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The Regio- and Stereoselective Synthesis of 1,4-Diarylbut-1-en-3-ynes Having Aryl Groups at the Mutual *Syn* Positions

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Abstract: (E)-1-aryl-2,4-bis(trimethylsilyl)but-1-en-3-ynes readily undergo protodesilylation and subsequent aerobic, copper-free Sonogashira cross-coupling with aryl halides to form (E)-1,4-diaryl-2-(trimethylsilyl)but-1-en-3-ynes. The proposed one-pot, two-step approach allows access to the isomers containing aryl substituents in mutual *syn* positions. The resulting 2-silyl enynes can be further converted by proto- or halodesilylation.

Keywords: Sonogashira cross-coupling; enynes; one-pot synthesis

1. Introduction

Conjugated enynes are valuable moieties in organic chemistry, providing convenient starting materials for constructing aromatic and heteroaromatic molecules [1–6]. Their structural motif is present in numerous biologically active molecules [7–10] and some functional materials [11,12]. A general method for the synthesis of enynes must ensure the regio- and stereoselective formation of the target compounds. The substitution pattern and stereoelectronic properties of the substituents significantly influence the reactivity, making a single and general synthetic route difficult to achieve. State-of-the-art catalytic methods for the synthesis of conjugated enynes have been reported in several reviews [9,13,14] and there has been significant progress in recent years. Several new examples of the synthesis and reactivity of conjugated enynes have been described [14]. The number of applications of conjugated enynes in the synthesis of organic compounds is steadily increasing [2–4,15,16].

The selective synthesis of 1,4-diarylbut-1-ene-3-ynes with the same substituents in positions 1 and 4 can be conveniently performed via selective alkyne homo-dimerization. However, if the substituents at positions 1 and 4 are different (Figure 1a), alkyne cross-dimerisation may not always be applicable due to low selectivity. In this case, other procedures may need to be applied (Scheme 1).

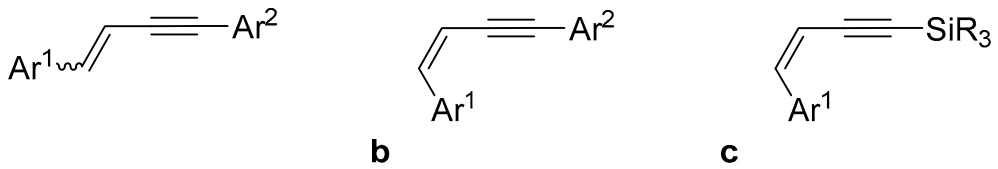

Figure 1. The conjugated enyne substitution patterns that are addressed in this paper.

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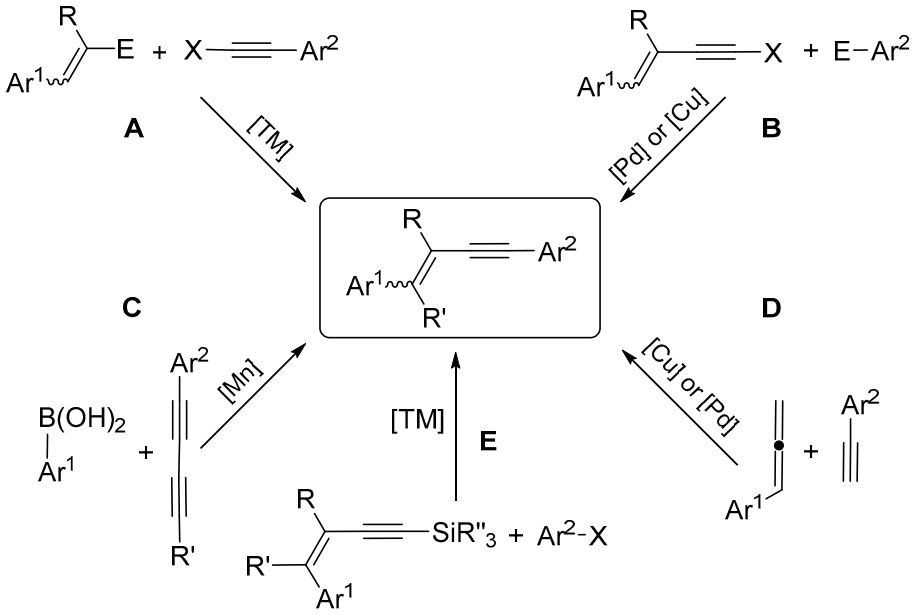
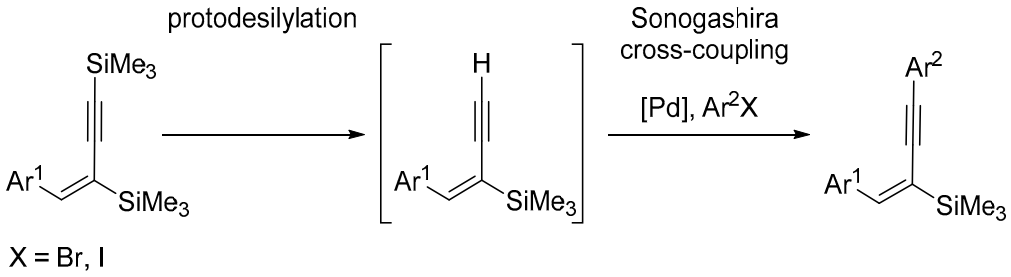


A a) E = $B(OH)_2$, SnR'_3, $Si(OEt)_3$; X = Br, I; b) E = Br, I; X = H; c) E = H, X = Br
B a) E = MgBr, X = Cl; b) E = $B(OH)_2$, X = I;
C R = H; R' = CH_2OH, CH_2OMe, CH_2OAc (see also ref. 28 and 29)
A-**C** R = H, R' = H
D R = Me; R' = H
E a) SiR''_3 = $SiMe_3$, $Si(i\text{-}Pr)_3$, X = Br, I; R = H (see also ref. S1-S6);
R' = H, Me, Ph, Bpin; TM = Pd and Cu;
sila-Sonogashira cross-coupling or protodesilylation/Sonogashira cross-coupling:
b) SiR''_3 = $SiMe_3$, X = Br, I; R = $SiMe_3$; R' = H; TM = Pd
one pot protodesilylation/Sonogashira cross-coupling (**this work**)

Scheme 1. General methods for the synthesis of conjugated 1,4-diarylenynes, where the substituents in the 1- and 4-positions are different. The available procedures include cross-coupling reactions, (i.e., Suzuki [17], Stille [18], Hiyama-Denmark [19], Sonogashira [20–24], Heck [25]) (**A**), Kumada [26], and Suzuki [27] (**B**), the hydroarylation of 1,3-diynes [28,29] (**C**), the hydroalkynylation of alkynes and/or allenes (**D**) [30,31], and a few less general procedures [32–35].

