Supporting Information For:

Palladium-Catalyzed Nucleomethylation of Alkynes for Synthesis of Methylated Heteroaromatic Compounds

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1. General

All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques, unless otherwise noted. All solvents and reagents were used as obtained from commercial sources without further purification. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded at room temperature on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC or NMR analysis.

2. General procedure for the synthesis of ortho-alkynylanilines

The ortho-alkynylanilines 1b-1k, 1ai, and 1aj were synthesized according to the reported procedures. 1b$^{[1]}$, 1c$^{[2]}$, 1d-1f$^{[3]}$, and 1g$^{[2]}$ were known compounds and all data were in agreement with the reported literatures.

\[
\begin{align*}
\text{Ar} & \quad \text{Br} & \quad \text{NH}_2 \\
\text{S1} & & \\
\begin{array}{c}
\text{R} \\
\text{Pd(PPh}_3\text{)}_2\text{Cl}_2, \text{CuI} \\
\text{Et}_3\text{N/DMF, 100 °C}
\end{array} & \rightarrow & \\
\text{Ar} & \quad \text{NH}_2 & \quad \text{R} \\
\text{S2} & & \\
\begin{array}{c}
\text{Pyridine, TsCl} \\
\text{DCM, r.t.}
\end{array} & \rightarrow & \\
\text{Ar} & \quad \text{NH} & \quad \text{R} \\
\text{1b-1k, 1ai, 1aj}
\end{align*}
\]

Synthesis of compound S2$^{[4]}$: Under nitrogen atmosphere, compound S1 (1.0 equiv.) Pd(PPh$_3$)$_2$Cl$_2$ (2 mol%), and CuI (4 mol%) were dissolved in $N,N$-dimethylformamide, then triethylamine and alkyne compounds (1.5 equiv.) were added. The mixture was stirred overnight in 100 °C oil bath. After completion of the reaction (monitored by TLC), the reaction was cooled to room temperature and quenched by aqueous saturated solution of sodium chloride. The aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S2.

Synthesis of compound 1$^{[5]}$: Under nitrogen atmosphere, to a solution of S2 (1.0 equiv.) in dichloromethane, the pyridine (2.0 equiv.) and sulfonyl chloride (1.2 equiv.) were added. The mixture was stirred at room temperature for 12 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 1b-1k, 1ai, and 1aj.

$N$-(2-fluoro-6-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (1h): the reaction was conducted at 3.5 mmol scale from S1, 377.1 mg, 29% yield, unknown compound, white solid, $R_t = 0.3$ (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.74–7.64 (m, 2H), 7.45–7.39 (m, 2H), 7.39–7.31 (m, 3H), 7.26–7.24 (m, 1H), 7.21–7.16 (m, 1H), 7.15–7.06 (m, 3H), 6.53 (s, 1H), 2.31 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.9 (d, $J_{CF} = 250.6$ Hz), 144.1, 137.2, 131.9, 129.7, 129.3, 128.6, 128.1 (d, $J_{CF} = 3.5$ Hz), 128.0 (d, $J_{CF} = 8.7$ Hz), 127.6, 125.5 (d, $J_{CF} = 13.5$ Hz), 122.5 (d, $J_{CF} =$}
2.6 Hz), 122.2, 117.3 (d, \( J_{CF} = 20.7 \) Hz), 96.2, 84.0 (d, \( J_{CF} = 4.3 \) Hz), 21.7. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -116.80. HRMS (ESI-QEplus) \( m/z \): [M+Na]\(^+\) Calcd for C\(_{21}\)H\(_{16}\)FNNaO\(_2\)S 388.0778; found 388.0773.

\( N-(4\text{-chloro-2-fluoro-6-(phenylethynyl)phenyl})\text{-4-methylbenzenesulfonamide (1i)} \): the reaction was conducted at 3.5 mmol scale from S1, 381.8 mg, 27% yield, unknown compound, white solid, \( R_f = 0.3 \) (petroleum ether/ethyl acetate 10/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.75–7.64 (m, 2H), 7.40–7.33 (m, 5H), 7.24 (s, 1H), 6.54 (s, 1H), 2.29 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 158.0 (d, \( J_{CF} = 254.0 \) Hz), 144.2, 137.0, 133.1 (d, \( J_{CF} = 10.9 \) Hz), 127.8, 124.3 (d, \( J_{CF} = 13.6 \) Hz), 123.9 (d, \( J_{CF} = 3.4 \) Hz), 121.7, 117.9 (d, \( J_{CF} = 23.9 \) Hz), 97.2, 83.0 (d, \( J_{CF} = 4.1 \) Hz), 21.7. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -113.89. HRMS (ESI-QEplus) \( m/z \): [M+Na]\(^+\) Calcd for C\(_{21}\)H\(_{15}\)ClFNNaO\(_2\)S 422.0388; found 422.0390.

\( N-(3,5\text{-difluoro-2-(phenylethynyl)phenyl})\text{-4-methylbenzenesulfonamide (1j)} \): the reaction was conducted at 3.5 mmol scale from S1, 389.8 mg, 29% yield, unknown compound, white solid, \( R_f = 0.3 \) (petroleum ether/ethyl acetate 10/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.75–7.61 (m, 2H), 7.49–7.31 (m, 5H), 7.19–7.08 (m, 2H), 7.04–6.94 (m, 1H), 6.93–6.82 (m, 1H), 6.36 (s, 1H), 2.30 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 160.9 (dd, \( J_{CF} = 248.2, 12.5 \) Hz), 158.9 (dd, \( J_{CF} = 253.4, 13.5 \) Hz), 144.2, 137.1, 132.0, 129.8, 128.6, 127.9 (d, \( J_{CF} = 3.7 \) Hz), 121.9 (d, \( J_{CF} = 13.8 \) Hz), 121.8, 114.9 (dd, \( J_{CF} = 23.8, 3.7 \) Hz), 105.9 (dd, \( J_{CF} = 24.9, 1.0 \) Hz), 97.0, 83.3 (dd, \( J_{CF} = 4.4, 3.4 \) Hz), 21.7. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -113.89. HRMS (ESI-QEplus) \( m/z \): [M+Na]\(^+\) Calcd for C\(_{21}\)H\(_{15}\)F\(_2\)NNaO\(_2\)S 406.0684; found 406.0675.

\( N-(2\text{-chboro-4-fluoro-6-(phenylethynyl)phenyl})\text{-4-methylbenzenesulfonamide (1k)} \): the reaction was conducted at 3.5 mmol scale from S1, 274.8 mg, 20% yield, unknown compound, white solid, \( R_f = 0.3 \) (petroleum ether/ethyl acetate 10/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.77–7.61 (m, 2H), 7.47–7.39 (m, 5H), 7.38–7.29 (m, 3H), 7.21–7.03 (m, 4H), 6.43 (s, 1H), 2.28 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 160.6 (d, \( J_{CF} = 248.2 \) Hz), 144.2, 137.6, 135.2 (d, \( J_{CF} = 11.2 \) Hz), 129.8, 128.5, 127.9 (d, \( J_{CF} = 11.2 \) Hz), 122.1, 118.5, 118.2, 118.0, 96.6, 84.6 (d, \( J_{CF} = 3.2 \) Hz), 21.7. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -113.89. HRMS (ESI-QEplus) \( m/z \): [M+Na]\(^+\) Calcd for C\(_{21}\)H\(_{15}\)ClFNNaO\(_2\)S 422.0388; found 422.0385.

\( N-(2\text{-((3,4-dimethoxyphenyl)ethynyl)-4-methoxyphenyl})\text{-4-methylbenzenesulfonamide (1ai)} \): the reaction was conducted at 10.0 mmol scale from S1, 714.8 mg, 16% yield, unknown compound, white solid, \( R_f = 0.25 \) (petroleum ether/ethyl acetate 10/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.62–7.57 (m, 2H), 7.57–7.53 (m, 1H), 7.21–7.03 (m, 4H), 3.94 (s, 3H), 3.93 (s, 3H), 3.77 (s, 3H), 2.33 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 157.0, 150.3,

N-(4-methoxy-2-((4-methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1aj): the reaction was conducted at 15.0 mmol scale from S1, 1489.7 mg, 24% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 7.59–7.54 (m, 3H), 7.39–7.31 (m, 2H), 7.17–7.09 (m, 2H), 6.95–6.80 (m, 5H), 3.86 (s, 3H), 3.76 (s, 3H), 2.33 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 160.4, 157.1, 143.9, 136.2, 133.3, 130.6, 129.7, 129.7, 127.5, 124.2, 117.7, 116.2, 115.9, 114.4, 114.2, 95.8, 83.0, 55.7, 55.6, 21.7. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C23H21NNaO4S 430.1083; found 430.1081.

The ortho-alkynylanilines 1a, 1l-1v, 1aa, 1ab, and 1ad were synthesized according to the reported procedures. 1a[6], 1l-1m[3], 1o[6], 1p[7], 1s-1t[3], 1u[7], 1v[8], 1ab[6], 1ac[7], and 1ad[9] were known compounds and all data were in agreement with the reported literatures.

Synthesis of compound S4:[5] Under nitrogen atmosphere, to a solution of S3 (1.0 equiv.) in tetrahydrofuran, Pd(PPh3)2Cl2 (2 mol%), CuI (4 mol%), triethylamine (1.2 equiv.) and the alkyne compound (1.2 equiv.) were added. The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S4.

Synthesis of compound 1:[5] Under nitrogen atmosphere, to a solution of S4 (1.0 equiv.) in dichloromethane, pyridine (2.0 equiv.) and sulfonyl chloride (1.2 equiv.) were added. The mixture was stirred at room temperature for 12 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 1a, 1l-1v, 1ab, 1ac, and 1ad.
**N-(2-((4-(tert-butyl)phenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1n):** the reaction was conducted at 4.0 mmol scale from S3, 1416.1 mg, 88% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 30/1); 1H NMR (400 MHz, CDCl3) δ 7.71–7.65 (m, 2H), 7.64–7.60 (m, 1H), 7.41 (s, 4H), 7.38–7.33 (m, 1H), 7.31–7.21 (m, 2H), 7.19–7.14 (m, 2H), 7.09–7.01 (m, 1H), 2.34 (s, 3H), 1.35 (s, 9H). 13C NMR (100 MHz, CDCl3) δ 152.7, 144.2, 137.7, 136.3, 132.1, 131.6, 129.8, 129.6, 127.5, 125.8, 124.7, 120.3, 119.2, 115.0, 96.6, 83.3, 35.1, 31.4, 21.7. HRMS (ESI-QEplus) m/z: [M+H]+ Calcd for C25H26NO2S 404.1679; found 404.1676.

**N-(2-((4-acetylphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1q):** the reaction was conducted at 5.0 mmol scale from S3, 1837.2 mg, 94% yield, unknown compound, yellow solid, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 8.02–7.94 (m, 2H), 7.71–7.65 (m, 2H), 7.64–7.60 (m, 1H), 7.58–7.51 (m, 2H), 7.43–7.37 (m, 1H), 7.36–7.30 (m, 1H), 7.22–7.14 (m, 3H), 7.13–7.06 (m, 1H), 2.64 (s, 3H), 2.34 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 197.4, 144.3, 137.9, 137.0, 136.2, 132.4, 131.9, 130.4, 129.9, 128.6, 127.4, 127.0, 124.9, 120.8, 114.3, 95.3, 87.1, 26.9, 21.7. HRMS (ESI-QEplus) m/z: [M+H]+ Calcd for C23H20NO3S 390.1158; found 390.1154.

**4-Methyl-N-(2-((4-nitrophenyl)ethynyl)phenyl)benzenesulfonamide (1r):** the reaction was conducted at 4.0 mmol scale from S3, 780.4 mg, 50% yield, unknown compound, yellow solid, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 8.31–8.19 (m, 2H), 7.72–7.65 (m, 2H), 7.64–7.56 (m, 3H), 7.45–7.40 (m, 1H), 7.39–7.33 (m, 1H), 7.24–7.15 (m, 3H), 7.14–7.08 (m, 1H), 2.35 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 147.6, 144.5, 138.1, 136.3, 132.7, 132.5, 130.9, 129.9, 129.1, 127.4, 125.0, 124.0, 120.9, 113.8, 94.0, 89.1, 21.8. HRMS (ESI-QEplus) m/z: [M-H]− Calcd for C21H15N2O4S 391.0758; found 391.0757.

The *ortho*-alkynylanilines 1w-1z were synthesized according to the reported procedures. 1w[1] and 1y[10] were known compounds and all data were in agreement with the reported literatures.

**Synthesis of compound S7:**[11] The mixture of S6 (1.0 equiv.), 4-dimethylaminopyridine (0.1 equiv.), triethylamine (1.2 equiv.) in dry dichloromethane was stirred at room temperature, then S5 was added into the system dropwise. The mixture was stirred at room temperature. After
completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S7. Then S7 was used to synthesize 1w-1z following the previous method.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl acetate (1x): the reaction was conducted at 3.1 mmol scale from S4, 842.1 mg, 76% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 7/1); 1H NMR (400 MHz, CDCl3) δ 7.71–7.64 (m, 2H), 7.60–7.54 (m, 1H), 7.29–7.25 (m, 2H), 7.24–7.20 (m, 3H) 7.03–6.97 (m, 1H), 4.24 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.5 Hz, 2H), 2.37 (s, 3H), 2.16 (s, 3H).

1H NMR (400 MHz, CDCl3) δ 171.3, 144.2, 138.1, 136.4, 131.2, 129.8, 129.5, 127.4, 124.4, 119.8, 114.4, 93.3, 77.0, 62.2, 21.7, 21.1, 20.3. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C19H19NNaO4S 380.0927; found 380.0920.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl benzoate (1z): the reaction was conducted at 4.8 mmol scale from S4, 865.8 mg, 43% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 6/1);

1H NMR (400 MHz, CDCl3) δ 8.15–8.06 (m, 2H), 7.70–7.62 (m, 2H), 7.61–7.53 (m, 2H), 7.50–7.43 (m, 2H), 7.33–7.20 (m, 3H), 7.20–7.14 (m, 2H), 7.03–6.95 (m, 1H), 4.49 (t, J = 6.6 Hz, 2H), 2.89 (t, J = 6.6 Hz, 2H), 2.33 (s, 3H).

13C NMR (100 MHz, CDCl3) δ 166.6, 144.1, 138.0, 136.4, 133.4, 132.4, 130.0, 129.9, 129.4, 128.7, 127.4, 124.4, 120.0, 114.5, 93.1, 77.2, 62.7, 21.7, 20.5. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C24H21NNaO4S 442.1083; found 442.1073.

The ortho-alkynylanilines 1aa were synthesized according to the reported procedures.

Synthesis of compound S8:[12] The mixture of 3-bromopropyne (1.2 equiv.), morpholine (1.0 equiv.), potassium carbonate (1.2 equiv.) in dry tetrahydrofuran was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (dichloromethane/ethyl acetate) to afford the desired compound S8. Then S8 was used to synthesize 1aa following the previous method.
4-Methyl-N-(2-(3-morpholinoprop-1-yn-1-yl)phenyl)benzenesulfonamide (1aa): the reaction was conducted at 5.9 mmol scale from S4, 1202.2 mg, 55% yield, unknown compound, yellow solid, Rf = 0.25 (dichloromethane/ethyl acetate 2/1); 1H NMR (400 MHz, CDCl3) δ 7.73–7.64 (m, 2H), 7.62–7.53 (m, 1H), 7.33–7.23 (m, 3H), 7.22–7.17 (m, 2H), 7.05–6.96 (m, 1H), 3.83–3.72 (m, 4H), 3.51 (s, 2H), 2.66–2.53 (m, 4H), 2.35 (s, 3H).

13C NMR (100 MHz, CDCl3) δ 144.2, 137.9, 136.4, 132.5, 129.7, 129.7, 127.4, 124.4, 119.6, 114.0, 91.6, 80.4, 66.9, 52.5, 48.1, 21.7. HRMS (ESI-QEplus) m/z: [M+H]+ Calcd for C20H23N2O3S 371.1424; found 371.1416.

The ortho-alkynylanilines 1ae-1ag were synthesized according to the reported procedures. The compound S9 was synthesized following the previous method.

