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Paper

Trifluoromethanesulfonyloxy-Group-Directed Regioselective (3+2) Cycloadditions of Benzynes for the Synthesis of Functionalized Benzo-Fused Heterocycles

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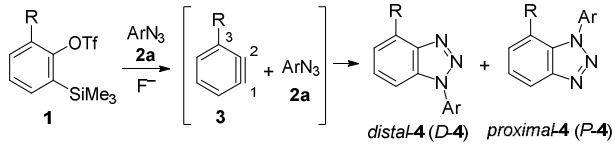
Highly regioselective (3+2) cycloadditions of (trifluoromethanesulfonyloxy)benzynes [(triflyloxy)benzynes] with 1,3-dipoles followed by cross-coupling reactions provided multisubstituted benzo-fused heterocycles. The triflyloxy group at the 3-position of benzynes, and even that at the remote 4-position, greatly affected the regiocontrol of the cycloaddition. These groups also served to install other substituents at their *ipso*-positions.

Introduction

The (3+2) cycloaddition reactions of benzynes[1] have been useful in the construction of benzo-fused heterocyclic skeletons, which are widely found in various biologically active compounds.[2,3] However, the regioselectivities of (3+2) cycloadditions of unsymmetrically-substituted benzynes were often low, and the reactions provided difficult-to-separate regioisomer mixtures.[4] For instance, the reactions of *p*-methoxyphenyl azide (**2a**) with either 3-methyl- (**3a**) or 3-fluorobenzyne (**3b**) afforded a 1:1 mixture of *distal*- and *proximal*-benzotriazoles (**4a** and **4b**, respectively) (Scheme 1).[4g] This problem could be solved by using a specific directing group that has a strong effect on controlling the orientation of the cycloaddition reactions, and that can also be subsequently converted into any other desired substituent. An alkoxy group at the 3-position of benzynes has been widely utilized as a distinguished directing group of various benzyne reactions such as nucleophilic addition,[5a] cycloaddition[4,5b] and transition-metal-catalysis.[5c] In fact, the reactions of 3-methoxybenzyne **3c**, generated from **1c**, with **2a** exclusively afforded the distal adduct, *distal*-**4a** (Scheme 1).[4g] However, the alkoxy groups on aryl rings have rarely been converted into other substituents after the reactions of alkoxybenzynes.

Garg *et al.* reported sulfamoyloxy (OSO_2NMe_2)-group-couplings after the cycloaddition, only a limited number of such directed regioselective reactions of 3,4-pyridyne.[6] Although this directing group could be transformed using nickel-catalyzed transformations are known and the substrate scopes of nickel-catalyzed couplings are much narrower than, for example, those of palladium.[7] Recently, we have reported silyl- or boryl-group-directed regioselective (3+2) cycloaddition reactions of benzynes.[8] These methods should be particularly valuable because the reactions of 3-silyl- and 3-borylbenzynes afforded products with complementary regioselectivities, and the directing groups were subsequently converted into various substituents under palladium-catalyzed and uncatalyzed conditions. The development of other directing groups of benzynes that have powerful regiocontrol and versatile convertibility should enrich diversity in synthetic methods and would be useful for organic and medicinal chemistries.

Herein, we report the use of a trifluoromethanesulfonyloxy (triflyloxy, OSO_2CF_3, OTf) group, at either the 3-position or 4-position of benzynes, in powerfully directed regioselective (3+2) cycloaddition reactions. Moreover, the OTf-group of the cycloadducts could be directly transformed into other substituents, such as aryl groups, using palladium-catalyzed couplings (Scheme 2).



Scheme 1 Regioselectivities in (3+2) Cycloaddition of 3-Substituted Benzynes **3**, Generated from **1**, with Azide **2a**.