If the synthesis target involves 1,4-diaryl-1,3-enynes that have aryl groups placed in mutual *syn* positions (Figure 1b), cross-coupling [17–19,26,36–38] is the only suitable synthetic route. Given the availability of procedures for the selective synthesis of silylated enynes (Figure 1c), the most convenient method for the preparation of (Z)-1,4-diaryl-1,3-enynes is the protodesilylation of the silyl derivatives followed by Sonogashira coupling with aryl halides [39–44]. Alternatively, a one-step sila-Sonogashira coupling of the silylated enynes with aryl halides (E in Scheme 1) can be used [45]. These reports are listed in Table S1 in the Supplementary Materials. However, such a sequence of reactions has not been developed into a general method for the synthesis of conjugated enynes with defined stereochemistry. To address this limitation, we report an efficient and general procedure for the synthesis of (E)-1,4-diaryl-2-(trimethylsilyl)but-1-en-3-ynes via the one-pot sequence of selective protodesilylation and Sonogashira coupling (Scheme 2).

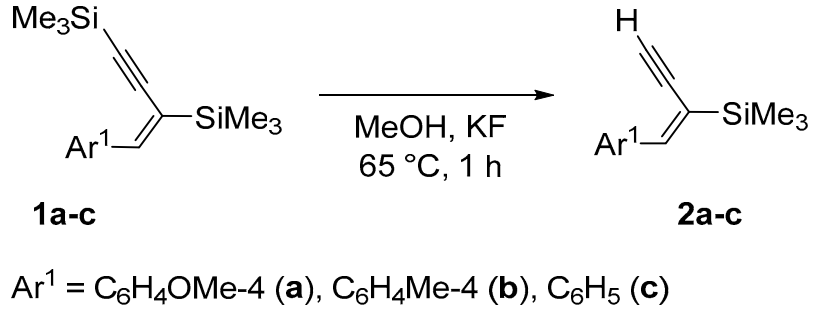


Scheme 2. One-pot synthesis of 1,4-diarylbut-1-en-3-ynes.

In addition, we describe preliminary studies on using the reactivity of the silyl group in position 2 for the modification of the synthesised enynes.

2. Results and Discussion

First, three bissilylated 1,3-enynes with different aryl groups (Scheme 3) were selected for the optimisation of the protodesilylation procedure. For the reaction starting conditions, we adopted the previously developed procedure for the protodesilylation of (E)-4-aryl-1,3-bis(trimethylsilyl)but-3-en-1-yne [46].



Scheme 3. Chemoselective protodesilylation of 2-silylsubstituted 1,3-enynes.

We started the study by treatment of a methanolic solution of bissilylated 1,3-enyne **1a** with an excess (5 equivalents) of KF. The reaction was carried out in air at 65 °C and led to the formation of the new compound in good yield after 3 h. GC-MS and NMR analyses showed the exclusive formation of the product **2a**, selectively desilylated at the acetylene moiety.

The protodesilylation procedure has been adapted for convenient use application in a one-pot sequence. The optimization research included the selection of the solvent, the base, and the reaction conditions.

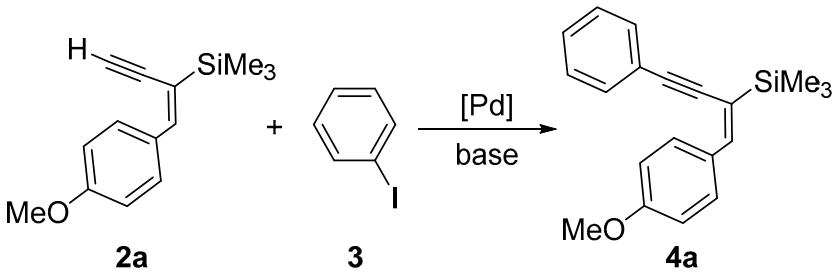
Of the bases tested, TBAF, KO*t*-Bu, and KOH resulted in the decomposition of **1a** and the formation of a mixture of unidentified compounds. In contrast, the reaction with KF, CsF, NaF, and K_2CO_3 in the MeOH solution was efficient even at room temperature. Raising the temperature to 65 °C reduced the reaction time required for complete conversion from 3 h to 1 h. Under these conditions, the silyl group at the Csp^2 carbon atom remained untouched. Solvents commonly used for Sonogashira connections, such as THF, DMF, and toluene, resulted in reduced conversion and yield. The results are summarised in Table 1.

After establishing the protodesilylation conditions, we investigated the Sonogashira coupling of terminal enyne with aryl bromides (or iodides) to find a convenient and efficient procedure. To find the optimum catalyst, base, and reaction conditions, studies were carried out using the cross-coupling of (E)-1-(4-methoxyphenyl)-2-trimethylsilylbut-1-en-3-yne (**2a**) with iodobenzene (Scheme 4) as a test reaction.

Table 1. Optimisation of the conditions for protodesilylation of **1a–c**.

Enyne	Base	Time [h]	Solvent	Conv.	Yield [%]
1a	KF	3	toluene	0	0
1a	K_2CO_3	3	toluene	0	0
1a	KF	3	DMF	27	22
1a	KF	3	THF	5	5
1a	KF	3	MeOH	100 [a]	99 [a]
1a	CsF	2.5	MeOH	100	99
1a	NaF	3	MeOH	65	65
1a	K_2CO_3	3	MeOH	100 [a]	99 [a]
1a	KF	1	MeOH	100	99
1a	TBAF	1	MeOH	100	5
1a	KO*t*-Bu	3	MeOH	100	30
1a	KOH	3	MeOH	100	22
1a	K_2CO_3	1	MeOH	100	99
1b	K_2CO_3	1	MeOH	100	98
1c	K_2CO_3	1	MeOH	100	96

Conditions: MeOH, base (5 equiv); 65 °C, [a] 25 °C.



Scheme 4. Sonogashira cross-coupling of **2a** with iodobenzene.

