Alkynylation of Aryl Bromides with Propargylamines Catalyzed by a Palladium-Tetraphosphine Complex

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Received 22 November 2004; revised 27 January 2005

Abstract: The tetraphosphine all-*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane in combination with $[Pd(C_3H_5)Cl]_2$ affords a very efficient catalyst for the alkynylation of aryl bromides with propargylamines. Higher reactions rates were observed with *N*,*N*-dialkylpropargylamines than with *N*-methylpropargylamine or propargylamine. A wide variety of substituents such as alkyl, phenyl, methoxy, dimethylamino, fluoro, trifluoromethyl, acetyl, benzoyl, formyl, carboxylate, nitro, or nitrile, on the aryl bromides are tolerated. High turnover numbers can be obtained with most of these aryl bromides. The coupling reaction of sterically very congested aryl bromides such as 9-bromoanthracene or 2,4,6-triisopropylbromobenzene also proceeds in good yields.

Key words: palladium, tetraphosphine, catalysis, alkynylation, propargylamine, aryl bromide

Substituted aryl propargylic amines bearing various substituents on the aromatic ring are of great biological interest since their structures display strong inhibitory activities towards several enzymes.[1] The palladium-catalyzed Sonogashira reaction is one of the most powerful methods for the formation of C–C bonds.[2] In recent years, several thermally stable palladium catalysts have been successfully used for Sonogashira reactions,[3] but most of these catalysts have not been tested in the synthesis of aryl propargylic amines by the coupling of aryl halides with propargylamine derivatives. The most popular ligand for the reaction of propargyl amine derivatives with aryl halides is triphenylphosphine. However, the catalyst formed by association of this ligand with palladium complexes is not very efficient in terms of substrate/catalyst ratio and 1–10 mol% of catalyst had to be used. Moreover, most of the results described involved very reactive substrates and the use of expensive aryl iodides.[4] Only a few results were described using less reactive aryl bromides.[5,6] We found only one example of the formation of such products using ligands other than triphenylphosphine; the reaction of *N*-propargylaniline with various heteroaryl bromides using Pd/C and several ligands was described by Lopez-Deber et al.[6] However, to our knowledge, low-catalyst loading Sonogashira alkynylation reactions using propargylamine derivatives have not been reported.

In order to obtain a highly stable palladium catalyst, we prepared the tetraphosphine ligand, all-*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane or tedicyp[7] (Figure 1). We have already reported the results obtained in allylic substitution,[7] Suzuki cross-coupling,[8] and for the Heck reaction[9] using tedicyp as the ligand. We have also reported recently the first results obtained for the Sonogashira reaction with this palladium catalyst.[10] In order to further expand the successful Sonogashira reaction with our catalyst, we herein report on the reaction of aryl bromides with propargylamine and *N*-substituted propargylamines.

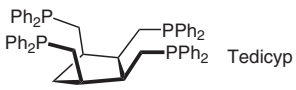
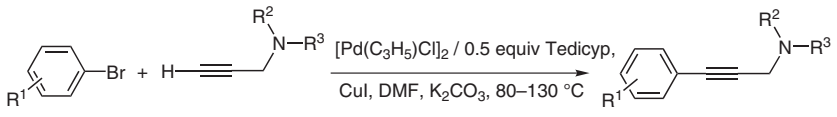


Figure 1

For this study, based on our previous results,[10] DMF was chosen as the solvent and potassium carbonate as the base. Copper(I) iodide (5 mol%) was added as co-catalyst. The reactions were performed at 80, 110, or 130 °C, under argon, in the presence of $[Pd(C_3H_5)Cl]_2$/tedicyp as catalyst in a ratio of 1:2.



R^1 = H, Me, *i*-Pr, *t*-Bu, OMe, F, CF_3, MeCO, PhCO, CHO, CO_2Me, CN, NO_2, NMe_2
R^2 and R^3 = H; R^2 and R^3 = Et; R^2 and R^3 = *n*-Pr; R^2 = H and R^3 = Me; R^2 = CH_2Ph and R^3 = Me

Scheme 1

SYNTHESIS 2005, No. 8, pp 1359–1367
Advanced online publication: 23.03.2005
DOI: 10.1055/s-2005-865284; Art ID: Z22104SS

First, we studied the influence of the *para*-substituents on the aryl bromide on the reaction rate for the coupling with the tertiary amine *N*,*N*-diethylpropargylamine (Scheme 1, Table 1). We observed that in most cases the reactions performed with *N*,*N*-diethylpropargylamine proceed very smoothly. As expected, electron-withdrawing groups on the aryl bromide support the reaction, while electron-donating groups are unfavorable. Complete conversions can be achieved with 0.1 mol% of this catalyst for activated substrates such as 4-bromoacetophenone, 4-bromobenzaldehyde, methyl 4-bromobenzoate, 4-bromobenzonitrile, and 4-bromonitrobenzene (Table 1, entries 2–9). With deactivated aryl bromides such as 4-bromoanisole and 4-dimethylaminobromobenzene lower reaction rates were observed and TONs of 232 and 92 were obtained, respectively (Table 1, entries 13–17). We also compared the reactivity of iodo- and bromobenzene and, as expected, we observed a much slower reaction with bromobenzene than with iodobenzene (Table 1, entries 1 and 12).

Then, we studied the influence of the presence of *meta*- and *ortho*-substituents on the aryl bromides on the reaction rate. As expected similar reaction rates were obtained with the *meta*-substituted 3-trifluoromethylbromobenzene and with the *para*-substituted 4-trifluoromethylbromobenzene (Table 1, entries 6 and 18). *Ortho*-substituents on the aryl bromides have a more important effect on the reaction rates. We observed that the coupling of 2-trifluoromethylbromobenzene with *N*,*N*-diethylpropargylamine also proceeds in the presence of 0.1 mol% of catalyst, however a low conversion of 46% was observed (Table 1, entry 25). With the other *ortho*-substituted aryl bromides, 2-bromoacetophenone, 2-bromobenzaldehyde, 2-bromobenzonitrile, or 2-bromonitrobenzene a similar tendency was observed; in all cases, they are less reactive than the *para*-substituted substrates (Table 1, entries 21–28).

Next, we tried to evaluate the difference of reaction rate between mono- and di-*ortho*-substituted aryl bromides, and we observed that even very hindered aryl bromides could be coupled efficiently with *N*,*N*-diethylpropargylamine. For example, with 9-bromoanthracene and 2,4,6-trimethylbromobenzene the aryl propargylic amines were obtained with excellent conversion, 100% and 85%, respectively, in the presence of 0.4 mol% and 2 mol% of catalyst (Table 1, entries 34–36). This coupling reaction also proceeds in the presence of a very sterically hindered substrate such as 1-bromo-2,4,6-triisopropylbenzene, but with this substrate the use of 4 mol% of catalyst was necessary (Table 1, entries 37 and 38). After this we investigated this reaction with 2- and 3-bromopyridines. The expected adducts were obtained in good yields in the presence of 0.4 mol% catalyst (Table 1, entries 39 and 40). Finally, the reactivity of two aryl chlorides was studied, 4-chloroacetophenone and 4-chlorobenzonitrile with *N*,*N*-diethylpropargylamine and 1 mol% catalyst led to the aryl propargylic amines in satisfactory yields (Table 1, entries 41 and 42).