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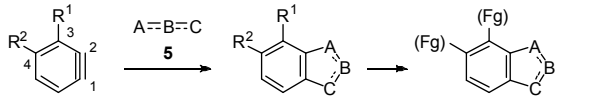
†Electronic Supplementary Information (ESI) available: Experimental *details*, full spectral data for all new compounds, distortion analysis, and Cartesian coordinate. see DOI: 10.1039/b000000x/



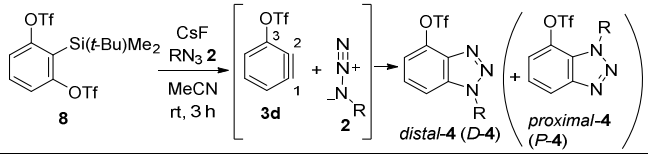
Scheme 2 Proposed OTf-Group-Directed Regioselective Cycloaddition Followed by Subsequent Transformation.

Results and discussion

Considering the strong electron-withdrawing nature of a triflyloxy group, we expected that it may act as a more powerful directing group of benzyne cycloadditions than any alkoxy groups. Moreover, it is well known that the triflyloxy groups on aromatic compounds are readily convertible into other various functional groups.[9] However, there have been no reports on the use of the triflyloxy group as a directing group for benzyne reactions.

To examine the feasibility of our idea, a new benzyne precursor **8** (Table 1) bearing two triflyloxy and one *tert*-butyldimethylsilyl groups on a benzene ring was synthesized from resorcinol in 5 steps (see the Supplementary Information), while 1,3-bis(triflyloxy)-2-(trimethylsilyl)benzene could not be synthesized due to the instability of 2-(trimethylsilyl)resorcinol.[10] Under mild conditions using CsF in MeCN at room temperature, novel benzyne **3d** was successfully generated, which was confirmed by the subsequent (3+2) cycloaddition reaction with aryl azide **2a** to form 1-(*p*-methoxyphenyl)-4-(triflyloxy)benzotriazole *distal*-**4d** (48% yield). To our delight, the regioselectivity of this reaction was exclusively distal (*distal*:*proximal* = >98:2; Entry 1). Under the same reaction conditions, benzyne **3d** reacted with benzyl, *p*-nitrobenzyl, and cyclohexyl azide **2b**, **2c**, and **2d**, to afford *distal*-adducts **4e**, **4f**, and **4g**, respectively (Entries 2–4), in superior yield to that of **4d**. In all cases, the *proximal*-**4** adducts were not observed by ^{1}H NMR analysis of crude reaction mixtures.

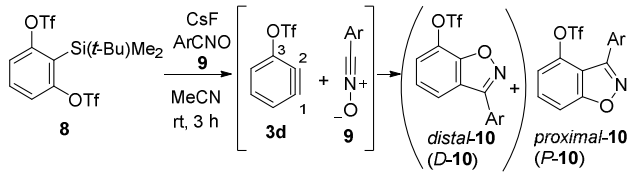
Table 1 Regioselective (3+2) Cycloaddition of 3-(Triflyloxy)benzyne **3d**, Generated from **8**, with Azides **2**.[a]



Entry	R	2	*D*-**4** : *P*-**4**[b]	4	Yield (%)[c]
1	C_6H_4-4-OMe	**2a**	>98 : 2	**4d**	48
2	Bn	**2b**	>98 : 2	**4e**	74
3	$CH_2C_6H_4$-4-NO_2	**2c**	>98 : 2	**4f**	70
4	cyclohexyl	**2d**	>98 : 2	**4g**	63

[a]Conditions: **8** (1.0 equiv), **2** (3.0 equiv), CsF (3.0 equiv), MeCN, rt. [b]Determined by ^{1}H NMR analysis of a crude product. [c]Isolated yield of *distal*-**4**.

