Synthesis of Aryl Triflones through the Trifluoromethanesulfonylation of Benzynes

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The direct synthesis of aryl triflones, that is, trifluoromethanesulfonyl arenes, was achieved through the trifluoromethanesulfonylation of benzenes. The trifluoromethanesulfonyl group, one of the fluorinated functional groups, is a highly electron-negative and mild lipophilic substituent. Aryl triflones have high potential in the synthesis of bioactive compounds and specialty materials. The treatment of 2-(trimethylsilyl)aryl trifluoromethanesulphonates with cesium fluoride in the presence of 15-crown-5 generated benzynes, which reacted with sodium trifluoromethanesulfinate followed by protonation with tBuOH under heating conditions, provided aryl triflones in moderated to good yields. Both symmetrical and unsymmetrical triflones were nicely accessed under the same reaction conditions. Interestingly, the trifluoromethanesulfonylation of unsymmetrical benzene precursors proceeded smoothly to furnish corresponding aryl triflones in good yields with good to high regioselectivities. The balance of polarization of electric charge as well as steric hindrance of the benzene intermediates are central factors to control the outcome of regioselectivity.

1. Introduction

Fluorinated aromatics are prevalent in specialty materials, pharmaceuticals, and agrochemicals.[1] Aryl fluorides (Ar–F) and benzotri fluorides (Ar–CF3) have served as two major contributors in the last half century. In recent years, arenes with heteroatom-linked trifluoromethyl modifications, such as trifluoromethoxy arenes (Ar–OCF3),[2] trifluoromethylthio arenes (Ar–SCF3),[3] and trifluoromethanesulfonyl arenes (aryl triflones, Ar–SO2CF3)[3d, 4–16] have been considerably targeted. Our group is interested in aryl triflones.[3d, 17] Aryl triflones have a functional group, trifluoromethanesulfonyl (SO2CF3), which is a stronger electron-withdrawing group than trifluoromethyl (CF3),[18] thus altering the stability and log P values of the original compounds. In fact, aryl triflones have been successfully used as central structural motifs in biologically active molecules,[19] functional materials,[20] and chiral catalysts.[8] The synthesis of aryl triflones has been explored over the last two decades, leading to its categorization into three methodologies: trifluoromethanesulfonylation of arenes,[14, 9] oxidation of aryl trifluoromethyl sulfides,[10] and trifluoromethylation of aryl sulfonyl fluorides or aryl sulfonates.[11] From the viewpoint of late-stage functionalization in pharmaceuticals, the direct trifluoromethanesulfonylation of aryl ethers is particularly attractive.[12] In this context, we envisaged the use of benzynes for the direct synthesis of aryl triflones. Benzynes have a strained triple bond, which is highly reactive towards a wide variety of addition reactions.[18] We, thus, started the investigation of the preparation of aryl triflones using benzynes. During our investigation,[13] the only example of the synthesis of trifluoromethanesulfonyl benzene from benzene was reported (Scheme 1a).[14] However, it focused exclusively on the phenylsulfonylation of benzenes, and thus a general preparation of aryl triflones has not yet been established. Later, Li and co-workers[15] and Zhao et al.[16] in this order, reported the synthesis of aryl triflones from benzenes (Schemes 1b and 1c), but they methods were limited to the preparation of ortho-substituted triflones. Finally, the direct mono-functionalization of benzene to triflones continues to have limitations except for the single example by Singh and co-workers.[16] Herein, we disclose a full account of our work for the synthesis of aryl triflones through the trifluoromethanesulfonylation of benzynes (Scheme 1d).[13]

A wide variety of aryl triflones can be nicely accessed in moderated to good yields through the reaction of sodium trifluoromethanesulfinate (NaSO2CF3; Langlois reagent)[19] with benzenes followed by the addition of tBuOH for protonation. Highly reactive benzene derivatives were generated in situ.
from 2-(trimethylsilyl)aryl trifluoromethanesulfonates with cesium fluoride in the presence of 15-crown-5. This method is useful not only for the synthesis of symmetrical aryl triflones, but also unsymmetrical aryl triflones. More importantly, regioselective trifluoromethanesulfonlation of unsymmetrical benzyne precursors was also achieved, depending on both the steric hindrance and polarization of electric charge of benzyne. An ionic pathway, rather than a radical pathway, for the introduction of the SO$_2$CF$_3$ moiety to reactive benzyne was suggested by the use of TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl) experiments. The regioselectivity observed was analyzed based on the computations.

