COUPLING REACTIONS OF *ortho*-SUBSTITUTED HALOBENZENES WITH ALKYNES. THE SYNTHESIS OF PHENYLACETYLENES AND SYMMETRICAL OR UNSYMMETRICAL 1,2-DIPHENYLACETYLENES

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The Pd- or Pd/Cu-catalyzed coupling reactions of halobenzenes bearing the methyl, hydroxymethyl, acetoxymethyl, methoxycarbonyl, or both methoxy and 4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl groups in the *ortho*-position with gaseous or metallated acetylene, (trialkylsilyl)acetylenes, and arylacetylenes have been systematically studied. Various functionalized aryl- or diarylacetylenes have been synthesized in good to excellent yields. Whereas additional fluoro, nitro, or methoxy group attached to the benzene ring does not interfere in the coupling reactions, the presence of a methoxycarbonyl requires a careful optimization of reaction conditions to achieve moderate yields.

Key words: Halobenzenes; Phenylacetylenes; Diphenylacetylenes; Cross-coupling reactions; Palladium catalysis; Arenes; Alkynes.

Arylacetylenes are both versatile synthetic intermediates and functional building blocks of a wide use[1]. As a result of enormous development of modern organometallic synthetic tools in the last two decades, cross-coupling reactions of aryl halides or triflates with alkynes under palladium(0 or II) catalysis and copper(I) co-catalysis have dominated in the preparation of aryl- and 1,2-diarylacetylene derivatives[2]. The unique position of the coupling methodology stems from the mild reaction conditions used, high tolerance to various functional groups, and broad variability of the experimental setup allowing a careful tuning of reaction conditions to achieve usually good preparative yields.

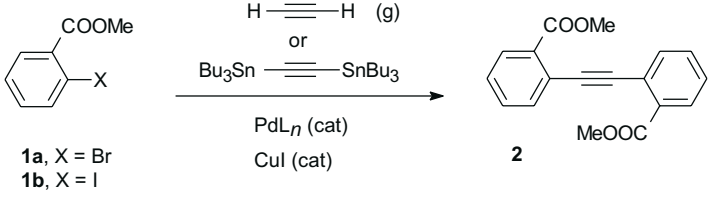
In connection with our interest in the development of novel strategies for the synthesis of helically chiral molecules[3], we required a general and efficient route to various *ortho*-functionalized arylacetylenes. Although plethora of phenyl- and naphthylacetylenes has been described in litera-

ture, only little attention has been paid to a systematic study of coupling acetylenes with aryl halides bearing various groups in the *ortho*-position. Recently, we have disclosed a report on the synthesis of 2-functionalized 1-ethynylnaphthalene derivatives[4]. In this paper, we describe a study on the coupling reaction of 2-substituted halobenzenes with gaseous or metallated acetylene as well as terminal alkynes under Pd or Pd/Cu catalysis.

RESULTS AND DISCUSSION

Coupling Reactions of 2-Halobenzoates with Gaseous or Metallated Acetylene

On treatment of 2-bromobenzoate **1a** with gaseous acetylene under $Pd(PPh_3)_2Cl_2$/CuI catalysis in piperidine[4], the educt was consumed but no expected bis-coupled product **2** was detected (Scheme 1; Table I, entry 1). Omitting the copper(I) co-catalyst, generally used to promote the coupling[1,2], the desired reaction took place but the product **2** was isolated in an unsatisfactory yield (Table I, entry 2). When bromine in **1a** was replaced by iodine and $Pd(PPh_3)_4$ was used as the catalyst, benzoate **1b** afforded the diarylacetylene **2** in an acceptable yield (52%; Table I, entry 3).



SCHEME 1

In order to compare the efficiency of an alternative synthetic methodology, we turned our attention to the cross-coupling reaction between aryl halides and alkynylstannanes[5]. On treatment of iodobenzoate **1b** with bis(tributylstannyl)acetylene under $Pd(PPh_3)_2Cl_2$ catalysis, the diarylacetylene **2** was obtained in the best yield achieved (56%; Table I, entry 4). The use of $Pd(PPh_3)_4$ instead of $Pd(PPh_3)_2Cl_2$ led to a lower yield of **2** (Table I, entry 5) in contrast to coupling halobenzoates with gaseous acetylene, *vide supra*. The $Pd(PPh_3)_4$-catalyzed reaction of iodobenzoate **1b** with alkynylzinc reagent[6] ClZn–C≡C–ZnCl did not afford the coupled product **2**.

Coupling Reactions of Halobenzenes with Gaseous Acetylene

The halobenzenes **3**–**7** bearing a methyl or hydroxymethyl group in the *ortho*-position have been found to undergo smoothly the Pd-catalyzed coupling reaction with gaseous acetylene to provide the corresponding diarylacetylenes **8**–**12** in high yields (76–99%; Table II, entries 1, 3–8). In all cases, a positive effect of the CuI co-catalyst on preparative yields was observed being most pronounced in the coupling reactions of the bromonitrobenzene **4** (Table II, *cf.* entries 2 and 3). Interestingly, the reaction course of the Pd/Cu-catalyzed couplings of halobenzenes with acetylene was almost invariant to the presence or absence of an additional 3-nitro, 3-methoxycarbonyl, and 4-methoxyl group.

TABLE I
Coupling reactions of 2-bromo- or 2-iodobenzoate with gaseous or metallated acetylene. Tuning reaction conditions

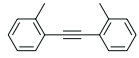
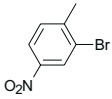
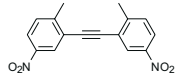
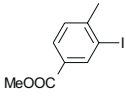
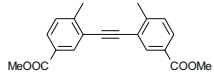
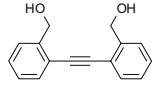
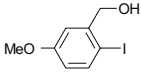
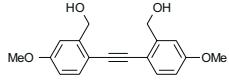
Entry	Educt	Acetylene[a] equivalent	PdL_n[b] mole %	CuI mole %	Solvent	Cond. °C; h	Yield[c] of **2**[d] %
1	**1a**	HC≡CH (g)	A, 5	5		80; 6	0[e]
2	**1a**	HC≡CH (g)	A, 5	0		80; 4	18
3	**1b**	HC≡CH (g)	B, 2.5	0		80; 3	52
4	**1b**	$Bu_3Sn–C≡C–SnBu_3$ 0.55	A, 5	0	THF	50; 18	56[f]
5	**1b**	$Bu_3Sn–C≡C–SnBu_3$ 0.55	B, 5	0	THF	50; 18	20[f]

[a] The reaction conducted under atmospheric pressure of gaseous acetylene unless noted otherwise (stannylated acetylene reacted under argon); [b] A: $Pd(PPh_3)_2Cl_2$, B: $Pd(PPh_3)_4$; [c] isolated; [d] see ref.[8]; [e] the starting material consumed, a complex mixture of products formed; [f] yield calculated from GC analysis of the reaction mixture with an internal standard.

Coupling Reactions of Halobenzenes with (Trialkylsilyl)acetylenes

The *ortho*-substituted halobenzenes **1a**, **1b**, **6a**, **6b**, **13**–**17** were treated with (trialkylsilyl)acetylenes under the $Pd(PPh_3)_4$ catalysis in the absence of CuI (ref.[4]) to furnish the silyl-protected arylacetylenes **18**, **20**–**23**, **25**, and **27** (Table III). Although good preparative yields were mostly attained (up to 99%), it was necessary to find out the best reacting (trialkylsilyl)acetylene by trial and error.

TABLE II
Coupling reactions of 2-substituted halobenzenes with gaseous acetylene

Entry	Educt		PdL_n[a] mole %	CuI mole %	Cond.[b] °C; h	Product		Yield[c] %
1		**3**	1.5	3	80; 0.25		**8**[d]	96
2		**4**	5	0	80; 4		**9**	9
3		**4**	5	10	80; 2.5		**9**	78
4		**5**	10	0	80; 0.75		**10**	76
5		**5**	5	10	80; 0.5		**10**	98
6		**6b**	1	2	r.t.; 1		**11**[d]	94
7		**7**	5	0	r.t.; 1		**12**	80
8		**7**	5	10	80; 0.1		**12**	99

[a] $Pd(PPh_3)_4$; [b] the reaction conducted in piperidine under atmospheric pressure of gaseous acetylene; [c] isolated; [d] see ref.[4].

TABLE III
Coupling reactions of 2-substituted halobenzenes with (trialkylsilyl)acetylenes

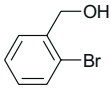
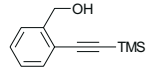
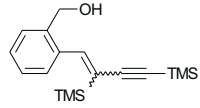
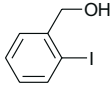
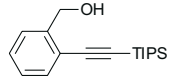
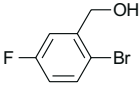
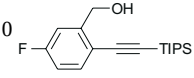
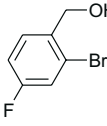
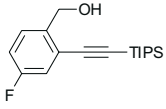
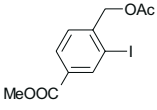
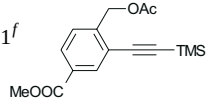
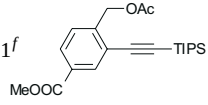
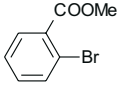
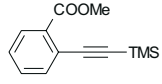
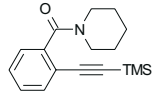
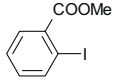
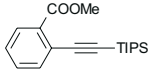
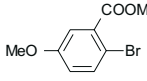
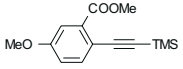
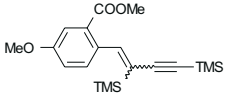
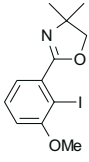
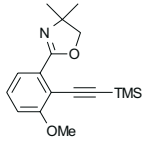
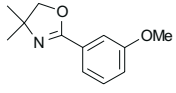
Entry	Educt		Acetylene[a] equivalent	PdL_n[b] mole %	Cond.[c] °C; h	Product		Yield[d] %
1		**6a**	A, 2.2	5	80; 6		**18a**[e]	54
							**19**	14
2		**6b**	A, 2.2	5	50; 20		**18a** **19**	46 25
3		**6b**	B, 1.2	5	80; 13		**18b**	97
4		**13**	B, 1.2	2.5	80; 20		**20**	86
5		**14**	B, 1.2	5	80; 22		**21**	99
6		**15**	A, 2.2	5	80; 1[f]		**22a**	73
7		**15**	B, 1.2	5	80; 1[f]		**22b**	28
8		**1a**	A, 2.2	5	80; 6		**23a**[g]	63
							**24**	6

TABLE III
(*Continued*)

Entry	Educt		Acetylene[a] equivalent	PdL_n[b] mole %	Cond.[c] °C; h	Product		Yield[d] %
9		**1b**	A, 2.2	5	80; 2		**23a** **24**	49 <5
10		**1b**	B, 1.2	5	80; 13		**23b**	44
11		**16**	A, 2.2	5	80; 4		**25**	42
							**26**	8
12		**17**	A, 2.2	10	80; 6		**27**	27
							**28**[h]	22

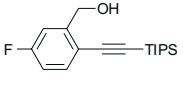
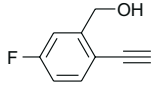
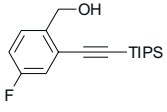
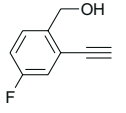
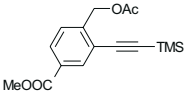
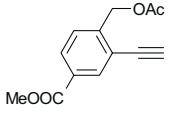
[a] A: $Me_3Si–C\equiv CH$, B: $iPr_3Si–C\equiv CH$; [b] $Pd(PPh_3)_4$; [c] the reaction conducted in piperidine; [d] isolated; [e] see ref.[9]; [f] the reaction conducted in diisopropylamine; [g] see refs[10,17]; [h] see ref.[11].

