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Site-Selective Suzuki–Miyaura and Sonogashira Cross Coupling Reactions of the Bis(triflate) of 2,4′-Bis(hydroxy)diphenyl Sulfone

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Described is the synthesis of novel arylated and alkynylated 2,4′-diphenyl sulfones based on what are, to the best of our knowledge, the first palladium(0)-catalyzed cross-coupling reactions of bis(triflates) of 2,4′-bis(hydroxy)diphenyl sulfone. The reactions proceed with very good site-selectivity.

Functionalized arylated sulfones are important structural motifs in medicinal chemistry.[1–14] Pharmacological properties include inhibition of the enzymes phospholipidase A_2,[1,2] catechol O-methyltransferase,[3] dihydropteroate synthase of *Escherichia coli* and the main protease of the recombinant SARS coronavirus.[4] Biological activities like antibacterial activity,[1] hypolipidemic,[5] cytotoxic against HeLa cells and the antipicornavirus,[6] neuropeptide Y_1 receptor binding,[7] anti-HIV,[8] anticholesteremic,[9] binding to human muscarinic M_1 and M_2 receptors,[10] histamine H_3-receptor antagonistic,[11] antiprotozoal,[12] and binding to the human cannabinoid CB_1 receptor[13] activities have also been reported. Alkynylated sulfones are potential candidates for liquid crystalline materials. Besides a vast range of bioactivities, conjugated enynes are also important synthetic intermediates.[14]

Known syntheses of diaryl sulfones include the oxidation of diaryl sulfides,[15] acylation of electron rich benzene derivatives with phenylsulfonyl chloride and benzenesulfonic acid.[16] Despite the usefulness of these methods, limitations related to scope and low regioselectivities exist, owing to the harsh reaction conditions. A number of mild transition metal-mediated approaches to diaryl sulfones have been reported. These include the CuI/proline-mediated reaction of sodium benzenesulfinate with aryl iodides[17a] and $Cu(OAc)_2$-catalyzed reaction sodium benzenesulfinate with 4-methoxybenzeneboronic acid.[17b] In addition, Suzuki reactions of phenylsulfonic acid chloride with arylboronic acids have been reported.[18] A different approach to diaryl sulfones relies on cyclization reactions of building blocks containing a sulfone moiety.[19] In recent years, site selective palladium catalyzed cross coupling reactions have been intensively studied. The selectivity of such reactions is generally controlled by electronic and steric parameters. The first attack usually occurs at the electronically more deficient or sterically less hindered position.[20–22] Recently, we reported[23] the synthesis of bis(diaryl) sulfones by site-selective Suzuki–Miyaura reactions of the bis(triflate) of 2,4′-bis(dihydroxy)diphenyl sulfone. Herein, we report full details of these studies. With regard to our preliminary communication, we have considerably extended the scope and report, for the first time, Sonogashira reactions which also proceed with excellent site-selectivity. This extension of synthetic scope could be of worth and interest because the regioselectivity in Sonogashira alkynylation reactions remains a challenge, owing to the low steric demand of alkynyl cuprates as reaction partners, Glaser homo-coupling as a side-reaction, and increased reactivity of the substrate after the first alkynylation step (owing to the electronic influence of the alkynyl group).[1c] Indeed, the product distribution of Sonogashira reactions of polyhalogenated substrates or polytriflates is not necessarily the same, as for Suzuki reactions of the same substrates, and the degree of regioselectivity of Sonogashira reactions is also not predictable, based on the results of the analogous Suzuki reactions. The products reported herein, arylated and alkynylated diaryl sulfones are of potential pharmacological relevance and have, to the best of our knowledge, not been reported so far. It can be expected that they are not readily available by other methods.

Results and Discussion

Bis(triflate) **2** was prepared in 81% yield by reaction of commercially available 2,4′-bis(hydroxy)-diphenyl sulfone (**1**) with triflic anhydride (Scheme 1).

