Copper-catalyzed decarboxylative cyclization via tandem C–P and C–N bond formation: access to 2-phosphorylmethyl indoles

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1. General Information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Flash column chromatography was performed using 200-300 mesh silica gel. $^1$H NMR spectra were recorded on 400 MHz spectrophotometers. Chemical shifts are reported in delta ($\delta$) units in parts per million (ppm) relative to the singlet (0 ppm) for tetramethylsilane (TMS). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constants (Hz) and integration. $^{13}$C NMR spectra were recorded on Varian Mercury 100 MHz with complete proton decoupling spectrophotometers (CDCl$_3$: 77.0 ppm). $^{31}$P NMR spectra were recorded on Varian Mercury 162 MHz spectrophotometers. HRMS was recorded on Bruker ultrafleXtreme MALDITOF/TOF mass spectrometer.

2. Preparation and Spectral Data of Substrates

2.1 General procedure for the preparation of substrates 1l-t and 2f-j.

Substrates(1l-t and 2f-j) were prepared according to the reported procedures$^{[1,2,3]}$. Ligands were synthesized according to the literature$^{[4]}$ or commercially available.

**Synthesis of substrate 1t**

![Chemical structure diagram]

**Procedure:** Under argon atmosphere, an oven dried 250 mL three-necked flask, equipped with a magnetic stirring bar, was charged with trimethylsilylacetylene (3.1 mL, 22 mmol) and anhydrous THF (100 mL). To this solution was added $n$-BuLi (8.8 mL, 2.5 M in hexane, 22 mmol) dropwise over 15 min at 0 °C, stirring for 30 min. Then the solution was cooled to -94 °C (liquid N$_2$/Acetone bath), and the $N$-(2-acetylphenyl)-4-methylbenzenesulfonamide$^{[5]}$ (2.89 g, 10 mmol) was added. The reaction was stirred for 0.5 h at the same temperature. After this interval, a solution of triphosgen (2.96 g, 10 mmol) in anhydrous THF (50 mL) was added dropwise over a period
of 0.5 h. The yellow solution was maintained at -94 °C for 1 h, and the reaction was then carefully quenched by dropwise addition of H2O over a period of 15 min. The resulting yellow solution was allowed to warm to room temperature. The organic phase was separated, and aqueous phases were extracted with EtOAc (50 mL×3). The combined organic layers were washed with brine, dried over Na2SO4, filtered and concentrated. The crude product was used directly without further purification.

The trimethylsilanylethynyl-benzoxazinanone from previous step was charged into a dry 100 mL flask along with anhydrous THF (50 mL). The flask was then cooled to -94 °C and TBAF (10.0 mL, 10.0 mmol, 1.0 M solution in THF) was added dropwise. The resulting solution was stirred for 5 min at -94 °C (liquid N2/Acetone bath). The reaction was quenched with H2O. The resulting red solution was allowed to warm to room temperature. The organic phase was separated, and aqueous phases were extracted with EtOAc (30 mL×3). The combined organic layers were washed with brine, dried over Na2SO4, filtered, and concentrated. The residue was purified by flash silica gel chromatography (PE/EtOAc/DCM = 20:1:1) to give the product as white solid (2.21 g, 65% yield over two steps).

References
2.2 Spectral data of the substrate 1t

4-Ethynyl-4-methyl-1-tosyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one (1t)

Yield of 1t: 65% as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.14 (d, $J$ = 1.8 Hz, 1H), 8.12 (d, $J$ = 1.8 Hz, 1H), 7.66 (dd, $J$ = 8.3 Hz, 1.0 Hz, 1H), 7.45 (m, 1H), 7.42 - 7.38 (m, 2H), 7.37 (s, 1H), 7.30 (m, 1H), 2.69 (s, 1H), 2.46 (s, 3H), 2.00 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 148.4, 145.8, 135.4, 133.4, 129.6, 129.5, 129.5, 129.3, 126.3, 123.4, 121.2, 81.0, 76.1, 75.5, 26.2, 21.8. M.P.: 164 – 166 $^\circ$C. HRMS (ESI) for C$_{18}$H$_{15}$NO$_4$S [M + Na]$^+$: calcd 364.0614, found 364.0609.

3. Optimization of the Reaction Conditions

3.1 The effect of solvent, base and the loading of base $^a$

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$^a$ Reaction Conditions: 1a (0.2 mmol), 2a (0.5 mmol), CuI (5 mol%) in 2 mL of solvent at rt for 1h. $^b$ Isolated yields. $^c$ a trace of 3a’ (<10% yield) was determined by $^1$H NMR. MTBE: methyl tert-butyl ether.
3.2 The effect of Ligand, copper and the loading of 2a

\[
\text{Copper, 6 mol\% Ligand, 2a (equiv.) Yield (3a %)}^{a}
\]

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\(^{a}\) Reaction Conditions: 1a (0.2 mmol), 2a (x mmol), Copper salt (5 mol\%), Ligand (6 mol\%), \(\text{PrRNEt (2.0 equiv.)}\) in 2 mL of MeOH at rt for 1h. \(^{b}\) Isolated yields.