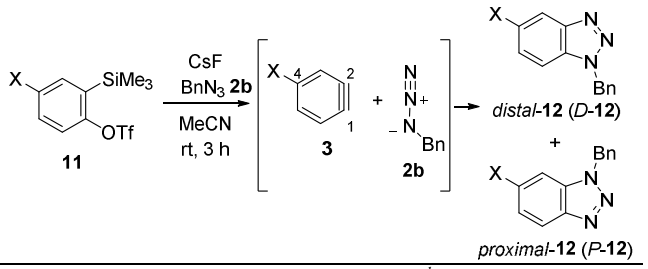
The reactions of **3d** generated from **8** with nitrile oxides (**9a** and **9b**)[11] were also achieved to provide proximal adducts (*proximal*-**10a** and -**10b**) exclusively (Scheme 3). Notably, the selectivities of the reactions using **3d** are much higher than that using 3-methoxybenzyne (*proximal*:*distal* = 80:20).[4h,12] These results suggest that the selectivities are derived not only from the electron-negativity of the oxygen atom but also from the strong electron-withdrawing nature of the sulfonyl group.



Scheme 3 Regioselective (3+2) Cycloadditions of 3-(Triflyloxy)benzyne 3d, Generated from 8, with Nitrile Oxides 9.

Next, we attempted the remote regiocontrol of (3+2) cycloadditions using substituents at the 4-position of benzyne, which has been long known as a much more difficult task than that using substituents at the adjacent 3-position.[13] Harrity *et al.* reported the directing effects of Br, CO_2Me, and CN groups attached at the 4-position of benzynes on the (3+2) cycloaddition with benzyl azide, which resulted in the production of two regioisomers in up to 2:1 ratio although the transformations of the directing groups have never been tried.[13f] Not surprisingly, the (3+2) cycloaddition of 4-methoxybenzyne **3f**, generated from precursor **11a**, with benzyl azide **2b** afforded a 52:48 mixture of two regioisomers (*distal*-**12a**:*proximal*-**12a**) (Table 2, Entry 1). On the other hand, a methanesulfonyloxy group in **3g** had a greater effect on the regiocontrol of the cycloaddition to afford a 72:28 mixture of *distal*-**12b**:*proximal*-**12b** (Entry 2). The regioselectivity became slightly better when using a triflyloxy group as the directing

Table 2 Regioselectivities in the (3+2) Cycloaddition of 4-Substituted Benzynes **3**, Generated from **11**, with Azide **2b**.[a]



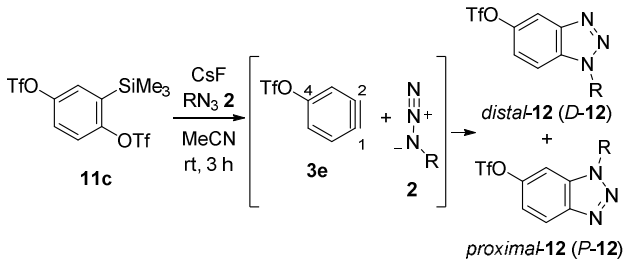
Entry	X	11	3	*D*-**12** : *P*-**12**[b]	12	Yield (%)[c]
1	OMe	**11a**	**3f**	52 : 48	**12a**	80
2	OMs	**11b**	**3g**	72 : 28	**12b**	65
3	OTf	**11c**	**3e**	77 : 23	**12c**	47
4[d]	OTf	**11c**	**3e**	75 : 25	**12c**	60

[a]Conditions: **11c** (1.0 equiv), 12 equiv of **2** (12 equiv), CsF (1.0 equiv), MeCN, rt. [b]Isolated product ratio. [c]Total isolated yield of *proximal*-**12** and *distal*-**12**.

group (*distal*-**12c**:*proximal*-**12c** = 77:23; Entry 3). The lower 47% yield of **12c** was improved to 60% by using 12 equiv of azide **2b** while maintaining similar regioselectivity (Entry 4). Delightfully, the triflyloxy group, which exhibited the highest regioselectivity as a directing group, would be the most promising for the subsequent transformations (*vide infra*, see Scheme 4).[9]