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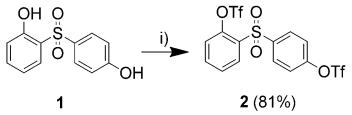
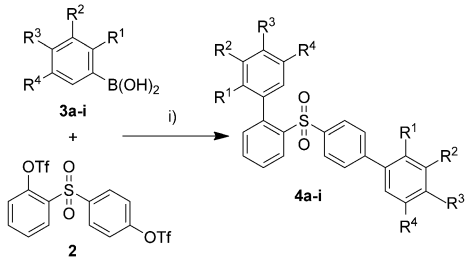


Scheme 1. Synthesis of **2**. Reagents and conditions: i) CH_2Cl_2, **1** (1.0 equiv), −78 °C, pyridine (4.0 equiv), Tf_2O (2.4 equiv), −78→0 °C, 4 h.

Suzuki–Miyaura reactions

2,4′-Bis(aryl)diphenyl sulfones **4a–i** were prepared in 55–75% yields by Suzuki–Miyaura reaction[24] of **2** with 2.6 equiv of arylboronic acids **3a–i** (Scheme 2, Table 1). The best yields were



Scheme 2. Synthesis of **4a–i**. Reagents and conditions: i) **2** (1.0 equiv), **3a–i** (2.6 equiv), K_3PO_4 (3.0 equiv), $[Pd(PPh_3)_4]$ (6 mol%), 1,4-dioxane (5 mL per 1 mmol of **2**), 110 °C, 4 h.

Table 1. Synthesis of 2,4′-bis(aryl)diphenyl sulfones **4a–i**.

3, 4	R^1	R^2	R^3	R^4	4 [%][a]
a	H	H	H	H	75
b	H	H	Me	H	70
c	H	CF_3	H	H	60
d	OMe	H	H	H	62
e	H	H	CF_3	H	65
f	H	H	*t*Bu	H	70
g	H	H	F	H	55
h	H	H	vinyl	H	65
i	H	Me	H	Me	60

[a] Yields of isolated products.

achieved when the reactions were carried out using $[Pd(PPh_3)_4]$ (6 mol%) as the catalyst, whereas employment of other catalysts, such as $[Pd(OAc)_2]$/XPhos, resulted in a decrease of the yield. Similar conditions were previously used in Suzuki reactions of related bis(triflates).[22] The use of potassium phosphate (K_3PO_4) as the base and 1,4-dioxane (110 °C, 4 h) gave optimal yields. The best yield was obtained for the reaction of simple phenylboronic acid. The lowest yield was obtained for 4-fluorophenylboronic acid, which might be attributed to its low nucleophilicity (owing to the electron-withdrawing fluorine atom). The structure of **4e** was independently confirmed by X-ray crystal structure analysis (Figure 1).[25]

2-Trifluoromethanesulfonyloxy-4′-(aryl)diphenyl sulfones **5a–d** were prepared in 62–76% yield by Suzuki–Miyaura reaction

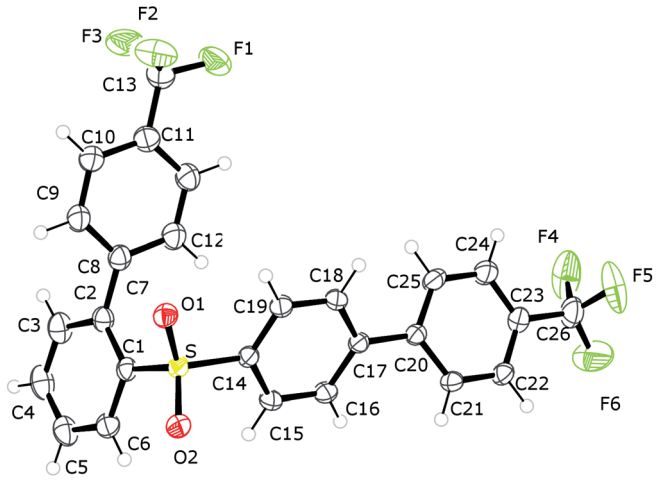
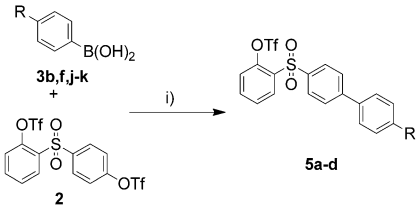


Figure 1. Crystal structure of **4e**.

of **2** with arylboronic acids **3b,f,j,k** (1.1 equiv) in the presence of $[Pd(PPh_3)_4]$ (3 mol%). The reactions proceeded with very good site-selectivity in favor of position C-4′ (Scheme 3,



Scheme 3. Synthesis of **5a–d**. Reagents and conditions: i) **2** (1.0 equiv), **3b,f,j,k** (1.1 equiv), K_3PO_4 (1.5 equiv), $[Pd(PPh_3)_4]$ (3 mol%), 1,4-dioxane (5 mL per 1 mmol of **2**), 70 °C, 4 h.