Table 1 Palladium-Catalyzed Coupling Reaction of Aryl Halides with *N*,*N*-Diethylpropargylamine (Scheme 1)[a]

Entry	Aryl bromide	Product	Ratio substrate/catalyst	Yield[b]
1	Iodobenzene	**1**	10000:1	100 (94)
2	4-Bromoacetophenone	**2**	1000:1	100 (92)
3	4-Bromobenzophenone	**3**	1000:1	100 (92)
4	4-Bromobenzaldehyde	**4**	1000:1	100 (94)
5	Methyl 4-bromobenzoate	**5**	1000:1	100 (90)
6	4-Trifluoromethylbromobenzene	**6**	1000:1	100 (93)
7	4-Bromobenzonitrile	**7**	1000:1	100 (93)
8	4-Bromonitrobenzene	**8**	1000:1	100 (89)
9	3,5-Bis(trifluoromethyl)bromobenzene	**9**	1000:1	100 (91)
10	4-Fluorobromobenzene	**10**	250:1	100 (90)
11	4-Fluorobromobenzene	**10**	1000:1	50
12	Bromobenzene	**1**	250:1	100 (92)
13	4-Bromotoluene	**11**	250:1	100 (90)
14	4-Bromotoluene	**11**	1000:1	51
15	4-*t*-Butylbromobenzene	**12**	250:1	100 (95)
16	4-Bromoanisole	**13**	250:1	93 (87)
17	4-Bromo-*N*,*N*-dimethylaniline	**14**	100:1	92 (84)
18	3-Trifluoromethylbromobenzene	**15**	1000:1	100 (92)
19	2-Bromo-6-methoxynaphthalene	**16**	250:1	100 (94)
20	2-Bromo-6-methoxynaphthalene	**16**	1000:1	88
21	2-Bromoacetophenone	**17**	250:1	100 (90)
22	2-Bromoacetophenone	**17**	1000:1	29
23	2-Bromobenzaldehyde	**18**	1000:1	100 (88)
24	2-Trifluoromethylbromobenzene	**19**	250:1	100 (93)
25	2-Trifluoromethylbromobenzene	**19**	1000:1	46
26	2-Bromobenzonitrile	**20**	250:1	100 (89)
27	2-Bromobenzonitrile	**20**	1000:1	62
28	2-Bromonitrobenzene	**21**	250:1	100 (88)
29	2-Fluorobromobenzene	**22**	250:1	100 (93)
30	2-Fluorobromobenzene	**22**	1000:1	47
31	1-Bromonaphthalene	**23**	250:1	100 (94)
32	2-Bromoanisole	**24**	250:1	100 (90)
33	2,6-Difluorobromobenzene	**25**	100:1	100 (91)
34	9-Bromoanthracene	**26**	250:1	100 (87)

Table 1 Palladium-Catalyzed Coupling Reaction of Aryl Halides with *N*,*N*-Diethylpropargylamine (Scheme 1)[a] (continued)

Entry	Aryl bromide	Product	Ratio substrate/catalyst	Yield[b]
35	2,4,6-Trimethylbromobenzene	**27**	50:1	85 (80)
36	2,4,6-Trimethylbromobenzene	**27**	100:1	50
37	2,4,6-Triisopropylbromobenzene	**28**	25:1	84 (78)
38	2,4,6-Triisopropylbromobenzene	**28**	100:1	25
39	2-Bromopyridine	**29**	250:1	100 (89)
40	3-Bromopyridine	**30**	250:1	100 (92)
41	4-Chloroacetophenone	**2**	100:1	61[c]
42	4-Chlorobenzonitrile	**7**	100:1	85[c]

[a] Conditions: $[ClPd(C_3H_5)]_2$/tedicyp (1:2), aryl halide (1 mmol), *N*,*N*-diethylpropargylamine (2 mmol), K_2CO_3 (2 mmol), CuI (0.05 mmol), DMF, 110 °C, 20 h, argon.
[b] Yields determined by GC and NMR; figures in parentheses are isolated yields.
[c] Reactions performed without CuI.

These results prompted us to investigate the arylation of a few other propargylamine derivatives and propargylamine (Table 2). As expected, with the two tertiary amines *N*,*N*-dipropylpropargylamine and *N*,*N*-benzylmethylpropargylamine very similar results to those with *N*,*N*-diethylpropargylamine were obtained (Table 2, entries 1–12). For example, the reaction of *N*,*N*-dipropylpropargylamine in the presence of 0.1 mol% catalyst with activated aryl bromides such as 4-bromoacetophenone led to the complete conversion to the expected adduct in (Table 2, entry 2). Sterically hindered 9-bromoanthracene and *N*,*N*-benzylmethylpropargylamine with 0.4 mol% catalyst gave 100% conversion to the expected product **40** (Table 2, entry 12). The secondary amine *N*-methylpropargylamine was found to be less reactive than the tertiary amines by a factor of ten (Table 2, entries 13–18), for example, a low TON of 32 was obtained for the reaction of 4-bromoanisole with *N*-methylpropargylamine (Table 2, entries 16 and 17). A TON of 232 had been obtained for the reaction of 4-bromoanisole with *N*,*N*-diethylpropargylamine (Table 1, entry 16), this lower reactivity results from the reaction being carried out at a lower temperature (80 °C). However, the reaction performed at the same temperature (80 °C) with the primary amine propargylamine gave even lower TONs of 14–18 (Table 2, entries 19–21). These results suggest that with secondary and especially primary propargylamines a possible interaction between the nitrogen atom and the palladium complex has a decelerating effect on the reaction rate. It should be noted that with these two propargyl amines no amination product was detected.

The use of the tetradentate ligand tedicyp associated to a palladium complex provides a convenient catalyst for the coupling reaction of propargylamine derivatives with substituted aryl bromides. The complex seems to possess a fine balance between steric and electronic properties which generally allows for fast catalytic processes. As expected, both the steric hindrance and the electronic properties of the aryl bromides have an effect on the reaction rate. Electron-poor aryl bromides can be reacted at higher substrate/catalyst ratios than electron-rich aryl bromides. The presence of *ortho*-substituents generally led to lower TONs than the reactions performed in the presence of *para*-substituted aryl bromides. Di-*ortho*-substituted aryl bromides also gave the coupling products, but a low TON was observed with the sterically very congested 2,4,6-triisopropylbromobenzene. The substituents on the nitrogen atom of the propargylamine derivatives also have an important influence on the reaction rates. *N*,*N*-Dialkylpropargylamines such as *N*,*N*-diethylpropargylamine are more reactive than *N*-methylpropargylamine. The lowest TONs were observed in the presence of propargylamine, with this substrate, 5 mol% catalyst had to be used. For many substrates, with *N*,*N*-dialkylpropargylamines the reaction can be performed with as little as 0.1 mol% catalyst without further optimization of the reaction conditions. We believe that this system compares favorably with the other catalysts that have been reported for this process. Due to the high cost of palladium, the practical advantage of such low catalyst loading reactions is becoming increasingly important for industrial processes.

