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Note

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Copper-catalyzed cascade phosphorylation initiated radical cyclization: access to 2-phosphorylated-pyrrolo[1,2-*a*]indole

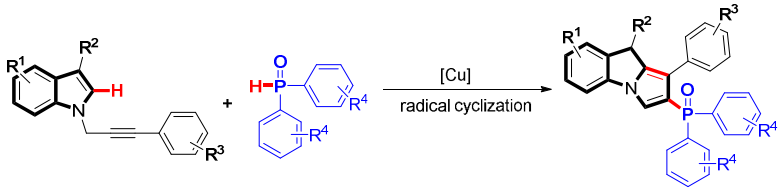
Honglin Zhang,[a] Weipeng Li,[a] and Chengjian Zhu[a,b]*

[a] *State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing, 210093, P. R. China.*

[b] State Key Laboratory of Organometallic Chemistry, *Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai,200032, P. R. China.*

cjzhu@nju.edu.cn

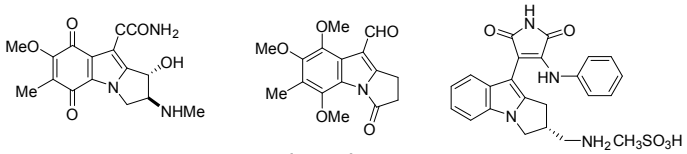
ABSTRACT



A copper-catalyzed tandem radical cyclization of 1-(3-phenylprop-2-yn-1-yl)-1*H*-indole with diphenylphosphine oxides was developed. C-P bond formation was achieved coupled with C(sp^2)-H functionalization. It provided an access to construct the pyrrolo[1,2-a]indole motif and a series of 2-phosphinoyl-9*H*-pyrrolo[1,2-a]indoles.

Polycyclic indole is one of important heterocycle classes, because of their biological and pharmacological activities.[1] For example, pyrrolo[1,2-a]indoles are important frameworks, which are present in numerous natural products and pharmaceutical chemicals, such as apo-Mitomycin B, Mitosene Lactam and protein kinase C-â inhibitor JTT-010 (Scheme 1).[2] There have been several methods to construct pyrrolo[1,2-a]indole scaffold.[3] Very recently, an effective silver-mediate tandem phosphinoylation/cyclization process to construct 2-phosphinoyl-9H-pyrrolo[1,2-a] indoles was developed by the Zhao and Tang group.[3c] Expensive transition-metal catalyst and high temperature are usually needed in these strategies. However, this motif remains interesting to organic synthetic chemists.[3]

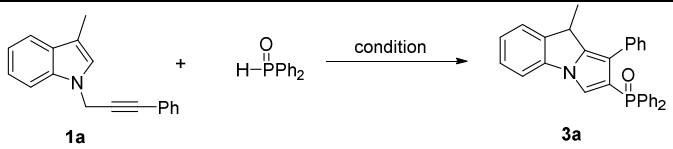
Scheme 1. Some of pyrrolo[1,2-a]indole derivatives.



Phosphonates are widely found in organic chiemcals such as functional materials,[4] nature products [5] and pharmaceutical chemicals. [6] Because of their special bioactivities,[6] it is of great importance to develop methods for construction of C-P bond. Enormous efforts have been devoted to the phosphorylation reactions catalyzed by transition-metals[7] or under metal-free conditions.[8] A variety of tandem reactions initiated by the addition of P-centered radicals to active alkenes were reported, providing a useful strategy to construct organophosphorus frameworks especially heterocycles.[9] Our group reported a silver-catalyzed cascade radical 6-endo-trig cyclization initiated by phosphorylation of *N*-methyl-*N*-phenylcinnamamides.[10] However, only several cascade reactions of P-centered radicals with alkynes through C-H functionalization were reported to date.[11] Thus it remains a challenge to explore efficient P-centered radical cascade reactions, which would provide an alternative strategy for synthesis of organophosphorus compounds. As our continuous research, herein, we report a copper-catalyzed cascade phosphorylation initiated radical cyclization, providing an access to 2-phosphorylated-pyrrolo[1,2-a]indole.