Table 2). In most cases, a small amount of the bis-coupled product could be detected in the crude product before chromatography (by ^1H NMR spectroscopy and GC–MS). Therefore, the yields of mono-substituted products **5** are often less than

Table 2. Synthesis of **5a–d**.

5	3	R	5 [%][a]
a	**b**	Me	62
b	**j**	Et	75
c	**f**	*t*Bu	70
d	**k**	MeO	76

[a] Yields of isolated products.

the yields of the corresponding disubstituted products **4**, because of practical difficulties during the chromatographic purification of products **5** and loss of material (because the R_f values of impurities were close the R_f value of the desired product. In case of the synthesis of products **4**, the reactions

were much cleaner and the chromatographic purifications much easier without much loss of material. All products were isolated in pure form by chromatographic purification. During the optimization, the temperature played a crucial role. It proved to be important to perform the reaction at 70 instead of 110 °C to induce a good selectivity.

The structure of **5b** was confirmed by 2D NMR spectroscopy (Figure 2). Assignments of chemical shifts of C and H were completed with the help of ^{1}H NMR, HMQC and COSY experiments. The NOESY correlation of CH_2 with H-3″/H-5″ and H-2″/H-6″ with H-3′/H-5′ provided the information that the aryl group is connected to carbon C-4′. The structure was further confirmed by strong HMBC correlations of H-2″/H-6″ with C-1″ & C-4′ and HMBC correlation from the other ring H-3′/H-5′ to C-1″. These careful and clear correlations proved, unambiguously, the connectivity of the first aryl group to C-4′.

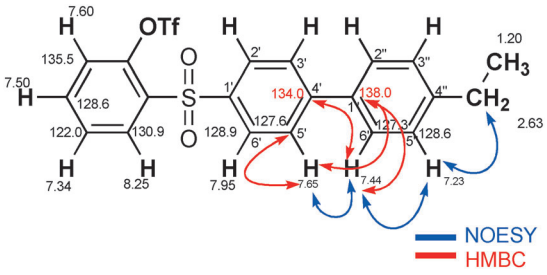
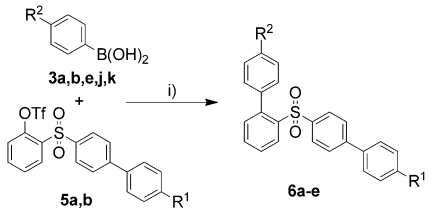


Figure 2. 2D NMR correlations (NOESY and HMBC) of **5b**.

The reaction of **5a** and **5c** with arylboronic acids **3a,b,e,j,k** (1.1 equiv) gave 2,4′-bis(aryl)diphenyl sulfones **6a–e** containing two different aryl groups in 50–64% yield (Scheme 4, Table 3). Interestingly, the yield of **6d** derived from the electron poor boronic acid **3e** proved to be the highest.



Scheme 4. Synthesis of **6a–e**. Reagents and conditions: i) **5** (1.0 equiv), **3a,b,e,j–k** (1.1 equiv), K_3PO_4 (1.5 equiv), $[Pd(PPh_3)_4]$ (3 mol%), 1,4-dioxane (5 mL per 1 mmol of **2**), 70 °C, 4 h.

Sonogashira reactions

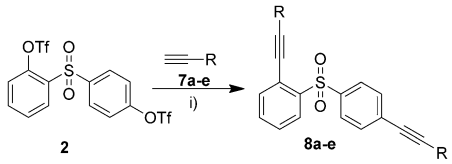
Recently, Takahashi et al. described the formation of highly substituted enynes by coupling reaction of alkenylzirconium compounds with alkynyl halides.[26] Gimeno et al. reported the stereoselective synthesis of chiral terminal (*E*)-1,3-enynes derived from optically active aldehydes.[27] The stereoselective synthesis of 1,3-enynylsulfides,[28] 1,3-enynylselenides,[29] 1,3-enynyltellurides,[30] 1,3-enynylsilanes,[31] 1,3-enynylstannanes[32] and fluoro or CF_3-substituted 1,3-enyne has previously been described in the literature. However, the synthesis of enynyl sulfones has received less attention[33] and enynyl sulfones have, to the best of our knowledge, not been reported so far.