Regardless of the halogen atom identity, coupling of (trimethylsilyl)acetylene with both the benzyl alcohols **6a** and **6b** afforded the ethynyl derivative **18a** in moderate yields along with the side product **19** arisen from **18a** by a subsequent carbopalladation (Table III, entries 1 and 2). By contrast, the use of (triisopropylsilyl)acetylene led exclusively to the formation of the ethynyl derivative **18b** in nearly quantitative yield (Table III, entry 3).

Similarly, the 4- and 3-fluorobenzyl alcohols **13** and **14** provided cleanly the fluorinated aryl acetylenes **20** and **21** in excellent yields (Table III, entries 4 and 5). Consequently, the presence of the bulky triisopropylsilyl group slowed down the coupling but, at the same time, it disallowed the undesirable addition of an organopalladium species on the triple bond. By contrast, the coupling of the 3-methoxycarbonyl derivative **15** with (trimethylsilyl)acetylene produced the arylacetylene **22a** in a good yield whereas the use of (triisopropylsilyl)acetylene resulted in a low yield of **22b** (Table III, *cf.* entries 6 and 7).

The coupling reactions of the 2-halobenzoates **1a**, **1b**, and **16** with (trimethylsilyl)- and (triisopropylsilyl)acetylene displayed a diminished ability of halobenzenes bearing an ester group in the *ortho*-position to produce corresponding ethynylated derivatives. On treatment with (trimethylsilyl)acetylene, all the halobenzoates **1a**, **1b**, and **16** provided the arylacetylenes **23a** and **25** in moderate yields (Table III, entries 8, 9, and 11). Moreover, two side products were detected: the amide **24** (Table III, entries 8 and 9) and the enyne **26** (Table III, entry 11)[17]. Application of (triisopropylsilyl)acetylene did not improve the yield of coupling (Table III, entry 10).

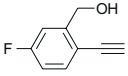
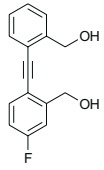
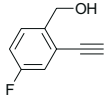
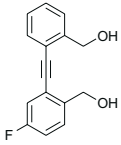
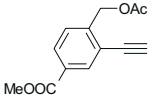
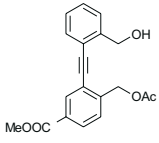
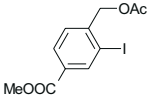
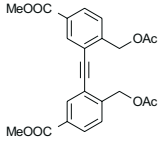
TABLE IV
Deprotection of silylated phenylacetylenes

Entry	Educt		TBAF[a] equiv.	Cond.[b] min	Product		Yield[c] %
1		**20**	1.7	15		**29**	99
2		**21**	1.4	5		**30**	85
3		**22a**	1.3	30		**31**	99

[a] 1.0 M Bu_4NF in THF; [b] room temperature; [c] isolated.

(Trimethylsilyl)acetylene reacted with the 2,6-disubstituted iodobenzene **17** to give the arylacetylene **27** in a low yield along with the dehalogenated product **28** (Table III, entry 12). It reveals that the reaction of (trimethylsilyl)acetylene with an arylpalladium(II) intermediate formed from **17** competes with its protonolysis.

TABLE V
Coupling reactions of *ortho*-substitued halobenzenes with phenylacetylenes

Entry	Educt	Acetylene[a]	PdL_n[b] mole %	Cond.[c] h	Product	Yield[d] %
1	 **6b**	 **29**	5	5	 **32**	72
2	**6b**	 **30**	10	2	 **33**	99
3	**6b**	 **31**	5	1[e]	 **34**	65
4	 **15**	**31**	5	1[e]	 **35**	11

[a] Equimolar amounts of halobenzene and arylacetylene reacted; [b] $Pd(PPh_3)_4$; [c] the reaction conducted at 80 °C in piperidine unless noted otherwise; [d] isolated; [e] the reaction conducted in diisopropylamine.

Coupling Reactions of Halobenzenes with Phenylacetylenes

Deprotection of the silylated arylacetylenes **20**, **21**, and **22a** proceeded smoothly in the presence of tetrabutylammonium fluoride to afford the terminal acetylenes **29**–**31** in high yields (Table IV, entries 1–3). These compounds were further used in the Pd-catalyzed coupling reactions with *ortho*-substituted halobenzenes, *vide infra*.

The yields of the couplings were strongly influenced by combination of the reaction partners. Whereas the Pd-catalyzed reaction of the arylacetylenes **29**–**31** with 2-iodobenzyl alcohol **6b** furnished the cross-coupled diarylacetylenes **32**–**34** in good to excellent yields (Table V, entries 1–3), the reaction between **15** and **31** led to the homo-coupled product **35** in a very low yield[7] (Table V, entry 4).

CONCLUSION

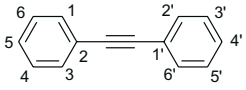
In the Pd- or Pd/Cu-catalyzed coupling reaction of gaseous acetylene, bis(tributylstannyl)acetylene, (trialkylsilyl)acetylenes, and arylacetylenes with halobenzenes bearing the methyl, hydroxymethyl, acetoxymethyl, and methoxycarbonyl group in the *ortho*-position, the target aryl- or diarylacetylenes can be synthesized in good to excellent yields. However, when coupling methoxycarbonyl derivatives, a careful optimization of the reaction conditions is required to get even moderate yields. The presence of additional substituents such as fluoro, nitro, and methoxy does not interfere with the coupling reaction.

EXPERIMENTAL

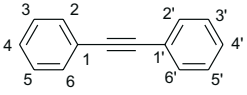
General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H NMR spectra were measured at 500 or 200 MHz, ^{13}C NMR spectra at 125 MHz, in $CDCl_3$ with TMS as an internal standard or in acetone-d_6 (referenced to acetone). ^{19}F NMR spectra were measured at 470.32 MHz in $CDCl_3$ or in acetone-d_6 with $CFCl_3$ as an internal standard. Chemical shifts are given in δ-scale, coupling constants J in Hz. For numbering of the skeleton see Fig. 1. IR spectra were measured in $CHCl_3$, CCl_4, and in KBr pellets (in cm^{-1}). EI MS spectra were determined at an ionizing voltage 70 eV. FAB MS spectra were measured using the thioglycerol–glycerol matrix and methanol as a solvent. HR MS spectra were obtained by the EI or FAB technique. GC MS analyses were carried out on a DB-5 column (0.25 × 30 m × 0.25 μm), EI MS spectra of separated compounds were measured at an ionizing voltage 70 eV. All reactions were performed in Schlenk or double-necked flasks equipped with rubber septa and connected *via* rubber tubings to a standard vacuum/argon line. All chemicals were reagent grade materials. Tetrahydrofuran was freshly distilled from sodium–benzophenone under ni-

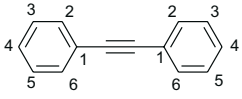
trogen; diisopropylamine and piperidine were distilled from calcium hydride under argon and degassed by three freeze-pump-thaw cycles before use, dimethylformamide was distilled from calcium hydride under reduced pressure and stored over 4Å molecular sieves. The reactions with gaseous acetylene under atmospheric pressure were performed in a vessel connected to a rubber balloon filled with acetylene directly from a cylinder[16].



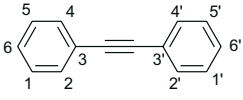
	Substituent			
32	1-CH_2OH		2'-CH_2OH	4'-F
33	1-CH_2OH		2'-CH_2OH	5'-F
34	1-CH_2OAc	4-COOMe	2'-CH_2OH	



	Substituent	
2	2-COOMe	2'-COOMe



	Substituent			
9	2-Me	5-NO_2	2-Me	5-NO_2
12	2-CH_2OH	4-OMe	2-CH_2OH	4-OMe



	Substituent			
10	1-COOMe	4-Me	1'-COOMe	4'-Me
35	1-COOMe	4-CH_2OAc	1'-COOMe	4'-CH_2OAc

FIG. 1
Numbering of diarylacetylene skeletons as utilized in ^1H and ^{13}C NMR spectra signal assignments

Bis(tributylstannyl)acetylene, (trimethylsilyl)- and (triisopropylsilyl)acetylene (Aldrich) were used as received. The starting halobenzenes were purchased from Aldrich (**3**, **4**, **6a**, 3-iodo-4-methylbenzoic acid, 1-bromo-4-fluoro-2-methylbenzene, 2-bromo-4-fluoro-1-methylbenzene), Acros Chimica (**1a**, **6b**), and Avocado (**1b**) or prepared according to the literature procedures[4] (**7**, **16**). The novel or modified syntheses of starting halobenzenes **5** (ref.[12]), **13**, **14**, **15**, and **17** or acetylenes **29**, **30**, and **31** are reported below. The compound **28** was prepared according to the literature procedure[11]. TLC was performed on Silica gel 60 F_{254}-coated aluminium sheets (Merck) and spots were detected by ceric sulfate–phosphomolybdic acid–sulfuric acid solution. Flash chromatography was performed on Silpearl silica gel (Kavalier Votice, Czech Republic) or Silica gel 60 (0.040–0.063 mm or <0.063 mm, Merck). Semipreparative HPLC was carried out on a silica gel column (Partisil M9, Whatman 10/50, 500 mm × 10 mm; sample injections on a 10–20 mg scale) using a refractometric detector.

General Procedure for the Coupling Reaction of Halobenzenes **1b**, **3**–**5**, **6b**, and **7** with Gaseous Acetylene

Method A). A Schlenk flask was charged with halobenzene (5.0 mmol), $Pd(PPh_3)_4$ (2.5–10 mole %), stoppered with a rubber septum, and flushed with argon. Piperidine (10 ml) was added and the mixture was briefly heated at 40–50 °C under stirring to get a clear solution. Then a rubber balloon filled with acetylene was attached to the side arm and the flask was purged of remaining argon using a needle introduced through the septum over the surface of the reaction medium. The mixture was stirred under atmospheric pressure of acetylene at ambient temperature or 80 °C for 0.75–4 h until the educt disappeared (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (2 × 5 ml). The combined fractions were evaporated to dryness *in vacuo* (at <50 °C) and the residue was chromatographed on silica gel to obtain the product.

Method B). It differs from the method *A*) in the presence of CuI (2–10 mole %).

Procedure for the Coupling Reaction of Halobenzene **1b** with Bis(tributylstannyl)acetylene

Method C). A Schlenk flask was charged with halobenzene **1b** (0.20 mmol), $Pd(PPh_3)_2Cl_2$ (5 mole %), stoppered with a rubber septum, and flushed with argon. THF (5 ml) was added and the mixture was stirred at room temperature for 5 min. Then bis(tributylstannyl)acetylene (60 μl, 0.114 mmol, 1.1 equivalent) was added with a syringe and the mixture was stirred at 50 °C for 18 h until the edduct disappeared (monitored by TLC or GC). The solution was evaporated to dryness *in vacuo* (at <50 °C) and the residue was chromatographed on silica gel to obtain the product.

General Procedure for the Coupling Reaction of Halobenzenes **1a**, **1b**, **6a**, **6b**, and **15**–**17** with (Trimethylsilyl)acetylene

Method D). A glass pressure tube with gas inlet was charged with halobenzene (1.0 mmol) and $Pd(PPh_3)_4$ (5–10 mole %). The tube was stoppered with a rubber septum and flushed with argon. Piperidine (or diisopropylamine; 3 ml) was added and the mixture was briefly heated under stirring at 40–50 °C to get a clear solution. After cooling to room temperature, (trimethylsilyl)acetylene (310 μl, 2.2 equivalent) was added. The septum was replaced in a stream of argon by a needle valve which was tightly closed. The reaction mixture was stirred

at 50 or 80 °C for 1–20 h until the educt disappeared (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (2 × 2 ml). The combined fractions were evaporated to dryness *in vacuo* (at <50 °C) and the residue was chromatographed on silica gel to obtain the product.