DMF analytical grade (99.8%) was not distilled before use. Potassium carbonate 99+ was used. All reactions were run under argon using vacuum lines in Schlenk tubes in oven-dried glassware. The reactions were followed by GC and NMR for high boiling point substrates and by GC for low boiling point substrates. ^1H (300 MHz) and ^{13}C (75 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shifts (δ) are reported in ppm relative to $CDCl_3$. Flash chromatography was performed on silica gel (230–400 mesh).

Preparation of the Pd-Tedicyp Catalyst[7]

An oven-dried 40-mL Schlenk tube equipped with a magnetic stirring bar, under argon atmosphere, was charged with $[Pd\text{-}\eta^3\text{-}C_3H_5)Cl]_2$ (4.2 mg, 11.6 μmol) and Tedicyp (20 mg, 23.2 μmol). Anhyd DMF (2.5 mL) was added, then the solution was stirred at r.t. for 10 min.

Palladium Calatalyzed Coupling Reaction; General Procedure

Aryl halide (1 mmol), alkyne (2 mmol), K_2CO_3 (0.276 g, 2 mmol), CuI (0.01 g, 0.05mmol), anhyd DMF (2 mL), and *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/0.5$[PdCl(C_3H_5)]_2$ complex under argon was heated at 80, 110, or 130 °C (see Tables 1 and 2). After this, H_2O (10 mL) was added and the product was extracted with Et_2O (**1**, **6**, **9**–**12**, **19**, **31**) or CH_2Cl_2 (**2**–**5**, **7**, **8**, **13**–**18**, **20**–**30**, **32**–**47**) (20 mL), the organic phase was dried ($MgSO_4$), and the solvent was evaporated. Chromatography on silica gel (**1**–**40**: Et_2O, then Et_2O–CH_2Cl_2; **41**–**47**: CH_2Cl_2, then CH_2Cl_2–MeOH) gave the desired coupled product.

3-(Diethylamino)-1-phenylpropyne (1)[4h]

The reaction of iodobenzene (0.204 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **1** in 94% (0.176 g) yield.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 2 H), 7.24 (m, 3 H), 3.60 (s, 2 H), 2.59 (q, 4 H, *J* = 7.2 Hz), 1.08 (t, 6 H, *J* = 7.2 Hz).

Table 2 Palladium-Catalyzed Coupling Reaction of Aryl Halides with Propargylamine Derivatives (Scheme 1)[a]

Entry	Aryl bromide	Alkyne	Product	Ratio substrate/catalyst	Yield[b]
1	Iodobenzene	*N*,*N*-Dipropylpropargylamine	**31**	10000:1	100 (90)
2	4-Bromoacetophenone	*N*,*N*-Dipropylpropargylamine	**32**	1000:1	100 (94)
3	4-*t*-Butylbromobenzene	*N*,*N*-Dipropylpropargylamine	**33**	250:1	100 (94)
4	1-Bromonaphthalene	*N*,*N*-Dipropylpropargylamine	**34**	250:1	100 (91)
5	1-Bromonaphthalene	*N*,*N*-Dipropylpropargylamine	**34**	1000:1	82
6	3-Trifluoromethylbromobenzene	*N*,*N*-Dipropylpropargylamine	**35**	1000:1	100 (92)
7	Iodobenzene	*N*,*N*-Benzylmethylpropargylamine	**36**	10000:1	100 (88)
8	4-Trifluoromethylbromobenzene	*N*,*N*-Benzylmethylpropargylamine	**37**	1000:1	100 (86)
9	4-*t*-Butylbromobenzene	*N*,*N*-Benzylmethylpropargylamine	**38**	250:1	100 (89)
10	4-*t*-Butylbromobenzene	*N*,*N*-Benzylmethylpropargylamine	**38**	1000:1	84
11	4-Bromoanisole	*N*,*N*-Benzylmethylpropargylamine	**39**	250:1	100 (90)
12	9-Bromoanthracene	*N*,*N*-Benzylmethylpropargylamine	**40**	250:1	100 (84)
13	Iodobenzene	*N*-Methylpropargylamine	**41**	250:1	100 (82)[c]
14	Iodobenzene	*N*-Methylpropargylamine	**41**	1000:1	83[c]
15	4-*t*-Butylbromobenzene	*N*-Methylpropargylamine	**42**	100:1	100 (84)[c]
16	4-Bromoanisole	*N*-Methylpropargylamine	**43**	25:1	100 (80)[c]
17	4-Bromoanisole	*N*-Methylpropargylamine	**43**	100:1	32[c]
18	1-Bromonaphthalene	*N*-Methylpropargylamine	**44**	250:1	100 (82)[c]
19	Iodobenzene	Propargylamine	**45**	20:1	88 (74)[c]
20	4-Bromotoluene	Propargylamine	**46**	20:1	72 (64)[c]
21	1-Bromonaphthalene	Propargylamine	**47**	20:1	86 (67)[c]

[a] Conditions: $[ClPd(C_3H_5)]_2$/tedicyp (1:2), aryl halide (1 mmol), alkyne (2 mmol), K_2CO_3 (2 mmol), CuI (0.05 mmol), DMF, 130 °C, 20 h, argon.
[b] Yields determined by GC and NMR; figures in parentheses are isolated yields.
[c] Reaction temperature: 80 °C.

1-(4-Acetylphenyl)-3-(diethylamino)propyne (2)
The reaction of 4-bromoacetophenone (0.199 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **2** in 92% (0.211 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, 2 H, *J* = 8.3 Hz), 7.48 (d, 2 H, *J* = 8.3 Hz), 3.67 (s, 2 H), 2.63 (q, 4 H, *J* = 7.2 Hz), 2.58 (s, 3 H), 1.12 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.1, 135.9, 131.6, 128.1, 128.0, 88.0, 84.3, 47.2, 41.4, 26.4, 12.4.

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.37; H, 8.19.

1-(4-Benzoylphenyl)-3-(diethylamino)propyne (3)
The reaction of 4-bromobenzophenone (0.261 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **3** in 92% (0.268 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (m, 4 H), 7.59 (t, 1 H, *J* = 7.4 Hz), 7.51 (d, 2 H, *J* = 8.1 Hz), 7.47 (t, 2 H, *J* = 7.2 Hz), 3.68 (s, 2 H), 2.65 (q, 4 H, *J* = 7.2 Hz), 1.13 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.6, 137.2, 136.4, 132.3, 131.3, 129.8, 129.7, 128.1, 127.4, 87.6, 84.3, 47.2, 41.4, 12.4.

Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26. Found: C, 82.21; H, 7.10.

3-(Diethylamino)-1-(4-formylphenyl)propyne (4)
The reaction of 4-bromobenzaldehyde (0.185 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **4** in 94% (0.202 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.99 (s, 1 H), 7.80 (d, 2 H, *J* = 8.2 Hz), 7.55 (d, 2 H, *J* = 8.2 Hz), 3.66 (s, 2 H), 2.62 (q, 4 H, *J* = 7.2 Hz), 1.11 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.2, 135.1, 132.1, 129.5, 129.3, 88.9, 84.2, 47.3, 41.5, 12.4.

