Metal-Free Sulfonylation of Arenes with N-Fluorobenzensulfonylimide 

via Cleavage of S-N Bonds: Expeditious Synthesis of Diarylsulfones 

(Supporting Information)

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General remarks

All manipulations were conducted with sealed tubes. $^1$H-NMR spectra were recorded on a Bruker AVIII-400 spectrometers. Chemical shifts (in ppm) were calibrated with Chloroform-d. $^{13}$C-NMR spectra were obtained by using the same NMR spectrometers and were calibrated with Chloroform-d. Analytical thin-layer chromatography (TLC) was conducted with TLC plates (Silica gel 60 F254, Qingdao Haiyang). Flash column chromatography was performed on silica gel 200-300 mesh with freshly distilled solvents. HRMS data were recorded on a maXis UHR-TOF mass spectrometer. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.
Table S1. Optimization of reaction conditions (Representative results).\textsuperscript{a,b}

\begin{center}
\begin{tabular}{cccc}
\hline
Entry & Acid (1.0 eq) & Time (h) & Yield\textsuperscript{b} (%) \\
\hline
1 & TfOH & 48 & 73 \\
2 & HCl (36\%) & 48 & 37 \\
3 & HNO\textsubscript{3} (65\%) & 48 & 65 \\
4 & AlCl\textsubscript{3} & 48 & 32 \\
5 & – & 48 & – \\
6 & TfOH & 30 & 75 \\
7 & TfOH & 36 & 79 \\
8 & TfOH & 44 & 75 \\
\hline
\end{tabular}
\end{center}

\textsuperscript{a} Reaction conditions: 2a (1.0 mmol) and acid in 1a (2 mL) at 130 °C under air.

\textsuperscript{b} Isolated yields.
Experimental procedure and characterization data

1) 1-Chloro-4-(phenylsulfonyl)benzene  (3a) \(^\text{[1]}\)

![Image of 1-Chloro-4-(phenylsulfonyl)benzene]

**Typical procedure:**
The reaction of chlorobenzene (2.5 mmol, 281.0 mg), N-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic acid (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 199.2 mg (79%) of 3a as solid: \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.93 (dd, \(J = 7.6, 1.6\) Hz, 2H), 7.89 (dd, \(J = 6.8, 2.0\) Hz, 2H), 7.58 (d, \(J = 7.6\) Hz, 1H), 7.52-7.47 (m, 4H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 141.1, 140.0, 139.8, 133.4, 129.5, 129.4, 129.1, 127.6. MS (70 eV): m/z (%): [M]\(^+\), 252 (45).

2) 1-Fluoro-4-(phenylsulfonyl)benzene (3b) \(^\text{[2]}\)

![Image of 1-Fluoro-4-(phenylsulfonyl)benzene]

The reaction of fluorobenzene (2.5 mmol, 240.3 mg), N-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic acid (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 178.7 mg (76%) of 3b as solid: \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.99-7.93 (m, 4H), 7.58 (d, \(J = 6.0\) Hz, 1H), 7.57-7.50 (m, 2H), 7.18 (t, \(J = 8.8\) Hz, 2H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 165.3 (d, \(^1J_{C-F} = 254.7\) Hz), 141.3, 137.5 (d, \(^4J_{C-F} = 2.5\) Hz), 133.3, 130.4 (d, \(^3J_{C-F} = 9.4\) Hz), 129.3, 127.5, 116.5 (d, \(^2J_{C-F} = 22.4\) Hz). \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\): -104.2 ppm. MS (70 eV): m/z (%): [M]\(^+\), 236 (50).