General Procedure for the Coupling Reaction of Halobenzenes **1b**, **6b**, and **13**–**15** with (Triisopropylsilyl)acetylene

Method E). A Schlenk flask was charged with halobenzene (1.0 mmol), $Pd(PPh_3)_4$ (2.5–5 mole %), and flushed with argon. Piperidine (or diisopropylamine; 3 ml) was added and the mixture was briefly heated under stirring at 40–50 °C to get a clear solution. (Triisopropylsilyl)acetylene (270 µl, 1.2 equivalent) was added and the reaction mixture was stirred at 80 °C for 1–22 h until the educt disappeared (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (2 × 2 ml). The combined fractions were evaporated to dryness *in vacuo* (at <50 °C) and the residue was chromatographed on silica gel to obtain the product.

General Procedure for the Coupling Reaction of Halobenzenes **6b** and **15** with Arylacetylenes **29**–**31**

Method F). A Schlenk flask was charged with halobenzene (1.0 mmol), $Pd(PPh_3)_4$ (5–10 mole %), and flushed with argon. Piperidine (or diisopropylamine; 2 ml) was added and the mixture was briefly heated under stirring at 40–50 °C to get a clear solution. Arylacetylene (1.0 mmol) in piperidine (or diisopropylamine; 1 ml) was added and the reaction mixture was stirred at 80 °C for 1–5 h until the educt disappeared (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (2 × 2 ml). The combined fractions were evaporated to dryness *in vacuo* (at <50 °C) and the residue was chromatographed on silica gel to obtain the product.

General Procedure for Desilylation of Halobenzenes **20**, **21**, and **22a**

Method G). A solution of trimethylsilyl or triisopropylsilyl derivative (0.30 mmol) in dry THF (3 ml) under argon was treated with tetrabutylammonium fluoride (1 M stock solution in THF, 1.3–1.7 equivalent) at room temperature for 5–30 min while stirred. The reaction mixture was evaporated *in vacuo* to dryness and the residue was chromatographed on silica gel to get the product.

Dimethyl 2,2′-Ethynediyldibenzoate[8] (**2**)

Method A). Compound **1b** (2.0 g, 7.63 mmol), $Pd(PPh_3)_4$ (220 mg, 0.19 mmol, 2.5 mole %), piperidine (25 ml), gaseous acetylene, 80 °C, 3 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 85 : 5 : 10) afforded **2** (583 mg, 52%). M.p. and IR in accord with the literature data[8]. ^{1}H NMR (500 MHz, $CDCl_3$): 3.96 (s, 6 H, 2 × CH_3); 7.40 (dt, 2 H, *J* = 7.7, 7.7, 1.4, 5,5′-H); 7.52 (dt, 2 H, *J* = 7.6, 7.6, 1.5, 4,4′-H); 7.73 (dd, 2 H, *J* = 7.8, 1.4, 3,3′-H); 7.99 (dd, 2 H, *J* = 7.9, 1.5, 6,6′-H). ^{13}C NMR ($CDCl_3$): 52.17 (q, 2 × CH_3), 93.09 (s, 2 × –C≡), 123.83 (s, C-2,2′), 128.13 (d, C-5,5′), 130.45 (d, C-6,6′), 131.74 (d, C-3,3′), 131.77 (s, C-1,1′), 134.32 (d, C-4,4′), 166.63 (s, C=O). EI MS (*m/z*, rel. intensity): 294 ($M^{+\bullet}$, 13), 279 (100), 264 (24), 248 (21), 220 (16), 132 (29), 116 (15), 102 (24), 88 (27), 75 (13), 28 (29).

Methyl 3-Iodo-4-methylbenzoate[12] (**5**)

The compound **5** was prepared according to the literature procedure[13]. Thionyl chloride (7.50 ml, 102.82 mmol, 4.0 equivalent) was added dropwise to absolute methanol (50 ml) at –30 °C under stirring. A solution of 3-iodo-4-methylbenzoic acid (6.76 g, 25.80 mmol) in absolute methanol (100 ml) was dropwise added over a 1 h period. The reaction mixture was stirred at –30 °C for 30 min, warmed up to room temperature, and finally heated at 40 °C for 1 h. Volatiles were removed *in vacuo* and the residue was filtered through a short column of alumina (eluted with petroleum ether) to afford **5** (6.98 g, 98%). ^{1}H NMR (200 MHz, $CDCl_3$): 2.48 (s, 3 H, CH_3); 3.91 (s, 3 H, CH_3O); 7.30 (d, 1 H, J = 7.9, 5-H); 7.91 (dd, 1 H, J = 7.9, 1.8, 6-H); 8.47 (d, 1 H, J = 1.8, 2-H). EI MS (*m/z*, rel. intensity): 276 ($M^{+\bullet}$, 100), 245 (80), 217 (12), 198 (4), 90 (14).

Bis(2-methyl-5-nitrophenyl)ethyne (**9**)

Method B). Compound **4** (537 mg, 2.49 mmol), $Pd(PPh_3)_4$ (144 mg, 0.125 mmol, 5 mole %), CuI (47 mg, 0.247 mmol, 10 mole %), piperidine (7 ml), 80 °C, 2.5 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 85 : 10 : 5) gave **9** as an amorphous solid (287 mg, 78%). IR ($CHCl_3$): 3 083 w, 2 959 w, 2 926 w, 1 613 w, 1 579 w, 1 525 s, 1 488 w, 1 448 w, 1 381 w, 1 351 vs, 1 304 w, 1 285 w, 1 266 w, 1 135 w, 1 074 w, 1 036 w, 906 w, 831 m, 823 m, 643 w, 445 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.65 (s, 6 H, 2 × CH_3); 7.44 (d, 2 H, J = 8.4, 2 × 3-H); 8.13 (dd, 2 H, J = 8.4, 2.5, 2 × 4-H); 8.38 (d, 2 H, J = 2.5, 2 × 6-H). ^{13}C NMR ($CDCl_3$): 21.23 (q, 2 × CH_3), 91.92 (s, 2 × –C≡), 123.56 (d, 2 × C-4), 123.78 (s, 2 × C-1), 126.92 (d, 2 × C-6), 130.54 (d, 2 × C-3), 146.19 (s, 2 × C-5), 147.60 (s, 2 × C-2). EI MS (*m/z*, rel. intensity): 296 ($M^{+\bullet}$, 100), 249 (11), 203 (50), 202 (49), 189 (27), 176 (9), 101 (6). HR EI MS: calculated for $C_{16}H_{12}N_2O_4$ 296.0797; found 296.0794.

Dimethyl 4,4′-Dimethyl-3,3′-ethynediyldibenzoate (**10**)

Method B). Compound **5** (1.23 g, 4.093 mmol), $Pd(PPh_3)_4$ (236 mg, 0.204 mmol, 5 mole %), CuI (78 mg, 0.410 mmol, 10 mole %), piperidine (5 ml), 80 °C, 0.5 h. Flash chromatography on silica gel (petroleum ether–ether 85 :15) provided **10** (645 mg, 98%), m.p. 136–137 °C (dichloromethane–acetone). IR ($CHCl_3$): 2 954 w, 1 719 vs, 1 606 w, 1 572 w, 1 499 w, 1 457 w (sh), 1 438 m, 1 418 w, 1 380 vw, 1 317 m, 1 297 m, 1 289 m, 1 248 s, 1 137 w, 1 103 w, 1 036 vw, 1 003 w, 915 w, 841 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.59 (s, 6 H, 2 × CH_3); 3.93 (s, 6 H, 2 × CH_3O); 7.33 (d, 2 H, J = 8.0, 5,5′-H); 7.91 (dd, 2 H, J = 8.0, 1.9, 6,6′-H); 8.19 (d, 2 H, J = 1.9, 2,2′-H). ^{13}C NMR ($CDCl_3$): 21.20 (q, 2 × CH_3), 52.16 (q, 2 × CH_3O), 92.01 (s, 2 × –C≡), 123.35 (s, C-3,3′), 127.97 (s, C-1,1′), 129.43 (d, C-5,5′), 129.71 (d, C-6,6′), 133.17 (d, C-2,2′), 145.25 (s, C-4,4′), 166.51 (s, 2 × C=O). EI MS (*m/z*, rel. intensity): 322 ($M^{+\bullet}$, 100), 291 (29), 277 (16), 263 (11), 231 (7), 204 (36), 203 (37), 202 (26), 189 (13), 130 (31), 101 (18), 89 (11), 77 (5). HR EI MS: calculated for $C_{20}H_{18}O_4$ 322.1205; found 322.1194.

Bis(2-hydroxymethyl-4-methoxyphenyl)ethyne (**12**)

Method B). Compound **7** (100 mg, 0.379 mmol), $Pd(PPh_3)_4$ (22 mg, 0.019 mmol, 5 mole %), CuI (7 mg, 0.037 mmol, 10 mole %), piperidine (3 ml), 80 °C, 0.1 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10 to 50 : 30 : 20) provided **12** as an oil (56 mg, 99%). IR (KBr): 3 322 m (br), 3 251 m (br), 3 091 w, 3 052 w, 3 007 w, 2 956 w,

2 936 m, 2 835 m, 1 612 s, 1 564 m, 1 500 vs, 1 463 m, 1 453 m, 1 438 m, 1 430 m, 1 363 w, 1 315 s, 1 295 vs, 1 274 s, 1 221 vs, 1 193 m, 1 158 m, 1 116 s, 1 057 s (sh), 1 050 s, 1 034 s, 886 w, 880 m, 819 m, 808 m, 724 m, 694 m, 681 m, 541 m, 444 w. ^{1}H NMR (500 MHz, $CDCl_3$): 3.92 (s, 6 H, 2 × CH_3); 4.93 (brs, 4 H, 2 × CH_2); 6.92 (ddt, 2 H, *J* = 8.5, 2.7, 0.6, 0.6, 2 × 5-H); 7.27 (dt, 2 H, *J* = 2.7, 1.0, 1.0, 2 × 3-H); 7.50 (d, 2 H, *J* = 8.5, 2 × 6-H). ^{13}C NMR ($CDCl_3$): 55.61 (q, 2 × CH_3), 63.13 (t, 2 × CH_2), 90.92 (s, 2 × –C≡), 112.79 (d, 2 × C-3), 113.06 (d, 2 × C-5), 113.73 (s, 2 × C-1), 133.74 (d, 2 × C-6), 146.49 (s, 2 × C-2), 160.91 (s, 2 × C-4). EI MS (*m/z*, rel. intensity): 298 ($M^{+\bullet}$, 100), 265 (45), 237 (26), 209 (22), 165 (28), 149 (30), 134 (91), 121 (19), 91 (18), 77 (16). HR EI MS: calculated for $C_{18}H_{18}O_4$ 298.1205; found 298.1157.

(2-Bromo-5-fluorophenyl)methanol (**13**)

A mixture of 1-bromo-4-fluoro-2-methylbenzene (9.53 g, 50.42 mmol), *N*-bromosuccinimide (9.66 g, 54.27 mmol, 1.08 equivalent), K_2CO_3 (100 mg), and 2,2′-azobis(isobutyronitrile) (100 mg) in CCl_4 (100 ml) was irradiated with an IR lamp to reflux for 1 h. The reaction mixture was cooled to room temperature, the precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel (petroleum ether) to obtain 1-bromo-2-bromomethyl-4-fluorobenzene[14] (9.13 g, 68%). ^{1}H NMR (200 MHz, $CDCl_3$): 4.55 (s, 2 H, CH_2); 6.92 (ddd, 1 H, *J* = 8.7, 7.8, 3.1, 5-H); 7.20 (dd, 1 H, *J* = 8.7, 3.1, 3-H); 7.54 (dd, 1 H, *J* = 8.7, 5.3, 6-H). EI MS (*m/z*, rel. intensity): 266 ($M^{+\bullet}$, 15), 189 (100), 187 (90), 108 (29), 91 (7).