The initial studies were carried out by selecting 3-methyl-1-(3-phenylprop-2-yn-1-yl)-1H-indole (**1a**) as model substrate to react with diphenylphosphine oxide in presence of 20 mol% $Cu(OAc)_2$ and 2 equiv $K_2S_2O_8$ in 2 mL of

Table 1. Optimization of reaction condition [a]



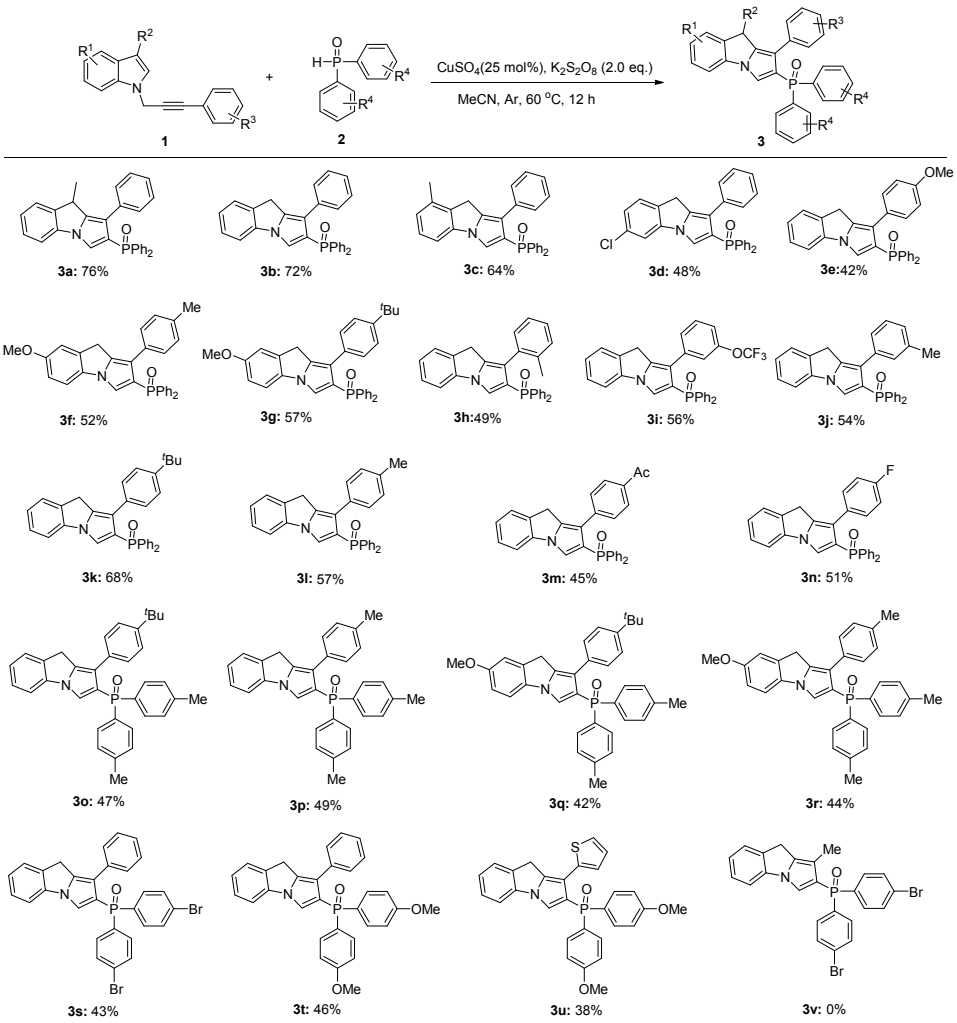
1a **3a**

Entry	Catalyst (mol%)	Oxidant (eq)	T (℃)	Yield of 3a (%) [b]
1	$Cu(OAc)_2$ (20)	$K_2S_2O_8$ (2)	60	42
2	$CuSO_4$ (20)	$K_2S_2O_8$ (2)	60	52
3	$Cu(OTf)_2$ (20)	$K_2S_2O_8$ (2)	60	30
4	$Fe(NO_3)_3$ (20)	$K_2S_2O_8$ (2)	60	trace
5[c]	-----	$AgNO_3$ (2)	60	35
6	$CuSO_4$ (20)	$(NH_4)_2S_2O_8$ (2)	60	30
7	$CuSO_4$ (20)	$Na_2S_2O_8$ (2)	60	46
8	$CuSO_4$ (20)	DDQ (2)	60	trace
9	$CuSO_4$ (20)	DTBP (2)	60	trace
10	$CuSO_4$ (25)	$K_2S_2O_8$ (2)	60	76
11	$CuSO_4$ (30)	$K_2S_2O_8$ (2)	60	57
12	$CuSO_4$ (25)	$K_2S_2O_8$ (3)	60	62
13	$CuSO_4$ (25)	$K_2S_2O_8$ (2)	70	66
14	$CuSO_4$ (25)	$K_2S_2O_8$ (2)	50	36
15	-----	$K_2S_2O_8$ (2)	60	15
16	$CuSO_4$ (25)	-----	60	trace

[a] Reaction condition: **1a** (0.1 mmol), diphenylphosphine oxide (0.2mmol), MeCN (2 mL), under Ar atmosphere, 12 h unless otherwise noted. [b] Isolated yield. [c] DMF(2 mL) was used.