With the optimized benzyne precursor **11c** and reaction conditions in hand, azide **2a**, along with **2c** and **2d**, were applied to the (3+2) cycloaddition reactions (Table 3). Aryl azide **2a** (Entry 1), primary alkyl azide **2c** (Entry 2), and secondary alkyl azide **2d** (Entry 3) successfully reacted with the *in situ* generated 4-(triflyloxy)benzyne **3e** to preferentially produce distal products (*distal*-**12**:*proximal*-**12** = 75–76:25–24). To the best of our knowledge, these are the best results among the reported regioselectivities of 4-substituted benzyne (3+2) cycloadditions.

Table 3 Regioselective (3+2) Cycloaddition of 4-(Triflyloxy)benzyne **3e**, Generated from **11c**, with Azides **2**.[a]

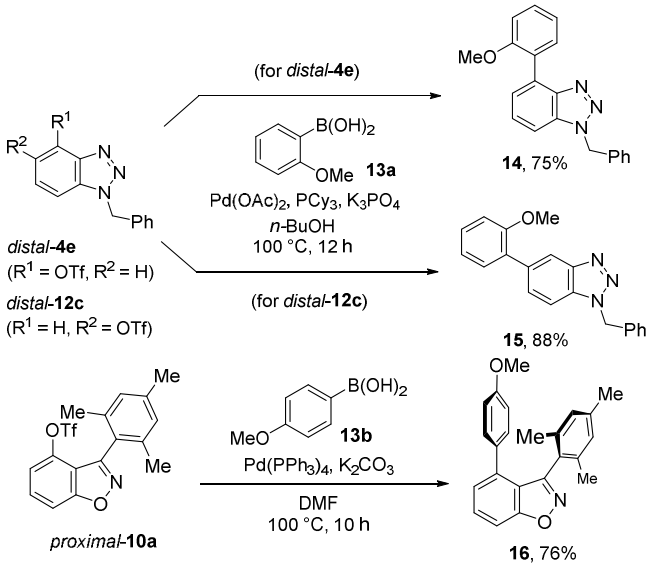


Entry	R	2	*D*-**12** : *P*-**12**[b]	12	Yield (%)[c]
1	C_6H_4-4-OMe	**2a**	76 : 24	**12d**	61
2	$CH_2C_6H_4$-4-NO_2	**2c**	75 : 25	**12e**	53
3	cyclohexyl	**2d**	76 : 24	**12f**	60

[a]Conditions: **11c** (1.0 equiv), 12 equiv of **2** (12 equiv), CsF (1.0 equiv), MeCN, rt. [b]Isolated product ratio. [c]Total isolated yield of *proximal*-**12** and *distal*-**12**.

Aryl trifluoromethanesulfonates have widely been used as good substrates for palladium-catalyzed coupling reactions.[7] The major cycloaddition products, *distal*-**4e**, *distal*-**12c**, and *proximal*-**10a**, were applied to the Suzuki coupling reactions with boronic acids **13a** and **13b** (Scheme 4). Reactions in the presence of a palladium catalyst, ligand, boronic acid, and base smoothly afforded biaryls **14**–**16** in 75–88% isolated yields even under unoptimized reaction conditions. These results suggest that the combination of the regioselective (3+2) cycloadditions of 3- or 4-(triflyloxy)benzynes and 1,3-dipoles, with subsequent transformations of the triflyloxy group provides a useful method for the synthesis of multisubstituted benzo-fused heterocyclic compounds.

