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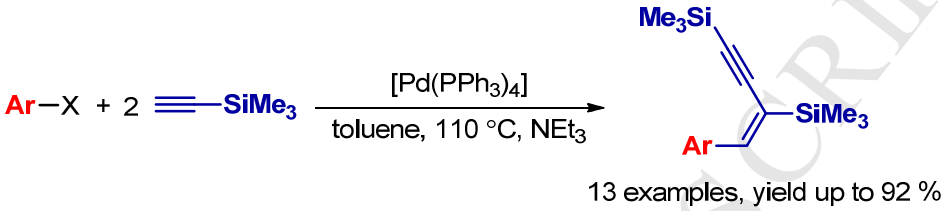

13 examples, yield up to 92 %

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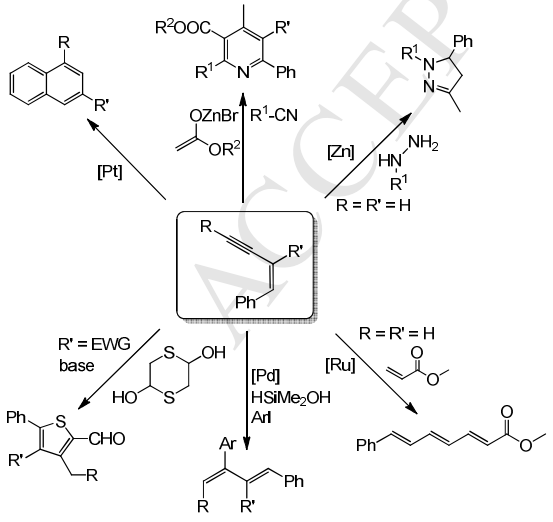
ABSTRACT

A practical and general synthetic approach to a series of 4-aryl-but-3-en-1-ynes is described. In the presence of palladium complexes a variety of aryl bromides (or iodides) undergo coupling with two equivalents of trimethylsilylacetylene with the formation of (*E*)-4-aryl-1,3-bis(trimethylsilyl)but-3-en-1-ynes. The protocol is simple, efficient, and affords synthesis of regio- and stereoselectively target products in good to high yields.

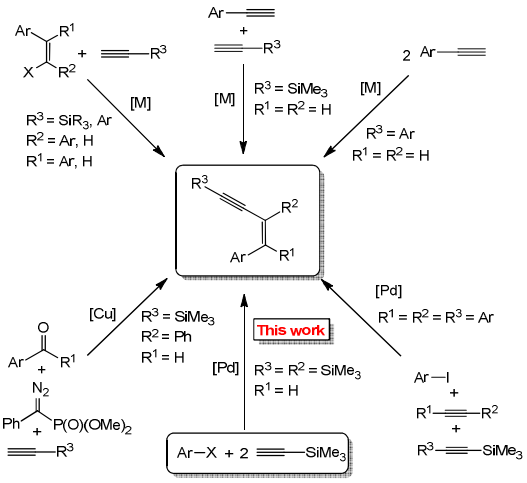
1. Introduction

Arylvinylacetylenes are valuable building blocks in organic synthesis[1] and are convenient starting materials in the construction of aromatic and heteroaromatic rings.[2,3,4] Moreover, aromatic and aliphatic derivatives of conjugated enynes are valuable precursors of a variety of functionalized compounds, such as conjugated dienes,[5] trienes,[6] pyridines,[7] pyrazolines,[8] thiophenes,[9] and others[10] (Scheme 1).



Scheme 1. Selected synthetic applications of arylvinylacetylenes.

In recent years, significant advancements have been made in the catalytic synthesis of arylvinylacetylenes with ethynyl and aromatic groups in *cis* arrangement.[1b,c] The most important synthetic approaches include dimerization of terminal arylacetylenes,[1b,c,11] co-dimerization of aryl and silylacetylenes,[12] Sonogashira coupling of corresponding *Z*-vinyl halides with alkynes,[13,14] cross-coupling of alkenyldialkylboranes with trimethylsilylethynyl bromide,[15] the sequence Wittig olefination of heteroaryl aldehydes / Sonogashira coupling,[16] sequence Cu(I)-catalysed cross-coupling of α-diazo phosphonates and alkynes / Horner−Wadsworth−Emmons (HWE) type reactions,[17] and arylalkynylation of aryl iodides, internal alkynes, and alkynylsilanes[18] (Scheme 2).



Scheme 2. Catalytic methods of synthesis of arylvinylacetylenes.

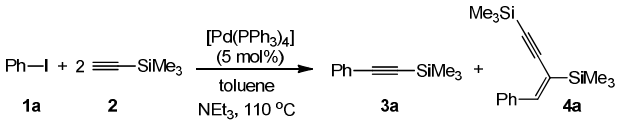
One example of arylvinylacetylene formation as the main product in a reaction of 1,8-diiodonaphthalene with 2-methylbut-3-yn-2-ol has been described by Echavarren.[19] Recently Hu has

described synthesis of a series of arylvinylacetylenes via the reaction of heteroaryl iodide with aryl and trimethylsilylacetylenes in DMF, in the presence of $[Pd(PPh_3)_4]$, NBu_3 and CuCl or $ZnBr_2$ as co-catalysts.[20] From amongst the accessible methods of arylvinylacetylene synthesis, homodimerization is efficient and atom-economical but usually leads to a mixture of stereo- and regioisomers. On the other hand, Sonogashira coupling, Suzuki coupling with alkynyl halides, and metal carbene coupling methods exhibit high stereo- and regioselectivity but suffer from limited accessibility of substrates.