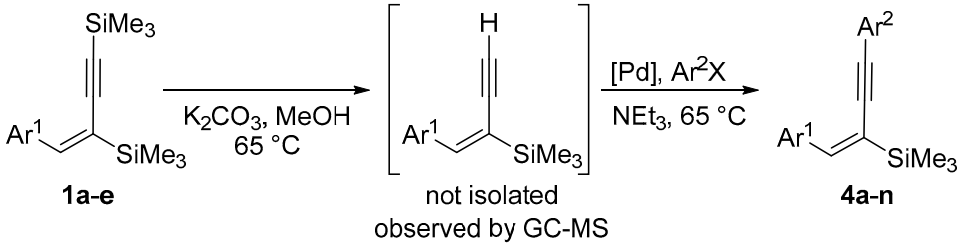
A series of commercially available palladium complexes such as $[PdCl_2(PPh_3)_2]$, $[Pd_2(dba)_3]/PPh_3$, $[Pd(PPh_3)_4]$, $PdCl_2$/dppf (dppf = 1,1′-bis(diphenylphosphino)ferrocene), $[PdCl_2(PhCN)_2]/PPh_3$, and PEPPSI-IPr ([1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridine)palladium(II) dichloride) were evaluated (Table 2). The greatest yields were observed for the phosphine-based catalysts $[Pd(PPh_3)_4]$ and $[PdCl_2(PPh_3)_2]$. The other palladium complexes exhibited lower activity. Among the bases tested, KF and NEt_3 gave the best performance. Finally, the high yields of Sonogashira cross-coupling under copper-free conditions prompted us to investigate the effect of the copper salt on the course of the reaction. Regardless of the amount of CuI used (1, 2, or 5 equivalents in relation to the catalyst), the course of the reaction was unaffected.

Next, reactions were carried out in the air, using commercially available solvents and reagents without further purification. Performing the reaction in MeOH at 65 °C in the presence of $[PdCl_2(PPh_3)_2]$ (1 mol%) and NEt_3 proved to be optimal. Under these conditions, product yields of up to 99% were obtained at a relatively low reaction temperature (65 °C) and catalyst loading (1 mol%). Following the optimisation studies, the one-pot syntheses of the 1,4-diarylbut-1-en-3-ynes were assessed according to Scheme 5.

Table 2. Optimisation of Sonogashira cross-coupling of **2a** with iodobenzene.

Cat.	Additive (Amount) [a]	Base	Conv. [%]	Yield [%]
$[Pd(PPh_3)_4]$	-	KF	100	99
$[Pd(PPh_3)_4]$	-	NEt_3	100	98
$[Pd(PPh_3)_4]$	CuI (see text)	KF	100	98
$[PdCl_2(PPh_3)_2]$	-	KF	100	98
$[PdCl_2(PPh_3)_2]$	-	NEt_3	100	99
$[PdCl_2(PPh_3)_2]$	-	NEt_3	98 [a]	98 [a]
$[PdCl_2(PPh_3)_2]$	CuI (see text)	KF	100	98
$[PdCl_2(PPh_3)_2]$	-	KF	97 [b]	96 [b]
$[PdCl_2(PPh_3)_2]$	-	K_2CO_3	90	90
PEPPSI-IPr	-	KF	99	95
PEPPSI-IPr	-	NEt_3	99	94
$[Pd_2(dba)_3]$	PPh_3 (2 equiv)	NEt_3	99	95
$[Pd_2(dba)_3]$	SPhos (2 equiv)	NEt_3	100	96
$PdCl_2$	dppf (1 equiv)	KF	75	75
$[PdCl_2(PhCN)_2]$	PPh_3 (2 equiv)	KF	87	86

Reaction conditions: MeOH, [Pd] (1 mol%), air, 3 h; 65 °C; [a] in relation to the catalyst; [b] 24 h, 25 °C.



Ar^1 = C_6H_4OMe-4 (**a**), C_6H_4Me-4 (**b**), C_6H_5 (**c**), 4-biphenyl (**d**), $C_6H_4CF_3$-4 (**e**)
X = I; Ar^2 = C_6H_5, 1-naphthyl, 4-biphenyl, C_6H_5OMe-4
X = Br; Ar^2 = $C_6H_5NH_2$-4, 9-anthracenyl, $C_6H_5NO_2$-3, C_6H_5Cl-3, 2-thienyl, $C_6H_5CF_3$-4, $C_6H_5NO_2$-4, 3-fluorenyl

Scheme 5. The one-pot procedure of protodesilylation/Sonogashira coupling sequence.

The silylated 1,3-enynes were found to undergo efficient protodesilylation/Sonogashira coupling with a wide range of aromatic bromides and iodides (Figure 2). Products **4a–o** were obtained by treating, in the first step, a methanolic solution of bissilylated 1,3-enynes (**1a–e**) with 5 equivalents of K_2CO_3 at 65 °C. The reaction was carried out for 1 h and the progress was monitored by GC-MS. After completion of the protodesilylation, the corresponding aromatic bromide or iodide was added together with NEt_3 and palladium catalyst $[PdCl_2(PPh_3)_2]$ (1 mol%) and the reaction was continued for a further 23 h. It was possible to obtain 1,3-enynes with overall isolated yields in the range of 60% to 92% (Figure 2).

Isomers with aryl groups in mutual *syn* positions were selectively formed. This method allows for the efficient conversion of reagents containing amine, nitro, methyl, methoxy, trifluoromethyl, and thiophenyl groups. Aryl halides containing conjugated aromatic rings, such as naphthyl and phenanthryl, were efficiently converted. *Meta*-substituted phenyl halides were also proved to be suitable reagents (see products **4d** and **4e**, Figure 2).

The reported method is not free from limitations. Reagents containing aldehyde, nitrile, and hydroxide groups could not be efficiently converted under the conditions used and generated products with yields below 15%. Furthermore, *ortho*-nitro and *ortho*-methyl substituted phenylacetylenes did not undergo Sonogashira cross-coupling with protodesilylated **1a** and trace amounts of the products were obtained. Nearly no conversion of aryl halides was observed. Other limitations relate to the optimisation of the one-pot process. For instance, THF and DMF are not suitable solvents in the proposed method.