4. General Procedure and Spectral Data of the Products

4.1 General procedure for the synthesis of 3

**Procedure:** Under argon atmosphere, a flame-dried 10 mL Schlenk tube was charged with CuI (0.01 mmol, 5 mol\%), pybox (0.012 mmol, 6 mol\%) and anhydrous MeOH (2 mL). The resulting solution was stirred for 5 min at room temperature. Then, \(\text{PrRNEt (0.4 mmol, 2.0 equiv.)}\) and 2 (0.4 mmol, 2.0 equiv.) were added, the resulting solution was stirred for 10 min at rt. Then ethynyl benzoazinanone 1 (0.2 mmol, 1.0 equiv.) was added. The resulting solution was stirred until complete conversion of ethynyl benzoazinanones (monitored by TLC). The product was purified by flash column chromatography on silica gel (petrol ether/EtOAc = 5/1 to 1/1) to give product 3.
4.2 Spectral data of the desired products 3a-3t and 3a’

Dimethyl ((1-tosyl-1H-indol-2-yl)methyl)phosphonate (3a)

Yield of 3a: 96% as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.13 – 8.07 (m, 1H), 7.66 – 7.60 (m, 2H), 7.47 – 7.41 (m, 1H), 7.29 (d, $J = 7.6$ Hz, 1H), 7.23 (dd, $J = 7.5$ Hz, 1.1 Hz, 1H), 7.20 (s, 1H), 7.17 (s, 1H), 6.84 – 6.78 (m, 1H), 3.82 (d, $J = 1.0$ Hz, 1H), 3.78 (s, 3H), 3.77 (d, $J = 1.0$ Hz, 1H), 3.76 (s, 3H), 2.33 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 144.8, 136.7, 135.2, 130.5 (d, $J = 4.0$ Hz), 129.7, 129.3 (d, $J = 1.0$ Hz), 126.2, 124.3, 123.6, 120.5, 114.8, 112.4 (d, $J = 5.0$ Hz), 52.9 (d, $J = 5.0$ Hz), 25.1 (d, $J = 94.0$ Hz), 21.3. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ = 26.40. HRMS (ESI) for C$_{18}$H$_{20}$NO$_5$PS [M + H]$^+$: calcd 394.0873, found 394.0866.

Diethyl ((1-tosyl-1H-indol-2-yl)methyl)phosphonate (3b)

Yield of 3b: 84% as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.11 (d, $J = 8.3$ Hz, 1H), 7.63 (d, $J = 8.1$ Hz, 2H), 7.43 (d, $J = 7.6$ Hz, 1H), 7.30 – 7.24 (m, 1H), 7.21 (d, $J = 7.5$ Hz, 1H), 7.18 (s, 1H), 7.16 (s, 1H), 6.83 (d, $J = 3.6$ Hz, 1H), 4.13 (m, 4H), 3.80 (s, 1H), 3.75 (s, 1H), 2.31 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 144.9, 136.9, 135.5, 131.0 (d, $J = 5.0$ Hz), 129.8, 129.5 (d, $J = 3.0$ Hz), 126.3, 124.4, 123.7, 120.6, 114.9, 112.4 (d, $J = 6.0$ Hz), 62.4 (d, $J = 6.0$ Hz), 26.0 (d, $J = 142.0$ Hz), 21.4, 16.3 (d, $J = 5.0$ Hz). $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ = 23.82. HRMS (ESI) for C$_{20}$H$_{24}$NO$_5$PS [M + Na]$^+$: calcd 444.1005, found 444.0998.

Dibutyl ((1-tosyl-1H-indol-2-yl)methyl)phosphonate (3c)

Yield of 3c: 65% as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.11 (d, $J = 8.3$ Hz, 1H), 7.62 (d, $J = 7.9$ Hz, 2H), 7.43 (d, $J = 7.7$ Hz, 1H), 7.27 (t, $J = 4.4$ Hz, 1H), 7.22 (d, $J = 7.5$ Hz, 1H), 7.18 (s, 1H), 7.16 (s, 1H), 6.83 (t, $J = 2.4$ Hz, 1H), 4.07 (dd, $J = 6.9$ Hz, 1.7 Hz, 2H), 4.03 (dd, $J = 6.9$ Hz, 1.8 Hz, 2H), 3.79 (s, 1H), 3.74 (s, 1H), 2.32 (d, $J = 1.9$ Hz, 3H), 1.61 (m, 4H), 1.35 (m, 4H), 0.89 (m, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 145.0, 137.0, 135.6, 131.1, 129.9, 129.7, 126.4, 124.5, 123.8, 120.7, 115.0, 112.6 (d, $J = 7.0$ Hz), 66.2 (d, $J = 7.0$ Hz), 32.5 (d, $J = 7.0$ Hz), 26.0 (d, $J = 142.0$ Hz), 21.6, 18.7, 13.6. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ = 23.87. HRMS (ESI) for C$_{24}$H$_{32}$NO$_5$PS [M + Na]$^+$: calcd 500.1631, found 500.1627.

