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Site-Selective Sonogashira Reactions of 1,4-Dibromo-2-fluorobenzene – Synthesis and Properties of Fluorinated Alkynylbenzenes

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Keywords: Synthetic methods / Regioselectivity / Homogeneous catalysis / Palladium / Fluorine / Alkynes / Organofluorine compounds / Liquid crystals / Luminescence

A variety of alkynyl-substituted fluorinated benzene derivatives have been prepared by Sonogashira cross-coupling reactions of 1,4-dibromo-2-fluorobenzene. The reactions proceed with very good site-selectivity in favor of the 4-position because of electronic and steric reasons. The regioselectivity is explained by the results of DFT calculations. The absorption and emission (fluorescence) properties of the products, mono- and dialkynylated fluorobenzenes, have been studied. In addition, the mesomorphic properties of the products have been investigated by polarization microscopy and differential scanning calorimetry. 1,4-Dialkynyl-2-fluorobenzenes show nematic liquid-crystalline properties over a long phase range.

Introduction

The unique properties of fluorine-containing carba- and heterocycles have led to their remarkable record in medicinal and agricultural chemistry, and they play an important role as lead compounds.[1,2] The solubility and bioavailability of fluorinated compounds are often enhanced compared to those of their nonfluorinated analogues.[3,4] Moreover, fluorinated arenes and hetarenes are useful substrates in transition-metal-catalyzed cross-coupling reactions.[5] Aryl fluorides are used as ligands[6] in catalytic reactions and as organocatalysts.[7] Since the early 1980s, a large number of liquid crystals with fluorine substituents have been synthesized. In recent years, liquid crystal displays (LCD) have become an important part of our daily life.[2] Initial interest in such materials was aroused by the greater nematic phase range, often dramatically increased, of laterally fluorinated liquid crystals compared to their nonfluorinated analogues. Later, it was found that liquid crystals that derive their molecular dipole moment from fluorine rather than cyano groups, so-called superfluorinated materials,[8–10] show excellent properties for materials to be used in active matrix LCDs.[11,12,13] Because of the degree of fluorination of many liquid crystals, a special methodology for the synthesis of fluorinated arenes has been developed.[2] Generally, the synthesis starts from aromatic building blocks that already have the required fluorination pattern. These building blocks can be functionalized by their commercially-available brominated derivatives. This includes, C–C coupling reactions such as Suzuki and Heck coupling[14] and the Wittig reaction.[15]

Among transition-metal-catalyzed coupling reactions, the Sonogashira coupling of aryl halides with terminal acetylenes provides an efficient method for C–C bond formation and has become a useful method to prepare arylated alkynes and conjugated enynes, which are relevant for the synthesis of important substructures of liquid crystals.[16,17] Referring to this, a number of site-selective Sonogashira reactions of polyhalogenated arenes and hetarenes have been developed in recent years. The site selectivity of these reactions is generally influenced by electronic and steric parameters.[18] Site-selective Sonogashira reactions of dibromides, diiodides, or bis(triflates) of fluorinated arenes have, to the best of our knowledge, not been reported. Herein, we report the results of our study of the site-selective Sonogashira reactions of 1,4-dibromo-2-fluorobenzene. These reactions provide a convenient approach to new fluorinated mono- and dialkynylbenzenes.[19] The products show interesting absorption and fluorescence properties. In addition, they exhibit long-range nematic liquid-crystal properties, which have been confirmed by polarization microscopy (POM) and differential scanning calorimetry (DSC).

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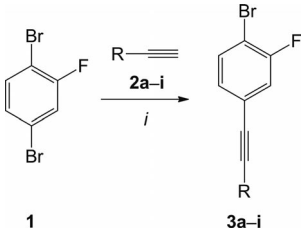
Results and Discussion

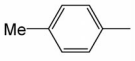
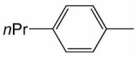
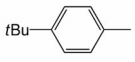
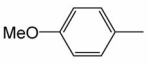
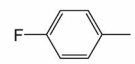
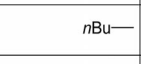
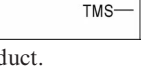
Synthesis

The Sonogashira reaction of commercially available 1,4-dibromo-2-fluorobenzene (**1**) with different substituted acetylenes **2a**–**i** (1.0 equiv.) afforded the corresponding alkynyl-substituted 4-bromo-3-fluorobenzene derivatives **3a**–**i** in moderate to good yields (Scheme 1, Table 1). The best yields were obtained using 1.0 equiv. of alkyne, $Pd(PPh_3)_4$ (3 mol-%) as the catalyst, and Et_3N (2.0 equiv.) as the base in tetrahydrofuran (THF) at 50 °C for 5 h. In some cases, the formation of a small amount of the other regioisomer was observed by GC–MS and ^{19}F NMR spectroscopy, which could not be separated preparatively by flash chromatography.



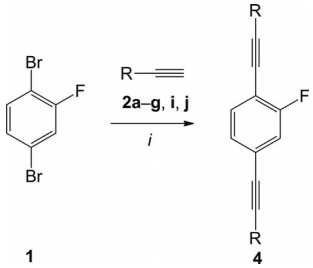
Scheme 1. Synthesis of **3a**–**i**. (i) **1** (1.0 equiv.), **2a**–**i** (1.0 equiv.), Et_3N (2.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), CuI (3 mol-%), THF, 50 °C, 5 h.

Table 1. Synthesis of **3a**–**i**.

2,3	R	% (3)[a]
a		69
b		68
c		56
d		65
e		62
f		71
g		66
h		51
i		61

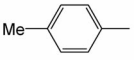
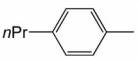
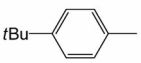
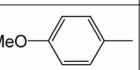
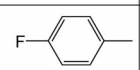
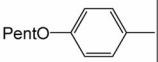
[a] Yield of isolated product.

The Sonogashira reaction of **1** with 2.0 equiv. of alkyne afforded the symmetrical *para*-substituted ethynyl-fluorobenzenes **4a**–**i** in moderate to good yields (Scheme 2, Table 2). The best yields were obtained using 2.1 equiv. of alkyne, $Pd(PPh_3)_4$ (3 mol-%) as the catalyst, CuI (3 mol-%), and Et_3N (2.5 equiv.) as the base in THF at 50 °C for 6 h.



Scheme 2. Synthesis of **4a**–**i**. (i) **1** (1.0 equiv.), **2** (2.1 equiv.), Et_3N (2.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), CuI (3 mol-%), THF, 50 °C, 6 h.

Table 2. Synthesis of **4a**–**i**.

4	2	R	% (4)[a]
a	a		74
b	b		70
c	c		68
d	d		70
e	e		63
f	f		69
g	g		68
h	i		73
i	j		69

[a] Yield of isolated product.

The synthesis of unsymmetrical *para*-substituted ethynyl-fluorobenzenes was studied next. The Sonogashira reaction of selected ethynyl-substituted 4-bromo-3-fluorobenzenes **3** with 1.1 equiv. of different substituted acetylenes **2** yielded *para*-substituted ethynylfluorobenzenes **5a**–**e**, which bear different ethynyl moieties (Scheme 3, Table 3).

The structures of all products were confirmed by spectroscopic methods. In addition, high resolution ^{13}C NMR spectroscopy confirmed the site-selectivity of these reactions. C-2 of the alkyne moiety showed long-range coupling with the fluorine atom over four bonds with a coupling constant of $^4J_{C-F}$ = 3.0 Hz. No coupling was observed for C-1. In case of the opposite regioisomer, long-range coupling over three bonds for C-2 of around 8.0 Hz and for C-1 of

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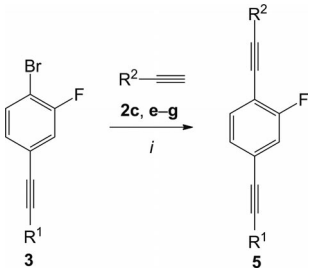


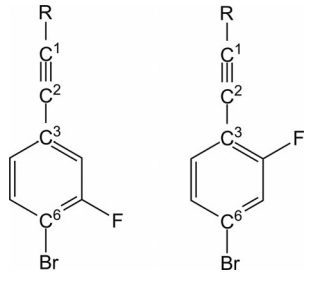
Scheme 3. Synthesis of **5a**–**e**. (i) **3** (1.0 equiv.), **2** (1.1 equiv.), Et_3N (2.0 equiv.), $Pd(PPh_3)_4$ (3 mol-%), CuI (3 mol-%), THF, 50 °C, 6 h.

Table 3. Synthesis of **5a**–**e**.

5	3	2	R^1	R^2	% (5)[a]
a	a	g		F	68
b	a	c		Me	61
c	a	e		*t*Bu	56
d	b	e	Me	*t*Bu	53
e	b	f	Me	MeO	68

[a] Yield of isolated product.

around 3.0 Hz should be observed. C-3 showed a coupling constant of $^3J_{C–F}$ = 8.0 Hz (124.0 ppm). C-6 (C–Br) resonated as a doublet at around 110.0 ppm and showed a typical coupling to the fluorine atom with a coupling constant of $^2J_{C–F}$ = 21.0 Hz (Scheme 4).



Scheme 4. Numbering of **3** (left) and opposite regioisomer (*not* observed, right).

The structures of **3b** and **4d** were independently confirmed by X-ray crystal structure analysis, which unambiguously proved their constituents (Figures 1 and 2).[20] Compound **3b** shows a planar structure, whereas **4d** and **5d** have a slight twist of the phenyl moieties along the alkyne bonds.

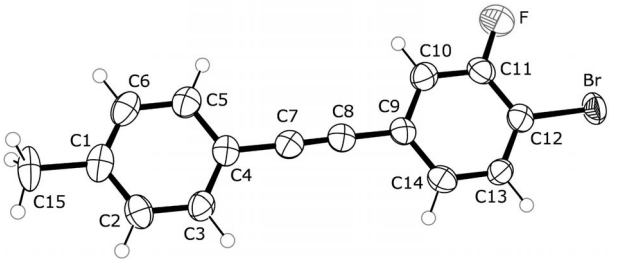
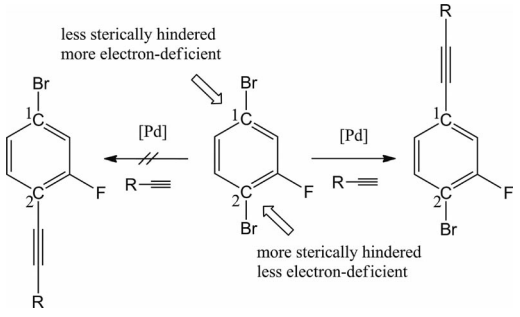


Figure 1. ORTEP plot of **3b**.