Synthesis of compound 1:[13] Under nitrogen atmosphere, to a solution of S10 (1.0 equiv.) in dichloromethane was added oxalyl chloride (2.0 equiv.) and N,N-dimethylformamide (a few drops). The mixture was stirred at room temperature for 0.5 h. The mixture was concentrated under reduced pressure. The resulting crude material was dissolved in tetrahydrofuran at 0 °C, then S9 (1.2 equiv.) and triethylamine (5.0 equiv.) were added into the system in the same temperature. The mixture was stirred at room temperature for 6 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 1ae-1ag.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 4-(N,N-dipropylsulfamoyl)benzoate (1ae): the reaction was conducted at 2.0 mmol scale from S10, 174.2 mg, 15% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 8.28–8.17 (m, 2H), 7.96–7.84 (m, 2H), 7.69–7.61 (m, 2H), 7.57–7.48 (m, 1H), 7.29–7.23 (m, 3H), 7.22–7.18 (m, 2H), 7.03–6.93 (m, 1H), 4.53 (t, J = 6.5 Hz, 2H), 3.15–3.04 (m, 4H), 2.92 (t, J = 6.5 Hz, 2H), 1.63–1.47 (m, 4H), 0.86 (t, J = 7.4 Hz, 6H). 13C NMR (100 MHz, CDCl3) δ 165.4, 144.8, 144.3, 138.1, 136.4, 133.2, 132.4, 130.6, 129.8, 129.6, 127.4, 124.4, 119.6, 114.1, 92.8, 77.4, 63.3, 50.2, 22.2, 21.8, 20.5, 11.4. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C30H34N2NaO6S2
4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 2-(6-methoxynaphthalen-2-yl)propanoate (1af): the reaction was conducted at 1.5 mmol scale from S10, 348.2 mg, 44% yield, unknown compound, colorless oil, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 7.73–7.65 (m, 2H), 7.65–7.60 (m, 3H), 7.56–7.49 (m, 1H), 7.45–7.37 (m, 1H), 7.24–7.19 (m, 1H), 7.19–7.14 (m, 3H), 7.12–7.03 (m, 3H), 6.96–6.87 (m, 1H), 4.24 (t, J = 6.5 Hz, 2H), 3.96 (q, J = 7.1 Hz, 1H), 3.90 (s, 3H), 2.67 (t, J = 6.5 Hz, 2H), 2.32 (s, 3H), 1.60 (d, J = 7.1 Hz, 3H). 
13C NMR (100 MHz, CDCl3) δ 174.9, 157.8, 144.1, 138.0, 136.5, 135.6, 133.9, 132.2, 129.8, 129.5, 129.4, 129.1, 127.5, 127.4, 126.4, 126.2, 124.4, 119.9, 119.2, 114.5, 105.8, 93.0, 77.1, 62.4, 55.5, 45.5. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C31H29NNaO5S 550.1659; found 550.1653.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 2-(4-isobutylphenyl)propanoate (1ag): the reaction was conducted at 2.0 mmol scale from S10, 886.4 mg, 88% yield, unknown compound, brown solid, Rf = 0.25 (petroleum ether/ethyl acetate 10/1); 1H NMR (400 MHz, CDCl3) δ 7.66 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.2 Hz, 1H), 7.26–7.17 (m, 7H), 7.05–7.03 (m, 2H), 7.00–6.96 (m, 1H), 4.27–4.18 (m, 2H), 3.80 (q, J = 7.0 Hz, 1H), 2.68 (t, J = 6.6 Hz, 2H), 2.40 (d, J = 7.2 Hz, 2H), 2.35 (s, 3H), 1.85–1.75 (m, 1H), 1.51 (d, J = 7.1 Hz, 3H), 0.87 (d, J = 6.6 Hz, 6H). 
13C NMR (100 MHz, CDCl3) δ 175.0, 144.2, 140.8, 138.0, 137.7, 136.5, 132.3, 129.8, 129.6, 129.4, 127.5, 127.4, 124.4, 120.0, 114.6, 93.0, 77.1, 62.4, 45.3, 45.2, 30.3, 22.6, 21.7, 20.3, 18.8. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C30H33NNaO4S 526.2023; found 526.2019.

The ortho-alkynylanilines 1ah were synthesized according to the reported procedures.

Synthesis of compound S11[14] Under nitrogen atmosphere, to a solution of lithocholic acid (3.0 mmol, 1.0 equiv.) in tetrahydrofuran (30.0 mL) was added sodium hydride (18.0 mmol, 6.0 equiv.) at 0 °C. The mixture was stirred in the same temperature for 10 min. Then methyl iodide (30 mmol, 10.0 equiv.) was added slowly into the system in the same temperature. The mixture
was stirred at 41 °C for 24 h. The reaction was quenched by saturated ammonium chloride aqueous solution, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S11.

**Synthesis of compound 1:**

Under nitrogen atmosphere, the reaction tube was charged with S11 (2.0 mmol, 1.0 equiv.), p-toluenesulfonic acid (0.2 mmol, 0.1 equiv.) and S9 (2.4 mmol, 1.2 equiv.) in toluene (10.0 mL) at room temperature. The mixture was stirred at 60 °C. After completion of the reaction (monitored by TLC), the reaction was quenched by saturated sodium chloride aqueous solution, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 1ah.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl (R)-4-((3R,5R,8S,9S,10R,13R,17R)-3-methoxy-5,10,13-trimethylhexadecahydro-1H-cyclopenta[al]phenanthren-17-yl)pentanoate (1ah): the reaction was conducted at 2.0 mmol scale from S11, 762.6 mg, 55% yield, unknown compound, white solid, Rf = 0.25 (petroleum ether/ethyl acetate 4/1); 1H NMR (400 MHz, CDCl3) δ 7.67 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.5 Hz, 1H), 7.25–7.20 (m, 5H), 7.00–6.97 (m, 1H), 4.24 (t, J = 6.5 Hz, 2H), 3.35 (s, 3H), 3.21–3.10 (m, 1H), 2.74 (t, J = 6.5 Hz, 2H), 2.48–2.40 (m, 1H), 2.37 (s, 3H), 2.34–2.27 (m, 1H), 1.92 (d, J = 12.3 Hz, 1H), 1.86–1.71 (m, 5H), 1.68 (d, J = 12.3 Hz, 1H), 1.55–1.47 (m, 1H), 1.42–1.32 (m, 7H), 1.27–1.16 (m, 5H), 1.14–0.95 (m, 6H), 0.94–0.87 (m, 6H), 0.61 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 174.6, 144.2, 138.1, 136.5, 132.2, 129.8, 129.5, 127.5, 124.4, 119.9, 114.5, 93.3, 80.6, 77.4, 62.0, 56.6, 56.1, 55.8, 42.9, 42.3, 40.5, 40.3, 36.0, 35.6, 35.5, 35.1, 33.0, 31.4, 31.2, 28.4, 27.8, 27.0, 26.6, 24.4, 23.6, 21.8, 21.0, 20.4, 18.5, 12.2. HRMS (ESI-QEplus) m/z: [M+Na]+ Caled for C42H57NNaO5S 710.3850; found 710.3838.

3. General procedure for the synthesis of ortho-alkynylphenols

The ortho-alkynylanilines 5a-5m were synthesized according to the reported procedures. 5a[16], 5b[17], 5c-5d[16], 5e[18], 5j-5l[7] were known compounds and all data were in agreement with the reported literatures.
Synthesis of compound S13:\[11]\) The mixture of S12 (1.0 equiv.) and triethylamine (1.2 equiv.) in dry dichloromethane was stirred at 0 °C. Then acetyl chloride (1.2 equiv.) was added dropwise, the mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S13.

Synthesis of compound S14:\[5]\) Under nitrogen atmosphere, to a solution of S13 (1.0 equiv.) in tetrahydrofuran was added Pd(PPh\(_3\))\(_2\)Cl\(_2\) (2 mol%), CuI (4 mol%), triethylamine (1.2 equiv.) and the alkyne compounds (1.2 equiv.). The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound S14.

Synthesis of compound 5:\[5]\) The mixture of S14 (1.0 equiv.) and potassium carbonate (2.0 equiv.) in methanol stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by water. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound 5a-5m.

### 5-Chloro-2-(phenylethynyl)phenol (5f): the reaction was conducted at 5.0 mmol scale from S12, 457.4 mg, 40% yield, unknown compound, yellow solid, R\(_f\) = 0.8 (petroleum ether); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.85–7.15 (m, 6H), 7.11–6.67 (m, 2H), 5.88 (s, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.5, 136.0, 132.6, 131.8, 129.2, 128.7, 122.3, 121.0, 115.7, 108.7, 97.1, 82.6. HRMS (ESI-QEplus) \(m/z\): [M-H] Calcd for C\(_{14}\)H\(_8\)ClO 227.0269; found 227.0270.

### 5-Fluoro-2-(phenylethynyl)phenol (5g): the reaction was conducted at 5.0 mmol scale from S12, 350.9 mg, 33% yield, unknown compound, yellow solid, R\(_f\) = 0.8 (petroleum ether); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.59–7.48 (m, 2H), 7.43–7.33 (m, 4H), 6.78–6.68 (m, 1H), 6.68–6.59 (m, 1H), 5.97 (s, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 164.1 (d, \(J_{C-F}\) = 247.8 Hz), 158.2 (d, \(J_{C-F}\) = 13.0 Hz), 133.0 (d, \(J_{C-F}\) = 10.1 Hz), 131.8, 129.2, 128.8, 122.4, 108.3 (d, \(J_{C-F}\) = 22.6 Hz), 106.1 (d, \(J_{C-F}\) = 3.0 Hz), 102.9 (d, \(J_{C-F}\) = 25.4 Hz), 96.4, 82.3. \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -107.63. HRMS (ESI-QEplus) \(m/z\): [M-H] Calcd for C\(_{14}\)H\(_8\)FO 211.0565; found 211.0564.

### 5-Methyl-2-(phenylethynyl)phenol (5h): the reaction was conducted at 5.0 mmol scale from S12, 386.3 mg, 37% yield, unknown compound, white solid, R\(_f\) = 0.8 (petroleum ether); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.66–7.45 (m, 2H), 7.42–7.23 (m, 4H), 6.90–6.64 (m, 2H), 5.79 (s, 1H), 2.33 (s, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 156.6, 141.4, 131.7, 131.6, 128.9, 128.7, 122.8,
2-Methyl-6-(phenylethynyl)phenol (5i): the reaction was conducted at 5.0 mmol scale from S12, unknown compound, 300.2 mg, 29% yield, white solid, R\textsubscript{f} = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.59–7.49 (m, 2H), 7.44–7.33 (m, 3H), 7.30–7.23 (m, 1H), 7.16–7.09 (m, 1H), 6.86–6.77 (m, 1H), 5.92 (s, 1H), 2.28 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 154.9, 132.0, 131.8, 129.3, 129.0, 128.7, 124.2, 122.7, 120.2, 109.1, 96.3, 83.6, 16.2. HRMS (ESI-QEplus) \(m/z\): [M-H]\textsuperscript{-} Calcd for C\textsubscript{15}H\textsubscript{11}O 207.0815; found 207.0815.

2-((2-Fluorophenyl)ethynyl)phenol (5j): the reaction was conducted at 5.0 mmol scale from S12, 477.5 mg, 45% yield, unknown compound, yellow solid, R\textsubscript{f} = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.57–7.48 (m, 1H), 7.47–7.40 (m, 1H), 7.39–7.23 (m, 2H), 7.21–7.07 (m, 2H), 7.05–6.96 (m, 1H), 6.95–6.84 (m, 1H), 5.96 (s, 1H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 162.7 (d, \textit{J}\textsubscript{C-F} = 249.8 Hz), 156.9, 133.1, 131.6, 131.1, 130.7 (d, \textit{J}\textsubscript{C-F} = 8.0 Hz), 124.4 (d, \textit{J}\textsubscript{C-F} = 3.6 Hz), 120.6, 115.8 (d, \textit{J}\textsubscript{C-F} = 20.9 Hz), 115.1, 111.4 (d, \textit{J}\textsubscript{C-F} = 15.3 Hz), 109.4, 89.9, 88.7 (d, \textit{J}\textsubscript{C-F} = 3.6 Hz). \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) \(\delta\) -109.84. HRMS (ESI-QEplus) \(m/z\): [M-H]\textsuperscript{-} Calcd for C\textsubscript{14}H\textsubscript{8}FO 211.0565; found 211.0565.

The \textit{ortho}-alkynylanilines 5n, 5o were synthesized according to the reported procedures. 5o\textsuperscript{[12]} was known compound and all data were in agreement with reported literature.

\[
\begin{align*}
\text{S12} & \quad \rightarrow \quad \text{Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2}, CuI, Et\textsubscript{3}N, r.t.} \quad \text{5n, 5o} \\
\end{align*}
\]

Synthesis of compound 5\textsuperscript{[12]} Under nitrogen atmosphere, to a solution of S13 (1.0 equiv.) in triethylamine was added Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (2 mol%), CuI (4 mol%) and the alkyne compound (1.2 equiv.). The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound 5n and 5o.

2-(3-(Tert-butyldimethylsilyl)oxy)prop-1-yn-1-yl)phenol (5n): the reaction was conducted at 3.0 mmol scale from S12, 140.0 mg, 18% yield, unknown compound, yellow solid, R\textsubscript{f} = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.35–7.30 (m, 1H), 7.27–7.21 (m, 1H), 6.96–6.92 (m, 1H), 6.89–6.83 (m, 1H), 5.81 (s, 1H), 4.59 (s, 2H), 0.94 (s, 9H), 0.17 (s, 6H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 157.0, 132.0, 130.7, 120.5, 114.9, 109.3, 95.4, 79.2, 52.4, 26.0, 18.5, -4.9. HRMS (ESI-QEplus) \(m/z\): [M-H]\textsuperscript{-} Calcd for C\textsubscript{15}H\textsubscript{22}O\textsubscript{2}Si 261.1316; found 261.1313.
4. General procedure for the synthesis of substrate alkynl-imines

The ortho-alkynylanilines 7a-7g were synthesized according to the reported procedures. 7a-7d\textsuperscript{[19]} were known compounds and all data were in agreement with the reported literature.

**Synthesis of compound S16:**\textsuperscript{[19]} Under nitrogen atmosphere, to a solution of S15 (1.0 equiv.), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (2 mol%), and CuI (1 mol%) in triethylamine, the appropriate acetylene (1.5 equiv.) was added at room temperature. The mixture was stirred overnight in 70 °C oil bath. After completion of the reaction (monitored by TLC), the reaction was cooled to room temperature and quenched by water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethanol) to afford the desired compound S16.

**Synthesis of compound 7:**\textsuperscript{[19]} To a suspension of tert-butylamine (2.0 equiv.) and 4Å MS in dichloromethane, compound S16 (1.0 equiv.) was added at room temperature. The mixture was stirred overnight, then the mixture was filtered and the filtrate was concentrated to give 7a-7g, which were used for the next step without purification.

**N-tert-butyl-1-(2-(2-fluorophenyl)ethynyl)phenyl)methanimine (7e):** the reaction was conducted at 3.0 mmol scale from S15, 536.4 mg, 64% yield, unknown compound, yellow oil; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 8.96 (s, 1H), 8.12–8.06 (m, 1H), 7.60–7.55 (m, 1H), 7.54–7.50 (m, 1H), 7.40–7.36 (m, 1H), 7.35–7.30 (m, 1H), 7.18–7.09 (m, 2H), 1.34 (s, 9H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 162.9 (d, J\textsubscript{C-F} = 250.4 Hz), 154.5, 138.2, 133.4, 132.4, 130.4 (d, J\textsubscript{C-F} = 7.9 Hz), 129.9, 129.2, 126.2, 124.3 (d, J\textsubscript{C-F} = 3.5 Hz), 123.7, 115.8 (d, J\textsubscript{C-F} = 20.4 Hz), 112.0 (d, J\textsubscript{C-F} = 15.3 Hz), 92.1 (d, J\textsubscript{C-F} = 2.8 Hz), 88.3, 58.1, 30.0. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) δ -109.53. HRMS (ESI-QEplus) m/z: [M+H]\textsuperscript{+} Calcd for C\textsubscript{19}H\textsubscript{19}FN 280.1496; found 280.1490.

**N-tert-butyl-1-(2-(hept-1-yn-1-yl)phenyl)methanimine (7f):** the reaction was conducted at 3.0 mmol scale from S15, 459.7 mg, 60% yield, unknown compound, brown oil; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 8.81 (s, 1H), 8.05–7.97 (m, 1H), 7.42–7.37 (m, 1H), 7.33–7.26 (m, 2H), 2.52–2.44 (m, 2H), 1.68–1.59 (m, 2H), 1.51–1.43 (m, 2H), 1.42–1.34 (m, 2H), 1.31 (s, 9H), 0.92 (t, J = 7.2 Hz, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 154.8, 137.9, 132.5, 129.8, 128.0, 126.0, 125.0, 96.4, 78.1, 57.8, 31.4, 30.0, 28.7, 22.5, 19.8, 14.2. HRMS (ESI-QEplus) m/z: [M+H]\textsuperscript{+} Calcd for C\textsubscript{18}H\textsubscript{26}N 256.2060; found 256.2054.
**N-tert-butyl-1-(2-((tert-butyldimethylsilyl)oxy)but-1-yn-1-yl)phenyl)methanimine (7g):** The reaction was conducted at 3.0 mmol scale from S15, 927.7 mg, 90% yield, unknown compound, brown oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.77 (s, 1H), 8.04–7.97 (m, 1H), 7.43–7.37 (m, 1H), 7.33–7.27 (m, 2H), 3.85 (t, $J$ = 7.2 Hz, 2H), 2.69 (t, $J$ = 7.2 Hz, 2H), 1.31 (s, 9H), 0.91 (s, 9H), 0.09 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.7, 138.0, 132.5, 129.8, 128.3, 126.0, 124.6, 92.9, 79.2, 62.3, 57.9, 30.0, 26.1, 24.2, 18.6, -5.1. HRMS (ESI-QEplus) $m/z$: [M+H]$^+$ Calcd for C$_{21}$H$_{34}$NOSi 344.2404; found 344.2397.