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 77.99; H, 7.82.

4-[3-(Diethylamino)prop-1-ynyl]benzoic Acid Methyl Ester (5)
The reaction of methyl 4-bromobenzoate (0.215 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **5** in 90% (0.221 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, 2 H, *J* = 8.2 Hz), 7.42 (d, 2 H, *J* = 8.2 Hz), 3.86 (s, 3 H), 3.61 (s, 2 H), 2.58 (q, 4 H, *J* = 7.2 Hz), 1.07 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 131.5, 129.3, 129.1, 128.0, 87.8, 84.2, 52.0, 47.2, 41.4, 12.5.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.57; H, 7.97.

3-(Diethylamino)-1-(4-trifluoromethylphenyl)propyne (6)
The reaction of 4-trifluoromethylbromobenzene (0.225 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **6** in 93% (0.237 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (d, 2 H, *J* = 8.7 Hz), 7.47 (d, 2 H, *J* = 8.7 Hz), 3.62 (s, 2 H), 2.59 (q, 4 H, *J* = 7.2 Hz), 1.08 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.8, 129.4 (q, *J* = 32.4 Hz), 127.0, 125.0 (q, *J* = 3.9 Hz), 123.8 (q, *J* = 272.2 Hz), 87.1, 83.7, 47.3, 41.4, 12.4.

Anal. Calcd for $C_{14}H_{16}F_3N$: C, 65.87; H, 6.32. Found: C, 65.74; H, 6.43.

1-(4-Cyanophenyl)-3-(diethylamino)propyne (7)
The reaction of 4-bromobenzonitrile (0.182 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **7** in 93% (0.197 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, 2 H, *J* = 8.4 Hz), 7.46 (d, 2 H, *J* = 8.4 Hz), 3.64 (s, 2 H), 2.60 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.8, 131.5, 127.8, 118.0, 110.8, 89.0, 83.3, 47.0, 41.2, 12.1.

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60. Found: C, 79.00; H, 7.68.

3-(Diethylamino)-1-(4-nitrophenyl)propyne (8)[1]
The reaction of 4-bromonitrobenzene (0.202 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **8** in 89% (0.207 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (d, 2 H, *J* = 8.5 Hz), 7.52 (d, 2 H, *J* = 8.5 Hz), 3.66 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.10 (t, 6 H, *J* = 7.2 Hz).

1-[3,5-Bis(trifluoromethyl)phenyl]-3-(diethylamino)propyne (9)
The reaction of 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **9** in 91% (0.294 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (s, 2 H), 7.75 (s, 1 H), 3.64 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.10 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.6 (q, *J* = 33.4 Hz), 131.4, 125.5, 122.5 (q, *J* = 272.8 Hz), 121.1 (m), 88.5, 82.1, 47.3, 41.3, 12.4.

Anal. Calcd for $C_{15}H_{15}F_6N$: C, 55.73; H, 4.68. Found: C, 55.91; H, 4.87.

3-(Diethylamino)-1-(4-fluorophenyl)propyne (10)
The reaction of 4-fluorobromobenzene (0.175 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **10** in 90% (0.185 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37 (dd, 2 H, *J* = 8.7, 5.5 Hz), 6.96 (t, 2 H, *J* = 8.7 Hz), 3.60 (s, 2 H), 2.60 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.2 (d, *J* = 248.6 Hz), 133.5 (d, *J* = 8.3 Hz), 119.4 (d, *J* = 3.3 Hz), 115.4 (d, *J* = 21.9 Hz), 84.1, 83.8, 47.3, 41.4, 12.9.

Anal. Calcd for $C_{13}H_{16}FN$: C, 76.06; H, 7.86. Found: C, 75.87; H, 7.99.

3-(Diethylamino)-1-(*p*-tolyl)propyne (11)[11]
The reaction of 4-bromotoluene (0.171 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **11** in 90% (0.181 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, 2 H, *J* = 8.1 Hz), 7.08 (d, 2 H, *J* = 8.1 Hz), 3.60 (s, 2 H), 2.60 (q, 4 H, *J* = 7.2 Hz), 2.31 (s, 3 H), 1.09 (t, 6 H, *J* = 7.2 Hz).

1-(4-*t*-Butylphenyl)-3-(diethylamino)propyne (12)
The reaction of 4-*t*-butylbromobenzene (0.213 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **12** in 95% (0.231 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (d, 2 H, *J* = 8.3 Hz), 6.31 (d, 2 H, *J* = 8.3 Hz), 3.62 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.29 (s, 9 H), 1.10 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.0, 131.3, 125.1, 120.1, 85.0, 83.2, 47.2, 41.3, 31.3, 31.0, 12.4.

Anal. Calcd for $C_{17}H_{25}N$: C, 83.89; H, 10.35. Found: C, 83.74; H, 10.21.

1-(*p*-Anisyl)-3-(diethylamino)propyne (13)[11]
The reaction of 4-bromoanisole (0.187 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **13** in 87% (0.189 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24 (d, 2 H, *J* = 8.7 Hz), 6.71 (d, 2 H, *J* = 8.7 Hz), 3.69 (s, 3 H), 3.51 (s, 2 H), 2.52 (q, 4 H, *J* = 7.2 Hz), 1.00 (t, 6 H, *J* = 7.2 Hz).

3-(Diethylamino)-1-(4-dimethylaminophenyl)propyne (14)
The reaction of 4-bromo-*N*,*N*-dimethylaniline (0.200 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **14** in 84% (0.194 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (d, 2 H, *J* = 8.8 Hz), 6.59 (d, 2 H, *J* = 8.8 Hz), 3.60 (s, 2 H), 2.93 (s, 6 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.7, 132.4, 111.5, 109.9, 85.7, 80.9, 47.0, 41.3, 40.0, 12.2.

Anal. Calcd for $C_{15}H_{22}N_2$: C, 78.21; H, 9.63. Found: C, 78.40; H, 9.51.

3-(Diethylamino)-1-(3-trifluoromethylphenyl)propyne (15)[12]
The reaction of 3-trifluoromethylbromobenzene (0.225 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **15** in 92% (0.235 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1 H), 7.57 (d, 1 H, *J* = 7.7 Hz), 7.52 (d, 1 H, *J* = 7.7 Hz), 7.40 (t, 1 H, *J* = 7.7 Hz), 3.64 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.11 (t, 6 H, *J* = 7.2 Hz).

3-(Diethylamino)-1-(6-methoxynaphthalen-2-yl)propyne (16)
The reaction of 2-bromo-6-methoxynaphthalene (0.237 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **16** in 94% (0.251 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (s, 1 H), 7.65 (d, 1 H, *J* = 7.3 Hz), 7.63 (d, 1 H, *J* = 7.3 Hz), 7.43 (dd, 1 H, *J* = 8.5, 1.5 Hz), 7.13 (dd, 1 H, *J* = 8.5, 2.4 Hz), 7.06 (d, 1 H, *J* = 2.4 Hz), 3.88 (s, 3 H), 3.68 (s, 2 H), 2.66 (q, 4 H, *J* = 7.2 Hz), 1.14 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 133.6, 130.8, 128.9, 128.8, 128.1, 126.4, 119.0, 117.9, 105.4, 85.2, 83.5, 55.0, 47.0, 41.2, 12.3.