The site-selective formation of **3a**–**i** and **5a**–**e** can be explained by steric and electronic factors. The first attack of palladium(0)-catalyzed cross-coupling reactions generally occurs at the more electron deficient and sterically less hindered position.[18,21] The 1-position in **1** is sterically less hindered because it is located next to two hydrogen atoms, whereas the 2-position is located next to a fluorine atom (Scheme 5). In addition, the 1-position (*meta* to the fluorine atom) is more electron deficient than the 2-position (*ortho* to the fluorine atom) because of π donation from the fluorine atom. The same observations were made in the synthesis of fluorinated terphenyls by site-selective Suzuki–Miyaura reactions of halogenated fluorobenzenes.[22,23]



Scheme 5. Possible explanation for the site-selectivity of cross-coupling reactions of **1**.

This assumption was confirmed by DFT calculations at the B3LYP level of theory using a 6-31G* basis set. In **1**, the C-1–Br bond is lengthened by about 1 pm compared to the C-1–Br bond with the neighboring fluorine atom (190.7 vs. 189.7 pm). Of course, the weaker C-1–Br bond

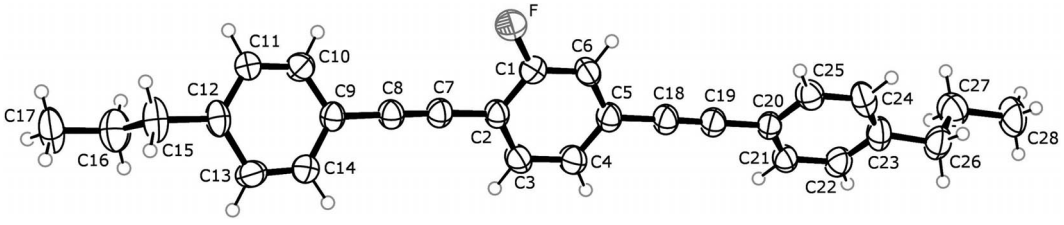


Figure 2. ORTEP plot of **4d**.

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will be preferentially attacked. The calculated natural charges from natural bond orbital analysis (NBO) support this view. The NBO charges at the reactive centers in **1** indicate that C-1 carries only half of the charge of C-2 (C-1: –0.107 a.u. vs. C-2: –0.192 a.u., see Scheme 5 for numbering). It is well known that the most electron-deficient position, which is C-2 in **1**, will be attacked preferentially. Furthermore, the NBO analysis shows that the higher charge at C-2 is related to the charge transfer from the neighboring fluorine atom, which strongly donates charge from its lone pairs into the C-2–C antibonding orbital. This charge transfer weakens the C-2–C bond and strengthens the neighboring C-2–Br bond, which leads to a shorter bond length relative to that of the C-1–Br bond. Of course, this effect is stronger for the fluorine atom located in the *ortho* position (see Supporting Information). A crude estimate of the C–Br bond strength can be obtained from the calculated energy differences (isodesmic reaction) between 1-bromo-2-fluorobenzene and 1-bromo-3-fluorobenzene. The latter compound is 5.4 kJ mol^{-1} lower in energy, which explains its higher reactivity empirically.

Liquid-Crystalline Properties

The synthesized fluorinated ethynylbenzenes were investigated with regard to their liquid-crystalline properties. It is known that fluorinated *para*-substituted arenes, e.g. fluorinated terphenyls or fluorinated phenol esters, can enhance the nematic phase range.[2] Characterization and determination of the liquid-crystalline phase range was carried out with a POM equipped with a hot stage. In all cases the transition temperatures were investigated in heating and cooling cycles. Although monosubstituted **3** showed no additional phases between the crystalline (solid) and isotropic (liquid) state, several symmetrical and unsymmetrical disubstituted **4** and **5** showed thermotropic nematic liquid-crystalline phases (Figure 3). The transition temperatures of **4** and **5** are given in Table 4. No smectic phases were observed in the textures of **4** and **5**, which is consistent with the work of Subramanya et al. and Gallardo et al. who concluded that the presence of lateral groups in liquid-crystalline compounds eliminates the smectic phase.[24,25]

Table 4. Transition temperatures of fluorinated dialkynylbenzenes **4a**–**i** and **5a**–**e**.[a]

Compd.	Trans. temp. [°C]	Compd.	Trans. temp. [°C]
4a	m.p. 170–171[b]	**4h**	m.p. 94–95[b]
4b	m.p. 200–202[b]	**4i**	C $\xleftrightarrow{135}$ N $\xleftrightarrow{224}$ I
4c	m.p. 103–104[b]	**5a**	m.p. 205–207[b]
4d	C $\xleftrightarrow{147}$ N $\xleftrightarrow{219}$ I	**5b**	m.p. 117–119[b]
4e	m.p. 235–237[b]	**5c**	m.p. 150–152[b]
4f	C $\xrightarrow{182}$ N $\xrightarrow{281}$ I	**5d**	m.p. 179–180[b]
4g	C $\xleftrightarrow{154}$ N $\xleftrightarrow{204}$ I	**5e**	C $\xrightarrow{182}$ N $\xrightarrow{256}$ I

[a] C, N, and I represent crystal, nematic, and isotropic phases, respectively. [b] Compounds **4a**–**c**, **e**, **h**, and **5a**–**d** do not show any mesophases.

As seen from Table 4, **4d**, **f**, **g**, **i**, and **5e**, which contain a *para*-alkoxy or *n*-alkyl substituent, showed a nematic phase, whereas unsubstituted **4a**, *para*-*tert*-butyl derivative **4e**, and *ortho*-substituted **4c** showed no mesophases. In addition, **4d**, **f**, **g**, **i**, and **5e** showed a long nematic phase range. The greatest phase range was observed for **4f**, which bears two *para*-methoxyphenyl moieties. This observation is in line with the statement of Goto et al. and Tarumi et al. who point out that the phase range of laterally fluorinated liquid crystals is often dramatically increased compared to their nonfluorinated analogues.[10,26] For **4f** and **5e**, it was only possible to investigate the phase transitions during the heating run because they decomposed at high temperatures.

In addition, the liquid-crystalline properties of **4d** and **4f** were investigated by DSC (Figures 4 and 5, respectively). The DSC curve for **4d** exhibits two peaks each for the heating and cooling runs for the corresponding phase transitions (heating run: 147 and 215 °C; cooling run: 211 and 140 °C). The bottom curve (cooling) shows a slight displacement of the NI and NC transition, partially due to supercooling and partially due to instrumental hysteresis,

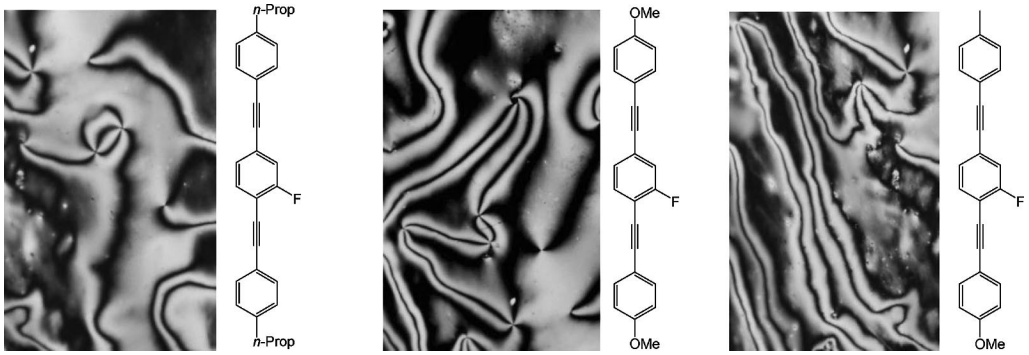

Figure 3. Nematic liquid crystals (schlieren texture) viewed by POM and structures of **4d**, **4f**, and **5e** (left to right).

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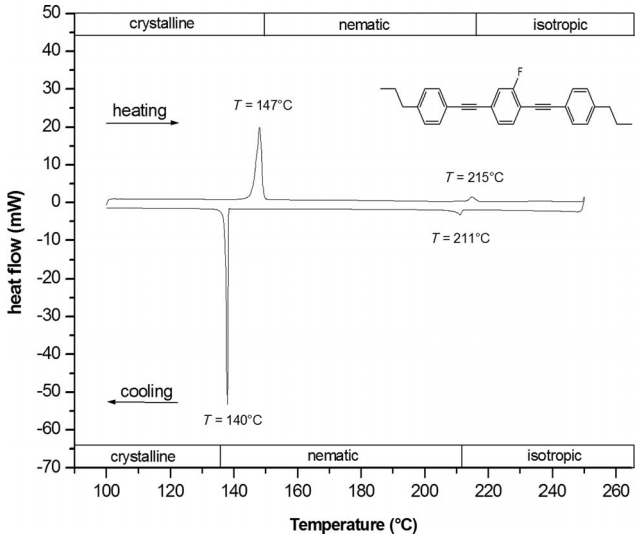

Figure 4. DSC plot with phase diagram of **4d**.

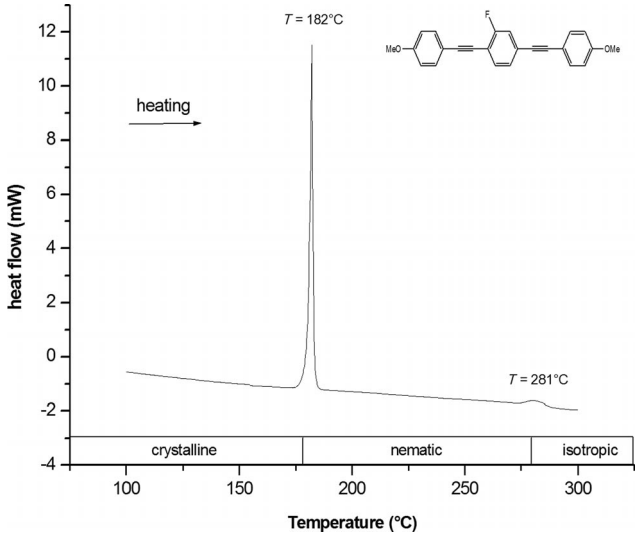

Figure 5. DSC plot with phase diagram of **4f**.

which is attributed to the temperature scan rate. The DSC curve for **4f** was measured during the heating run and shows two endothermic peaks at 182 and 281 °C, which correspond to a sudden phase transition from the crystal to nematic (182 °C) and nematic to isotropic phases (281 °C).