Herein, we report an efficient, regio- and stereoselective synthesis of terminal arylvinylacetylene skeletons with cis arrangement of aryl and acetylene moieties from easily accessible and commercially available starting materials in the presence of simple palladium complexes, without the use of Cu or Zn-based co-catalyst.

2. Results and Discussion

We started our investigations with treatment of iodobenzene with two equivalents of trimethylsilylacetylene in the presence of $[Pd(PPh_3)_4]$ and NH_3 as a base. The reaction was performed in toluene at 110 °C and led to the formation of Sonogashira product **3a** together with a major amount of an unknown compound. On the basis of NMR and GC-MS analyses we established the structure of the product **4a** and we proposed the equation for the reaction (Scheme 2).



Scheme 3. Coupling of iodobenzene with two equivalents of trimethylsilylacetylene

The geometry around the double bond in product **4a** was assigned through observation of through-space interactions of hydrogens H_a, H_b, and $Si(CH_3)_3$ (Figure 1). NOESY spectrum showed strong cross peaks between H^a and H^b at δ = 6.81 and 8.01 ppm, respectively, and a weak one between H^a and hydrogens of the $Si(CH_3)_3$ group (δ=0.19 ppm), indicating *E* configuration of the double bond (ESI, S13).

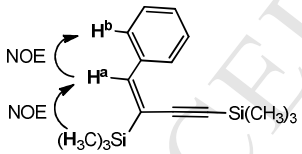


Figure 1: Structure determination of compound **4a**

Rentgenostructural analysis of the coupling product of 9-bromoanthracene with trimethylsilylacetylene (**4m)** (Figure 2) provided additional confirmation of the proposed structure of the synthesized enyne.

Formation of enynes as by-products in the study of Sonogashira coupling of aryl halides with arylacetylenes has already been reported.[21] We have made attempts to develop procedures in order to use this reaction for an efficient synthesis of enynes. For this purpose, the reaction conditions (temperature, solvent, catalyst and base) were optimized (Table 1). It was found that heating the reagents in boiling toluene, in the presence of 5 mol% of $[Pd(PPh_3)_4]$ results in product yield of up to 92% within 5 hours. Lowering the catalyst loading leads to a significant reduction in the reaction yield (entry 5). The

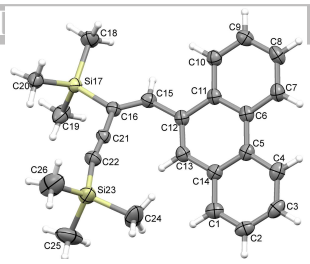


Figure 2. Perspective view of the molecule 4m; ellipsoids are drawn at the 50% probability level, hydrogen atoms are shown as spheres of arbitrary radii. Only one set of the disordered atoms is shown.

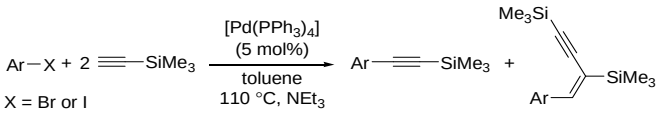
selectivity of the reaction depends on the temperature. At 80 °C, the formation of enyne is accompanied by significant amounts of Sonogashira product (entries 1-3). Increasing the reaction temperature to 110 °C resulted in a significant increase in the yield of enyne (entry 4). Among different bases tested in the process, triethylamine turned out to be the most efficient (entries 4 and 8-11).

Table 1. Optimization of the reaction conditions

entry	catalyst	base	Conv [%]	yield of **4**[a] [%]	yield of **3**[a] [%]
1	$PdCl_2(PPh_3)_2$	NEt_3	68	35[b]	30
2	$PdCl_2(PhCN)_2$	NEt_3	55	26[b]	25
3	$Pd(PPh_3)_4$	NEt_3	80	53[b]	25
4	$Pd(PPh_3)_4$	NEt_3	100	92	6
5	$Pd(PPh_3)_4$	NEt_3	85	75[c]	8
6	$Pd(OAc)_2$	NEt_3	30	0	30
7	PEPPSI-iPr	NEt_3	30	0	28
8	$Pd(PPh_3)_4$	K_2CO_3	100	79	20
9	$Pd(PPh_3)_4$	Cs_2CO_3	100	77	21
10	$Pd(PPh_3)_4$	KO*t*Bu	100	70	28
11	$Pd(PPh_3)_4$	HN*i*Pr$_2$	100	85	12

Reaction conditions: argon, closed system, toluene, 110 °C, cat. 5 mol%, [ArX]:[C≡C] = 1:2; 5 h; a) GC yield, b) THF, 80 °C, 24 h, c) 2.5 mol% of [Pd];

In order to determine the scope of the reaction, a series of aryl bromides and iodides were treated with trimethylsilylacetylene in the optimized reaction conditions (Scheme 4 and Figure 3).



Scheme 4. Coupling of aryl halides with excess of trimethylsilylacetylene

The reaction afforded a series of conjugated 1,3-enynes in good yields and in a regio- and stereoselective manner. The reaction proceeded efficiently in the presence of a variety of functional groups including amine, chloro, methoxy, trifluoromethyl, and vinyl. Moreover, highly conjugated aromatic groups such as naphthyl, anthracenyl, and phenanthryl were also found to be suitable reagents producing desirable 1,3-enynes with yields up to 90%. Unfortunately, heteroaryl substrates such as pyridine and pyrrole iodides and bromides did not result in the desired enynes, reacting quantitatively with the formation of Sonogashira products. The usefulness of the compounds obtained in the synthesis is related to the ease of the silyl group removal from

acetylene moiety. The tests performed permitted determination of conditions allowing a practically quantitative course of the reaction. The desilylation tests performed for selected derivatives in optimized conditions are summarized in Scheme 5.