Table 3. Synthesis of **6a–e**.

6	5	3	R^1	R^2	6 [%][a]
a	**a**	**a**	Me	H	57
b	**a**	**j**	Me	Et	60
c	**a**	**k**	Me	OMe	50
d	**a**	**e**	Me	CF_3	64
e	**c**	**b**	*t*Bu	Me	61

[a] Yields of isolated products.

The Sonogashira reaction[34] of **2** with alkynes **7a–e** (2.2 equiv) gave the 2,4′-bis(alkynyl)diphenyl sulfones **8a–e** containing two different aryl groups in 85–92% yield (Scheme 5, Table 4). The reaction was carried using catalytic amounts of CuI (10 mol%), $[Pd(PPh_3)_2Cl_2]$ (2.5 mol%), and $(Bu)_4NI$ (15 mol%). In the reaction Et_3N (1.25 equiv) was used as the base and DMF as the solvent (60 °C, 1 h). The structure of **8b** was independently confirmed by X-ray crystal structure analysis (Figure 3).[25] Copper-free Sonogashira reactions have been previously reported.[35] The application of copper free conditions to the synthesis of product **8a** failed (no conversion).



Scheme 5. Synthesis of **8a–e**. Reagents and conditions: i) **2** (1.0 equiv), **7a–e** (2.2 equiv), $(Bu)_4NI$ (15 mol%), CuI (10 mol%), $[Pd(PPh_3)_2Cl_2]$ (5 mol%), Et_3N (2.5 equiv), DMF, 80 °C, 4 h.

Table 4. Synthesis of **8a–e**.

8,7	R	8 [%][a]
a	C_6H_5	88
b	4-MeC_6H_4	92
c	*n*-Pr	85
d	*n*-Pent	88
e	*n*-Oct	90

[a] Yields of isolated products.

2-Trifluoromethanesulfonyloxy-4′-(alkynyl)diphenyl sulfones **9a–d** were prepared in 83–91% yield by Sonogashira reaction of **2** with alkynes **7b,d,e,g** (1.1 equiv) in the presence of 2.5 mol% of $[Pd(PPh_3)_2Cl_2]$. The reactions proceeded with very good site-selectivity in favor of position C-4′ (Scheme 6, Table 5). In most cases, a small amount of the bis-coupled product could be detected in the crude product before chro-

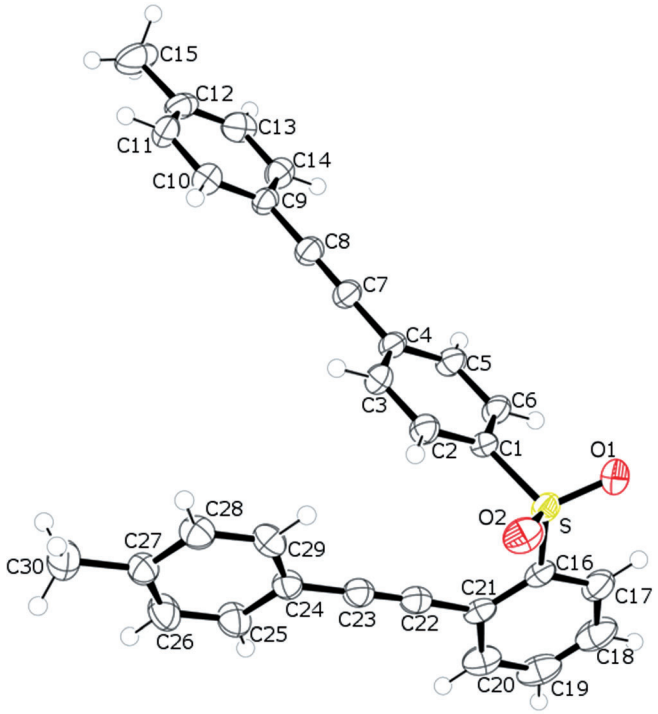
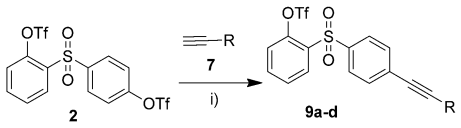


Figure 3. Ortep plot of **8b** (50% probability level).



