Trifluoroborane-Catalyzed C-H Functionalization/S-H Insertion Reaction:
Construction of $N,S$-Acetal Quaternary Centers

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General Comments.

All reactions and manipulations were performed using standard Schlenk techniques. Solvents were dried and distilled prior to use according to the standard methods. Unless otherwise indicated, all materials were obtained from commercial sources, and used as purchased without dehydration. Flash column chromatography was performed on silica gel (particle size 10-40 μm, Ocean Chemical Factory of Qingdao, China). Nitrogen gas (99.999%) was purchased from Boc Gas Inc. ¹H NMR, ¹³C NMR and ³¹P NMR spectra were recorded in CDCl₃ at Bruker 400 MHz spectrometers, TMS served as internal standard (δ = 0 ppm) for ¹H NMR and ¹³C NMR, H₃PO₄ served as internal standard (δ = 0 ppm) for ³¹P NMR. The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer. Melting points were determined on a T-4 melting point apparatus (uncorrected). Optical rotations were recorded on a Perkin Elemer 241 Polarimeter.

The synthesis pathway of α-diazophosphonate 1:¹
General procedure for the preparation of 3 and 4:

3.6 μL BF₃·Et₂O (0.028 mmol) and 1.4 mmol mercaptan or thiophenol dissolved in 2 mL dry CH₂Cl₂ was injected to an oven-dried Schlenk tube under nitrogen. Dialkyl α-diazoephosphonates 1 (0.28 mmol) was diluted with 2 mL of dry CH₂Cl₂ and was drawn into a gastight syringe. It was then added to the reaction mixture dropwise over a period of 1.5h with the help of a syringe pump. After the addition was complete, the reaction mixture was stirred for another 6 hour at 25 °C. The solvent was then removed under reduced pressure and the crude residue was purified by silica gel chromatography with the eluent (CH₂Cl₂/EtOAc = 15:1) to afford the corresponding products 3 and 4.

Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-(ethylthio)propyl)phosphonate (3a):

Colourless oil; ¹H NMR (400 MHz, CDCl₃): δ 7.80-7.82 (m, 2H, Ph), 7.69-7.71 (m, 2H, Ph), 3.93-4.07 (m, 5H, 2OCH₂, CH₂-P), 2.72-2.80 (m, 1H, S CH₂), 2.55-2.68 (m, 1H, S CH₂), 2.41 (s, 3H, CH₃), 2.15-2.26 (m, 1H, CH₂-P), 1.18 (dd, J = 15.6, 7.4 Hz, 6H, 2CH₃), 1.11 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 168.64 (s, C=O), 134.07, 131.65, 123.06 (s, Ph), 65.24 (d, J = 5.0 Hz, N-C), 61.77 (d, J = 3.0 Hz, OCH₂), 61.71 (d, J = 3.0 Hz, OCH₂), 36.58 (d, J = 135.2 Hz, C-P), 27.92 (s, CH₃), 23.90 (d, J = 2.8 Hz, S CH₂), 16.24 (d, J = 6.4 Hz, CH₃), 16.12 (d, J = 6.4 Hz, CH₃), 13.72 (s, CH₃); ³¹P NMR (162 MHz, CDCl₃): δ 24.22 (s); ESI-HRMS calcd for [C₁₇H₂₄NO₅PS, M+Na]⁺: 408.1005, Found: 408.1007.
Diethyl (2-(1,3-dioxoisindolin-2-yl)-2-(ethylthio)-3-methylbutyl)phosphonate (3b):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.77-7.83 (m, 2H, Ph), 7.66-7.71 (m, 2H, Ph), 3.97-4.09 (m, 4H, 2OCH$_2$), 3.62-3.72 (m, 1H, CH), 3.25 (dd, $J$ = 20.7, 15.6 Hz, 1H, CH$_2$P), 2.90-3.00 (m, 1H, SCH$_2$), 2.74-2.87 (m, 2H, SCH$_2$, CH$_2$P), 1.14-1.23 (m, 15H, 5CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 169.10 (s, C=O), 133.91, 131.74, 122.96 (s, Ph), 62.04 (d, $J$ = 5.2 Hz, N-C), 61.78 (d, $J$ = 3.3 Hz, OCH$_2$), 61.72 (d, $J$ = 3.3 Hz, OCH$_2$), 33.99 (d, $J$ = 5.0 Hz, CH), 31.14 (d, $J$ = 139.1 Hz, C-P), 25.80 (s, SCH$_2$), 19.05 (s, CH$_3$), 18.26 (s, CH$_3$), 16.24 (d, $J$ = 2.6 Hz, CH$_3$), 16.18 (d, $J$ = 2.6 Hz, CH$_3$), 13.31 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 25.15 (s); ESI-HRMS calcd for [C$_{19}$H$_{28}$NO$_5$PS, M+Na]$^+$: 436.1318, Found: 436.1320.
Diethyl (2-(1,3-dioxoisindolin-2-yl)-2-(ethylthio)-4-methylpentyl)phosphonate (3c):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.80-7.84 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 4.00-4.13 (m, 4H, 2OCH$_2$), 3.49 (dd, $J = 18.6$, 15.9 Hz, 1H, CH$_2$P), 3.02 (dd, $J = 20.2$, 15.8 Hz, 1H, CH$_2$P), 2.71-2.86 (m, 2H, SCH$_2$), 2.59-2.69 (m, 2H, CH$_2$), 1.95-2.06 (m, 1H, CH), 1.27 (t, $J = 7.0$ Hz, 3H, CH$_3$), 1.22 (t, $J = 7.0$ Hz, 3H, CH$_3$), 1.17 (t, $J = 7.5$ Hz, 3H, CH$_3$), 1.11 (d, $J = 6.6$ Hz, 3H, CH$_3$), 1.04 (d, $J = 6.6$ Hz, 3H, CH$_3$);