MeCN at 60 ℃ for 12 h under Ar atmosphere. To our delight, (9-methyl-1-phenyl-9*H*-pyrrolo[1,2-a]indol-2-yl)-diphenylphosphine oxide (**3a**) was obtained with 42% yield (Table 1, entry 1). Different metal catalysts were screened, and anhydrous $CuSO_4$ shows best catalytic activity with 52% yield of **3a** (Table 1, entries 1-5). Oxidants were tested and no better result was obtained (Table 1, entries 6-9), indicating that $K_2S_2O_8$ is the most suitable oxidant. As 25 mol% anhydrous $CuSO_4$ was loaded, **3a** was generated with 76% yield (Table 1, entry 10). However, increasing the amount of $CuSO_4$ did not result in increase of the yield (Table 1, entry 11). Similarly, the yield decreased to 62% as 3 equiv $K_2S_2O_8$ was loaded (Table 1, entry 12). When the reactions were carried out under higher or lower temperature, the yield decreased (Table 1, entries 13, 14), showing that 60 ℃ is the most suitable reaction temperature. Without $CuSO_4$, **3a** was obtained only in 15% yield (Table 1, entry 15). While trace of **3a** was obtained when no $K_2S_2O_8$ was loaded (Table 1, entry 16). This result showed that $CuSO_4$ is of great importance for this transformation.

As the optimized reaction condition was estiblished, it was applied to a series of 1-(3-phenylprop-2-yn-1-yl)-1H-indoles. The results showed that both electron-withdrawing and electron-donating functional groups were well



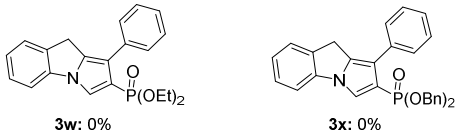


Figure 1. Copper-catalyzed tandom cyclization of 1-(3-phenylprop-2-yn-1-yl)-1H-indoles with diphenylphosphine oxide. Standard condition: 1-(3-phenylprop-2-yn-1-yl)-1H-indole (0.1 mmol), diphenylphosphine oxide (0.2 mmol), anhydrous $CuSO_4$ (25 mol%), $K_2S_2O_8$ (2.0 equiv), MeCN (2.0 mL), 60℃, 12 h under Ar atmosphere. An isolated yield was provided.

torlerated (Figure 1). The corresponding products could be also obtained with middle yield when indoles were substituted by chlorine atoms (Figure 1, **3d**). It provided a possiblity for further transformation of these products. When substituent groups (such as Me, OMe, OCF_3, F, Ac, *t*Bu) were on phenyl ring attacted to carbon-carbon triple bond, the reaction efficiency were almost not affected, generating the desired products with moderate to good yield (Figure 1, **3f-3n**). Diphenylphosphine oxides substituted by Me, OMe or Br were also scoped, and the corresponding products were obtained with moderate yields (Figure 1, **3o-3x**). When phenyl ring attached to the carbon-carbon triple bond was replaced by thiophene ring, product 3u was generated in 38% yield (Figure 1, **3u**). However, it did not work when methyl group was used (Figure 1, **3v**). Diethyl phosphite and dibenzyl phosphite could not react with 1-(3-phenylprop-2-yn-1-yl)-1H-indole, either (Figure 1, **3w-3x**). Further more, a gram-scale reaction of 1b and diphenylphosphine oxide was performed, generating product **3b** in 65% yield (Figure 2).

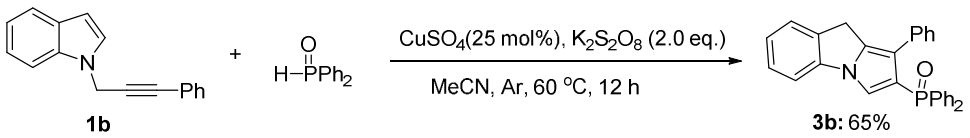
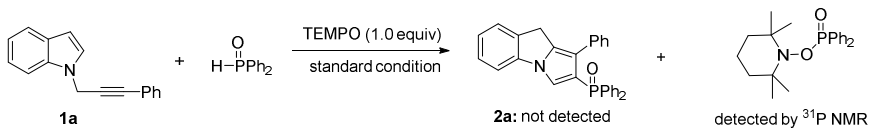