### Optimization of the Conditions for synthesis of 3-methyl-1-tosyl-1H-indole

**Table S1: Base screening**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>3a Yield (%)</th>
<th>3a:4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMAP</td>
<td>0</td>
<td>0:1</td>
</tr>
<tr>
<td>2</td>
<td>NaOEt</td>
<td>29</td>
<td>1:0.17</td>
</tr>
<tr>
<td>3</td>
<td>NaOMe</td>
<td>60</td>
<td>1:0.45</td>
</tr>
<tr>
<td>4</td>
<td>KOMe</td>
<td>32</td>
<td>1:0.09</td>
</tr>
<tr>
<td>5</td>
<td>KO'Bu</td>
<td>36</td>
<td>1:0.06</td>
</tr>
<tr>
<td>6</td>
<td>NaO2CH</td>
<td>70</td>
<td>1:0.42</td>
</tr>
<tr>
<td>7</td>
<td>KOAc</td>
<td>60</td>
<td>1:0.66</td>
</tr>
<tr>
<td>8</td>
<td>CsOAc</td>
<td>56</td>
<td>1:0.71</td>
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<tr>
<td>9</td>
<td>K$_2$CO$_3$</td>
<td>81</td>
<td>1:0.05</td>
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<tr>
<td>10</td>
<td>K$_3$PO$_4$</td>
<td>84</td>
<td>1:0.12</td>
</tr>
</tbody>
</table>

*a1a (0.1 mmol), 2a (0.3 mmol), Pd(OAc)$_2$ (10 mol%), Xantphos (11 mol%), base (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h. Yields of 3a and ratios of 3a:4a were determined by $^1$H NMR (1,3,5-trimethoxybenzene as internal standard).*
Table S2: Solvent screening

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<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>3a Yield (%)</th>
<th>3a:4a</th>
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<tr>
<td>1</td>
<td>THF</td>
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<td>2</td>
<td>DCM</td>
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<td>N.D.</td>
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<tr>
<td>3</td>
<td>Ethyl ether</td>
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<td>N.D.</td>
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<tr>
<td>4</td>
<td>EA</td>
<td>69</td>
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<tr>
<td>5</td>
<td>MeOH</td>
<td>&lt;5</td>
<td>N.D.</td>
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<td>6</td>
<td>TFE</td>
<td>33</td>
<td>N.D.</td>
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<tr>
<td>7</td>
<td>NMP</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>8</td>
<td>DMSO</td>
<td>&lt;5</td>
<td>N.D.</td>
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<tr>
<td>9</td>
<td>DMF</td>
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<td>&gt;20:1</td>
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<td>1:4.60</td>
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<td>11</td>
<td>Benzene</td>
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<td>1:2.60</td>
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<td>12</td>
<td>Benzotrifluoride</td>
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<td>13</td>
<td>1,4-dioxane</td>
<td>78</td>
<td>1:0.27</td>
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*a* 1a (0.1 mmol), 2a (0.3 mmol), Pd(OAc)$_2$ (10 mol%), Xantphos (11 mol%), K$_3$PO$_4$ (1.5 equiv.), solvent (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h. Yields of 3a and ratios of 3a:4a were determined by $^1$H NMR (1,3,5-trimethoxybenzene as internal standard).
### Table S3: Metal precursor screening

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<th>Entry</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd(OAc)$_2$</td>
<td>84</td>
<td>1:0.12</td>
</tr>
<tr>
<td>2$^b$</td>
<td>PdCl$_2$</td>
<td>33</td>
<td>1:0.03</td>
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<tr>
<td>3</td>
<td>PdBr$_2$</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>4</td>
<td>Pd(PPh$_3$)$_2$Cl$_2$</td>
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<td>N.D.</td>
</tr>
<tr>
<td>5</td>
<td>Pd(TFA)$_2$</td>
<td>97</td>
<td>1:0.03</td>
</tr>
</tbody>
</table>

$^a$1a (0.1 mmol), 2a (0.3 mmol), cat. Pd (10 mol%), Xantphos (11 mol%), K$_3$PO$_4$ (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h. Yields of 3a and ratios of 3a:4a were determined by $^1$H NMR (1,3,5-trimethoxybenzene as internal standard). $^b$2.0 mg 2,2’-diphenyl-1,1’-ditosyl-1H,1’H- 3,3’-biindole was isolated, 6% yield, known compound$^{[36]}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.37–8.27 (m, 2H), 7.36–7.30 (m, 2H), 7.22–7.13 (m, 2H), 7.12–6.94 (m, 10H), 6.72 (s, 4H), 6.62–6.57 (m, 2H), 2.35 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.7, 139.7, 137.9, 134.6, 132.0, 130.8, 129.3, 128.3, 127.2, 127.0, 125.4, 124.6, 119.8, 117.2, 117.2, 21.8.
Table S4: Ligand screening

<table>
<thead>
<tr>
<th>Ligands</th>
<th>Reactions</th>
<th>Yield</th>
<th>3a:4a Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>L₁: Tri-o-tolylphosphine</td>
<td>$\text{PhCH} = \text{CHPh} + \text{MeB(OH)}_2 \rightarrow \text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>5%</td>
<td>3a:4a = 1:13.4</td>
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<tr>
<td>L₂: PhDave-Phos</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Me}$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>4%</td>
<td>3a:4a = 1:0.60</td>
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<tr>
<td>L₃: 'BuMePhos</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Ph}_2$ to $\text{Ph}_3\text{P('Bu)}_3\text{Me}$</td>
<td>10%</td>
<td>3a:4a = 1:19.0</td>
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<tr>
<td>L₄: dppbenz</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Ph}_2$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>20%</td>
<td>3a:4a = 1:1.10</td>
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<tr>
<td>L₅: Dppm</td>
<td>$\text{Fe}\text{PPh}_2\text{Ph}_2$ to $\text{Fe}\text{PPh}_2\text{Ph}_2$</td>
<td>23%</td>
<td>3a:4a = 1:0.25</td>
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<tr>
<td>L₆: Dppe</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Me}$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>20%</td>
<td>3a:4a = 1:1.67</td>
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<tr>
<td>L₇: Dppp</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Me}$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>42%</td>
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<tr>
<td>L₈: Dppb</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Me}$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>48%</td>
<td>3a:4a = 1:1.10</td>
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<td>L₉: DPPF</td>
<td>$\text{Fe}\text{PPh}_2\text{Ph}_2$ to $\text{Fe}\text{PPh}_2\text{Ph}_2$</td>
<td>46%</td>
<td>3a:4a = 1:0.37</td>
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<tr>
<td>L₁₀: DPEPhos</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Ph}_2$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>12%</td>
<td>3a:4a = 1:1.67</td>
</tr>
<tr>
<td>L₁₁: DPEPhos</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Ph}_2$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>92%</td>
<td>3a:4a = 1:1.10</td>
</tr>
<tr>
<td>L₁₂: XantPhos</td>
<td>$\text{Ph}_3\text{PMe}_2\text{Ph}_2$ to $\text{Ph}_3\text{PMe}_2\text{Ph}_2$</td>
<td>97%</td>
<td>3a:4a = 1:0.03</td>
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</table>

$^a$1a (0.1 mmol), 2a (0.3 mmol), Pd(TFA)$_2$ (10 mol%), ligand (11 mol%), K$_3$PO$_4$ (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h. Yields of 3a and ratios of 3a:4a were determined by $^1$H NMR (1,3,5-trimethoxybenzene as internal standard).
Table S5: The other reaction conditions screening

<table>
<thead>
<tr>
<th>Entry</th>
<th>PG</th>
<th>MeB(OR)₂</th>
<th>T(°C)</th>
<th>3a Yield (%)</th>
<th>3a:4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ts</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>50</td>
<td>95</td>
<td>1:0.03</td>
</tr>
<tr>
<td>2</td>
<td>Boc</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Ac</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Ts</td>
<td>MeB(OH)₂ (1.2 eq)</td>
<td>50</td>
<td>27</td>
<td>1:0.30</td>
</tr>
<tr>
<td>5</td>
<td>Ts</td>
<td>MeB(OH)₂ (2.0 eq)</td>
<td>50</td>
<td>59</td>
<td>1:0.10</td>
</tr>
<tr>
<td>6</td>
<td>Ts</td>
<td>Trimethylboroxine (3.0 eq)</td>
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<td>60</td>
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</tr>
<tr>
<td>7</td>
<td>Ts</td>
<td>MeBF₃K (3.0 eq)</td>
<td>50</td>
<td>56</td>
<td>1:0.08</td>
</tr>
<tr>
<td>8</td>
<td>Ts</td>
<td>MeB(pin) (3.0 eq)</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>Ts</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>30</td>
<td>85</td>
<td>1:0.02</td>
</tr>
<tr>
<td>10⃣</td>
<td>Ts</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>60</td>
<td>94</td>
<td>1:0.06</td>
</tr>
<tr>
<td>11⃣</td>
<td>Ts</td>
<td>MeB(OH)₂ (3.0 eq)</td>
<td>50</td>
<td>95</td>
<td>1:0.05</td>
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</tbody>
</table>

4⃣1a (0.1 mmol), 2 (0.3 mmol), Pd(TFA)₂ (10 mol%), Xantphos (11 mol%), K₃PO₄ (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O₂ balloon, 50 °C, 10 h. Yields of 3a and ratios of 3a:4a were determined by ¹H NMR (1,3,5-trimethoxybenzene as internal standard). 5⃣5 mol% cat Pd, 5.5 mol% ligand. 6⃣Isolated yields.

6. General procedure for synthesis of 3-methylindoles

In the glovebox, a Schlenk tube was charged with 1 (1.0 equiv.), 2a (3.0 equiv.), Pd(TFA)₂ (5 mol%), Xantphos (5.5 mol%), potassium phosphate (1.5 equiv.), 4Å MS and tetrahydrofuran. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compounds 3.
3-Methyl-2-phenyl-1-tosyl-1H-indole (3a): the reaction was conducted at 0.1 mmol scale, 34.3 mg, 95% yield, known compound[20], white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.40–8.26 (m, 1H), 7.53–7.40 (m, 4H), 7.39–7.25 (m, 6H), 7.12–6.96 (m, 2H), 2.29 (s, 3H), 2.03 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.5, 137.4, 136.9, 135.3, 132.0, 131.8, 131.6, 129.4, 128.6, 127.6, 127.0, 125.2, 124.1, 120.0, 119.2, 116.4, 21.7, 9.7.

3,5-Dimethyl-2-phenyl-1-tosyl-1H-indole (3b): the reaction was conducted at 0.1 mmol scale, 36.0 mg, 96% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.22–8.14 (m, 1H), 7.47–7.38 (m, 3H), 7.38–7.31 (m, 2H), 7.22–7.15 (m, 2H), 7.08–6.99 (m, 2H), 2.44 (s, 3H), 2.28 (s, 3H), 2.01 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.4, 137.0, 135.6, 135.2, 133.8, 132.3, 131.9, 131.5, 129.4, 128.5, 127.6, 127.0, 126.5, 120.0, 119.2, 116.2, 21.7, 21.6, 9.7. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C23H21NNaO2S 398.1185; found 398.1184.

5-Methoxy-3-methyl-2-phenyl-1-tosyl-1H-indole (3c): the reaction was conducted at 0.1 mmol scale, 37.5 mg, 96% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.24–8.16 (m, 1H), 7.47–7.40 (m, 3H), 7.39–7.31 (m, 2H), 7.09–7.01 (m, 2H), 6.88–6.80 (m, 1H), 3.85 (s, 3H), 2.28 (s, 3H), 2.01 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 157.2, 144.4, 137.9, 135.0, 133.3, 131.9, 131.8, 131.5, 129.3, 128.6, 127.6, 127.0, 120.2, 117.6, 113.5, 101.9, 55.8, 21.7, 9.8. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C23H21NNaO3S 414.1134; found 414.1134.

5-Chloro-3-methyl-2-phenyl-1-tosyl-1H-indole (3d): the reaction was conducted at 0.1 mmol scale, 19.7 mg, 50% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.29–8.20 (m, 1H), 7.48–7.41 (m, 3H), 7.40–7.37 (m, 1H), 7.36–7.29 (m, 3H), 7.11–7.02 (m, 2H), 2.31 (s, 3H), 2.00 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.9, 137.7, 137.4, 135.2, 131.6, 131.2, 131.0, 130.4, 129.6, 128.8, 127.7, 127.1, 124.6, 119.9, 119.4, 116.5, 21.8, 9.6. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C22H18ClNNaO2S 418.0639; found 418.0633.

5-Fluoro-3-methyl-2-phenyl-1-tosyl-1H-indole (3e): the reaction was conducted at 0.1 mmol scale, 33.1 mg, 87% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.30–8.23 (m, 1H), 7.48–7.41 (m, 3H), 7.38–7.31 (m, 2H), 7.13–7.01 (m, 4H), 2.30 (s, 3H), 2.00 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 160.3 (d, J_C= 239.8 Hz), 144.8, 138.7, 134.9, 133.6, 133.3 (d, J_C= 9.4 Hz), 131.5, 131.4, 129.5, 128.8, 127.7, 127.0, 119.8 (d, J_C= 4.0 Hz), 117.7 (d, J_C= 9.2 Hz), 112.8 (d, J_C= 25.1 Hz), 104.9 (d, J_C= 23.7 Hz), 21.8, 9.7. 19F NMR (376 MHz, CDCl3) δ -118.79. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C22H18FNNaO2S 402.0934; found 402.0930.
3,6-Dimethyl-2-phenyl-1-tosyl-1H-indole (3f): the reaction was conducted at 0.1 mmol scale, 34.5 mg, 92% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.14 (s, 1H), 7.47–7.38 (m, 3H), 7.36–7.31 (m, 2H), 7.30–7.26 (m, 3H), 7.15–7.11 (m, 1H), 7.09–7.02 (m, 2H), 2.54 (s, 3H), 2.30 (s, 3H), 2.01 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.4, 137.8, 136.2, 135.4, 135.2, 131.9, 131.6, 129.8, 129.4, 128.4, 127.6, 127.0, 125.5, 120.0, 118.8, 116.6, 22.3, 21.7, 9.7. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C23H25ClFNNaO2S 398.1185; found 398.1184.

6-Chloro-3-methyl-2-phenyl-1-tosyl-1H-indole (3g): the reaction was conducted at 0.1 mmol scale, 19.3 mg, 49% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.36 (s, 1H), 7.48–7.39 (m, 3H), 7.36–7.24 (m, 6H), 7.14–7.03 (m, 2H), 2.32 (s, 3H), 2.00 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.9, 137.7, 137.4, 135.2, 131.6, 131.2, 131.0, 130.4, 129.6, 128.8, 127.7, 127.1, 124.6, 119.9, 119.4, 116.5, 21.8, 9.6. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C23H18ClNaO2S 418.0639; found 418.0642.

7-Fluoro-3-methyl-2-phenyl-1-tosyl-1H-indole (3h): the reaction was conducted at 0.1 mmol scale, 32.2 mg, 85% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 7.48–7.42 (m, 5H), 7.41–7.36 (m, 2H), 7.25–7.17 (m, 2H), 7.16–7.10 (m, 2H), 7.09–7.02 (m, 1H), 2.34 (s, 3H), 2.08 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 151.5 (d, JCF = 251.6 Hz), 144.6, 139.8, 136.7 (d, JCF = 2.9 Hz), 135.4, 132.2, 130.7, 129.4, 128.5, 127.9, 127.5 (d, JCF = 1.5 Hz), 125.4 (d, JCF = 7.2 Hz), 120.3 (d, JCF = 1.8 Hz), 115.2 (d, JCF = 3.6 Hz), 112.7 (d, JCF = 21.7 Hz), 21.8, 10.0. 19F NMR (376 MHz, CDCl3) δ -116.45. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C22H18FNNaO2S 402.0934; found 402.0931.

5-Chloro-7-fluoro-3-methyl-2-phenyl-1-tosyl-1H-indole (3i): the reaction was conducted at 0.1 mmol scale, 29.0 mg, 70% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 7.48–7.42 (m, 4H), 7.41 (s, 1H), 7.39–7.34 (m, 2H), 7.20–7.17 (m, 1H), 7.16–7.12 (m, 2H), 7.10–7.05 (m, 1H), 2.36 (s, 3H), 2.04 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 150.9 (d, JCF = 256.3 Hz), 144.9, 141.3, 137.2 (d, JCF = 3.8 Hz), 135.2, 131.7, 130.7, 130.2 (d, JCF = 9.1 Hz), 129.5, 128.8, 128.0, 127.5 (d, JCF = 0.8 Hz), 123.9 (d, JCF = 9.5 Hz), 119.6 (d, JCF = 2.0 Hz), 115.2 (d, JCF = 3.9 Hz), 113.3 (d, JCF = 25.3 Hz), 21.8, 9.9. 19F NMR (376 MHz, CDCl3) δ -113.73. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C22H17ClFNNaO2S 436.0554; found 436.0552.

4,6-Difluoro-3-methyl-2-phenyl-1-tosyl-1H-indole (3j): the reaction was conducted at 0.1 mmol scale, 36.4 mg, 92% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 7.49–7.42 (m, 3H), 7.41 (s, 1H), 7.40–7.34 (m, 3H), 7.17–7.09 (m, 2H), 6.91–6.79 (m, 2H), 2.35 (s, 3H), 2.03 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 160.0 (dd, JCF = 242.8, 10.2 Hz), 151.2 (dd, JCF = 255.2, 13.1 Hz), 144.9, 141.6, 137.0 (dd, JCF = 10.7, 4.4 Hz), 134.9, 131.8, 130.7, 129.5, 128.8, 128.0, 127.5 (d, JCF = 0.3 Hz), 121.9 (dd, JCF = 9.4, 2.3 Hz), 120.4 (dd, JCF = 3.8, 2.4 Hz), 101.9, 101.6, 101.4, 101.4, 101.4, 101.2,
7-Chloro-5-fluoro-3-methyl-1-tosyl-1H-indole (3k): the reaction was conducted at 0.1 mmol scale, 37.9 mg, 92% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 7.41–7.35 (m, 3H), 7.34–7.27 (m, 2H), 7.18–7.10 (m, 3H), 7.07–7.00 (m, 2H), 6.98–6.92 (m, 1H), 2.35 (s, 3H), 2.01 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 160.4 (d, J\textsuperscript{C-F} = 244.9 Hz), 144.7, 143.2, 138.4 (d, J\textsuperscript{C-F} = 10.0 Hz), 134.5, 133.9 (d, J\textsuperscript{C-F} = 2.1 Hz), 131.5, 130.6, 129.0, 128.7, 127.9, 127.6, 125.6 (d, J\textsuperscript{C-F} = 11.6 Hz), 121.7 (d, J\textsuperscript{C-F} = 4.1 Hz), 115.4 (d, J\textsuperscript{C-F} = 27.4 Hz), 104.3 (d, J\textsuperscript{C-F} = 23.2 Hz), 21.8, 10.0. 19F NMR (376 MHz, CDCl3) δ -115.73. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C\textsubscript{22}H\textsubscript{17}F\textsubscript{2}NNaO\textsubscript{2}S 436.0545; found 436.0546.

2-(4-Methoxyphenyl)-3-methyl-1-tosyl-1H-indole (3l): the reaction was conducted at 0.1 mmol scale, 31.3 mg, 80% yield, known compound\textsuperscript{34}, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.35–8.27 (m, 1H), 7.43–7.34 (m, 2H), 7.32–7.23 (m, 5H), 7.09–7.01 (m, 2H), 7.00–6.92 (m, 2H), 3.89 (s, 3H), 2.29 (s, 3H), 2.02 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 159.9, 144.5, 137.3, 136.8, 135.4, 132.9, 132.0, 129.4, 127.0, 125.0, 124.1, 123.9, 119.5, 119.1, 116.4, 113.1, 55.5, 21.7, 9.7.