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.81 (s, C=O), 134.09, 131.46, 123.05 (s, Ph), 70.87 (d, $J = 1.5$ Hz, N-C), 61.82 (d, $J = 6.6$ Hz, OCH$_2$), 61.64 (d, $J = 6.6$ Hz, OCH$_2$), 42.69 (s, CH$_2$), 32.62 (d, $J = 141.4$ Hz, C-P), 25.14 (s, CH), 24.51 (s, CH$_3$), 24.17 (s, CH$_3$), 23.81 (s, SCH$_2$), 16.35 (d, $J = 6.4$ Hz, CH$_3$), 16.27 (d, $J = 6.4$ Hz, CH$_3$), 12.94 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.55 (s); ESI-HRMS calcd for [C$_{20}$H$_{30}$NO$_5$PS, M+Na]$^+$: 450.1475, Found: 450.1472.
Diethyl (2-(1,3-dioxoisooindolin-2-yl)-2-(ethylthio)-3-phenylpropyl)phosphonate (3d):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.82 (m, 2H, Ph), 7.68-7.73 (m, 2H, Ph), 7.45-7.50 (m, 2H, Ph), 7.21-7.26 (m, 3H, Ph), 4.25 (d, $J$ = 14.1 Hz, 1H, CH$_2$), 4.04-4.14 (m, 3H, CH$_2$, OCH$_2$), 3.93-4.03 (m, 2H, OCH$_2$), 3.26 (dd, $J$ = 18.4, 15.9 Hz, 1H, CH$_3$P), 2.60-2.80 (m, 3H, CH$_2$P, SCH$_2$), 1.26 (t, $J$ = 7.1 Hz, 3H, CH$_3$), 1.17 (t, $J$ = 7.5 Hz, 3H, CH$_3$), 1.13 (t, $J$ = 7.1 Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.62 (s, C=O), 135.76, 134.19, 131.75, 131.40, 127.93, 127.04, 123.14 (s, Ph), 70.72 (s, C-N), 62.01 (d, $J$ = 6.6 Hz, OCH$_2$), 61.62 (d, $J$ = 6.6 Hz, OCH$_2$), 39.77 (s, CH$_2$), 31.97 (d, $J$ = 140.4 Hz, C-P), 24.11 (s, SCH$_2$), 16.37 (d, $J$ = 6.1 Hz, CH$_3$), 16.16 (d, $J$ = 6.1 Hz, CH$_3$), 12.99 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.47 (s); ESI-HRMS calcd for [C$_{23}$H$_{28}$NO$_5$PS, M+Na]$^+$: 484.1318, Found: 484.1323.
Diethyl (2,6-bis(1,3-dioxoisindolin-2-yl)-2-(p-tolylthio)hexyl)phosphonate (3e):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.93-7.99 (m, 2H, Ph), 7.80-7.87 (m, 4H, Ph), 7.75-7.80 (m, 2H, Ph), 7.25 (d, $J$ = 7.8 Hz, 2H, Ph), 7.05 (d, $J$ = 7.8 Hz, 2H, Ph), 4.03-4.14 (m, 4H, 2OCH$_2$), 3.82-3.94 (m, 3H, CH$_2$P, CH$_2$), 2.90 (dd, $J$ = 18.9, 8.3 Hz, 1H, CH$_3$P), 2.53-2.72 (m, 2H, CH$_2$), 2.35 (s, 3H, CH$_3$), 1.95-2.04 (m, 1H, CH$_2$), 1.74-1.91 (m, 3H, CH$_2$), 1.27 (t, $J$ = 7.1 Hz, 3H, CH$_3$), 1.21 (t, $J$ = 7.1 Hz, 3H, CH$_3$), $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.40, 168.35 (s, C=O), 140.03, 136.67, 133.99, 133.88, 132.22, 131.44, 129.79 (s, Ph), 127.08 (d, $J$ = 3.5 Hz, Ph), 123.18, 122.98 (s, Ph), 73.53 (d, $J$ = 3.7 Hz, N-C), 61.75 (s, OCH$_2$), 38.23 (s, CH$_2$), 34.72 (s, CH$_2$), 31.15 (d, $J$ = 136.9 Hz, C-P), 28.60 (s, CH$_3$), 22.23 (s, CH$_2$), 21.26 (s, CH$_2$), 16.21 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.17 (s); ESI-HRMS calcd for [C$_{33}$H$_{35}$N$_2$O$_7$PS, M+Na]$^+$: 657.1795, Found: 657.1797.
4-(3-(Diethoxyphosphoryl)-2-(1,3-dioxoisooindolin-2-yl)-2-(\(\rho\)-tolylthio)propyl)phenyl acetate (3f):