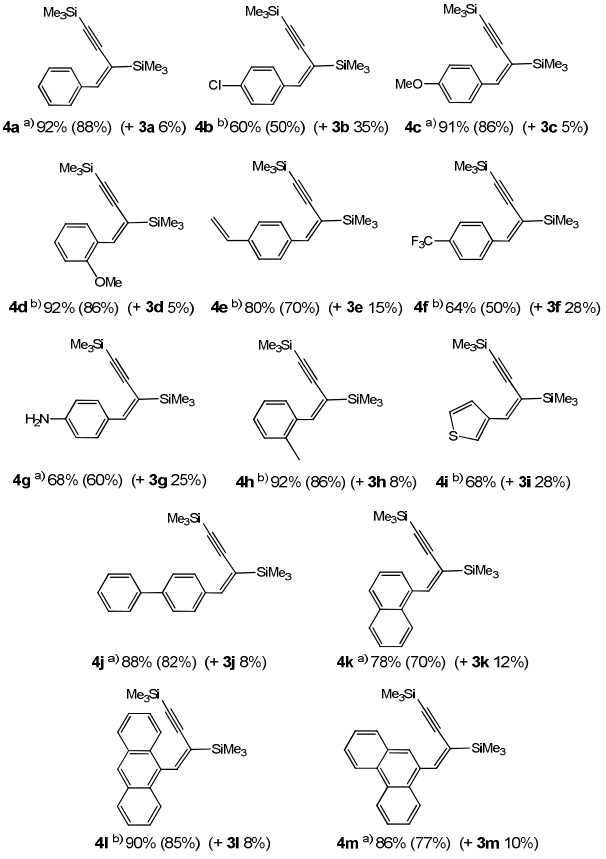
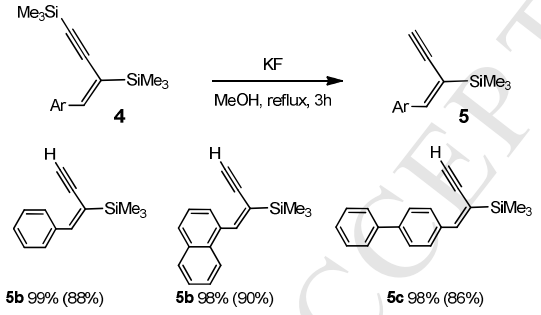
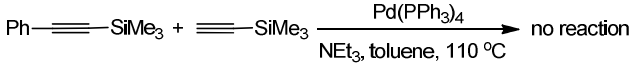


Figure 3: The scope of the reaction. Reaction conditions: argon, [Pd(PPh$_3$)$_4$] (5 mol%); toluene, 110 °C; NEt$_3$; closed system, GC yields, isolated yields in parentheses, [a)] obtained from aryl iodide, [b)] obtained from aryl bromide



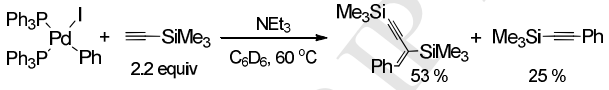
Scheme 5: Selective desilylation of **4** at acetylene moiety

In order acquire insight into the reaction mechanism, the Sonogashira product (**3a**) was treated with silylacetylene (**2**) in the presence of [Pd(PPh$_3$)$_4$]. The reaction did not lead to the formation of any product, which permitted exclusion of the formation of **4a** by hydroethynylation of **3a** (Scheme 6).



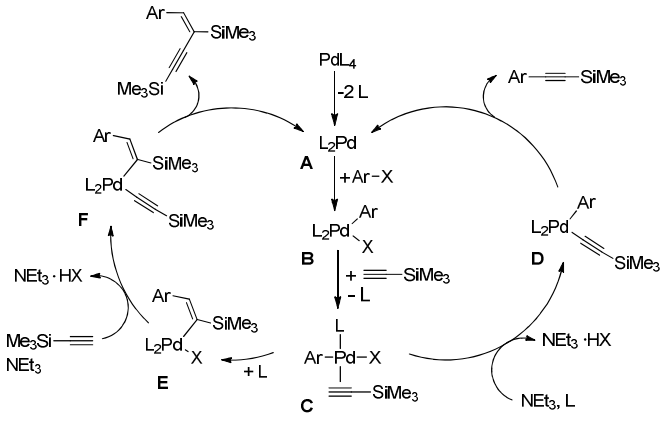
Scheme 6: Hydroalkynylation of **3a**

In the hope of detecting the reaction intermediates, the complex [PdIPh(PPh$_3$)$_2$] was synthesized according to the published method[22,23] and reacted with an excess of trimethylsilylacetylene. The reaction was performed in an NMR tube in C_6D_6 and monitored by ^{1}H NMR spectroscopy. The spectra showed gradual a disappearance of the signals characteristic of the starting palladium complex (δ = 5.91 and 6.42 ppm) and formation of 1,3-enyne (**4a**) along with Sonogashira product (**3a**) (Scheme 7). No reaction intermediates were observed. Attempts to observe the relevant intermediates at reduced temperatures also failed. This could be an indication that carbometallation is a rate limiting step. The experiment also indicates that oxidative addition of aryl iodide to palladium(0) is involved in the catalytic cycle.