Diphenyl ((1-tosyl-1H-indol-2-yl)methyl)phosphonate (3d)
Yield of 3d: 93% as a yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ = 8.12 (d, J = 8.3 Hz, 1H), 7.62 (s, 1H), 7.61 – 7.59 (m, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.29 (s, 1H), 7.27 (s, 2H), 7.24 (d, J = 6.9 Hz, 2H), 7.21 (d, J = 7.4 Hz, 1H), 7.17 – 7.13 (m, 4H), 7.13 – 7.09 (m, 4H), 6.97 (d, J = 3.5 Hz, 1H), 4.15 (s, 1H), 4.10 (s, 1H), 2.27 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 150.3 (d, J = 9.0 Hz), 145.1, 137.1, 135.6, 129.9, 129.8, 129.7 (d, J = 4.0 Hz), 129.5 (d, J = 3.0 Hz), 126.4, 125.4, 124.8, 123.9, 120.9, 120.6 (d, J = 5.0 Hz), 115.1, 113.1 (d, J = 6.0 Hz), 26.4 (d, J = 144.0 Hz), 21.6. **³¹P NMR** (162 MHz, CDCl₃) δ = 16.93. **HRMS (ESI)** for C₂₈H₂₄NO₅PS [M + Na]+: calcd 540.1005, found 540.1002.

**Diphenyl((1-tosyl-1H-indol-2-yl)methyl)phosphine oxide (3e)**

Yield of 3e: 94% as a white solid. **¹H NMR** (400 MHz, CDCl₃) δ = 8.02 (d, J = 8.3 Hz, 1H), 7.81 (s, 1H), 7.78 (d, J = 4.2 Hz, 2H), 7.76 (s, 1H), 7.55 (s, 1H), 7.52 (d, J = 6.7 Hz 2H), 7.50 (s, 1H), 7.45 (m, 4H), 7.37 (d, J = 7.6 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 7.19 – 7.14 (m, 2H), 7.13 (s, 1H), 7.02 (d, J = 2.4 Hz, 1H), 4.27 (s, 1H), 4.24 (s, 1H), 2.32 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 145.0, 136.8, 135.4, 132.6, 132.1 (d, J = 3.0 Hz), 131.6, 131.1, 131.0, 129.9, 128.7 (d, J = 12.0 Hz), 126.3, 124.5, 123.8, 120.9, 114.9, 113.5 (d, J = 6.0 Hz), 30.0 (d, J = 68.0 Hz), 21.6. **³¹P NMR** (162 MHz, CDCl₃) δ = 28.82. **M.P.**: 176 – 178 °C. **HRMS (ESI)** for C₂₈H₂₄NO₃PS [M + H]+: calcd 486.1287, found 486.1283.

**Di-p-tolyl((1-tosyl-1H-indol-2-yl)methyl)phosphine oxide (3f)**

Yield of 3f: 96% as a white solid. **¹H NMR** (400 MHz, CDCl₃) δ = 8.03 (d, J = 8.3 Hz, 1H), 7.67 (s, 1H), 7.65 (d, J = 3.6 Hz, 2H), 7.63 (s, 1H), 7.54 (s, 1H), 7.52 (s, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.25 (s, 2H), 7.23 (s, 3H), 7.15 (t, J = 10.8 Hz, 3H), 7.02 (s, 1H), 4.21 (s, 1H), 4.18 (s, 1H), 2.37 (s, 6H), 2.32 (d, J = 3.0 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ = 145.0, 142.7, 136.8, 135.4, 131.7 (d, J = 10.0 Hz), 131.1 (d, J = 9.0 Hz), 129.9, 129.8, 129.6, 129.4, 126.3, 124.4, 123.8, 120.9, 114.9, 113.7, 30.0 (d, J = 67.0 Hz), 29.3, 21.6 (d, J = 6.0 Hz). **³¹P NMR** (162 MHz, CDCl₃) δ = 29.42. **M.P.**: 193 – 194 °C. **HRMS (ESI)** for C₃₀H₂₈NO₃PS [M + Na]+: calcd 536.1420, found 536.1417.