3-Methyl-2-(p-tolyl)-1-tosyl-1H-indole (3m): the reaction was conducted at 0.1 mmol scale, 33.2 mg, 88% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.34–8.28 (m, 1H), 7.42–7.33 (m, 2H), 7.32–7.27 (m, 3H), 7.26–7.23 (m, 5H), 7.07–7.00 (m, 2H), 2.44 (s, 3H), 2.28 (s, 3H), 2.03 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.5, 138.4, 137.3, 137.0, 135.2, 132.1, 131.4, 129.4, 128.8, 128.4, 127.0, 125.0, 124.1, 123.9, 119.5, 119.1, 116.4, 113.1, 55.5, 21.7, 9.7. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C\textsubscript{23}H\textsubscript{21}NNaO\textsubscript{2}S 398.1185; found 398.1184.

2-(4-(Tert-butyl)phenyl)-3-methyl-1-tosyl-1H-indole (3n): the reaction was conducted at 0.1 mmol scale, 34.4 mg, 82% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.34–8.28 (m, 1H), 7.43–7.40 (m, 3H), 7.38–7.33 (m, 1H), 7.30–7.25 (m, 5H), 7.07–6.99 (m, 2H), 2.29 (s, 3H), 2.04 (s, 3H), 1.40 (s, 9H). 13C NMR (100 MHz, CDCl3) δ 151.4, 144.4, 137.4, 137.1, 135.3, 132.1, 131.2, 129.3, 128.6, 127.1, 125.0, 124.5, 124.0, 119.7, 119.1, 116.4, 34.9, 31.6, 21.7, 9.8. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C\textsubscript{26}H\textsubscript{27}NNaO\textsubscript{2}S 440.1655; found 440.1652.

2-(4-Fluorophenyl)-3-methyl-1-tosyl-1H-indole (3o): the reaction was conducted at 0.1 mmol scale, 28.4 mg, 75% yield, unknown compound, white solid, Rf = 0.3 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.36–8.27 (m, 1H), 7.45–7.36 (m, 2H), 7.34–7.24 (m, 5H), 7.17–7.09 (m, 2H), 7.08–7.02 (m, 2H), 2.23 (s, 3H), 2.02 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 163.0 (d, J\textsuperscript{C-F} = 246.8 Hz), 144.7, 137.4, 135.7, 135.3, 133.3 (d, J\textsuperscript{C-F} = 38.1 Hz), 131.8, 129.5, 127.7 (d, J\textsuperscript{C-F} = 3.3 Hz), 126.9, 125.3, 124.2, 120.2, 119.2, 116.4, 114.8 (d, J\textsuperscript{C-F} = 21.6 Hz), 21.7,
9.6. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -112.83. HRMS (ESI-QEplus) $m/z$: [M+Na]$^+$ Calcd for C$_{22}$H$_{18}$FNNaO$_2$S 402.0934; found 402.0935.

2-(4-Chlorophenyl)-3-methyl-1-tosyl-1H-indole (3p): the reaction was conducted at 0.1 mmol scale, 23.7 mg, 60% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36–8.28 (m, 1H), 7.45–7.36 (m, 4H), 7.34–7.30 (m, 1H), 7.29–7.26 (m, 4H), 7.10–7.01 (m, 2H), 2.30 (s, 3H), 2.03 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.7, 137.5, 135.6, 135.2, 134.7, 134.7, 130.2, 129.5, 128.0, 127.0, 125.5, 124.3, 120.5, 119.3, 116.5, 21.8, 9.7. HRMS (ESI-QEplus) $m/z$: [M+Na]$^+$ Calcd for C$_{22}$H$_{18}$ClNNaO$_2$S 418.0639; found 418.0611.

1-(4-(3-Methyl-1-tosyl-1H-indol-2-yl)phenyl)ethan-1-one (3q): the reaction was conducted at 0.1 mmol scale, 30.1 mg, 75% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 30/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35–8.29 (m, 1H), 8.08–8.02 (m, 2H), 7.53–7.47 (m, 2H), 7.46–7.37 (m, 2H), 7.35–7.27 (m, 2H), 7.09–7.03 (m, 2H), 2.69 (s, 3H), 2.30 (s, 3H), 2.06 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 198.0, 144.8, 137.7, 136.8, 136.7, 135.7, 134.8, 132.1, 131.6, 129.5, 127.7, 126.9, 125.7, 124.5, 121.5, 119.5, 116.6, 26.9, 21.8, 9.8. HRMS (ESI-QEplus) $m/z$: [M+Na]$^+$ Calcd for C$_{24}$H$_{21}$NNaO$_3$S 426.1134; found 426.1131.

3-Methyl-2-(4-nitrophenyl)-1-tosyl-1H-indole (3r): the reaction was conducted at 0.1 mmol scale, 28.0 mg, 69% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 30/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35–8.29 (m, 3H), 7.62–7.54 (m, 2H), 7.48–7.41 (m, 2H), 7.37–7.31 (m, 1H), 7.30–7.24 (m, 2H), 7.10–7.05 (m, 2H), 2.31 (s, 3H), 2.09 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.7, 145.1, 138.7, 137.9, 134.6, 132.1, 131.9, 129.6, 126.9, 126.2, 124.7, 123.1, 122.9, 122.5, 119.7, 116.7, 21.8, 9.8. HRMS (ESI-QEplus) $m/z$: [M-H]$^-$. Calcd for C$_{22}$H$_{17}$N$_2$O$_4$S 405.0915; found 405.0906.

3-Methyl-2-(m-tolyl)-1-tosyl-1H-indole (3s): the reaction was conducted at 0.1 mmol scale, 31.9 mg, 85% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35–8.29 (m, 1H), 7.45–7.39 (m, 1H), 7.39–7.22 (m, 6H), 7.17–7.08 (m, 2H), 7.08–7.01 (m, 2H), 2.40 (s, 3H), 2.29 (s, 3H), 2.03 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.5, 137.4, 137.1, 137.0, 135.4, 132.3, 132.0, 131.6, 129.4, 128.6, 127.5, 127.1, 125.1, 124.0, 119.7, 119.2, 116.4, 21.7, 21.7, 9.7. HRMS (ESI-QEplus) $m/z$: [M+Na]$^+$ Calcd for C$_{23}$H$_{21}$NNaO$_2$S 398.1185; found 398.1183.

2-(3-Chlorophenyl)-3-methyl-1-tosyl-1H-indole (3t): the reaction was conducted at 0.1 mmol scale, 32.7 mg, 83% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35–8.27 (m, 1H), 7.45–7.35 (m, 4H), 7.34–7.24 (m, 4H), 7.23–7.20 (m, 1H), 7.10–7.04 (m, 2H), 2.31 (s, 3H), 2.04 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.8, 137.5, 135.2, 133.5, 131.7, 131.3, 129.9, 129.5, 128.9, 128.7, 127.0, 125.5, 124.2, 120.6,
119.4, 116.4, 21.8, 9.6. HRMS (ESI-QEplus) m/z: [M+Na]^+ Calcd for C_{22}H_{18}CINaO_{2}S 418.0639; found 418.0641.

2-(2-Methoxyphenyl)-3-methyl-1-tosyl-1H-indole (3u): the reaction was conducted at 0.1 mmol scale, 36.8 mg, 94% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, CDCl_3) δ 8.29–8.22 (m, 1H), 7.45–7.42 (m, 2H), 7.40–7.36 (m, 2H), 7.35–7.30 (m, 1H), 7.29–7.24 (m, 1H), 7.15–7.13 (m, 1H), 7.09–6.98 (m, 3H), 6.97–6.93 (m, 1H), 3.72 (s, 3H), 2.29 (s, 3H), 1.99 (s, 3H). ^13C NMR (100 MHz, CDCl_3) δ 158.7, 144.2, 137.1, 136.1, 133.3, 133.1, 131.7, 130.6, 129.3, 127.1, 124.7, 123.5, 120.8, 119.8, 119.4, 119.1, 115.7, 110.8, 55.5, 21.7, 9.5. HRMS (ESI-QEplus) m/z: [M+Na]^+ Calcd for C_{23}H_{21}NNaO_3S 414.1134; found 414.1130.

2-(2-Fluorophenyl)-3-methyl-1-tosyl-1H-indole (3v): the reaction was conducted at 0.1 mmol scale, 33.8 mg, 89% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, CDCl_3) δ 8.31–8.24 (m, 1H), 7.49–7.42 (m, 2H), 7.40–7.27 (m, 5H), 7.26–7.21 (m, 1H), 7.20–7.14 (m, 1H), 7.10–7.04 (m, 2H), 2.28 (s, 3H), 2.03 (s, 3H). ^13C NMR (100 MHz, CDCl_3) δ 160.8 (d, _J_{C-F} = 247.1 Hz), 144.7, 137.4, 135.3, 133.7 (d, _J_{C-F} = 2.7 Hz), 131.6, 131.0 (d, _J_{C-F} = 8.5 Hz), 130.2, 129.5, 127.0, 125.3, 124.0, 123.5 (d, _J_{C-F} = 3.6 Hz), 121.4, 119.9 (d, _J_{C-F} = 15.1 Hz), 119.3, 116.0, 115.7 (d, _J_{C-F} = 21.7 Hz), 21.7, 9.6 (d, _J_{C-F} = 0.9 Hz). ^19F NMR (376 MHz, CDCl_3) δ -111.42. HRMS (ESI-QEplus) m/z: [M+Na]^+ Calcd for C_{22}H_{18}FNNaO_2S 402.0934; found 402.0928.

2-(2-(Benzyloxy)ethyl)-3-methyl-1-tosyl-1H-indole (3w): the reaction was conducted at 0.1 mmol scale, 39.9 mg, 95% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, CDCl_3) δ 8.21–8.14 (m, 1H), 7.59–7.52 (m, 2H), 7.42–7.37 (m, 1H), 7.33–7.21 (m, 7H), 7.16–7.09 (m, 2H), 4.52 (s, 2H), 3.79 (t, _J = 6.7 Hz), 2.32 (s, 3H), 2.16 (s, 3H). ^13C NMR (100 MHz, CDCl_3) δ 144.7, 136.9, 136.3, 132.4, 131.4, 130.0, 126.4, 124.8, 123.7, 119.4, 118.9, 115.3, 73.2, 70.1, 27.6, 21.7, 9.3. HRMS (ESI-QEplus) m/z: [M+Na]^+ Calcd for C_{23}H_{25}NNaO_4S 442.1447; found 442.1445.

2-(5-Methyl-1-tosyl-1H-indol-2-yl)ethyl acetate (3x): the reaction was conducted at 0.1 mmol scale, 33.4 mg, 90% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^1H NMR (400 MHz, CDCl_3) δ 8.21–8.13 (m, 1H), 7.61–7.53 (m, 2H), 7.42–7.37 (m, 1H), 7.33–7.23 (m, 2H), 7.19–7.12 (m, 2H), 4.38 (t, _J = 6.7 Hz), 3.34 (t, _J = 6.7 Hz), 2.32 (s, 3H), 2.17 (s, 3H), 2.03 (s, 3H). ^13C NMR (100 MHz, CDCl_3) δ 171.2, 144.8, 136.8, 136.1, 132.4, 131.4, 130.0, 126.4, 124.8, 123.7, 119.4, 118.9, 115.3, 64.0, 26.3, 21.7, 21.2, 9.2. HRMS (ESI-QEplus) m/z: [M+Na]^+ Calcd for C_{23}H_{23}NNaO_4S 394.1083; found 394.1078.
2-(2-(((Tert-butyldimethylsilyl)oxy)ethyl)-3-methyl-1-tosyl-1H-indole (3y): the reaction was conducted at 0.1 mmol scale, 35.1 mg, 79% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.20–8.14 (m, 1H), 7.59–7.52 (m, 2H), 7.40–7.34 (m, 1H), 7.30–7.20 (m, 2H), 7.17–7.10 (m, 2H), 3.92 (t, $J$ = 6.7 Hz, 2H), 3.21 (t, $J$ = 6.6 Hz, 2H), 2.31 (s, 3H), 2.17 (s, 3H), 0.85 (s, 9H), -0.03 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.6, 136.8, 136.3, 133.8, 131.7, 129.9, 126.4, 124.4, 123.6, 119.1, 118.6, 115.3, 63.3, 30.5, 26.1, 21.7, 18.5, 9.5, -5.2. HRMS (ESI-QEplus) m/z: [M+Na]$^+$ Calcd for C$_{24}$H$_{33}$NNaO$_3$Si 466.1843; found 466.1834.

2-(3-Methyl-1-tosyl-1H-indol-2-yl)ethyl benzoate (3z): the reaction was conducted at 0.1 mmol scale, 36.8 mg, 85% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 15/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.22–8.16 (m, 1H), 8.03–7.95 (m, 2H), 7.63–7.57 (m, 2H), 7.56–7.50 (m, 1H), 7.45–7.35 (m, 3H), 7.34–7.28 (m, 1H), 7.27–7.22 (m, 1H), 7.19–7.12 (m, 2H), 4.65 (t, $J$ = 6.6 Hz, 2H), 3.48 (t, $J$ = 6.6 Hz, 2H), 2.31 (s, 3H), 2.17 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.7, 144.8, 136.9, 136.2, 133.1, 132.4, 131.4, 130.4, 130.0, 129.8, 128.5, 126.4, 124.8, 123.7, 119.5, 118.9, 115.3, 64.4, 26.4, 21.7, 9.3. HRMS (ESI-QEplus) m/z: [M+Na]$^+$ Calcd for C$_{25}$H$_{23}$NNaO$_4$S 456.1240; found 456.1234.

4-((3-Methyl-1-tosyl-1H-indol-2-yl)methyl)morpholine (3aa): the reaction was conducted at 0.1 mmol scale, 18.5 mg, 48% yield, unknown compound, white solid, R$_f$ = 0.3 (dichloromethane/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.16–8.08 (m, 1H), 8.07–7.98 (m, 2H), 7.49–7.40 (m, 1H), 7.35–7.28 (m, 1H), 7.26–7.21 (m, 1H), 7.21–7.12 (m, 2H), 3.88 (s, 2H), 3.53 (br s, 4H), 2.50 (br s, 4H), 2.34 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.4, 137.4, 136.6, 132.2, 129.5, 127.3, 125.0, 123.2, 119.2, 119.1, 114.9, 66.9, 53.4, 52.1, 21.7, 9.5. HRMS (ESI-QEplus) m/z: [M+H]$^+$ Calcd for C$_{21}$H$_{25}$N$_2$O$_3$S 385.1580; found 385.1577.

2-Cyclopropyl-3-methyl-1-tosyl-1H-indole (3ab): the reaction was conducted at 0.1 mmol scale, 27.7 mg, 85% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.21–8.14 (m, 1H), 7.67–7.59 (m, 2H), 7.39–7.33 (m, 1H), 7.31–7.20 (m, 2H), 7.18–7.12 (m, 2H), 2.33 (s, 3H), 2.21 (s, 3H), 2.06–1.93 (m, 1H), 1.06–0.97 (m, 2H), 0.69–0.61 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.4, 137.4, 136.6, 132.2, 129.5, 127.3, 125.0, 123.2, 119.2, 119.1, 114.9, 66.9, 53.4, 52.1, 21.7, 9.5. HRMS (ESI-QEplus) m/z: [M+Na]$^+$ Calcd for C$_{19}$H$_{19}$NNaO$_2$S$_2$ 348.1029, found 348.1027.

2-(Tert-butyl)-3-methyl-1-tosyl-1H-indole (3ac): the reaction was conducted at 0.1 mmol scale, 30.4 mg, 89% yield, unknown compound, white solid, R$_f$ = 0.3 (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.03–7.96 (m, 1H), 7.27–7.23 (m, 2H), 7.21–7.16 (m, 1H), 7.14–7.08 (m, 2H), 6.97–6.90 (m, 2H), 2.22 (s, 6H), 1.66 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 147.6, 143.8, 139.9, 135.4, 132.7, 128.6, 127.0, 124.9, 124.7, 124.6, 118.5, 118.2, 36.1, 32.1, 21.7, 12.9. HRMS (ESI-QEplus) m/z: [M+Na]$^+$ Calcd for C$_{26}$H$_{23}$NNaO$_2$S 364.1342; found 364.1340.
3-Methyl-1-tosyl-2-(trimethylsilyl)-1H-indole (3ad): the reaction was conducted at 0.1 mmol scale, 35.7 mg, 99% yield, unknown compound, white solid, Rₜ = 0.3 (petroleum ether/ethyl acetate 50/1); ¹H NMR (400 MHz, CDCl₃) δ 7.97–7.92 (m, 1H), 7.46–7.41 (m, 2H), 7.38–7.34 (m, 1H), 7.26–7.21 (m, 1H), 7.19–7.13 (m, 1H), 7.08–7.02 (m, 2H), 2.32 (s, 3H), 2.24 (s, 3H), 0.52 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 144.1, 139.5, 138.1, 133.4, 129.4, 126.7, 125.5, 123.6, 119.2, 115.6, 21.7, 12.1, 2.7. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C₁₉H₂₃NNaO₂Si 380.1111; found 380.1108.

2-(3-Methyl-1-tosyl-1H-indol-2-yl)ethyl 3-(N,N-dipropylsulfamoyl)benzoate (3ae): the reaction was conducted at 0.1 mmol scale, 44.1 mg, 74% yield, unknown compound, white solid, Rₜ = 0.3 (petroleum ether/ethyl acetate 15/1); ¹H NMR (400 MHz, CDCl₃) δ 8.22–8.16 (m, 1H), 8.14–8.05 (m, 2H), 7.88–7.81 (m, 2H), 7.62–7.54 (m, 2H), 7.39–7.37 (m 1H), 7.35–7.22 (m, 2H), 7.20–7.12 (m, 2H), 4.69 (t, J = 6.5 Hz, 2H), 3.50 (t, J = 6.5 Hz, 2H), 3.15–3.04 (m, 4H), 2.32 (s, 3H), 2.16 (s, 3H), 1.55–1.49 (m, 4H), 0.86 (t, J = 7.4 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 165.4, 144.9, 144.4, 136.9, 136.0, 133.7, 132.1, 131.3, 130.4, 130.0, 127.2, 126.4, 124.9, 123.8, 119.6, 118.9, 115.3, 65.1, 50.1, 26.3, 22.1, 21.7, 11.3, 9.3. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C₃₁H₃₆N₂NaO₆S₂ 619.1907; found 619.1908.