Scheme 7: Reaction of [PdIPh(PPh$_3$)$_2$] with excess of trimethylsilylacetylene

Based on the obtained results and mechanistic studies reported by Woo[21b] and Mårtensson[24] a reasonable reaction scheme explaining catalytic formation of enynes (**4**) was proposed (Scheme 8). The right cycle in Scheme 8 is consistent with the copper-free Sonogashira coupling[25] and includes a sequence of oxidative addition of an aryl halide to palladium(0) complex, formation of π-acetylene intermediate, deprotonation of acetylene in the presence of a base leading to σ-acetylide complex **D** which subsequently undergoes reductive elimination resulting in formation of Sonogashira product, and regeneration of palladium(0) complex. The deprotonation mechanism of copper-free Sonogashira has recently been supported by DFT calculations.[24,26] π- Acetylene complex **C** may undergo two competitive processes, i.e. deprotonation (right cycle) or regio- and stereoselective carbopalladation, leading to complex **E**. The regiochemistry of the carbopalladation step is controlled primarily by steric effects so that the aryl group is transferred to the less hindered position of the alkyne molecule. The observed stereochemistry originates from *syn* addition of the organic residue and the palladium moiety to the carbon–carbon triple bond.[27] Complex **E** subsequently may be transformed to σ-acetylide complex **F** via a substitution/deprotonation sequence. Finally, complex **F** undergoes reductive elimination, resulting in the final product (**4**) and the regeneration of the catalytically active species. Competition between deprotonation and carbopalladation is crucial for the selectivity of the process. σ-vinyl



Scheme 8: Proposed reaction scheme explaining catalytic formation of **4** and competitive Sonogashira coupling.[28]

The use of at least a twofold excess of silylacetylene in relation to aryl halide is decisive for switching the selectivity of the reaction towards the formation of enyne **4**. The use of aryl halides containing electron-donating groups promotes the formation of enynes. In contrast, reaction of 1-bromo-4 nitrobenzene with trimethylsilylacetylene (**2**) leads to exclusive formation of Sonogashira product.

3. Conclusions

Palladium-catalysed coupling of aryl halides with two equivalents of trimethylsilylacetylene offers a new general, regio- and stereoselective method for the synthesis of terminal arylvinylacetylenes. This methodology is efficient for a series of aryl iodides and bromides bearing a variety of functional groups. The demonstrated selective desilylation of the acetylenic moiety in synthesized enynes opens the potential for their further functionalization.

4. Experimental section

4.1. General methods and chemicals:

Unless written otherwise, all operations were performed by using standard Schlenk techniques. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian 400 operating at 402.6 and 101.2 MHz, respectively. NOE, COSY, HSQC and HMBC spectra were recorded on a Bruker Avance DRX 600, operating at frequency of 600.13 MHz (^{1}H). All spectra were recorded at 298 K. GC analyses were carried out on a Bruker Scion 436-GC (column: DB-5 30 m I.D. 0.53mm) equipped with TCD. The GC/MS analyses were performed on a Varian Saturn 2100T equipped with (DB-1, 30 m capillary column, I.D. 0.25 mm) and Ion Trap Detector. The chemicals were obtained from the following sources: triethylamine, iodobenzene, 4-chlorobromobenzene, 4-methoxybromobenzene, 2-methoxybromobenzene, 4-bromostyrene, 4-trifluoromethylstyrene, 4-iodoaniline, 2-bromoaniline, 4-iodobiphenyl, 1-iodonaphtalene, 9-bromoantracene, 3-bromotiophene, Cs_2CO_3, $AgNO_3$, CuI, KF, $Pd(OAc)_2$, PEPPSI-iPr, trimethylsilylacetylene and $CDCl_3$ were purchased from Sigma-Aldrich. Toluene, tetrahydrofuran and K_2CO_3 were purchased from Chempur. Toluene was distilled prior to use from sodium, tetrahydrofuran was distilled from Na/benzophenone and the solvents were stored under argon over molecular sieves 4 Å. Complexes $[PdIPh(PPh_3)_2]$, $[Pd(PPh_3)_4]$, $[PdCl_2(PPh_3)_4]$, $[PdCl_2(PhCN)_2]$ were synthesized according to literature data.[20,21]

4.2. Procedure for the optimization tests

An oven dried 20 mL Schlenk flask closed with a Rotaflo valve, equipped with a magnetic stirring bar was charged under argon with 0.026 g (2.25×10^{-5} mol) of $[Pd(PPh_3)_4]$, 3 mL of toluene or THF, 0.5 mL of NEt_3 and 0.25 mL of dodecane (internal standard). Then 48 µL (4.5×10^{-4} mol) of iodobenzene was added to the reaction mixture followed by 137 µL (9.9×10^{-4} mol) of trimethylsilylacetylene. The mixture was heated at 110 °C in a closed system in an oil bath for 5h. Reaction course was monitored by gas chromatography.

4.3. Representative synthesis of (*E*)-1-Aryl-2,4-(bis)trimethylsilyl-1,3-enynes

All operations were performed by using standard Schlenk techniques. The synthesis was carried out in a Schlenk flask with a capacity of 20 mL, equipped with a magnetic stirring bar and closed with a Rotaflo valve. The flask was charged under argon with 0.052 g (4.5×10^{-5} mol) of $[Pd(PPh_3)_4]$, 6 mL of toluene, 1 mL of NEt_3, (9.0×10^{-4} mol) of corresponding aryl iodide or bromide and 274 µL (1.98×10^{-3} mol) of trimethylsilylacetylene. The reaction was carried out in a closed system at 110 °C for 24 h. After completion of the reaction, the resulting mixture was filtered through a short pad of Celite, evaporated to dryness, and the residue was purified using silica gel column chromatography.