Scheme 6. Synthesis of **9a–d**. Reagents and conditions: i) **2** (1.0 equiv), **7b,d,e,g** (1.0 equiv), $(Bu)_4NI$ (15 mol%), CuI (10 mol%), $[Pd(PPh_3)_2Cl_2]$ (2.5 mol%), Et_3N (1.25 equiv), DMF, 60 °C, 1 h.

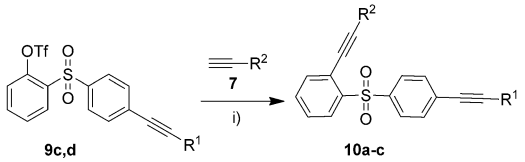
Table 5. Synthesis of **9a–d**.

9	7	R	9 [%][a]
a	**b**	4-MeC_6H_4	83
b	**g**	4-*t*BuC_6H_4	88
c	**d**	*n*-Pent	86
d	**e**	*n*-Oct	91

[a] Yields of isolated products.

matography (by ^1H NMR spectroscopy and GC–MS). All products were isolated in pure form by chromatographic purification. Therefore, similar to the synthesis of mono-Suzuki products **5**, the yields of mono-Sonogashira products **9** are often less than the yields of the corresponding disubstituted products **8**, because of difficulties during the chromatographic purification of products **9** and loss of material. During the optimization, the rate of addition of the acetylene played a crucial role. It proved to be important to perform the reaction at 70 rather than 110 °C with drop-wise addition of the acetylene to achieve a good site-selectivity.

The Sonogashira cross-coupling reaction of monoalkynylated diaryl sulfones **9c,d** with terminal alkynes (1.0 equiv), in the presence of $[Pd(PPh_3)_2Cl_2]$ (2.5 mol%), CuI (10 mol%), $(Bu)_4NI$ (15 mol%), Et_3N (2.5 equiv) (DMF, 80 °C, 4 h), gave products **10a–c** in 79–87% yield (Scheme 7, Table 6).



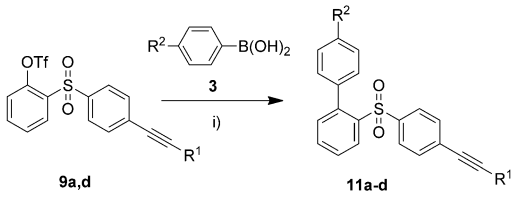
Scheme 7. Synthesis of **10a–c**. Reagents and conditions: i) **9c,d** (1.0 equiv), **7a,g,h** (1.0 equiv), $(Bu)_4NI$ (15 mol%), CuI (10 mol%), $[Pd(PPh_3)_2Cl_2]$ (2.5 mol%), Et_3N (1.25 equiv), DMF, 60 °C, 4 h.

Table 6. Synthesis of **10a–c**.

10	9	7	R^1	R^2	10 [%][a]
a	**d**	**h**	*n*-Pent	*n*-But	87
b	**e**	**a**	*n*-Oct	C_6H_5	83
c	**e**	**g**	*n*-Oct	4-*t*BuC_6H_4	79

[a] Yields of isolated products.

The Suzuki–Miyaura reaction of **9a,d** with arylboronic acids **3a,e,j,k** in the presence of $[Pd(PPh_3)_4]$ and K_3PO_4, gave sulfones **11a–d** (Scheme 8). All these reactions proceeded in good yields (80–91%) (Scheme 8, Table 7).



Scheme 8. Synthesis of **11a–d**. Reagents and conditions: *i)* **9a,d** (1.0 equiv), $ArB(OH)_2$ (1.1 equiv), $[Pd(PPh_3)_4]$ (2.5 mol%), K_3PO_4 (1.5 equiv), Dioxane, 100 °C, 6 h.

Table 7. Synthesis of **11a–d**.

11	3	9	R^1	R^2	11 [%][a]
a	**a**	**d**	*n*-Oct	H	88
b	**j**	**d**	*n*-Oct	4-Et	91
c	**e**	**d**	*n*-Oct	CF_3	85
d	**k**	**a**	4-MeC_6H_4	OMe	80

[a] Yields of isolated products.

Conclusions

We have reported the synthesis of novel arylated and alkynylated 2,4′-diphenyl sulfones based on what are, to the best of

our knowledge, the first palladium(0)-catalyzed cross-coupling reactions of bis(triflates) of 2,4′-bis(hydroxy)diphenyl sulfone. The reactions proceed with very good site-selectivity.