Absorption and Fluorescence

The UV/Vis and fluorescence spectroscopic data of several fluorinated ethynylbenzenes, measured in dichloromethane at 25 °C, are summarized in Tables 5 and 6. All the compounds contain a diphenylacetylene core as the chromophore. The absorption wavelengths of monosubstituted **3** are in the UV region (285–318 nm), and they exhibit four conspicuous transitions ($\lambda_{abs1–4}$) (Figures 6 and 7) and four shoulders, which are not considered in the following discussion.[27] For the methoxy and *tert*-butyl derivatives, the absorptions are slightly redshifted to higher wavelengths, which is due to the positive mesomeric and inductive effect of these substituents, respectively. Surprisingly, the electron-withdrawing effect of one fluorine atom in the *para* position causes no significant shift to shorter wavelengths relative to unsubstituted **3a**.

The absorption spectra of **4** are similar to those of **3**. However, all transitions of **4** appear at longer wavelengths compared to those of **3**, which is because of the extension of the π-electron system. In contrast to the spectra of **3**, no shoulders between the first and second transitions were observed. The presence of substituents located at the *para* position of the phenyl ring has the same effect on the spectra of **3** and **4**. Electron-donating groups, such as methoxy and *tert*-butyl, cause a slight shift to higher wavelengths, whereas the electron-withdrawing effect of the fluorine atom has nearly no influence. This trend is also observed in the emission spectra. Diethynylbenzenes, which contain two substituted aryl groups, exhibit absorptions in the UV region of $\lambda_{3max,abs}$ = 321–331 nm and emissions in the range of $\lambda_{5max,em}$ = 369–396 nm. Compound **4f** showed an absorption of $\lambda_{3max,abs}$ = 331 nm and an emission of $\lambda_{5max,em}$

Table 5. Absorption spectroscopic data for **3a**, **e**–**g** (CH_2Cl_2, $c = 1 \times 10^{-5}$ mol L^{-1}). The numbers of the absorptions refer to Figure 6.

	λ_{1abs} [nm]	log ε λ_{1abs}	λ_{2abs} [nm]	log ε λ_{2abs}	λ_{3abs} [nm]	log ε λ_{3abs}	λ_{4abs} [nm]	log ε λ_{4abs}
3a	226	4.289	285	4.583	298	4.513	307	4.577
3e	228	4.882	293	5.232	302	5.180	312	5.242
3f	228	4.952	286	5.163	301	5.301	318	5.295
3g	228	4.129	285	4.506	297	4.430	307	4.486

Table 6. Absorption and emission spectroscopic data of **4a**, **e**–**g** (CH_2Cl_2, $c = 1 \times 10^{-5}$ mol L^{-1}). The numbers of the absorptions refer to Figure 7.

	λ_{1abs} [nm]	log ε λ_{1abs}	$\lambda_{2abs(sh)}$ [nm]	log ε λ_{2abs}	$\lambda_{3max,abs}$ [nm]	log ε λ_{3abs}	λ_{4abs} [nm]	log ε λ_{4abs}	$\lambda_{5max,em}$ [nm]	$\lambda_{6em(sh)}$ [nm]	Stokes shift (λ_5– λ_3) [nm]
4a	230	4.488	303	4.659	323	4.797	343	4.623	369	376	46
4e	231	4.933	304	5.144	329	5.339	349	5.171	379	388	50
4f	237	4.084	318	4.366	331	4.506	357	4.390	396	402	65
4g	228	4.094	303	4.129	321	4.276	343	4.127	369	373	48

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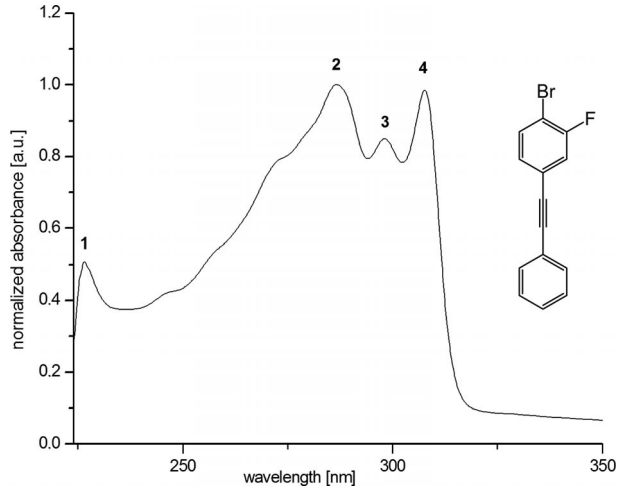

Figure 6. Absorption spectrum of **3a** (in CH_2Cl_2).

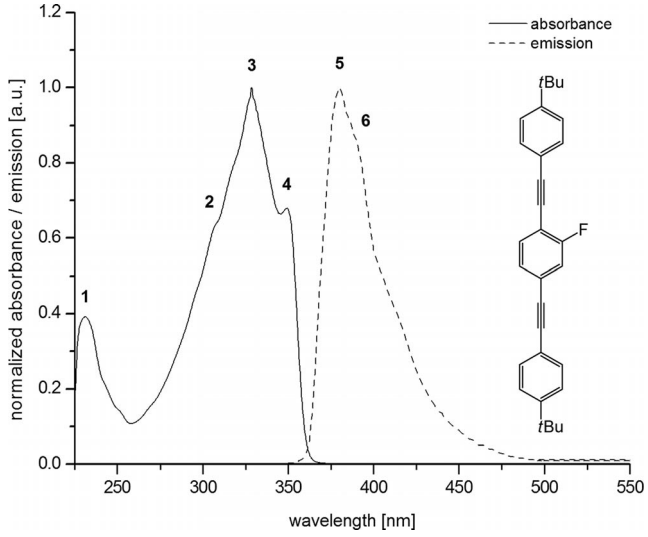

Figure 7. Absorption and emission spectra of **4e** (in CH_2Cl_2).

= 396 nm with a large Stokes shift of 65 nm. In fact, a large Stokes shift generally corresponds to better fluorescence properties. The bathochromic shift in the spectra of **4f** and the large Stokes shift might be associated with the push–pull substitution pattern of **4f**, which contains two methoxy groups as electron-donating substituents and the fluorine atom as an electron-withdrawing substituent. In contrast, a hypsochromic effect is observed for **4g**, which contains a fluorine atom instead of methoxy groups. Thus, the electron-donating 4-methoxyphenyl group of **4f** seems to be advantageous. This result is in agreement with our earlier work related to alkynylated pyrimidines.[28]

Conclusion

We have demonstrated an easy, applicable route for the synthesis of mono- and disubstituted ethynylfluorobenzenes by site-selective Sonogashira reactions of 1,4-dibromo-2-fluorobenzene. The site-selectivity in favor of the 4-position can be explained by steric and electronic reasons. The mesomorphic properties and optical textures of the products were investigated by DSC and POM. The existence of nematic phases (schlieren texture) was confirmed. Disubstituted ethynylbenzenes showed long-range nematic liquid-crystalline properties. Monosubstituted fluorobenzenes show absorptions in the range of λ_{abs} = 285–318 nm. Diethynylbenzenes exhibit absorptions and emissions (fluorescence) in the range of $\lambda_{abs,max}$ = 321–331 nm and $\lambda_{em,max}$ = 369–396 nm. Diethynylbenzenes represent promising fluorescence dyes and liquid crystals.

Experimental Section

General: All reactions were carried out in oven-dried pressure tubes under an argon atmosphere. Tetrakis(triphenylphosphane)palladium(0) was prepared according to the literature method.[29] 1,4-Dibromo-2-fluorobenzene (TCI), copper iodide (Acros), and the corresponding alkynes (Acros, AlfaAesar) were purchased from a commercial source. THF was distilled and purged with argon before use. Triethylamine was purchased from a commercial source (Acros) and purged with argon before use. TLC was performed with Merck precoated aluminium plates (Si 60 F254). Column chromatography was performed with Merck silica gel 60 (0.043–0.06 mm). NMR spectra were recorded with Bruker ARX 300 and Bruker ARX 400 spectrometers. ^{13}C and ^{1}H NMR spectra were referenced to signals of the deuterated solvents. GC–MS was carried out with an Agilent HP-5890 instrument with an Agilent HP-5973 Mass Selective Detector (EI) and HP-5 capillary column using helium carrier gas. HRMS (ESI) measurements were performed with an Agilent 1969A TOF mass spectrometer. UV/Vis spectra were recorded with a Lambda 5 (Perkin–Elmer) spectrophotometer with a solution concentration of 1×10^{-5} mol L^{-1}. Fluorescence spectra were recorded with a Hitachi F-4010 fluorescence spectrophotometer using similar solution concentrations. The solvent used (dichloromethane) was distilled before use. The mesomorphic properties and optical textures were investigated by POM (LaborLux 12 Pol-5, Leica) and by DSC (Mettler Toledo/DSC 823e/2007).

Calculations: Geometry optimizations were carried out with the Gaussian 03 programme package. We used the B3LYP method, which included the Becke-3-parameter gradient corrected exchange functional combined with the gradient-corrected correlation LYP functional by Lee, Yang and Parr, to calculate the structures of the compounds. No imaginary frequencies were found, which indicated that all geometries represent at least local minima on the potential energy surface. For all structures the calculations were performed with the 6-31G* basis set implemented in Gaussian 03.[30] In addition, we calculated the natural atomic charges by applying the NBO program as implemented in Gaussian 03. All calculations were carried out on the HPPC-Cluster in Rostock.