3) 1-Bromo-4-(phenylsulfonyl)benzene  (3c) \(^\text{[2]}\)
The reaction of bromobenzene (2.5 mmol, 392.5 mg), N-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 203.3 mg (68%) of 3c as solid. 1H NMR (400 MHz, CDCl3) δ: 7.92 (t, J = 1.2 Hz, 2H), 7.81 (dd, J = 6.4, 2.0 Hz, 2H), 7.65 (dd, J = 6.8, 2.0 Hz, 2H), 7.58 (d, J = 7.2 Hz, 1H), 7.52 (dd, J = 8.0, 7.2 Hz, 2H). 13C NMR (100 MHz, CDCl3) δ: 141.0, 140.6, 133.4, 132.5, 129.4, 129.1, 128.4, 127.6. MS (70 eV): m/z (%): [M]+, 296 (35).

4) 1-Iodo-4-(phenylsulfonyl)benzene (3d) [1]

The reaction of iodobenzene (2.5 mmol, 510.0 mg), N-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 218.0 mg (63%) of 3d as solid. 1H NMR (400 MHz, CDCl3) δ: 7.93 (dd, J = 7.6, 1.6 Hz, 2H), 7.86 (dd, J = 6.4, 2.0 Hz, 2H), 7.65 (dd, J = 6.8, 2.0 Hz, 2H), 7.58 (d, J = 7.2 Hz, 1H), 7.52 (dd, J = 8.4, 6.8 Hz, 2H). 13C NMR (100 MHz, CDCl3) δ: 141.2, 141.0, 138.5, 133.4, 129.3, 129.0, 127.5, 101.0. MS (70 eV): m/z (%): [M]+, 344 (100).

5) Sulfonyldibenzene (3e) [2]

The reaction of benzene (1.25 mmol, 97.6 mg), N-fluorobenzenesulfonimide (2a) (0.25 mmol, 78.9 mg), trifluoromethanesulfonic (150 mol %, 33 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 158.4 mg (73%) of 3e as solid. 1H NMR (400 MHz,
CDCl$_3$ δ: 7.95 (dd, $J = 8.0$, 1.2 Hz, 4H), 7.56 (dd, $J = 4.0$, 1.2 Hz, 2H), 7.51 (dd, $J = 8.0$, 7.2 Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 141.4, 133.1, 129.2, 127.6. MS (70 eV): m/z (%): [M]$^+$, 218 (25).

6) 1-Methyl-4-(phenylsulfonyl)benzene (3f)

![Chemical structure](image)

The reaction of toluene (2.5 mmol, 230.4 mg), $N$-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 185.8 mg (80%) (1.3:1) of 3f as solid.

(major): $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.93 (t, $J = 1.6$ Hz, 2H), 7.83 (d, $J = 8.4$ Hz, 2H), 7.54 (d, $J = 7.6$ Hz, 1H), 7.49 (t, $J = 6.8$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 144.1, 141.9, 138.6, 133.0, 129.9, 129.2, 127.7, 127.4, 21.5. (minor): $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.22 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.86 (t, $J = 1.2$ Hz, 2H), 7.57 (d, $J = 7.2$ Hz, 1H), 7.52-7.47 (m, 3H), 7.41 (d, $J = 8.0$ Hz, 1H), 7.23 (d, $J = 7.6$ Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 141.2, 138.7, 137.9, 133.6, 133.0, 132.6, 129.4, 129.0, 127.6, 126.4, 20.2. MS (70 eV): m/z (%): [M]$^+$, 232 (100).

7) 1-Isopropyl-4-(phenylsulfonyl)benzene (3g)

![Chemical structure](image)

The reaction of cumene (2.5 mmol, 300.4 mg), $N$-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 256.2 mg (97%) (4:1) of 3g as solid.