The oxidative addition of palladium usually occurs first at the most electron deficient carbon atom. Carbon atoms C-2 and C-4′ of bis(triflate) **2** are expected to be equally electron deficient. The site-selective formation of **5a–d** and **9a–d** can be explained by the fact that carbon atom C-4′ is less sterically hindered. Interestingly, excellent site-selectivities could be obtained not only for Suzuki–Miyaura reactions, but also for Sonogashira reactions (which rely on the use of sterically undemanding alkynes).

Experimental Section

General procedure A for the synthesis of 4a–i, 5a–d 6a–e and 11a–d

In a pressure tube, 1,4-dioxane solution of arylboronic acid, K_3PO_4, $[Pd(PPh_3)_4]$ and **2** or **5** was stirred at 110 °C for 4 h under an argon atmosphere. After cooling to 20 °C, a saturated aqueous solution of NH_4Cl was added. The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by using column chromatography.

2-(Biphenyl-4-ylsulfonyl)biphenyl (4a)

Starting with **2** (205 mg, 0.40 mmol), K_3PO_4 (254 mg, 1.2 mmol), $[Pd(PPh_3)_4]$ (28 mg, 6 mol%), phenylboronic acid (122 mg, 1.0 mmol) and 1,4-dioxane (2 mL), following general procedure A, **4a** was isolated as a white solid (111 mg, 75%). M.p. 131 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86–6.93 (m, 3H), 7.31–7.39 (m, 5H), 7.44–7.48 (m, 3H), 7.59–7.63 (m, 4H), 7.88–7.91 (m, 2H), 8.35–8.38 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 126.0, 126.5, 126.9, 127.5, 128.3, 128.5, 128.7, 129.1, 129.9, 131.1, 132.7, 132.9 (CH), 135.2, 139.2, 140.1, 145.0, 150.8, 151.8 ppm (C); IR (KBr): $\tilde{\nu}$ = 3066, 2923, 2852, 1595, 1466 (w), 1317 (m), 1291 (w), 1195 (m), 1126 (s), 1091, 1003 (m), 834, 759, 690 (s), 732, 572 cm^{-1} (m); GC–MS (EI, 70 eV): *m/z* (%): 370 ([*M*]$^+$, 100), 305 (43), 291 (11), 289 (40), 215 (11), 207 (49), 201 (17), 184 (10), 169 (26), 152 (95), 141 (15), 127 (11), 115 (13), 44 (17); HRMS (EI, 70 eV): calcd for $C_{24}H_{18}O_2S$ [*M*]$^+$: 370.10275; found 370.102731.

2-(4′-Methylbiphenyl-4-ylsulfonyl)phenyl trifluoromethanesulfonate (5a)

Starting with with **2** (205 mg, 0.4 mmol), K_3PO_4 (127 mg, 0.60 mmol), $[Pd(PPh_3)_4]$ (14 mg, 3 mol%), 4-methylphenylboronic acid (60 mg, 0.44 mmol) and 1,4-dioxane (2 mL), following general procedure A, **5a** was isolated as a white solid (113 mg, 62%). M.p. 91 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 7.19–7.22 (d, *J* = 8.0 Hz, 2H, ArH), 7.32–7.35 (m, 1H, ArH), 7.41 (d, *J* = 8.2 Hz, 2H, ArH), 7.47–7.53 (m, 1H, ArH), 7.58–7.61 (m, 1H, ArH), 7.63–7.66 (m, 2H, ArH), 7.95 (d, *J* = 8.6 Hz, 2H, ArH), 8.23–8.27 ppm (m, 1H, ArH); ^{19}F NMR (282 MHz, $CDCl_3$): δ = −73.1; ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.1 (CH_3), 122.2 (CH), 124.0 (q, $J_{F,C}$ = 321.7 Hz, CF_3), 127.2, 127.5, 128.5, 128.9, 129.7, 130.9 (CH), 134.4 (C), 135.5 (CH), 136.0, 138.3, 138.8, 146.5, 146.8 ppm (C); IR (KBr): $\tilde{\nu}$ = 2959, 2928, 2869 (w), 1590, 1514, 1467, 1392 (m), 1313, 1151 (s), 1093, 1003 (m), 820 (s), 752, 623, 565 cm^{-1} (m); GC–MS (EI, 70 eV): *m/z* (%): 456 ([*M*]$^+$, 100), 332 (21), 304 (14), 198 (28), 259 (10), 244 (26), 215 (21), 183 (16), 165 (15), 152 (18); HRMS (EI, 70 eV): calcd for $C_{20}H_{15}F_3O_5S_2$ [*M*]$^+$: 456.03075; found 456.030612.