A solution of 1-bromo-2-bromomethyl-4-fluorobenzene (1.80 g, 6.72 mmol) in dioxane (20 ml) was added portionwise under stirring to a suspension of $CaCO_3$ (3.72 g, 37.17 mmol, 5.5 equivalent) in water (25 ml) at 100 °C. The mixture was refluxed for 20 h. The solvents were removed *in vacuo* and the residue was triturated with dichloromethane. The organic portion was washed with 5% hydrochloric acid (1 ×), saturated $KHCO_3$ (2 ×), and dried over Na_2SO_4. The solution was evaporated to dryness and the residue was chromatographed on silica gel (hexane–ether–acetone 80 : 10 : 10) to provide **13** (948 mg, 69%), m.p. 88–90 °C (chloroform). IR ($CHCl_3$): 3 615 m, 3 464 w (br), 3 077 vw, 3 029 vw, 2 933 w, 2 884 w, 1 606 m, 1 583 s, 1 468 vs, 1 414 m, 1 376 w, 1 268 s, 1 239 m, 1 145 s, 1 106 s, 1 052 m, 1 026 s, 950 w, 875 s, 813 s, 620 m, 590 m, 561 w, 544 w, 492 w, 443 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.01 (t, 1 H, *J* = 6.2, OH); 4.72 (dt, 2 H, *J* = 6.2, 0.7, 0.7, CH_2); 6.89 (dddt, 1 H, *J* = 8.7, 7.8, 3.1, 0.7, 0.7, 4-H); 7.27 (ddt, 1 H, *J* = 9.2, 3.1, 0.8, 0.8, 6-H); 7.48 (dd, 1 H, *J* = 8.7, 5.2, 3-H). ^{13}C NMR ($CDCl_3$): 64.48 (t, CH_2), 115.56 (dd, $J_{C–F}$ = 23.8, C-6), 115.76 (d, $J_{C–F}$ = 2.8, C-2), 115.85 (dd, $J_{C–F}$ = 22.9, C-4), 133.61 (dd, $J_{C–F}$ = 8.2, C-3), 142.00 (d, $J_{C–F}$ = 7.2, C-1), 162.30 (d, $J_{C–F}$ = 247.7, C-5). ^{19}F NMR ($CDCl_3$): –114.60 (ddd, $J_{F–H}$ = 9.3, 7.8, 5.1). EI MS (*m/z*, rel. intensity): 204 ($M^{+\bullet}$, 79), 187 (7), 175 (13), 125 (100), 107 (13), 97 (70), 96 (53), 95 (44), 77 (22), 75 (20). HR EI MS: calculated for C_7H_6BrFO 203.9586; found 203.9573.

(2-Bromo-4-fluorophenyl)methanol (**14**)

A mixture of 2-bromo-4-fluoro-1-methylbenzene (947 mg, 5.01 mmol), *N*-bromosuccinimide (1.02 g, 5.73 mmol, 1.14 equivalent), K_2CO_3 (50 mg), and 2,2′-azobis(isobutyronitrile) (50 mg) in CCl_4 (20 ml) was irradiated with an IR lamp to reflux for 1 h. The reaction mixture was cooled to room temperature, the precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel (petroleum ether) to obtain

2-bromo-1-bromomethyl-4-fluorobenzene[15] (767 mg, 57%). ^{1}H NMR (200 MHz, $CDCl_3$): 4.58 (s, 2 H, CH_2); 7.03 (ddd, 1 H, *J* = 8.5, 7.9, 2.8, 5-H); 7.33 (dd, 1 H, *J* = 8.1, 2.8, 3-H); 7.44 (dd, 1 H, *J* = 8.5, 5.8, 6-H). EI MS (*m/z*, rel. intensity): 266 ($M^{+\bullet}$, 8), 189 (88), 187 (100), 108 (35), 107 (18).

A solution of 2-bromo-1-bromomethyl-4-fluorobenzene (476 mg, 1.78 mmol) in dioxane (10 ml) was added portionwise under stirring to a suspension of $CaCO_3$ (925 mg, 9.24 mmol, 5.2 equivalent) in water (10 ml) at 100 °C. The mixture was refluxed for 6 h. The solvents were removed *in vacuo* and the residue was triturated with dichloromethane. The organic portion was washed with 5% hydrochloric acid (1 ×), saturated $KHCO_3$ (2 ×), and dried over Na_2SO_4. The solution was evaporated to dryness and the residue was chromatographed on silica gel (hexane–ether–acetone 80 : 10 : 10) to provide **14** (297 mg, 82%), m.p. 68.5–69.5 °C (chloroform). IR ($CHCl_3$): 3 609 m, 3 462 w (br), 3 062 vw, 3 027 vw, 2 933 w, 2 888 w, 1 600 s, 1 590 s, 1 488 vs, 1 399 w, 1 383 w, 1 265 m, 1 230 s, 1 177 w, 1 121 w, 1 029 m, 863 s, 588 w, 564 w (br), 460 w, 445 w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.96 (t, 1 H, *J* = 6.1, OH); 4.72 (d, 2 H, *J* = 6.1, CH_2); 7.05 (ddd, 1 H, *J* = 8.5, 8.1, 2.5, 5-H); 7.31 (dd, 1 H, *J* = 8.1, 2.6, 3-H); 7.46 (ddt, 1 H, *J* = 8.5, 6.0, 0.7, 0.7, 6-H). ^{13}C NMR ($CDCl_3$): 64.41 (t, CH_2), 114.65 (dd, J_{C-F} = 21.0, C-5), 119.90 (dd, J_{C-F} = 34.4, C-3), 122.52 (d, J_{C-F} = 9.7, C-2), 129.94 (dd, J_{C-F} = 8.8, C-6), 135.70 (d, J_{C-F} = 3.4, C-1), 161.81 (d, J_{C-F} = 250.5, C-4). ^{19}F NMR ($CDCl_3$): –113.25 (dtt, J_{F-H} = 8.1, 8.1, 6.1, 1.0, 1.0). EI MS (*m/z*, rel. intensity): 204 ($M^{+\bullet}$, 84), 187 (16), 175 (11), 125 (100), 107 (16), 97 (93), 96 (71), 95 (53), 75 (23). HR EI MS: calculated for C_7H_6BrFO 203.9586; found 203.9573.

2-Iodo-4-(methoxycarbonyl)benzyl Acetate (**15**)

A mixture of **5** (4.35 g, 15.76 mmol), *N*-bromosuccinimide (3.07 g, 17.25 mmol, 1.09 equivalent), K_2CO_3 (100 mg), and 2,2′-azobis(isobutyronitrile) (100 mg) in CCl_4 (15 ml) was irradiated with an IR lamp to reflux for 1 h. The reaction mixture was cooled to room temperature, the precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel (petroleum ether–ether 95 : 5) to furnish methyl 4-bromomethyl-3-iodobenzoate (3.90 g, 70%). IR ($CHCl_3$): 1 724 vs, 1 597 w, 1 558 m, 1 482 w, 1 437 s, 1 294 vs, 1 285 vs, 1 263 vs, 1 226 m, 1 120 s, 1 036 m, 971 m, 608 w. ^{1}H NMR (200 MHz, $CDCl_3$): 3.93 (s, 3 H, CH_3); 4.60 (s, 2 H, CH_2); 7.54 (d, 1 H, *J* = 8.0, 5-H); 7.99 (dd, 1 H, *J* = 8.0, 1.8, 6-H); 8.51 (d, 1 H, *J* = 1.8, 2-H). EI MS (*m/z*, rel. intensity): 354 ($M^{+\bullet}$, 14), 275 (84), 245 (16), 229 (9), 149 (15), 117 (16), 89 (41), 63 (24), 39 (100). HR EI MS: calculated for $C_9H_8BrIO_2$ 353.8752; found 353.8752.

Methyl 4-bromomethyl-3-iodobenzoate (1.47 g, 4.14 mmol) in *N*,*N*-dimethylformamide (10 ml) was treated with anhydrous sodium acetate (840 mg, 10.24 mmol, 2.47 equivalent) under stirring at 80 °C for 2 h. The reaction mixture was cooled to room temperature, diluted with water, and extracted with ether (3 ×). The combined ethereal extracts were washed with water (2 ×) and dried over Na_2SO_4. Ether was removed *in vacuo* and the crude product was purified by flash chromatography on silica gel (petroleum ether–ether–acetone 95 : 5 : 0 to 80 : 10 : 10) to get **15** as an oil (1.13 g, 82%). IR ($CHCl_3$): 1 740 vs (sh), 1 725 vs, 1 600 w, 1 560 m, 1 484 w, 1 437 s, 1 291 vs, 1 259 vs, 1 247 vs, 1 141 w, 1 119 s, 1 054 m, 1 030 s, 971 m, 805 w, 602 w, 463 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.18 (s, 3 H, CH_3CO_2); 3.92 (s, 3 H, CH_3O_2C); 5.14 (brs, 2 H, CH_2); 7.43 (dtt, 1 H, *J* = 8.0, 0.8, 0.8, 0.3, 0.3, 6-H); 8.01 (ddq, 1 H, *J* = 8.0, 1.7, 0.2, 0.2, 0.2, 5-H); 8.50 (brd, 1 H, *J* = 1.7, 3-H). ^{13}C NMR ($CDCl_3$): 20.79 (q, CH_3CO_2), 52.40 (q, $\mathbf{C}H_3O_2C$), 69.57 (t, CH_2), 96.95 (s, C-2), 128.47 (d,

C-6), 129.39 (d, C-5), 131.31 (s, C-4), 140.44 (d, C-3), 143.15 (s, C-1), 165.27 (s, CH_3O_2C), 170.36 (s, CH_3CO_2). EI MS (*m/z*, rel. intensity): 334 ($M^{+\bullet}$, 3), 303 (7), 275 (7), 207 (54), 165 (100), 147 (16), 89 (7), 43 (28). HR EI MS: calculated for $C_{11}H_{11}IO_4$ 333.9702; found 333.9703.

2-(2-Iodo-3-methoxyphenyl)-4,4-dimethyl-4,5-dihydro-1,3-oxazole (**17**)

A solution of **28** (ref.[11]) (107 mg, 0.521 mmol) in dry THF (2 ml) under argon was cooled to –45 °C and butyllithium (1.6 M in hexanes, 500 µl, 0.80 mmol, 1.5 equivalent) was added. The reaction mixture was stirred at –45 °C for 1.5 h. Iodine (215 mg, 0.847 mmol, 1.6 equivalent) in dry THF (1 ml) was added and the mixture was allowed to reach room temperature during 1.5 h. Solvents were evaporated *in vacuo* and the residue was dissolved in dichloromethane. The solution was washed with aqueous $Na_2S_2O_3$ (5%, 1 ×), water (1 ×), dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) to get **17** (100 mg, 58%), m.p. 102–103 °C (petroleum ether–ether–acetone). IR ($CHCl_3$): 3 075 w, 2 840 m, 1 665 s, 1 587 s, 1 567 s, 1 467 vs, 1 443 m, 1 424 vs, 1 386 m, 1 367 s, 1 353 s, 1 318 vs, 1 282 s, 1 264 vs, 1 187 s, 1 175 m, 1 127 s, 1 094 m, 1 045 vs, 967 s, 523 w, 431 w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.43 (s, 6 H, 2 × CH_3); 3.90 (s, 3 H, CH_3O); 4.15 (s, 2 H, CH_2); 6.87 (dd, 1 H, *J* = 8.2, 1.5, 4-H); 7.12 (dd, 1 H, *J* = 7.6, 1.5, 6-H); 7.32 (dd, 1 H, *J* = 8.2, 7.6, 5-H). ^{13}C NMR ($CDCl_3$): 28.19 (q, 2 × CH_3), 56.72 (q, CH_3O), 68.16 (s, CH_3C), 79.50 (t, CH_2), 87.94 (s, C-2), 112.30 (d, C-4), 122.83 (d, C-6), 129.22 (d, C-5), 136.77 (s, C-1), 158.56 (s, C=N), 163.24 (s, C-3). EI MS (*m/z*, rel. intensity): 331 ($M^{+\bullet}$, 100), 316 (59), 301 (31), 288 (6), 260 (24), 245 (7), 161 (12). HR EI MS: calculated for $C_{12}H_{14}INO_2$ 331.0069; found 330.9792; calculated for $C_{11}H_{11}INO_2$ (M – CH_3) 315.9835; found 315.9770.