**Bis(3,5-dimethylphenyl)((1-tosyl-1H-indol-2-yl)methyl)phosphine oxide (3g)**
Yield of 3g: 93% as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta =$ 8.00 (d, $J = 8.3$ Hz, 1H), 7.55 (d, $J = 2.1$ Hz, 1H), 7.53 (s, 1H), 7.41 (s, 2H), 7.37 (d, $J = 7.4$ Hz, 3H), 7.22 (d, $J = 7.7$ Hz, 1H), 7.17 (d, $J = 17.4$ Hz, 2H), 7.12 (s, 3H), 7.00 (s, 1H), 4.21 (d, $J = 13.6$ Hz, 2H), 2.31 (s, 15H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta =$ 144.9, 138.4 (d, $J = 13.0$ Hz), 136.8, 135.5, 133.8 (d, $J = 3.0$ Hz), 132.4, 131.4 (d, $J = 5.0$ Hz), 129.9 (d, $J = 2.0$ Hz), 129.9, 128.5 (d, $J = 9.0$ Hz), 126.3, 124.3, 123.7, 120.9, 114.9, 113.5 (d, $J = 6.0$ Hz), 30.0 (d, $J = 67.0$ Hz), 21.6, 21.3. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta =$ 29.40. M.P.: 172 – 174 °C. HRMS (ESI) for C$_{32}$H$_{32}$NO$_3$PS [M + Na]$^+$: calcd 564.1733, found 564.1737.

Bis(4-fluorophenyl)((1-tosyl-1H-indol-2-yl)methyl)phosphine oxide (3h)

Yield of 3h: 96% as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta =$ 7.98 (d, $J = 8.3$ Hz, 1H), 7.78 (m, 4H), 7.52 (d, $J = 1.9$ Hz, 1H), 7.51 (d, $J = 1.9$ Hz, 1H), 7.31 (d, $J = 7.8$ Hz, 1H), 7.25 – 7.19 (m, 1H), 7.18 – 7.13 (m, 3H), 7.12 (d, $J = 2.3$ Hz, 3H), 7.10 (d, $J = 2.2$ Hz, 1H), 7.02 (d, $J = 3.0$ Hz, 1H), 4.36 (s, 1H), 4.33 (s, 1H), 2.30 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta =$ 166.5 (d, $J = 4.0$ Hz), 164.0 (d, $J = 3.0$ Hz), 145.2, 136.9, 135.2, 133.7 (dd, $J = 10.0$ Hz, 8.0 Hz), 129.9, 129.6 (d, $J = 2.0$ Hz), 126.2, 124.7, 124.0, 120.9, 116.4 (d, $J = 13.0$ Hz), 116.2 (d, $J = 13.0$ Hz), 115.0, 114.0 (d, $J = 6.0$ Hz), 30.5 (d, $J = 68.0$ Hz), 21.6. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta =$ 27.55. HRMS (ESI) for C$_{28}$H$_{22}$F$_2$NO$_3$PS [M + H]$^+$: calcd 522.1099, found 522.1110.

Bis(4-chlorophenyl)((1-tosyl-1H-indol-2-yl)methyl)phosphine oxide (3i)

Yield of 3i: 99% as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta =$ 8.04 – 7.99 (m, 1H), 7.73 (d, $J = 1.9$ Hz, 1H), 7.71 (t, $J = 2.3$ Hz, 2H), 7.69 (d, $J = 1.9$ Hz, 1H), 7.52 (d, $J = 1.9$ Hz, 1H), 7.50 (d, $J = 1.9$ Hz, 1H), 7.44 (d, $J = 2.4$ Hz, 2H), 7.42 (d, $J = 2.3$ Hz, 2H), 7.41 – 7.37 (m, 1H), 7.26 – 7.22 (m, 1H), 7.18 (m, 1H), 7.15 (s, 1H), 7.13 (s, 1H), 6.99 (d, $J = 2.7$ Hz, 1H), 4.29 – 4.25 (m, 1H), 4.25 – 4.21 (m, 1H), 2.32 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta =$ 145.1, 138.9 (d, $J = 4.0$ Hz), 136.0 (d, $J = 155.0$ Hz), 132.3 (d, $J = 11.0$ Hz), 130.6, 130.1 (d, $J = 5.0$ Hz), 129.9, 129.5 (d, $J = 2.0$ Hz), 129.2, 129.1, 126.1, 124.7, 123.9, 120.8, 114.9, 113.6 (d, $J = 6.0$ Hz), 30.0 (d, $J = 68.0$ Hz), 21.5. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta =$ 27.55. M.P.: 170 – 172 °C. HRMS (ESI) for C$_{28}$H$_{22}$Cl$_2$NO$_3$PS [M +
H]+: calcd 554.0508, found 554.0502.

