2,4-Diphenyl-3-(phenylethynyl)pyridine (10a). Pale yellow solid, mp: 123–124 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.66 (d, J = 5.0 Hz, 1H), 8.02–7.99 (m, 2H), 7.73–7.71 (m, 2H), 7.54–7.45 (m, 6H), 7.31 (d, J = 5.0 Hz, 1H), 7.26–7.21 (m, 3H), 7.11–7.09 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.2, 152.6, 148.1, 140.1, 138.8, 131.3, 129.8, 129.4, 128.9, 128.8, 128.6, 128.4, 128.3, 128.1, 127.9, 123.2, 122.3, 116.5, 97.9, 87.3; HRMS (ESI) m/z calcd for C$_{25}$H$_{18}$N (M + H)$^+$: 332.1439, found 332.1441.

4-(4-Methoxyphenyl)-2-phenyl-3-(phenylethynyl)pyridine (10b). Colorless solid, mp: 85–86 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.62 (d, J = 5.0 Hz, 1H), 7.99–7.97 (m, 2H), 7.71 (d, J = 8.6 Hz, 2H), 7.52–7.44 (m, 3H), 7.29–22 (m, 4H), 7.15–7.13 (m, 2H), 7.04 (d, J = 8.6 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.4, 160.3, 152.0, 148.0, 140.2, 131.2, 131.0, 130.7, 129.8, 128.8, 128.6, 128.4, 127.9, 123.2, 122.2, 116.3, 113.7, 97.7, 87.6, 55.5; HRMS (ESI) m/z calcd for C$_{26}$H$_{20}$NO (M + H)$^+$: 362.1545, found 362.1544.

4-(4-Chlorophenyl)-2-phenyl-3-(phenylethynyl)pyridine (10c). Colorless solid, mp: 155–156 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H

(ppm): 8.68 (d, J = 5.0 Hz, 1H), 8.02–7.99 (m, 2H), 7.71–7.67 (m, 2H), 7.55–7.47 (m, 5H), 7.33–7.26 (m, 4H), 7.16–7.13 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.5, 151.2, 148.3, 139.9, 137.2, 135.1, 131.3, 130.7, 129.8, 129.0, 128.8, 128.6, 128.5, 128.0, 123.0, 122.1, 116.4, 98.2, 86.9; HRMS (ESI) m/z calcd for C$_{25}$H$_{17}$ClN (M + H)$^+$: 366.1050, found 366.1053.

4-(3-Nitrophenyl)-2-phenyl-3-(phenylethynyl)pyridine (10d). Colorless solid, mp: 180–181 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.72 (d, J = 5.0 Hz, 1H), 8.67–8.66 (m, 1H), 8.36–8.33 (m, 1H), 8.05–7.98 (m, 3H), 7.72–7.68 (m, 1H), 7.53–7.47 (m, 3H), 7.34 (d, J = 5.0 Hz, 1H), 7.27–7.21 (m, 3H), 7.10–7.07 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.7, 149.6, 148.5, 148.3, 140.4, 139.7, 135.4, 131.3, 129.7, 129.4, 129.2, 129.0, 128.6, 128.1, 124.4, 123.7, 122.5, 121.9, 116.4, 99.0, 86.3; HRMS (ESI) m/z calcd for C$_{25}$H$_{17}$N$_2$O$_2$ (M + H)$^+$: 377.1290, found 377.1291.

4-(Naphthalen-1-yl)-2-phenyl-3-(phenylethynyl)pyridine (10e). Colorless gummy liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.77 (d, J = 4.8 Hz, 1H), 8.15–8.12 (m, 2H), 8.01–7.98 (m, 2H), 7.76–7.74 (m, 1H), 7.63–7.59 (m, 1H), 7.56–7.45 (m, 6H), 7.39 (d, J = 4.8 Hz, 1H). 7.17–7.06 (m, 3H), 6.63–6.60 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 160.3, 152.5, 148.0, 139.8, 137.0, 133.6, 131.2, 131.1, 129.8, 129.0, 128.9, 128.4, 128.4, 128.1, 127.9, 127.2, 126.5, 126.1, 126.1, 125.2, 123.6, 122.8, 118.5, 98.7, 86.9; HRMS (ESI) m/z calcd for C$_{29}$H$_{20}$N (M + H)$^+$: 382.1598, found 382.1596.