[2-(2-Trimethylsilylethyn-1-yl)phenyl]methanol[9] (**18a**)

Method D). Compound **6a** (100 mg, 0.535 mmol), trimethylsilylacetylene (165 µl, 1.168 mmol, 2.2 equivalent), $Pd(PPh_3)_4$ (31 mg, 0.027 mmol, 5 mole %), piperidine (2 ml), 80 °C, 6 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) afforded a mixture of **18a** and **19** (4 : 1 according to ^{1}H NMR). Compounds **18a** and **19** were separated by semipreparative HPLC on a silica gel column (petroleum ether–acetone 90 : 10) to provide **18a** (59 mg, 54%) and more polar **19** (22 mg, 14%) as oils. IR ($CHCl_3$): 3 608 m, 3 070 w, 2 962 s, 2 928 m, 2 901 m, 2 876 m, 2 153 s, 1 599 w, 1 570 w, 1 482 m, 1 451 m, 1 252 s, 1 037 m, 1 008 m, 867 vs, 844 vs, 645 m. ^{1}H NMR (500 MHz, $CDCl_3$): 0.27 (s, 9 H, $(CH_3)_3Si$); 2.22 (brt, 1 H, *J* = 6.1, OH); 4.82 (d, 2 H, *J* = 6.1, CH_2); 7.24 (dt, 1 H, *J* = 7.5, 7.5, 1.5, 4-H); 7.33 (dt, 1 H, *J* = 7.5, 7.5, 1.5, 5-H); 7.41 (brd, 1 H, *J* = 7.6, 3-H); 7.47 (dd, 1 H, *J* = 7.6, 1.5, 6-H). ^{13}C NMR ($CDCl_3$): –0.11 (q, $(CH_3)_3Si$), 64.10 (t, CH_2), 99.60 (s, C≡C–Si), 102.60 (s, C≡C–Si), 121.20 (s, C-2), 127.22 (d, C-6), 127.37 (d, C-4), 128.95 (d, C-5), 132.45 (d, C-3), 143.16 (s, C-1). EI MS (*m/z*, rel. intensity): 204 ($M^{+\bullet}$, 58), 189 (27), 171 (26), 161 (13), 145 (16), 131 (50), 129 (52), 115 (31), 87 (15), 73 (69), 61 (100).

[2-(2-Triisopropylsilylethyn-1-yl)phenyl]methanol (**18b**)

Method E). Compound **6b** (65 mg, 0.278 mmol), triisopropylsilylacetylene (75 µl, 0.334 mmol, 1.2 equivalent), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol, 5 mole %), piperidine (2 ml), 80 °C, 13 h. Flash chromatography on silica gel (petroleum ether–ether 85 : 15) furnished **18b** (75 mg, 97%)

as an oil. IR ($CHCl_3$): 3 610 w, 3 570 w (sh); 3 469 w (br), 3 071 w, 2 959 s, 2 944 vs, 2 925 s (sh), 2 891 s, 2 866 vs, 2 151 m, 1 600 w, 1 570 vw, 1 481 m, 1 462 s, 1 450 m, 1 383 m,1 367 w, 1 243 w, 1 160 w (sh), 1 102 w, 1 072 w, 1 035 m, 1 011 m, 997 m, 995 w, 883 w, 852 m, 844 m, 809 w, 678 s, 663 s, 640 m, 611 w, 599 w, 538 w, 460 w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.14 (s, 21 H, 3 × $(CH_3)_2CH$); 2.26 (brt, 1 H, J = 6.1, OH); 4.85 (d, 2 H, J = 6.1, CH_2); 7.24 (dt, 1 H, J = 7.6, 7.6, 1.2, 4-H); 7.33 (dt, 1 H, J = 7.8, 7.8, 1.2, 5-H); 7.42 (brdd, 1 H, J = 7.8, 1.2, 6-H); 7.49 (dd, 1 H, J = 7.6, 1.4, 3-H). ^{13}C NMR ($CDCl_3$): 11.26 (d, 3 × $(CH_3)_2CH$), 18.64 (q, 3 × $(CH_3)_2CH$), 64.15 (t, CH_2), 96.01 (s, C≡C–Si), 104. 41 (s, C≡C–Si), 121.52 (s, C-2), 127.11 (d, C-4), 127.32 (d, C-6), 128.78 (d, C-5), 132.75 (d, C-3), 143.08 (s, C-1). EI MS (*m/z*, rel. intensity): 288 ($M^{+\bullet}$, 1), 245 (26), 203 (47), 175 (100), 161 (9), 115 (15), 75 (5), 61 (11). FAB MS (*m/z*): 289 ($(M + H)^+$), 271, 245, 229, 203, 201, 175, 159, 145, 115, 103, 87, 73, 59. HR FAB MS: calculated for $C_{18}H_{29}OSi$ (M + H) 289.1988; found 289.2028.

{2-[2,4-Bis(trimethylsilyl)but-1-en-3-yn-1-yl]phenyl}methanol (**19**)

For preparation, see compound **18a**. ^{1}H NMR (200 MHz, $CDCl_3$) in a mixture with **18a**: 0.18 (s, 9 H, $(CH_3)_3Si$–C≡); 0.25 (s, 9 H, $(CH_3)_3Si$–C=); 4.74 (s, 2 H, CH_2); 7.19–7.49 (m, 5 H, arom. and –CH=). EI MS from the GC MS analysis of a mixture of **18a** and **19** (*m/z*, rel. intensity): 302 ($M^{+\bullet}$, 2), 243 (6), 229 (33), 213 (6), 197 (33), 155 (6), 119 (61), 75 (36), 73 (100).

{5-Fluoro-2-[2-(triisopropylsilyl)ethyn-1-yl]phenyl}methanol (**20**)

Method E). Compound **13** (500 mg, 2.439 mmol), triisopropylsilylacetylene (660 µl, 2.942 mmol, 1.2 equivalent), $Pd(PPh_3)_4$ (70 mg, 0.061 mmol, 2.5 mole %), piperidine (8 ml), 80 °C, 20 h. Flash chromatography on silica gel (hexane–ether 90 : 10) gave **20** (640 mg, 86%) as an oil. IR ($CHCl_3$): 3 621 w, 3 568 w (sh), 3 455 w (br), 3 076 vw, 3 046 vw, 2 959 vs, 2 945 vs, 2 866 vs, 2 152 s, 1 607 s, 1 583 m, 1 488 vs, 1 462 s, 1 423 m, 1 383 m, 1 367 m, 1 344 w, 1 272 s, 1 245 m, 1 187 m, 1 145 s, 1 095 m, 1 034 s, 1 018 s, 996 s, 955 m, 940 m, 883 vs, 825 s (sh), 814 s, 678 s, 661 s, 617 m, 607 m (sh), 536 m, 491 m, 460 m, 445 m. ^{1}H NMR spectrum (500 MHz, $CDCl_3$): 1.13 (brs, 21 H, 3 × $(CH_3)_2CH$); 2.17 (brs, 1 H, OH); 4.84 (brd, 2 H, J = 5.0, CH_2); 6.92 (dt, 1 H, J = 8.5, 8.5, 2.7, 4-H); 7.19 (ddt, 1 H, J = 9.7, 2.7, 0.9, 0.9, 6-H); 7.45 (dd, 1 H, J = 8.4, 5.6, 3-H). ^{13}C NMR ($CDCl_3$): 11.25 (d, 3 × $(CH_3)_2$**C**H), 18.65 (q, 3 × (**C**$H_3)_2CH$), 63.49 (t, CH_2), 95.72 (s, C≡C–Si), 103.21 (s, C≡C–Si), 113.94 (dd, $J_{C–F}$ = 23.9, C-6), 114.20 (dd, $J_{C–F}$ = 22.9, C-4), 117.07 (d, $J_{C–F}$ = 2.9, C-2), 134.44 (dd, $J_{C–F}$ = 8.2, C-3), 145.94 (d, $J_{C–F}$ = 7.3, C-1), 162.77 (d, $J_{C–F}$ = 250.0, C-5). ^{19}F NMR ($CDCl_3$): –110.18 (ddd, $J_{F–H}$ = 9.4, 8.6, 5.6). EI MS (*m/z*, rel. intensity): 306 ($M^{+\bullet}$, 2), 263 (10), 221 (49), 193 (100), 179 (10), 141 (7), 133 (15), 115 (7), 75 (8), 61 (7). HR EI MS: calculated for $C_{18}H_{27}FOSi$ 306.1815; found 306.1784.

{4-Fluoro-2-[2-(triisopropylsilyl)ethyn-1-yl]phenyl}methanol (**21**)

Method E). Compound **14** (100 mg, 0.488 mmol), triisopropylsilylacetylene (130 µl, 0.580 mmol, 1.2 equivalent), $Pd(PPh_3)_4$ (28 mg, 0.024 mmol, 5 mole %), piperidine (2 ml), 80 °C, 22 h. Flash chromatography on silica gel (hexane–ether 90 : 10) provided **21** (148 mg, 99%) as an oil. IR ($CHCl_3$): 3 610 m, 3 572 w (sh), 3 452 w (br), 3 075 vw, 3 039 vw, 2 960 s, 2 944 s, 2 866 vs, 2 150 m, 1 608 s, 1 581 s, 1 493 s, 1 479 s, 1 463 s, 1 414 m, 1 384 m, 1 367 m, 1 344 w, 1 268 s, 1 254 m, 1 151 s, 1 097 s, 1 072 m, 1 039 m, 1 012 s, 997 s, 959 s, 883 s, 828 m, 822 m, 679 s, 543 m, 446 m. ^{1}H NMR (500 MHz, $CDCl_3$): 1.14 (m, 21 H,

3 × $(CH_3)_2CH$); 2.12 (t, 1 H, *J* = 6.5, OH); 4.81 (brd, 2 H, *J* = 6.5, CH_2); 7.03 (dt, 1 H, *J* = 8.4, 8.4, 2.7, 5-H); 7.18 (dd, 1 H, *J* = 9.0, 2.7, 3-H); 7.40 (ddq, 1 H, *J* = 8.6, 5.8, 0.6, 0.6, 0.6, 6-H). ^{13}C NMR ($CDCl_3$): 11.24 (d, 3 × $(CH_3)_2CH$), 18.64 (q, 3 × $(CH_3)_2CH$), 63.46 (t, CH_2), 97.27 (s, C≡C–Si), 103.07 (s, C≡C–Si), 115.91 (dd, $J_{C–F}$ = 21.1, C-5), 119.25 (dd, $J_{C–F}$ = 22.9, C-3), 123.21 (d, $J_{C–F}$ = 9.2, C-2), 128.95 (dd, $J_{C–F}$ = 8.7, C-6), 138.99 (d, $J_{C–F}$ = 3.0, C-1), 161.54 (d, $J_{C–F}$ = 246.8, C-4). ^{19}F NMR ($CDCl_3$): –115.54 (dddt, $J_{F–H}$ = 9.0, 8.3, 5.7, 0.8, 0.8). EI MS (*m/z*, rel. intensity): 306 ($M^{+\bullet}$, 1), 263 (25), 221 (29), 193 (100), 179 (9), 141 (9), 131 (18), 103 (14), 75 (19), 61 (12). HR EI MS: calculated for $C_{15}H_{20}FOSi$ (M – C_3H_7) 263.1267; found 263.1211.