2-(3-Methyl-1-tosyl-1H-indol-2-yl)ethyl 2-(6-methoxynaphthalen-2-yl)propanoate (3af): the reaction was conducted at 0.1 mmol scale, 29.4 mg, 54% yield, unknown compound, white solid, Rₜ = 0.3 (petroleum ether/ethyl acetate 15/1); ¹H NMR (400 MHz, CDCl₃) δ 8.17–8.11 (m, 1H), 7.60–7.58 (m, 2H), 7.55–7.53 (m, 1H), 7.52–7.46 (m, 2H), 7.32–7.18 (m, 4H), 7.13–7.03 (m, 4H), 4.40 (t, J = 6.5 Hz, 2H), 3.91 (s, 3H), 3.79 (q, J = 7.1 Hz, 1H), 3.33–3.21 (m, 2H), 2.27 (s, 3H), 1.94 (s, 3H), 1.53 (d, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 174.8, 157.8, 144.7, 136.9, 136.1, 135.8, 133.8, 132.3, 131.4, 129.9, 129.5, 129.1, 127.3, 126.4, 126.1, 124.7, 123.6, 119.6, 119.1, 118.9, 115.3, 105.8, 64.4, 55.5, 45.7, 26.2, 21.7, 18.7, 9.0. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C₃₂H₃₆N₂NaO₆S 564.1815; found 564.1812.

2-(3-Methyl-1-tosyl-1H-indol-2-yl)ethyl 2-(4-isobutylphenyl)propanoate (3ag): the reaction was conducted at 0.1 mmol scale, 32.6 mg, 63% yield, unknown compound, white solid, Rₜ = 0.3 (petroleum ether/ethyl acetate 15/1); ¹H NMR (400 MHz, CDCl₃) δ 8.18–8.12 (m, 1H), 7.56–7.49 (m, 2H), 7.36 –7.21 (m, 1H), 7.16–7.08 (m, 4H), 7.02–6.96 (m, 2H), 4.44–4.32 (m, 2H), 3.63 (q, J = 7.0 Hz, 1H), 3.35–3.22 (m, 2H), 2.41 (d, J = 7.1 Hz, 2H), 2.30 (s, 3H), 2.02 (s, 3H), 1.88–1.76 (m, 1H), 1.44 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 6.6 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 174.9, 144.7, 136.9, 136.1, 133.8, 132.3, 131.4, 129.9, 129.5, 129.1, 127.3, 126.4, 126.1, 124.7, 123.6, 119.6, 119.1, 118.9, 115.3, 64.3, 45.3, 45.2, 30.4, 29.9, 26.2, 22.6, 21.7, 18.8, 9.1. HRMS (ESI-QEplus) m/z: [M+Na]⁺ Calcd for C₃₃H₃₅NNaO₆S 540.2179; found 540.2174.
2-(3-Methyl-1-tosyl-1H-indol-2-yl)ethyl \((R)\)-4-((3R,5R,8R,9S,10S,13R,14S,17R)-3-methoxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoate (3ah): the reaction was conducted at 0.1 mmol scale, 51.8 mg, 74% yield, unknown compound, white solid, \(R_f = 0.3\) (petroleum ether/ethyl acetate 10/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.21–8.14 (m, 1H), 7.61–7.52 (m, 2H), 7.40–7.38 (m, 1H), 7.31–7.27 (m, 1H), 7.26–7.21 (m, 1H), 7.18–7.10 (m, 2H), 4.38 (t, \(J = 6.6\) Hz, 2H), 3.48–3.28 (m, 5H), 3.23–3.09 (m, 1H), 2.36–2.26 (m, 4H), 2.23–2.11 (m, 4H), 1.95–1.89 (m, 1H), 1.86–1.63 (m, 7H), 1.43–1.32 (m, 6H), 1.30–1.17 (m, 6H), 1.15–0.96 (m, 6H), 0.91 (s, 3H), 0.87 (d, \(J = 6.4\) Hz, 3H), 0.61 (s, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 174.4, 144.8, 136.9, 136.2, 132.5, 131.4, 130.0, 126.4, 124.7, 123.7, 119.4, 118.8, 115.3, 80.6, 63.8, 56.6, 56.1, 55.7, 42.9, 42.2, 40.5, 40.3, 36.0, 35.5, 35.1, 33.0, 31.5, 31.1, 28.3, 27.5, 27.0, 26.6, 26.3, 24.4, 23.6, 21.7, 21.0, 18.4, 12.2, 9.3. HRMS (ESI-QEplus) \(m/z\): [M+H]\(^+\) Calcd for C\(_{43}\)H\(_{60}\)NNaO\(_5\)S 702.4187; found 702.4173.
7. Optimization of the Conditions for synthesis of 3-methyl-2-phenylbenzofuran

Table S6: Solvent screening

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$^a$5a (0.1 mmol), 2a (0.3 mmol), Pd(TFA)$_2$ (10 mol%), Xantphos (11 mol%), K$_3$PO$_4$ (1.5 equiv.), solvent (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h, isolated yields.
Table S7: Base screening

\[
\begin{align*}
\text{OH} & \quad + \quad \text{MeB(OH)}_2 \\
\text{5a} & \quad 2a \\
\rightarrow & \quad \text{Ph} \\
\text{6a}
\end{align*}
\]

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*5a (0.1 mmol), 2a (0.3 mmol), Pd(TFA)₂ (10 mol%), Xantphos (11 mol%), base (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O₂ balloon, 50 °C, 10 h, isolated yields.

Table S8: Metal precursor screening

\[
\begin{align*}
\text{OH} & \quad + \quad \text{MeB(OH)}_2 \\
\text{5a} & \quad 2a \\
\rightarrow & \quad \text{Ph} \\
\text{6a}
\end{align*}
\]

<table>
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<tr>
<th>Entry</th>
<th>Pd-cat</th>
<th>6a Yield(%)</th>
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<td>1</td>
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<tr>
<td>2</td>
<td>[PdCl(Allyl)]₂</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>Pd[(CH₃)₂CO₂]</td>
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</tr>
<tr>
<td>4</td>
<td>PdCl₂(CN)₂</td>
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</tr>
<tr>
<td>5</td>
<td>Pd(acac)₂</td>
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<tr>
<td>6</td>
<td>PdCl₂(Amphos)</td>
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<tr>
<td>8</td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>&lt;5</td>
</tr>
<tr>
<td>9</td>
<td>PdCl₂</td>
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</tbody>
</table>

*5a (0.1 mmol), 2a (0.3 mmol), cat. Pd (10 mol%), Xantphos (11 mol%), K₃PO₄ (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O₂ balloon, 50 °C, 10 h, isolated yields.
Table S9: Ligand screening

\[
\begin{align*}
\text{5a} & \quad + \quad \text{MeB(OH)}_2 & \quad \xrightarrow{\text{Pd(TFA)}_2/\text{ligand, K}_3\text{PO}_4} & \quad \text{6a}
\end{align*}
\]

\[
\begin{align*}
\text{L}_1: \text{Dppm} & \quad & \text{L}_2: \text{Dppe} & \quad & \text{L}_3: \text{Dppp} & \quad & \text{L}_4: \text{Dppb} \\
\text{L}_5: \text{dppbenz} & \quad & \text{L}_6: \text{DPPF} & \quad & \text{L}_7 & \quad & \text{L}_8: \text{DPEPhos} \\
\text{L}_9: \text{XantPhos} & \quad & \text{L}_{10}: \text{N-XantPhos} & \quad & \text{L}_{11}: \text{tBuXantPhos}
\end{align*}
\]

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<th>Entry</th>
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<th>(6a) Yield(%)</th>
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<tr>
<td>11</td>
<td>L11</td>
<td>6</td>
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</tbody>
</table>

\(5a\) (0.1 mmol), \(2a\) (0.3 mmol), Pd(TFA)$_2$ (10 mol%), ligand (11 mol%), K$_3$PO$_4$ (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O$_2$ balloon, 50 °C, 10 h, isolated yields.
8. General procedure for synthesis of 3-methylbenzofurans

\[
\begin{align*}
\text{Ar} + \text{MeB(OH)}_2 & \xrightarrow{\text{Pd(TFA)}_2/\text{Xantphos, K}_3\text{PO}_4, \text{O}_2, 4\text{Å MS, 1,4-dioxane, 50} \ C}\ \text{O} \ \text{Me} \\
\text{5} & \rightarrow \text{6a} \ (\text{R}^1) \\
\text{6a} & \rightarrow \text{3-Methyl-2-phenylbenzofuran (6a):} \\
\text{6b} & \rightarrow \text{5-Fluoro-3-methyl-2-phenylbenzofuran (6b):} \\
\text{6c} & \rightarrow \text{3,5-Dimethyl-2-phenylbenzofuran (6c):} \\
\text{6d} & \rightarrow \text{5-(Tert-butyl)-3-methyl-2-phenylbenzofuran (6d):}
\end{align*}
\]

In the glovebox, a Schlenk tube was charged with 5 (1.0 equiv.), 2a (3.0 equiv.), Pd(TFA)\(_2\) (10 mmol%), Xantphos (11 mol%), potassium phosphate (1.5 equiv.), 4Å MS and 1,4-dioxane. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compounds 6.

3-Methyl-2-phenylbenzofuran (6a): the reaction was conducted at 0.1 mmol scale, 13.3 mg, 64% yield, known compound\(^{[21]}\), white solid, \(R_f = 0.8\) (petroleum ether); \(\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.89–7.77 \ (m, 2H), 7.58–7.52 \ (m, 1H), 7.52–7.43 \ (m, 3H), 7.40–7.33 \ (m, 1H), 7.32–7.24 \ (m, 2H), 2.49 \ (s, 3H).} \)

13\(\text{C NMR (100 MHz, CDCl}_3\) \(\delta 154.0, 150.9, 131.6, 131.4, 128.8, 128.1, 126.9, 124.5, 122.5, 119.5, 111.5, 111.1, 9.7.} \)

5-Fluoro-3-methyl-2-phenylbenzofuran (6b): the reaction was conducted at 0.1 mmol scale, 10.0 mg, 44% yield, known compound\(^{[21]}\), white solid, \(R_f = 0.8\) (petroleum ether); \(\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.83–7.76 \ (m, 2H), 7.52–7.44 \ (m, 2H), 7.42–7.34 \ (m, 2H), 7.42–7.34 \ (m, 1H), 7.05–6.95 \ (m, 1H), 2.44 \ (s, 3H).} \)

13\(\text{C NMR (100 MHz, CDCl}_3\) \(\delta 159.4 \ (d, J_{\text{C-F}} = 236.4 \ Hz), 152.8, 150.2, 132.3 \ (d, J_{\text{C-F}} = 10.1 \ Hz), 131.3, 128.9, 128.4, 127.0, 112.1 \ (d, J_{\text{C-F}} = 26.0 \ Hz), 111.7 \ (d, J_{\text{C-F}} = 9.5 \ Hz), 111.7 \ (d, J_{\text{C-F}} = 3.8 \ Hz), 105.1 \ (d, J_{\text{C-F}} = 24.6 \ Hz), 9.7.} \)

19\(\text{F NMR (376 MHz, CDCl}_3\) \(\delta -121.32.} \)

3,5-Dimethyl-2-phenylbenzofuran (6c): the reaction was conducted at 0.1 mmol scale, 12.9 mg, 58% yield, known compound\(^{[21]}\), white solid, \(R_f = 0.8\) (petroleum ether); \(\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.85–7.76 \ (m, 2H), 7.51–7.43 \ (m, 2H), 7.40–7.33 \ (m, 1H), 7.32–7.24 \ (m, 2H), 2.47 \ (s, 3H), 2.47 \ (s, 3H).} \)

13\(\text{C NMR (100 MHz, CDCl}_3\) \(\delta 152.4, 151.0, 132.0, 131.8, 131.5, 128.8, 128.0, 126.9, 125.8, 119.4, 111.3, 110.7, 21.6, 9.7.} \)

5-(Tert-butyl)-3-methyl-2-phenylbenzofuran (6d): the reaction was conducted at 0.1 mmol scale, 17.7 mg, 67% yield, known compound\(^{[22]}\), white solid, \(R_f = 0.8\) (petroleum ether); \(\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.84–7.76 \ (m, 2H), 7.54–7.50 \ (m, 1H), 7.49–7.43 \ (m, 2H), 7.42–7.39 \ (m, 1H), 7.38–7.31 \ (m, 2H), 2.49 \ (s, 3H), 1.41 \ (s, 9H).} \)

13\(\text{C NMR (100 MHz, CDCl}_3\) \(\delta 152.3, 151.1, 145.7, 131.9, 130.9, 128.8, 127.9, 126.9, 122.5, 115.5, 111.7, 110.5, 35.0, 32.1, 9.7.} \)
5-Methoxy-3-methyl-2-phenylbenzofuran (6e): the reaction was conducted at 0.1 mmol scale, 10.0 mg, 42% yield, known compound\cite{21}, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.83–7.76 (m, 2H), 7.52–7.44 (m, 2H), 7.41–7.31 (m, 2H), 7.01–6.96 (m, 1H), 6.93–6.87 (m, 1H), 3.89 (s, 3H), 2.46 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 156.0, 151.8, 149.0, 131.9, 131.7, 128.8, 128.1, 126.9, 113.2, 111.6, 111.6, 102.1, 56.2, 9.8.

6-Chloro-3-methyl-2-phenylbenzofuran (6f): the reaction was conducted at 0.1 mmol scale, 6.3 mg, 26% yield, known compound\cite{22}, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.85–7.74 (m, 2H), 7.54–7.45 (m, 3H), 7.44–7.41 (m, 1H), 7.40–7.34 (m, 1H), 7.25–7.20 (m, 1H), 2.46 (s, 3H).

6-Fluoro-3-methyl-2-phenylbenzofuran (6g): the reaction was conducted at 0.1 mmol scale, 7.2 mg, 32% yield, known compound\cite{21}, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.81–7.75 (m, 2H), 7.52–7.41 (m, 3H), 7.39–7.33 (m, 1H), 7.23–7.17 (m, 1H), 7.06–6.97 (m, 1H), 2.47 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 161.3 (d, \textit{J}_{C-F} = 270.1 Hz), 153.9 (d, \textit{J}_{C-F} = 13.1 Hz), 151.7 (d, \textit{J}_{C-F} = 4.0 Hz), 131.4, 128.9, 128.2, 127.7 (d, \textit{J}_{C-F} = 1.2 Hz), 126.8, 119.8 (d, \textit{J}_{C-F} = 10.0 Hz), 111.3, 110.8 (d, \textit{J}_{C-F} = 23.8 Hz), 99.0 (d, \textit{J}_{C-F} = 24.6 Hz), 9.6. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) δ -117.45.

3,6-Dimethyl-2-phenylbenzofuran (6h): the reaction was conducted at 0.1 mmol scale, 15.9 mg, 71% yield, unknown compound, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.83–7.76 (m, 2H), 7.51–7.43 (m, 2H), 7.42–7.38 (m, 1H), 7.37–7.31 (m, 1H), 7.30–7.27 (m, 1H), 7.11–7.04 (m, 1H), 2.49 (s, 3H), 2.46 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 156.4, 150.3, 134.8, 131.7, 129.0, 128.8, 127.8, 126.4, 124.0, 119.0, 111.4, 22.0, 9.8. HRMS (ESI-QEplus) m/z: [M+H]\textsuperscript{+} Caled for C\textsubscript{16}H\textsubscript{15}O 223.1117; found 223.1116.

3,7-Dimethyl-2-phenylbenzofuran (6i): the reaction was conducted at 0.1 mmol scale, 15.8 mg, 71% yield, unknown compound, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.87–7.79 (m, 2H), 7.53–7.44 (m, 2H), 7.42–7.38 (m, 1H), 7.37–7.31 (m, 1H), 7.30–7.27 (m, 1H), 7.11–7.04 (m, 1H), 2.32 (d, \textit{J} = 2.7 Hz, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 155.0, 150.6, 131.9, 130.8, 128.8, 128.0, 126.9, 125.5, 122.6, 121.4, 117.0, 111.8, 15.2, 9.8. HRMS (ESI-QEplus) m/z: [M+H]\textsuperscript{+} Caled for C\textsubscript{16}H\textsubscript{15}O 223.1117; found 223.1117.

2-(2-Fluorophenyl)-3-methylbenzofuran (6j): the reaction was conducted at 0.1 mmol scale, 17.6 mg, 78% yield, unknown compound, white solid, R_t = 0.8 (petroleum ether); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.69–7.61 (m, 1H), 7.53–7.44 (m, 2H), 7.40–7.32 (m, 2H), 7.20–7.13 (m, 1H), 7.12–7.05 (m, 1H), 2.57 (s, 3H), 2.47 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 159.7 (d, \textit{J}_{C-F} = 249.6 Hz), 154.7, 146.5, 130.9 (d, \textit{J}_{C-F} = 3.3 Hz), 130.7, 130.6 (d, \textit{J}_{C-F} = 8.1 Hz), 124.7, 124.4 (d, \textit{J}_{C-F} =
3.4 Hz), 122.6, 119.8, 119.4 (d, \( J_{C,F} = 14.2 \) Hz), 116.5 (d, \( J_{C,F} = 22.0 \) Hz), 114.4, 111.3, 9.2 (d, \( J_{C,F} = 6.4 \) Hz). 19F NMR (376 MHz, CDCl3) \( \delta \) -111.93. HRMS (ESI-QEplus) \( m/z \): [M+H]+ Calcd for C15H12FO 227.0867; found 227.0866.