General Procedure for the Synthesis of 3a–i: A suspension of 1,4-dibromo-2-fluorobenzene (**1**), $Pd(PPh_3)_4$ (3 mol-%), and CuI (3 mol-%) in THF (3 mL/mmol **1**) in an oven-dried pressure tube was degassed by bubbling argon through the solution for 10 min. The acetylene **2** (1.0 equiv.) and triethylamine (2.0 equiv.) were added by syringe. The mixture was heated at 50 °C for 5 h. The cooled reaction mixture was filtered, and the residue was washed with CH_2Cl_2. The filtrate was washed with a saturated solution of ammonium chloride (2 × 25 mL) and water (2 × 25 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered,

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and the solvent was removed in vacuo. The product was purified by column chromatography (silica gel, EtOAc/heptanes).

1-Bromo-2-fluoro-4-(2-phenylethynyl)benzene (3a): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2a** (0.11 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3a** was isolated as a colorless solid (0.189 g, 69%); m.p. 88–89 °C, R_F = 0.51 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.08 (ddd, $^3J_{H-F}$ = 8.4, $^4J_{H-H}$ = 1.8, $^5J_{H-H}$ = 0.7 Hz, CH next to CF), 7.10 (dd, $^3J_{H-H}$ = 9.1, $^4J_{H-H}$ = 1.8 Hz, CH), 7.14–7.19 (m, 3 H of Ph), 7.30–7.38 (m, 2 H of Ph, 1 H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 87.4 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 91.3 (C, alkyne), 109.5 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.3 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 122.5 (C of Ph), 124.4 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 127.5 (CH of Ph), 127.5 (CH of Ph), 128.5 (CH of Ph), 128.7 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr),131.7 (CH of Ph), 131.7 (CH of Ph), 134.1 (CH), 158.8 (d, $^1J_{C-F}$ = 246.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.4 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3081 (w), 3053 (w), 2204 (m), 1610 (w), 1593 (w), 1275 (w), 1094 (w), 1069 (w), 952 (w), 834 (w), 820 (m), 786 (s), 683 (s), 543 (s), 524 (s), 431 (s), 379 (s) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 274 (98) $[M]^+$, 195 (6), 194 (38), 175 (14), 138 (5), 137 (7), 98 (4). HRMS: calcd. for $C_{14}H_8BrF$ $[M]^+$ 273.97879; found 273.97811.

1-Bromo-2-fluoro-4-(2-*p*-tolylethynyl)benzene (3b): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2b** (0.13 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3b** was isolated as a colorless solid (0.195 g, 68%); m.p. 134–136 °C, R_F = 0.52 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, CH_3), 7.07–7.11 (m, 2 H of Me–Ph and 1 H next to CF), 7.16–7.21 (m, H of Br–Ph), 7.32–7.45 (m, 2 H of Me–Ph and 1 H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (CH_3), 86.7 (C, alkyne), 91.5 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 109.2 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.3 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 124.5 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 127.4 (C next to alkyne of Me–Ph), 128.4 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr), 129.2 (CH of Me–Ph), 129.3 (CH of Me–Ph), 131.6 (CH of Me–Ph), 131.6 (CH of Me–Ph), 133.5 (CH), 139.1 (C of Me–Ph), 158.7 (d, $^1J_{C-F}$ = 246.8 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.9 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3024 (w), 2919 (m), 2852 (m), 2727 (w), 2550 (w), 2353 (w), 2209 (m), 1906 (m), 1738 (m), 1591 (m), 1556 (m), 1472 (m), 1404 (s), 1321 (w), 1215 (m), 1117 (m), 1036 (m), 950 (m), 809 (s), 751 (s), 526 (s), 455 (m), 419 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 288 (99) $[M]^+$, 287 (14), 209 (12), 208 (17), 207 (48), 189 (10), 183 (10), 145 (5), 123 (4), 105 (7), 104 (8), 63 (4). HRMS: calcd. for $C_{15}H_{10}BrF$ $[M]^+$ 287.99444; found 287.99497. $C_{15}H_{10}BrF$ (289.14): calcd. C 62.31, H 3.49; found C 62.27, H, 3.55.

1-Bromo-2-fluoro-4-(2-*o*-tolylethynyl)benzene (3c): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2c** (0.13 mL, 1.00 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.00 mL), **3c** was isolated as a colorless oil (0.161 g, 56%). R_F = 0.45 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, CH_3), 7.08–7.13 (m, H next to CF and H of 2-Me–Ph next to Me), 7.15–7.24 (m, 2 H of 2-Me–Ph and 1 H of Br–Ph), 7.39–7.58 (m, 1 H of 2-Me–Ph and 1 H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 90.3 (C, alkyne), 91.2 (d, $^4J_{C-F}$ = 3.0 Hz, 1 C, alkyne), 109.3 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.2 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 122.3 (C next to alkyne of Me–Ph), 124.6 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 125.7 (CH of Me–Ph), 127.5 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr), 128.4 (CH of Me–Ph), 129.6 (CH of Me–Ph), 132.0 (CH of Me–Ph), 133.5 (CH), 140.4 (C of Me–Ph), 158.8 (d, $^1J_{C-F}$ = 246.8 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.6 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3023 (w), 2950 (m), 2207 (m), 1590 (m), 1554 (s), 1485 (s), 1470 (s), 1456 (m), 1241 (m), 1217 (m), 1198 (m), 1036 (m), 949 (m), 818 (s), 753 (s), 715 (s), 611 (s), 524 (m), 449 (s), 416 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 288 (100) $[M]^+$, 287 (14), 210 (14), 209 (90), 208 (31), 207 (86), 189 (15), 183 (28), 144 (5), 104 (31), 94 (10), 92 (17), 63 (4). HRMS: calcd. for $C_{15}H_{10}BrF$ $[M]^+$ 287.99444; found 287.99422. $C_{15}H_{10}BrF$ (289.14): calcd. C 62.31, H 3.49; found C 62.25, H 3.304.

1-Bromo-2-fluoro-4-[(4-propylphenyl)ethynyl]benzene (3d):[19] Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2d** (0.16 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3d** was isolated as a slight yellow solid (0.212 g, 65%); m.p. 78–80 °C, R_F = 0.48 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, $^3J_{H-H}$ = 8.4 Hz, CH_3), 1.65 (m, CH_2), 2.61 (t, $^3J_{H-H}$ = 7.7 Hz, CH_2), 7.17 (d, $^3J_{H-H}$ = 8.2 Hz, 2 H of *n*Pr–Ph), 7.18 (d, $^3J_{H-F}$ = 8.1 Hz, H of Br–Ph), 7.26 (dd, $^3J_{H-H}$ = 9.2, $^4J_{H-H}$ = 1.7 Hz, H of Br–Ph), 7.41–7.46 (m, 2 H of *n*Pr–Ph), 7.51 (dd, $^3J_{H-H}$ = 8.3, $^4J_{H-F}$ = 7.2 Hz, H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 24.6 (CH_2), 38.0 (CH_2), 86.8 (C, alkyne), 91.6 (C, alkyne), 109.2 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.3 (d, $^2J_{C-F}$ = 24.0 Hz, CH next to CF), 119.7 (C, *n*Pr–Ph next to alkyne), 124.6 (d, $^3J_{C-F}$ = 8.8 Hz, C next to alkyne), 128.4 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr), 128.7 (CH, *n*Pr–Ph), 128.7 (CH, *n*Pr–Ph), 133.5 (CH, *n*Pr–Ph), 133.5 (CH, *n*Pr–Ph), 133.5 (CH), 143.9 (C next to *n*Pr), 158.7 (d, $^1J_{C-F}$ = 246.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.6 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2957 (m), 2924 (m), 2856 (m), 2210 (m), 1893 (w), 1591 (m), 1556 (m), 1509 (s), 1471 (s), 1404 (s), 1216 (s), 1116 (m), 1036 (m), 950 (m), 814 (s), 766 (m), 609 (m), 531 (m), 425 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 316 (56) $[M]^+$, 290 (16), 289 (99), 288 (17), 287 (100), 220 (4), 208 (17), 207 (47). HRMS: calcd. for $C_{17}H_{14}BrF$ $[M]^+$ 316.02574; found 316.02569. $C_{17}H_{14}BrF$ (317.2): C, 64.37; H, 4.45; found C 64.13, H 4.47.

4-[2-(4-*tert*-Butylphenyl)ethynyl]-1-bromo-2-fluorobenzene (3e): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2e** (0.16 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3e** was isolated as a colorless solid (0.205 g, 62%); m.p. 77–79 °C, R_F = 0.51 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 9 H, *t*Bu), 7.18 (ddd, $^3J_{H-F}$ = 8.2, $^4J_{H-H}$ = 2.0, $^5J_{H-H}$ = 0.9 Hz, H next to CF), 7.25 (dd, $^3J_{H-H}$ = 9.1, $^4J_{H-H}$ = 1.6 Hz, H of Br–Ph), 7.41–7.45 (m, 4 H of *t*Bu–Ph), 7.51 (dd, $^3J_{H-H}$ = 8.2, $^4J_{H-F}$ = 7.2 Hz, H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.2 (CH_3), 31.2 (CH_3), 31.2 (CH_3), 34.9 (C of *t*Bu), 86.7 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 91.5 (C, alkyne), 109.2 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.3 (d, $^2J_{C-F}$ = 24.0 Hz, CH next to CF), 119.5 (C of *t*Bu–Ph), 124.6 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 125.5 (CH of *t*Bu–Ph), 125.5 (CH of *t*Bu–Ph), 128.4 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to C–Br), 131.5 (CH of *t*Bu–Ph), 131.5 (CH of *t*Bu–Ph), 133.5 (CH), 152.2 (C of *t*Bu–Ph), 158.7 (d, $^1J_{C-F}$ = 246.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.6 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3086 (w), 2959 (m), 2924 (m), 2864 (m), 2212 (m), 1910 (w), 1590 (w), 1555 (w), 1405 (w), 1362 (m), 1243 (m), 1220 (m), 1099 (m), 951 (m), 872 (s), 830 (s), 817 (s), 711 (m), 556 (m), 448 (w), 432 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 330 (49) $[M]^+$, 318 (17), 317 (100), 316 (19), 315 (100), 289 (15), 287 (15), 236 (10), 221 (13), 220 (18), 207 (10), 196 (10), 144 (17), 143 (17). HRMS: calcd. for $C_{18}H_{16}BrF$ $[M]^+$ 330.04139; found 330.040588. $C_{18}H_{16}BrF$ (331.22): calcd. C 65.27, H 4.87; found C 65.01, H 5.23.