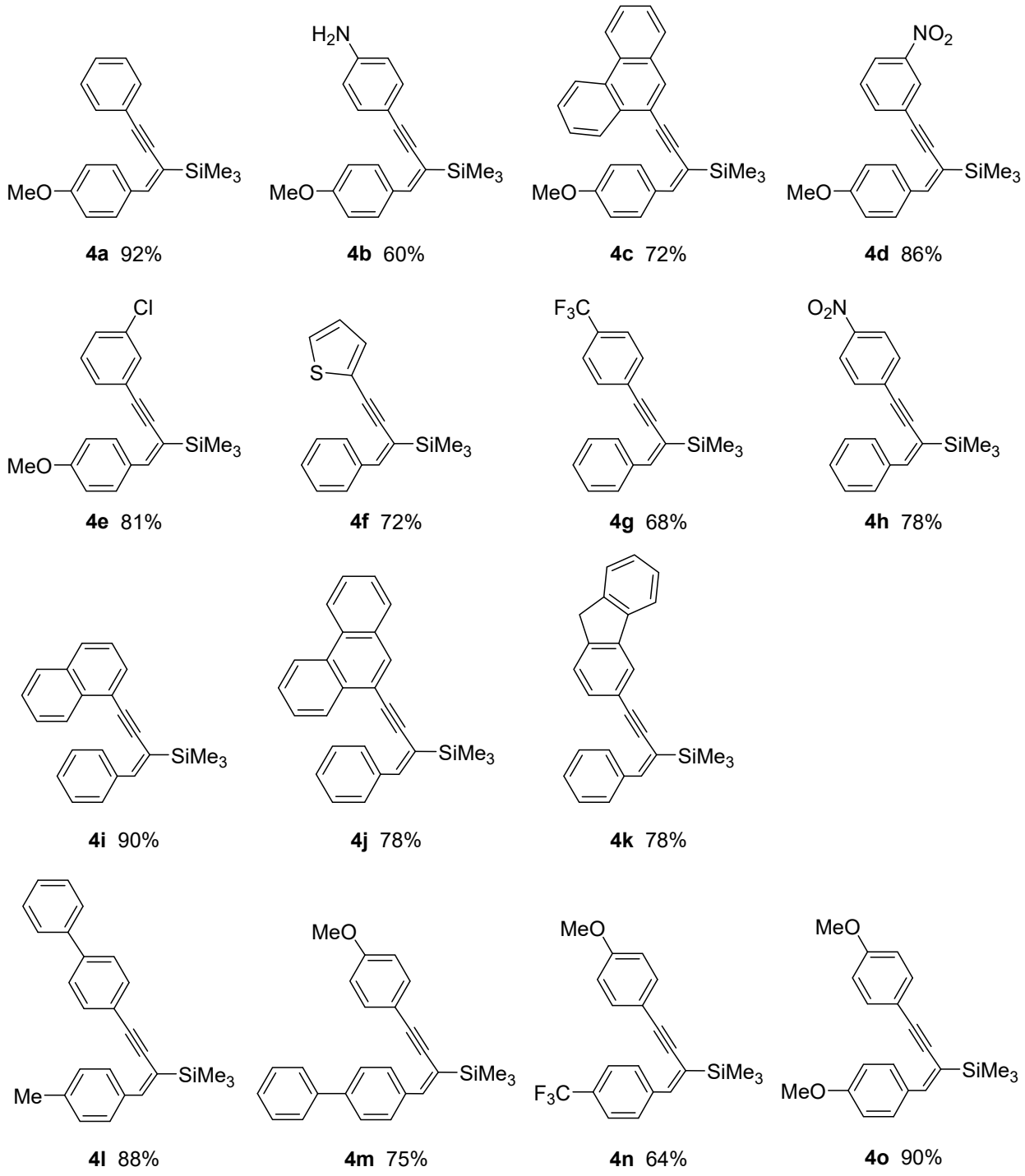
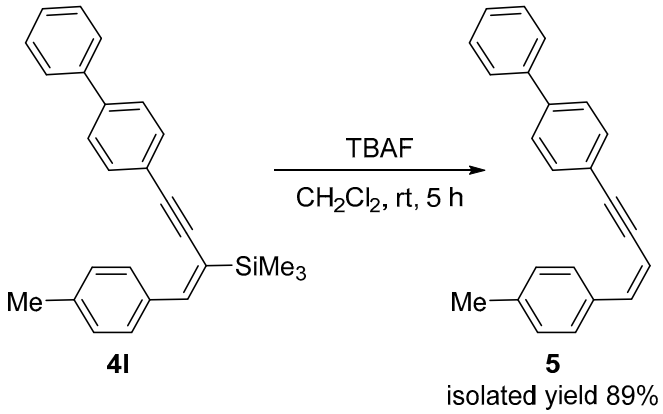


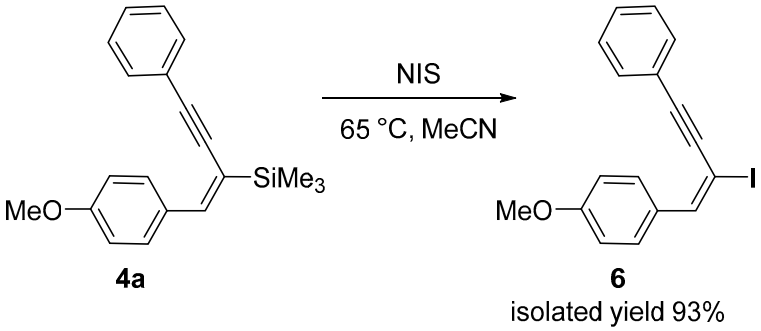
Figure 2. Synthesised enynes (isolated yields are given).

Moreover, the reactivity of the silyl group attached to the enyne double bond allows further transformations. Treatment of **4l** with KO*t*-Bu or KOH resulted in a mixture of unidentified products, and using KF as a desilylation agent had no effect. In contrast, desilylation with TBAF in CH_2Cl_2 solution at room temperature yielded 89% of the protodesilylated product (**5**) (Scheme 6).



Scheme 6. Protodesilylation of 2-silylsubstituted 1,4-(diaryl)but-1-en-3-yne.

The method described by Pawluć and Marciniec [47] was adapted for the iododesilylation of **4a**. Halodesilylation of 1,3-enyne with *N*-iodosuccinimide (NIS) at room temperature did not lead to the formation of **6**. Treatment of an acetonitrile solution of (E)-1-(4-methoxyphenyl)-2-(trimethylsilyl)-4-(phenyl)but-1-en-3-yne (**4a**) with NIS at 65 °C for 5 h afforded the compound **6** in 93% yield (Scheme 7). We only found one paper in the literature describing a similar iododesilylation at position 2 of conjugated enyne [48].