2-(4′-Methylbiphenyl-4-ylsulfonyl)biphenyl (6a)

Starting with **5a** (182 mg, 0.40 mmol), K_3PO_4 (127 mg, 0.6 mmol), $[Pd(PPh_3)_4]$ (14 mg, 3 mol%), phenylboronic acid (53 mg, 0.44 mmol) and 1,4-dioxane (2 mL), following the general procedure A,**6a** was isolated as a solid (87 mg, 57%). M.p. 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 6.91 (d, *J* = 7.0 Hz, 2H, ArH), 7.08–7.14 (m, 3H, ArH), 7.16–7.20 (m, 4H, ArH), 7.29–7.33 (m, 1H, ArH), 7.28 (d, *J* = 8.0 Hz, 2H, ArH), 7.34 (d, *J* = 8.2 Hz, 2H, ArH), 7.49–7.53 (m, 2H, ArH), 8.36–8.39 ppm (m, 1H, ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.1 (CH_3), 126.6, 127.0, 127.2, 127.5, 127.6, 128.1, 128.4, 129.7, 130.0, 132.6, 132.8 (CH), 136.4, 138.1, 138.5, 139.0, 139.9, 142.1, 145.2 ppm (C); IR (KBr): $\tilde{\nu}$ = 3052, 2918, 2852 (w), 1591, 1464 (m), 1297, 1147 (s), 1090, 1005, 813, 757, 702, 690, 625, 582 (s), 541 cm^{-1} (m); GC–MS (EI, 70 eV): *m/z* (%): 384 ([*M*]$^+$, 100), 320 (28), 304 (19), 289 (19), 215 (13), 183 (43), 165 (26), 152 (75); HRMS (EI, 70 eV): calcd for $C_{25}H_{20}O_2S$ [*M*]$^+$: 384.11785; found 384.117575.

General procedure B for the synthesis of (8a–e), (9a–d) and (10a–c)

In a pressure tube (glass bomb) a suspension of $[Pd(PPh_3)_2Cl_2]$ (2.5–5.0 mol%), **2** (257 mg, 0.5 mmol), alkyne (0.50–1.10 mmol), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mol%), Et_3N (0.62–1.25 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C for 10 min. The reaction mixture was stirred at 60 −80 °C for 2–4 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were washed with H_2O (3×20 mL), dried (Na_2SO_4), concentrated in vacuo and the residue was purified by chromatography (flash silica gel, heptanes/EtOAc) to give **8a–e, 9a–e** and **10a–c**.

2-(Phenylethynyl)-1-[4-(phenylethynyl)benzenesulfonyl]benzene (8a)

Starting with **2** (257 mg, 0.50 mmol), $[Pd(PPh_3)_2Cl_2]$ (18 mg, 5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.18 mL, 1.25 mmol), ethynylbenzene (0.13 mL, 1.1 mmol) and DMF (5 mL), following the general procedure B, **8a** was isolated as a white solid (184 mg, 88%). M.p. 87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.27 (m, 4H, ArH), 7.31–7.34 (m, 3H, ArH), 7.40–7.56 (m, 8H, ArH), 7.77–7.80 (m, 2H, ArH), 8.18 ppm (dd, 1H, *J* = 1.8, 7.8 Hz, ArH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 85.8, 87.8, 93.0, 98.2 (C≡), 122.3, 122.4, 122.7 (C), 128.3, 128.4, 128.5, 129.0, 129.1, 129.2, 131.6, 131.7, 131.8, 132.3, 133.1, 134.8 (CH), 135.2, 139.7, 141.0 ppm (C); IR (KBr): $\tilde{\nu}$ = 3060, 2924, 2853 (w), 1780, 1597, 1587, 1491, 1465, 1441, 1395, 1359 (m), 1319, 1279, 1249, 1220, 1155 (s), 1123, 1086, 916, 834 (m), 746, 688, 673, 622, 583 (s), 548 cm^{-1} (m); GC–MS (EI, 70 eV): *m/z* (%): 418 ([*M*]$^+$, 21), 352 (33), 313 (100), 284 (21), 213 (10); HRMS (EI, 70 eV): calcd for $C_{28}H_{18}O_2S$ [*M*]$^+$: 418.10220; found: 418.102241.