White solid; m.p: 165-168 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.73-7.79 (m, 4H, Ph), 7.69-7.73 (m, 2H, Ph), 7.29 (d, \(J = 6.5\) Hz, 2H, Ph), 7.06 (d, \(J = 8.2\) Hz, 2H, Ph), 6.96 (d, \(J = 8.2\) Hz, 2H, Ph), 4.37 (d, \(J = 14.4\) Hz, 1H, CH\(_2\)), 4.20 (d, \(J = 14.4\) Hz, 1H, CH\(_2\)), 4.05-4.15 (m, 2H, OCH\(_2\)), 3.93-4.04 (m, 2H, OCH\(_2\)), 3.39 (dd, \(J = 18.4, 16.1\) Hz, 1H, CH\(_2\)P), 2.67 (dd, \(J = 19.8, 15.7\) Hz, 1H, CH\(_2\)P), 2.31 (s, 3H, CH\(_3\)), 2.24 (s, 3H, CH\(_3\)), 1.27 (t, \(J = 7.1\) Hz, 3H, CH\(_3\)), 1.14 (t, \(J = 7.1\) Hz, 3H, CH\(_3\)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 169.43, 168.32 (s, C=O), 149.79, 139.91, 136.69, 134.07, 133.67, 133.18, 131.32, 129.76, 127.50, 122.90, 120.98 (s, Ph), 73.03 (d, \(J = 2.2\) Hz, N-C), 62.08 (d, \(J = 6.5\) Hz, OCH\(_2\)), 61.65 (d, \(J = 6.5\) Hz, OCH\(_2\)), 40.09 (s, CH\(_2\)), 32.28 (d, \(J = 138.1\) Hz, C-P), 21.18 (s, CH\(_3\)), 16.32 (d, \(J = 6.2\) Hz, CH\(_3\)), 16.13 (d, \(J = 6.2\) Hz, CH\(_3\)); \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta\) 24.52 (s); ESI-HRMS calcd for [C\(_{30}\)H\(_{32}\)NO\(_7\)PS, M+Na\(^+\)]: 604.1529, Found: 604.1525.
Diethyl(2-(1,3-dioxoisooindolin-2-yl)-4-(methylthio)-2-(ρ-tolylthio)butyl)phosphonate (3g):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75-7.79 (m, 2H, Ph), 7.68-7.72 (m, 2H, Ph), 7.22 (d, $J$ = 8.0 Hz, 2H, Ph), 6.99 (d, $J$ = 8.0 Hz, 2H, Ph), 3.95-4.09 (m, 4H, 2OCH$_2$), 3.79-3.90 (m, 1H, CH$_2$P), 2.81-3.15 (m, 4H, 2CH$_2$), 2.45 (dd, $J$ = 19.6, 15.7 Hz, 1H, CH$_2$P), 2.27 (s, 3H, CH$_3$), 2.16 (s, 3H, CH$_3$), 1.22 (t, $J$ = 7.1 Hz, 3H, CH$_3$), 1.12 (t, $J$ = 7.1 Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.30 (s, C=O), 140.28, 136.83, 134.10, 131.34, 129.87(s, Ph), 126.69 (d, $J$ = 3.5 Hz, Ph), 123.04 (s, Ph), 72.83 (d, $J$ = 4.0 Hz, N-C), 61.92 (d, $J$ = 4.3 Hz, OCH$_2$), 61.86 (d, $J$ = 4.3 Hz, OCH$_2$), 35.28 (s, CH$_2$), 31.19 (d, $J$ = 136.8 Hz, C-P), 28.94 (s, CH$_2$), 21.29 (s, CH$_3$), 16.29 (d, $J$ = 6.4 Hz, CH$_3$), 16.16 (d, $J$ = 6.4 Hz, CH$_3$), 15.47 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 23.82 (s); ESI-HRMS calecd for [C$_{24}$H$_{30}$NO$_5$PS$_2$, M+Na]$^+$: 530.1195, Found: 530.1192.
Diethyl (2-(1,3-dioxoisindolin-2-yl)-2-(p-tolythio)propyl)phosphonate (3h):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.83 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 7.26 (d, $J = 8.0$ Hz, 2H, Ph), 7.04 (d, $J = 8.0$ Hz, 2H, Ph), 3.92-4.11 (m, 5H, 2OCH$_2$, CH$_2$P), 2.31 (s, 3H, CH$_3$), 2.21-2.29 (m, 4H, CH$_2$P, CH$_3$), 1.20 (t, $J = 7.1$ Hz, 3H, CH$_3$), 1.11 (t, $J = 7.1$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.23 (s, C=O), 140.16, 137.12, 134.05, 131.59, 129.79 (s, Ph), 127.23 (d, $J = 3.2$ Hz, Ph), 123.05 (s, Ph), 67.76 (d, $J = 5.0$ Hz, N-C), 61.75 (d, $J = 6.5$ Hz, OCH$_2$), 36.51 (d, $J = 134.8$ Hz, C-P), 27.96 (s, CH$_3$), 21.31 (s, CH$_3$), 16.25 (d, $J = 6.3$ Hz, CH$_3$), 16.14 (d, $J = 6.3$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.36 (s); ESI-HRMS calcd for [C$_{22}$H$_{26}$NO$_5$PS, M+Na]$^+$: 470.1162, Found: 470.1164.
Diethyl (2-(1,3-dioxoisooindolin-2-yl)-2-((4-fluorophenyl)thio)propyl)phosphonate (3i):