2. Results and Discussion

We first investigated the trifluoromethanesulfonlation of benzynes by using 2-(trimethylsilyl)naphthalen-3-yl trifluoromethanesulfonate (1a) as a benzyne precursor. Under conventional conditions$^{[15,16]}$ with KSO$_2$CF$_3$ (2.0 equiv)$^{[18]}$ and KF (4.0 equiv) in tetrahydrofuran (THF) at room temperature, no desired trifluoromethanesulfonlated product 2a was observed (Table 1, entry 1). We next attempted the reaction by using NaSO$_2$CF$_3$ and CsF in MeCN at room temperature. Desired 2a$^{[19]}$ was obtained in a low yield of 15% (entry 2). Screening the fluorides did not improve this transformation (entries 3–5), whereas the addition of 15-crown-5 increased the yield slightly to 19% (entry 6). The amount of CsF affected the conversion to 2a, increasing the yield to 44% (entry 7). Heating the reaction shortened the reaction time without affecting significantly the yield (entries 8, 9). We further examined the proton source. The use of H$_2$O was not effective (entry 10), but the addition of 1.0 equivalent of BuOH improved the yield to 50% (entry 11). The reaction was not inhibited in the presence of TEMPO, thus an ionic reaction was suggested (entry 12). We also attempted the reaction using sodium methanesulfinate (NaSO$_2$CH$_3$) instead of NaSO$_2$CF$_3$, but no desired SO$_2$CH$_3$-containing product, 2-methanesulfonyl naphthalene, was obtained (entry 13). The structure of product 2a was confirmed by spectroscopic analysis ($^1$H NMR δ: -78.69 ppm (triflone, SO$_2$CF$_3$)) and also by a comparison with an authentic sample of 2a, which was prepared by the oxidation of 2-trifluoromethylthio-naphthalene (see the Supporting Information).

With the optimal reaction conditions in hand, we examined the substrate scope for the trifluoromethanesulfonlation of symmetrical benzynes derived from corresponding precursors, 2-(trimethylsilyl)phenyl trifluoromethanesulfonate derivatives 1a–e (Table 2). The simple benzyne generated from 1b provided the trifluoromethanesulfonyl benzene (2b) in a moderate yield of 43% (entry 2). The alkyl-substituted benzyne derived from 4,5-dimethyl-substituted 1c gave 2c in 63% yield. It should be noted that the sterically demanding 3,6-dimethyl benzyne precursor 1d was nicely converted to the dimethylphenyl-triflone 2d in 76% yield (entry 4). The 5-trimethylsilyl-6-trifluoromethanesulfonyloxy indane 1e also provided the corresponding 5-trifluoromethanesulfonlated indane 2e in 74% yield (entry 5). We next investigated the trifluoromethanesulfonlation of unsymmetrical benzynes generated from 4- or 6-substituted 1-trimethylsilyl-2-trifluoromethanesulfonate arenes 1f–n (Table 3). 4-Methyl benzyne precursor 1f gave a mixture of aryl triflones 2f and 2f' in a 48:52 regioisomeric ratio in a combined yield of 58% (entry 1). The bulky 8-bu-substituted benzyne precursor 1g gave the corresponding regioisomeric aryl triflones 2g and 2g' in 47% yield in a ratio of 33:67 (entry 2). 4-Methoxy-substituted benzyne precursor 1h provided regioisomeric products 2h and 2h' in 57% yield (ratio, 74:26) selectively (entry 3). High regioselectivities were observed by the reaction of halogen-substituted benzyne precursors 1i and 1j to furnish the aryl triflones 2i and 2i' in 63% yield (ratio, 81:19) and 2j and 2j' in 41% yield (ratio, 85:15), respectively (en-