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92. Found: C, 80.97; H, 7.80.

1-(2-Acetylphenyl)-3-(diethylamino)propyne (17)
The reaction of 2-bromoacetophenone (0.199 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **17** in 90% (0.206 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, 1 H, *J* = 7.8 Hz), 7.50 (d, 1 H, *J* = 7.8 Hz), 7.45–7.30 (m, 2 H), 3.68 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.3, 140.8, 134.2, 130.9, 128.2, 127.8, 121.4, 90.6, 83.8, 47.3, 41.5, 29.7, 12.5.

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.40; H, 8.41.

3-(Diethylamino)-1-(2-formylphenyl)propyne (18)
The reaction of 2-bromobenzaldehyde (0.185 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **18** in 88% (0.190 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.54 (s, 1 H), 7.89 (d, 1 H, *J* = 7.8 Hz), 7.52 (m, 2 H), 7.40 (m, 1 H), 3.71 (s, 2 H), 2.62 (q, 4 H, *J* = 7.2 Hz), 1.11 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.3, 135.6, 133.5, 133.3, 128.1, 126.7, 126.6, 91.9, 80.4, 47.2, 41.3, 12.4.

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.34; H, 7.77.

3-(Diethylamino)-1-(2-trifluoromethylphenyl)propyne (19)
The reaction of 2-trifluoromethylbromobenzene (0.225 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **19** in 93% (0.237 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, 1 H, *J* = 8.0 Hz), 7.55 (d, 1 H, *J* = 7.8 Hz), 7.45 (t, 1 H, *J* = 7.6 Hz), 7.36 (t, 1 H, *J* = 7.6 Hz), 3.69 (s, 2 H), 2.62 (q, 4 H, *J* = 7.2 Hz), 1.10 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.1, 131.2, 131.3 (q, *J* = 30.2 Hz), 127.6, 125.5 (q, *J* = 4.9 Hz), 123.2 (q, *J* = 273.4 Hz), 121.3 (q, *J* = 2.1 Hz), 90.4, 81.0, 47.2, 41.1, 12.4.

Anal. Calcd for $C_{14}H_{16}F_3N$: C, 65.87; H, 6.32. Found: C, 65.61; H, 6.18.

1-(2-Cyanophenyl)-3-(diethylamino)propyne (20)
The reaction of 2-bromobenzonitrile (0.182 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **20** in 89% (0.189 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, 1 H, *J* = 7.5 Hz), 7.42 (m, 2 H), 7.28 (m, 1 H), 3.64 (s, 2 H), 2.58 (q, 4 H, *J* = 7.2 Hz), 1.02 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 132.3, 132.1, 132.1, 127.9, 126.9, 117.4, 115.0, 91.2, 81.2, 47.2, 41.2, 12.4.

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60. Found: C, 78.97; H, 7.51.

3-(Diethylamino)-1-(2-nitrophenyl)propyne (21)[13]
The reaction of 2-bromonitrobenzene (0.202 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **21** in 88% (0.204 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, 1 H, *J* = 8.0 Hz), 7.58 (d, 1 H, *J* = 7.7 Hz), 7.51 (t, 1 H, *J* = 7.7 Hz), 7.40 (t, 1 H, *J* = 7.6 Hz), 3.69 (s, 2 H), 2.63 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

3-(Diethylamino)-1-(2-fluorophenyl)propyne (22)
The reaction of 2-fluorobromobenzene (0.175 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **22** in 93% (0.191 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40 (t, 1 H, *J* = 7.5 Hz), 7.25 (m, 1 H), 7.05 (m, 2 H), 3.68 (s, 2 H), 2.63 (q, 4 H, *J* = 7.2 Hz), 1.11 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.4 (d, *J* = 250.8 Hz), 133.3, 129.3 (d, *J* = 8.2 Hz), 123.6 (d, *J* = 3.9 Hz), 115.1 (d, *J* = 20.8 Hz), 111.5 (d, *J* = 15.9 Hz), 89.5 (d, *J* = 3.3 Hz), 78.1, 47.1, 41.3, 12.4.

Anal. Calcd for $C_{13}H_{16}FN$: C, 76.06; H, 7.86. Found: C, 76.21; H, 8.04.

3-(Diethylamino)-1-(naphthalen-1-yl)propyne (23)[14]
The reaction of 1-bromonaphthalene (0.207 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **23** in 94% (0.223 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, 1 H, *J* = 8.5 Hz), 7.83 (d, 1 H, *J* = 7.9 Hz), 7.79 (d, 1 H, *J* = 8.4 Hz), 7.66 (d, 1 H, *J* = 8.3 Hz), 7.56 (t, 1 H, *J* = 7.5 Hz), 7.52 (t, 1 H, *J* = 7.5 Hz), 7.40 (t, 1 H, *J* = 7.4 Hz), 3.83 (s, 2 H), 2.73 (q, 4 H, *J* = 7.2 Hz), 1.18 (t, 6 H, *J* = 7.2 Hz).

1-(*o*-Anisyl)-3-(diethylamino)propyne (24)
The reaction of 2-bromoanisole (0.187 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **24** in 90% (0.196 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (dd, 1 H, *J* = 7.4, 1.9 Hz), 7.22 (td, 1 H, *J* = 7.5, 1.9 Hz), 6.84 (td, 1 H, *J* = 7.5, 1.9 Hz), 6.82 (d, 1 H, *J* = 7.5 Hz), 3.83 (s, 3 H), 3.67 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7, 133.2, 129.0, 120.0, 112.2, 110.4, 88.0, 81.0, 55.4, 47.0, 41.4, 12.3.

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 77.21; H, 8.94.

3-(Diethylamino)-1-(2,6-difluorophenyl)propyne (25)
The reaction of 2,6-difluorobromobenzene (0.193 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **25** in 91% (0.203 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (m, 1 H), 6.86 (m, 2 H), 3.70 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.09 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.6 (d, *J* = 253.1 Hz), 129.1 (t, *J* = 9.8 Hz), 110.0 (d, *J* = 24.7 Hz), 102.1 (t, *J* = 19.7 Hz), 94.8 (t, *J* = 3.2 Hz), 71.7, 47.2, 41.4, 12.5.

Anal. Calcd for $C_{13}H_{15}F_2N$: C, 69.94; H, 6.77. Found: C, 70.12; H, 6.84.

1-(Anthracen-9-yl)-3-(diethylamino)propyne (26)
The reaction of 9-bromoanthracene (0.257 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **26** in 87% (0.250 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.55 (d, 2 H, *J* = 8.7 Hz), 8.39 (s, 1 H), 7.99 (d, 2 H, *J* = 8.7 Hz), 7.55 (t, 2 H, *J* = 7.0 Hz), 7.50 (t, 2

H, *J* = 7.0 Hz), 4.01 (s, 2 H), 2.80 (q, 4 H, *J* = 7.2 Hz), 1.23 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 132.7, 131.1, 128.6, 127.2, 126.7, 126.4, 125.5, 117.4, 95.6, 81.5, 47.6, 41.8, 12.8.