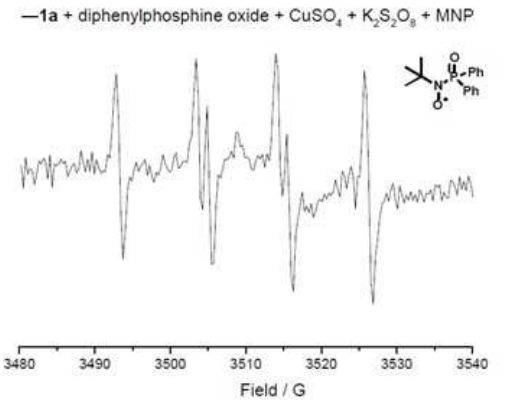
Figure 2. Gram-scale reaction

For further investagation of the mechanism, some control experiments were carried out. When 1 equiv radical inhibitor 2,2,6,6-tetramethylpiperidine oxide (TEMPO) was loaded, the reaction was totally shut down and no **3a** was detected (Scheme 2). The TEMPO-P(O)Ph_2 adduct was observed by LC-MS (mass calcd for $C_{21}H_{29}NO_2P$ $[M + H]^+$: 358.18, found 358.92) and ^{31}P NMR (δ 33.5).[12] Meanwhile, a EPR experiments was conducted to detected the P-centered radical by addtion of 2-methyl-2-nitrosopropane (MNP), a radical spin trapping agent. When MNP was added to the reaction system, an EPR signal was recorded (Scheme 2(b)). It showed that a P-centered radical generated and trapped by MNP, forming a relatively stable radical A (a_N = 10.56 G, a_P = 12.02 G).[13] The result suggested that this reaction undergoes a radical pathway.

Scheme 2. Radical trapping experiment



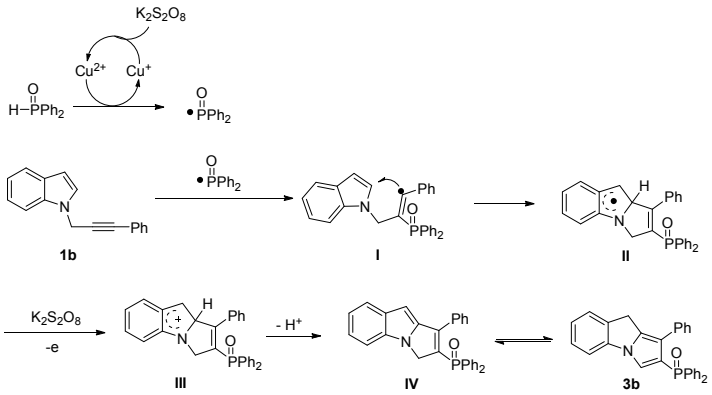
Scheme 3. EPR experment



The electron paramagnetic resonance (EPR) spectra (X band, 0.5 GHz, room temperature) of the reaction mixture of 1a, diphenylphosphine oxide, $CuSO_4$ and $K_2S_2O_8$ in MeCN at 60 °C.

On the basis of above results and previous literatures reports,[14] we suggested a plausible mechanism (Scheme 4). Firstly, a P-centered radical formed when diphenylphosphine oxide was oxidized by Cu(II) and Cu(I) was given out.[14a] Oxidized by $K_2S_2O_8$, Cu(I) transformed to Cu(II). Then a vinyl radical **I** was generated after the addition of P-cantered radical to the C-C triple bond.[14b] Radical intermediate **II** was afforded as vinyl radical **I** underwent a intramolecular cyclization.[14c] Oxidized by $K_2S_2O_8$ or Cu(II), radical **II** transformed to be cation **III**.[14a] Finally, deprotonation of the cation **III** generated intermediate **IV**,[14c] which transformed to the final product **3b** through an isomerization process.

Scheme 4. Plausible reaction mechanism



In conclusion, we have reported a copper catalyzed tandom C-H functionalization/radical cyclization initiated by phosphorylation. In this reaction, both P-H and C-H bonds were activated. A direct access to 2-phosphorylated-pyrrolo[1,2-a]indoles was provided. A series of functional groups were well tolerated, giving the corresponding products in middle to

good yields. Meanwhile, a method to synthesis polycyclic indoles was developed, which may be applied in organic synthetic chemistry.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from chemical supliers and used without further purification. 1-(3-phenylprop-2-yn-1-yl)-1H-indoles were prepared according to literature reports. [11c,15] The radical cyclization were performed under Ar atmosphere. The reaction was detected by TLC. The products were seperated by TLC. HRMS datas were carried out by a TOF LC-MS. ^{1}H, ^{19}F, ^{31}P and ^{13}C NMR spectra were recorded using a 400 MHz spectrometer using $CDCl_3$ as solvent.

Experimental Procedure for the Copper-catalyzed Cyclization of 1-(3-phenylprop-2-yn-1-yl)-1H-indole with Diphenyl-phosphine Oxide. 1-(3-phenylprop-2-yn-1-yl)-1H-indole (0.1 mmol), diphenylphosphine oxide (0.2 mmol, 2.0 equiv), $CuSO_4$ (0.025 mmol, 25 mol%), $K_2S_2O_8$ (0.2 mmol, 2.0 equiv), MeCN (2.0 mL) and a stir bar were added to a sealed tube under Ar atmosphere. Then the tube was heated to 60 ℃ for 12 h. The tube was cooled to room temperature and the mixture was concentraed in vacuum. The corresponding product **3** was seperated by TLC using ethyl acetate and petroleum (1: 1~ 2:1) as solvents.