4.4. Characterization of the products

*4.4.1. (E)-1-phenyl-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4a)**.* The product was isolated by column chromatography over silica gel and using *n*-hexane as an eluent. The product was obtained as a yellow oil with a yield of 88%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.03-8.01 (m, 2H, Ph), 7.39-7.30 (m, 3H Ph), 6.83 (s, 1H, =CH), 0.27 (s, 9H, $SiMe_3$), 0.26 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 145.0, 137.60, 128.80, 128.57, 128.08, 124.01, 107.23, 105.80, 0.03, -2.02; GC-MS (EI): m/z (rel intensity): 73 (17), 241 (19), 257 (100), 258 (24), 272 (20, M^+). HRMS (EI): calc: 272.1417; found: 272.1416.

*4.4.2. (E)-2-(4-Chlorophenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4b)**.* The product was isolated by column chromatography over silica gel and using *n*-hexane as an eluent. The product was obtained as a yellow oil with a yield of 50%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 7.95-7.92 (m, 2H, C_6H_4), 7.32-7.29 (m, 2H, C_6H_4), 6.74 (s, 1H, =CH), 0.24 (s, 9H, $SiMe_3$), 0.23 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 143.36, 136.03, 133.95, 129.97, 128.22, 124.94, 108.11, 105.42, -0.08, -2.09. GC-MS (EI): m/z (rel intensity): 45 (31), 73 (100), 74 (11), 75 (10), 97 (17), 147 (10), 155 (64), 156 (11), 163 (13), 218 (10), 255 (12), 275 (67), 276 (18), 277 (30), 291 (50), 292 (14), 293 (21), 306 (44, M^+), 307 (15), 308 (18). HRMS (EI): calc: 306.1027; found: 306.1023.

*4.4.3. (E)-1-(4-Methoxyphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4c)**.* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as a yellow oil with a yield of 86%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.00-7.96 (m, 2H, C_6H_4), 6.89-6.85 (m, 2H, C_6H_4), 6.74 (s, 1H, =CH), 3.83 (s, 3H, OCH_3), 0.25 (s, 9H, $SiMe_3$), 0.23 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 159.73, 144.49, 130.89, 130.37, 129.83, 120.59, 113.36, 106.21, 55.26, 0.01, -2.00. GC-MS (EI): m/z (rel intensity): 73 (20), 271 (47), 272 (24), 287 (23), 302 (100, M^+), 303 (30); HRMS (EI): calc: 302.1522; found: 302.1528.

*4.4.4. (E)-1-(2-Methoxyphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4d)**.* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as a yellow oil with a yield of 86%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.63 (dd, J = 7.8, 1.7 Hz, 1H, C_6H_4), 7.30 (s, 1H, =CH), 7.29-7.25 (m, 1H, C_6H_4), 6.96-6.92 (m, 1H, C_6H_4), 6.87 (dd, J = 8.3, 1.0 Hz, 1H, C_6H_4), 3.84 (s, 3H, OCH_3), 0.25 (s, 9H, $SiMe_3$), 0.22 (s, 9H, $SiMe_3$). ^{13}C NMR ($CDCl_3$; ppm) δ: 156.78, 138.98, 129.75, 128.65, 126.42, 123.12, 119.82, 110.37, 106.31, 55.51, -0.03, -1.96. GC-MS (EI): m/z (rel intensity): 119 (15), 257 (16), 287 (100), 288 (30), 302 (95, M^+), 303 (24). HRMS (EI): calc: 302.1522; found: 302.1525.

*4.4.5. (E)-1-(4-Vinylphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4e)**.* Compound is unstable. GC-MS (EI): m/z (rel intensity): 45 (37), 73 (100), 74 (11), 75 (11), 97 (18), 131 (11), 147 (12), 155 (48), 195 (21), 209 (30), 210 (18), 267 (95), 267 (30), 269 (11), 283 (56), 284 (15), 298 (80, M^+), 299 (23).

*4.4.6. (E)-1-(4-trifluoromethyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne **(4f)**.* The product was isolated as a yellow oil by column

chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. Isolated yield = 50%; ^{1}H NMR ($CDCl_3$; ppm) δ: 8.10-8.08 (m, 2H, C_6H_4), 7.61-7.58 (m, 2H, C_6H_4), 6.82 (s, 1H, =CH), 0.26 (s, 9H, $SiMe_3$), 0.25 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 142.93, 140.66, 128.79, 128.59, 127.78, 125.02 (m), 122.75, 109.04, 105.15, 0.12, -2.12. GC-MS (EI): m/z (rel intensity): 73 (65), 77 (15), 97 (17), 155 (11), 165 (12), 233 (12), 309 (22), 321 (29), 325 (100), 326 (28), 340 (12, M^+); HRMS (EI): calc: 340.1290; found: 340.1280.

*4.4.7. (E)-1-(4-aminophenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4g**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as an orange oil with a yield of 60%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 7.88-7.86 (m, 2H, C_6H_4), 6.68 (s, 1H, =CH), 6.65-6.62 (m, 2H, C_6H_4), 3.79 (brs, 2H, NH_2), 0.23 (s, 9H, $SiMe_3$), 0.21 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 146.85, 145.12, 130.47, 128.96, 118.29, 114.26, 106.69, 105.52, 0.05, -1.95. GC-MS (EI): m/z (rel intensity): 256 (34), 257 (11), 272 (20), 287 (100), 288 (30); HRMS (EI): calc: 287.1526; found: 287.1520.