The origin of the regioselectivity in the (3+2) cycloadditions was analyzed using density functional theory (DFT) calculation[14] and a natural bond orbital (NBO) method.[15] Firstly, the structures of **3c**–**f** were optimized by DFT [B3LYP/6-31G(d)], and then the electron densities of their reacting π-orbitals were calculated by NBO 6.0.[16] Thereby, the



Scheme 4 Transformations of Cycloaddition Products, *distal*-**4e**, *distal*-**12c**, and *proximal*-**10a**.

selectivities of both 3- and 4-substituted benzynes could be rationally explained using the electron densities of the NBO (Figure 1).[15–20] The electron density in the π-orbital at the C1 of **3c** (0.826) and that of **3d** (0.781) were lower than those at the C2 (1.010 and 1.031, respectively). A similar tendency was observed for **3f** and **3e**; however, the difference between the electron densities of **3f** (C2–C1 = 0.0005) and that of **3e** (C2–C1 = 0.046) were found to be much smaller than those of **3c** and **3d** (C2–C1 = 0.184 and 0.250, respectively). These calculated differences were parallel with the magnitudes of regioselectivities. For example, the (3+2) cycloadditions of **3c** and **3d** with benzyl azide **2b** exhibited complete *distal* regioselectivities (Scheme 1 and Table 2, Entry 2), while that of **3e** afforded moderate distal selectivity. Moreover, very poor selectivity was observed using **3f**. These results indicated that the inductive effect of the oxygen atom at the 3-position was greater than that at the 4-position, thus inducing a larger difference in electron density between the C1 and C2 orbitals, which resulted in higher regioselectivities. An additional sulfonyl group at the 4-position could amplify the electron-withdrawing inductive effect and achieve directed benzyne (3+2) cycloaddition reactions.

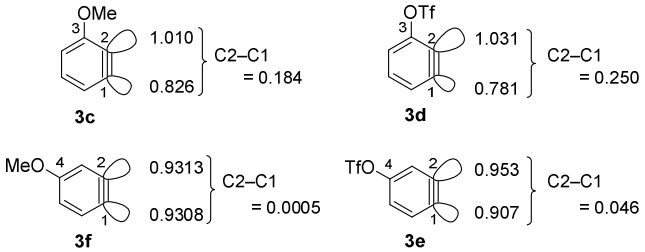


Fig. 1 Natural Bond Orbital (NBO) Analysis of Substituted Benzynes **3c–f**. Optimized structures of benzynes **3c–f** were calculated by DFT [B3LYP6/31G(d)]. Electron densities of the reacting *p*-orbitals were determined by NBO analysis.

Conclusions

In conclusion, the regiocontrolled (3+2) cycloadditions of benzynes with azides and nitrile oxides were demonstrated by the use of a triflyloxy group at either the 3- or 4-position of benzynes. In particular, this method provides the highest reported selectivity for 4-substituted-group-directed benzyne cycloaddition reactions. The sequential combination of regioselective cycloaddition and palladium-catalyzed coupling of the aryl triflates could be implemented in the synthesis of polysubstituted heterocycles. The applications of this chemistry to a wide range of benzyne reactions and detailed mechanistic investigations are now underway in our laboratory.

Experimental

General Procedure for Regioselective Cycloadditions of Triflyloxybenzynes 3 with dipoles (Tables 1–3, and Scheme 3)

CsF (1.5 equiv) was flame-dried under reduced pressure in a flask equipped with a three-way stopcock, and back-filled with Ar. Azide **2** or nitrile oxide **9** (7.0 equiv) with a stir bar was loaded into the flask and evacuated and backfilled with Ar (This process was repeated three times). MeCN (One-fifth of its total volume) was added into the flask via a syringe. A solution of precursor **8**, or **11** (1.0 equiv) in anhydrous MeCN (one-fifth of its total volume) was added to the flask through a cannula and washed with MeCN (three-fifth of its total volume). The mixture was stirred at rt for the period shown in Tables 2–4 and Scheme 3. H_2O and EtOAc were added to the reaction mixture, and the aqueous phase was extracted thrice with EtOAc. The combined organic phase was washed with a saturated aqueous NaCl solution (brine). The organic phase was dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was subjected to ^{1}H NMR analysis for calculating the ratio of the two regioisomers (*distal*- and *proximal*-**4**, **10**, or **12**). The crude product was purified by flash column chromatography on silica gel (hexane, a mixture of hexane and EtOAc, or CH_2Cl_2) to afford *distal*- and *proximal*-**4**, **10**, or **12**.