1-Bromo-2-fluoro-4-[2-(4-methoxyphenyl)ethynyl]benzene (3f): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%),

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CuI (5.7 mg, 3 mol-%), **2f** (0.12 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3f** was isolated as a colorless solid (0.215 g, 71%); m.p. 93–95 °C, R_F = 0.65 (hexane/ethyl acetate = 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, MeO), 6.86–6.90 (m, 2 H, MeO–Ph), 7.16 (ddd, $^3J_{H-F}$ = 8.1, $^4J_{H-H}$ = 1.9, $^5J_{H-H}$ = 0.8 Hz, H next to CF), 7.25 (dd, $^3J_{H-H}$ = 9.1, $^4J_{H-H}$ = 1.7 Hz, H of Br–Ph), 7.43–7.52 (m, 2 H of MeO–Ph and 1 H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 86.2 (C, alkyne), 91.4 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 109.0 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 114.1 (CH of MeO–Ph), 114.1 (CH of MeO–Ph), 114.6 (C, MeO–Ph next to alkyne), 119.1 (d, $^2J_{C-F}$ = 24.3 Hz, CH next to CF), 124.6 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 128.3 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to C–Br), 133.4 (CH), 133.2 (CH of MeO–Ph), 133.2 (CH of MeO–Ph), 158.6 (d, $^1J_{C-F}$ = 246.8 Hz, CF), 160.1 (C–OMe) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.7 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2964 (m), 2933 (w), 2841 (w), 2205 (w), 1602 (m), 1509 (m), 1403 (m), 1288 (m), 1217 (w), 1108 (m), 1025 (m), 951 (m), 821 (s), 721 (m), 695 (m), 612 (m), 537 (m), 471 (w), 401 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 304 (100) $[M]^+$, 291 (37), 289 (37), 263 (14), 261 (15), 194 (5), 182 (29), 181 (45), 155 (6). HRMS: calcd. for $C_{15}H_{10}OBrF$ $[M]^+$ 303.98936; found 303.99005. $C_{15}H_{10}OBrF$ (305.1): calcd. C 59.04, H 3.30; found C 59.12, H 3.44.

1-Bromo-2-fluoro-4-[2-(4-fluorophenyl)ethynyl]benzene (3g): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2g** (0.114 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3g** was isolated as a colorless solid (0.199 g, 66%); m.p. 88–89 °C, R_F = 0.51 (hexane/CH_2Cl_2 = 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.02–7.08 (m, 2 H), 7.15–7.19 (m, H of Br–Ph), 7.24–7.29 (m, H of Br–Ph), 7.48–7.55 (m, 2 H of F–Ph and 1 H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 87.0 (C alkyne), 90.1 (C, alkyne), 109.6 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 115.7 (d, $^2J_{C-F}$ = 21.8 Hz CH, F–Ph), 115.9 (d, $^2J_{C-F}$ = 21.8 Hz CH, F–Ph), 118.6 (d, $^4J_{C-F}$ = 3.0 Hz, C F–Ph next to alkyne), 119.3 (d, $^2J_{C-F}$ = 24.0 Hz, CH next to CF), 124.2 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 127.3 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr), 133.3 (CH), 133.7 (d, $^3J_{C-F}$ = 8.3 Hz CH, F–Ph), 133.7 (d, $^3J_{C-F}$ = 8.3 Hz CH, F–Ph), 158.7 (d, $^1J_{C-F}$ = 246.8 Hz, CF), 162.8 (d, $^1J_{C-F}$ = 249.0 Hz, CF of F–Ph) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.4 (t, CF of Br–Ph), –109.5 (m, CF of F–Ph) ppm. IR (ATR): $\tilde{\nu}$ = 3070 (m), 2921 (w), 2210 (w), 1900 (w), 1557 (m), 1508 (s), 1471 (m), 1403 (m), 1321 (m), 1213 (s), 1152 (s), 827 (s), 757 (m), 670 (m), 611 (m), 530 (m), 499 (m), 611 (w), 424 (m), 405 (m) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 292 (39) $[M]^+$, 212 (32), 193 (17), 192 (9), 168 (4), 167 (3), 147 (7), 96 (5). HRMS: calcd. for $C_{14}H_7BrF_2$ $[M]^+$ 291.96937; found 291.96989. $C_{14}H_7BrF_2$ (293.1): calcd. C 57.37, H 2.41; found C 57.53, H 2.341.

1-Bromo-2-fluoro-4-(hex-1-ynyl)benzene (3h): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2h** (0.12 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3h** was isolated as a colorless oil (0.118 g, 50%). R_F = 0.61 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, $^3J_{H-H}$ = 7.3 Hz, CH_3), 1.41–1.59 (m, 4 H, 2 CH_2), 2.37 (t, $^3J_{H-H}$ = 7.3 Hz, CH_2), 7.02 (ddd, $^3J_{H-F}$ = 8.4, $^4J_{H-H}$ = 1.8, $^5J_{H-H}$ = 0.7 Hz, H next to CF), 7.09–7.30 (m, H of Br–Ph), 7.42 (dd, $^3J_{H-H}$ = 8.1, $^4J_{H-F}$ = 7.2 Hz, H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_3), 19.1, 22.1, 30.6 (CH_2), 78.8 (d, $^4J_{C-F}$ = 3.0 Hz, C alkyne), 92.7 (C, alkyne), 108.5 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.4 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 127.2 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 128.5 (d, $^3J_{C-F}$ = 3.8 Hz, CH next to CBr), 133.2 (CH), 158.6 (d, $^1J_{C-F}$ = 246.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –107.0 (t, CF of Br–Ph) ppm. IR (ATR): $\tilde{\nu}$ = 2957 (m), 2930 (m), 2872 (m), 2233 (w), 1598 (w), 1558 (w), 1486 (s), 1476 (s), 1404 (s), 1178 (s), 1043 (m), 868 (s), 814 (s), 614 (s), 456 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 254 (39) $[M]^+$, 241 (28), 239 (31), 213 (47), 200 (21), 198 (17), 175 (10), 161 (11), 160 (100), 159 (30), 147 (48), 146 (84), 145 (10), 134 (21), 133 (45), 132 (35), 131 (24), 105 (15), 81 (7), 41 (10). HRMS: calcd. for $C_{12}H_{12}BrF$ $[M]^+$ 254.01009; found 254.01034.

1-Bromo-2-fluoro-4-[(trimethylsilyl)ethynyl]benzene (3i): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2i** (0.10 mL, 1.0 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (3.0 mL), **3i** was isolated as a colorless oil (0.166 g, 61%). R_F = 0.70 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, $^3J_{H-H}$ = 7.3 Hz, CH_3), 1.41–1.59 (m, 4 H, 2 CH_2), 2.37 (t, $^3J_{H-H}$ = 7.3 Hz, CH_2), 7.02 (ddd, $^3J_{H-F}$ = 8.4, $^4J_{H-H}$ = 1.8, $^5J_{H-H}$ = 0.7 Hz, H next to CF), 7.09–7.30 (m, H of Br–Ph), 7.42 (dd, $^3J_{H-H}$ = 8.1, $^4J_{H-F}$ = 7.2 Hz, H of Br–Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (CH_3; TMS), 96.9 (C, alkyne), 102.9 (d, $^4J_{C-F}$ = 3.0 Hz, 1 C, alkyne), 110.0 (d, $^2J_{C-F}$ = 21.0 Hz, C–Br), 119.9 (d, $^2J_{C-F}$ = 23.2 Hz, CH, next to CF), 124.4 (d, $^3J_{C-F}$ = 8.3 Hz, C next to alkyne), 129.0 (d, $^3J_{C-F}$ = 3.8 Hz, C next to C–Br), 133.6 (CH), 158.8 (d, $^1J_{C-F}$ = 246.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –106.6 (t, $^4J_{F-H}$ = 5.6, $^3J_{F-H}$ = 11.3 Hz, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2960 (m), 2899 (w), 2160 (s), 2114 (w), 1559 (m), 1474 (s), 1401 (s), 1250 (s), 1159 (s), 1042 (m), 958 (m), 837 (s), 757 (s), 689 (m), 657 (s), 615 (s), 514 (m) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 270 (19) $[M]^+$, 258 (16), 257 (100), 256 (16), 255 (99), 146 (4), 128 (4), 127 (3). HRMS: calcd. for $C_{11}H_{12}BrFSi$ $[M]^+$ 269.98702; found 269.98671.

General Procedure for the Synthesis of 4a–i: A suspension of **1**, $Pd(PPh_3)_4$ (3 mol-%), and CuI (3 mol-%) in THF (4 mL/mmol **1**) in an oven-dried pressure tube was degassed by bubbling argon through the solution for 10 min. The acetylene **2** (2.1 equiv.) and triethylamine (2.5 equiv.) were added by syringe. The mixture was heated at 50 °C for 6 h. The cooled reaction mixture was filtered, and the residue was washed with CH_2Cl_2. The filtrate was washed with a saturated solution of ammonium chloride (2 × 25 mL) and water (2 × 25 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and the solvent was removed in vacuo. The product was purified by column chromatography (silica gel, EtOAc/heptanes).

2-Fluoro-1,4-bis(phenylethynyl)benzene (4a):[19] Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2a** (0.23 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4a** was isolated as a colorless solid (0.219 g, 74%); m.p. 170–171 °C, R_F = 0.44 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.20 (m, 2 H), 7.26–7.31 (m, 6 H), 7.40–7.50 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 82.6 (C of alkyne), 88.1 (d, $^3J_{C-F}$ = 4.5 Hz, C of alkyne), 92.1 (C of alkyne), 96.1 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 112.1 (d, $^2J_{C-F}$ = 15.8 Hz, C next to CF), 118.5 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 122.7 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 124.9 (C of Ph), 125.0 (C of Ph), 127.4 (d, $^3J_{C-F}$ = 3.8 Hz, CH), 128.5 (2 CH of Ph), 128.8 (4 CH of Ph), 133.3 (4 CH of Ph), 133.3 (d, $^4J_{C-F}$ = 2.3 Hz, CH), 162.2 (d, $^1J_{C-F}$ = 250.5 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.5 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3053 (m), 2204 (w), 1610 (w), 1511 (m), 1412 (m), 1328 (w), 1275 (w), 1204 (w), 1157 (w), 1094 (w), 1025 (w), 952 (w), 834 (w), 820 (m), 751 (s), 683 (s), 524 (m), 494 (m), 470 (m), 431 (m), 379 (m) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 296 (100) $[M]^+$, 294 (19), 292 (7), 148 (17), 122 (3). HRMS: calcd. for $C_{22}H_{13}F$ $[M]^+$ 296.09958; found 296.10000. $C_{16}H_{21}F$ (296.33): calcd. C 89.17, H 4.42; found C 89.51, H 4.384.