*4.4.8. (E)-1-(2-methylphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4h**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as a yellow oil with a yield of 86%. ^{1}H NMR ($CDCl_3$; ppm) δ: 8.43-8.38 (m, 1H, C_6H_4), 7.21-7.17 (m, 3H, C_6H_4), 7.07 (s, 1H, 1H, =CH), 2.90 (s, 3H, CH_3), 0.26 (s, 9H, $SiMe_3$), 0.21 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: ^{13}C NMR (75 MHz, cdcl$_3$) δ 143.02, 136.14, 136.06, 130.04, 128.32, 128.05, 125.31, 124.68, 105.94, 105.61, 19.71, -0.05, -1.95; GC-MS (EI): m/z (rel intensity): 45 (38), 73 (100), 182 (30), 196 (20), 197 (58), 198 (18), 212 (75), 253 (75), 254 (19), 270 (32), 286 (10); HRMS (EI): calc: 286.1573; found: 286.1580

*4.4.9. (E)-1-(3-thiophenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4i**).* Compound is unstable. It decomposes during isolation. GC-MS (EI): m/z (rel intensity): 263 (100), 264 (27), 265 (14), 278 (24, M^+).

*4.4.10. (E)-1-Biphenyl-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4j**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as a yellow microcrystalline solid with a yield of 82%. Spectroscopic characterization: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.09 (d, *J* = 8.2 Hz, 2H, Ph), 7.65-7.58 (m, 3H Ph), 7.55 (s, 1H, Ph), 7.47-7.43 (m, 2H, Ph), 7.38-7.34 (m, 1H, Ph), 7.26 (s, 1H, =CH), 0.27 (s, 9H, $SiMe_3$), 0.26 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 144.42, 141.11, 140.64, 136.68, 132.37, 129.24, 128.76, 127.41, 127.00, 126.70, 124.10, 107.56, 105.95, -0.01, -2.01. GC-MS (EI): m/z (rel intensity): 259 (10), 317 (22), 333 (65), 334 (27), 348 (100, M^+), 349 (40); HRMS (EI): calc: 348.1730; found: 348.1717.

*4.4.11. (E)-1-(1-Naphthyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4k**).* The product was isolated by column chromatography over silica gel and using *n*-hexane as an eluent. The product was recrystallized from *n*-hexane and obtained as a yellow crystalline solid with a yield of 70%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.46 (d, *J* = 7.3 Hz, 1H, Ar), 8.09-8.06 (m, 1H, Ar), 7.87-7.81 (m, 2H, Ar), 7.63 (s, 1H, =CH), 7.55-7.47 (m, 3H, Ar), 0.34 (s, 9H, $SiMe_3$), 0.19 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 150.36, 142.25, 133.61, 133.55, 131.29, 128.75, 128.63, 126.53, 126.03, 125.55, 125.02, 123.31, 105.81, 105.61, -0.05, -1.87; GC-MS (EI): m/z (rel intensity): 45 (35), 73 (100), 74 (12), 75 (10), 97 (14), 152 (64), 153 (11), 155 (11), 219 (33), 233 (55), 234 (45), 235 (15), 247 (20), 248 (21), 249 (19), 291 (53), 292 (19), 307 (25), 322 (31, M^+), 323 (11); HRMS (EI): calc: 322.1573; found: 322.1576.

*4.4.12. (E)-1-(9-Anthracenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4l**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained after recrystallization from *n*-hexane as an orange microcrystalline solid with a yield of 85%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.47 (s, 1H, Ar), 8.28 (dq, *J* = 8.6, 1.0 Hz, 1H, Ar), 8.10 (ddd, *J* = 8.6, 1.2, 0.7 Hz, 1H, Ar), 8.00 (d, *J* = 8.4 Hz, 1H, Ar), 7.81 (d, *J* = 6.6 Hz, 1H, Ar), 7.62-7.57 (m, 3H, Ar, =CH), 7.49-7-43 (m, 1H, Ar), 7.15 (dd, *J* = 5.2, 0.6 Hz, 1H, Ar), 0.17 (s, 9H, $SiMe_3$), 0.08 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 140.25, 134.32, 130.28, 128.07, 128.00, 127.72, 127.53, 127.35, 126.83, 125.76, 124.72, 124.18, 1.94; GC-MS (EI): m/z (rel intensity): 73 (87), 97 (11), 202 (100), 203 (22), 269 (25), 283 (51), 284 (54), 285 (17), 298 (26), 299 (20), 372 (48), 373 (22); HRMS (EI): calc: 372.1730.; found: 372.1738.

*4.4.13. (E)-1-(9-Phenanthryl)-2,4-bis(trimethylsilyl)but-1-en-3-yne (**4m**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained after recrystallization from *n*-hexane as a yellow crystalline solid with a yield of 77%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.75-8.73 (m, 1H, Ar), 8.68-8.66 (m, 1H, Ar), 8.67 (s, 1H, Ar), 8.11 (dd, *J* = 8.1, 1.4 Hz, 1H, Ar), 7.88 (dd, *J* = 7.7, 1.6 Hz, 1H, Ar), 7.69-7.58 (m, 5H, Ar and =CH), 0.36 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 142.56, 132.02, 131.40, 130.57, 130.37, 128.91, 127.74, 126.96, 126.85, 126.70, 126.55, 126.27, 124.00, 123.07, 122.46, 106.17, 105.41, 0.06, -1.85. GC-MS (EI): m/z (rel intensity): 73 (11), 269 (13), 283 (16), 357 (23), 371 (14), 372 (100, M^+), 373 (35); HRMS (EI): calc: 372.1730; found: 372.1742.

4.5. Representative procedure for selective protodesilylation

A 10 mL two neck round bottom flask, equipped with a condenser and a magnetic stirring bar was charged with 0.1 g (3.68×10^{-4} mol) of (*E*)-1-phenyl-2,4-bis(trimethylsilyl)but-1-en-3-yne, 0.21 g (3.68×10^{-3} mol) of KF and 5 mL of methanol. The mixture was heated at 65 °C for 3 h. After this time the solvent was evaporated under vacuum and the product was purified by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent.