### Table 1. Optimization of reaction conditions$^{[20]}$

| Entry | F source [equiv] | Additive | Temp. [°C] | Time [h] | Yield [%] |
|-------|-----------------|----------|------------|----------|-----------|
| 1$^{[1]}$ | KF (4.0) | 18-crown-6 | RT | 24 | NR |
| 2 | CsF (4.0) | - | RT | 24 | 15 |
| 3 | TMAF (4.0) | - | RT | 24 | 9 |
| 4 | TBAF·3H$_2$O (4.0) | - | RT | 24 | trace |
| 5 | TBAF (4.0) | - | RT | 24 | trace |
| 6 | CsF (4.0) | 15-crown-5 | RT | 24 | 19 |
| 7 | CsF (6.0) | 15-crown-5 | RT | 24 | 44 |
| 8 | CsF (6.0) | 15-crown-5 | 40 | 4 | 45 |
| 9 | CsF (6.0) | 15-crown-5 | 50 | 4 | 42 |
| 10$^{[2]}$ | CsF (6.0) | 15-crown-5 | 40 | 3 | 42 |
| 11$^{[2]}$ | CsF (6.0) | 15-crown-5 | 40 | 3 | 50 |
| 12$^{[2]}$ | CsF (6.0) | 15-crown-5 | 40 | 3 | 49 |
| 13$^{[2]}$ | CsF (6.0) | 15-crown-5 | 40 | 3 | NR$^{[2]}$ |

[a] Reaction was carried out with 1a, NaSO$_2$CF$_3$ (2.0 equiv), an F source, and an additive (2.0 equiv) in MeCN (1.0 mL). [b] KSO$_2$CF$_3$ was used instead of NaSO$_2$CF$_3$ 18-crown-6 (6.0 equiv), with THF as the solvent. [c] H$_2$O (1.0 equiv) was added. [d] BuOH (1.0 equiv) was added. [e] TEMPO (2.0 equiv) was added. [f] Reaction was carried out using NaSO$_2$CH$_3$ instead of NaSO$_2$CF$_3$. [g] No desired product, 2-methanesulfonyl naphthalene, was obtained.
tries 4 and 5). On the other hand, phenyl-substituted benzyne precursor 1k gave the aryl triflones 2k and 2k' in 77% yield in a ratio of 48:52 at a higher reaction temperature (50 °C) (entry 6). The unsymmetrical naphthalene-containing aryne precursor 1l provided the trifluoromethanesulfonylated naphthalenes 2l (2a) and 2l' (2a') in 64% yield in a ratio of 67:33 (entry 7). It should be pointed out that 6-substituted 1-trimethylsilyl-2-trifluoromethanesulfonate benzyne precursors 1m and 1n solely provided the 3-substituted phenyl triflones 2m' (2h') and 2n' (2j') in moderate yields, 42 and 27%, respectively (entries 8 and 9).

According to previous studies of regioselectivity of substituted benzenes,[18,21] the regioselectivity observed in Table 2 could be rationally explained by both the balance of polarization of the electric charge and steric hindrance of the benzyne intermediates I (Scheme 2). Initially, Cs⁺ is captured by 15-crown-5 to generate naked fluoride anion, which attacks the silicon atom of 1 to generate highly reactive benzyne I. Then, SO₂CF₃ anion attacks benzynes I followed by protonation with tBuOH to provide desired aryl triflones 2 (Scheme 2). The formation of the major meta-isomer 2g' (R=tBu) can be explained by the preferential attack of the SO₂CF₃ anion to C3, as C4 is more negative because of the electron-donating effect of the tBu substituent (positive inductive effect, Figure 1a).

On the other hand, for the MeO-, Cl- and Br-substituted benzyne precursors 1f and 1k (R=Me, Ph) suggest that there is no significant difference between steric and electronic factors on C3 and C4 (Figure 1c). Complete regioselective formation of meta-substituted isomers 2m' (2h') and 2n' (2j') from 1m and 1n should be explained by both the steric effect and polarization of the electric charge on C2 and C3 (Figure 1d).