2-Fluoro-1,4-bis(2-*p*-tolylethynyl)benzene (4b): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg,

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3 mol-%), **2b** (0.26 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4b** was isolated as a colorless solid (0.226 g, 70%); m.p. 200–202 °C, R_F = 0.41 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 6 H, CH_3), 7.17 (d, $^3J_{H-H}$ = 7.9 Hz, 4 H of Me–Ph), 7.41–7.52 (m, 5 H), 7.63–7.71 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 20.7 (CH_3), 86.4 (C of alkyne), 90.9 (C of alkyne), 91.9 (C of alkyne), 95.2 (C of alkyne), 112.2 (d, $^2J_{C-F}$ = 15.7 Hz, C next to CF), 118.4 (d, $^2J_{C-F}$ = 22.0 Hz, CH next to CF), 122.3 (C of 2-Me–Ph), 122.5 (C of 2-Me–Ph), 124.9 (d, $^3J_{C-F}$ = 8.8 Hz, C next to alkyne), 125.6 (CH of 2 Me–Ph), 125.7 (CH of 2 Me–Ph), 127.2 (d, $^3J_{C-F}$ = 3.8 Hz, CH), 128.8 (CH of 2 Me–Ph), 128.8 (CH of 2 Me–Ph), 129.5 (CH of 2 Me–Ph), 129.6 (CH of 2 Me–Ph), 131.9 (CH of 2 Me–Ph), 132.0 (CH of 2 Me–Ph), 133.0 (d, $^4J_{C-F}$ = 2.3 Hz, CH), 140.4 (CH_3 of 2-Me–Ph), 140.5 (CH_3 of 2-Me–Ph), 162.1 (d, $^1J_{C-F}$ = 250.5 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, CDCl3): δ = –109.7 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3022 (w), 2918 (m), 2851 (m), 2213 (m), 1901 (w), 1723 (w), 1603 (w), 1538 (s), 1518 (s), 1436 (s), 1413 (s), 1181 (m), 1019 (w), 954 (m), 838 (w), 809 (s), 749 (s), 719 (s), 693 (m), 612 (m), 538 (s), 504 (s), 471 (m) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 324 (100) $[M]^+$, 323 (11), 162 (7), 161 (5). HRMS: calcd. for $C_{24}H_{17}F$ $[M]^+$ 324.13088; found 324.13098.

2-Fluoro-1,4-bis[(2-methylphenyl)ethynyl]benzene (4c): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2c** (0.26 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4c** was isolated as a colorless solid (0.221 g, 68%); m.p. 103–104 °C, R_F = 0.27 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, CH_3), 2.59 (s, 3 H, CH_3), 7.21–7.27 (m, 2 H), 7.29–7.37 (m, 6 H), 7.51–7.59 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 20.8 (CH_3), 86.5 (C of alkyne), 91.1 (C of alkyne), 92.0 (C of alkyne), 95.2 (C of alkyne), 112.3 (d, $^2J_{C-F}$ = 16.8 Hz, C next to CF), 118.3 (d, $^2J_{C-F}$ = 22.5 Hz, CH next to CF), 122.4 (C of 2-Me–Ph), 122.6 (C of 2-Me–Ph), 125.0 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 125.7 (CH of 2 Me–Ph), 125.7 (CH of 2 Me–Ph), 127.3 (d, $^3J_{C-F}$ = 3.8 Hz, CH), 128.9 (CH of 2 Me–Ph), 128.9 (CH of 2 Me–Ph), 129.6 (CH of 2 Me–Ph), 129.6 (CH of 2 Me–Ph), 132.0 (CH of 2 Me–Ph), 132.0 (CH of 2 Me–Ph), 133.0 (d, $^4J_{C-F}$ = 2.3 Hz, CH), 140.5 (CH_3 of Me–Ph), 140.6 (CH_3 of Me–Ph), 162.1 (d, $^1J_{C-F}$ = 250.5 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.4 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3017 (m), 1901 (w), 1598 (m), 1536 (m), 1507 (m), 1414 (m), 1212 (m), 1083 (m), 1037 (m), 954 (m), 935 (m), 862 (m), 817 (m), 755 (s), 710 (m), 616 (m), 551 (m), 444 (s), 396 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 324 (100) $[M]^+$, 323 (16), 320 (8), 307 (12), 162 (8), 147 (3), 115 (5). HRMS: calcd. for $C_{24}H_{17}F$ $[M]^+$ 324.13088; found 324.13091. $C_{24}H_{17}F$ (408.55): calcd. C 88.86, H 5.28; found C 89.00, H 5.24.

2-Fluoro-1,4-bis[2-(4-propylphenyl)ethynyl]benzene (4d):[19] Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2b** (0.33 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4b** was isolated as a colorless solid (0.267 g, 70%); m.p. 147–149 °C, R_F = 0.31 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, $^3J_{H-H}$ = 8.6 Hz, 6 H, CH_3), 1.59–1.71 (m, 4 H, CH_2), 2.61 (t, $^3J_{H-H}$ = 7.7 Hz, 4 H, CH_2), 7.17 (d, $^3J_{H-H}$ = 8.5 Hz, 4 H of *n*Pr–Ph), 7.23–7.29 (m, 2 H), 7.42–7.49 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 24.6 (CH_2), 38.3 (CH_2), 82.3 (C of alkyne), 87.8 (d, $^3J_{C-F}$ = 4.5 Hz, C of alkyne), 92.6 (C of alkyne), 96.6 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 112.5 (d, $^2J_{C-F}$ = 16.7 Hz, C next to CF), 118.5 (d, $^2J_{C-F}$ = 23.4 Hz, C next to alkyne), 120.2 (d, $^2J_{C-F}$ = 13.3 Hz, CH next to CF), 125.2 (d, $^3J_{C-F}$ = 10.2 Hz, C next to alkyne), 127.5 (d, $^3J_{C-F}$ = 4.1 Hz, CH), 128.9 (2CH of *n*Pr–Ph), 128.9 (2CH of *n*Pr–Ph), 131.9 (2CH of *n*Pr–Ph), 131.9 (2 CH of *n*Pr–Ph), 133.4 (d, $^4J_{C-F}$ = 2.1 Hz, CH), 162.4 (d, $^1J_{C-F}$ = 253.7 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.8 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3029 (w), 2955 (m), 2927 (m), 2867 (m), 2215 (w), 1914 (w), 1603 (m), 1515 (m), 1412 (s), 1211 (s), 1093 (s), 954 (s), 865 (s), 816 (s), 621 (s), 538 (s), 461 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 380 (100) $[M]^+$, 352 (18), 351 (66), 322 (30), 161 (23). HRMS: calcd. for $C_{28}H_{25}F$ $[M]^+$ 380.19348; found 380.19424. $C_{28}H_{25}F$ (380.50): calcd. C 88.38, H 6.62; found C 88.14, H 6.21.

1,4-Bis[2-(4-*tert*-butylphenyl)ethynyl]-2-fluorobenzene (4e): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2e** (0.331 g, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4e** was isolated as a colorless solid (0.256 g, 63%); m.p. 235–237 °C, R_F = 0.29 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 18 H, CH_3), 7.15–7.21 (m, 2 H), 7.28–7.32 (m, 4 H), 7.36–7.44 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.2 (6 CH_3), 34.9 (2 C of *t*Bu), 82.0 (C of alkyne), 87.6 (C of alkyne), 92.2 (C of alkyne), 96.3 (d, $^3J_{C-F}$ = 3.8 Hz, C of alkyne), 112.1 (d, $^2J_{C-F}$ = 16.0 Hz, C next to CF), 118.4 (d, $^2J_{C-F}$ = 22.5 Hz, CH next to CF), 119.7 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 124.9 (C of *t*Bu–Ph), 125.0 (C of *t*Bu–Ph), 127.3 (2 CH of *t*Bu–Ph), 127.3 (2 CH of *t*Bu–Ph), 127.4 (d, $^3J_{C-F}$ = 3.8 Hz, CH), 131.5 (2 CH of *t*Bu–Ph), 131.5 (2 CH of *t*Bu–Ph), 133.2 (d, $^4J_{C-F}$ = 1.5 Hz, CH), 152.2 (2C next to *t*Bu), 162.1 (d, $^1J_{C-F}$ = 250.5 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.7 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2957 (m), 2865 (m), 2216 (w), 1914 (m), 1667 (m), 1611 (m), 1514 (m), 1488 (m), 1413 (s), 1362 (m), 1264 (s), 1212 (m), 1101 (m), 955 (m), 870 (m), 833 (s), 697 (m), 561 (s), 431 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 408 (100) $[M]^+$, 394 (29), 393 (88), 335 (5), 309 (5), 189 (21), 161 (14). HRMS: calcd. for $C_{30}H_{30}F$ $[M]^+$ 409.2326; found 409.2322. $C_{30}H_{29}F$ (408.55): calcd. C 88.20, H 7.15; found C 88.43, H 7.075.