Anal. Calcd for $C_{21}H_{21}N$: C, 87.76; H, 7.36. Found: C, 87.56; H, 7.49.

3-(Diethylamino)-1-(2,4,6-trimethylphenyl)propyne (27)[15]
The reaction of 2,4,6-trimethylbromobenzene (0.199 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **27** in 80% (0.183 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.83 (s, 2 H), 3.73 (s, 2 H), 2.62 (q, 4 H, *J* = 7.2 Hz), 2.36 (s, 6 H), 2.25 (s, 3 H), 1.11 (t, 6 H, *J* = 7.2 Hz).

3-(Diethylamino)-1-(2,4,6-triisopropylphenyl)propyne (28)
The reaction of 2,4,6-triisopropylbromobenzene (0.283 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **28** in 78% (0.245 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.95 (s, 2 H), 3.75 (s, 2 H), 3.50 (septet, 2 H, *J* = 7.0 Hz), 2.85 (septet, 1 H, *J* = 7.0 Hz), 2.62 (q, 4 H, *J* = 7.2 Hz), 1.24 (d, 18 H, *J* = 7.0 Hz), 1.12 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 148.6, 120.1, 118.6, 91.4, 81.9, 47.5, 41.3, 34.5, 31.7, 23.9, 23.7, 12.8.

Anal. Calcd for $C_{22}H_{35}N$: C, 84.28; H, 11.25. Found: C, 84.41; H, 11.34.

3-(Diethylamino)-1-(pyridin-2-yl)propyne (29)[1]
The reaction of 2-bromopyridine (0.158 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **29** in 89% (0.168 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53 (d, 1 H, *J* = 4.5 Hz), 7.60 (td, 1 H, *J* = 7.7, 1.7 Hz), 7.37 (d, 1 H, *J* = 7.8 Hz), 7.18 (dd, 1 H, *J* = 7.8, 4.5 Hz), 3.65 (s, 2 H), 2.61 (q, 4 H, *J* = 7.2 Hz), 1.08 (t, 6 H, *J* = 7.2 Hz).

3-(Diethylamino)-1-(pyridin-3-yl)propyne (30)[16]
The reaction of 3-bromopyridine (0.158 g, 1 mmol) and *N*,*N*-diethylpropargylamine (0.222 g, 2 mmol) afforded **30** in 92% (0.173 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66 (m, 1 H), 8.54 (m, 1 H), 7.67 (d, 1 H, *J* = 7.7 Hz), 7.21 (m, 1 H), 3.62 (s, 2 H), 2.59 (q, 4 H, *J* = 7.2 Hz), 1.07 (t, 6 H, *J* = 7.2 Hz).

3-(Dipropylamino)-1-phenylpropyne (31)[12]
The reaction of iodobenzene (0.204 g, 1 mmol) and *N*,*N*-dipropylpropargylamine (0.278 g, 2 mmol) afforded **31** in 90% (0.194 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (m, 2 H), 7.56 (m, 3 H), 3.52 (s, 2 H), 2.41 (t, 4 H, *J* = 7.2 Hz), 1.42 (m, 4 H), 0.83 (t, 6 H, *J* = 7.2 Hz).

1-(4-Acetylphenyl)-3-(dipropylamino)propyne (32)
The reaction of 4-bromoacetophenone (0.199 g, 1 mmol) and *N*,*N*-dipropylpropargylamine (0.278 g, 2 mmol) afforded **32** in 94% (0.242 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δEt_2O= 7.83 (d, 2 H, *J* = 8.3 Hz), 7.44 (d, 2 H, *J* = 8.3 Hz), 3.58 (s, 2 H), 2.53 (s, 3 H), 2.44 (t, 4 H, *J* = 7.2 Hz), 1.46 (m, 4 H), 0.87 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.1, 135.8, 131.7, 128.3, 128.0, 88.7, 84.2, 55.8, 42.7, 26.4, 20.6, 11.8.

Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 79.09; H, 8.87.

1-(4-*tert*-Butylphenyl)-3-(dipropylamino)propyne (33)
The reaction of 4-*tert*-butylbromobenzene (0.213 g, 1 mmol) and *N*,*N*-dipropylpropargylamine (0.278 g, 2 mmol) afforded **33** in 94% (0.255 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (d, 2 H, *J* = 8.6 Hz), 7.29 (d, 2 H, *J* = 8.6 Hz), 3.58 (s, 2 H), 2.47 (t, 4 H, *J* = 7.2 Hz), 1.49 (m, 4 H), 1.27 (s, 9 H), 0.89 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.9, 131.3, 125.1, 120.3, 84.9, 83.9, 55.8, 42.7, 31.2, 31.0, 20.6, 11.8.

Anal. Calcd for $C_{19}H_{29}N$: C, 84.07; H, 10.77. Found: C, 84.27; H, 10.60.

3-(Dipropylamino)-1-(naphthalen-1-yl)propyne (34)
The reaction of 1-bromonaphthalene (0.207 g, 1 mmol) and *N*,*N*-dipropylpropargylamine (0.278 g, 2 mmol) afforded **34** in 91% (0.242 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.35 (d, 1 H, *J* = 8.5 Hz,), 7.83 (d, 1 H, *J* = 7.9 Hz), 7.79 (d, 1 H, *J* = 8.4 Hz), 7.66 (d, 1 H, *J* = 8.3 Hz), 7.56 (t, 1 H, *J* = 7.5 Hz), 7.52 (t, 1 H, *J* = 7.5 Hz), 7.39 (t, 1 H, *J* = 7.4 Hz), 3.78 (s, 2 H), 2.60 (t, 4 H, *J* = 7.2 Hz), 1.58 (m, 4 H), 0.96 (t, 6 H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 133.3, 133.1, 130.3, 128.2, 128.1, 126.5, 126.2, 126.1, 125.1, 121.1, 89.7, 82.9, 56.0, 42.9, 20.8, 11.9.

Anal. Calcd for $C_{19}H_{23}N$: C, 85.99; H, 8.74. Found: C, 86.15; H, 8.86.

3-(Dipropylamino)-1-(3-trifluoromethylphenyl)propyne (35)[12]
The reaction of 3-trifluoromethylbromobenzene (0.225 g, 1 mmol) and *N*,*N*-dipropylpropargylamine (0.278 g, 2 mmol) afforded **35** in 92% (0.261 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (s, 1 H), 7.56 (d, 1 H, *J* = 7.7 Hz), 7.52 (d, 1 H, *J* = 7.7 Hz), 7.40 (t, 1 H, *J* = 7.7 Hz), 3.60 (s, 2 H), 2.47 (t, 4 H, *J* = 7.2 Hz), 1.50 (m, 4 H), 0.91 (t, 6 H, *J* = 7.2 Hz).

3-(Benzylmethylamino)-1-(phenyl)propyne (36)[17]
The reaction of iodobenzene (0.204 g, 1 mmol) and *N*,*N*-benzylmethylpropargylamine (0.318 g, 2 mmol) afforded **36** in 88% (0.207 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.25 (m, 9 H), 3.63 (s, 2 H), 2.50 (s, 2 H), 2.39 (s, 3 H).