2-(4-Fluorophenyl)-3-methylbenzofuran (6k): the reaction was conducted at 0.1 mmol scale, 13.8 mg, 61% yield, known compound[23], white solid, \( R_f = 0.8 \) (petroleum ether); 1H NMR (400 MHz, CDCl3) \( \delta \) 7.82–7.73 (m, 2H), 7.56–7.50 (m, 1H), 7.49–7.45 (m, 1H), 7.33–7.22 (m, 2H), 2.45 (s, 3H). 13C NMR (100 MHz, CDCl3) \( \delta \) 162.6 (d, \( J_{C,F} = 246.9 \) Hz), 153.9, 150.1, 131.3, 128.7 (d, \( J_{C,F} = 8.2 \) Hz), 127.9 (d, \( J_{C,F} = 3.6 \) Hz), 124.6, 122.7, 119.5, 115.9 (d, \( J_{C,F} = 21.6 \) Hz), 111.1, 9.6. 19F NMR (376 MHz, CDCl3) \( \delta \) -113.13.

3-Methyl-2-(p-tolyl)benzofuran (6l): the reaction was conducted at 0.1 mmol scale, 13.8 mg, 62% yield, known compound[24], white solid, \( R_f = 0.8 \) (petroleum ether); 1H NMR (400 MHz, CDCl3) \( \delta \) 7.74–7.67 (m, 2H), 7.56–7.50 (m, 1H), 7.49–7.44 (m, 1H), 7.32–7.20 (m, 4H), 2.46 (s, 3H), 2.41 (s, 3H). 13C NMR (100 MHz, CDCl3) \( \delta \) 153.9, 151.2, 138.1, 131.5, 129.6, 128.8, 126.9, 124.3, 122.5, 119.4, 111.1, 110.8, 21.6, 9.7.

2-(4-Methoxyphenyl)-3-methylbenzofuran (6m): the reaction was conducted at 0.1 mmol scale, 16.0 mg, 67% yield, known compound[24], white solid, \( R_f = 0.8 \) (petroleum ether); 1H NMR (400 MHz, CDCl3) \( \delta \) 7.79–7.70 (m, 2H), 7.55–7.49 (m, 1H), 7.48–7.43 (m, 1H), 7.31–7.20 (m, 2H), 7.06–6.98 (m, 2H), 3.87 (s, 3H), 2.45 (s, 3H). 13C NMR (100 MHz, CDCl3) \( \delta \) 159.6, 153.8, 151.1, 131.5, 128.4, 124.4, 124.1, 122.5, 119.2, 114.3, 111.0, 109.9, 55.6, 9.6.

Tert-butlyldimethyl(3-methylbenzofuran-2-yl)methoxy)silane (6n): the reaction was conducted at 0.1 mmol scale, 13.3 mg, 48% yield, unknown compound[25], white solid, \( R_f = 0.8 \) (petroleum ether); 1H NMR (400 MHz, CDCl3) \( \delta \) 7.49–7.46 (m, 1H), 7.44–7.41 (m, 1H), 7.29–7.24 (m, 1H), 7.23–7.19 (m, 1H), 4.78 (s, 2H), 2.25 (s, 3H), 0.92 (s, 9H), 0.12 (s, 6H). 13C NMR (100 MHz, CDCl3) \( \delta \) 154.3, 151.7, 130.2, 124.4, 122.3, 119.6, 112.4, 111.3, 56.9, 26.1, 18.7, 8.2, -5.0. HRMS (ESI-QEplus) \( m/z \): [M-’Bu]+ Calcd for C12H15O2Si 219.0836; found 219.0833.

Trimethyl(3-methylbenzofuran-2-yl)silane (6o): the reaction was conducted at 0.1 mmol scale, 15.9 mg, 78% yield, known compound[25], white solid, \( R_f = 0.8 \) (petroleum ether); 1H NMR (400 MHz, CDCl3) \( \delta \) 7.49–7.46 (m, 1H), 7.44–7.41 (m, 1H), 7.29–7.24 (m, 1H), 7.23–7.19 (m, 1H), 4.78 (s, 2H), 2.25 (s, 3H), 0.92 (s, 9H), 0.12 (s, 6H). 13C NMR (100 MHz, CDCl3) \( \delta \) 157.6, 157.6, 130.1, 125.3, 124.4, 122.0, 119.4, 111.3, 9.1, -0.9.
9. General procedure for synthesis of 4-methylisoquinolines

\[
\begin{align*}
7 & \quad + \quad \text{MeB(OH)}_2 \quad \xrightarrow{\text{Pd(TFA)}_2/Xantphos, K_3\text{PO}_4, O_2, 4\,\text{Å MS, THF, } 50\,\text{oC}} \quad 8
\end{align*}
\]

In the glovebox, a Schlenk tube was charged with 7 (1.0 equiv.), 2a (3.0 equiv.), Pd(TFA)$_2$ (10 mol%), Xantphos (11 mol%), potassium phosphate (1.5 equiv.), 4Å MS, and tetrahydrofuran. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compounds 8.

4-Methyl-3-phenylisoquinoline (8a): the reaction was conducted at 0.1 mmol scale, 12.1 mg, 55% yield, known compound[26], white solid, R$_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 9.21 (s, 1H), 8.10–8.05 (m, 1H), 8.03–7.97 (m, 1H), 7.81–7.73 (m, 1H), 7.66–7.56 (m, 3H), 7.53–7.45 (m, 2H), 7.44–7.37 (m, 1H), 2.66 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 152.1, 150.4, 141.5, 136.5, 130.6, 130.1, 128.3, 127.8, 127.5, 126.9, 124.3, 123.8, 15.8.

3-(4-Fluorophenyl)-4-methylisoquinoline (8b): the reaction was conducted at 0.1 mmol scale, 12.5 mg, 53% yield, unknown compound, white solid, R$_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 9.19 (s, 1H), 8.11–8.04 (m, 1H), 8.03–7.97 (m, 1H), 7.82–7.75 (m, 1H), 7.68–7.60 (m, 1H), 7.59–7.52 (m, 2H), 7.22–7.11 (m, 2H), 2.65 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.6 (d, $J_{C-F}$ = 245.0 Hz), 151.0, 150.4, 137.6 (d, $J_{C-F}$ = 3.5 Hz), 136.4, 131.8 (d, $J_{C-F}$ = 8.1 Hz), 130.8, 128.4, 127.5, 127.0, 124.3, 123.8, 115.3 (d, $J_{C-F}$ = 2.1 Hz), 15.8. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -114.77. HRMS (ESI-QEplus) m/z: [M+H]$^+$ Calcd for C$_{16}$H$_{13}$FN 238.1027; found 238.1020.

3-(4-Chlorophenyl)-4-methylisoquinoline (8c): the reaction was conducted at 0.1 mmol scale, 11.2 mg, 44% yield, unknown compound, white solid, R$_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 9.19 (s, 1H), 8.12–8.05 (m, 1H), 8.03–7.98 (m, 1H), 7.83–7.74 (m, 1H), 7.69–7.60 (m, 1H), 7.58–7.51 (m, 2H), 7.49–7.42 (m, 2H), 2.65 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.6 (d, $J_{C-F}$ = 245.0 Hz), 151.0, 150.4, 137.6 (d, $J_{C-F}$ = 3.5 Hz), 136.4, 131.8 (d, $J_{C-F}$ = 8.1 Hz), 130.8, 128.4, 127.5, 127.0, 124.3, 123.8, 115.3 (d, $J_{C-F}$ = 2.1 Hz), 15.8. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -114.77. HRMS (ESI-QEplus) m/z: [M+H]$^+$ Calcd for C$_{16}$H$_{13}$ClN 254.0731; found 254.0725.

3-(4-Methoxyphenyl)-4-methylisoquinoline (8d): the reaction was conducted at 0.1 mmol scale, 14.7 mg, 59% yield, unknown compound, white solid, R$_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 9.19 (s, 1H), 8.09–8.02 (m, 1H), 8.01–7.95 (m, 1H), 7.80–7.72 (m, 1H), 7.66–
7.59 (m, 1H), 7.57–7.48 (m, 2H), 7.06–6.99 (m, 2H), 3.88 (s, 3H), 2.67 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.4, 151.8, 150.3, 136.5, 134.0, 131.4, 130.6, 128.3, 127.3, 126.7, 123.9, 123.8, 113.8, 55.6, 15.9. HRMS (ESI-QEplus) $m/z$: [M+H]$^+$ Calcd for C$_{17}$H$_{16}$NO 250.1226; found 250.1220.

3-(2-Fluorophenyl)-4-methylisoquinoline (8e): the reaction was conducted at 0.1 mmol scale, 12.7 mg, 54% yield, unknown compound, white solid, $R_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.21 (s, 1H), 8.11–8.05 (m, 1H), 8.04–7.99 (m, 1H), 7.82–7.75 (m, 1H), 7.70–7.61 (m, 1H), 7.58–7.50 (m, 1H), 7.46–7.38 (m, 1H), 7.32–7.26 (m, 1H), 2.56 (d, $J$ = 2.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.7 (d, $J$ $^{13}$C-$^1$F = 245.5 Hz), 150.6, 146.7, 136.0, 132.2 (d, $J$ $^{13}$C-$^1$F = 3.4 Hz), 130.7, 130.0 (d, $J$ $^{13}$C-$^1$F = 8.4 Hz), 129.2 (d, $J$ $^{13}$C-$^1$F = 16.0 Hz), 128.3, 127.8, 127.2, 126.5, 124.5 (d, $J$ $^{13}$C-$^1$F = 3.6 Hz), 123.8, 115.8 (d, $J$ $^{13}$C-$^1$F = 22.4 Hz), 15.3 (d, $J$ $^{13}$C-$^1$F = 3.6 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -115.21. HRMS (ESI-QEplus) $m/z$: [M+H]$^+$ Calcd for C$_{16}$H$_{13}$FN 238.1027; found 238.1020.

4-Methyl-3-pentylisoquinoline (8f): the reaction was conducted at 0.1 mmol scale, 15.0 mg, 70% yield, unknown compound, colorless oil, $R_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.08 (s, 1H), 8.01–7.95 (m, 1H), 7.94–7.87 (m, 1H), 7.74–7.65 (m, 1H), 7.57–7.48 (m, 1H), 3.06–2.96 (m, 2H), 2.61 (s, 3H), 1.82–1.69 (m, 2H), 1.50–1.32 (m, 4H), 0.93 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 153.5, 150.1, 136.2, 130.2, 128.2, 127.1, 125.9, 123.5, 123.2, 36.2, 32.2, 29.9, 22.9, 14.3, 13.8. HRMS (ESI-QEplus) $m/z$: [M+H]$^+$ Calcd for C$_{15}$H$_{20}$N 214.1590; found 214.1584.

3-(2-(((Tert-butyldimethylsilyl)oxy)ethyl)-4-methylisoquinoline (8g): the reaction was conducted at 0.1 mmol scale, 10.3 mg, 34% yield, unknown compound, white liquid, $R_f$ = 0.25 (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.08 (s, 1H), 8.01–7.96 (m, 1H), 7.94–7.88 (m, 1H), 7.73–7.66 (m, 1H), 7.57–7.50 (m, 1H), 4.05 (t, $J$ = 6.9 Hz, 2H), 3.25 (t, $J$ = 6.9 Hz, 2H), 2.65 (s, 3H), 0.83 (s, 9H), -0.07 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.3, 150.2, 136.0, 132.2, 128.2, 127.2, 126.1, 125.0, 123.3, 63.5, 39.2, 26.1, 18.5, 14.1, -5.2. HRMS (ESI-QEplus) $m/z$: [M+H]$^+$ Calcd for C$_{18}$H$_{28}$NOSi 302.1935; found 302.1928.

10. Scale-up experiment for synthesis of 3ad and 6o

In the glovebox, a Schlenk tube was charged with 1ad (343.5 mg, 1.0 mmol), 2a (180.0 mg, 3.0 mmol), Pd(TFA)$_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 oC oil bath. After completion of
the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 3ad as white solid (350.0 mg, 98% yield).

![Chemical structure](image)

In the glovebox, a Schlenk tube was charged with 5o (380.0 mg, 2 mmol), 2a (360.0 mg, 6 mmol), Pd(TFA)2 (66.0 mg, 0.2 mmol), Xantphos (127.3 mg, 0.22 mmol), potassium phosphate (636.0 mg, 3 mmol), and 4Å MS (2000.0 mg) in the 1,4-dioxane (40.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound 6o as white solid (319.4 mg, 77% yield).

11. Further synthetic transformations of product 3ad

![Chemical structure](image)

Synthesis of (3-methyl-1-tosyl-1H-indol-2-yl)(phenyl)methanone 9: In a nitrogen-filled Schlenk tube, to a solution of the 3ad (35.7 mg, 0.1 mmol) and benzoyl chloride (15.5 mg, 1.1 mmol) in dichloromethane (2.0 mL) was added dropwise a solution of titanium tetrachloride in dichloromethane (3.0 M, 0.13 mL, 0.4 mmol) at 0 °C. The mixture was stirred for 0.5 h, the reaction was quenched by water, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 9 as white solid (22.2 mg, 57% yield), unknown compound, Rf = 0.25 (petroleum ether/ethyl acetate 30/1); 1H NMR (400 MHz, CDCl3) δ 8.14–8.06 (m, 1H), 7.96–7.88 (m, 2H), 7.74–7.67 (m, 2H), 7.62–7.56 (m, 1H), 7.52–7.40 (m, 4H), 7.34–7.28 (m, 1H), 7.19–7.13 (m, 2H), 2.31 (s, 3H), 2.18 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 189.8, 145.1, 138.6, 136.6, 134.0, 133.8, 133.6, 131.4, 129.8, 129.7, 128.8, 127.5, 126.9, 124.8, 124.5, 120.6, 115.5, 21.8, 9.6. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C23H19NNaO3S 412.0975; found 412.0971.

Synthesis of 2-bromo-3-methyl-1-tosyl-1H-indole 10: Under nitrogen atmosphere, the
mixture of 3ad (35.7 mg, 0.1 mmol) and N-bromosuccinimide (35.6 mg, 0.2 mmol) in dichloromethane (2.0 mL) was stirred for 2h in 40 °C oil bath. Then the reaction was cooled to room temperature and quenched by water, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 10 as white solid (24.4 mg, 67% yield), unknown compound, Rf = 0.25 (petroleum ether/ethyl acetate 30/1); 1H NMR (400 MHz, CDCl3) δ 8.31–8.24 (m, 1H), 7.77–7.70 (m, 2H), 7.41–7.36 (m, 1H), 7.35–7.29 (m, 1H), 7.29–7.22 (m, 1H), 7.22–7.15 (m, 2H), 2.34 (s, 3H), 2.16 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 145.2, 137.5, 135.5, 130.6, 129.9, 127.3, 125.2, 124.0, 121.9, 118.7, 115.7, 109.2, 21.8, 10.6. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C16H14BrNNaO2S 385.9821; found 385.9816.

Synthesis of 3-methyl-1-tosyl-1H-indole 11: Under nitrogen atmosphere, to a solution of the 3ad (35.7 mg, 0.1 mmol) in tetrahydrofuran (2.0 mL) was added dropwise a solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 0.3 mL, 0.3 mmol). The mixture was stirred for 12 h. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 11 as white solid (22.5 mg, 79% yield), known compound[27], white solid, Rf = 0.25 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 8.01–7.94 (m, 1H), 7.77–7.69 (m, 2H), 7.47–7.40 (m, 1H), 7.34–7.27 (m, 2H), 7.26–7.14 (m, 2H), 2.30 (s, 3H), 2.23 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 144.8, 135.6, 135.5, 132.0, 130.0, 126.9, 124.8, 123.3, 123.2, 119.6, 118.8, 113.9, 21.7, 9.9.

Synthesis of 1,3-dimethyl-1H-indole 12: Under nitrogen atmosphere, the mixture of 3ad (35.7 mg, 0.1 mmol) and potassium methoxide (14.0 mg, 0.2 mmol) in acetonitrile (2.0 mL) was stirred overnight. After completion of the reaction (monitored by TLC), the reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 12 as white solid (12.1 mg, 83% yield), known compound[27], white solid, Rf = 0.25 (petroleum ether/ethyl acetate 50/1); 1H NMR (400 MHz, CDCl3) δ 7.60–7.54 (m, 1H), 7.30–7.24 (m, 1H), 7.23–7.17 (m, 1H), 7.14–7.06 (m, 1H), 6.80 (s, 1H), 3.71 (s, 3H), 2.32 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 137.2, 128.8, 126.7, 121.6, 119.1, 118.7, 110.3, 109.2, 32.7, 9.7.
12. Synthesis of bioactive molecules and drugs

Synthesis of 2-(3,4-dimethoxyphenyl)-5-methoxy-3-methyl-1H-indole 3ai: In the glovebox, a Schlenk tube was charged with 1ai (438.0 mg, 1.0 mmol), 2a (180.0 mg, 3.0 mmol), Pd(TFA)$_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 3ai as white solid (375.0 mg, 83% yield), unknown compound, $R_f = 0.3$ (petroleum ether/ethyl acetate 10/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.24–8.18 (m, 1H), 7.29–7.24 (m, 2H), 7.07–7.01 (m, 2H), 7.00–6.95 (m, 1H), 6.94–6.89 (m, 1H), 6.89–6.82 (m, 3H), 3.96 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 2.30 (s, 3H), 2.01 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.1, 149.3, 148.0, 144.4, 137.7, 135.3, 133.2, 131.8, 129.3, 127.0, 124.0, 124.0, 119.7, 117.5, 115.1, 113.3, 110.0, 101.8, 56.1, 56.0, 55.8, 21.7, 9.9. HRMS (ESI-QEplus) $m/z$: [M+Na]$^+$ Calcd for C$_{25}$H$_{25}$NNaO$_5$S 474.1346; found 474.1344.