(major): $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.96-7.94 (m, 2H), 7.86 (dd, $J = 6.4$, 1.6 Hz, 2H), 7.54 (t, $J = 0.8$ Hz, 1H), 7.52-7.48 (m, 4H), 7.39 (s, 1H), 7.35 (d, $J = 8.4$ Hz, 2H), 2.94 (d, $J = 6.8$ Hz, 1H), 1.25 (d, $J = 7.6$ Hz, 3H), 1.23 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 154.8, 141.9, 138.8, 133.0, 129.2, 127.8, 127.6, 127.4, 34.2, 23.6. (minor): $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.21 (dd, $J = 8.0$, 1.6
Hz, 1H), 7.86 (dd, J = 6.8, 1.6 Hz, 2H), 7.57-7.48 (m, 4H), 7.31 (d, J = 7.6 Hz, 1H), 2.86 (dd, J = 15.2, 7.2 Hz, 2H), 1.03 (t, J = 7.6 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 144.1, 141.9, 138.4, 133.7, 132.9, 130.9, 129.5, 129.0, 127.4, 126.2, 25.5, 15.0. MS (70 eV): m/z (%): [M]$^+$, 260 (80).

8) 1-(tert-Butyl)-4-(phenylsulfonyl)benzene (3h)$^{[5]}$

![Structure of 1-(tert-Butyl)-4-(phenylsulfonyl)benzene (3h)]

The reaction of tert-butylbenzene (2.5 mmol, 335.6 mg), N-fluorobenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 $\mu$L), was carried out in 0.5 mL trifluoroacetic acid at 60 $^\circ$C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 251.4 mg (92%) of 3h as solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.96-7.94 (m, 2H), 7.86 (dd, J = 6.4, 1.6 Hz, 2H), 7.54 (t, J = 0.8 Hz, 1H), 7.52-7.48 (m, 4H), 1.31 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 154.8, 141.9, 138.8, 133.0, 129.2, 127.8, 127.6, 127.4, 34.2, 23.6. MS (70 eV): m/z (%): [M]$^+$, 274 (25).

9) 1-Cyclohexyl-4-(phenylsulfonyl)benzene (3i)

![Structure of 1-Cyclohexyl-4-(phenylsulfonyl)benzene (3i)]

The reaction of cyclohexylbenzene (2.5 mmol, 400.7 mg), N-fluorobenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 $\mu$L), was carried out in 0.5 mL trifluoroacetic acid at 80 $^\circ$C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 224.8 mg (75%) (4:1) of 3i as solid. (major): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.95 (d, J = 7.2 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.57-7.48 (m, 3H), 7.31 (t, J = 8.4 Hz, 2H), 2.55 (d, J = 8.4 Hz, 1H), 1.84-1.74 (d, J = 6.4 Hz, 4H), 1.43-1.22 (m, 6H). $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$: 153.9, 141.9, 138.7, 133.0, 129.2, 127.8, 127.7, 127.5, 44.5, 34.0, 26.6, 26.0. (minor): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.27 (dd, J = 8.4, 1.6 Hz, 1H), 7.86 (dd, J = 7.2, 1.6 Hz, 2H), 7.56 (t, J = 4.4 Hz, 2H), 7.51 (t, J = 1.6 Hz, 2H), 7.40-7.36 (m, 2H), 1.67 (d, J = 6.8 Hz, 4H), 1.23 (t, J = 6.4 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 147.8, 142.5, 138.0, 133.8, 132.8, 129.0, 128.9, 128.8, 127.4, 126.0, 39.5, 33.7, 26.7, 25.9. HRMS
(EI), m/z calcd. for C₁₈H₂₀O₂S [M⁺]: 300.1184, found: 300.1177.

10) 1-Methoxy-4-(phenylsulfonyl)benzene  (3j)

\[
\text{MeO} \quad \text{S} \quad \text{O} \quad \text{Ph}
\]

The reaction of anisole (2.5 mmol, 270.4 mg), N-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 224.0 mg (90%) (1.5:1) of 3j as solid.

(major): ¹H NMR (400 MHz, CDCl₃) δ: 7.92 (t, J = 6.8 Hz, 2H), 7.88 (dd, J = 7.2, 2.0 Hz, 2H), 7.54 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 1.6 Hz, 2H), 6.97 (dd, J = 7.2, 2.4 Hz, 2H), 3.85 (s, 3H).