3-(Benzylmethylamino)-1-(4-trifluoromethylphenyl)propyne (37)
The reaction of 4-trifluoromethylbromobenzene (0.225 g, 1 mmol) and *N*,*N*-benzylmethylpropargylamine (0.318 g, 2 mmol) afforded **37** in 86% (0.261 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60 (m, 4 H), 7.45–7.25 (m, 5 H), 3.68 (s, 2 H), 2.57 (s, 2 H), 2.46 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.3, 131.9, 129.8 (q, *J* = 32.4 Hz), 129.1, 128.3, 127.3, 127.1, 125.1 (q, *J* = 3.9 Hz), 123.9 (q, *J* = 271.8 Hz), 87.3, 84.4, 60.3, 45.7, 42.0.

Anal. Calcd for $C_{18}H_{16}F_3N$: C, 71.28; H, 5.32. Found: C, 71.48; H, 5.32.

3-(Benzylmethylamino)-1-(4-*tert*-butylphenyl)propyne (38)
The reaction of 4-*t*-butylbromobenzene (0.213 g, 1 mmol) and *N*,*N*-benzylmethylpropargylamine (0.318 g, 2 mmol) afforded **38** in 89% (0.259 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.22 (m, 9 H), 3.64 (s, 2 H), 3.51 (s, 2 H), 2.40 (s, 3 H), 1.32 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.2, 138.5, 131.4, 129.3, 128.3, 127.2, 125.3, 120.3, 85.7, 83.6, 60.2, 45.7, 41.9, 34.7, 31.2.

Anal. Calcd for $C_{21}H_{25}N$: C, 86.55; H, 8.65. Found: C, 86.40; H, 8.52.

1-(*p*-Anisyl)-3-(benzylmethylamino)propyne (39)
The reaction of 4-bromoanisole (0.187 g, 1 mmol) and *N*,*N*-benzylmethylpropargylamine (0.318 g, 2 mmol) afforded **39** in 90% (0.239 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.10 (m, 7 H), 6.73 (d, 2 H, *J* = 8.5 Hz), 3.68 (s, 3 H), 3.53 (s, 2 H), 3.40 (s, 2 H), 2.29 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 138.5, 133.0, 129.2, 128.2, 127.1, 115.4, 113.8, 85.4, 82.8, 60.2, 55.2, 45.8, 41.9.

Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22. Found: C, 81.21; H, 7.01.

1-(Anthracen-9-yl)-3-(benzylmethylamino)propyne (40)
The reaction of 9-bromoanthracene (0.257 g, 1 mmol) and *N*,*N*-benzylmethylpropargylamine (0.318 g, 2 mmol) afforded **40** in 84% (0.282 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, 2 H, *J* = 8.6 Hz), 8.42 (s, 1 H), 8.01 (d, 2 H, *J* = 8.6 Hz), 7.70–7.20 (m, 9 H), 3.89 (s, 2 H), 3.84 (s, 2 H), 2.61 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.5, 132.7, 131.1, 129.3, 128.6, 128.4, 127.3, 127.2, 126.7, 126.5, 125.6, 117.5, 95.9, 82.3, 60.3, 46.3, 42.3.

Anal. Calcd for $C_{25}H_{21}N$: C, 89.51; H, 6.31. Found: C, 89.71; H, 6.14.

3-(Methylamino)-1-(phenyl)propyne (41)[4d]
The reaction of iodobenzene (0.204 g, 1 mmol) and *N*-methylpropargylamine (0.138 g, 2 mmol) afforded **41** in 82% (0.119 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (m, 2 H), 7.18 (m, 3 H), 3.49 (s, 2 H), 2.42 (s, 3 H).

1-(4-*tert*-Butylphenyl)-3-(methylamino)propyne (42)
The reaction of 4-*tert*-butylbromobenzene (0.213 g, 1 mmol) and *N*-methylpropargylamine (0.138 g, 2 mmol) afforded **42** in 84% (0.169 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (d, 2 H, *J* = 8.5 Hz), 7.34 (d, 2 H, *J* = 8.5 Hz), 3.65 (s, 2 H), 2.56 (s, 3 H), 2.39 (s, 1 H), 1.29 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.4, 131.4, 125.5, 120.0, 86.4, 83.7, 40.6, 35.1, 34.7, 31.1.

Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51. Found: C, 83.29; H, 9.38.

1-(*p*-Anisyl)-3-(methylamino)propyne (43)
The reaction of 4-bromoanisole (0.187 g, 1 mmol) and *N*-methylpropargylamine (0.138 g, 2 mmol) afforded **43** in 80% (0.140 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, 2 H, *J* = 7.8 Hz), 6.78 (d, 2 H, *J* = 7.8 Hz), 3.75 (s, 3 H), 3.55 (s, 2 H), 2.49 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 132.8, 114.7, 113.6, 86.2, 84.1, 55.0, 40.2, 34.6.

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48. Found: C, 75.61; H, 7.67.

3-(Methylamino)-1-(naphthalen-1-yl)propyne (44)
The reaction of 1-bromonaphthalene (0.207 g, 1 mmol) and *N*-methylpropargylamine (0.138 g, 2 mmol) afforded **44** in 82% (0.160 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, 1 H, *J* = 8.5 Hz), 7.83 (d, 1 H, *J* = 7.9 Hz), 7.79 (d, 1 H, *J* = 8.4 Hz), 7.65 (d, 1 H, *J* = 8.3 Hz), 7.55 (t, 1 H, *J* = 7.5 Hz), 7.49 (t, 1 H, *J* = 7.5 Hz), 7.40 (t, 1 H, *J* = 7.4 Hz), 3.77 (s, 2 H), 2.62 (s, 3 H), 2.15 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 133.2, 133.1, 130.3, 128.4, 128.2, 126.6, 126.3, 126.1, 125.1, 120.8, 86.7, 81.3, 41.0, 35.4.

Anal. Calcd for $C_{14}H_{13}N$: C, 86.12; H, 6.71. Found: C, 86.33; H, 6.57.

3-Phenylprop-2-ynylamine (45)[18]
The reaction of iodobenzene (0.204 g, 1 mmol) and propargylamine (0.110 g, 2 mmol) afforded **45** in 74% (0.097 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (m, 2 H), 7.17 (m, 3 H), 3.52 (s, 2 H).

3-(*p*-Tolyl)prop-2-ynylamine (46)[19]
The reaction of 4-bromotoluene (0.171 g, 1 mmol) and propargylamine (0.110 g, 2 mmol) afforded **46** in 64% (0.093 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, 2 H, *J* = 8.0 Hz), 7.07 (d, 2 H, *J* = 8.0 Hz), 3.60 (s, 2 H), 2.31 (s, 3 H).

3-(Naphthalen-1-yl)prop-2-ynylamine (47)
The reaction of 1-bromonaphthalene (0.207 g, 1 mmol) and propargylamine (0.110 g, 2 mmol) afforded **47** in 67% (0.122 g) yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (d, 1 H, *J* = 8.5 Hz), 7.82 (d, 1 H, *J* = 7.9 Hz), 7.78 (d, 1 H, *J* = 8.4 Hz), 7.63 (d, 1 H, *J* = 8.3 Hz), 7.55 (t, 1 H, *J* = 7.5 Hz), 7.49 (t, 1 H, *J* = 7.5 Hz), 7.39 (t, 1 H, *J* = 7.4 Hz), 3.78 (s, 2 H), 1.68 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 133.2, 133.1, 130.2, 128.4, 128.2, 126.6, 126.3, 126.0, 125.1, 120.8, 95.1, 80.4, 32.4.