Colourless oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.73-7.81 (m, 2H, Ph), 7.66-7.71 (m, 2H, Ph), 7.28-7.36 (m, 2H, Ph), 6.89 (t, \(J = 8.5\) Hz, 2H, Ph), 3.90-4.06 (m, 5H, 2OCH\(_2\), CH\(_2\)P), 2.17-2.29 (m, 4H, CH\(_3\), CH\(_3\)P), 1.16 (t, \(J = 7.1\) Hz, 3H, CH\(_3\)), 1.08 (t, \(J = 7.1\) Hz, 3H, CH\(_3\)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 168.14 (s, C=O), 139.23, 139.14, 134.15, 131.47, 123.09, 116.30, 116.09 (s, Ph), 67.89 (d, \(J = 5.9\) Hz, N-C), 61.78 (s, OCH\(_2\)), 36.52 (d, \(J = 135.5\) Hz, C-P), 28.00 (s, CH\(_3\)), 16.24 (d, \(J = 6.3\) Hz, CH\(_3\)), 16.13 (d, \(J = 6.3\) Hz, CH\(_3\)); \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta\) 24.04 (s); ESI-HRMS calcld for [C\(_{21}\)H\(_{23}\)FNO\(_5\)PS, M+Na]\(^+\): 474.0911, Found: 474.0912.
Diethyl(2-(1,3-dioxoisindolin-2-yl)-2-((4-methoxyphenyl)thio)propyl)phosphonate (3j):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75-7.82 (m, 2H, Ph), 7.67-7.72 (m, 2H, Ph), 7.28 (d, $J = 8.7$ Hz, 2H, Ph), 6.73 (d, $J = 8.7$ Hz, 2H, Ph), 3.94-4.09 (m, 5H, 2OCH$_2$, CH$_2$P), 3.75 (s, 3H, OCH$_3$), 2.17-2.31 (m, 4H, CH$_3$, CH$_2$P), 1.18 (t, $J = 7.1$ Hz, 3H, CH$_3$), 1.10 (t, $J = 7.1$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.22 (s, C=O), 161.05, 138.73, 134.05, 131.57, 123.02, 114.48 (s, Ph), 67.80 (s, N-C), 61.73 (d, $J = 6.5$ Hz, OCH$_2$), 55.28 (s, OCH$_3$), 36.36 (d, $J = 134.7$ Hz, C-P), 27.89 (s, CH$_3$), 16.25 (d, $J = 6.3$ Hz, CH$_3$), 16.14 (d, $J = 6.3$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.42 (s); ESI-HRMS calcd for [C$_{22}$H$_{26}$NO$_6$PS, M+Na]$^+$: 486.1111, Found: 486.1113.
Diethyl (2-(1,3-dioxoisindolin-2-yl)-2-(o-tolylthio)propyl)phosphonate (3k):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.85 (m, 2H, Ph), 7.69-7.75 (m, 2H, Ph), 7.22-7.32 (m, 3H, Ph), 6.96-7.04 (m, 1H, Ph), 3.94-4.17 (m, 5H, 2OCH$_2$, CH$_2$P), 2.45 (s, 3H, CH$_3$), 2.32 (dd, $J = 20.1$, 15.4 Hz, 1H, CH$_2$P), 2.22 (s, 3H, CH$_3$), 1.20 (t, $J = 7.1$ Hz, 3H, CH$_3$), 1.11 (t, $J = 7.1$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.28 (s, C=O), 143.89, 138.23, 134.10, 131.64, 130.75 (s, Ph), 130.42 (d, $J = 2.8$ Hz, Ph), 130.07, 126.28, 123.09 (s, Ph), 68.48 (d, $J = 4.8$ Hz, N-C), 61.79 (d, $J = 2.1$ Hz, OCH$_2$), 61.72 (d, $J = 2.1$ Hz, OCH$_2$), 37.06 (d, $J = 134.2$ Hz, C-P), 27.64 (s, CH$_3$), 21.34 (s, CH$_3$), 16.26 (d, $J = 6.3$ Hz, CH$_3$), 16.13 (d, $J = 6.3$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.18 (s); ESI-HRMS calcd for [C$_{22}$H$_{26}$NO$_5$PS, M+Na]$^+$: 470.1162, Found: 470.1165.
Diethyl (2-(1,3-dioxoisooindolin-2-yl)-2-(isopropylthio)propyl)phosphonate (3l):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.77-7.82 (m, 2H, Ph), 7.65-7.70 (m, 2H, Ph), 3.82-4.04 (m, 5H, 2OCH$_2$, CH$_2$P), 3.18-3.32 (m, 1H, CH), 2.43 (s, 3H, CH$_3$), 2.17 (dd, $J = 19.9$, 15.4 Hz, 1H, CH$_2$P), 1.22 (d, $J = 6.9$ Hz, 3H, CH$_3$), 1.11-1.19 (m, 6H, 2CH$_3$), 1.07 (t, $J = 7.0$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 168.59 (s, C=O), 134.04, 131.73, 123.07 (s, Ph), 65.59 (d, $J = 4.4$ Hz, N-C), 61.71 (d, $J = 6.7$ Hz, OCH$_2$), 37.07 (d, $J = 134.2$ Hz, C-P), 34.55 (d, $J = 2.9$ Hz, CH), 28.02 (s, CH$_3$), 24.90 (s, CH$_3$), 24.41 (s, CH$_3$), 16.24 (d, $J = 6.4$ Hz, CH$_3$), 16.10 (d, $J = 6.4$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): δ 24.11 (s); ESI-HRMS calcd for [C$_{18}$H$_{26}$NO$_5$PS, M+Na]$^+$: 422.1162, Found: 422.1164.
Diethyl (2-(tert-butylthio)-2-(1,3-dioxoisindolin-2-yl)propyl)phosphonate (3m):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.80-7.84 (m, 2H, Ph), 7.67-7.73 (m, 2H, Ph), 3.82-4.07 (m, 5H, 2OCH$_2$, CH$_2$P), 2.55 (s, 3H, CH$_3$), 2.20 (dd, $J$ = 19.9, 15.3 Hz, 1H, CH$_2$P), 1.36 (s, 9H, 3CH$_3$), 1.18 (t, $J$ = 7.1 Hz, 3H, CH$_3$), 1.08 (t, $J$ = 7.1 Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.60 (s, C=O), 134.01, 131.81, 123.06 (s, Ph), 67.06 (d, $J$ = 4.0 Hz, N-C), 61.70 (d, $J$ = 6.6 Hz, OCH$_2$), 47.62 (s, S-C(Me)$_3$), 37.60 (d, $J$ = 133.8 Hz, C-P), 32.11 (s, CH$_3$), 29.78 (s, CH$_3$), 16.23 (d, $J$ = 6.3 Hz, CH$_3$), 16.07 (d, $J$ = 6.3 Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.00 (s); ESI-HRMS calcd for [C$_{19}$H$_{28}$NO$_5$PS, M+Na]$^+$: 436.1318, Found: 436.1320.
Dimethyl (2-(1,3-dioxoisoxindolin-2-yl)-2-ethylthio)propylphosphonate (3n):