¹³C NMR (100 MHz, Chloroform-d) δ: 163.3, 142.3, 133.0, 132.8, 129.9, 129.2, 127.3, 114.5, 55.6. (minor): ¹H NMR (400 MHz, CDCl₃) δ: 8.17 (dd, J = 7.6, 1.6 Hz, 1H), 7.97 (t, J = 1.2 Hz, 2H), 7.56 (dd, J = 7.6, 2.0 Hz, 2H), 7.49 (t, J = 7.2 Hz, 2H), 7.12 (d, J = 7.6 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ: 157.0, 141.1, 135.5, 132.9, 129.8, 128.9, 128.4, 128.3, 120.5, 112.4, 55.8. MS(70 eV): m/z (%): [M⁺], 248 (60).

11) 4-(Phenylsulfonyl)phenol  (3k)

\[
\text{O} \quad \text{S} \quad \text{O} \quad \text{Ph}
\]

The reaction of phenol (0.8 mmol, 75.3 mg), N-fluorobenzenesulfonylimide (2a) (0.4 mmol, 126.4 mg), trifluoromethanesulfonic (500 mol %, 177 μL), was carried out in 1.0 mL trifluoroacetic acid at 100 °C under air for 12 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 29.2 mg (16%) of 3k as solid. ¹H NMR (400 MHz, CDCl₃) δ: 7.94-7.90 (m, 2H), 7.86-7.82 (m, 2H), 7.57-7.47 (m, 3H), 6.93-6.89 (m, 2H), 5.62 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ: 160.6, 141.8, 133.7, 132.07, 130.0, 129.3, 127.1, 116.2. HRMS: m/z [M+Na⁺]: calcd for C₁₂H₁₀NaO₃S: 257.0243; found: 257.0241.

12) 1,4-Dimethyl-2-(phenylsulfonyl)benzene (3m)
The reaction of \( p \)-xylene (2.5 mmol, 268.1 mg), \( N \)-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 \( \mu \)L), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 152.3 mg (62%) of 3m as solid. \(^1\)H NMR (400 MHz, CDCl\( _3 \)) \( \delta \): 8.05 (d, \( J = 0.8 \) Hz, 1H), 7.86 (t, \( J = 1.6 \) Hz, 2H), 7.56 (d, \( J = 7.2 \) Hz, 1H), 7.50 (dd, \( J = 8.0, 6.8 \) Hz, 2H), 7.28 (d, \( J = 0.8 \) Hz, 1H), 7.11 (d, \( J = 8.0 \) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl\( _3 \)) \( \delta \): 141.2, 138.2, 136.3, 134.6, 134.3, 132.8, 132.5, 129.6, 128.9, 127.4, 20.8, 19.6. MS (70 eV): m/z (%): [M]\(^+\), 246 (90).

13) 1-Chloro-4-methyl-2-(phenylsulfonyl)benzene (3n)

The reaction of 1-chloro-4-methylbenzene (2.5 mmol, 316.5 mg), \( N \)-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 \( \mu \)L), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 170.0 mg (64%) of 3n as solid. \(^1\)H NMR (400 MHz, CDCl\( _3 \)) \( \delta \): 8.22 (d, \( J = 2.0 \) Hz, 1H), 7.88 (t, \( J = 1.6 \) Hz, 2H), 7.60 (d, \( J = 7.2 \) Hz, 1H), 7.53 (dd, \( J = 8.0, 6.8 \) Hz, 2H), 7.45 (dd, \( J = 8.0, 2.4 \) Hz, 1H), 7.17 (d, \( J = 8.0 \) Hz, 1H), 2.40 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\( _3 \)) \( \delta \): 140.5, 140.3, 136.3, 134.0, 133.5, 133.4, 132.5, 129.2, 129.1, 127.8, 19.6. HRMS (EI), m/z calcd. for C\(_{13}\)H\(_{11}\)ClO\(_2\)S [M]\(^+\): 266.0168, found: 266.0174.