4-Methoxycarbonyl-2-[2-(trimethylsilyl)ethyn-1-yl]benzyl Acetate (**22a**)

Method D). Compound **15** (100 mg, 0.299 mmol), trimethylsilylacetylene (95 µl, 0.672 mmol, 2.2 equivalent), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol, 5 mole %), diisopropylamine (2 ml), 80 °C, 1 h. Flash chromatography on silica gel (petroleum ether–ether 90 : 10) provided **22a** (66 mg, 73 %) as an oil. IR ($CHCl_3$): 2 900 w, 2 157 w, 1 763 s, 1 745 m (sh), 1 610 w, 1 570 w , 1 491 w, 1 438 m, 1 410 w, 1 380 m, 1 362 w, 1 300 s, 1 290 s (sh), 1 252 s, 1 097 m, 1 043 w, 1 030 w, 991 w, 980 w (sh), 921 w, 854 s, 847 s, 701 w, 647 w. ^{1}H NMR (500 MHz, $CDCl_3$): 0.26 (s, 9 H, $(CH_3)_3Si$); 2.16 (s, 3 H, CH_3CO_2); 3.92 (s, 3 H, CH_3O_2C); 5.30 (s, 2 H, CH_2); 7.44 (brd, 1 H, *J* = 8.3, 6-H); 7.97 (dd, 1 H, *J* = 8.3, 2.0, 5-H); 8.14 (d, 1 H, *J* = 2.0, 3-H). ^{13}C NMR ($CDCl_3$): 0.19 (q, $(CH_3)_3Si$), 20.82 (q, CH_3CO_2), 52.30 (q, CH_3O_2C), 64.13 (t, CH_2), 100.82 (s, C≡C–Si), 101.10 (s, C≡C–Si), 122.46 (s, C-2), 127.54 (d, C-6), 129.55 (d, C-5), 129.77 (s, C-4), 133.63 (d, C-3), 142.60 (s, C-1), 166.09 (s, CH_3O_2C), 170.54 (s, CH_3CO_2). EI MS (*m/z*, rel. intensity): 304 ($M^{+\bullet}$, 47), 289 (100), 273 (13), 261 (27), 247 (64), 232 (20), 215 (15), 187 (11), 157 (21), 128 (18), 91 (19), 73 (25), 59 (12). HR EI MS: calculated for $C_{16}H_{20}O_4Si$ 304.1131; found 304.1118.

4-Methoxycarbonyl-2-[2-(triisopropylsilyl)ethyn-1-yl]benzyl Acetate (**22b**)

Method E). Compound **15** (85 mg, 0.254 mmol), triisopropylsilylacetylene (70 µl, 0.312 mmol, 1.2 equivalent), $Pd(PPh_3)_4$ (15 mg, 0.013 mmol, 5 mole %), diisopropylamine (2 ml), 80 °C, 1 h. Flash chromatography on silica gel (petroleum ether–ether 90 : 10) gave **22b** (14 mg, 28%) as an oil. IR ($CHCl_3$): 2 945 vs, 2 893 s, 2 866 s, 2 155 w, 1 746 vs (sh), 1 723 vs, 1 609 w, 1 570 w, 1 494 w, 1 462 s, 1 438 s, 1 410 m, 1 381 s, 1 362 m, 1 292 vs, 1 250 vs, 1 232 vs, 1 137 m (sh), 1 124 s, 1 097 s, 1 045 s, 1 029 s, 996 s, 965 w (br, sh), 920 s, 901 m, 883 s, 845 w, 679 s, 665 m, 605 w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.14 (m, 21 H, 3 × $(CH_3)_2CH$); 2.14 (s, 3 H, CH_3CO_2); 3.93 (s, 3 H, CH_3O_2C); 5.33 (brs, 2 H, CH_2); 7.46 (dq, 1 H, *J* = 8.1, 0.6, 0.6, 0.6, 6-H); 7.97 (dd, 1 H, *J* = 8.1, 1.7, 5-H); 8.14 (brd, 1 H, *J* = 1.7, 3-H). ^{13}C NMR ($CDCl_3$): 11.25 (d, 3 × $(CH_3)_2CH$), 18.64 (q, 3 × $(CH_3)_2CH$), 20.83 (q, CH_3CO_2), 52.29 (q, CH_3O_2C), 64.33 (t, CH_2), 97.66 (s, C≡C–Si), 102.69 (s, C≡C–Si), 122.88 (s, C-2), 127.6 7 (d, C-6), 129.40 (d, C-5), 129.81 (s, C-4), 133.74 (d, C-3), 142.51 (s, C-1), 166.14 (s, CH_3O_2C), 170.51 (s, CH_3CO_2). EI MS (*m/z*, rel. intensity): 388 ($M^{+\bullet}$, 0.5), 334 (5), 303 (9), 275 (8), 207 (62), 165 (100), 147 (15), 89 (8). HR EI MS: calculated for $C_{19}H_{25}O_4Si$ (M – C_3H_7) 345.1522; found 345.1519.

Methyl 2-[2-(Trimethylsilyl)ethyn-1-yl]benzoate[10,18] (**23a**)

Method D). Compound **1a** (100 mg, 0.465 mmol), trimethylsilylacetylene (145 µl, 1.026 mmol, 2.2 equivalent), $Pd(PPh_3)_4$ (27 mg, 0.023 mmol, 5 mole %), piperidine (2 ml), 80 °C, 6 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) yielded **23a** (68 mg, 63%) and more polar **24** (8 mg, 6%) as oils. IR (CCl_4): 3 070 w, 3 023 w, 2 995 w, 2 900 m, 2 160 m, 1 738 vs, 1 722 vs, 1 597 m, 1 568 m, 1 483 s, 1 447 s, 1 434 s, 1 408 w, 1 297 vs, 1 272 s, 1 250 vs, 1 191 m, 1 163 m, 870 vs, 844 vs, 700 s, 643 m. ^{1}H NMR (500 MHz, $CDCl_3$): 0.28 (s, 9 H, $(CH_3)_3Si$); 3.92 (s, 3 H, CH_3O_2C); 7.36 (dt, 1 H, *J* = 7.7, 7.7, 1.5, 5-H); 7.44 (dt, 1 H, *J* = 7.6, 7.6, 1.4, 4-H); 7.58 (dd, 1 H, *J* = 7.7, 1.4, 3-H); 7.90 (dd, 1 H, *J* = 7.8, 1.5, 6-H). ^{13}C NMR ($CDCl_3$): –0.16 (q, $(CH_3)_3Si$), 51.95 (q, CH_3O_2C), 99.65 (s, C≡C–Si), 103.26 (s, C≡C–Si), 123.18 (s, C-2), 128.16 (d, C-5), 130.24 (d, C-6), 131.46 (d, C-3), 132.57 (s, C-1), 134.51 (d, C-4), 166.90 (s, CH_3O_2C). EI MS (*m/z*, rel. intensity): 232 ($M^{+\bullet}$, 13), 217 (39), 201 (5), 187 (100), 158 (27), 143 (34), 129 (15), 115 (18), 101 (16), 93 (15), 86 (14), 79 (11), 59 (5).

Methyl 2-[2-(Triisopropylsilyl)ethyn-1-yl]benzoate (**23b**)

Method E). Compound **1b** (160 mg, 0.611 mmol), triisopropylsilylacetylene (165 µl, 0.736 mmol, 1.2 equivalent), $Pd(PPh_3)_4$ (35 mg, 0.030 mmol, 5 mole %), piperidine (2 ml), 80 °C, 13 h. Flash chromatography on silica gel (petroleum ether–ether 97 : 3) gave **23b** (84 mg, 44%) as an oil. IR ($CHCl_3$): 3 070 w, 2 960 vs (sh), 2 945 vs, 2 930 s (sh), 2 892 s, 2 866 vs, 2 156 m, 1 728 vs, 1 714 vs, 1 596 m, 1 568 m, 1 482 s, 1 463 s, 1 447 s, 1 434 s, 1 383 m, 1 367 w, 1 300 vs, 1 276 s, 1 254 s, 1 191 m, 1 163 w, 1 130 s, 1 081 s, 1 068 w (sh), 1 043 m, 996 m, 965 m, 883 s, 858 m, 847 s, 809 m, 701 m, 679 vs, 660 s, 636 s, 545 w, 463 w. ^{1}H NMR (500 MHz, $CDCl_3$): 1.15 (s, 21 H, 3 × $(CH_3)_2CH$); 3.91 (s, 3 H, CH_3O_2C); 7.35 (dt, 1 H, *J* = 7.6, 7.6, 1.2, 4-H); 7.43 (dt, 1 H, *J* = 7.6, 7.6, 1.5, 5-H); 7.59 (ddd, 1 H, *J* = 7.8, 1.7, 0.5, 3-H); 7.88 (ddd, 1 H, *J* = 7.8, 1.5, 0.5, 6-H). ^{13}C NMR ($CDCl_3$): 11.33 (d, 3 × $(CH_3)_2CH$), 18.63 (q, 3 × $(CH_3)_2CH$), 52.13 (q, CH_3O_2C), 96.31 (s, C≡C–Si), 105.13 (s, C≡C–Si), 123.42 (s, C-1), 127.98 (d, C-5), 130.17 (d, C-6), 131.33 (d, C-3), 132.64 (s, C-2), 134.93 (d, C-4), 167.19 (s, CH_3O_2C). EI MS (*m/z*, rel. intensity): 316 ($M^{+\bullet}$, 1), 273 (100), 243 (29), 231 (7), 201 (20), 173 (19), 129 (11), 59 (9). FAB MS (*m/z*): 317 ($(M + H)^+$), 285, 279, 273, 243, 215, 197, 185, 173, 155, 145, 129, 113, 93, 73, 59. HR FAB MS: calculated for $C_{19}H_{29}O_2Si$ (M + H) 317.1937; found 317.1963.

1-[Piperidin-1-yl)amino]carbonyl-2-[(trimethylsilyl)ethynyl]benzene (**24**)

For preparation, see **23a**. ^{1}H NMR (200 MHz, $CDCl_3$): 0.23 (s, 9 H, $(CH_3)_3Si$); 1.35–1.78 (m, 6 H, $NCH_2C\mathbf{H}_2C\mathbf{H}_2C\mathbf{H}_2CH_2$); 3.11–3.28 (m, 2 H, $NC\mathbf{H}_2CH_2CH_2CH_2C\mathbf{H}_2$); 3.69–3.80 (m, 2 H, $NC\mathbf{H}_2CH_2CH_2CH_2C\mathbf{H}_2$); 7.24–7.76 (m, 4 H, arom.).

Methyl 5-Methoxy-2-[2-(trimethylsilyl)ethyn-1-yl]benzoate (**25**)

Method D). Compound **16** (100 mg, 0.408 mmol), trimethylsilylacetylene (125 µl, 0.884 mmol, 2.2 equivalent), $Pd(PPh_3)_4$ (24 mg, 0.021 mmol, 5 mole %), piperidine (2 ml), 80 °C, 4 h. Flash chromatography on silica gel (petroleum ether–ether 90 : 10) yielded **25** (45 mg, 42%) and more lipophilic **26** (12 mg, 8%) as oils. IR ($CHCl_3$): 3 083 w, 2 901 m, 2 841 m, 2 155 s, 1 715 s (br), 1 604 s, 1 560 m, 1 495 vs, 1 465 s, 1 446 s, 1 437 s, 1 421 m, 1 415 m,

1 322 vs, 1 293 vs, 1 250 vs, 1 183 m, 1 138 m, 1 079 s, 1 036 s, 899 m, 859 vs, 844 vs, 825 s, 700 w, 637 m, 573 m. ^{1}H NMR (500 MHz, $CDCl_3$): 0.26 (s, 9 H, $(CH_3)_3Si$); 3.84 (s, 3 H, CH_3O); 3.92 (s, 3 H, CH_3O_2C); 6.97 (dd, 1 H, *J* = 8.6, 2.8, 4-H); 7.41 (d, 1 H, *J* = 2.8, 6-H); 7.50 (d, 1 H, *J* = 8.6, 3-H). ^{13}C NMR ($CDCl_3$): 0.24 (q, $(CH_3)_3Si$), 52.32 (q, CH_3O_2C), 55.77 (q, CH_3O), 97.76 (s, C≡C–Si), 103.59 (s, C≡C–Si), 115.01 (d, C-6), 115.63 (s, C-2), 118.33 (d, C-4), 134.21 (s, C-1), 136.16 (d, C-3), 159.46 (s, C-5), 167.03 (s, CH_3O_2C). EI MS (*m/z*, rel. intensity): 262 ($M^{+\bullet}$, 51), 247 (24), 231 (7), 217 (100), 202 (6), 173 (7), 116 (5). HR EI MS: calculated for $C_{14}H_{18}O_3Si$ 262.1025; found 262.0980.