Scheme 7. Iododesilylation of 2-silylsubstituted 1,4-(diaryl)but-1-en-3-yne.

3. Conclusions

1,4-diaryl-2-(trimethylsilyl)but-1-en-3-ynes with aryl groups in mutual *syn* positions can be obtained selectively by the one-pot sequence of protodesilylation of (E)-1-aryl-2,4-bis(trimethylsilyl)but-1-en-3-ynes followed by the aerobic, copper-free Sonogashira cross-coupling of terminal enynes with aryl halides. This method allows for the synthesis of a wide range of 1,4-diaryl-2-silyl-1,3-enynes in moderate to high yields. The synthesised enynes can undergo proto- and halodesilylation, yielding useful building blocks.

4. Experimental

General methods and chemicals. All activities were conducted in the air. ^{1}H and ^{13}C NMR spectra were recorded using a Varian 400 instrument at 402.6 and 101.2 MHz, respectively. All spectra were recorded at 298 K. GC analyses were performed using a Bruker Scion 436-GC (column: DB-5 30 m I.D. 0.53 mm) equipped with a TCD. GC/MS analyses were performed using a Varian Saturn 2100T instrument equipped with (DB-1, 30 m capillary column, 0.25 mm I.D.) and an ion trap detector. IR spectra were recorded on Jasco FT/IR-4600 spectrometer. HRMS analyses were performed using a QTOF mass spectrometer (Impact HD, Bruker Daltonics). Chemicals: KF, all aryl bromides, iodides, $PdCl_2$, PPh_3, methanol (99.6%), tetrahydrofuran, and K_2CO_3 were purchased from Merck. The complexes [$Pd(PPh_3)_4$], [$PdCl_2(PPh_3)_2$], and [$PdCl_2(PhCN)_2$] were synthesised according to the published procedures [49,50].

Optimisation of protodesilylation. A 10 mL two-neck round bottom flask, equipped with a magnetic stirring bar, was charged with 0.069 g (0.225 mmol) of representative (E)-1-(4-methoxyphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne, 5 mL of MeOH, 0.2 g of K_2CO_3, and 0.03 mL of dodecane (internal standard). The vial was closed under air and then stirred and heated at temperatures ranging from 25 to 65 °C in an oil bath for a given reaction time. The reaction course was monitored by gas chromatography.

Optimisation of Sonogashira coupling. First, 25 µL (0.225 mmol) of iodobenzene, 0.15 mL of NEt_3, and 0.0045 mmol of Pd catalyst were added to the methanol solution of desilylated 1,3-enyne. The reaction mixture was heated at various temperatures ranging from 25 to 65 °C in an oil bath for a given reaction time. The reaction course was monitored by gas chromatography.

Representative one-pot synthesis. The synthesis was carried out in a two-neck round bottom flask with a capacity of 100 mL and equipped with a magnetic stirring bar under a closed system. The flask was charged with 0.25 g (0.817 mmol) of (E)-1-(4-methoxyphenyl)-2,4-bis(trimethylsilyl)but-1-en-3-yne, 20 mL of MeOH, and 0.58 g of K_2CO_3 (4.09 mmol). The reaction mixture was stirred and heated at 65 °C in an oil bath for 1 h. Afterwards, 0.9 mL (0.817 mmol) of iodobenzene, 0.5 mL of NEt_3, and 0.006 g (0.0817 mmol) of $[PdCl_2(PPh_3)_2]$ were added to the reaction mixture, and the heating was continued for an additional 23 h. Then, the solvent was removed under vacuum, and the solid residue was purified by column chromatography over silica gel and using hexane/ethyl acetate (25:1) as an eluent. Products characterisation

4a. Isolated as a yellow oil, 225 mg (92% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.99 (d, *J* = 8.5 Hz, 2H, C_6H_4), 7.50–7.47 (m, 2H, Ph), 7.31–7.35 (m, 3H, Ph), 6.91 (d, *J* = 8.9 Hz, 2H, C_6H_4), 6.80 (s, 1H, =CH), 3.84 (s, 3H, OMe), 0.29 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.67, 143.46, 132.35, 131.24, 130.59, 130.30, 128.33, 127.80, 124.50, 113.74, 113.57, 90.59, 55.28, −1.79; **IR** (ν_{max}, cm^{-1}): 3065, 2954, 2838, 2553, 1684, 1599, 1509, 1447, 1422, 1248, 1170, 1109, 1025, 835, 757, 693, 610, 546; **GC-MS** (EI): *m/z* (rel intensity): 45 (10), 59 (10), 73 (50), 292 (38), 306 (100, M^+); **HRMS** (ESI+): calc for $[C_{20}H_{22}OSi + H]^+$: 307.1513; found: 307.1512.

4b. Isolated as a yellow oil, 155 mg (60% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.99–7.97 (m, 2H, C_6H_4), 7.34 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.83 (broad, *J* = 8.7 Hz, 2H), 6.74 (s, 1H, =CH), 5.08 (brs, 2H, -NH_2, 3.83 (s, 3H, OMe), 0.27 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.51, 142.47, 132.64, 132.16, 131.11, 130.16, 124.80, 120.62, 116.59, 113.59, 100.63, 89.48, 55.27, −2.04. **IR** (ν_{max}, cm^{-1}): 3459, 3369, 2953, 2836, 2548, 2166, 1890, 1599, 1504, 1457, 1403, 1303, 1244, 1171, 1112, 1025, 826, 756, 690, 589, 526; **GC-MS** (EI): *m/z* (rel intensity): 73 (11), 306 (30), 307 (10), 321 (100, M^+); **HRMS** (ESI+): calc for $[C_{20}H_{23}NOSi + H]^+$: 322.1622; found: 322.1616.