General Procedure for Pd-Catalyzed Couplings of Cycloaddition Products *distal*- and *proximal*-4, 10, or 12

An oven dried Schlenk tube was charged with *distal*- and *proximal*-**4**, **10**, or **12** (1.0 equiv), phenylboronic acid **13** (1.5 equiv), Pd source (0.10 equiv), ligand (0.20 equiv, if applicable), base (2.0 equiv), evacuated and back-filled with Ar. An anhydrous solvent (0.56 mL) was added via syringes, and the reaction mixture was stirred at 100 °C for several hours and filtered through a pad of silica gel cake using EtOAc. The eluent was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc) to provide the biaryl compound **14**–**16**.

Synthesis of benzyne precursors 8, 11b and 11c

2-Bromoresorcinol (17):[22,23] To a solution of resorcinol (11 g, 0.10 mol) in $CHCl_3$ (63 mL, 0.50 M) was added Br_2 (15 mL, 0.30 mol) at 0 °C. After stirring for 10 h at rt, the mixture was concentrated in vacuo. The residue was recrystallized from $CHCl_3$ to give 2,4,6-tribromoresorcinol (27 g, 77%). To a solution of 2,4,6-tribromoresorcinol (17 g, 50 mmol) in H_2O/MeOH (0.35 L, H_2O/MeOH = 6:1, 0.50 M) were added NaOH (15 mL, 0.30 mol) and Na_2SO_3 at rt. After stirring for 10 h at rt, the mixture was concentrated in vacuo. The residue was recrystallized from $CHCl_3$ to give the titled compound **17** (7.3 g, 78%) as a colourless solid. Mp: 101–102 °C (Lit. 101–102 °C).[23] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.39 (2 OH, s), 6.60 (2 H, d, J = 8.5 Hz), 7.11 (1 H, t, J = 8.5 Hz).

1,3-Bis(*tert*-butyldimethylsilyloxy)-2-bromobenzene (18): To a solution of **17** (6.0 g, 32 mmol) in DMF (63 mL, 0.50 M) were added imidazol (6.5 g, 95 mmol) and TBSCl (14 g, 95 mmol) at 0 °C. After stirring for 1 h at rt, the reaction was stopped by adding a saturated aqueous solution of NH_4Cl and the mixture was extracted with hexane. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 20:1) to provide the titled compound **18** (13 g, quant) as a colourless solid. Mp: 40–42 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.23 (12 H, s), 1.04 (18 H, s), 6,51 (2 H, d, J = 8.5 Hz), 6.99 (1 H, t, J = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: –4.22, 18.4, 25.8, 109.3, 113.0, 127.3, 154.1. IR (neat): 1252, 1464 cm^{-1}. HRMS (MALDI) Calcd for $C_{18}H_{34}O_2Si_2Br$ $[M+H]^+$: 417.1275, found 417.1257.

2-(*tert*-Butyldimethylsilyl)-3-[(*tert*-butyldimethylsilyl)oxy]phenol (19): To a solution of **18** (10 g, 24 mmol) in THF (0.12 L, 0.20 M) was added 1.6 M *n*-BuLi in hexane (18 mL, 29 mmol) slowly at –78 °C. After stirring for 40 min, the reaction was stopped by adding a saturated aqueous solution of NH_4Cl and the mixture was extracted with hexane. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 15:1) to provide the titled compound **19** (8.1 g, 85%) as a colourless solid. Mp: 57–60 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.31 (6 H, s), 0.37 (6 H, s), 0.93 (9 H, s), 1.00 (9 H, s), 4.87 (OH, s), 6.30 (1 H, d, J = 8.0 Hz), 6.40 (1 H, d, J = 8.0 Hz), 7.05 (1 H, t, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –2.95, –1.37, 18.6, 19.5, 26.9, 27.0, 107.8, 110.5, 112.0, 130.6, 162.3, 162.3. IR (neat): 1254, 1437, 3512 cm^{-1}. HRMS (MALDI) Calcd for $C_{18}H_{35}O_2Si_2$ $[M+H]^+$:339.2170, found 339.2170.