(9-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3a**): m.p.: 194.1-196.4 °C, light yellow solid (33.6 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.70 – 7.63 (m, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.50 – 7.47 (m, 1H), 7.45 – 7.40 (m, 2H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.34 – 7.15 (m, 7H), 7.11 (t, *J* = 7.5 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.94 (d, *J* = 3.9 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 1H), 1.31 (d, *J* = 7.2 Hz, 3H).^{13}C NMR (100MHz, $CDCl_3$) δ 140.7, 140.5, 140.4, 138.8, 134.0 (d, *J* = 107.0 Hz), 133.8, 133.5, 132.8, 131.9, 131.8, 131.7, 131.3, 131.3, 131.2, 131.1, 129.3, 128.2, 128.1, 128.0, 127.8, 127.7, 126.3, 125.0, 124.8, 122.2, 122.1, 118.8, 118.6, 118.3, 117.1, 110.4, 36.2, 17.1. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.10. HRMS (ESI) calcd. for $C_{30}H_{24}NNaOP^+$ ($M+Na^+$): 468.1488, found: 468.1484.

diphenyl(1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (3b): 259.5-262.0 °C, light yellow solid (30.9 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.71 (m, 4H), 7.64 – 7.57 (m, 2H), 7.42 (m, 3H), 7.38 – 7.28 (m, 6H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.19 – 7.13 (m, 3H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 4.0 Hz, 1H), 4.02 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 135.4, 135.3, 134.5, 134.2, 133.8 (d, *J*= 107.3 Hz), 131.9, 131.8, 131.3, 131.3, 128.7, 128.3, 128.2, 128.0, 127.7, 126.2, 126.1, 124.7, 121.9, 121.9, 119.5, 119.3, 117.9, 116.8, 110.6, 29.6. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.33. HRMS (ESI) calcd. for $C_{29}H_{22}NNaOP^+$ ($M+Na^+$): 454.1331, found:454.1326.

(8-methyl-1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (3c) : m.p.: 236.4-238.6 °C, light yellow solid (28.3 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.71 (m, 4H), 7.63 – 7.60 (m, 2H), 7.45 – 7.40 (m, 2H), 7.37 –

7.32 (m, 4H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 2H), 7.10 – 7.04 (m, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 4.0 Hz, 1H), 3.92 (s, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$)δ 139.4, 135.9, 135.3, 134.9 (d, *J*= 109.5 Hz),133.3, 131.9, 131.8, 131.3, 131.3, 128.7, 128.1, 128.0, 127.8, 126.1, 125.8, 119.6, 119.3, 108.0, 28.6, 18.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.47. HRMS (ESI) calcd. for $C_{30}H_{24}NNaOP^+$ ($M+Na^+$): 468.1488, found: 468.1493.

(6-chloro-1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3d**): m.p.: 281.5-283.2 °C, light yellow solid (25.5 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 4H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.44 – 7.41 (m, 2H), 7.38 – 7.33 (m, 5H), 7.23 (d, *J* = 1.7 Hz, 1H), 7.18-7.13 (m, 3H), 7.07-7.03 (m, 1H), 6.89 (d, *J* = 3.9 Hz, 1H), 3.99 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 133.8, 133.6, 133.5 (d, *J* = 107.2 Hz), 131.9, 131.8, 131.4, 128.7, 128.2, 128.1, 127.0, 126.3, 124.6, 119.5, 119.3, 111.3, 29.2. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.10. HRMS (ESI) calcd. for $C_{29}H_{21}NClNaOP^+$ ($M+Na^+$): 488.0941, found: 488.0943.

(1-(4-methoxyphenyl)-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3e**): m.p.: 133.9-135.1 °C, light yellow solid (19.2 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 4H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.43 (dd, *J* = 7.8, 1.9 Hz, 3H), 7.38 – 7.34 (m, 4H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.17 (dd, *J* = 7.9, 7.0 Hz, 1H), 6.93 (d, *J* = 3.9 Hz, 1H), 6.70 (d, *J* = 8.7 Hz, 2H), 3.99 (s, 2H), 3.72 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 157.9, 139.8, 134.9, 134.6, 133.8 (d, *J* = 107.2 Hz), 131.9, 131.8, 131.3, 129.9, 128.2, 128.0, 127.7, 126.8, 126.2, 124.6, 119.2, 119.0, 113.5, 110.5, 55.2, 29.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.47. HRMS (ESI) calcd. for $C_{30}H_{24}NNaO_2P^+$ ($M+Na^+$): 484.1437, found: 484.1439.