4c. Isolated as a yellow-orange solid, 235 mg (72% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.72–8.65 (m, 2H, Ar), 8.55–8.53 (m, 1H, Ar), 8.11–8.09 (m, 2H, C_6H_4), 8.00 (s, 1H, Ar), 7.91–7.87 (m, 2H, Ar), 7.73–7.59 (m, 3H, Ar), 6.95–6.93 (m, 2H, C_6H_4), 6.92 (s, 1H, =CH), 3.84 (s, 3H, OMe), 0.38 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.82, 151.68, 143.97, 131.29, 130.42, 130.01, 128.47, 127.22, 127.19, 126.97, 126.94, 126.92, 126.89, 126.54, 122.76, 122.61, 113.67, 98.40, 95.09, 55.31, −1.56. **IR** (ν_{max}, cm^{-1}): 3059, 2954, 2838, 2648, 2170, 1683, 1600, 1506, 1447, 1420, 1292, 1247, 1171, 1103, 1029, 834, 745, 724, 616, 510 **GC-MS** (EI): *m/z* (rel intensity): 406 (100, M^+); **HRMS** (ESI+): calc for $[C_{28}H_{26}OSi + H]^+$: 407.1826; found: 407.1814.

4d. Isolated as a yellow powder, 242 mg (86% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.28 (m, 1H, Ar), 8.16–8.14 (m, 1H, Ar), 7.93 (d, *J* = 8.6 Hz, 2H, C_6H_4), 7.74 (dt, J = 7.6, 1.4 Hz, 1H, Ar), 7.53–7.49 (m, 1H, Ar), 6.93 (d, *J* = 8.6 Hz, 2H, C_6H_4), 6.88 (s, 1H, =CH), 3.84 (s, 3H, OMe), 0.29 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 160.07, 145.43, 136.89, 133.31, 130.35, 129.27, 126.28, 125.82, 122.35, 113.81, 97.11, 93.40, 55.34, −1.57. **IR** (ν_{max}, cm^{-1}): 3060, 2951, 2831, 2183, 1657, 1590, 1515, 1402, 1331, 1250, 1179, 1101, 1008, 832, 750, 684, 630; **GC-MS** (EI): *m/z* (rel intensity): 73 (10), 262 (12), 336 (10), 351 (100, M^+) **HRMS** (ESI+): calc for $[C_{20}H_{21}NO_3Si + Na]^+$: 374.1188; found: 374.1180.

4e. Isolated as a yellow oil, 222 mg (81% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.95 (d, *J* = 8.4 Hz, 2H, C_6H_4), 7.44–7.43 (m, 1H, Ar), 7.35–7.33 (m, 1H, Ar), 7.28–7.27 (m, 2H, Ar), 6.92 (d, *J* = 8.4 Hz, 2H, C_6H_4), 6.82 (s, 1H, =CH), 3.85 (s, 3H, OMe), 0.28 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.89, 144.37, 134.17, 130.97, 130.35, 129.51, 129.39, 127.99, 126.22, 119.83, 113.67, 104.38, 98.54, 91.89, 55.32, −1.77; **IR** (ν_{max}, cm^{-1}): 3032, 2911, 2883, 2143, 1662, 1618, 1599, 1565, 1372, 1334, 1258, 1149, 1191, 1108, 832, 721, 654, 629; **GC-MS** (EI): *m/z* (rel intensity): 73 (20), 202 (12), 251 (10), 326 (14), 340 (100, M^+); **HRMS** (ESI+): calc for $[C_{20}H_{21}ClOSi + Na]^+$: 363.0948; found: 363.1416.

4f. Isolated as a yellow oil, 163 mg (72% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.97 (d, *J* = 7.1 Hz, 2H, Ph), 7.40 (t, *J* = 7.7 Hz, 2H, Ph), 7.33–7.31 (m, 1H, Ph), 7.30 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.22 (dd, *J* = 3.6, 1.3 Hz, 1H), 7.03 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.86 (s, 1H, =CH), 0.32 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: ^{13}C NMR (101 MHz, cdcl$_3$) δ 143.76, 137.66, 131.12, 128.66, 128.52, 128.27, 127.27, 127.18, 124.43, 123.10, 94.47, 94.02, −2.10. **IR** (ν_{max}, cm^{-1}): 3059, 2954, 2890, 2163, 1685, 1597, 1491, 1445, 1410, 1246, 1181, 1046, 990, 837, 753, 692, 631; **GC-MS** (EI): 45 (39), 73 (83), 75 (13), 141 (17), 164 (29), 171 (23), 182 (11), 191 (10), 280 (100), 281 (25), 282 (10, M^+); **HRMS** (ESI+): calc for $[C_{17}H_{18}SSi + H]^+$: 283.0971; found: 283.0976.

4g. Isolated as a yellow oil, 188 mg (68% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.99–7.96 (m, 2H, C_6H_4), 7.62–7.55 (m, 4H, Ph, C_6H_4), 7.42–7.30 (m, 3H, Ph), 6.93 (s, 1H, =CH), 0.31 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 147.02, 145.32, 137.46, 131.45, 130.22, 128.82, 128.78, 128.40, 128.34, 125.31 (q, *J* = 3.8 Hz) 123.03, 99.16, 92.75, −2.05. **IR** (ν_{max}, cm^{-1}): 3069, 2956, 2171, 1705, 1611, 1492, 1448, 1408, 1321, 1248, 1165, 1123, 1065, 1015, 834, 754, 692, 630, 593; **GC-MS** (EI): *m/z* (rel intensity): 251 (24), 252 (17), 323 (15), 325 (32), 326 (83), 327 (48), 343 (21), 344 (100, M^+); **HRMS** (ESI+): calc for $[C_{20}H_{19}F_3Si + Na]^+$: 367.1100; found: 367.1115.

4h. Isolated as a dark yellow solid, 201 mg (78% yield). Spectroscopic characterization: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.21 (d, *J* = 9.0 Hz, 2H, C_6H_4), 7.96–7.93 (m, 2H, Ph), 7.58 (d, *J* = 9.0 Hz, 2H, C_6H_4), 7.42–7.34 (m, 3H, Ph), 6.97 (s, 1H, =CH), 0.33 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: ^{13}C NMR (101 MHz, cdcl$_3$) δ 153.48, 146.25, 137.38, 131.85, 131.20, 128.99, 128.83, 128.36, 128.07, 123.69, 98.42, 95.90, 29.68, −2.09. **IR** (ν_{max}, cm^{-1}): 3063, 2956, 2851, 2173, 1687, 1591, 1515, 1406, 1337, 1250, 1174, 1103, 1017, 834, 751, 689, 632; **GC-MS (EI)**: *m/z* (rel intensity): 45 (37), 73 (100), 75 (17), 200 (28), 215 (14), 230 (22), 243 (18), 257 (13), 288 (20), 304 (22), 320 (38), 321 (10, M^+); **HRMS** (ESI+): calc for $[C_{19}H_{19}NO_2Si + Na]^+$: 344.1077; found: 344.1090.