2-(*tert*-Butyldimethylsilyl)benzene-1,3-diol (20): To a solution of **19** (2.0 g, 5.0 mmol) in THF (50 mL, 0.10 M) was added TBAF (5.0 mL, 5.0 mmol) slowly at 0 °C. After stirring for 1 h, the reaction was stopped by adding a saturated aqueous solution of NH_4Cl and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was recrystallized from $CHCl_3$ to provide the titled compound **20** (0.86 mg, 77%) as a colourless solid. Mp: 128–131 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.41 (6 H, s), 0.94 (9 H, s), 4.90 (2 OH, s), 6.29 (2 H, d, J = 8.0 Hz), 7.07 (1 H, t, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –2.09, 18.4, 26.8, 107.7, 108.0, 131.4, 162.1. IR (neat): 1263, 1327, 1445, 3518 cm^{-1}. HRMS (MALDI) Calcd for $C_{12}H_{21}O_2Si$ $[M+H]^+$: 225.1305, found 225.1298.

2-(*tert*-Butyldimethylsilyl)-1,3-bis(trifluoromethanesulfonyloxy)benzene (8): To a solution of **20** (0.20 g, 0.89 mmol) in CH_2Cl_2 (4.5 mL, 0.20 M) were added DIPEA (0.47 mL, 2.7 mmol) and Tf_2O (0.45 mL, 2.7 mmol) at 0 °C. After stirring for 1 h at rt, the reaction was

stopped by adding $NaHCO_3$ aq. and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 20:1) to provide the titled compound **8** (0.37 g, 86%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.53 (6 H, s), 0.98 (9 H, s), 7.49 (2 H, d, J = 9.0 Hz), 7.56 (1 H, t, J = 9.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –2.00, 18.6, 26.5, 117.9, 118.6 (q, J = 318 Hz), 122.4, 132.3, 156.0. ^{19}F NMR (280 MHz, $CDCl_3$) δ: –73.8. IR (neat): 1215, 1424 cm^{-1}. Anal. Calcd for $C_{14}H_{18}F_6O_6S_2Si$: C, 34.42; H, 3.71. Found: C, 34.54; H, 3.72.

2-Bromohydroquinone (21):[24,25] To a solution of hydroquinone (6.4 g, 58 mmol) in $CHCl_3$ (0.29 L, 0.20 M) was added Br_2 (3.0 mL, 58 mmol) at 0 °C. After stirring for 1 h at rt, the mixture was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1) to provide the titled compound **21** (6.0 g, 55%) as a colourless solid. Mp: 111–114 °C (Lit. 112 °C).[25] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.12 (2 OH, brs), 6.73 (1 H, dd, J = 3.0, 9.0 Hz), 6.90 (1 H, d, J = 9.0 Hz), 6.99 (1 H, d, J = 3.0 Hz).

1,4-Bis(trimethylsilyloxy)-2-bromobenzene (22): To a solution of **21** (2.5 g, 13 mmol) in THF (65 mL, 0.20 M) were added Et_3N (5.4 mL, 39 mmol) and TMSCl (4.9 mL, 39 mmol). After stirring for 1 h at rt, the mixture was concentrated in vacuo. The residue was filtered through Celite pad (washed with hexane) and concentrated in vacuo as a colourless oil (4.3 g, quant). This compound **22** was used for next reaction without purification due to the instability on silica gel column chromatography.