Synthesis of 2-(3,4-dimethoxyphenyl)-5-methoxy-3-methyl-1H-indole 13: Under nitrogen atmosphere, the mixture of 3ai (135.5 mg, 0.3 mmol) and potassium hydroxide (50.5 mg, 0.9 mmol) in ethanol (6.0 mL) was stirred overnight in 100 °C oil bath. The reaction was cooled to room temperature and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 13 as white solid (84.7 mg, 95% yield), known compound[28], $R_f = 0.3$ (petroleum ether/ethyl acetate 15/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 (s, 1H), 7.28–7.25 (m, 1H), 7.14–7.10 (m, 1H), 7.09–7.06 (m, 1H), 7.04–7.01 (m, 1H), 6.99–6.95 (m, 1H), 6.88–6.82 (m, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.89 (s, 3H), 2.42 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.3, 149.3, 148.7, 135.3, 131.0, 130.7, 130.7, 126.5, 120.5, 112.3, 111.6, 111.5, 112.2, 107.9, 100.9, 56.2, 9.9.

Synthesis of 4-(5-hydroxy-3-methyl-1H-indol-2-yl)benzene-1,2-diol 14: Under nitrogen atmosphere, to a solution of the 13 (29.7 mg, 0.1 mmol) in dichloromethane (2.0 mL) was added
dropwise a solution of boron tribromide in dichloromethane (1 M, 0.9 mL, 0.9 mmol) in 0 °C. The mixture was stirred for 1.5 h at room temperature. The reaction was quenched by water, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 14 as yellow solid (20.4 mg, 80% yield), known compound[28], \( R_f = 0.25 \) (petroleum ether/ethyl acetate 4/1); \(^1H\) NMR (400 MHz, CD₃OD) δ 7.17–7.14 (m, 1H), 7.09–7.08 (m, 1H), 6.98–6.95 (m, 1H), 6.90–6.85 (m, 2H), 6.66–6.64 (m, 1H), 2.35 (s, 3H). \(^13C\) NMR (100 MHz, CD₃OD) δ 150.4, 145.7, 145.1, 136.2, 131.7, 131.4, 126.6, 119.9, 115.9, 115.4, 111.4, 111.3, 105.6, 102.8, 9.4.

**Synthesis of 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1H-indole 3aj:** In the glovebox, a Schlenk tube was charged with 1aj (407.5 mg, 1.0 mmol), 2a (180.0 mg, 3.0 mmol), Pd(TFA)₂ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 3aj as white solid (384.0 mg, 91% yield), unknown compound, \( R_f = 0.3 \) (petroleum ether/ethyl acetate 50/1); \(^1H\) NMR (400 MHz, CDCl₃) δ 8.24–8.16 (m, 1H), 7.28–7.22 (m, 4H), 7.08–7.00 (m, 2H), 6.99–6.92 (m, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.29 (s, 3H), 2.00 (s, 3H). \(^13C\) NMR (100 MHz, CDCl₃) δ 159.9, 157.1, 144.4, 137.8, 135.1, 133.3, 132.8, 131.8, 129.3, 127.0, 124.0, 119.7, 117.6, 113.3, 113.1, 101.9, 55.9, 55.5, 21.7, 9.8. HRMS (ESI-QEplus) m/z: [M+Na]+ Calcd for C₂₄H₂₃NNaO₄S 444.1240; found 444.1235.

**Synthesis of 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1H-indole 15:** Under nitrogen atmosphere, the mixture of 3aj (380.0 mg, 0.9 mmol) and potassium hydroxide (151.5 mg, 2.7 mmol) in ethanol (20.0 mL) was stirred overnight in 100 °C oil bath. The reaction was cooled to room temperature and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 15 as white solid (235.8 mg, 98% yield), known compound[29], \( R_f = 0.3 \) (petroleum ether/ethyl acetate 15/1); \(^1H\) NMR (400 MHz, CDCl₃) δ 7.53–7.44 (m, 2H), 7.27–7.20 (m, 1H), 7.06–6.96 (m, 3H), 6.88–6.80 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 2.40 (s, 3H). \(^13C\) NMR (100 MHz, CDCl₃) δ 159.1, 154.2, 135.2, 131.0, 130.6, 129.1,
Synthesis of 1-(4-(2-(azepan-1-yl)ethoxy)benzyl)-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1H-indole 17: Under nitrogen atmosphere, the mixture of 15 (26.7 mg, 0.1 mmol) and potassium hydroxide (50.5 mg, 0.3 mmol) in N,N-dimethylformamide (3.0 mL) was stirred for 1h. Then the compound 16 (32.1 mg, 0.12 mmol) was added into the mixture. The reaction was stirred for 24 h and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate/triethylamine) to afford the desired compound 17 as yellow oil (47.7 mg, 96% yield), known compound\[10\], Rf = 0.25 (petroleum ether/ethyl acetate/triethylamine 10/1/1); 1H NMR (400 MHz, CDCl3) δ 7.27–7.20 (m, 2H), 7.09–7.03 (m, 2H), 6.96–6.90 (m, 2H), 6.87–6.83 (m, 2H), 6.82–6.78 (m, 1H), 6.78–6.71 (m, 2H), 5.11 (s, 2H), 4.00 (t, J = 6.2 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 3H), 2.91 (t, J = 6.2 Hz, 2H), 2.80–2.71 (m, 4H), 2.25 (s, 3H), 1.70–1.54 (m, 8H). 13C NMR (100 MHz, CDCl3) δ 159.5, 158.0, 154.2, 138.5, 132.1, 131.9, 131.0, 129.3, 127.4, 124.6, 114.8, 114.0, 111.8, 111.1, 108.5, 100.9, 66.4, 56.4, 56.2, 56.0, 55.5, 47.3, 27.8, 27.2, 9.7.

Synthesis of Bazedoxifene 18: Under nitrogen atmosphere, to a solution of the 17 (24.9 mg, 0.05 mmol) in chloroform (1.0 mL) was added dropwise a solution of boron tribromide in dichloromethane (1 M, 0.3 mL, 0.3 mmol) at -30 °C. The reaction was stirred for 16 h in at -10 °C. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (dichloromethane/methanol) to afford the desired compound 18 as yellow solid (8.0 mg, 34% yield), known compound\[30\], yellow solid, Rf = 0.25 (dichloromethane/methanol 10/1); 1H NMR (400 MHz, DMSO-d6) δ 7.16–7.11 (m, 2H), 7.07–7.02 (m, 1H), 6.91–6.86 (m, 2H), 6.82–6.79 (m, 1H), 6.77–6.71 (m, 4H), 6.60–6.56 (m, 1H), 5.10 (s, 2H), 3.92 (t, J = 6.2 Hz, 2H), 2.77 (t, J = 6.0 Hz, 2H), 2.67–2.60 (m, 4H), 2.10 (s, 3H), 1.58–1.45 (m, 8H). 13C NMR (100 MHz, DMSO-d6) δ 157.9, 157.8, 151.4, 138.5, 131.8, 131.8, 131.1, 131.1, 131.1, 127.8, 127.8, 115.9, 114.8, 111.2, 106.9, 103.0, 66.6, 56.5, 55.6, 28.3, 27.0, 9.9.
Synthesis of 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1H-indole 19: Under nitrogen atmosphere, the mixture of 15 (80.0 mg, 0.3 mmol) and sodium hydride (10.8 mg, 0.45 mmol) in N,N-dimethylformamide (3.0 mL) was stirred for 15 min. Then a solution of iodoethane in N,N-dimethylformamide was added into the mixture. The reaction was stirred overnight and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 19 as white solid (75.0 mg, 85% yield), known compound[31], R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^1^H NMR (400 MHz, CDCl_3) δ 7.39–7.31 (m, 2H), 7.31–7.24 (m, 1H), 7.11–7.01 (m, 3H), 6.97–6.87 (m, 1H), 4.05 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 2.24 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^1^C NMR (100 MHz, CDCl_3) δ 159.3, 153.9, 137.8, 131.7, 131.2, 128.9, 124.8, 113.9, 111.5, 110.2, 108.2, 100.8, 56.1, 55.4, 38.7, 15.5, 9.4.

Synthesis of Zindoxifene 20: Under nitrogen atmosphere, to a solution of the 19 (29.7 mg, 0.1 mmol) in dichloromethane (2.0 mL) was added dropwise a solution of boron tribromide in dichloromethane (1 M, 0.4 mL, 0.4 mmol) in -60 °C. After 30 min the cooling bath was removed and the mixture was stirred overnight. The reaction was quenched by an aqueous solution of sodium bicarbonate, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was used for next acetylation step without further purification.

Under nitrogen atmosphere, to a solution of the crude material in pyridine (1.0 mL) was added acetic anhydride (61.3 mg, 0.6 mmol). After refluxing in 110 °C oil bath for 2 h. The reaction was cooled to room temperature and quenched by aqueous dilute solution of hydrochloric acid, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 20 as white solid (32.3 mg, 92% yield), known compound[32], R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^1^H NMR (400 MHz, CDCl_3) δ 7.41–7.35 (m, 2H), 7.34–7.29 (m, 1H), 7.28–7.26 (m, 1H), 7.24–7.18 (m, 2H), 6.97–6.91 (m, 1H), 4.04 (q, J = 7.1 Hz, 2H), 2.34 (s, 3H), 2.33 (s, 3H), 2.18 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H). ^1^C NMR (100 MHz, CDCl_3) δ 170.8, 169.6, 150.6, 144.2, 137.8, 134.1, 131.7, 129.9, 129.0, 121.8, 115.8, 111.2, 110.1, 109.5, 39.0, 21.4, 15.6, 9.4.
Synthesis of 3-methylbenzofuran-2-carbaldehyde 21: Under nitrogen atmosphere, to a solution of the 6o (306.5 mg, 1.5 mmol) in tetrahydrofuran (2.0 mL) was added dropwise a solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 0.3 mL, 0.3 mmol). The reaction was stirred overnight and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was used for next acetylation step without further purification.

Under nitrogen atmosphere, to a solution of the crude material in tetrahydrofuran (10.0 mL) was added dropwise a solution of n-butyllithium (2.5 M, 0.4 mL, 1.6 mmol) in tetrahydrofuran at -78 °C. After 1 h the N,N-dimethylformamide (0.3 mL, 3.0 mmol) was added to the mixture and the reaction was stirred for 5h. The reaction was quenched by a saturated aqueous solution of ammonium chloride, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 21 as white solid (192.2 mg, 80% yield), known compound[33], R<sub>f</sub> = 0.25 (petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 10.04 (s, 1H), 7.73–7.68 (m, 1H), 7.58–7.49 (m, 2H), 7.38–7.31 (m, 1H), 2.64 (s, 3H).<br><br>13C NMR (100 MHz, CDCl<sub>3</sub>) δ 179.9, 155.6, 148.3, 129.6, 128.9, 123.8, 122.0, 112.8, 8.63.

Synthesis of N-methyl-1-(3-methylbenzofuran-2-yl)methanamine 22: Under nitrogen atmosphere, the reaction tube was charged with methylamine hydrochloride (20.3 mg, 0.3 mmol), potassium carbonate (20.7 mg, 0.15 mmol) and methanol (1 mL), and the reaction was stirred at 0 ºC for 30 min. Then the compound 21 (32.2 mg, 0.2 mmol) was added to mixture, and the reaction was stirred at r.t. for 1 h. The reaction was cooled to 0 ºC and sodium borohydride (11.4 mg, 0.3 mmol) was added. The reaction was stirred at room temperature for 4 h. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate/triethylamine) to afford the desired compound 22 as white solid (26.4 mg, 75% yield), unknown compound, R<sub>f</sub> = 0.2 (petroleum ether/ethyl acetate/triethylamine 20/1/1); <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 7.51–7.46 (m, 1H), 7.41–7.35 (m, 1H), 7.26–7.17 (m, 2H), 3.82 (s, 2H), 2.37 (s, 3H), 2.23 (s, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD) δ 155.0, 151.0, 130.4, 124.6, 122.7, 119.7, 113.3, 111.0, 34.7, 7.2. HRMS (ESI-QEplus) m/z: [M+H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>14</sub>NO 176.1070; found 176.1068.
13. Mechanism studies

In the glovebox, a Schlenk tube was charged with 4a (24.5 mg, 0.07 mmol), 2a (12.6 mg, 0.21 mmol), Pd(TFA)$_2$ (1.2 mg, 0.0035 mmol), Xantphos (2.2 mg, 0.00385 mmol), potassium phosphate (22.3 mg, 0.105 mmol), and 4Å MS (70.0 mg) in the tetrahydrofuran (1.4 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 5 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford 25.1 mg compound and confirmed as 4a by $^1$H NMR.

2-phenyl-1-tosyl-1H-indole 4a: known compound$^{[34]}$, white solid, $R_f = 0.2$ (petroleum ether/ethyl acetate 50/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35–8.28 (m, 1H), 7.54–7.47 (m, 2H), 7.47–7.39 (m, 4H), 7.39–7.32 (m, 1H), 7.31–7.22 (m, 3H), 7.08–6.99 (m, 2H), 6.54 (s, 1H), 2.28 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.7, 142.3, 138.5, 134.9, 132.6, 130.8, 130.6, 129.4, 128.9, 127.7, 127.0, 125.0, 124.5, 120.9, 116.9, 113.8, 21.7.

Preparation of (Xantphos)Pd(TFA)$_2$: In the glovebox, the reaction tube was charged with Pd(CH$_3$CN)$_2$Cl$_2$ (31.1 mg, 0.12 mmol), Xantphos (69.4 mg, 0.12 mmol) and dichloromethane (4.0 mL). Then the mixture was stirred in room temperature for 3 h. Filtration through Celite yielded a clear yellow solution, which was concentrated under reduced pressure. Then ethyl ether was added,
and the solution was cooled at -35 °C for 12 h. The resulting yellow crystals were washed two times with ethyl ether and dried in vacuo. Under nitrogen atmosphere, the reaction tube was charged with the resulting yellow crystals, silver trifluoroacetate (106.0 mg, 0.48 mmol), dichloromethane (5.0 mL) and acetonitrile (0.5 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear green solution, which was concentrated under reduced pressure. The resulting green crystals were washed two times with ethyl ether and dried in vacuo to afford \( \text{24} \) as yellow solid (79.0 mg, 75% yield), unknown compound, yellow solid; \( \text{\textsuperscript{1}H NMR (400 MHz, CD}_{2}\text{Cl}_{2}) \delta 7.69–7.60 \text{ (m, 2H), 7.40–7.25 \text{ (m, 12H), 7.20–7.13 \text{ (m, 8H), 7.11–7.06 \text{ (m, 2H), 6.56–6.45 \text{ (m, 2H), 1.67 (s, 6H). \text{\textsuperscript{13}C NMR (100 MHz, CD}_{2}\text{Cl}_{2}) \delta 155.3, 155.3, 135.4, 135.4, 133.9, 133.8, 132.0, 132.0, 131.2, 131.2, 129.1, 128.5, 128.4, 125.8, 125.3, 125.3, 125.2, 117.2, 116.7, 36.8, 26.8. \text{\textsuperscript{19}F NMR (376 MHz, CD}_{2}\text{Cl}_{2}) \delta -74.80. \text{\textsuperscript{31}P NMR (161 MHz, CD}_{2}\text{Cl}_{2}) \delta 8.81. HRMS (ESI-QEplus) m/z: \text{[M-2TFA]}^{2+} \text{Calcd for C}_{39}\text{H}_{32}\text{OP}_{2}\text{Pd 342.0476; found 342.0472.}} \)

The reaction was conducted at 0.02 mmol scale using 1.0 equiv. (Xantphos)Pd(TFA)_2 24:
In the glovebox, a Schlenk tube was charged with \( \text{1a} \) (6.9 mg, 0.02 mmol), \( \text{2a} \) (3.6 mg, 0.06 mmol), \( \text{24} \) (17.6 mg, 0.02 mmol), potassium phosphate (6.4 mg, 0.03 mmol), 4Å MS (20.0 mg) and tetrahydrofuran (0.5 mL). Then the Schlenk tube was removed from glovebox and the mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound \( \text{3a} \) (7.1 mg, 98% yield).