14) 2,4-Dimethyl-1-(phenylsulfonyl)benzene (3o) \(^6\)

The reaction of \( m \)-xylene (2.5 mmol, 265.0 mg), \( N \)-fluorobenzenesulfonylimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 \( \mu \)L), was carried out in 0.5 mL trifluoroacetic
acids at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 208.0 mg (84%) of 3o as solid. $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.11 (d, $J$ = 0.8 Hz, 1H), 7.84 (t, $J$ = 1.6 Hz, 2H), 7.60 (d, $J$ = 7.6 Hz, 1H), 7.51-7.47 (m, 2H), 7.20 (d, $J$ = 8.0 Hz, 1H), 7.04 (s, 1H), 2.39 (s, 3H), 2.37 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 144.4, 141.5, 137.7, 135.8, 133.3, 132.8, 129.6, 128.9, 127.5, 127.0, 21.3, 20.1. MS (70 eV): m/z (%): [M]$^+$, 246 (60).

15) 2,4-Dichloro-1-(phenylsulfonyl)benzene (3p)

The reaction of 1,3-dichlorobenzene (2.5 mmol, 371.2 mg), N-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 169.6 mg (59%) of 3p as solid. $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.31 (d, $J$ = 8.8 Hz, 1H), 7.94 (dd, $J$ = 7.2, 5.6 Hz, 2H), 7.62 (d, $J$ = 7.6 Hz, 1H), 7.53 (t, $J$ = 7.2 Hz, 2H), 7.49-7.45 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 140.6, 139.6, 137.0, 133.9, 133.7, 132.0, 131.8, 129.0, 128.5, 127.6. HRMS (EI), m/z calcd. for C$_{12}$H$_8$Cl$_2$O$_2$S [M]$^+$: 285.9622, found: 285.9625.

16) 2-Chloro-1-methyl-4-(phenylsulfonyl)benzene (3q) $^{[7]}$

The reaction of 1-chloro-2-methylbenzene (2.5 mmol, 316.5 mg), N-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 225.6 mg (85%) (3.5:1) of 3q as solid. (major): $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.96 (m, 2H), 7.81 (d, $J$ = 2.0 Hz, 1H), 7.71 (dd, $J$ = 8.4, 2.0 Hz, 1H), 7.58 (d, $J$ = 6.0 Hz, 1H), 7.56-7.49 (m, 2H), 7.45 (d, $J$ = 8.4 Hz, 1H), 2.40
(d, J = 2.4 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 141.2, 139.9, 139.7, 137.7, 133.3, 129.9, 129.7, 129.3, 127.6, 126.3, 20.1. (minor): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.95 – 7.91 (m, 3H), 7.72 (dd, J = 8.0, 2.4 Hz, 1H), 7.59 -7.57 (m, 1H), 7.54-7.50 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 2.41 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 142.2, 139.9, 139.7, 137.7, 133.3, 129.7, 129.3, 127.6, 126.3, 20.1.

17) 1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (3r)$^{[1]}$

![1,3,5-Trimethyl-2-(phenylsulfonyl)benzene (3r)](image)

The reaction of mesitylene (2.5 mmol, 300.5 mg), N-fluorobenzenesulfonimide (2a) (0.5 mmol, 157.7 mg), trifluoromethanesulfonic (150 mol %, 66 $\mu$L), was carried out in 0.5 mL trifluoroacetic acid at 80 $^\circ$C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 183.2 mg (70%) of 3s as solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.78 (t, J = 1.2, Hz, 2H), 7.54 (s, 1H), 7.47 (t, J = 1.6, Hz, 2H), 6.94 (s, 2H), 2.59 (s, 6H), 2.30 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 143.4, 143.4, 140.0, 133.7, 132.5, 132.2, 128.8, 126.2, 22.8, 21.0 ppm. MS (70 eV): m/z (%): [M]$^+$, 260 (40).