Table 2. Trifluoromethanesulfonylation of symmetrical benzyne precursors 1a–e.

| Entry | Substrate Product | Yield [%] |
|-------|------------------|-----------|
| 1     | 1a               | 50        |
| 2     | 1b               | 43        |
| 3     | 1c               | 63        |
| 4     | 1d               | 76        |
| 5     | 1e               | 74        |

[a] Reaction was carried out with 1, NaSO₂CF₃ (2.0 equiv), CsF (6.0 equiv), 15-crown-5 (2.0 equiv), and tBuOH (1.0 equiv) in MeCN (1.0 mL) at 40 °C for 3 h.

Table 3. Trifluoromethanesulfonylation of unsymmetrical benzyne precursors 1f–n.

| Entry | Substrate Product | Yield [%] |
|-------|------------------|-----------|
| 1     | 1f               | 57        |
| 2     | 1g               | 63        |
| 3     | 1h               | 57        |
| 4     | 1i               | 41        |
| 5     | 1j               | 77        |
| 6     | 1k               | 64        |
| 7     | 1l               | 42        |
| 8     | 1m               | 27        |

[a] Reaction was carried out with 1a, NaSO₂CF₃ (2.0 equiv), CsF (6.0 equiv), 15-crown-5 (2.0 equiv), tBuOH (1.0 equiv) in MeCN (1.0 mL) at 40 °C for 3 h. [b] The ratios of regioisomers are shown in parentheses and were determined by crude products of ¹⁹F NMR spectroscopy. [c] Carried out at 50 °C.

Scheme 2. Proposed reaction mechanism for the reaction of 1 to 2.
The preferred formation of 2-SO$_2$CF$_3$ naphthalene 2 (2a) is the result of sterically favored attack on C2, owing to the steric repulsion by peri-hydrogen in the 1,2-naphthalene (Figure 1e).\[22\]

Finally, the regioselectivity was analyzed by computations. The structures of benzynes were initially optimized by density functional theory (DFT) [B3LYP/6-31G(d)],\[23\] and then the electron densities of their reacting π orbitals were calculated by using a natural bond orbital (NBO) 6.0.\[24, 25\] The differences of the electron densities in the π orbital at the triple bond are shown in Figure 2 and they are in good agreement with the experimental observations of the selectivity. In the case of 1-tBu substitution of 3,4-benzene, the electron density in the π orbital at C3 (0.9103) was lower than that at C4 (0.9576) (Figure 2a). On the other hand, the electron densities in the π orbitals at C4 of 1-Cl- and Br-substituted 3,4-benzenes were lower than those at C3 (Figure 2b). For 1-OMe-substituted 3,4-benzene, the direction of the Me group against the triple bond strongly affected the bias of the electron density, and the electron densities in the cis-configuration of 1-OMe 3,4-benzene are in good agreement with the experimental observation, whereas those of trans-configuration are not. In the case of Me- and Ph-substituted 3,4-benzene, the difference between the electron densities are small, resulting in low regioselectivities (Figure 2c). Excellent regioselectivity was observed for MeO- and Br-substituted 2,3-benzynes, which could be well explained based on the large difference of electron densities in the π orbital at C3 and C2 (Figure 2d). The preferred formation of 2-SO$_2$CF$_3$ naphthalene is also in good agreement with the calculations (Figure 2e).

3. Conclusions

We have succeeded in synthesizing aryl triflones through the direct trifluoromethanesulfonfylolation of benzynes. A wide variety of 1-trimethylsilyl-2-trifluoromethanesulfonate arenues are feasible as precursors to generate highly reactive benzynes upon treatment with CsF and 5-crown-15 followed by the reaction with NaSO$_2$CF$_3$ to furnish a variety of aryl triflones in moderate to good yields. Regioselective trifluoromethanesulfonylation was achieved, depending on the substrate structures and selectivity, by balancing the polarization of electric charge and steric hindrance of the benzene intermediates. All aryl triflones are expected to serve as building blocks for biologically active molecules and materials. As excess amounts of the reagents are necessary in the present method, further improvement of the reaction conditions are required. Applications of this methodology, including the synthesis of heteroaryl triflones,\[4\] are also under investigation.