Methyl phenyl(1-tosyl-1H-indol-2-yl)methylphosphinate (3j)

Yield of 3j: 72% as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$)  δ = 8.03 (d, $J$ = 8.2 Hz, 1H), 7.77 (dd, $J$ = 11.9 Hz, 7.6 Hz, 2H), 7.55 (m, 3H), 7.44 (m, 3H), 7.20 (m, 2H), 7.13 (d, $J$ = 8.0 Hz, 2H), 6.81 (d, $J$ = 3.3 Hz, 1H), 3.98 (d, $J$ = 6.9 Hz, 1H), 3.93 (d, $J$ = 5.5 Hz, 1H), 3.67 (dd, $J$ = 11.1 Hz, 1.9 Hz, 3H), 2.30 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 144.8, 136.8, 135.5, 132.6 (d, $J$ = 2.0 Hz), 132.0 (d, $J$ = 9.0 Hz), 130.6 (d, $J$ = 5.0 Hz), 129.8, 129.7, 129.5 (d, $J$ = 3.0 Hz), 128.6 (d, $J$ = 12.0 Hz), 126.2, 124.3, 123.7, 120.6, 114.9, 112.7 (d, $J$ = 7.0 Hz), 51.6 (d, $J$ = 7.0 Hz), 29.7 (d, $J$ = 98.0 Hz), 21.5. $^{31}$P NMR (162 MHz, CDCl$_3$) δ = 39.52. HRMS (ESI) for C$_{23}$H$_{22}$NO$_4$PS [M + H]+: calcd 440.1080, found 440.1085.

(6-((1-Tosyl-1H-indol-2-yl)methyl)dibenzo[c,e][1,2]oxaphosphinine 6-oxide (3k)

Yield of 3k: 98% as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.96 – 7.88 (m, 2H), 7.88 – 7.81 (m, 1H), 7.71 (dd, $J$ = 8.0 Hz, 1.5 Hz), 7.66 (t, $J$ = 7.8 Hz, 1H), 7.47 (s, 1H), 7.45 (d, $J$ = 2.6 Hz, 2H), 7.30 (d, $J$ = 7.6 Hz, 1H), 7.26 (d, $J$ = 7.6 Hz, 1H), 7.21 (d, $J$ = 7.5 Hz, 1H), 7.19 – 7.17 (m, 1H), 7.17 – 7.13 (m, 1H), 7.12 – 7.07 (m, 1H), 7.06 (s, 1H), 7.04 (s, 1H), 6.66 (d, $J$ = 3.7 Hz, 1H), 4.13 (t, $J$ = 17.1 Hz, 1H), 3.98 (t, $J$ = 16.7 Hz, 1H), 2.24 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 149.3 (d, $J$ = 8.0 Hz), 144.8, 136.7, 136.1 (d, $J$ = 7.0 Hz), 135.0, 133.5, 130.6 (d, $J$ = 10.0 Hz), 130.3, 129.6, 129.4, 129.3 (d, $J$ = 5.0 Hz), 128.3 (d, $J$ = 13.0 Hz), 126.1, 124.8, 124.3 (d, $J$ = 6.0 Hz), 124.0, 123.6, 123.5 (d, $J$ = 10.0 Hz), 122.7, 121.8 (d, $J$ = 11 Hz), 120.5, 120.1 (d, $J$ = 6.0 Hz), 114.8, 113.5 (d, $J$ = 7.0 Hz), 29.8 (d, $J$ = 92.0 Hz), 21.4. $^{31}$P NMR (162 MHz, CDCl$_3$) δ = 32.28. M.P.: 170 – 171 °C. HRMS (ESI) for C$_{28}$H$_{22}$NO$_4$PS [M + H]+: calcd 500.1080, found 500.1073.

Dimethyl ((5-methoxy-1-tosyl-1H-indol-2-yl)methyl)phosphonate) (3l)

Yield of 3l: 84% as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.00 (d, $J$ = 9.8 Hz, 1H), 7.59 (d, $J$ = 8.1 Hz, 2H), 7.16 (d, $J$ = 8.1 Hz, 2H), 6.93 – 6.85 (m, 2H), 6.74 (d, $J$ = 3.6 Hz, 1H), 3.79 (d, $J$ = 3.6 Hz, 4H), 3.77 (s, 3H), 3.74 (s, 4H), 2.31 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 156.7, 144.9, 135.3, 131.6, 131.4 (d, $J$ = 7.0 Hz), 130.6 (d, $J$ = 3.0 Hz), 129.8, 126.3, 116.0, 113.4, 113.0 (d, $J$ = 7.0 Hz), 103.1, 55.6, 53.1 (d, $J$ = 7.0 Hz), 25.4 (d, $J$ = 142.0 Hz), 21.5. $^{31}$P NMR
(162 MHz, CDCl₃) δ = 26.37. HRMS (ESI) for C₁₉H₂₂NO₆PS [M + Na]⁺: calcd 446.0798, found 446.0801.