Colourless oil; $^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ 7.74-7.95 (m, 2H, Ph), 7.57-7.74 (m, 2H, Ph), 3.97 (t, $J = 16.5$ Hz, 1H, CH$_2$P), 3.63 (d, $J = 11.0$ Hz, 3H, OCH$_3$), 3.60 (d, $J = 11.0$ Hz, 3H, OCH$_3$), 2.67-2.81 (m, 1H, SCH$_2$), 2.55-2.66 (m, 1H, SCH$_2$), 2.37 (s, 3H, CH$_3$), 2.22 (dd, $J = 20.1, 15.5$ Hz, 1H, CH$_2$P), 1.15 (t, $J = 7.5$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.71 (s, C=O), 134.09, 131.62, 123.11 (s, Ph), 65.13 (s, N-C), 52.60 (d, $J = 6.6$ Hz, OCH$_3$), 52.26 (d, $J = 6.6$ Hz, OCH$_3$), 35.83 (d, $J = 135.4$ Hz, C-P), 27.97 (s, CH$_3$), 23.95 (d, $J = 2.4$ Hz, SCH$_2$), 13.72 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 26.93 (s); ESI-HRMS calcd for [C$_{15}$H$_{20}$NO$_5$PS, M+Na]$^+$: 380.0692, Found: 380.0691.
Diisopropyl (2-(1,3-dioxoisoindolin-2-yl)-2-(ethylthio)propyl)phosphonate (3o):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.81-7.87 (m, 2H, Ph), 7.70-7.76 (m, 2H, Ph), 4.57-4.72 (m, 2H, 2OCH), 3.89-4.03 (m, 1H, CH$_2$P), 2.72-2.88 (m, 1H, SCH$_2$), 2.58-2.69 (m, 1H, SCH$_2$), 2.44 (s, 3H, CH$_3$), 2.16 (dd, $J$ = 20.3, 15.3 Hz, 1H, CH$_2$P), 1.25-1.32 (m, 3H, CH$_3$), 1.21-1.25 (m, 6H, 2CH$_3$), 1.13-1.19 (m, 6H, 2CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.69 (s, C=O), 134.02, 131.78, 123.04 (s, Ph), 70.37 (m, OCH), 65.42 (d, $J$ = 4.9 Hz, N-C), 37.80 (d, $J$ = 136.1 Hz, C-P), 27.98 (d, $J$ = 1.5 Hz, CH$_3$), 24.04 (d, $J$ = 3.8 Hz, SCH$_2$), 23.96 (d, $J$ = 4.0 Hz, CH$_3$), 23.88 (d, $J$ = 3.9 Hz, CH$_3$), 23.76 (d, $J$ = 4.6 Hz, CH$_3$), 13.77 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 22.35 (s); ESI-HRMS calcd for [C$_{19}$H$_{28}$NO$_5$PS, M+Na]$^+$: 436.1318, Found: 436.1320.
Dibutyl (2-(1,3-dioxoisindolin-2-yl)-2-(ethylthio)propyl)phosphonate (3p):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.85 (m, 2H, Ph), 7.66-7.75 (m, 2H, Ph), 3.88- 4.05 (m, 5H, 2OCH$_2$, CH$_2$P), 2.69-2.84 (m, 1H, SCH$_2$), 2.56-2.68 (m, 1H, SCH$_2$), 2.41 (s, 3H, CH$_3$), 2.14-2.28 (m, 1H, CH$_2$P), 1.46-1.54 (m, 2H, CH$_2$), 1.37-1.45 (m, 2H, CH$_2$), 1.23-1.33 (m, 4H, 2CH$_2$), 1.17 (t, $J = 7.5$ Hz, 3H, CH$_3$), 0.86 (t, $J = 7.4$ Hz, 3H, CH$_3$), 0.81 (t, $J = 7.4$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.66 (s, C=O), 134.05, 131.70, 123.09 (s, Ph), 65.50 (s, OCH$_2$), 65.29 (d, $J = 4.6$ Hz, N-C), 36.48 (d, $J = 135.1$ Hz, C-P), 32.39 (s, CH$_2$), 27.99 (s, CH$_3$), 23.93 (d, $J = 2.7$ Hz, SCH$_2$), 18.68 (d, $J = 4.1$ Hz, CH$_2$), 13.74 (s, CH$_3$), 13.57 (d, $J = 1.6$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.35 (s); ESI-HRMS calcd for [C$_{21}$H$_{32}$NO$_5$PS, M+Na]$^+$: 464.1631, Found: 464.1636.
Diethyl (2-(1,3-dioxoindolin-2-yl)-3-phenyl-2-(p-tolylthio)propyl)phosphonate (3q):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.73-7.78 (m, 2H, Ph), 7.67-7.71 (m, 4H, Ph), 7.27-7.36 (m, 5H, Ph), 6.95 (d, $J = 7.9$ Hz, 2H, Ph), 4.35 (d, $J = 14.3$ Hz, 1H, CH$_2$), 4.20 (d, $J = 14.3$ Hz, 1H, CH$_2$), 4.09-4.17 (m, 2H, OCH$_2$), 3.99-4.07 (m, 2H, OCH$_2$), 3.77 (dd, $J = 18.4$, 15.9 Hz, 1H, CH$_2$P), 2.79 (dd, $J = 20.0$, 15.7 Hz, 1H, CH$_2$P), 2.23 (s, 3H, CH$_3$), 1.29 (t, $J = 7.1$ Hz, 3H, CH$_3$), 1.18 (t, $J = 7.1$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.36 (s, C=O), 139.81, 136.68, 136.10, 134.06, 132.04, 131.30, 129.72, 127.98, 127.64, 127.02, 122.88 (s, Ph), 73.10 (d, $J = 1.7$ Hz, N-C), 62.05 (d, $J = 6.6$ Hz, OCH$_2$), 61.64 (d, $J = 6.6$ Hz, OCH$_2$), 40.61 (s, CH$_2$), 32.62 (d, $J = 138.9$ Hz, C-P), 21.18 (s, CH$_3$), 16.34 (d, $J = 6.4$ Hz, CH$_3$), 16.19 (d, $J = 6.4$ Hz, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.69 (s);