18) 1-Chloro-4-tosylbenzene (4a)$^{[8]}$

![1-Chloro-4-tosylbenzene (4a)](image)

The reaction of chlorobenzene (2.5 mmol, 281.0 mg), N-fluoro-4-methyl-N-tosylbenzenesulfonamide (2b) (0.5 mmol, 171.7 mg), trifluoromethanesulfonic (150 mol %, 66 $\mu$L), was carried out in 0.5 mL trifluoroacetic acid at 60 $^\circ$C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 204.3 mg (76%) of 4a as solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.86 (dd, J = 19.2, 6.8 Hz, 4H), 7.46 (d, J = 6.8 Hz, 2H), 7.31 (d, J =8.0 Hz, 2H), 2.41 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 144.1, 141.9, 133.0, 129.9, 129.2, 127.7, 127.5, 21.6. MS (70 eV): m/z (%): [M]$^+$, 266 (60).

19) 1-Fluoro-4-tosylbenzene (4b)$^{[21]}$
The reaction of fluorobenzene (2.5 mmol, 242.7 mg), N-fluoro-4-methyl-N-tosylbenzenesulfonamide (4b) (0.5 mmol, 171.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 204.7 mg (82%) of 4b as solid. 1H NMR (400 MHz, CDCl3) δ: 7.94 (dd, J = 8.8, 5.6 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.16 (dd, J = 8.8, 7.6 Hz, 2H), 2.40 (s, 3H). 13C NMR (100 MHz, CDCl3) δ: 165.3 (d, 1J_{C-F} = 253.6 Hz), 144.3, 138.4, 138.0 (d, 4J_{C-F} = 2.5 Hz), 130.3 (d, 3J_{C-F} = 9.4 Hz), 130.0, 127.6, 116.5 (d, 2J_{C-F} = 21.9 Hz), 21.6. 19F NMR (376 MHz, CDCl3): δ -104.2 ppm. MS (70 eV): m/z (%): [M]+, 250 (100).

20) 4,4'-Sulfonylbis(methylbenzene) (4c)[8]

The reaction of toluene (2.5 mmol, 230.4 mg), N-fluoro-4-methyl-N-tosylbenzenesulfonamide (2b) (0.5 mmol, 171.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 201.7 mg (82%) (3:1) of 4c as solid. (major): 1H NMR (400 MHz, CDCl3) δ: 7.81 (d, J = 7.6 Hz, 4H), 7.26 (d, J = 8.0 Hz, 4H), 2.35 (s, 6H). 13C NMR (100 MHz, CDCl3) δ: 143.8, 138.8, 129.7, 127.3, 21.3. (minor): 1H NMR (400 MHz, CDCl3) δ: 8.19 (dd, J = 7.6, 1.2 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.47 (td, J = 7.5, 1.6 Hz, 1H), 7.42 - 7.33 (m, 1H), 7.32 - 7.27 (m, 2H), 7.22 (dd, J = 7.4, 1.4 Hz, 1H), 2.44 (s, 3H), 2.41 (s, 3H). 13C NMR (100 MHz, CDCl3) δ: 143.9, 139.0, 138.1, 133.4, 132.5, 129.6, 129.2, 127.7, 126.4, 21.5, 20.1. HRMS: m/z [M+Na]+: calcld for C14H14NaO2S: 269.0607; found: 269.0605.

21) 1-Methyl-4-(phenylsulfonyl)benzene (3f)[2]

The reaction of benzene (2.5 mmol, 195.3 mg), N-fluoro-4-methyl-N-tosylbenzenesulfonamide (2b) (0.5 mmol, 171.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL
trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 80.1 mg (34%) of 3f as solid. $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.93 (t, $J = 1.6$ Hz, 2H), 7.83 (d, $J = 8.4$ Hz, 2H), 7.54 (d, $J = 7.6$ Hz, 2H), 7.49 (t, $J = 6.8$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 144.1, 141.9, 138.6, 133.0, 129.9, 129.2, 127.7, 127.4, 21.5. MS (70 eV): m/z (%): [M]$^+$, 232 (100).