*4.5.1. (E)-1-Phenyl-2-trimethylsilylbut-1-en-3-yne (**5a**).* The product was isolated by column chromatography over silica gel and using *n*-hexane/ethyl acetate (25:1) as an eluent. The product was obtained as a yellow oil with a yield of 88%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 7.97 (d, *J* = 7.6 Hz, 2H, Ph), 7.38-7.29 (m, 3H, Ph), 6.90 (s, 1H, =CH), 3.69 (s, 1H, ≡C-H), 0.26 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 146.14, 137.38, 128.76, 128.65, 128.18, 122.93, 88.90, 84.01, 76.98, -2.09. GC-MS (EI): m/z (rel intensity): 45 (27), 59 (15), 73 (88), 83 (27), 159 (14), 169 (20), 172 (29), 183 (59), 185 (100), 186 (18), 199 (12, M^+); HRMS (EI): calc: 200.1021; found: 200.1019.

*4.5.2. (E)-1-(1-Naphthyl)-2-trimethylsilylbut-1-en-3-yne (**5b**).* The product was isolated by column chromatography over silica gel and using *n*-hexane as an eluent. The product was obtained as a yellow oil with a yield of 92%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.26 (dt, *J* = 7.3, 0.9 Hz, 1H, Ar), 8.04-8.02 (m, 1H, Ar), 7.87-7.81 (m, 2H, Ar), 7.67 (s, 1H, =CH), 7.55-7.48 (m, 3H, Ar), 3.45 (s, 1H, ≡C-H), 0.34 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 144.08, 133.80, 133.52, 131.22, 128.77, 128.63, 126.42, 126.11, 125.87, 125.68, 125.17, 123.45,

87.19, 83.71, -1.94; HRMS (EI): calc: 250.1178; found: 250.1178.

4.5.3. *(E)-1-Biphenyl-2-trimethylsilylbut-1-en-3-yne (**5c**).* The product was isolated by column chromatography over silica gel and using *n*-hexane as an eluent. The product was obtained as a yellow oil with a yield of 90%. Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 8.05 (d, *J* = 9.1 Hz, 2H, Ar), 7.65-7.60 (m, 5H, Ar), 7.47-7.33 (m, 4H, Ar), 6.93 (s, 1H, =CH), 3.74 (s, 1H, ≡C-H), 0.28 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$; ppm) δ: 145.62, 141.22, 140.60, 136.45, 129.17, 128.77, 127.43, 126.99, 126.83, 123.02, 89.21, 84.17, -2.06; HRMS (EI): calc: 276.1334; found: 276.1330.

4.6. ^{1}H NMR spectroscopic study of equimolar reaction of [PdIPh(PPh$_3$)$_2$] with 2.

An NMR tube equipped with a rotaflo valve was charged under argon with 0.01g (1.2×10^{-5} mol) complex, 0.65 mL of C_6D_6 and anthracene as an internal standard. After this, the starting NMR spectrum was recorded. Then 3.0 μL (2.4×10^{-5} mol) of triethylamine and 3.0 μL (2.64×10^{-5} mol) trimethylsilylacetylene was added under argon by microliter syringe to the reaction mixture. The reaction was heated at 60 °C for 24 h. The progress of the reaction was monitored by ^{1}H NMR. After the given reaction time the mixture was additionally analysed by GC-MS.

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Supplementary Material

Supplementary data associated with this article can be found in the online version, at