(7-methoxy-1-(p-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3f**): m.p.: 153.4-155.6 °C, light yellow solid (24.5 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.71 (m, 4H), 7.48-7.41 (m, 4H), 7.37-7.32 (m, 4H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.00 (d, *J* = 1.9 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.87 (d, *J* = 3.8 Hz, 1H), 6.83-6.79 (m, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 136.2, 135.6, 135.1, 135.0, 133.9 (d, *J*= 107.1 Hz),133.7, 132.0, 131.9, 131.2, 131.2, 128.7, 128.6, 128.1, 128.0, 122.0, 119.2, 119.0, 112.6, 112.5, 110.9, 55.8, 29.8, 21.1. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.83. HRMS (ESI) calcd. for $C_{31}H_{27}NO_2P^+$ ($M+H^+$): 476.1774, found: 476.1777.

(1-(4-(tert-butyl)phenyl)-7-methoxy-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3g**): m.p.: 116.3-118.7 °C, light yellow solid (29.2 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 12.1, 7.1 Hz, 4H), 7.45-7.37 (m, 4H), 7.35-7.30 (m, 4H), 7.15-7.10 (m, 3H), 7.00 (d, *J* = 1.9 Hz, 1H), 6.92 (d, *J* = 3.7 Hz, 1H), 6.83 – 6.79 (m, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 148.8, 136.2, 134.9, 134.8, 133.8 (d, *J*= 107.3 Hz), 133.7, 132.0, 131.9, 131.2, 131.2, 128.4, 128.1, 128.0, 124.8, 121.9, 121.9, 119.1, 118.9, 116.9, 115.7, 112.6, 112.5, 110.9, 55.8, 34.3, 31.2, 29.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.49. HRMS (ESI) calcd. for $C_{34}H_{32}NNaO_2P^+$ ($M+Na^+$): 540.2063, found: 540.2057.

diphenyl(1-(o-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3h**): m.p.: 216.3-217.9 °C, light yellow solid (21.7 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 4H), 7.40 (d, *J* = 7.1 Hz, 4H), 7.35-7.27 (m, 6H), 7.19 – 7.15 (m, 1H), 7.12 (d, *J* = 7.4 Hz, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.95-6.88 (m, 2H), 3.67 (s, 2H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.01, 137.16, 135.42, 134.79, 133.02, 131.78, 131.67, 131.16, 129.33, 127.97, 127.85, 127.78, 127.24, 126.23, 124.95, 124.50, 120.38, 118.33, 110.64, 28.93, 19.84. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.64. HRMS (ESI) calcd. for $C_{30}H_{25}NOP^+$ ($M+H^+$): 446.1668, found: 446.1662.

diphenyl(1-(3-(trifluoromethoxy)phenyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3i**) : m.p.: 195.3-196.7 °C, light yellow solid (28.6 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.72 (m, 4H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.47 – 7.42 (m, 4H), 7.39-7.34 (m, 4H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.13 (m, 3H), 6.95 (d, *J* = 4.0 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 4.02 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 139.5, 136.3, 136.0, 135.9, 134.3, 133.3 (d, *J*= 107.5 Hz), 131.9, 131.8, 131.5, 131.5, 129.4, 128.2, 128.1, 127.8, 127.5, 126.3, 124.9, 121.7, 120.8, 120.5, 120.4, 119.6, 119.4, 118.5, 118.2, 117.1, 110.7, 29.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.63. ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.93. HRMS (ESI) calcd. for $C_{30}H_{21}F_3NNaO_2P^+$ ($M+Na^+$): 538.1154, found: 538.1150.

diphenyl(1-(m-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3j**): m.p.: 278.2-280.5 °C, light yellow solid (23.8 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 4H), 7.45-7.41 (m, 3H), 7.38 – 7.33 (m, 6H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 4.0 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 4.01 (s, 2H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 137.4, 135.2, 134.6, 134.0, 133.9 (d, *J* = 107.1 Hz), 131.9, 131.8, 131.6, 131.2, 129.8, 128.4, 128.1, 128.0, 127.9, 127.7, 126.9, 126.7, 126.2, 125.5, 124.6, 119.4, 119.2, 110.6, 29.6, 21.3. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.04. HRMS (ESI) calcd. for $C_{30}H_{25}NOP^+$ ($M+H^+$) 446.1668, found: 446.1673.