2-Fluoro-1,4-bis[(4-methoxyphenyl)ethynyl]benzene (4f): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.65 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2f** (0.25 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4f** was isolated as a colorless solid (0.244 g, 69%); m.p. 182–184 °C, R_F = 0.33 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, MeO), 6.79–6.84 (m, 4 H), 7.34–7.44 (m, 2 H), 7.34–7.44 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3 (CH_3 of MeO), 81.4 (C of alkyne), 87.0 (C of alkyne), 92.0 (C of alkyne), 96.1 (C of alkyne), 112.1 (d, $^2J_{C-F}$ = 16.5 Hz, C next to CF), 114.1 (2 CH of MeO–Ph), 114.1 (2 CH of MeO–Ph), 114.7 (C of Me–Ph), 114.9 (C of Me–Ph), 118.2 (d, $^2J_{C-F}$ = 22.5 Hz, CH next to CF), 124.9 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 127.2 (d, $^3J_{C-F}$ = 3.0 Hz, CH), 133.2 (2 CH of MeO–Ph), 133.3 (2 CH of MeO–Ph), 133.2 (d, $^4J_{C-F}$ = 2.0 Hz, CH), 160.0 (2 C of MeO–Ph), 161.9 (d, $^1J_{C-F}$ = 249.8 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –110.0 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2933 (w), 2836 (w), 2210 (m), 1603 (m), 1540 (m), 1517 (s), 1458 (m), 1414 (m), 1289 (m), 1242 (s), 1168 (s), 1028 (s), 954 (m), 839 (s), 826 (s), 798 (s), 585 (m), 529 (m), 465 (s), 424 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 356 (100) $[M]^+$, 341 (32), 313 (4), 270 (7), 178 (11), 122 (4). HRMS: calcd. for $C_{24}H_{17}O_2F$ $[M]^+$ 356.12071; found 356.12046. $C_{16}H_{21}F$ (296.33): calcd. C 89.17, H 4.42; found C 89.51, H 4.38.

2-Fluoro-1,4-bis[2-(4-fluorophenyl)ethynyl]benzene (4g): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2g** (0.24 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4g** was isolated as a colorless solid (0.226 g, 68%); m.p. 154–155 °C, R_F = 0.28 (hexane/CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.02–7.11 (m, 4 H), 7.22–7.28 (m, 2 H), 7.43-7.59 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 82.3 (C of alkyne), 87.7 (C of alkyne), 91.0 (C of alkyne), 95.0

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(d, $^3J_{C-F}$ = 5.5 Hz, C of alkyne), 112.0 (d, $^2J_{C-F}$ = 18.4 Hz, C next to CF), 115.8 (dd, $^2J_{C-F}$ = 21.9 Hz, 4 CH of F–Ph), 118.4 (d, $^2J_{C-F}$ = 23.4 Hz, CH next to CF), 118.7 (dd, $^4J_{C-F}$ = 3.0 Hz, 2 C of F–Ph), 124.7 (d, $^3J_{C-F}$ = 10.0 Hz, C next to alkyne), 127.3 (d, $^3J_{C-F}$ = 4.0 Hz, CH), 133.2 (d, $^4J_{C-F}$ = 2.0 Hz, CH), 133.7 (dd, $^3J_{C-F}$ = 8.0 Hz, 4 CH of F–Ph), 162.3 (d, $^1J_{C-F}$ = 249.5 Hz, F–Ph, CF), 162.6 (d, $^1J_{C-F}$ = 252.8 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.5 (m, 3 CF) ppm. IR (ATR): $\tilde{\nu}$ = 3062 (w), 2924 (w), 2215 (w), 1613 (w), 1599 (m), 1538 (m), 1599 (m), 1538 (m), 1515 (m), 1415 (m), 1231 (m), 1209 (m), 1154 (m), 1094 (m), 956 (m), 838 (s), 812 (s), 785 (m), 739 (m), 526 (s), 386 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 332 (100) $[M]^+$, 330 (10), 310 (5), 166 (13). HRMS: calcd. for $C_{22}H_{11}F_3$ $[M]^+$ 332.08074; found 332.08099. $C_{22}H_{11}F_3$ (332.32): calcd. C 79.51, H 3.34; found C 79.61, H 3.40.

2-Fluoro-1,4-bis[2-(trimethylsilyl)ethynyl]benzene (4h):[19] Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2i** (0.26 mL, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4h** was isolated as a colorless solid (0.212 g, 73%); m.p. 94–95 °C, R_F = 0.57 (hexane/ethyl acetate = 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.24 (s, 9 H, TMS), 0.25 (s, 9 H, TMS), 7.12–7.18 (m, 2 H), 7.36 (dd, $^3J_{H-H}$ = 8.2, $^4J_{H-F}$ = 7.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.00 (6 CH_3, TMS), 97.7 (C of alkyne), 97.7 (C of alkyne), 102.3 (C of alkyne), 103.4 (C of alkyne), 112.3 (d, $^2J_{C-F}$ = 16.0 Hz, C next to CF), 118.8 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 125.1 (d, $^3J_{C-F}$ = 8.0 Hz, C next to alkyne), 127.7 (d, $^3J_{C-F}$ = 3.0 Hz, CH), 133.8 (d, $^4J_{C-F}$ = 2.3 Hz, CH), 162.6 (d, $^1J_{C-F}$ = 250.5 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.4 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2955 (w), 2897 (w), 2157 (m), 1608 (w), 1539 (w), 1488 (m), 1406 (m), 1246 (m), 961 (m), 836 (s), 753 (s), 696 (m), 626 (m), 534 (w), 461 (w), 420 (w), 398 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 288 (45) $[M]^+$, 275 (10), 274 (27), 273 (100), 196 (8), 129 (19). HRMS: calcd. for $C_{16}H_{21}FSi_2$ $[M]^+$ 288.11603; found 288.11609. $C_{16}H_{21}FSi_2$ (288.51): calcd. C 66.61, H 7.34; found C 66.73, H 7.23.

1-[2-{3-Fluoro-4-(2-{4-(pentyloxy)phenyl}ethynyl)phenyl}ethynyl]-4-(pentyloxy)benzene (4i): Starting with **1** (253 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2j** (0.394 g, 2.1 mmol), Et_3N (0.35 mL, 2.5 mmol), and THF (4.0 mL), **4i** was isolated as a colorless solid (0.321 g, 69%); m.p. 135–136 °C, R_F = 0.36 (hexane/CH_2Cl_2 = 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, $^3J_{H-H}$ = 7.7 Hz, 6 H, CH_3), 1.35–1.47 (m, 8 H, CH_2), 1.75–1.84 (m, 4 H, CH_2), 3.97 (t, $^3J_{H-H}$ = 6.7 Hz, 4 H, OCH_2), 6.85–6.89 (m, 4 H), 6.85–6.89 (m, 2 H), 7.41–7.50 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.5 (CH_2), 28.2 (CH_2), 28.9 (CH_2), 68.1 (OCH_2), 81.4 (C of alkyne), 86.9 (d, $^3J_{C-F}$ = 4.5 Hz, C of alkyne), 92.2 (C of alkyne), 96.2 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 112.1 (d, $^2J_{C-F}$ = 16.0 Hz, C next to CF), 114.5 (4 CH of PentO–Ph), 114.6 (C of PentO–Ph), 114.7 (C of PentO–Ph), 118.2 (d, $^2J_{C-F}$ = 22.0 Hz, CH next to CF), 124.9 (d, $^3J_{C-F}$ = 9.0 Hz, C next to alkyne), 127.2 (d, $^3J_{C-F}$ = 3.0 Hz, CH), 133.2 (2 CH of PentO–Ph), 133.3 (2 CH of PentO–Ph), 133.2 (d, $^4J_{C-F}$ = 2.0 Hz, CH), 159.7 (C, PentO), 162.0 (d, $^1J_{C-F}$ = 250.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –110.1 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 2955 (w), 2929 (m), 2870 (m), 2216 (m), 1603 (m), 1566 (w), 1516 (m), 1467 (m), 1416 (m), 1285 (s), 1248 (s), 1211 (s), 1172 (s), 1049 (m), 983 (m), 955 (m), 866 (m), 828 (s), 621 (m), 534 (m), 418 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 468 (67) $[M]^+$, 398 (17), 329 (22), 328 (100), 327 (16), 299 (13), 55 (14). HRMS: calcd. for $C_{32}H_{33}O_2F$ $[M]^+$ 468.24591; found 468.24541. $C_{32}H_{33}O_2F$ (468.602): calcd. C 82.02, H 7.10; found C 81.94, H 7.04.

General Procedure for the Synthesis of 5a–e: A suspension of substituted **3**, $Pd(PPh_3)_4$ (3 mol-%), and CuI (3 mol-%) in THF (3 mL/mmol 3) in an oven-dried pressure tube was degassed by bubbling argon through the solution for 10 min. The acetylene **2** (1.1 equiv.) and triethylamine (2.0 equiv.) were added by syringe. The mixture was heated at 50 °C for 6 h. The cooled reaction mixture was filtered, and the residue was washed with CH_2Cl_2. The filtrate was washed with a saturated solution of ammonium chloride (2 × 25 mL) and water (2 × 25 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and the solvent was removed in vacuo. The product was purified by column chromatography (silica gel, EtOAc/heptanes).

2-Fluoro-1-[2-(4-fluorophenyl)ethynyl]-4-(2-phenylethynyl)benzene (5a): Starting with **3a** (275 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2g** (0.125 mL, 1.1 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (2.0 mL), **5a** was isolated as a colorless solid (0.212 g, 68%); m.p. 205–207 °C, R_F = 0.34 (hexane/CH_2Cl_2 = 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.02–7.19 (m, 2 H), 7.23–7.31 (m, 2 H), 7.34–7.40 (m, 3 H), 7.45–7.58 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 82.3 (C of alkyne), 87.9 (d, $^3J_{C-F}$ = 5.8 Hz, C of alkyne), 92.1 (C of alkyne), 95.0 (d, $^4J_{C-F}$ = 4.3 Hz, C of alkyne), 111.9 (d, $^2J_{C-F}$ = 16.4 Hz, C next to CF), 115.8 (d, $^2J_{C-F}$ = 21.0 Hz, 2 CH of F–Ph), 118.5 (d, $^2J_{C-F}$ = 21.0 Hz, CH next to CF), 118.8 (d, $^4J_{C-F}$ = 2.8 Hz, C of F–Ph), 122.6 (C of Ph), 125.5 (d, $^3J_{C-F}$ = 10.0 Hz, 1 C), 127.4 (d, $^3J_{C-F}$ = 3.4 Hz, CH), 128.5 (2 CH of Ph), 128.8 (CH of Ph), 131.7 (2CH of Ph), 133.2 (d, $^4J_{C-F}$ = 2.0 Hz, CH), 133.7 (d, $^3J_{C-F}$ = 8.1 Hz, 2 CH of F–Ph), 162.0 (d, $^1J_{C-F}$ = 250.0 Hz, CF), 162.8 (d, $^1J_{C-F}$ = 255.0 Hz, CF of F–Ph) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.5 (m, 2 CF) ppm. IR (ATR): $\tilde{\nu}$ = 3058 (w) 3046 (w), 2927 (w), 1612 (w), 1595 (w), 1539 (w), 1512 (s), 1415 (s), 1210 (s), 1153 (m), 1095 (m), 955 (m), 866 (m), 833 (s), 752 (s), 685 (s), 597 (s), 525 (s), 478 (s), 395 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 314 (100) $[M]^+$, 312 (20), 157 (20). HRMS: calcd. for $C_{22}H_{12}F_2$ $[M]^+$ 314.09016; found 314.09072.