**Dimethyl ((5-methyl-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3m)**

Yield of 3m: 99% colorless oil. ¹H NMR (400 MHz, CDCl₃) δ = 7.97 (d, J = 8.5 Hz, 1H), 7.62 (d, J = 1.7 Hz, 1H), 7.60 (d, J = 1.9 Hz, 1H), 7.21 (d, J = 1.7 Hz, 1H), 7.18 (s, 1H), 7.16 (s, 1H), 7.11 – 7.07 (m, 1H), 6.75 – 6.72 (m, 1H), 3.81 – 3.79 (m, 1H), 3.77 (s, 3H), 3.74 (s, 4H), 2.38 (s, 3H), 2.31 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ = 144.8, 135.5, 135.1, 133.4, 130.6, 129.7, 126.3, 125.8, 120.5, 114.7, 112.5 (d, J = 7.0 Hz), 53.0 (d, J = 6.0 Hz), 25.2 (d, J = 142.0 Hz), 21.4, 21.1. ³¹P NMR (162 MHz, CDCl₃) δ = 26.42. HRMS (ESI) for C₁₉H₂₂NO₆PS [M + Na]⁺: calcd 430.0849, found 430.0854.

**Dimethyl ((5-chloro-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3n)**

Yield of 3n: 97% as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ = 8.03 (d, J = 8.9 Hz, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 2.1 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.22 (d, J = 4.2 Hz, 2H), 7.19 (s, 1H), 6.76 (d, J = 3.6 Hz, 1H), 3.82 (s, 1H), 3.79 (s, 3H), 3.76 (s, 4H), 2.34 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ = 145.6, 135.6, 135.5, 132.5 (d, J = 6.0 Hz), 131.0 (d, J = 3.0 Hz), 130.3, 129.9, 126.7, 125.0, 120.5, 116.4, 112.2 (d, J = 7.0 Hz), 53.6 (d, J = 6.0 Hz), 25.6 (d, J = 142.0 Hz), 21.9. ³¹P NMR (162 MHz, CDCl₃) δ = 25.99. HRMS (ESI) for C₁₈H₁₉ClNO₅PS [M + Na]⁺: calcd 450.0302, found 450.0302.

**Dimethyl ((5-bromo-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3o)**

Yield of 3o: 99% as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ = 8.0 (d, J = 8.9 Hz, 1H), 7.6 (s, 1H), 7.6 (s, 1H), 7.4 (d, J = 8.9 Hz, 1H), 7.2 (s, 1H), 7.2 (s, 1H), 6.7 (d, J = 3.5 Hz, 1H), 3.8 (s, 1H), 3.8 (s, 3H), 3.8 (s, 4H), 2.3 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ = 144.8, 135.5, 135.1, 133.4, 130.6, 129.7, 126.3, 125.8, 120.5, 114.7, 112.5 (d, J = 7.0 Hz), 53.0 (d, J = 6.0 Hz), 25.2 (d, J = 142.0 Hz), 21.4. ³¹P NMR (162 MHz, CDCl₃) δ = 25.94. HRMS (ESI) for C₁₈H₁₉BrNO₅PS [M + Na]⁺: calcd 493.9797, found 493.9798.

**Dimethyl ((4-fluoro-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3p)**

Yield of 3p: 97% as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ = 7.89 (d, J = 8.4 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.21 (d, J = 7.9 Hz, 3H), 6.95 – 6.84 (m, 2H), 3.81 (s, 1H), 3.80 (d, J = 8.4 Hz, 1H), 7.25 (d, J = 3.5 Hz, 1H), 7.12 (d, J = 3.5 Hz, 1H), 6.7 (d, J = 3.5 Hz, 1H), 3.8 (s, 1H), 3.8 (s, 3H), 3.8 (s, 4H), 2.3 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ = 144.8, 135.5, 135.1, 133.4, 130.6, 129.7, 126.3, 125.8, 120.5, 114.7, 112.5 (d, J = 7.0 Hz), 53.0 (d, J = 6.0 Hz), 25.2 (d, J = 142.0 Hz), 21.4. ³¹P NMR (162 MHz, CDCl₃) δ = 25.94. HRMS (ESI) for C₁₈H₁₉BrNO₅PS [M + Na]⁺: calcd 493.9797, found 493.9798.
1.1 Hz, 3H), 3.78 – 3.75 (m, 4H), 2.34 (s, 3H). **13C NMR** (100 MHz, CDCl3) δ = 155.2 (d, J = 248.0 Hz), 145.3, 138.9 (d, J = 9.0 Hz), 135.3, 131.0 (d, J = 6.0 Hz), 129.9, 126.4, 125.2 (d, J = 8.0 Hz), 118.5 (dd, J = 3.0 Hz), 111.0 (d, J = 4.0 Hz), 109.1 (d, J = 19.0 Hz), 107.6 (d, J = 7.0 Hz), 53.1 (d, J = 6.0 Hz), 25.3 (d, J = 142.0 Hz), 21.5. **31P NMR** (162 MHz, CDCl3) δ = 25.93. **HRMS (ESI)** for C18H19FNO5PS [M + Na]+: calcd 434.0598, found 434.0604.