4i. Isolated as a yellow solid, 235 mg (90% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.43–8.41 (m, 1H, Ar), 8.11–8.09 (m, 2H, Ph), 7.88–7.80 (m, 2H, Ar), 7.71 (dd, *J* = 7.1, 1.2 Hz, 1H, Ar), 7.57–7.53 (m, 2H, Ar), 7.49–7.39 (m, 3H, Ph), 7.36–7.30 (m, 1H, Ar), 6.96 (s, 1H, =CH), 0.38 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 144.16, 137.80, 135.22, 134.99, 133.25, 133.07, 130.27, 128.80, 128.53, 128.49, 128.41, 128.29, 127.98, 126.65, 126.37, 125.37, 123.86, 99.02, 95.03, −1.67. **IR** (ν_{max}, cm^{-1}): 3363, 3055, 2954, 2165, 1686, 1636, 1590, 1505, 1445, 1398, 1246, 1173, 1107, 1022, 961, 835, 799, 772, 692, 630, 592; **GC-MS** (EI): *m/z* (rel intensity): 45 (27), 59 (13), 73 (79), 172 (14), 197 (13), 209 (15), 252 (37), 253 (24), 295 (13), 311 (16), 326 (100, M^+); **HRMS** (ESI+): calc for $[C_{23}H_{22}Si + H]^+$: 327.1564; found: 327.1552.

4j. Isolated as a yellow-orange solid, 235 mg (78% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.73–8.65 (m, 2H, Ar), 8.54–8.51 (m, 1H, Ar), 8.14–8.10 (m, 2H, Ph), 8.00 (s, 1H, Ar), 7.90–7.87 (m, 2H, Ar), 7.72–7.61 (m, 3H, Ar), 7.46–7.33 (m, 3H, Ph), 6.99 (s, 1H, =CH), 0.40 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 151.81, 144.43, 137.85, 131.51, 130.15, 128.84, 128.57, 128.51, 128.33, 127.30, 127.17, 127.00, 126.96, 126.93, 123.88, 122.75, 122.61, 120.85, 99.13, 94.68, −1.61. **IR** (ν_{max}, cm^{-1}): 3062, 2956, 2838, 2645, 2170, 1683, 1600, 1506, 1450, 1420, 1292, 1247, 1171, 1113, 1029, 834, 745, 725, 623; **GC-MS** (EI): *m/z* (rel intensity): 45 (19), 73 (50), 302 (23), 303 (19), 361 (11), 376 (100, M^+); **HRMS** (ESI+): calc for $[C_{27}H_{24}Si + H]^+$: 377.1720; found: 377.1712.

4k. Isolated as a yellow crystalline solid, 228 mg (78% yield). Purified by column chromatography over silica gel using n-hexane as an eluent, then recrystallized from n-hexane. Spectroscopic characterization: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.04 (d, *J* = 7.9 Hz, 2H, Ph), 7.80–7.77 (m, 3H, Ar), 7.58–7.55 (m, 3H, Ph), 7.41–7.40 (m, 2H, Ar), 7.35–7.33 (m, 2H, Ar), 6.87 (s, 1H, =CH), 3.92 (s, 2H, -CH_2-), 0.33 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 143.62, 141.12, 137.83, 131.56, 130.28, 128.74, 128.41, 128.35, 128.27, 127.84, 127.09, 126.90, 125.08, 123.78, 120.15, 119.79, 101.93, 90.41, 36.74, −1.77. **IR** (ν_{max}, cm^{-1}): 3056, 2954, 2206, 1711, 1685, 1603, 1489, 1451, 1400, 1247, 1180, 1101, 1023, 950, 916, 834, 750, 731, 689, 589; **GC-MS** (EI): *m/z* (rel intensity): 45 (10), 73 (11), 364 (100, M^+); **HRMS** (ESI+): calc. for $[C_{26}H_{24}Si + Na]^+$: 387.1539; found: 387.1544.

4l. Isolated as a yellow powder, 258 mg (88% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 7.94 (d, *J* = 8.0 Hz, 2H, C_6H_4), 7.63–7.59 (m, 4H, Ar), 7.56–7.55 (m, 2H, Ar), 7.48–7.45 (m, 2H, Ar), 7.39–7.36 (m, 1H, Ar), 7.22 (d, *J* = 8.0 Hz, 2H, C_6H_4), 6.86 (s, 1H, =CH), 2.39 (s, 3H, Me), 0.32 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 144.01, 140.61, 140.47, 138.55, 135.19, 131.69, 128.97, 128.85, 128.75, 127.55, 127.04, 126.98, 123.43, 122.19, 100.60, 91.31, 21.42, −1.98. **IR** (ν_{max}, cm^{-1}): 3046, 2930, 2850, 2505, 2140, 1688, 1525, 1480, 1413, 1332, 1250, 1181, 1116, 1054, 828, 750, 702, 568, 481; **GC-MS (EI)**: *m/z* (rel intensity): 45 (10), 73 (12), 366 (100, M^+) **HRMS** (ESI+): calc for $[C_{26}H_{26}Si + Na]^+$: 389.1696; found: 389.1687.

4m. Isolated as a yellow powder, 230 mg (75% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.10 (d, *J* = 7.9 Hz, 2H, C_6H_4), 7.66–7.61 (m, 4H, C_6H_4, Ph), 7.37–7.35 (m, 1H, Ph), 6.90 (d, *J* = 7.9 Hz, 2H, C_6H_4), 6.87 (s, 1H, =CH), 3.84 (s, 3H, OMe), 0.31 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.48, 142.53, 140.68, 136.98, 132.77, 131.84, 129.12, 128.67, 127.43, 127.10, 126.83, 123.93, 116.60, 113.96, 101.57, 89.30, 55.32, −2.00; **IR** (ν_{max}, cm^{-1}): 3042, 2910, 2820, 2158, 1689, 1525, 1483, 1410, 1330, 1259, 1181, 1084, 822, 751, 698, 560, 496; **GC-MS** (EI): *m/z* (rel intensity): 73 (12), 368 (8), 382 (100, M^+); **HRMS** (ESI+): calc for $[C_{26}H_{26}OSi + Na]^+$: 405.1651; found: 405.1676.