ESI-HRMS calcd for [C$_{28}$H$_{30}$NO$_5$PS, M+Na]$^+$: 546.1475, Found: 546.1477.
Diisopropyl(2-(1,3-dioxoisoindolin-2-yl)-2-(ethylthio)-3-phenylpropyl)phosphonate (3r):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.77-7.85 (m, 2H, Ph), 7.67-7.73 (m, 2H, Ph), 7.52 (d, $J$ = 6.5 Hz, 2H, Ph), 7.21-7.29 (m, 3H, Ph), 4.54-4.77 (m, 2H, 2OCH), 4.29 (d, $J$ = 14.1 Hz, 1H, CH$_2$), 4.12 (d, $J$ = 14.1 Hz, 1H, CH$_2$), 3.23 (dd, $J$ = 18.9, 15.9 Hz, 1H, CH$_2$P), 2.71-2.83 (m, 1H, SCH$_2$), 2.59-2.68 (m, 1H, SCH$_2$), 2.53 (dd, $J$ = 20.1, 15.6 Hz, 1H, CH$_2$P), 1.22-1.29 (m, 6H, 2CH$_3$), 1.12-1.19 (m, 6H, 2CH$_3$), 1.06 (d, $J$ = 6.2 Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.61 (s, C=O), 135.93, 134.12, 131.97, 131.54, 127.80, 126.97, 123.10 (s, Ph), 70.94 (d, $J$ = 2.7 Hz, N-C), 70.73 (d, $J$ = 6.8 Hz, OCH), 70.25 (d, $J$ = 6.8 Hz, OCH), 39.56 (s, CH$_2$), 32.96 (d, $J$ = 139.8 Hz, C-P), 24.10 (d, $J$ = 3.6 Hz, SCH$_2$), 23.92 (d, $J$ = 4.4 Hz, CH$_3$), 23.72 (d, $J$ = 4.4 Hz, CH$_3$), 12.99 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 22.53 (s); ESI-HRMS calcd for [C$_{25}$H$_{32}$NO$_5$PS, M+Na]$^+$: 512.1631, Found: 512.1635.
Dibutyl (2-(1,3-dioxoisindolin-2-yl)-2-(ethylthio)-3-phenylpropyl)phosphonate (3s):

Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.77-7.82 (m, 2H, Ph), 7.67-7.72 (m, 2H, Ph), 7.46 (d, $J = 6.1$ Hz, 2H, Ph), 7.20-7.27 (m, 3H, Ph), 4.25 (d, $J = 14.1$ Hz, 1H, CH$_2$), 4.10 (d, $J = 14.1$ Hz, 1H, CH$_2$), 3.96-4.05 (m, 2H, OCH$_2$), 3.87-3.95 (m, 2H, OCH$_2$), 3.26 (dd, $J = 18.5$, 15.9 Hz, 1H, CH$_2$P), 2.59-2.82 (m, 3H, SCH$_2$, CH$_2$P), 1.51-1.63 (m, 2H, CH$_2$), 1.39-1.48 (m, 2H, CH$_2$), 1.30-1.37 (m, 2H, CH$_2$), 1.22-1.29 (m, 2H, CH$_2$), 1.17 (t, $J = 7.5$ Hz, 3H, CH$_3$), 0.88 (t, $J = 7.4$ Hz, 3H, CH$_3$), 0.81 (t, $J = 7.4$ Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.60 (s, C=O), 135.78, 134.17, 131.76, 131.40, 127.91, 127.03, 123.14 (s, Ph), 70.74 (s, N-C), 65.76 (d, $J = 6.8$ Hz, OCH$_2$), 65.40 (d, $J = 6.8$ Hz, OCH$_2$), 39.73 (s, CH$_2$), 32.53 (d, $J = 6.5$ Hz, CH$_2$), 32.40 (s, CH$_2$), 31.76 (d, $J = 116.0$ Hz, C-P), 24.13 (s, SCH$_2$), 18.77 (s, CH$_2$), 18.68 (s, CH$_2$), 13.60 (d, $J = 4.2$ Hz, CH$_3$), 13.00 (s, CH$_3$); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 24.57 (s); ESI-HRMS calcd for [C$_{27}$H$_{36}$NO$_5$PS, M+Na]$^+$: 540.1944, Found: 540.1950.
(Z)-diethyl 2-(1,3-dioxoisoindolin-2-yl)-4-(methylthio)but-1-enylphosphonate (4g):