Experimental Section

General Procedure of Trifluoromethanesulfonfylolation

To a stirred solution of 2-(trimethylsilyl)aryl trifluoromethanesulfonates 1\[26\] (0.1 mmol), sodium trifluoromethanesulfinate (31.2 mg, 0.2 mmol, 2.0 equiv) in acetonitrile (1.0 mL) was added with 15-crown-5 (39.7 μL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 μL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) at room temperature under a nitrogen atmosphere. After the reaction mixture was stirred at 40°C for 3 h, it was cooled to room temperature, water was added, and the whole mixture was extracted with Et$_2$O. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure to give the crude product. The residue was purified by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel to give trifluoromethanesulfonfyl benzene 2.
A reaction of 2-(trimethylsilyl)naphthalen-3-yl trifluoromethanesulfonate 1a (34.8 mg, 0.1 mmol), sodium trifluoromethanesulfonate (31.2 mg, 0.2 mmol, 2.0 equiv), 15-crown-5 (39.7 µL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 µL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 40 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave 2-(trifluoromethylsulfonyl)naphthalene 2a (13.1 mg, 50%) as a yellow solid.

2: H NMR (CDCl₃, 300 MHz) δ: 7.69–7.81 (m, 2H), 7.94–8.01 (m, 2H), 8.06–8.11 (m, 2H), 8.67 (s, 1 H) ppm; ¹³C NMR (CDCl₃, 282 MHz) δ: −78.7 (s, 3F) ppm; ¹¹B NMR (CDCl₃, 150.9 MHz) δ: 119.9 (q, J = 325.9 Hz), 123.7, 128.0, 128.1, 128.3, 129.8, 130.2, 130.8, 132.0, 134.0 (m), 136.3 ppm; IR (KBr): 3083, 2952, 2877, 2609, 2375, 1930, 1790, 1654, 1564, 1558, 1541, 1521, 1507, 1473, 1456, 1417, 1418, 1373, 1074 cm⁻¹; MS (EI): m/z: 260 (M+); HRMS (EI): calcd for C₁₃H₁₁F₂O₅S: 260.0119; found: 260.0135.

A reaction of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 1b (29.8 mg, 0.1 mmol), sodium trifluoromethanesulfonate (31.2 mg, 0.2 mmol, 2.0 equiv), 15-crown-5 (39.7 µL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 µL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 40 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave 1-(trifluoromethylsulfonyl)benzene 2b (9.0 mg, 43%) as a colorless oil.

δ: 7.67–7.72 (m, 2H), 7.83–7.88 (m, 1H), 8.06 (d, J = 8.1 Hz, 2H) ppm; ¹³C NMR (CDCl₃, 282 MHz) δ: −78.9 (s, 3F) ppm; ¹¹B NMR (CDCl₃, 150.9 MHz) δ: 119.8 (q, J = 325.9 Hz), 129.9, 130.8, 131.3, 136.6 ppm; IR (NaCl): 2360, 1844, 1793, 1771, 1734, 1716, 1699, 1684, 1635, 1635, 1617, 1558, 1541, 1521, 1507, 1473, 1456, 1417, 1418, 1373, 1074 cm⁻¹; MS (EI, m/z): 141 (M-CF₃); HRMS (EI): calcd for C₁₀H₇F₂O₅S: 210.0055, found: 210.0054.

A reaction of 4,5-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 1c (32.6 mg, 0.1 mmol), sodium trifluoromethanesulfonate (31.2 mg, 0.2 mmol, 2.0 equiv), 15-crown-5 (39.7 µL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 µL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 40 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave 1,2-dimethyl-4-(trifluoromethylsulfonyl)benzene 2c (15.1 mg, 63%) as a white solid.