4n. Isolated as a yellow oil, 195 mg (64% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.09 (d, *J* = 8.1 Hz, 2H, C_6H_4-CF_3), 7.62 (d, *J* = 8.1 Hz, 2H, C_6H_4-CF_3), 7.41 (d, *J* = 8.9 Hz, 2H C_6H_4-OMe), 6.90 (d, *J* = 8.9 Hz, 2H, C_6H_4-OMe), 6.83 (s, 1H, =CH), 3.84 (s, 3H, OMe), 0.31 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.79, 141.03, 141.00, 133.04, 132.89, 129.69, 128.65, 127.64, 125.08, 116.09, 114.14, 102.72, 88.62, 55.35, −1.89; **IR** (ν_{max}, cm^{-1}): 3039, 2942, 2131, 1675, 1601, 1462, 1408, 1329, 1242, 1165, 1119, 1034, 1022, 831, 772, 690, 630; **GC-MS** (EI): *m/z* (rel intensity): 73 (15), 267(10), 282 (10), 355 (16), 374 (100, M^+); **HRMS** (ESI+): calc for $[C_{21}H_{21}F_3OSi + H]^+$: 375.1392; found: 375.1416.

4o. Isolated as a yellow oil, 202 mg (90% yield). Spectroscopic characterisation: **^{1}H NMR** ($CDCl_3$; ppm) δ: 8.02 (d, *J* = 8.9 Hz, 2H, C_6H_4), 7.45 (d, *J* = 8.9 Hz, 2H, C_6H_4), 6.93, (d, *J* = 8.9 Hz, 2H, C_6H_4), 6.91 (d, *J* = 8.9 Hz, 2H, C_6H_4), 6.80 (s, 1H, =CH), 3.85 (s, 3H, OMe), 3.84 (s, 3H, OMe), 0.31 (s, 9H, $SiMe_3$); **^{13}C NMR** ($CDCl_3$; ppm) δ: 159.57, 159.34, 142.62, 132.64, 131.10, 130.18, 120.59, 116.72, 114.00, 113.52, 100.38, 89.35, 55.25, 55.22, −1.96; **IR** (ν_{max}, cm^{-1}): 3001, 2953, 2835, 2540, 2173, 2055, 1889, 1603, 1566, 1503, 1461, 1441, 1286, 1242, 1171, 1105, 1025, 864, 826, 754, 693, 614, 531; **GC-MS** (EI): *m/z* (rel intensity): 321 (10), 336 (100, M^+); **HRMS** (ESI+): calc for $[C_{21}H_{24}NaO_2Si + Na]^+$: 359.1438; found: 359.1452.

Protodesilylation of **4l**. A 10 mL two-neck round bottom flask, which was equipped with a magnetic stirring bar, was charged with 0.082 g (0.225 mmol) of (E)-1-(4-methylphenyl)-2-(trimethylsilyl)-4-biphenylbut-1-en-3-yne (**4l**), 5 mL of CH_2Cl_2, 0.18 g (0.675 mmol) of TBAF and 5 mL of CH_2Cl_2. The mixture was stirred at room temperature for 24 h. The solvent was then removed under vacuum, and the solid residue was purified by column chromatography on silica gel with hexane/ethyl acetate (25:1).

5. Isolated as a yellow oil, 59 mg (89% yield). Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 7.88 (d, 2H, J = 8.2 Hz, C_6H_4), 7.64–7.58 (m, 6H, Ar), 7.48–7.46 (m, 2H, Ar), 7.40–7.37 (m, 1H, Ar), 7.24 (d, 2H, J = 8.2 Hz, C_6H_4), 6.71 (d, 1H, J = 11.9 Hz, =CH), 5.91 (d, 1H, J = 11.9 Hz, =CH), 2.41 (s, 3H, -CH_3); ^{13}C NMR ($CDCl_3$; ppm) δ: 140.97, 140.30, 138.66,

138.58, 133.89, 131.81, 129.00, 128.85, 128.73, 127.63, 127.06, 126.98, 122.46, 106.31, 95.55, 88.97, 21.39. IR (ν_{max}, cm^{-1}): 3028, 2921, 2853, 2182, 1913, 1677, 1602, 1512, 1485, 1448, 1403, 1321, 1259, 1180, 1112, 1078, 1036, 1006, 822, 761, 721, 692, 556, 499, 447; GC-MS (EI): *m/z* (rel intensity): 213 (2), 278 (5), 279 (7), 294 (100, M^+); HRMS (ESI+): calc for $[C_{23}H_{18}Si + Na]^+$: 317.1306; found: 317.1311.

Iododesilylation of **4a**. A 10 mL two-neck round bottom flask, equipped with a magnetic stirring bar, was charged with 0.069 g (0.25 mmol) of (E)-1-(4-methoxyphenyl)-2-(trimethylsilyl)-4-phenylbut-1-en-3-yne (**4a**), 0.1 g (0.45 mmol) of NIS and 5 mL of MeCN. The mixture was stirred and heated in a closed system at 65 °C in an oil bath for 5 h. The solvent was removed under vacuum, and the solid residue was purified by column chromatography on silica gel with hexane/ethyl acetate (25:1).

6. Isolated as an orange-yellow oil, 83 mg (93% yield). Spectroscopic characterisation: ^{1}H NMR ($CDCl_3$; ppm) δ: 7.77–7.75 (m, 2H, C_6H_4), 7.50–7.49 (m, 2H, Ph), 7.38–7.37 (m, 3H, Ph), 7.34 (s, 1H, =CH), 6.88 (d, 2H, J = 9.0 Hz, C_6H_4), 3.83 (s, 3H, OMe); ^{13}C NMR ($CDCl_3$; ppm) δ: 160.08, 146.59, 131.49, 130.23, 129.85, 128.98, 128.39, 122.41, 113.82, 97.05, 91.10, 64.90, 55.31. IR (ν_{max}, cm^{-1}): 3001, 2929, 2837, 2167, 1883, 1717, 1685, 1598, 1507, 1443, 1293, 1254, 1175, 1026, 894, 823, 779, 755, 691, 631, 534; GC-MS (EI): *m/z* (rel intensity): 360 (100, M^+); HRMS (ESI+): calc for $[C_{17}H_{13}IO + H]^+$: 361.0089; found: 361.0069.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/org4020017/s1, Table S1: Literature reports on the application of silylenynes in the synthesis of 1,4-(diaryl)but-1-en-3-ynes substituted in positions 1 and 4 by different aryl groups, ^{1}H and ^{13}C, spectra of the products **4a-4o**, **5** and **6**.

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