5. References and notes

1. (a) Garcia-Garrido, S. E. In *Modern Alkyne Chemistry*; Trost, BM, Li, C-J, Eds.; Wiley-VCH: Weinheim, 2015; pp 301–334; (b) Trost BM.; Masters JT. *Chem. Soc. Rev*. 2016; 45:2212–2238; (c) Zhou Y, Zhanga Y, Wang J. *Org. Biomol. Chem.* 2016; 14:6638–6650.
2. Aguilar E, Sanz R, Fernández-Rodríguez MA, García-García P. *Chem. Rev.* 2016, 116:8256–8311.
3. Gilmore K, Alabugin IV. *Chem. Rev.* 2011; 111:6513–6556.
4. Kang D, Kim J, Oh S, Ho Lee P. *Org. Lett.* 2012; 14:5636–5639.
5. (a) Zhou H, Moberg C. *Org. Lett.* 2013; *15*:1444–1447; (b) Eberlin L, Carboni B, Whiting A. *J. Org. Chem*. 2015; 80:6574–6583; (c) Xu S, Zhang Y, Li B, Liu S-Y. *J. Am. Chem. Soc.* 2016; 137:14566–14569; (d) Choudhury PP, Junker CS, Pidaparthi RR, Welker ME. *J. Organomet. Chem*. 2014; 754: 88–93.
6. Schabel T, Plietker B. *Chem. Eur. J.* 2013; 19:6938–6941.
7. Chun YS, Lee JH, Kim JH, Ko YO, Lee S. *Org. Lett.* 2011; 13:6390–6393.
8. Patil NT, Singh V. *Chem. Commun.* 2011, 47:11116–11118.
9. Bharathiraja G, Sathishkannan G, Punniyamurthy T. *J. Org. Chem.* 2016; 81:2670–2674.
10. (a) Cai H, Nie J, Zheng Y, Ma J-A. *J. Org. Chem.* 2014; 79:5484–5493; (b) Jadhav AM, Gawade SA, Vasu D, Dateer RB, Liu R-S. *Chem. Eur. J.* 2014; 20:1813–1817; (c) Shashidhar J, Reddy KM, Ghosh S. *Tetrahedron Lett.* 2011; 52:3106–3109; (d) Hoshi M, Yamazaki H, Okimoto, M. *Synlett* 2010; 16:2461–2464; (e) Yang Z-Y, Liu T-L, Zheng Y, Li S, Ma J-A. *Eur. J. Org. Chem.* 2015; 18:3905–3912; (f) Hoshi M, Okimoto M, Nakamura S, Takahashi S. *Synthesis* 2011; 23:3839–3847; (g) Cao J, Huang X. *Org. Lett.* 2010; 12:5048–5051.
11. For selected examples see: (a) Nishiura M, Hou Z, Makatsuki Y, Yamaki T, Miyamoto T. *J. Am. Chem. Soc.* 2003; 125:1184–1185; (b) Funayama A, Satoh T, Miura M. *J. Am. Chem. Soc*. 2005; 127:15354–15355; (c) Tsukada N, Ninomiya S, Aoyama Y, Inoue Y. *Org. Lett.* 2007; 9:2919–2921; (d) Nishimura T, Guo X-X, Ohnishi K, Hayashi T. *Adv. Synth. Catal*. 2007; 349:2669–2672; (e) Shibata Y, Tanaka K. *Angew. Chem. Int. Ed*. 2011; 50:10917–10921; (f) Jahier C, Zatolochnaya OV, Zvyagintsev NV, Ananikov VP, Gevorgyan V. *Org. Lett.* 2012; 14:2846–2849; (g) Xu C, Du W, Zeng Y, Dai B, Guo H. *Org. Lett.* 2014; 16:948–951; (h) Babu MH, Dwivedi V, Kant R, Reddy MS. *Angew. Chem. Int. Ed*. 2015; 54:3783–3786.
12. (a) Katayama H, Yari H, Tanaka M, Ozawa F. *Chem. Commun.* 2005; 4336–4338; (b) Rivada-Wheelaghan O, Chakraborty S, Shimon LJW, Ben-David Y, Milstein D. *Angew. Chem. Int. Ed.* 2016; 55:6942–6945; (c) Ogata K, Oka O, Toyota A, Suzuki N, Fukuzawa S. *Synlett* 2008; 17:2663–2666.
13. For reviews on Sonogashira coupling see: (a) Negishi E-I, Anastasia L. *Chem. Rev*. 2003; 103:1979–2017; (b) Chinchilla R, Najera C. *Chem. Rev*. 2007; 107:874–922; (c) Doucet H, Hierso J-C. *Angew. Chem. Int. Ed*. 2007; 46:834–871; (d) Chinchilla R, Najera C. *Chem. Soc. Rev*. 2011; 40:5084–5121.
14. (a) Teplý F, Stará IG, Starý I, Kollárovič A, Šaman D, Rulíšek L, Fiedler P. *J. Am. Chem. Soc.* 2002; 124:9175–9180; (b) Yasuike S, Ohta H, Shiratori S, Kurita J, Tsuchiya T. *J. Chem. Soc., Chem. Commun.* 1993; 1817–1818; (c) Sonoda M, Itahashi K, Tobe Y. *Tetrahedron Lett*. 2002; 43:5269–5272; (d) Rahman SMA, Sonoda M, Ono M, Miki K, Tobe Y. *Org. Lett*. 2006; 8:1197–1200.
15. (a) Hoshi M, Nakayabu H, Shirakawa K. *Synthesis* 2005; 1991–2007; (b) Hoshi M, Suzuki S, Saitoh S, Okimoto M, Shirakawa K. *Tetrahedron Lett.* 2007; 48:119–124; (c) Hoshi M, Kawamura N, Shirakawa K. *Synthesis* 2006; 1961–1970.
16. (a) Hayford A, Kaloko Jr. J, El-Kazaz S, Bass G, Harrison C, Corprew T. *Org. Lett*. 2005; 7:2671–2673; (b) Kaloko J, Hayford A. *Org. Lett*. 2005; 7:4305–4308.
17. Zhou Y, Ye F, Zhou Q, Zhang Y, Wang J. *Org. Lett.* 2016; 18:2024−2027.
18. Sakai N, Komatsu R, Uchida N, Ikeda R, Konakahara T. *Org. Lett.* 2010; 12:1300–1303.
19. Gonzalez JJ, Francesch A, Cardenas DJ, Echavarren AM. *J. Org. Chem.* 1998; 63:2854–2857.
20. Liu Y, Jin S, Wang Z, Song L, Hu Y. *Org. Lett*. 2014; 16:3524−3527.
21. (a) Djakovitch L, Rollet P. *Adv. Synth. Catal.* 2004; 346:1782–1792; (b) Roberts GM, Lu W, Woo LK. *RSC Adv*. 2015; 5:18960–18971; (c) Batenburg-Nguyen U, Ung AT, Pyne SG. *Tetrahedron* 2009; 65:318–327; (d) Filatova EA, Gulevskaya AVA, Pozharskii F, Ozeryanskii VA. *Tetrahedron* 2016; 72:1547–1557.
22. Komiya, S. *Synthesis of organometallic compounds*, John Wiley and Sons: Chichester, 1997.
23. Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: New York, 1985.
24. Ljungdahl T, Bennur T, Dallas A, Emtenas H, Martensson J. *Organometallics* 2008; 27:2490–2498.
25. Soheili A, Albaneze-Walker J, Murry JA, Dormer PG, Hughes DL. *Org. Lett*. 2003; 5:4191–4194.
26. García-Melchor M, Pacheco MC, Nájera C, Lledós A, Ujaque G. *ACS Catal*. 2012; 2:135−144.
27. Cacchi, S.; Fabrizi, G. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, 2002, vol. 1, pp. 1335–1367.
28. Scheme is simplified and does not discuss details. For detailed DFT study of the copper-free Sonogashira mechanisms see ref. 26.