δ: 2.39 (s, 3H), 2.41 (s, 3H), 7.42 (d, J = 7.5 Hz, 1H), 7.76–7.78 (m, 2H) ppm; ¹³C NMR (CDCl₃, 282 MHz) δ: −79.2 (s, 3F) ppm; ¹¹B NMR (CDCl₃, 150.9 MHz) δ: 19.8, 20.3, 119.8 (q, J = 325.9 Hz), 128.1, 128.3, 130.1, 131.2, 139.0, 147.1 ppm; IR (KBr): 3083, 2952, 2877, 2609, 2375, 1930, 1790, 1654, 1596, 1483, 1451, 1362, 1304, 1125, 1082, 1042, 893, 826, 763, 705, 672, 608, 509 cm⁻¹; MS (EI, m/z): 250 (M⁺); HRMS (EI): calcd for C₁₃H₁₀F₂O₅S: 250.0275, found: 250.0276.

A reaction of 4-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 1f (32.1 mg, 0.2 mmol), sodium trifluoromethanesulfonate (31.2 mg, 0.2 mmol, 2.0 equiv), 15-crown-5 (39.7 µL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 µL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 40 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave inseparable mixture of 1-Methyl-4-(trifluoromethylsulfonyl)benzene 2f (12.8 mg, 57%, 48:52) as a colorless oil.

δ: 2.50 (s, 3H), 2.52 (s, 3H), 7.47 (d, J = 7.8 Hz, 2H), 7.53–7.58 (m, 1H), 7.63–7.65 (m, 1H), 7.82–7.86 (m, 2H), 7.93 (d, J = 8.4 Hz, 2H) ppm; ¹³C NMR (CDCl₃, 282 MHz) δ: 25.2, 32.5, 33.2, 119.9 (q, J = 325.9 Hz), 125.6, 126.4, 128.7, 129.2, 146.5, 154.8 ppm; IR (KBr): 3066, 2969, 1931, 1814, 1598, 1573, 1437, 1413, 1363, 1263, 1216, 1063, 886, 828, 763, 686, 607, 518, 460, 417 cm⁻¹; MS (EI, m/z): 250 (M⁺); HRMS (EI): calcd for C₁₃H₁₀F₂O₅S: 250.0275, found: 250.0302.
1-Chloro-4-(trifluoromethylsulfonyl)benzene (2b)[28] and 1-Chloro-3-(trifluoromethylsulfonyl)benzene (2c)[28]

A reaction of 4-chloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 11 (33.3 mg, 0.1 mmol), sodium trifluoromethanesulfonate (31.2 mg, 0.2 mmol, 2.0 equiv), 15-crown-5 (39.7 µL, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (9.5 µL, 0.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 40 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave a mixture of 1-chloro-4-(trifluoromethylsulfonyl)benzene 2b and 1-chloro-3-(trifluoromethylsulfonyl)benzene 2c (10.0 mg, 41 %, 81:19) as a white semisolid.

2f: Colorless oil. 1H NMR (CDCl3, 300 MHz) δ: 7.64 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 8.03 (s, 1H) ppm; 13C NMR (CDCl3, 75 MHz) δ: 111.0 (M-SO2F) ppm; HRMS (EI): calcd for C15H10F3O2S: 266.0588, found: 266.0631.

1-Chloro-4-(trifluoromethylsulfonyl)benzene (2b)[28] and 1-Chloro-3-(trifluoromethylsulfonyl)benzene (2c)[28]
4-(Trifluoromethylsulfonyl) biphenyl (2k) \(^{5a,11b}\) and 3-(Trifluoromethylsulfonyl) biphenyl (2k’)

A reaction of 4-phenyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1k) (31.2 mg, 0.2 mmol, 2.0 equiv), tert-butyl alcohol (95.1 mg, 1.1 mmol, 1.0 equiv), and cesium fluoride (91.2 mg, 0.6 mmol, 6.0 equiv) in acetonitrile (1.0 mL) proceeded at 50 °C for 3 h. Subsequent purification by column chromatography (n-hexane/ethyl acetate = 95/5) on silica gel gave 4-(trifluoromethylsulfonyl) biphenyl 2k and 3-(trifluoromethylsulfonyl) biphenyl 2k’ (18.3 mg, 64%, 48:52) as a white solid.

Confict of Interest

The authors declare no conflict of interest.

Keywords: benzylcine · fluorine · pharmaceuticals · trifluoromethanesulfonan group · trifluoromethanesulfonanlonation

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Theoretical Synthesis

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