Methyl 2-[2,4-Bis(trimethylsilyl)but-1-en-3-yn-1-yl]-5-methoxybenzoate (**26**)

For preparation, see **25**. IR ($CHCl_3$): 3 083 w, 2 900 m, 2 840 m, 2 113 m, 1 716 s (br), 1 605 s, 1 580 m, 1 492 s, 1 465 s, 1 444 m, 1 435 s, 1 408 m, 1 315 s, 1 291 s, 1 250 vs, 1 232 s, 1 182 m, 1 142 m, 1 074 s, 1 038 s, 982 m, 865 vs, 845 vs, 697 m, 635 m. ^{1}H NMR (500 MHz, $CDCl_3$): 0.18 (s, 9 H, $(CH_3)_3Si$–C≡); 0.24 (s, 9 H, $(CH_3)_3Si$–C=); 3.86 (s, 3 H, CH_3O); 3.88 (s, 3 H, CH_3O_2C); 7.01 (ddd, *J* = 8.7, 2.8, 0.6, 4-H); 7.41 (d, 1 H, *J* = 2.8, 6-H); 7.49 (brt, 1 H, *J* = 0.6, –CH=); 8.39 (d, 1 H, *J* = 8.7, 3-H). ^{13}C NMR ($CDCl_3$): –1.99 (q, $(CH_3)_3Si$–C=), 0.03 (q, $(CH_3)_3Si$–C≡), 52.13 (q, CH_3O_2C), 55.48 (q, CH_3O), 105.10 (s, C≡C–Si), 105.59 (s, C≡C–Si), 114.69 (d, C-6), 117.40 (d, C-4), 123.72 (s, C-2), 130.26 (s, C-1), 131.04 (d, C-3), 131.12 (s, C=C–Si), 143.62 (d, C=C–Si), 158.87 (s, C-5), 167.57 (s, CH_3O_2C). EI MS (*m/z*, rel. intensity): 360 ($M^{+\bullet}$, 100), 345 (64), 329 (30), 315 (9), 287 (36), 271 (24), 257 (18), 241 (93), 226 (6), 213 (8), 89 (41), 73 (90), 59 (22). HR EI MS: calculated for $C_{19}H_{28}O_3Si_2$ 360.1577; found 360.1530.

2-{3-Methoxy-2-[2-(trimethylsilyl)ethyn-1-yl]phenyl}-4,4-dimethyl-4,5-dihydrooxazole (**27**)

Method D). Compound **17** (80 mg, 0.242 mmol), trimethylsilylacetylene (75 µl, 0.531 mmol, 2.2 equivalent), $Pd(PPh_3)_4$ (28 mg, 0.024 mmol, 10 mole %), piperidine (2 ml), 80 °C, 6 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) furnished **27** (20 mg, 27%) and more lipophilic **28** (11 mg, 22%) as oils. Compound **27**: IR ($CHCl_3$): 3 073 w, 2 899 m, 2 841 m, 2 155 m, 1 657 s (br), 1 591 m, 1 571 s, 1 462 s, 1 438 s, 1 385 m, 1 366 m, 1 318 s, 1 288 s, 1 268 vs, 1 250 vs, 1 188 m, 1 176 m, 1 126 m, 1 081 m, 1 048 vs, 900 m (sh), 865 vs, 845 vs, 699 w, 631 w, 543 w. ^{1}H NMR (500 MHz, $CDCl_3$): 0.26 (s, 9 H, $(CH_3)_3Si$); 1.40 (s, 6 H, $(CH_3)_2C$); 3.89 (s, 3 H, CH_3O); 4.11 (s, 2 H, CH_2); 6.94 (dd, 1 H, *J* = 7.7, 1.9, 4-H); 7.27 (t, 1 H, *J* = 7.8, 5-H); 7.30 (dd, 1 H, *J* = 7.9, 1.9, 6-H). ^{13}C NMR ($CDCl_3$): 0.03 (q, $(CH_3)_3Si$), 28.37 (q, $(CH_3)_2C$), 56.37 (q, CH_3O), 67.85 (s, $(CH_3)_2C$), 79.35 (t, CH_2), 98.61 (s, C≡C–Si), 103.74 (s, C≡C–Si), 112.31 (s, C-2), 112.92 (d, C-4), 121.77 (d, C-6), 129.04 (d, C-5), 133.04 (s, C-1), 161.24 (s, C=N), 162.28 (s, C-3). EI MS (*m/z*, rel. intensity): 301 ($M^{+\bullet}$, 30), 286 (39), 270 (8), 246 (21), 228 (100), 214 (25), 184 (22), 160 (7), 73 (33). HR EI MS: calculated for $C_{17}H_{23}NO_2Si$ 301.1498; found 301.1470.

(2-Ethynyl-5-fluorophenyl)methanol (**29**)

Method G). Compound **20** (100 mg, 0.326 mmol), tetrabutylammonium fluoride (555 µl of 1 M solution in THF, 0.555 mmol, 1.7 equivalent), THF (3 ml), room temperature, 15 min. Flash chromatography on silica gel (hexane–ether–acetone 80 : 10 : 10) yielded **29** (49 mg, 99%) as an oil. IR ($CHCl_3$): 3 611 w, 3 413 w (br), 3 305 s, 2 960 s, 2 872 s, 2 106 w, 1 608 s, 1 585 m, 1 487 s, 1 467 m, 1 458 m, 1 424 m, 1 379 m, 1 349 w (sh), 1 277 s, 1 233 m, 1 150 m,

1 095 m, 1 036 m, 1 022 m (sh), 877 m, 824 m, 661 m, 616 m, 582 m. ^{1}H NMR (500 MHz, $CDCl_3$): 2.09 (brs, 1 H, OH); 3.30 (d, 1 H, J = 0.8, HC≡); 4.83 (s, 2 H, CH_2); 6.94 (dtt, 1 H, J = 8.4, 8.4, 2.7, 0.6, 0.6, 4-H); 7.21 (ddt, 1 H, J = 8.4, 2.7, 0.9, 0.9, 6-H); 7.47 (dd, 1 H, J = 8.4, 5.5, 3-H). ^{13}C NMR ($CDCl_3$): 63.17 (t, CH_2), 80.20 (s, HC≡C), 81.74 (d, HC≡C), 114.17 (dd, $J_{C–F}$ = 22.9, C-6), 114.39 (dd, $J_{C–F}$ = 22.9, C-4), 115.71 (d, $J_{C–F}$ = 4.0, C-2), 134.61 (dd, $J_{C–F}$ = 8.2, C-3), 146.20 (d, $J_{C–F}$ = 7.3, C-1), 163.05 (d, $J_{C–F}$ = 250.9, C-5). ^{19}F NMR ($CDCl_3$): –109.61 (dt, $J_{F–H}$ = 8.7, 8.7, 5.6). EI MS (*m/z*, rel. intensity): 150 ($M^{+\bullet}$, 72), 133 (11), 121 (40), 101 (45), 85 (45), 71 (65), 57 (100), 43 (73). HR EI MS: calculated for C_9H_7FO 150.0481; found 150.0462.

(2-Ethynyl-4-fluorophenyl)methanol (**30**)

Method G). Compound **21** (320 mg, 1.044 mmol), tetrabutylammonium fluoride (1.50 ml of 1 M solution in THF, 1.5 mmol, 1.4 equivalent), THF (4 ml), room temperature, 5 min. Flash chromatography on silica gel (hexane–ether–acetone 80 : 10 : 10) yielded **30** (133 mg, 85%) as an oil. IR ($CHCl_3$): 3 609 m, 3 460 vw (br), 3 304 vs, 3 076 vw, 2 928 m, 2 883 w, 2 107 vw, 1 610 s, 1 583 vs, 1 493 vs, 1 414 w, 1 386 w, 1 344 w, 1 302 w, 1 265 s, 1 250 s, 1 195 w, 1 146 m, 1 092 m, 1 039 m, 1 009 m, 942 m, 876 s, 830 m, 661 s, 628 s, 606 w (sh), 541w, 457 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.01 (brs, 1 H, OH); 3.37 (s, 1 H, HC≡); 4.80 (brs, 2 H, CH_2); 7.07 (dt, 1 H, J = 8.4, 8.4, 2.7, 5-H); 7.20 (dd, 1 H, J = 8.9, 2.7, 3-H); 7.42 (dq, 1 H, J = 8.5, 5.6, 0.6, 0.6, 0.6, 6-H). ^{13}C NMR ($CDCl_3$): 63.15 (t, CH_2), 80.11 (d, $J_{C–F}$ = 2.8, HC≡C), 82.76 (d, HC≡C), 116.46 (dd, $J_{C–F}$ = 21.1, C-5), 119.46 (dd, $J_{C–F}$ = 22.9, C-3), 121.98 (d, $J_{C–F}$ = 10.1, C-2), 129.24 (dd, $J_{C–F}$ = 9.2, C-6), 139.19 (d, $J_{C–F}$ = 3.7, C-1), 161.54 (d, $J_{C–F}$ = 247.3, C-4). ^{19}F NMR ($CDCl_3$): –115.13 (dt, $J_{F–H}$ = 8.5, 8.5, 5.6). EI MS (*m/z*, rel. intensity): 150 ($M^{+\bullet}$, 100), 149 (72), 133 (20), 122 (29), 121 (26), 101 (61), 95 (9), 85 (8), 57 (15), 43 (9). HR EI MS: calculated for C_9H_7FO 150.0481; found 150.0473.

2-Ethynyl-4-(methyloxycarbonyl)benzyl Acetate (**31**)

Method G). Compound **22a** (410 mg, 1.347 mmol), tetrabutylammonium fluoride (1.75 ml of 1 M solution in THF, 1.75 mmol, 1.3 equivalent), THF (4 ml), room temperature, 30 min. Flash chromatography on silica gel (petroleum ether–ether 90 : 10) yielded **31** (311 mg, 99%) as an oil. IR ($CHCl_3$): 3 305 s, 1 743 vs (sh), 1 724 vvs, 1 610 m, 1 573 w, 1 496 w, 1 438 s, 1 408 m, 1 301 vs, 1 291 vs, 1 250 vs, 1 232 vs, 1 124 s, 1 094 m, 1 046 s, 1 031 m, 987 m, 919 w, 847 w, 807 w, 661 m, 627 m, 606 w. ^{1}H NMR (500 MHz, $CDCl_3$): 2.16 (s, 3 H, CH_3CO_2); 3.38 (s, 1 H, HC≡); 3.93 (s, 3 H, CH_3O_2C); 5.33 (s, 2 H, CH_2); 7.49 (dq, 1 H, J = 8.1, 0.7, 0.7, 0.7, 6-H); 8.02 (dd, 1 H, J = 8.1, 1.8, 5-H); 8.18 (brd, 1 H, J = 1.8, 3-H). ^{13}C NMR ($CDCl_3$): 20.80 (q, CH_3CO_2), 52.33 (q, CH_3O_2C), 63.96 (t, CH_2), 79.73 (s, HC≡C), 83.23 (d, HC≡C), 121.32 (s, C-2), 127.59 (d, C-6), 129.87 (s, C-4), 129.92 (d, C-5), 133.96 (d, C-3), 142.88 (s, C-1), 165.95 (s, CH_3O_2C), 170.55 (s, CH_3CO_2). EI MS (*m/z*, rel. intensity): 232 ($M^{+\bullet}$, 34), 207 (11), 201 (27), 190 (100), 173 (25), 165 (16), 159 (25), 149 (26), 145 (15), 131 (70), 114 (26), 101 (16), 75 (14), 62 (18), 45 (34), 43 (88). HR EI MS: calculated for $C_{13}H_{12}O_4$ 232.0736; found 232.0731.