Anal. Calcd for $C_{13}H_{11}N$: C, 86.15; H, 6.12. Found: C, 86.42; H, 5.97.

Acknowledgment

We thank the CNRS for providing financial support.

References

(1) Olivi, N.; Spruyt, P.; Peyrat, J.-F.; Alami, M.; Brion, J.-D. *Tetrahedron Lett.* **2004**, *45*, 2607.
(2) For reviews on the palladium-catalyzed reaction of aryl halides with alkynes see: (a) Sonogashira, K. *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: New York, **1998**. (b) Brandsma, L.; Vasilevsky, S. F.; Verkruijsse, H. D. *Application of Transition Metal Catalysts in Organic Synthesis*; Springer-Verlag: Berlin, **1998**. (c) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.
(3) For examples of efficient Pd-catalysts for the alkynylation of aryl halides: (a) Herrmann, W. A.; Reisinger, C.-P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93. (b) Nakamura, K.; Okubo, H.; Yamaguchi, M. *Synlett* **1999**, 549. (c) Herrmann, W. A.; Böhm, V.; Reisinger, C.-P. *J. Organomet. Chem.* **1999**, *576*, 23. (d) McGuinness, D.; Cavell, K. *Organometallics* **2000**, *19*, 741. (e) Böhm, V. P. W.; Herrmann, W. A. *Eur. J. Org. Chem.* **2000**, 3679. (f) Hundertmark, T.; Littke, A.; Buchwald, S.; Fu, G. *Org. Lett.* **2000**, *2*, 1729. (g) Buchmeiser, M.; Schareina, T.; Kempe, R.; Wurst, K. *J. Organomet. Chem.* **2001**, *634*, 39. (h) Batey, R. A.; Shen, M.; Lough, A. J. *Org. Lett.* **2002**, *4*, 1411. (i) Yang, C.; Nolan, S. *Organometallics* **2002**, *21*, 1020. (j) Alonso, D.; Najera, C.; Pacheco, C. *Tetrahedron Lett.* **2002**, *43*, 9365. (k) Méry, D.; Heuzé, K.; Astruc, D. *Chem. Commun.* **2003**, 1934. (l) Köllhofer, A.; Pullmann,

T.; Plenio, H. *Angew. Chem. Int. Ed.* **2003**, *42*, 1056. (m) Köllhofer, A.; Plenio, H. *Chem.–Eur. J.* **2003**, *9*, 1416. (n) Gelman, D.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2003**, *42*, 5993. (o) Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P.; Doucet, H.; Santelli, M.; Ivanov, V. V. *Org. Lett.* **2004**, *6*, 3473.

(4) For selected examples of Pd-catalyzed reaction of aryl iodides with propargylamine derivatives using PPh_3 as a ligand: (a) Gotteland, J.-P.; Dax, C.; Halazy, S. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1153. (b) Chaudhuri, G.; Kundu, N. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 775. (c) Kundu, N. G.; Chaudhuri, G. *Tetrahedron* **2001**, *57*, 6833. (d) Nomak, R.; Snyder, J. K. *Tetrahedron Lett.* **2001**, *42*, 7929. (e) Conn, C.; Shimmon, R.; Cordaro, F.; Hargraves, T.-L.; Ibrahim, P. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2565. (f) Kundu, N. G.; Chaudhuri, G.; Upadhyay, A. *J. Org. Chem.* **2001**, *66*, 20. (g) Kundu, N. G.; Nandi, B. *J. Org. Chem.* **2001**, *66*, 4563. (h) Nakamura, H.; Kamakura, T.; Ishikura, M.; Biellmann, J.-F. *J. Am. Chem. Soc.* **2004**, *126*, 5958.

(5) For selected examples of Pd-catalyzed reaction of aryl bromides with propargylamine derivatives using PPh_3 as ligand: (a) Unroe, M. R.; Reinhardt, B. A. *Synthesis* **1987**, 981. (b) Bleicher, L. S.; Cosford, N. D. P.; Herbaut, A.; McCallum, J. S.; McDonald, I. A. *J. Org. Chem.* **1998**, *63*, 1109. (c) Inouye, M.; Fujimoto, K.; Furusyo, M.; Nakazumi, H. *J. Am. Chem. Soc.* **1999**, *121*, 1452. (d) Basak, A.; Shain, J. C.; Khamrai, K.; Rudra, K. R.; Basak, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1955.

(6) Lopez-Deber, M. P.; Castedo, L.; Granja, J. R. *Org. Lett.* **2001**, *3*, 2823.

(7) Laurenti, D.; Feuerstein, M.; Pèpe, G.; Doucet, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 1633.

(8) Feuerstein, M.; Laurenti, D.; Bougeant, C.; Doucet, H.; Santelli, M. *Chem. Commun.* **2001**, 325.

(9) Feuerstein, M.; Doucet, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 5923.

(10) (a) Feuerstein, M.; Berthiol, F.; Doucet, H.; Santelli, M. *Org. Biomol. Chem.* **2003**, *1*, 2235. (b) Feuerstein, M.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2004**, *45*, 1630. (c) Feuerstein, M.; Berthiol, F.; Doucet, H.; Santelli, M. *Synthesis* **2004**, 1281. (d) Feuerstein, M.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2004**, *45*, 8443.

(11) Babayan, A. T.; Chukhadzhyan, E. O.; Chukhadzhyan, E. O. *Zh. Org. Khim.* **1973**, *9*, 467.

(12) Kwatra, M. M.; Simon, D. Z.; Salvador, R. L.; Cooper, P. D. *J. Med. Chem.* **1978**, *21*, 253.

(13) Mannich, C. *Ber. Dtsch. Chem. Ges. B.* **1933**, *66*, 418.

(14) Chukhadzhyan, E. O.; Shakhatuni, K. G.; Chukhadzhyan, E. H.; Babayan, A. T. *Arm. Khim. Zh.* **1991**, *44*, 241.

(15) Kostrovskii, V. G.; Shvartsberg, M. S.; Andrievskii, V. N.; Kotlyarevskii, I. L. *Izv. Akad. Nauk, Ser. Khim.* **1968**, 2454.

(16) Izyumov, E. G.; Norina, O. A.; Andrievskaya, E. K.; Fedenok, L. G.; Kotlyarevskii, I. L. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Biol. Med. Nauk* **1968**, 113.

(17) Dupont, J.; Basso, N. R.; Meneghetti, M. R.; Konrath, R. A.; Burrow, R.; Horner, M. *Organometallics* **1997**, *16*, 2386.

(18) Moody, C. J.; Rahimtoola, K. F.; Porter, B.; Ross, B. C. *J. Org. Chem.* **1992**, *57*, 2105.

(19) Campi, E. M.; Jackson, W. R.; Nilsson, Y. *Tetrahedron Lett.* **1991**, *32*, 1093.