4-(Naphthalen-2-yl)-2-phenyl-3-(phenylethynyl)pyridine (10f). Colorless gummy liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.69 (d, J = 5.0 Hz, 1H), 8.22 (s, 1H), 8.04–7.86 (m, 6H), 7.59–7.46 (m, 5H), 7.42 (d, J = 5.0 Hz, 1H), 7.26–7.16 (m, 3H), 7.05–7.04 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.5, 152.4, 148.2, 140.1, 136.3, 133.4, 133.2, 131.3, 129.8, 128.9, 128.8, 128.6, 128.5, 128.4, 127.9, 127.8, 127.1, 126.9, 126.6, 123.1, 122.6, 121.3, 116.7, 98.1, 87.4; HRMS (ESI) m/z calcd for C$_{29}$H$_{20}$N (M + H)$^+$: 382.1596, found 382.1597.

2-Phenyl-3-(phenylethynyl)-4-(p-tolyl)pyridine (10g). Yellow gummy liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.65 (d, J = 8.6 Hz, 1H), 8.02 (d, J = 7.4 Hz, 2H), 7.66 (d, J = 7.8 Hz, 2H), 7.54–7.48 (m, 3H), 7.34–7.27 (m, 6H), 7.16–7.15 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.3, 152.4, 148.0, 140.1, 138.8, 135.8, 131.2, 129.8, 129.2, 128.9, 128.8, 128.5, 128.4, 127.9, 123.2, 122.3, 116.4, 97.7, 87.4, 21.5; HRMS (EI) m/z calcd for C$_{26}$H$_{19}$N (M$^+$): 345.1517, found 345.1521.

4-(3,4-Dimethoxyphenyl)-2-phenyl-3-(phenylethynyl)pyridine (10h). Light yellowish brown gummy liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.63 (d, J = 5.0 Hz, 1H), 7.98 (d, J = 6.8 Hz, 2H), 7.52–7.46 (m, 3H), 7.38–7.37 (m, 1H), 7.31–7.26 (m, 5H), 7.13–7.11 (m, 2H), 7.02–7.00 (m, 1H), 3.97 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 161.6, 152.1, 149.7, 148.5, 148.1, 140.2, 131.4, 131.3, 129.8, 128.9, 128.7, 128.5, 127.9, 123.2, 122.2, 122.0, 116.3, 112.8, 111.0, 97.9, 87.6, 56.2, 56.1; HRMS (EI) m/z calcd for C$_{27}$H$_{21}$NO$_2$ (M$^+$): 391.1572, found 391.1573.

4-Phenyl-2-(p-tolyl)-3-(p-tolylethynyl)pyridine (10i). Light yellowish brown gummy liquid, ^{1}H NMR (400 MHz, CDCl$_3$) δ_H (ppm): 8.63 (d, J = 5.0 Hz, 1H), 7.95–7.93 (m, 2H), 7.72–7.69 (m, 2H), 7.53–7.46 (m, 3H), 7.31–7.25 (m, 3H), 7.06–7.01 (m, 4H), 2.45 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ_C (ppm): 160.9,

152.6, 147.9, 139.0, 138.8, 137.3, 131.2, 129.7, 129.4, 129.2, 128.7, 128.6, 128.2, 122.1, 120.2, 116.5, 98.1, 86.9, 21.7, 21.6; HRMS (EI) m/z calcd for C$_{27}$H$_{21}$N (M$^+$): 359.1674, found 359.1675.

Conclusions

In conclusion, an approach for the synthesis of unsymmetrical functionalized (CHO, CN, COOEt) 1,3-butadiene-3-yne derivatives is reported starting from β-halo styrene derivatives and phenyl acetylenes in the presence of PdCl$_2$ and CuI catalysts. Good yields and wide substrate scope makes this protocol noteworthy. Also, these 1,3-buta-diene-3-ynals are utilized for the synthesis of novel 2,3,5-trisubstituted pyridine derivatives. Further efforts to synthesize complex heterocyclic derivatives from 1,3-buta-diene-3-ynals are currently underway in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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