2-(Trimethylsilyl)hydroquinone (23):[26] To a solution of **22** (4.3 g, 13 mmol) in THF (65 mL, 0.20 M) was added 2.3 M *n*-BuLi in hexane (11 mL, 26 mmol) slowly at –78 °C. After stirring for 1 h at rt, the reaction was stopped by adding a saturated aqueous solution of NH_4Cl and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **23** (2.1 g, 89%) as a colourless solid. Mp: 126–127 °C (Lit. 126–127 °C).[26] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.30 (9 H, s), 4.49 (OH, s), 4.54 (OH, s), 6.57 (1 H, d, J = 8.5 Hz), 6.70 (1 H, dd, J = 3.5, 8.5 Hz), 6.82 (1 H, d, J = 3.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –1.08, 115.5, 116.2, 117.0, 121.4, 149.0, 154.2. IR (neat): 1362, 3349 cm^{-1}. HRMS (MALDI) Calcd for $C_9H_{14}O_2Si$ $[M+H]^+$: 182.0758, found 182.0759.

1-(Methanesulfonyloxy)-3-(trimethylsilyl)-4-(trifluoromethanesulfonyloxy)benzene (11b): To a solution of **23** (0.90 g, 4.9 mmol) in CH_2Cl_2 (25 mL, 0.20 M) were added pyridine (2.6 mL, 32 mmol) and MsCl (1.9 mL, 25 mmol) at 0 °C. After stirring for 2 h at rt, the reaction was stopped by adding H_2O and the mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (toluene/EtOAc = 6:1) to provide the mixture of **11b** and 1,4-bis(methansulfonyloxy)-3-(trimethylsilyl)benzene (1.3 g). To a solution of the mixture in CH_2Cl_2 (14 mL) were added pyridine (1.9 mL, 24 mmol) and Tf_2O (3.1 mL, 18 mmol) at 0 °C. After stirring for 3 h at rt, the reaction was stopped by adding H_2O and the mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **11b** [1.0 g, 52% (2 steps)] as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.38 (9 H, s), 3.18 (3 H, s), 7.36 (1 H, dd, J = 3.0, 8.5 Hz), 7.21 (1 H, d, J = 8.5 Hz), 7.40 (1 H, d, J = 3.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –1.21, 37.6, 118.3 (q, J = 317 Hz), 121.2, 124.5, 129.3, 135.9, 147.5, 152.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ: –73.8. IR (neat): 1373, 1420 cm^{-1}. HRMS (APCI) Calcd for $C_{11}H_{16}F_3O_6S_2Si$ $[M+H]^+$: 393.01097, found 393.01356.

1,4-Bis(trifluoromethanesulfonyloxy)-3-(trimethylsilyl)benzene (11c): To a solution of **23** (1.0 g, 5.5 mmol) in CH_2Cl_2 (28 mL, 0.20 M) were added pyridine (2.0 mL, 25 mmol) and Tf_2O (2.8 mL, 17 mmol) at 0 °C. After stirring for 19 h at rt, the reaction was stopped by adding a saturated aqueous solution of NH_4Cl and the mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 15:1) to provide the titled compound **11c** (2.3 g, 95%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.39 (9 H, s), 7.34 (1 H, dd, J = 3.0, 9.0 Hz), 7.38 (1 H, d, J = 3.0 Hz), 7.44 (1 H, d, J = 9.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: –1.21, 118.4 (q, J = 318 Hz), 118.7 (q, J = 319 Hz), 121.5, 123.9, 128.6, 136.7, 147.9, 153.3. ^{19}F NMR (280 MHz, $CDCl_3$) δ: –73.7, –72.6. IR (neat): 1427 cm^{-1}. HRMS (APCI) Calcd for $C_{12}H_{13}F_6O_6S_2Si$ $[M+H]^+$: 446.98270, found 446.98508.

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$$\rho^{i}_{C_A} = n_i \times d_{C_A} \quad (1)$$

where n_i is occupancy of the *i*th NBO and d_{C_A} is percentage contribution from each carbon atom C_A for the *i*th NBO (Fig. 1).

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