**Dimethyl ((6-fluoro-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3q)**

Yield of 3q : 93% as a yellow oil. **1H NMR** (400 MHz, CDCl3) δ = 7.85 (dd, J = 10.4 Hz, 2.3 Hz, 1H), 7.65 (s, 1H), 7.63 (d, J = 1.9 Hz, 1H), 7.36 (dd, J = 8.6 Hz, 5.4 Hz, 1H), 7.22 (s, 1H), 7.20 (s, 1H), 6.97 (m, 1H), 6.78 (d, J = 3.6 Hz, 1H), 3.78 (s, 4H), 3.75 (s, 3H), 3.73 (s, 3H), 2.34 (s, 3H). **13C NMR** (100 MHz, CDCl3) δ = 160.8 (d, J = 240.0 Hz), 145.3, 137.2, 135.3, 131.1 – 131.0 (m), 130.0, 126.4, 126.0 – 125.2 (m), 121.3 (d, J = 10.0 Hz), 112.3, 112.2 – 112.0 (m), 102.6 (d, J = 29.0 Hz), 53.1 (d, J = 7.0 Hz), 25.3 (d, J = 142.0 Hz), 21.6. **31P NMR** (162 MHz, CDCl3) δ = 26.24. **HRMS (ESI)** for C18H19ClNO5PS [M + Na]+: calcd 450.0302, found 450.0297.

**Dimethyl ((6-chloro-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3r)**

Yield of 3r : 93% as a yellow oil. **1H NMR** (400 MHz, CDCl3) δ = 8.15 (s, 1H), 7.65 (s, 1H), 7.63 (d, J = 1.4 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.25 (d, J = 15.1 Hz, 1H), 7.22 – 7.18 (m, 2H), 6.78 (d, J = 3.5 Hz, 1H), 3.78 (d, J = 1.4 Hz, 4H), 3.75 (d, J = 1.3 Hz, 3H), 3.72 (s, 1H), 2.35 (s, 3H). **13C NMR** (100 MHz, CDCl3) δ = 145.3, 137.2, 135.3, 131.4 (d, J = 6.0 Hz), 130.5, 130.0, 127.9 (d, J = 3.0 Hz), 126.4, 124.5, 121.3, 115.1, 112.0 (d, J = 7.0 Hz), 53.1 (d, J = 6.0 Hz), 25.2 (d, J = 142.0 Hz), 21.5. **31P NMR** (162 MHz, CDCl3) δ = 26.04. **HRMS (ESI)** for C18H19ClNO5PS [M + Na]+: calcd 450.0302, found 450.0297.

**Dimethyl ((7-methyl-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3s)**

Yield of 3s : 99% as a yellow oil. **1H NMR** (400 MHz, CDCl3) δ = 7.84 (s, 1H), 7.53 (s, 1H), 7.51 (s, 1H), 7.22 (d, J = 7.9 Hz, 1H), 7.10 (s, 1H), 7.08 (s, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.67 (d, J = 3.6 Hz, 1H), 3.70 (s, 1H), 3.69 – 3.66 (m, 3H), 3.65 (s, 4H), 2.37 (s, 3H), 2.22 (s, 3H). **13C NMR** (100 MHz, CDCl3) δ = 144.8, 137.3, 135.5, 134.5, 129.8, 129.7, 127.1 (d, J = 3.0 Hz), 126.2, 125.2,
120.1, 115.1, 112.5 (d, $J = 7.0$ Hz), 53.0 (d, $J = 6.0$ Hz), 25.2 (d, $J = 141.0$ Hz), 21.9, 21.4.

$^{31}$P NMR (162 MHz, CDCl$_3$) $\delta =$ 26.51. **HRMS (ESI)** for C$_{19}$H$_{22}$NO$_5$PS [M + Na]$^+$: calcd 430.0849, found 430.0849.