(1-(4-(tert-butyl)phenyl)-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3k**): m.p.: 138.4-143.7 °C, light yellow solid (32.9 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 4H), 7.46 – 7.39 (m, 5H), 7.35 – 7.30 (m, 5H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 3.9 Hz, 1H), 4.02 (s, 2H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$)δ 148.8, 139.8, 135.0, 134.9, 134.6, 133.9 (d, *J*= 107.2 Hz), 131.9, 131.8, 131.2, 128.4, 128.1, 128.0, 127.7, 126.2, 124.8, 124.6, 121.9, 121.8, 119.2, 119.0, 118.0, 116.8, 110.5, 34.3, 31.2, 29.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.34. HRMS (ESI) calcd. for $C_{33}H_{30}NNaOP^+$ ($M+Na^+$) 510.1957, found: 510.1954.

diphenyl(1-(p-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3l**): m.p.: 260.1-264.3 °C, light yellow solid (25.1 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.70 (m, 4H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.46 – 7.40 (m, 3H), 7.38-7.32 (m, 4H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.19-7.15 (m, 1H), 6.99-6.91 (m, 3H), 4.01 (s, 2H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 135.7, 135.2, 135.1, 134.6, 133.9 (d, *J*= 107.1 Hz), 131.9, 131.8, 131.2, 131.2,

128.7, 128.6, 128.1, 128.0, 127.7, 126.2, 124.6, 121.9, 119.3, 119.1, 110.5, 29.6, 21.1. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.58. HRMS (ESI) calcd. for $C_{30}H_{25}NOP^+$ ($M+H^+$) 446.1668, found: 446.1665.

1-(4-(2-(diphenylphosphoryl)-9H-pyrrolo[1,2-a]indol-1-yl)phenyl)ethan-1-one (**3m**): m.p.: 263.8-267.6 °C, light yellow solid (21.1 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.72 (m, 8H), 7.48 – 7.43 (m, 3H), 7.39-7.34 (m, 4H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.25 – 7.18 (m, 2H), 6.91 (d, *J* = 4.1 Hz, 1H), 4.06 (s, 2H), 2.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 139.4, 139.3, 136.6, 136.5, 134.5, 134.2, 133.3 (d, *J* = 107.7 Hz), 132.6, 131.9, 131.8, 131.6, 131.6, 131.3, 130.8, 130.7, 129.0, 128.9, 128.5, 128.3, 128.2, 127.9, 126.3, 125.0, 120.9, 120.9, 120.2, 119.9, 118.0, 116.8, 110.7, 30.0, 26.6. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.61. HRMS (ESI) calcd. for $C_{31}H_{25}NO_2P^+$ ($M+H^+$) 474.1617, found: 474.1622.

(1-(4-fluorophenyl)-9H-pyrrolo[1,2-a]indol-2-yl)diphenylphosphine oxide (**3n**): m.p.: 265.5-267.9 °C, light yellow solid (22.7 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.69 (m, 4H), 7.62 – 7.55 (m, 2H), 7.48-7.41 (m, 3H), 7.38 – 7.33 (m, 4H), 7.30 (d, *J* = 7.1 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.20-7.16 (m, 1H), 6.93 (d, *J* = 4.0 Hz, 1H), 6.84 (t, *J* = 8.8 Hz, 2H), 3.99 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ161.3 (d, *J* = 243.7 Hz), 139.7, 135.3, 135.2, 134.4, 133.6 (d, *J*= 107.2 Hz), 131.9, 131.8, 131.4, 131.4, 130.4, 130.3, 128.2, 128.1, 127.8, 126.2, 124.7, 121.0, 120.9, 119.3, 119.1, 118.1, 116.9, 115.0, 114.7, 110.6, 29.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.40. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.15. HRMS (ESI) calcd. for $C_{29}H_{22}FNOP^+$ ($M+H^+$) 450.1418, found: 450.1416.

(1-(4-(tert-butyl)phenyl)-9H-pyrrolo[1,2-a]indol-2-yl)di-p-tolylphosphine oxide (**3o**) : m.p.: 105.5-106.8 °C, light yellow solid (24.0 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.58 (m, 4H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.17 – 7.10 (m, 7H), 6.97 (d, *J* = 4.0 Hz, 1H), 4.01 (s, 2H), 2.32 (s, 6H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 141.3, 141.3, 139.8, 134.9, 134.8, 134.6, 131.9, 131.8, 131.5, 131.4, 130.9 (d, *J* = 109.6 Hz), 128.8, 128.7, 128.4, 127.7, 126.2, 124.7, 124.5, 121.8, 121.7, 119.2, 119.0, 118.6, 117.4, 110.5, 34.3, 31.3, 29.5, 21.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.49. HRMS (ESI) calcd. for $C_{35}H_{35}NOP^+$ ($M+H^+$) 516.2451, found: 516.2454.

di-p-tolyl(1-(p-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3p**): m.p.: 94.3-96.0 °C, light yellow solid (23.0 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.57 (m, 4H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.18 – 7.13 (m, 5H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 4.0 Hz, 1H), 4.00 (s, 2H), 2.35 (s, 6H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 139.8, 135.5, 135.2, 135.1, 134.6, 131.9, 131.8, 131.5, 130.9 (d, *J* = 109.7 Hz), 128.9, 128.8, 128.7, 128.6, 127.6, 126.2, 124.5, 119.3, 119.1, 110.5, 29.6, 21.6, 21.1. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.68. HRMS (ESI) calcd. for $C_{32}H_{28}NNaOP^+$ ($M+Na^+$) 496.1801, found: 496.1805.