22) 1-Methyl-4-(phenylsulfonyl)benzene (3f)$^{[2]}$

![Chemical structure of 1-Methyl-4-(phenylsulfonyl)benzene](image)

The reaction of benzene (2.5 mmol, 195.3 mg), N-fluoro-4-methyl-N-(phenylsulfonyl)benzenesulfonamide (2c) (0.5 mmol, 164.7 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 100 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 70.1 mg (60%) of 3f as solid. $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.93 (t, $J = 1.6$ Hz, 2H), 7.83 (d, $J = 8.4$ Hz, 2H), 7.54 (d, $J = 7.6$ Hz, 2H), 7.49 (t, $J = 6.8$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 144.1, 141.9, 138.6, 133.0, 129.9, 129.2, 127.7, 127.4, 21.5. MS (70 eV): m/z (%): [M]$^+$, 232 (100).

23) Sulfonyldibenzene (3e)$^{[2]}$

![Chemical structure of Sulfonyldibenzene](image)

The reaction of benzene (2.5 mmol, 195.3 mg), N-fluoro-4-nitro-N-(phenylsulfonyl)benzenesulfonamide (2d) (0.5 mmol, 180.2 mg), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 40.1 mg (35%) of 3e as solid. $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.95 (dd, $J = 8.0$, 1.2 Hz, 4H), 7.56 (dd, $J = 4.0$, 1.2 Hz, 2H), 7.51 (dd, $J = 8.0$, 7.2 Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 141.4, 133.1, 129.2, 127.6. MS (70 eV): m/z (%): [M]$^+$, 218 (25).
Structural modification of β-estradiol derivative 5

(8R,9S,13S,14S)-3,17-Dimethoxy-13-methyl-2-(phenylsulfonyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (5)

The reaction of (8R,9S,13S,14S)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (0.25 mmol, 75.0 mg), N-fluoro-N-(phenylsulfonyl)benzenesulfonamide (2a) (0.0625 mmol, 19.8 mg), trifluoromethanesulfonic (600 mol %, 33 μL), was carried out in 0.5 mL trifluoroacetic acid at 30 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 30.2 mg (55%) of 5 as solid.

1H NMR (400 MHz, CDCl3) δ: 8.04 (s, 1H), 7.97-7.95 (m, 2H), 7.56-7.52 (m, 1H), 7.46 (dd, J = 14.8, 7.6 Hz, 2H), 6.58 (s, 1H), 3.69 (s, 3H), 3.47 (s, 3H), 3.32 (dd, J = 16.8, 8.4 Hz, 1H), 2.85 (dd, J = 8.8, 4.2 Hz, 2H), 2.42 (dt, J = 12.9, 3.5 Hz, 1H), 2.27- 2.14 (m, 1H), 2.08 (ddd, J = 13.8, 9.5, 3.5 Hz, 2H), 1.88 (ddt, J = 12.3, 4.4, 2.5 Hz, 1H), 1.75-1.22 (m, 8H). 13C NMR (100 MHz, CDCl3) δ: 154.7, 145.4, 141.9, 133.1, 132.6, 128.4, 128.2, 126.8, 126.9, 126.1, 112.7, 90.6, 76.7, 57.9, 55.8, 50.2, 43.7, 43.2, 38.3, 37.8, 30.1, 27.7, 26.7, 26.4, 23.0, 11.5. HRMS (EI), m/z calcd. for C26H32O4S [M]+: 440.2021, found: 440.2028.