**Dimethyl ((3-methyl-1-tosyl-1H-indol-2-yl)methyl)phosphonate (3t)**

Yield of 3t: 40% as a yellow oil. **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta =$ 8.09 (d, $J =$ 8.1 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.38 (dd, $J =$ 6.9 Hz, 1.7 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.26 – 7.20 (m, 1H), 7.14 (s, 1H), 7.12 (s, 1H), 3.86 (s, 1H), 3.81 (s, 1H), 3.76 (d, $J =$ 1.3 Hz, 3H), 3.73 (d, $J =$ 1.3 Hz, 3H), 2.30 (s, 3H), 2.21 (dd, $J =$ 4.8 Hz, 1.3 Hz, 3H). **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta =$ 144.8, 137.3, 135.5, 134.5, 129.8, 129.7, 127.1 (d, $J =$ 3.0 Hz), 126.2, 125.2, 120.1, 115.1, 112.5 (d, $J =$ 7.0 Hz), 53.0 (d, $J =$ 6.0 Hz), 25.2 (d, $J =$ 141.0 Hz), 21.9, 21.4. **$^{31}$P NMR** (162 MHz, CDCl$_3$) $\delta =$ 26.51. **HRMS (ESI)** for C$_{19}$H$_{22}$NO$_5$PS [M + Na]$^+$: calcd 430.0849, found 430.0848.

**Dimethyl (2-methyl-1-tosyl-1H-indol-3-yl)methyl)phosphonate (3a’)**

Yield of 3a’: a yellow oil. **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta =$ 8.23 (m, 1H), 7.77 (dd, $J =$ 7.8 Hz, 1.4 Hz, 1H), 7.74 (s, 1H), 7.72 (s, 1H), 7.34 (m, 1H), 7.30 (m, 1H), 7.27 (s, 1H), 7.25 (s, 1H), 3.74 (d, $J =$ 0.7 Hz, 3H), 3.71 (d, $J =$ 0.7 Hz, 3H), 2.94 (d, $J =$ 2.2 Hz, 3H), 2.38 (s, 3H). **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta =$ 147.0 (d, $J =$ 28.0 Hz), 145.6, 136.5 (d, $J =$ 13.0 Hz), 135.8, 130.1, 128.8 (d, $J =$ 12.0 Hz), 126.7, 124.9, 124.2, 120.9, 114.4, 105.0 (d, $J =$ 210.0 Hz), 52.3 (d, $J =$ 5.0 Hz), 21.6, 14.2. **$^{31}$P NMR** (162 MHz, CDCl$_3$) $\delta =$ 18.18. **HRMS (ESI)** for C$_{18}$H$_{20}$NO$_5$PS [M + H]$^+$: calcd 394.0873, found 394.0877.
5. X-ray Crystal Structure Determination of 3e.

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6. Copies of $^1$H NMR, $^{13}$C NMR and $^{31}$P NMR Spectra.

$^1$H NMR Spectrum of 1t

$^{13}$C NMR Spectrum of 1t
$^1$H NMR Spectrum of 3a

$^{13}$C NMR Spectrum of 3a
$^{31}$P NMR Spectrum of 3a

$^{1}$H NMR Spectrum of 3b
$^{13}$C NMR Spectrum of 3b

$^{31}$P NMR Spectrum of 3b
\(^1\)H NMR Spectrum of 3c

\[^{13}\]C NMR Spectrum of 3c
$^{13}$C NMR Spectrum of 3d

31P NMR Spectrum of 3d
$^1$H NMR Spectrum of 3e

$^{13}$C NMR Spectrum of 3e
$^{31}$P NMR Spectrum of 3e

$^1$H NMR Spectrum of 3f
$^{13}$C NMR Spectrum of 3f

$^{31}$P NMR Spectrum of 3f
$^{13}$C NMR Spectrum of $3h$

$^{31}$P NMR Spectrum of $3h$
$^{13}$C NMR Spectrum of 3j

31P NMR Spectrum of 3j
$^{1} \text{H NMR Spectrum of } 3\text{m}$

$^{13} \text{C NMR Spectrum of } 3\text{m}$
$^{31}$P NMR Spectrum of $3m$

$^1$H NMR Spectrum of $3n$
$^{13}$C NMR Spectrum of 3n

$^{31}$P NMR Spectrum of 3n
$^{13}$C NMR Spectrum of 3p

$^1$H NMR Spectrum of 3p
$^1$H NMR Spectrum of 3q

$^1$H NMR Spectrum of 3r
$^1$H NMR Spectrum of 3s

$^{13}$C NMR Spectrum of 3s
$^1$H NMR Spectrum of 3s

$^1$H NMR Spectrum of 3t
$^1$H NMR Spectrum of 3a' 

$^{13}$C NMR Spectrum of 3a'
$^{31}$P NMR Spectrum of 3a'