{2-[2-(4-Fluoro-2-hydroxymethylphenyl)ethyn-1-yl]phenyl}methanol (**32**)

Method F). Compound **6b** (125 mg, 0.534 mmol), **29** (80 mg, 0.534 mmol, 1.0 equivalent), $Pd(PPh_3)_4$ (31 mg, 0.027 mmol, 5 mole %), piperidine (3 ml), 80 °C, 5 h. Flash chromatogra-

phy on silica gel (hexane–ether–acetone 80 : 10 : 10 to 50 : 30 : 20) afforded **32** (98 mg, 72%) as an oil. IR ($CHCl_3$): 3 628 w (sh), 3 607 m, 3 459 w (br), 3 068 w, 1 608 m, 1 600 w, 1 583 w, 1 570 w (sh), 1 497 vs, 1 480 w (sh), 1 452 w, 1 424 w, 1 384 w, 1 275 m, 1 233 m, 1 152 w, 1 102 w, 1 090 w, 1 034 m, 1 020 m (br), 948 w, 825 m. ^{1}H NMR (500 MHz, $CDCl_3$): 2.45 (brs, 1 H, OH); 2.82 (brs, 1 H, OH); 4.86 (brs, 2 H, CH_2Ar'); 4.87 (brs, 2 H, CH_2Ar); 7.01 (dt, 1 H, *J* = 8.4, 8.4, 2.7, 5′-H); 7.19 (ddt, 1 H, *J* = 9.2, 2.7, 0.5, 0.5, 3′-H); 7.32 (dt, 1 H, *J* = 7.4, 7.4, 1.5, 4-H); 7.37 (dt, 1 H, *J* = 7.5, 7.5, 1.5, 5-H); 7.44 (ddq, 1 H, *J* = 7.4, 1.4, 0.6, 0.6, 0.6, 6-H); 7.54 (dd, 1 H, *J* = 8.5, 5.6, 6′-H); 7.56 (ddd, 1 H, *J* = 7.3, 1.6, 0.6, 3-H). ^{13}C NMR ($CDCl_3$): 63.79 (t, CH_2Ar'), 64.50 (t, CH_2Ar), 90.58 (s, C≡C–Ar′), 91.25 (s, C≡C–Ar′), 114.75 (dd, J_{C-F} = 22.0, C-3′), 115.11 (dd, J_{C-F} = 22.9, C-5′), 117.60 (d, J_{C-F} = 3.2, C-1′), 121.87 (s, C-2), 127.90 (d, C-4), 128.09 (d, C-6), 128.89 (d, C-5), 132.39 (d, C-3), 134.14 (dd, J_{C-F} = 8.2, C-6′), 142.10 (s, C-1), 145.23 (d, J_{C-F} = 7.8, C-2′), 162.71 (d, J_{C-F} = 250.9, C-4′). ^{19}F NMR ($CDCl_3$): –110.29 (ddd, J_{F-H} = 9.2, 8.3, 5.6). EI MS (*m/z*, rel. intensity): 256 ($M^{+\bullet}$, 9), 238 (96), 220 (11), 209 (100), 196 (22), 189 (16), 183 (40), 137 (21), 119 (17), 109 (11), 91 (13), 77 (11), 63 (7), 51 (8). HR EI MS: calculated for $C_{16}H_{13}FO_2$ 256.0899; found 256.0886.

{2-[2-(5-Fluoro-2-hydroxymethylphenyl)ethyn-1-yl]phenyl}methanol (**33**)

Method F). Compound **6b** (170 mg, 0.726 mmol), **30** (109 mg, 0.726 mmol, 1.0 equivalent), $Pd(PPh_3)_4$ (84 mg, 0.073 mmol, 10 mole %), piperidine (3 ml), 80 °C, 2 h. Flash chromatography on silica gel (hexane–ether–acetone 80 : 10 : 10) afforded **33** (184 mg, 99%) as an oil. IR ($CHCl_3$): 3 608 m, 3 465 w (br), 3 072 w, 2 933 w, 2 882 w, 2 209 vw, 1 581 vs, 1 508 s, 1 496 vs, 1 480 w (sh), 1 464 w, 1 418 w, 1 384 w, 1 345 vw, 1 308 m, 1 263 w, 1 199 m, 1 138 w, 1 108 w, 1 083 w, 1 011 s, 1 034 m, 950 m, 875 m, 829 m, 607 w, 538 w. ^{1}H NMR (500 MHz, acetone-d_6): 4.94 (brd, 2 H, *J* = 6.3, CH_2Ar); 4.97 (brd, 2 H, *J* = 6.3, CH_2Ar'); 7.27 (dt, 1 H, *J* = 8.6, 8.6, 2.7, 4′-H); 7.38 (dd, 1 H, *J* = 9.4, 2.7, 6′-H); 7.40 (dtt, 1 H, *J* = 7.6, 7.6, 1.5, 0.7, 0.7, 5-H); 7.51 (dt, 1 H, *J* = 7.6, 7.6, 1.5, 4-H); 7.64 (brdd, 1 H, *J* = 7.6, 1.5, 6-H); 7.70 (ddt, 1 H, *J* = 8.6, 5.9, 0.9, 0.9, 3′-H); 7.70 (ddt, 1 H, *J* = 7.6, 1.5, 0.9, 0.9, 3-H). ^{13}C NMR (acetone-d_6): 62.71 (t, CH_2Ar), 63.25 (t, CH_2Ar'), 91.02 (d, J_{C-F} = 3.2, C≡C–Ar′), 93.21 (s, C≡C–Ar′), 116.35 (dd, J_{C-F} = 21.1, C-4′), 118.73 (dd, J_{C-F} = 22.9, C-6′), 121.23 (s, C-2), 123.46 (d, J_{C-F} = 9.7, C-1′), 127.63 (d, C-6), 127.73 (d, C-4), 129.69 (d, J_{C-F} = 8.2, C-3′), 129.84 (d, C-5), 132.78 (d, C-3), 141.03 (s, C-1), 145.02 (d, J_{C-F} = 3.4, C-2′), 162.16 (d, J_{C-F} = 242.7, C-5′). ^{19}F NMR (acetone-d_6): –112.99 (tt, J_{F-H} = 8.8, 5.4). EI MS (*m/z*, rel. intensity): 256 ($M^{+\bullet}$, 3), 238 (100), 221 (13), 209 (65), 207 (18), 196 (16), 189 (9), 183 (25), 137 (13), 119 (13), 109 (5), 91 (9), 77 (6). HR EI MS: calculated for $C_{16}H_{11}FO$ ($M - H_2O$) 238.0794; found 238.0799.

2-[2-(2-Hydroxymethylphenyl)ethyn-1-yl]-4-(methoxycarbonyl)benzyl Acetate (**34**)

Method F). Compound **6b** (105 mg, 0.449 mmol), **31** (104 mg, 0.448 mmol, 1.0 equivalent), $Pd(PPh_3)_4$ (26 mg, 0.022 mmol, 5 mole %), diisopropylamine (5 ml), 80 °C, 1 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) afforded **34** (99 mg, 65%) as an oil. IR ($CHCl_3$): 3 607 w, 2 954 w, 2 880 vw, 2 210 vw, 1 746 m (sh), 1 724 vs, 1 608 w, 1 572 w, 1 497 w, 1 483 w, 1 450 w, 1 438 m, 1 413 w, 1 380 w, 1 363 w, 1 318 m, 1 282 m, 1 255 s, 1 156 w, 1 133 w (sh), 1 106 w, 1 043 w, 1 030 w, 1 008 w, 989 w, 916 w, 845 vw. ^{1}H NMR (500 MHz, $CDCl_3$): 2.15 (s, 3 H, CH_3CO_2); 2.51 (brs, 1 H, OH); 3.95 (s, 3 H,

CH_3O_2C); 4.92 (s, 2 H, C**H**$_2$OH); 5.41 (brs, 2 H, CH_2OAc); 7.31 (dt, 1 H, *J* = 7.6, 7.6, 1.5, 4′-H); 7.39 (dt, 1 H, *J* = 7.6, 7.6, 1.5, 5′-H); 7.51 (ddt, 1 H, *J* = 7.5, 1.5, 0.6, 0.6, 3′-H); 7.53 (dq, 1 H, *J* = 8.1, 0.6, 0.6, 0.6, 6-H); 7.57 (dd, 1 H, *J* = 7.7, 1.5, 6′-H); 8.01 (dd, 1 H, *J* = 8.1, 1.8, 5-H); 8.22 (d, 1 H, *J* = 1.8, 3-H). ^{13}C NMR ($CDCl_3$): 20.87 (q, CH_3CO_2), 52.37 (q, CH_3O_2C), 63.84 (t, CH_2OH), 64.33 (t, CH_2OAc), 89.98 (s, C≡C–Ar′), 92.85 (s, C≡C–Ar′), 120.87 (s, C-1′), 122.52 (s, C-2), 127.60 (d, C-3′), 127.68 (d, C-4′), 128.07 (d, C-6), 129.27 (d, C-5′), 129.55 (d, C-5), 130.04 (s, C-4), 132.45 (d, C-6′), 133.29 (d, C-3), 141.86 (s, C-2′), 142.49 (s, C-1), 166.06 (s, CH_3O_2C), 170.84 (s, CH_3CO_2). EI MS (*m/z*, rel. intensity): 338 ($M^{+\bullet}$, 26), 307 (12), 295 (39), 277 (100), 263 (11), 219 (59), 201 (12), 191 (53), 189 (42), 178 (17), 69 (24), 57 (26), 43 (44). HR EI MS: calculated for $C_{20}H_{18}O_5$ 338.1154; found 338.1175.

Dimethyl 4,4′-Bis(acetoxymethyl)-3,3′-ethynediyldibenzoate (**35**)

Method F). Compound **15** (144 mg, 0.431 mmol), **31** (100 mg, 0.431 mmol, 1.0 equivalent), $Pd(PPh_3)_4$ (25 mg, 0.022 mmol, 5 mole %), diisopropylamine (5 ml), 80 °C, 1 h. Flash chromatography on silica gel (petroleum ether–ether–acetone 80 : 10 : 10) afforded **35** (20 mg, 11%) as an oil. IR ($CHCl_3$): 2 954 w, 2 933 vw, 1 746 m (sh), 1 724 vs, 1 608 w, 1 575 w, 1 499 vw, 1 481 w, 1 463 w, 1 457 w, 1 439 m, 1 422 w, 1 317 w, 1 293 m, 1 278 w (sh), 1 248 vs, 1 157 w, 1 135 w (sh), 1 103 w, 1 046 w, 1 030 w, 994 w, 917 w, 845 vw. ^{1}H NMR (500 MHz, $CDCl_3$): 2.17 (s, 6 H, 2 × CH_3CO_2); 3.95 (s, 6 H, 2 × CH_3O_2C); 5.41 (s, 4 H, 2 × CH_2); 7.53 (d, 2 H, *J* = 8.1, 5,5′-H); 8.04 (dd, 2 H, *J* = 8.1, 1.9, 6,6′-H); 8.23 (d, 2 H, *J* = 1.9, 2,2′-H). ^{13}C NMR ($CDCl_3$): 20.87 (q, CH_3CO_2), 52.40 (q, CH_3O_2C), 64.03 (t, CH_2OAc), 91.25 (s, ≡C–), 121.92 (s, C-3,3′), 127.98 (d, C-5,5′), 129.94 (d, C-6,6′), 130.06 (s, C-1,1′), 133.57 (d, C-2,2′), 142.23 (s, C-4,4′), 165.99 (s, 2 × CH_3O_2C), 170.56 (s, 2 × CH_3CO_2). EI MS (*m/z*, rel. intensity): 438 ($M^{+\bullet}$, 23), 407 (16), 378 (55), 363 (28), 336 (48), 321 (20), 304 (30), 277 (62), 249 (18), 218 (16), 189 (38), 59 (14), 43 (100). HR EI MS: calculated for $C_{24}H_{22}O_8$ 438.1315; found 438.1305.

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