Synthesis of the intermediate 6 of an inhibitor of Farnesyl-protein transferase

4-Bromo-2-methyl-1-(phenylsulfonyl)benzene (6) [9]

The reaction of 1-bromo-3-methylbenzene (1.25 mmol, 427.6 mg), N-fluoro-N-(phenylsulfonyl)benzenesulfonamide (2a) (0.5 mmol, 158.0 mg), trifluoromethanesulfonic (0.75 mmol, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 196.0 mg (63%) of 6 as solid. (major): 1H NMR (400 MHz, CDCl3) δ: 8.04 (s, 1H), 7.97-7.95 (m, 2H), 7.56-7.52 (m, 1H), 7.46 (dd, J = 14.8, 7.6 Hz, 2H), 6.58 (s, 1H), 3.69 (s, 3H), 3.47 (s, 3H), 3.32 (dd, J = 16.8, 8.4 Hz, 1H), 2.85 (dd, J = 8.8, 4.2 Hz, 2H), 2.42 (dt, J = 12.9, 3.5 Hz, 1H), 2.27- 2.14 (m, 1H), 2.08 (ddd, J = 13.8, 9.5, 3.5 Hz, 2H), 1.88 (ddt, J = 12.3, 4.4, 2.5 Hz, 1H), 1.75-1.22 (m, 8H).
MHz, CDCl$_3$) $\delta$: 8.08 (d, $J = 8.4$ Hz, 1H), 7.85 (m, 2H), 7.59 (d, $J = 3.6$ Hz, 1H), 7.54-7.50 (m, 3H), 7.40 (d, $J = 1.2$ Hz, 1H), 2.41 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 140.8, 139.9, 138.0, 135.4, 133.2, 130.9, 129.7, 129.1, 128.5, 127.6, 20.0 ppm. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 56.1 mg (18%) of 6 (minor) as solid. (minor): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.29 (d, $J = 8.0$ Hz, 1H), 7.94 (d, $J = 7.6$ Hz, 2H), 7.58 (d, $J = 3.6$ Hz, 1H), 7.52-7.48 (m, 3H), 7.33 (d, $J = 8.0$ Hz, 1H), 2.39 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 146.0, 140.2, 136.9, 136.0, 133.2, 131.3, 128.7, 128.5, 128.4, 120.9, 21.0. HRMS: m/z [M+Na]$^+$: calcd for C$_{13}$H$_{11}$BrNaO$_2$S: 332.9555; found: 332.9553.

Gram-scale synthesis of EPAC2 antagonist 8

1,3,5-Trimethyl-2-tosylbenzene (8) $^{[6]}$

![1,3,5-Trimethyl-2-tosylbenzene (8)]

The reaction of mesitylene (23.1 mmol, 2.78 g), N-fluoro-4-methyl-N-tosylbenzenesulfonamide (2b) (4.62 mmol, 1.59 g), trifluoromethanesulfonic (150 mol %, 66 $\mu$L), was carried out in 0.5 mL CH$_3$CN at 130 $^\circ$C under air for 36 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford 2.38 g (94%) of 8 as solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.67 (d, $J = 8.4$ Hz, 2H), 7.26 (t, $J = 5.6$ Hz, 2H), 6.93 (s, 2H), 2.59 (s, 6H), 2.40 (s, 3H), 2.29 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 143.3, 143.1, 140.5, 139.9, 134.1, 132.1, 129.4, 126.2, 22.8, 21.5, 21.0 ppm. HRMS: m/z [M+Na]$^+$: calcd for C$_{16}$H$_{18}$NaO$_2$S: 297.0920; found: 297.0917.
**Scheme S1** Control Experiments

Typical procedure:

The reaction of chlorobenzene 1a (2.5 mmol, 281.0 mg), 2 (0.5 mmol), trifluoromethanesulfonic (150 mol %, 66 μL), was carried out in 0.5 mL trifluoroacetic acid at 60 °C under air for 24 h as monitored by TLC. The resulting mixture was concentrated and purified by flash chromatography on silica gel to afford the product.
References

$^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra for products
3J (minor)
4c (minor)