2-Fluoro-4-(2-phenylethynyl)-1-[2-(2-tolyl)ethynyl]benzene (5b): Starting with **3a** (275 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2c** (0.138 mL, 1.1 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (2.0 mL), **5b** was isolated as a colorless solid (0.188 g, 61%); m.p. 117–119 °C, R_F = 0.39 (hexane/CH_2Cl_2 = 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, CH_3), 7.10–7.14 (m, 6 H), 7.27–7.32 (m, 3 H), 7.38–7.51 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3), 86.4 (C of alkyne), 88.1 (C of alkyne), 92.0 (C of alkyne), 95.3 (C of alkyne), 112.5 (d, $^2J_{C-F}$ = 22.4 Hz, C next to CF), 118.3 (d, $^2J_{C-F}$ = 24.0 Hz, CH next to CF), 122.5 (CH of 2 Me–Ph), 122.6 (C of 2 Me–Ph), 124.7 (d, $^3J_{C-F}$ = 9.8 Hz, 1 C), 125.7 (CH of 2 Me–Ph), 127.4 (d, $^3J_{C-F}$ = 3.7 Hz, CH), 128.5 (CH of Ph), 128.5 (2 CH of Ph), 128.8 (CH of Ph), 128.8 (CH of Ph), 129.6 (CH of 2 Me–Ph), 131.7 (CH of 2 Me–Ph), 131.9 (CH of 2 Me–Ph), 133.0 (d, $^4J_{C-F}$ = 2.0 Hz, CH), 140.5 (C), 162.1 (d, $^1J_{C-F}$ = 250.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, CDCl3): δ = –109.5 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3053 (w), 3016 (w), 2922 (w), 2733 (w), 1609 (m), 1596 (m), 1509 (m), 1413 (m), 1206 (m), 1155 (m), 1088 (m), 952 (m), 818 (m), 791 (w), 751 (s), 684 (s), 612 (m), 526 (m), 453 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 310 (100) $[M]^+$, 309 (31), 308 (10), 307 (21), 289 (11). HRMS: calcd. for $C_{22}H_{12}F_2$ $[M]^+$ 310.11523; found 310.11527. $C_{22}H_{12}F_2$ (310.364): calcd. C 89.01, H 4.87; found C 89.20, H 4.81.

1-[2-(4-*tert*-Butylphenyl)ethynyl]-2-fluoro-4-(2-phenylethynyl)benzene (5c): Starting with **3a** (275 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2e** (0.174 g, 1.1 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (2.0 mL), **5c** was isolated as a colorless solid (0.198 g, 56%); m.p. 144–146 °C, R_F = 0.32 (hexane/

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CH_2Cl_2 = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.24 (s, 9 H, *t*Bu), 7.17–7.22 (m, 2 H), 7.26–7.32 (m, 6 H), 7.37–7.49 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.5 (CH_3, *t*Bu), 35.3 (C of *t*Bu), 82.4 (C of alkyne), 87.9 (C of alkyne), 92.6 (C of alkyne), 96.6 (C of alkyne), 112.5 (d, $^2J_{C-F}$ = 23.3 Hz, C next to CF), 118.8 (d, $^2J_{C-F}$ = 23.3 Hz, CH next to CF), 119.6 (C of *t*Bu–Ph), 124.7 (d, $^3J_{C-F}$ = 8.7 Hz, 1 C), 125.8 (2 CH of *t*Bu–Ph), 125.9 (3 CH of Ph), 127.5 (d, $^3J_{C-F}$ = 4.1 Hz, CH), 131.8 (2CH of *t*Bu–Ph), 131.9 (2CH of Ph), 133.5 (d, $^4J_{C-F}$ = 2.7 Hz, CH), 152.5 (2C of *t*Bu),162.6 (d, $^1J_{C-F}$ = 250.0 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.6 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3055 (w), 2959 (w), 2901 (w), 2866 (w), 1612 (w), 1541 (w), 1415 (m), 1362 (m), 1330 (w), 1267 (m), 1107 (m), 1092 (m), 1015 (w), 864 (m), 833 (s), 751 (s), 685 (s), 670 (w), 560 (s), 526 (m), 430 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 352 (89) $[M]^+$, 338 (27), 337 (100), 322 (10), 309 (14), 296 (11), 186 (14), 154 (30). HRMS: calcd. for $C_{26}H_{21}F$ $[M]^+$ 352.16218; found 352.16211. $C_{26}H_{21}F$ (352.443): calcd. C 88.60, H 6.01; found C 89.01, H 6.41.

1-[2-(4-*tert*-Butylphenyl)ethynyl]-2-fluoro-4-[2-(4-methylphenyl)ethynyl]benzene (5d): Starting with **3b** (287 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2e** (0.174 g, 1.1 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (2.0 mL), **5d** was isolated as a colorless solid (0.194 g, 53%); m.p. 179–180 °C, R_F = 0.31 (hexane/CH_2Cl_2 = 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*Bu), 2.38 (s, 3 H, CH_3), 7.17 (d, $^3J_{H-H}$ = 7.7 Hz, 2 H of 4 Me–Ph), 7.23–7.30 (m, 1 H), 7.36–7.51 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 (CH_3 of Me–Ph), 31.2 (CH_3 of *t*Bu), 34.9 (C of *t*Bu), 82.0 (C of alkyne), 87.5 (d, $^3J_{C-F}$ = 4.8 Hz, C of alkyne), 92.2 (C of alkyne), 96.3 (d, $^4J_{C-F}$ = 3.0 Hz, C of alkyne), 112.1 (d, $^2J_{C-F}$ = 20.0 Hz, C next to CF), 118.3 (d, $^2J_{C-F}$ = 23.0 Hz, CH next to CF), 119.6 (C of *t*Bu–Ph), 119.7 (C of Me–Ph), 124.9 (d, $^3J_{C-F}$ = 8.6 Hz, 1 C), 125.5 (CH of *t*Bu–Ph), 125.5 (CH of *t*Bu–Ph), 127.3 (d, $^3J_{C-F}$ = 4.1 Hz, CH), 129.2 (CH of Me–Ph), 129.3 (CH of Me–Ph), 131.4 (CH of Me–Ph), 131.4 (CH of Me–Ph), 131.6 (CH of *t*Bu–Ph), 131.7 (CH of *t*Bu–Ph), 133.2 (d, $^4J_{C-F}$ = 2.7 Hz, CH), 139.0 (C of Me–Ph), 152.2 (C of *t*Bu–Ph),162.6 (d, $^1J_{C-F}$ = 249.8 Hz, CF) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.8 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3036 (w), 2953 (w), 2902 (w), 2864 (w), 1603 (w), 1515 (w), 1362 (m), 1267 (m), 1212 (m), 1106 (m), 956 (m), 1014 (m), 868 (m), 832 (s), 818 (s), 749 (s), 620 (m), 560 (m), 529 (w), 463 (w), 395 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 366 (100) $[M]^+$, 352 (28), 351 (98), 323 (17), 175 (18), 161 (25). HRMS: calcd. for $C_{27}H_{23}F$ $[M]^+$ 366.17783; found 366.17798. $C_{27}H_{23}F$ (366.470): calcd. C 88.49, H 6.33; found C 88.32, H 6.43.

2-Fluoro-1-[2-(4-methoxyphenyl)ethynyl]-4-[2-(4-methylphenyl)ethynyl]benzene (5e): Starting with **3b** (287 mg, 1.0 mmol), $Pd(PPh_3)_4$ (34.6 mg, 3 mol-%), CuI (5.7 mg, 3 mol-%), **2f** (0.129 g, 1.1 mmol), Et_3N (0.28 mL, 2.0 mmol), and THF (2.0 mL), **5e** was isolated as a colorless solid (0.233 g, 68%); m.p. 182 °C, R_F = 0.56 (heptane/ethyl acetate = 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.89 (d, $^3J_{H-H}$ = 9.3 Hz, 2 H of 4 Me–Ph), 7.15–7.28 (m, 3 H), 7.40–7.53 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 (CH_3), 55.4 (MeO), 81.4 (C of alkyne), 87.5 (d, $^3J_{C-F}$ = 4.9 Hz, C of alkyne), 92.2 (C of alkyne), 96.2 (d, $^4J_{C-F}$ = 2.8 Hz, C of alkyne), 112.2 (d, $^2J_{C-F}$ = 16.3 Hz, C next to CF), 112.2 (CH of MeO–Ph), 112.3 (CH of MeO–Ph), 114.9 (C of MeO–Ph), 118.4 (d, $^2J_{C-F}$ = 21.0 Hz, CH next to CF), 119.6 (C of Me–Ph), 124.7 (d, $^3J_{C-F}$ = 8.1 Hz, C), 127.3 (d, $^3J_{C-F}$ = 4.0 Hz, CH), 129.2 (2 CH of Me–Ph), 131.6 (2 CH of MeO–Ph), 133.1 (d, $^4J_{C-F}$ = 2.7 Hz, CH), 133.3 (2 CH of Me–Ph), 139.1 (C of Me–Ph), 160 (C of MeO–Ph) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –110.0 (t, CF) ppm. IR (ATR): $\tilde{\nu}$ = 3023 (w), 2919 (w), 2853 (w), 2839 (w), 2211 (w), 1899 (w), 1601 (w), 1516 (s), 1414 (m), 1247 (m), 1172 (s), 1031 (s), 810 (s), 524 (s), 457 (m), 393 (w) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%) = 340 (100) $[M]^+$, 325 (28), 297 (11), 170 (11.8). HRMS: calcd. for $C_{24}H_{17}OF$ $[M]^+$ 340.12579; found 340.12593.

Supporting Information (see footnote on the first page of this article): Copies of NMR spectra, DFT-calculated structures.

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