The reaction was conducted at 0.1 mmol scale using 0.1 equiv. (Xantphos)Pd(TFA)_2 24:
In the glovebox, a Schlenk tube was charged with \( \text{1a} \) (34.7 mg, 0.1 mmol), \( \text{2a} \) (18.0 mg, 0.3 mmol), \( \text{24} \) (8.8 mg, 0.01 mmol), potassium phosphate (31.8 mg, 0.15 mmol), 4Å MS (100.0 mg) and tetrahydrofuran (2.0 mL). Then the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound \( \text{3a} \) (31.6 mg, 88% yield).

\[
\text{\textsuperscript{1}H NMR (400 MHz, CD}_{2}\text{Cl}_{2}) \delta 7.69–7.60 \text{ (m, 2H), 7.40–7.25 \text{ (m, 12H), 7.20–7.13 \text{ (m, 8H), 7.11–7.06 \text{ (m, 2H), 6.56–6.45 \text{ (m, 2H), 1.67 (s, 6H). \text{\textsuperscript{13}C NMR (100 MHz, CD}_{2}\text{Cl}_{2}) \delta 155.3, 155.3, 135.4, 135.4, 133.9, 133.8, 132.0, 132.0, 131.2, 131.2, 129.1, 128.5, 128.4, 125.8, 125.3, 125.3, 125.2, 117.2, 116.7, 36.8, 26.8. \text{\textsuperscript{19}F NMR (376 MHz, CD}_{2}\text{Cl}_{2}) \delta -74.80. \text{\textsuperscript{31}P NMR (161 MHz, CD}_{2}\text{Cl}_{2}) \delta 8.81. HRMS (ESI-QEplus) m/z: \text{[M-2TFA]}^{2+} \text{Calcd for C}_{39}\text{H}_{32}\text{OP}_{2}\text{Pd 342.0476; found 342.0472.}} \]

In the glovebox, a Schlenk tube was charged with \( \text{1a} \) (34.7 mg, 0.1 mmol), Pd(TFA)_2 (1.7 mg, 0.005 mmol), Xanthos (3.2 mg, 0.0055 mmol), potassium phosphate (31.8 mg, 0.15 mmol), 4Å MS (100.0 mg) and tetrahydrofuran (2.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was analyzed by \( \text{\textsuperscript{1}H NMR using 1,3,5-trimethoxybenzene as internal standard and yield of 4a is 6%}. \)
Preparation of (Xantphos)PdMeCl·25: In the glovebox, the reaction tube was charged with (cod)PdMeCl (88.0 mg, 0.29 mmol), Xantphos (167.8 mg, 0.29 mmol) and dichloromethane (7.0 mL). Then the mixture was stirred in room temperature for 3 h. Filtration through Celite yielded a clear yellow solution, which was concentrated under reduced pressure. Then pentane was added, and the solution was cooled at -35 °C for 12 h. The resulting yellow crystals were washed twice with pentane and dried in vacuo to afford 25 as green solid, known compound[33]; ¹H NMR (400 MHz, CD₂Cl₂) δ 7.58–7.52 (m, 2H), 7.48–7.34 (m, 8H), 7.26–7.13 (m, 12H), 7.12–7.07 (m, 2H), 7.06–7.01 (m, 2H), 1.67 (s, 6H), 0.30 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂) δ 155.3, 155.2, 155.2, 134.8, 134.8, 134.8, 134.5, 134.4, 134.4, 131.8, 131.6, 131.4, 131.0, 129.8, 128.2, 128.2, 128.1, 127.0, 124.4, 124.4, 36.3, 27.6, 0.8. ³¹P NMR (162 MHz, CD₂Cl₂) δ 15.21. HRMS (ESI-QEplus) m/z: [M-Cl]+ Calcd for C₄₀H₃₅OP₂Pd+ 699.1192; found 699.1197.

The reaction was conducted at 0.02 mmol scale using 1.5 equiv. (Xantphos)PdMeCl·25: Under nitrogen atmosphere, the reaction tube was charged with 25 (22.1 mg, 0.03 mmol), silver trifluoroacetate (6.6 mg, 0.03 mmol), dichloromethane (1.0 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear brown solution, which was concentrated under reduced pressure. The resulting solid is dissolved in tetrahydrofuran (1.0 mL), then 1a (6.9 mg, 0.02 mmol), potassium phosphate (6.4 mg, 0.03 mmol) and 4Å MS (20.0 mg) was added into the system. The mixture was stirred in 50 ºC oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 3a (5.9 mg, 82% yield) and 4a (0.3 mg, 4% yield).

The reaction was conducted at 0.1 mmol scale using 0.15 equiv. (Xantphos)PdMeCl·25: Under nitrogen atmosphere, the reaction tube was charged with 25 (11.0 mg, 0.015 mmol), silver trifluoroacetate (3.4 mg, 0.015 mmol), dichloromethane (1.0 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear brown solution, which was concentrated under reduced pressure. The resulting solid is dissolved in tetrahydrofuran (2.0 mL), then 1a (34.7 mg, 0.1 mmol), potassium phosphate (31.8 mg, 0.15 mmol) and 4Å MS (100.0 mg)
was added into the system. Then the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound 3a (4.9 mg, 14% yield) and 4a (14.2 mg, 41% yield).

**Determination of intermediate 25-TFA**: In the glovebox, a seal tube was charged with 2a (6.0 mg, 0.1 mmol), Pd(TFA)₂ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (21.2 mg, 0.1 mmol), and 4Å MS (100.0 mg) in the tetrahydrofuran (2.0 mL). Then the seal tube was removed from glovebox and oscillated several times. The mixture was filtered and diluted with methanol, analyzed by HRMS immediately. HRMS (ESI-QEplus) m/z: [M-X]⁺ Calcd for C₄₀H₃₅OP₂Pd⁺ 699.1192; found 699.1209.

**Determination of intermediate 26**: In the glovebox, a seal tube was charged with 1a (34.7 mg, 0.1 mmol), 2a (18.0 mg, 0.3 mmol), Pd(TFA)₂ (3.3 mg, 0.01 mmol), Xantphos (6.4 mg, 0.011 mmol), potassium phosphate (31.8 mg, 0.15 mmol), and 4Å MS (100.0 mg) in the tetrahydrofuran (2.0 mL). Then the seal tube was removed from glovebox and oscillated several times. The
mixture was filtered and diluted with methanol, analyzed by HRMS immediately. HRMS (ESI-QEplus) m/z: [M+H]^+ Calcd for C_{61}H_{52}NO_3P_2PdS 1046.2172; found 1046.1764.

Fig. S2 HRMS analysis of intermediate 26
14. Kinetic studies

14.1 Kinetic order of catalyst

In the glovebox, a Schlenk tube was charged with 1a (104.0 mg, 0.3 mmol), 2a (53.9 mg, 0.9 mmol), trimethoxybenzene (50.5 mg, 0.3 mmol), Pd(TFA)$_2$, Xantphos, potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath and analyzed by $^1$H NMR along time. The experimental details and results were shown in the tables below.

Table S10: The amount of materials used for kinetic order test of catalyst

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<th>Entry</th>
<th>Pd</th>
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<th>2a</th>
<th>K$_3$PO$_4$</th>
<th>Trimethoxybenzene</th>
<th>THF</th>
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</thead>
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<tr>
<td></td>
<td>mg</td>
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<td>mg</td>
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<tr>
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<td>95.5</td>
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<td>6</td>
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<td>2</td>
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<td>104</td>
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<td>95.5</td>
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<tr>
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<td>50.5</td>
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Table S11: Concentration of 3a over time with reactions performed with varying concentration of catalyst

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<th>Time/min</th>
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<th>12</th>
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<td>3 mol%</td>
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<td>3a/M</td>
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<td>4 mol%</td>
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<td>3a/M</td>
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<td>6 mol%</td>
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Fig. S3 Plot of concentration of 3a over time with reactions performed with varying concentration of catalyst

Table S12: Relationship between initial rate and concentration of catalyst

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<th>Cat/M</th>
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<td>Initial rate/M·min⁻¹</td>
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<td>-Ln(cat)</td>
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<td>-Ln(v)</td>
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Fig. S4 Plot of \(-\ln(v)\) vs. \(-\ln(cat)\) for reaction

\[ y = 1.2977x - 0.8252, \ R^2 = 0.9963 \]
14.2 Kinetic order of 1a

In the glovebox, a Schlenk tube was charged with 1a, 2a (53.9 mg, 0.9 mmol), trimethoxybenzene (50.5 mg, 0.3 mmol), Pd(TFA)$_2$ (4.0 mg, 0.012 mmol), Xantphos (7.6 mg, 0.013 mmol), potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath and analyzed by $^1$H NMR along time. The detailed amount of each substrate was shown in the table below.

Table S13: The amount of materials used for kinetic order test of 1a

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<th>Entry</th>
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<th>1a (mg)</th>
<th>2a (mg)</th>
<th>K$_3$PO$_4$ (mg)</th>
<th>Trimethoxybenzene (mg)</th>
<th>THF (mL)</th>
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Table S14: Concentration of 3a over time with reactions performed with varying concentration of 1a

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Fig. S5 Plot of concentration of 3a over time with reactions performed with varying concentration of 1a

Table S15: Relationship between initial rate and concentration of 1a

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<tr>
<th>1a/M</th>
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</table>

| -Ln(1a) | 3.17725 | 2.99573 | 2.84215 | 2.69267 |
| -Ln(v)  | 7.25873 | 7.25166 | 7.25731 | 7.25307 |

kinetic study with 1a

\[ y = 0.0074x + 7.2335, \ R^2 = 0.2094 \]

Fig. S6 Plot of -ln(v) vs. -ln(1a) for reaction
14.3 Kinetic order of 2a

In the glovebox, a Schlenk tube was charged with 1a (104.0 mg, 0.3 mmol), 2a, trimethoxybenzene (50.5 mg, 0.3 mmol), Pd(TFA)$_2$ (4.0 mg, 0.012 mmol), Xantphos (7.6 mg, 0.013 mmol), potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath and analyzed by $^1$H NMR along time. The detailed amount of each substrate was shown in the table below.

Table S16: The amount of materials used for kinetic order test of 2a

<table>
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<tr>
<th>Entry</th>
<th>Pd</th>
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<th>2a</th>
<th>K$_3$PO$_4$</th>
<th>Trimethoxybenzene</th>
<th>THF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>7.6</td>
<td>104</td>
<td>35.9</td>
<td>95.5</td>
<td>50.5</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>7.6</td>
<td>104</td>
<td>53.9</td>
<td>95.5</td>
<td>50.5</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>7.6</td>
<td>104</td>
<td>71.8</td>
<td>95.5</td>
<td>50.5</td>
<td>6</td>
</tr>
</tbody>
</table>

Table S17: Concentration of 3a over time with reactions performed with varying concentration of 2a

<table>
<thead>
<tr>
<th></th>
<th>Time/min</th>
<th>2</th>
<th>5</th>
<th>7</th>
<th>10</th>
<th>12</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 M 2a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a/M</td>
<td></td>
<td>0.00238</td>
<td>0.00358</td>
<td>0.005665</td>
<td>0.007095</td>
<td>0.00906</td>
<td>0.010955</td>
</tr>
<tr>
<td>0.15 M 2a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a/M</td>
<td></td>
<td>0.002065</td>
<td>0.0045</td>
<td>0.006225</td>
<td>0.00804</td>
<td>0.00984</td>
<td></td>
</tr>
<tr>
<td>0.2 M 2a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a/M</td>
<td></td>
<td>0.002185</td>
<td>0.00317</td>
<td>0.005285</td>
<td>0.0066</td>
<td>0.00926</td>
<td></td>
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</table>
**Fig. S7** Plot of concentration of 3a over time with reactions performed with varying concentration of 2a

**Table S18**: Relationship between initial rate and concentration of 2a

<table>
<thead>
<tr>
<th>2a/M</th>
<th>0.1</th>
<th>0.15</th>
<th>0.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial rate/M·min⁻¹</td>
<td>0.000709</td>
<td>0.000706</td>
<td>0.000706</td>
</tr>
</tbody>
</table>

| -Ln(2a) | 2.302585093 | 1.897119985 | 1.609437912 |
| -Ln(v)  | 7.251655031  | 7.25589532  | 7.25589532  |

**kinetic study with 2a**

\[ y = -0.0064x + 7.2669, \quad R^2 = 0.8294 \]

**Fig. S8** Plot of -ln(v) vs. -ln(2a) for reaction
15. References

27. Hodnik, Ž.; Peterlin Mašič, L.; Tomasić, T.; Smodiš, D.; D’Amore, C.; Fiorucci, S.; Kikelj,


16. Copy of NMR for compounds

**1h**

$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$\text{NH}$

$\text{Ts}$

$\text{F}$

$\text{1i}$

$^1\text{H NMR (400 MHz CDCl}_3\text{)}$

---

$\text{Cl}$

$\text{NH}$

$\text{Ts}$

$\text{F}$

$\text{1i}$

$^{13}\text{C NMR (100 MHz CDCl}_3\text{)}$
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
1H NMR (376 MHz CDCl₃)

1k
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)

1r

1r

NH

NO$_2$

NH

NO$_2$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{13}C$ NMR (100 MHz CDCl$_3$)

$^1$H NMR (400 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
$\text{H NMR (400 MHz CDCl}_3\text{)}$

$\text{\textbf{1ai}}$

$\text{\textbf{13C NMR (100 MHz CDCl}_3\text{)}}$

$\text{\textbf{1ai}}$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
**5g**

$^1$H NMR (400 MHz CDCl$_3$)

F

**5g**

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{H NMR (400 MHz CDCl}_3\text{)}$

$\text{C NMR (100 MHz CDCl}_3\text{)}$
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_{3}$)

$^{13}C$ NMR (100 MHz CDCl$_{3}$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)  

- 0.09 s
- 0.80 t

C$_5$H$_{11}$N$_t$Bu

$^13$C NMR (100 MHz CDCl$_3$)  

- 99.36
- 78.14
- 77.56
- 77.33
- 76.92

C$_5$H$_{11}$N$_t$Bu

$^1$C NMR (100 MHz CDCl$_3$)  

- 154.81
- 137.82
- 132.39
- 128.81
- 128.64
- 128.59
- 126.02

$^1$H NMR (400 MHz CDCl$_3$)  

- 8.5669
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^1$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^13$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)

![Chemical Structure]

$3h$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

3k

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (376 MHz CDCl$_3$)

3k

$^1$F NMR (376 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

3l

$^{13}C$ NMR (100 MHz CDCl$_3$)

3l
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{Me}$

$\text{Ts}$

$\text{3o}$

$^{19}\text{F NMR (376 MHz CDCl}_3\text{)}$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
\(^1\)H NMR (400 MHz CDCl₃)

\(^{13}\)C NMR (100 MHz CDCl₃)
$\text{Me}$

$\text{Ts}$

$\text{NO}_2$

$\text{3r}$

$^1\text{H NMR (400 MHz CDCl}_3)$

$\text{Me}$

$\text{Ts}$

$\text{NO}_2$

$\text{3r}$

$^{13}\text{C NMR (100 MHz CDCl}_3)$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{Me}$

$\text{Cl}$

$\text{Ts}$

$\text{3t}$

$^1\text{H NMR (400 MHz CDCl}_3\text{)}$

$\text{Me}$

$\text{Cl}$

$\text{Ts}$

$\text{3t}$

$^{13}\text{C NMR (100 MHz CDCl}_3\text{)}$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)

3v

Me F

Ts

N

Me

Ts

F
$^{19}$F NMR (376 MHz CDCl$_3$)

3v

Me F

Ts

Ts
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^13$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
3ae

$^1$H NMR (400 MHz CDCl$_3$)

3ae

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
**S125**

3ag

$^1$H NMR (400 MHz CDCl$_3$)

![NMR Spectrogram](image_1)

3ag

$^{13}$C NMR (100 MHz CDCl$_3$)

![NMR Spectrogram](image_2)
3ah

$^1$H NMR (400 MHz CDCl$_3$)

3ah

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{H NMR (400 MHz CDCl}_3$)

F

Me

Ph

6b

$\text{C NMR (100 MHz CDCl}_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{H NMR (400 MHz CDCl}_3\text{)}$

$\text{^13C NMR (100 MHz CDCl}_3\text{)}$
$\text{MeO}$

6e

$^1\text{H NMR (400 MHz CDCl}_3\text{)}$

\[
\begin{array}{c}
\text{MeO} \\
\text{Me} \\
\text{Ph}
\end{array}
\]

6e

$^{13}\text{C NMR (100 MHz CDCl}_3\text{)}$

\[
\begin{array}{c}
\text{MeO} \\
\text{Me} \\
\text{Ph}
\end{array}
\]
$\text{H NMR (400 MHz CDCl}_3\text{)}$

$\text{C NMR (100 MHz CDCl}_3\text{)}$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
\[ \text{Me} \quad 6i \]

$^{1}H$ NMR (400 MHz CDCl$_3$)

\[ \text{Me} \quad \text{Ph} \]

\[ \text{Me} \quad 6i \]

$^{13}C$ NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^1$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^6$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
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$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$\text{H NMR (400 MHz CDCl}_3\text{)}$
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^1$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

8d

$^{13}$C NMR (100 MHz CDCl$_3$)

8d
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{19}$F NMR (376 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
**1H NMR (400 MHz CDCl₃)**

![NMR Spectrogram](image)

**13C NMR (100 MHz CDCl₃)**

![NMR Spectrogram](image)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
**$^1$H NMR (400 MHz CDCl$_3$)**

![H NMR spectrum of compound 13](image1)

**$^{13}$C NMR (100 MHz CDCl$_3$)**

![C NMR spectrum of compound 13](image2)
**H NMR (400 MHz CD$_3$OD)**

**C NMR (100 MHz CD$_3$OD)**
$^1$H NMR (400 MHz CDCl$_3$)

$^{13}$C NMR (100 MHz CDCl$_3$)
**1H NMR (400 MHz CDCl₃)**

![1H NMR Spectrum](image)

**13C NMR (100 MHz CDCl₃)**

![13C NMR Spectrum](image)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
18: Bazedoxifene

$^1$H NMR (400 MHz DMSO-$d_6$)

18: Bazedoxifene

$^{13}$C NMR (100 MHz DMSO-$d_6$)
1H NMR (400 MHz CDCl₃)

13C NMR (100 MHz CDCl₃)
20: Zindoxifene

$^1$H NMR (400 MHz CDCl$_3$)

20: Zindoxifene

$^{13}$C NMR (100 MHz CDCl$_3$)
$^{1}H$ NMR (400 MHz CDCl$_3$)

$^{13}C$ NMR (100 MHz CDCl$_3$)
**H NMR (400 MHz CD$_3$OD)**

**C NMR (100 MHz CD$_3$OD)**
**1H NMR (400 MHz CDCl₃)**

**13C NMR (100 MHz CDCl₃)**
2,2'-diphenyl-1,1'-ditosyl-1H,1'H-3,3'-biindole

$^1$H NMR (400 MHz CDCl$_3$)

2,2'-diphenyl-1,1'-ditosyl-1H,1'H-3,3'-biindole

$^{13}$C NMR (100 MHz CDCl$_3$)
\[ \text{H NMR (400 MHz CD}_2\text{Cl}_2) \]

\[ \text{C NMR (100 MHz CD}_2\text{Cl}_2) \]
$^{19}$F NMR (376 MHz CD$_2$Cl$_2$)

$^{31}$P NMR (162 MHz CD$_2$Cl$_2$)
**1H NMR (400 MHz CD$_2$Cl$_2$)**

![1H NMR spectrum](image1)

**13C NMR (100 MHz CD$_2$Cl$_2$)**

![13C NMR spectrum](image2)
$^{31}$P NMR (162 MHz CD$_2$Cl$_2$)