diphenyl(1-(m-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3q**): m.p.: 71.6-72.8 °C, light yellow solid (22.7 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.57 (m, 4H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.13 (t, *J* = 8.7 Hz, 7H), 7.00 (s, 1H),

6.93 (d, *J* = 3.5 Hz, 1H), 6.81 (d, *J* = 6.9 Hz, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 2.32 (s, 6H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 148.7, 141.3, 136.2, 133.8, 131.9, 131.8, 131.4, 130.9 (d, *J* = 109.4 Hz), 128.8, 128.7, 128.4, 124.7, 119.0, 118.7, 112.6, 112.5, 110.8, 55.8, 31.2, 29.8, 21.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.39. HRMS (ESI) calcd. for $C_{36}H_{37}NO_2P^+$ ($M+H^+$) 546.2556, found: 546.2550.

(7-methoxy-1-(p-tolyl)-9H-pyrrolo[1,2-a]indol-2-yl)di-p-tolylphosphine oxide (**3r**): m.p.: 83.1-84.5 °C, light yellow solid (22.0 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.56 (m, 4H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.17-7.10 (m, 5H), 7.01-7.94 (m, 3H), 6.86 (d, *J* = 4.0 Hz, 1H), 6.83-6.78(m, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 2.34 (s, 6H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 141.4, 136.2, 135.4, 134.9, 133.8, 131.9, 131.8, 131.6, 131.0 (d, *J* = 109.7 Hz), 128.8, 128.7, 128.7, 128.5, 121.8, 119.1, 118.9, 112.6, 112.5, 110.8, 55.8, 29.9, 21.6, 21.1. ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.02. HRMS (ESI) calcd. for $C_{33}H_{31}NO_2P^+$ ($M+H^+$) 504.2087, found: 504.2083.

bis(4-bromophenyl)(1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3s**): m.p.: 238.2-239.7 °C, light yellow solid (25.3 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 6H), 7.50 – 7.44 (m, 5H), 7.33 – 7.27 (m, 2H), 7.18 (t, *J* = 7.5 Hz, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 4.0 Hz, 1H), 4.02 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 135.7, 135.5, 134.5, 133.9, 133.4, 133.3, 132.5 (d, *J* = 109.0 Hz), 131.5, 131.4, 128.7, 128.2, 127.8, 127.4, 126.7, 126.6, 126.5, 126.3, 124.9, 122.0, 121.9, 119.3, 119.1, 116.9, 115.7, 110.7, 29.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.88. $C_{29}H_{21}Br_2NOP^+$($M+H^+$) 587.9722, f ound: 587.9721.

bis(4-methoxyphenyl)(1-phenyl-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3t**): m.p.: 183.4-185.2 °C, light yellow solid (22.3 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.65 – 7.61 (m, 5H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.19 – 7.14 (m, 3H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 4.1 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.2 Hz, 4H), 4.01 (s, 2H), 3.79 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 161.9, 139.8, 135.4, 135.3, 134.5, 134.4, 133.7, 133.5, 131.8, 129.5, 128.7, 128.6, 128.0, 127.8(d, *J* = 104.0 Hz), 127.7, 126.2, 126.0, 125.9, 125.0, 124.5, 121.8, 121.7, 119.4, 119.1, 118.9, 117.7, 113.7, 113.6, 110.5, 55.3, 29.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.11. $C_{31}H_{26}NNaO_3P^+$($M+Na^+$)514.1543, found: 514.1546.

bis(4-methoxyphenyl)(1-(thiophen-2-yl)-9H-pyrrolo[1,2-a]indol-2-yl)phosphine oxide (**3u**): m.p.: 213.7-214.9 °C, light yellow solid (18.6 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.61 (m, 6H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.30 (s, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 3.6 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 4.1 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.1 Hz, 4H), 4.02 (s, 2H), 3.80 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.88, 161.85, 139.77, 135.40, 135.30, 134.48, 134.37, 133.64, 133.53, 131.81, 129.48, 128.71, 128.59, 128.27, 128.00, 127.86, 127.68, 127.23, 126.4 (d, *J* = 106.3 Hz),

126.15, 126.03, 125.01, 124.91, 124.53, 121.78, 121.70, 119.34, 119.13, 118.86, 117.68, 113.67, 113.54, 110.48, 77.37, 77.05, 76.74, 55.25, 29.64. ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.83. $C_{29}H_{25}NO_3PS^+(M+H^+)$ 498.1287, found: 498.1289.

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Supporting Information:

^{1}H, ^{31}P, ^{19}F and ^{13}C NMR spectra of compounds **3a**-**3u**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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