2-[4-(*p*-Tolylethynyl)phenylsulfonyl]phenyl trifluoromethanesulfonate (9a)

Starting with **2** (257 mg, 0.50 mmol), $[Pd(PPh_3)_2Cl_2]$ (9 mg, 2.5 mol%), $(Bu)_4NI$ (27 mg, 15 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 1-ethynyl-4-methylbenzene (0.06 mL, 0.5 mmol) and DMF (4 mL), following general procedure B, (**9b**) was prepared as a reddish oil (199 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.30$ (s, 3H, CH_3), 7.10 (d, $J = 7.9$ Hz, 2H, ArH), 7.31–7.36 (m, 3H, ArH), 7.48–7.55 (m, 2H, ArH), 7.57–7.65 (m, 2H, ArH), 7.87 (d, $J = 8.7$ Hz, 2H, ArH), 8.21–8.25 ppm (m, 1H, ArH); ^{19}FNMR (282.4 MHz, $CDCl_3$): $\delta = -73.1$; ^{13}CNMR (75.5 MHz, $CDCl_3$): $\delta = 21.5$ (CH_3), 87.1, 94.1 (C≡), 116.3, 120.5 (C), 119.8 (q, $J_{F,C} = 321.0$ Hz, CF_3), 122.3, 128.3, 128.6, 129.2,130.9, 131.7, 132.0, 135.7 (CH), 129.8, (CH), 135.7, 138.9, 139.5, 146.5 ppm (C); IR (KBr): $\tilde{\nu} =$ 3068, 2919 (w), 1586 (m), 1426, 1332 (s), 1231, 1198, 1157 (m), 1127 (s), 1087 (m), 882 (s), 771, 719, 608 (m), 572 cm^{-1} (s); GC–MS (EI, 70 eV): *m/z* (%) = 480 ([*M*]$^+$, 100), 282 (18), 268 (33), 239 (27), 189 (16); HRMS (EI, 70 eV): calcd for $C_{22}H_{15}F_3O_5S_2$ [*M*]$^+$: 480.03075; found: 480.030830.

1-[4-(Hept-1-ynyl)benzenesulfonyl]-2-hex-1-ynyl-benzene (10a)

Starting with **9c** (230 mg, 0.5 mmol), $[Pd(PPh_3)_2Cl_2]$ (9 mg, 2.5 mol%), CuI (10 mg, 10 mol%), triethylamine (0.09 mL, 0.62 mmol), 1-heptyne (0.06 mL, 0.5 mmol) and DMF (5 mL) following general procedure B, **10a** was isolated as a reddish oil (171 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.77$–0.93 (m, 6H, $2CH_3$), 1.18–1.24 (m, 2H, CH_2), 1.29–1.61 (m, 8H, $4CH_2$), 2.30–2.36 (m, 4H, $2CH_2$), 7.36–7.42 (m, 5H, ArH), 7.74–7.78 (m, 2H, ArH), 8.16–8.19 ppm (m, 1H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 13.6$, 14.0 (CH_3), 19.5, 22.1, 22.6, 28.4, 29.1, 30.2, 31.8 (CH_2), 78.1, 79.5, 94.8, 100.4 (C≡), 123.5 (C), 127.6, 128.1, 128.9 (CH), 129.3 (C), 131.4, 132.9, 135.1 (CH), 139.1, 140.7 ppm (C); IR (KBr): $\tilde{\nu} = 3063$, 2924 (w), 2929, 2859, 1590, 1467 (m), 1318, 1153 (s), 1089, 835, 754, 730 (m), 612, 581 cm^{-1} (s); GC–MS (EI, 70 eV): *m/z* (%): 392 ([*M*]$^+$, 100), 365 (17), 350 (16), 349 (56), 228 (10), 205 (38), 163 (12), 115 (12); HRMS (EI, 70 eV): calcd for $C_{25}H_{28}O_2S$ [*M*]$^+$: 392.18045; found: 392.180237.

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