Colorless oil; yield: 0.053g (57%).

\[^1\]H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta 7.86-7.94\) (m, 2H, Ph), \(7.72-7.77\) (m, 2H, Ph), \(5.98\) (d, \(J = 9.7\) Hz, 1H, \(=CH\)), \(3.99-4.10\) (m, 4H, 2OCH\textsubscript{2}), \(2.76-2.84\) (m, 2H, CH\textsubscript{2}), \(2.64-2.74\) (m, 2H, CH\textsubscript{2}), \(2.12\) (s, 3H, SCH\textsubscript{3}), \(1.27\) (t, \(J = 7.1\) Hz, 6H, 2CH\textsubscript{3}).

\[^{13}\]C NMR (101 MHz, CDCl\textsubscript{3}): \(\delta 166.86\) (s, C=O), \(148.49\) (s, N-C=), \(134.12, 132.23, 123.71\) (s, Ph), \(118.63\) (d, \(J = 184.5\) Hz, \(=C-P\)), \(62.14\) (d, \(J = 5.0\) Hz, OCH\textsubscript{2}), \(37.35\) (d, \(J = 15.6\) Hz, CH\textsubscript{2}), \(30.72\) (s, CH\textsubscript{2}), \(16.24\) (d, \(J = 6.5\) Hz, CH\textsubscript{3}), \(15.39\) (s, CH\textsubscript{3}).

\(^{31}\)P NMR (162 MHz, CDCl\textsubscript{3}): \(\delta 11.84\) (s).

ESI-HRMS calcd for [C\textsubscript{17}H\textsubscript{22}NO\textsubscript{5}PS, M+H]\textsuperscript{+}: 384.1029, Found: 384.1031.
Single Crystal X-Ray Analysis 3e (CCDC 969832 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk.)

Table 1. Crystal data and structure refinement for shelx.

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<td></td>
<td>b = 9.4953(19) Å, β = 95.99(3)°</td>
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<td></td>
<td>c = 23.856(5) Å, γ = 90°</td>
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<td>Z, Calculated density</td>
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<td>Theta range for data collection</td>
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<td>Limiting indices</td>
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<tr>
<td>Reflections collected / unique</td>
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<td>Absorption correction</td>
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Max. and min. transmission        0.9752 and 0.9592
Refinement method               Full-matrix least-squares on F^2
Data / restraints / parameters   5204/248/436
Goodness-of-fit on F^2           1.024
Final R indices [I>2sigma(I)]    R1 = 0.0771, wR2 = 0.2364
R indices (all data)             R1 = 0.0941, wR2 = 0.2577
Extinction coefficient           0.040(6)
Largest diff. peak and hole      0.476 and -0.340 e.A^-3

Reference: