Supporting Information
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Supporting Information

Ag-Catalyzed [3 + 3] Annulation of Glycine Imino Esters with Seyferth-Gilbert Reagent to access Tetrahydro-1,2,4-triazine-carboxylate Esters

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General information

$^1$H, $^{13}$C, $^{31}$P, and $^{19}$F NMR spectra were recorded on Bruker AV 400 MHz instrument at 400 MHz ($^1$H NMR), 100 MHz ($^{13}$C NMR), 162 MHz ($^{31}$P NMR), and 376 MHz ($^{19}$F NMR), respectively. Chemical shifts were reported in ppm down field from internal Me$_4$Si and external CHCl$_3$, respectively. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), pentet (p), m (multiplet). Coupling constants were reported in Hertz (Hz). High resolution mass spectrometry (HRMS) spectra were obtained on a Bruker miorOTOF-QII instrument. Melting points were measured on a SGW X-4A digital melting point apparatus and are uncorrected. X-ray structural analysis was conducted on the XtaLAB mini instrument. The diastereomeric ratio (dr) of the tetrahydro-1,2,4-triazine-carboxylate ester products 3 were determined by $^{31}$P NMR spectroscopy.

Materials: Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone prior to use. CH$_2$Cl$_2$ was distilled from CaH$_2$. 1,4-Dioxane, DMF, DMSO, and NMP were dried with 4 Å molecular sieves prior to use. All purchased reagents were used without further purification. Flash chromatography separations were carried out using silica gel (200–300 mesh, Qingdao Marine Chemical Inc.). Glycine imino esters 1 and Seyferth-Gilbert reagent 2 were prepared according to the reported procedures.
General procedure for the [3+3] annulation reaction of glycine imino esters 1 with Seyferth-Gilbert reagent 2.

An oven-dried 10 mL Schlenk tube equipped with a stirring bar and capped with a rubber septum was charged with glycine imino ester (1, 1.5 equiv, 0.45 mmol), AgF (0.03 mmol, 10 mol %), and Cs₂CO₃ (1 equiv, 0.30 mmol). The tube was evacuated in vacuo and then backfilled with argon (for three times), and THF (1.5 mL) was transferred into the tube via a syringe under a positive argon pressure. Seyferth-Gilbert reagent 2 (1 equiv, 0.3 mmol) was then dissolved into THF (1.5 mL), and the resulting solution of 2 was transferred into the reaction mixture via syringe under the positive argon pressure. The resulting mixture was then stirred under an argon atmosphere at room temperature for 12 h. At this point, the reaction mixture was concentrated in vacuo with the aid of rotary evaporator. The residue was purified by flash chromatography on silica gel, eluted with petroleum ether/EtOAc followed by EtOAc/MeOH as eluents (20:1), to afford the title compounds 3. The diastereomeric ratio (dr) of the isolated compounds 3 were found to be identical to that of the crude products as determined by ³¹P NMR spectroscopy. Unless otherwise noted, the diastereomeric ratio (dr) of the isolated title compound 3 were >99:1.

Methyl 5-(4-chlorophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3a): The title compound was synthesized using the general procedure. Brown solid. 85.6 mg, 73% yield. M.p.: 120-122 °C. ¹H NMR (400 MHz, Chloroform-d) δ 7.34 – 7.29 (m, 2H), 7.25 – 7.21 (m, 2H), 5.73 (s, 1H), 5.56 (t, J = 2.2 Hz, 1H), 4.78 – 4.83 (m, 1H), 4.11 – 3.90 (m, 4H), 3.86 (s, 3H), 3.21 – 3.17 (m,
$^1$H, 1.24 (t, $J = 7.1$ Hz, 3H), 1.12 (t, $J = 7.1$ Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-$d$) $\delta$ 20.08 (p, $J = 8.0$ Hz). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 162.1, 138.7 (d, $J = 4.5$ Hz), 136.2, 134.5, 129.0, 128.8, 63.0 (d, $J = 6.7$ Hz), 62.7 (d, $J = 7.0$ Hz), 54.2, 53.1, 52.9 (d, $J = 154.1$ Hz), 16.5 (d, $J = 5.9$ Hz), 16.3 (d, $J = 6.1$ Hz).

HRMS (ESI) calcd for C$_{15}$H$_{22}$ClN$_3$O$_5$P$^+$ [M + H]$^+$ 390.0980; found m/z 390.0981.

Methyl 5-(4-bromophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3b): The title compound was synthesized using the general procedure. Pale yellow solid. 95.2 mg, 73% yield. M.p.: 134-136 °C. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.52 – 7.39 (m, 2H), 7.24 – 7.08 (m, 2H), 5.75 (s, 1H), 5.66 – 5.50 (m, 1H), 4.92 – 4.68 (m, 1H), 4.09 – 3.89 (m, 4H), 3.84 (s, 3H), 3.18 (dd, $J = 9.2$, 5.1 Hz, 1H), 1.22 (t, $J = 7.1$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-$d$) $\delta$ 20.09 (p, $J = 7.9$ Hz). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 162.0, 139.3 (d, $J = 4.7$ Hz), 136.1, 131.9, 129.1, 122.6, 63.0 (d, $J = 6.7$ Hz), 62.7 (d, $J = 7.0$ Hz), 54.1, 53.1, 52.8 (d, $J = 153.7$ Hz), 16.4 (d, $J = 5.8$ Hz), 16.2 (d, $J = 6.1$ Hz).

HRMS (ESI) calcd for C$_{15}$H$_{22}$BrN$_3$O$_5$P$^+$ [M + H]$^+$ 434.0475; found m/z 434.0479.

Methyl 6-(diethoxyphosphoryl)-5-(4-fluorophenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3c): The title compound was synthesized using the general procedure. Pale yellow solid. 49.7 mg, 44% yield. M.p.: 150-152 °C. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.28 – 7.24 (m, 2H), 7.01 (t, $J = 8.7$ Hz, 2H), 5.76 (s, 1H), 5.55 (t, $J = 2.2$ Hz, 1H), 4.85 – 4.75 (m, 1H), 4.08 – 3.88 (m, 4H), 3.84 (s, 3H), 3.18 (dd, $J = 9.1$, 5.4 Hz, 1H), 1.21 (t, $J = 7.1$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-$d$) $\delta$ 20.12 (p, $J = 8.1$ Hz). $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -113.2. $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 162.8 (d, $J = 247.5$ Hz).
(t, J = 3.8 Hz), 129.2 (d, J = 8.3 Hz), 115.6 (d, J = 21.6 Hz),
63.0 (d, J = 6.7 Hz), 62.6 (d, J = 7.0 Hz), 54.2, 53.1 (d, J = 154.1 Hz), 53.0, 16.4 (d, J = 5.8 Hz), 16.2 (d, J = 6.1 Hz). **HRMS** (ESI) calcd for C$_{13}$H$_{22}$F$_{3}$N$_{3}$O$_{5}$P$^+$ [M + H]$^+$ 374.1276; found m/z 374.1262.

**Methyl 5-(3,4-dichlorophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3d):** The title compound was synthesized using the general procedure. Pale yellow solid. 74.2 mg, 58% yield, dr = 96:4. **M.p:** 52-54 ºC. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.40 – 7.32 (m, 2H), 7.10 (dd, J = 8.3, 2.2 Hz, 1H), 5.82 (s, 1H), 5.73 (t, J = 2.1 Hz, 1H), 4.88 – 4.75 (m, 1H), 4.09 – 3.89 (m, 4H), 3.81 (s, 3H), 3.18 (dd, J = 9.4, 4.4 Hz, 1H), 1.21 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H). **$^{31}$P NMR** (162 MHz, Chloroform-d) δ 20.14 (p, J = 7.8 Hz). **$^{13}$C NMR** (101 MHz, Chloroform-d) δ 161.9, 141.1 (d, J = 5.9 Hz), 135.8, 132.8, 132.4, 130.6, 129.2, 126.5, 63.0 (d, J = 6.8 Hz), 62.8 (d, J = 7.1 Hz), 53.3 (d, J = 1.6 Hz), 53.0, 52.4 (d, J = 152.5 Hz), 16.4 (d, J = 5.7 Hz), 16.2 (d, J = 5.9 Hz). **HRMS** (ESI) calcd for C$_{15}$H$_{21}$Cl$_{2}$N$_{3}$O$_{5}$P$^+$ [M + H]$^+$ 424.0590; found m/z 424.0588.

**Methyl 6-(diethoxyphosphoryl)-5-(4-(methoxycarbonyl)phenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3e):** The title compound was synthesized using the general procedure. Pale yellow solid. 91.4 mg, 74% yield, dr = 94:6. **M.p.:** 48-50 ºC. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.96 – 7.90 (m, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.78 (s, 1H), 5.74 (d, J = 3.0 Hz, 1H), 4.88 – 4.72 (m, 1H), 4.07 – 3.87 (m, 4H), 3.83 (s, 3H), 3.79 (s, 3H), 3.20 (dd, J = 9.2, 4.5 Hz, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H). **$^{31}$P NMR** (162 MHz, Chloroform-d) δ 20.33 (p, J = 7.9 Hz). **$^{13}$C NMR** (101 MHz, Chloroform-d) δ 166.5, 161.9, 145.6 (d, J = 5.4 Hz), 135.9,
130.1, 129.9, 127.2, 62.9 (d, $J = 6.8$ Hz), 62.7 (d, $J = 7.0$ Hz), 54.1, 52.9, 52.3 (d, $J = 152.7$ Hz), 52.1, 16.3 (d, $J = 5.8$ Hz), 16.2 (d, $J = 6.0$ Hz). **HRMS** (ESI) calcd for $\text{C}_{17}\text{H}_{25}\text{N}_{3}\text{O}_{7}\text{P}^+$ 414.1425 [M + H]$^+$; found m/z 414.1430.

**Methyl 6-(diethoxyphosphoryl)-5-(3-nitrophenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3f):** The title compound was synthesized using the general procedure. Pale yellow solid. 53.8 mg, 45% yield, dr = 95:5. **M.p.:** 86-88 °C. **$^1$H NMR** (400 MHz, Chloroform- $d$) $\delta$ 8.17 – 8.11 (m, 2H), 7.63 (dt, $J = 7.8$, 1.4 Hz, 1H), 7.57 – 7.48 (m, 1H), 5.85 (s, 1H), 5.82 – 5.75 (m, 1H), 4.51 – 4.97 (m, 1H), 4.17 – 3.92 (m, 4H), 3.85 (s, 3H), 3.30 – 3.25 (m, $J = 1$H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.13 (t, $J = 7.1$ Hz, 3H). **$^{31}$P NMR** (162 MHz, Chloroform- $d$) $\delta$ 19.96 (p, $J = 8.0$ Hz). **$^{13}$C NMR** (101 MHz, Chloroform- $d$) $\delta$ 161.9, 148.5, 143.1 (d, $J = 5.9$ Hz), 135.8, 133.3, 129.8, 123.4, 122.3, 63.1 (d, $J = 6.9$ Hz), 62.9 (d, $J = 7.0$ Hz), 53.7 (d, $J = 1.6$ Hz), 53.1, 52.5 (d, $J = 152.6$ Hz), 16.5 (d, $J = 5.7$ Hz), 16.3 (d, $J = 6.0$ Hz). **HRMS** (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{N}_{4}\text{O}_{7}\text{P}^+$ [M + H]$^+$; 401.1221; found m/z 401.1213.

**Methyl 6-(diethoxyphosphoryl)-5-(4-(trifluoromethyl)phenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3g):** The title compound was synthesized using the general procedure. Pale yellow solid. 94.5 mg, 75% yield, dr = 95:5. **M.p.:** 117-119 °C. **$^1$H NMR** (400 MHz, Chloroform- $d$) $\delta$ 7.59 (d, $J = 8.1$ Hz, 2H), 7.41 (d, $J = 8.1$ Hz, 2H), 5.78 (s, 1H), 5.67 (t, $J = 2.1$ Hz, 1H), 5.03 – 4.85 (m, 1H), 4.11 – 3.90 (m, 4H), 3.85 (s, 3H), 3.23 (dd, $J = 9.3$, 4.7 Hz, 1H)$^-$ 1.22 (t, $J = 7.1$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H). **$^{31}$P NMR** (162 MHz, Chloroform- $d$) $\delta$ 20.03 (p, $J = 7.6$ Hz). **$^{19}$F NMR** (376
MHz, Chloroform-\(d\) \(\delta\) -62.7. \(\text{\(^{13}\)C NMR}\) (101 MHz, Chloroform-\(d\)) \(\delta\) 162.0, 144.5 (d, \(J = 5.5\) Hz), 136.0, 130.9 (q, \(J = 32.6\) Hz), 127.8, 125.7 (q, \(J = 3.7\) Hz), 124.0 (q, \(J = 272.2\) Hz), 63.0 (d, \(J = 6.7\) Hz), 62.8 (d, \(J = 7.0\) Hz), 54.2, 53.1, 52.7 (d, \(J = 153.3\) Hz), 16.4 (d, \(J = 5.8\) Hz), 16.2 (d, \(J = 6.2\) Hz). \(\text{HRMS (ESI)}\) calcd for C\(_{16}\)H\(_{22}\)F\(_{3}\)O\(_{5}\)P\(^{+}\) [M + H]\(^{+}\); 424.1244; found m/z 424.1249.

**Methyl 5-(4-cyanophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3h):** The title compound was synthesized using the general procedure. Brown oil. 39.2 mg, yield, dr = 80:20, 34% yield. \(\text{\(^{1}H NMR}\) (400 MHz, Chloroform-\(d\)) \(\delta\) 7.66 – 7.62 (m, 2H), 7.45 – 7.39 (m, 2H), 5.79 (s, 1H), 5.71 – 5.66 (m, 1H), 4.93 – 4.97 (m, 1H), 4.13 – 3.95 (m, 4H), 3.87 (s, 3H), 3.24 (dd, \(J = 9.5, 4.2\) Hz, 1H), 1.26 (t, \(J = 7.1\) Hz, 3H), 1.16 (t, \(J = 7.1\) Hz, 3H). \(\text{\(^{31}\)P NMR}\) (162 MHz, Chloroform-\(d\)) \(\delta\) 20.00 (p, \(J = 7.8\) Hz). \(\text{\(^{13}\)C NMR}\) (101 MHz, Chloroform-\(d\)) \(\delta\) 162.0, 146.1 (d, \(J = 5.9\) Hz), 135.8, 132.6, 128.1, 118.4, 112.5, 63.1 (d, \(J = 6.9\) Hz), 63.0 (d, \(J = 7.4\) Hz), 54.0 (d, \(J = 1.6\) Hz), 53.2, 52.4 (d, \(J = 153.0\) Hz), 16.5 (d, \(J = 5.7\) Hz), 16.4 (d, \(J = 5.8\) Hz). \(\text{HRMS (ESI)}\) calcd for C\(_{16}\)H\(_{22}\)N\(_{4}\)O\(_{5}\)P\(^{+}\) [M + H]\(^{+}\) 381.1322; found m/z 381.1317.

**Methyl 6-(diethoxyphosphoryl)-5-(4-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3i):** The title compound was synthesized using the general procedure. Pale yellow solid. 35.0 mg, 30% yield. \(\text{M.p.:} 125-127^\circ\text{C}\). \(\text{\(^{1}H NMR}\) (400 MHz, Chloroform-\(d\)) \(\delta\) 7.24 – 7.15 (m, 2H), 6.92 – 6.81 (m, 2H), 5.73 (s, 1H), 5.47 (t, \(J = 2.2\) Hz, 1H), 4.72 – 4.77 (m, 1H), 4.06 – 3.87 (m, 4H), 3.84 (s, 3H), 3.77 (s, 3H), 3.18 (dd, \(J = 9.0, 5.9\) Hz, 1H), 1.21 (t, \(J = 7.0\) Hz, 3H), 1.09 (t, \(J = 7.0\) Hz, 3H). \(\text{\(^{31}\)P NMR}\) (162 MHz, Chloroform-\(d\)) \(\delta\) 20.28 (p, \(J = 7.9\) Hz). \(\text{\(^{13}\)C NMR}\) (101 MHz, Chloroform-\(d\)) \(\delta\) 162.2, 160.0, 136.6, 131.8 (d, \(J = 3.5\) Hz), 128.7, 114.2, 62.9 (d, \(J = 272.2\) Hz), 63.0 (d, \(J = 6.7\) Hz), 62.8 (d, \(J = 7.0\) Hz), 54.2, 53.1, 52.7 (d, \(J = 153.3\) Hz), 16.4 (d, \(J = 5.8\) Hz), 16.2 (d, \(J = 6.2\) Hz).
6.6 Hz), 62.5 (d, J = 6.8 Hz), 55.4, 54.6, 53.2 (d, J = 154.8 Hz), 53.0, 16.4 (d, J = 5.8 Hz), 16.2 (d, J = 6.2 Hz). \textbf{HRMS} (ESI) calcd for C$_{16}$H$_{25}$N$_{3}$O$_{6}$P$^+$ [M + H]$^+$ 386.1475; found m/z 386.1470.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{image1}
\caption{Structure of Methyl 6-(diethoxyphosphoryl)-5-(3-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3j).}
\end{figure}

**Methyl 6-(diethoxyphosphoryl)-5-(3-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3j):** The title compound was synthesized using the general procedure in the presence of 2 equiv of \textit{II}. Pale yellow oil. 66.8 mg, 58% yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.26 – 7.19 (m, 1H), 6.88 – 6.84 (m, 1H), 6.84 – 6.78 (m, 2H), 5.78 (s, 1H), 5.66 – 5.52 (m, 1H), 4.80 – 4.76 (m, 1H), 4.08 – 3.88 (m, 4H), 3.83 (s, 3H), 3.75 (s, 3H), 3.22 (dd, $J$ = 9.1, 5.2 Hz, 1H), 1.21 (t, $J$ = 7.1 Hz, 3H), 1.09 (t, $J$ = 7.1 Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-$d$) $\delta$ 20.42 (p, $J$ = 8.0 Hz). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 162.0, 159.9, 141.8 (d, $J$ = 4.6 Hz), 136.3, 129.8, 119.5, 113.9, 113.1, 62.9 (d, $J$ = 6.7 Hz), 62.6 (d, $J$ = 7.0 Hz), 55.3, 54.7, 53.0, 52.7 (d, $J$ = 153.6 Hz), 16.4 (d, $J$ = 5.8 Hz), 16.2 (d, $J$ = 6.2 Hz). \textbf{HRMS} (ESI) calcd for C$_{16}$H$_{25}$N$_{3}$O$_{6}$P$^+$ [M + H]$^+$: 386.1475; found m/z 386.1468.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{image2}
\caption{Structure of Methyl 6-(diethoxyphosphoryl)-5-(2-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3k).}
\end{figure}

**Methyl 6-(diethoxyphosphoryl)-5-(2-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3k):** The title compound was synthesized using the general procedure. Pale yellow solid. 35.5 mg, 31% yield. M.p.: 135-137 °C. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.26 – 7.22 (m, 1H), 7.18 (dd, $J$ = 7.7, 1.7 Hz, 1H), 6.92 (t, $J$ = 7.5 Hz, 1H), 6.85 (d, $J$ = 8.2 Hz, 1H), 5.89 (s, 1H), 5.62 (d, $J$ = 4.2 Hz, 1H), 5.32 – 5.28 (m, 1H), 4.16 – 3.96 (m, 4H), 3.85 (s, 3H), 3.82 (s, 3H), 3.51 (dd, $J$ = 9.2, 3.3 Hz, 1H), 1.27 (t, $J$ = 7.1 Hz, 3H), 1.21 (t, $J$ = 7.1 Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-$d$) $\delta$ 21.76 (p, $J$ = 7.6 Hz). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 162.1, 156.2, 136.1, 129.4, 129.3, 128.2, 120.8, 110.5, 62.7, 62.6, 55.4, 52.9, 50.1 (d, $J$ = 148.9 Hz), 49.1 (d, $J$ = 2.8 Hz), 16.5 (d, $J$ = 6.0 Hz), 16.4 (d, $J$ = 6.2 Hz). \textbf{HRMS} (ESI)
calcd for C_{16}H_{25}N_{3}O_{6}P^{+} [M + H]^{+} 386.1475; found m/z 386.1469

**Methyl 5-(3-(dibenzylamino)phenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3l):** The title compound was synthesized using the general procedure. Pale yellow oil. 61.4 mg, 37% yield. ¹H NMR (400 MHz, Chloroform-d) δ 7.33 – 7.28 (m, 4H), 7.28 – 7.20 (m, 6H), 7.16 – 7.08 (m, 1H), 6.73 – 6.59 (m, 3H), 5.72 (s, 1H), 5.46 (t, J = 2.1 Hz, 1H), 4.74 – 4.54 (m, 5H), 4.01 – 3.86 (m, 4H), 3.84 (s, 3H), 3.16 (dd, J = 8.9, 5.5 Hz, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H). ³¹P NMR (162 MHz, Chloroform-d) δ 20.42 (p, J = 7.7 Hz). ¹³C NMR (101 MHz, Chloroform-d) δ 162.0, 149.3, 140.9 (d, J = 3.9 Hz), 138.4, 136.3, 129.6, 128.7, 127.0, 126.7, 115.5, 112.8, 111.6, 62.8 (d, J = 6.6 Hz), 62.4 (d, J = 6.8 Hz), 55.3, 54.5, 52.9, 52.7 (d, J = 153.8 Hz), 16.4 (d, J = 5.9 Hz), 16.2 (d, J = 6.3 Hz). HRMS (ESI) calcd for C_{29}H_{36}N_{4}O_{5}P^{+} [M + H]^{+} 551.2418; found m/z 551.2424.

**Methyl 5-([1,1′-biphenyl]-4-yl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3m):** The title compound was synthesized using the general procedure. Pale yellow solid. 75.3 mg, 58% yield. M.p.: 165-167 °C. ¹H NMR (400 MHz, Chloroform-d) δ 7.60 – 7.53 (m, 4H), 7.48 – 7.40 (m, 2H), 7.39 – 7.31 (m, 3H), 5.78 (s, 1H), 5.61 (t, J = 2.1 Hz, 1H), 4.90 – 4.86 (m, 1H), 4.12 – 3.90 (m, 4H), 3.87 (s, 3H), 3.35 – 3.23 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H). ³¹P NMR (162 MHz, Chloroform-d) δ 20.26 (p, J = 8.0 Hz). ¹³C NMR (101 MHz, Chloroform-d) δ 162.2, 141.7, 140.6, 139.0 (d, J = 4.1 Hz), 136.4, 128.9, 127.9, 127.6, 127.5 127.1, 63.0 (d, J = 6.6 Hz), 62.6 (d, J = 6.9 Hz), 54.7, 53.04, 53.01 (d, J = 154.2 Hz), 16.5 (d, J = 5.9 Hz), 16.2 (d, J = 6.4 Hz). HRMS (ESI) calcd for C_{21}H_{27}N_{3}O_{5}P^{+} [M + H]^{+} 432.1683; found m/z 432.1688.
Methyl 6-(diethoxyphosphoryl)-5-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3n): The title compound was synthesized using the general procedure. Pale yellow solid. 30.0 mg, 28% yield. M.p.: 95-97 °C. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.38 – 7.27 (m, 5H), 5.79 (s, 1H), 5.55 (s, 1H), 4.84 – 4.80 (m, 1H), 4.08 – 3.87 (m, 4H), 3.86 (s, 3H), 3.24 (dd, $J$ = 9.0, 5.5 Hz, 1H), 1.22 (t, $J$ = 7.2 Hz, 3H), 1.08 (t, $J$ = 7.1 Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-d) $\delta$ 20.24 (p, $J$ = 7.6 Hz). $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 162.2, 139.9 (d, $J$ = 4.0 Hz), 136.5, 128.8, 128.7, 127.5, 63.0 (d, $J$ = 6.7 Hz), 62.6 (d, $J$ = 6.9 Hz), 55.0, 53.04, 53.01 (d, $J$ = 154.4 Hz), 29.8, 16.5 (d, $J$ = 5.7 Hz), 16.2 (d, $J$ = 6.3 Hz). HRMS (ESI) calcd for C$_{15}$H$_{23}$N$_3$O$_5$P$^+$ [M + H]$^+$ 356.1370; found m/z 356.1361.

Methyl 6-(diethoxyphosphoryl)-5-(naphthalen-2-yl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3o): The title compound was synthesized using the general procedure. Pale yellow oil. 81.2 mg, 69% yield. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.83 – 7.75 (m, 3H), 7.74 (d, $J$ = 1.8 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.35 (dd, $J$ = 8.6, 1.8 Hz, 1H), 5.78 (s, 1H), 5.71 (t, $J$ = 2.1 Hz, 1H), 5.06 – 4.92 (m, 1H), 4.07 – 3.85 (m, 4H), 3.84 (s, 3H), 3.32 (dd, $J$ = 9.1, 5.2 Hz, 1H), 1.15 (t, $J$ = 7.1 Hz, 3H), 0.97 (t, $J$ = 7.1 Hz, 3H). $^{31}$P NMR (162 MHz, Chloroform-d) $\delta$ 20.43 (p, $J$ = 8.0 Hz). $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 162.1, 137.4 (d, $J$ = 4.4 Hz), 136.4, 133.3, 133.1, 128.7, 128.0, 127.6, 126.8, 126.45, 126.40, 124.5, 62.9 (d, $J$ = 6.7 Hz), 62.5 (d, $J$ = 7.0 Hz), 54.9, 53.0, 52.8 (d, $J$ = 153.8 Hz), 16.3 (d, $J$ = 5.7 Hz), 16.0 (d, $J$ = 6.1 Hz). HRMS (ESI) calcd for C$_{19}$H$_{25}$N$_3$O$_5$P$^+$ [M + H]$^+$ 406.1526; found m/z 406.1532.
Methyl 6-(diethoxyphosphoryl)-5-(naphthalen-1-yl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3p): The title compound was synthesized using the general procedure. Pale yellow oil. 34.4 mg, 28% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.15 – 8.08 (m, 1H), 7.87 (dd, \(J = 8.0, 1.5\) Hz, 1H), 7.82 – 7.75 (m, 1H), 7.58 – 7.35 (m, 4H), 5.90 – 5.76 (m, 2H), 5.69 (s, 1H), 4.10 – 3.99 (m, 4H), 3.89 (s, 3H), 3.56 – 3.50 (m, 1H), 1.25 (t, \(J = 7.1\) Hz, 3H), 1.17 (t, \(J = 7.1\) Hz, 3H). \(^{31}\)P NMR (162 MHz, Chloroform-\(d\)) \(\delta\) 21.64 (p, \(J = 6.8\) Hz). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 162.2, 137.0 (d, \(J = 7.5\) Hz), 136.0, 133.9, 129.9, 129.2, 128.8, 126.8, 125.9, 125.4, 125.0, 122.3, 62.8 (d, \(J = 7.3\) Hz), 62.7 (d, \(J = 7.0\) Hz), 53.0, 51.3 (d, \(J = 148.4\) Hz), 50.5, 16.5 (d, \(J = 5.9\) Hz), 16.3 (d, \(J = 6.1\) Hz). HRMS (ESI) calcd for C\(_{19}\)H\(_{25}\)N\(_3\)O\(_5\)P\(^+\) [M + H]\(^+\) 406.1526; found m/z 406.1519.

Methyl 5-(anthracen-9-yl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3q): The title compound was synthesized using the general procedure. Pale yellow solid. 48.1 mg, 35% yield. M.p.: 213-215 °C. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.56 – 8.35 (m, 2H), 8.19 (d, \(J = 7.6\) Hz, 1H), 7.98 (d, \(J = 7.9\) Hz, 2H), 7.60 – 7.37 (m, 4H), 6.30 (t, \(J = 7.6\) Hz, 1H), 5.99 (s, 1H), 5.86 (d, \(J = 3.1\) Hz, 1H), 4.27 (dd, \(J = 9.5, 7.6\) Hz, 1H), 3.84 (s, 3H), 3.77 – 3.53 (m, 2H), 3.45 – 3.35 (m, 1H), 3.35 – 3.26 (m, 1H), 0.95 (t, \(J = 7.1\) Hz, 3H), 0.45 (t, \(J = 7.1\) Hz, 3H). \(^{31}\)P NMR (162 MHz, Chloroform-\(d\)) \(\delta\) 19.64 (p, \(J = 8.5\) Hz). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 162.0 (d, \(J = 1.9\) Hz), 136.4, 131.9, 131.5, 131.1, 129.84, 129.80, 129.2, 127.0, 126.6, 126.4, 125.0, 124.7, 124.0, 63.0 (d, \(J = 6.7\) Hz), 62.0 (d, \(J = 6.7\) Hz).
Hz), 53.0, 50.3, 49.4 (d, J = 159.8 Hz), 16.1 (d, J = 5.9 Hz), 15.3 (d, J = 6.5 Hz).

**HRMS** (ESI) calcd for C_{23}H_{27}N_{3}O_{5}P^+ [M + H]^+ 456.1683; found m/z 456.1687.

**Oxidation of 3a to 4.**

An oven-dried 10 mL Schlenk tube equipped with a stirring bar and capped with a rubber septum was charged with methyl 1,4,5,6-tetrahydro-1,2,4-triazine carboxylate 3a (0.2 mmol, 1 equiv), 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ, 0.4 mmol, 4 equiv), and THF (2 mL). The reaction mixture was then stirred at 50 °C in an oil bath for 12 h. At this point, the reaction mixture was concentrated *in vacuo* with the aid of rotary evaporator. The residue was extracted with EtOAc (20 mL) and saturated NaHCO₃ solution (20 mL). The aqueous layer was further extracted with EtOAc (10 mL x 2). The combined organic fraction was concentrated with the aid of rotary evaporator. The residue was purified by flash chromatography on silica gel using petroleum ether / EtOAc (3:2) as an eluent to afford the title compounds 4.

![Chemical Structure](image)

**Methyl 5-(4-chlorophenyl)-6-(diethoxyphosphoryl)-1,2,4-triazine-3-carboxylate (4).** Pale yellow solid. 67.0 mg, 87% yield. \(^1\)H NMR (400 MHz, Chloroform-d) δ 8.05 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 4.24 – 4.18 (m, 4H), 4.08 (s, 3H), 1.18 (t, J = 7.1 Hz, 6H). \(^{31}\)P NMR (162 MHz, Chloroform-d) δ 5.97 (p, J = 7.9 Hz). \(^{13}\)C NMR (101 MHz, Chloroform-d) δ 162.4 (d, J = 3.4 Hz), 159.7 (d, J = 21.2 Hz), 155.1 (d, J = 1.4 Hz), 154.0 (d, J = 217.8 Hz), 138.8, 132.8, 131.6, 129.0, 64.7, 64.7, 54.0, 16.1, 16.0.
References


NMR spectra

$^1$H NMR Spectrum of Methyl 5-(4-chlorophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3a).
$^{31}$P NMR Spectrum of (3a).

$^{13}$C NMR Spectrum of (3a).
$^1$H NMR Spectrum of Methyl 5-(4-bromophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3b).
$^{31}\text{P NMR Spectrum of (3b).}$

$^{13}\text{C NMR Spectrum of (3b).}$
$^1$H NMR Spectrum of Methyl 6-(diethoxycarbonyl)-5-(4-fluorophenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3c).
$^{31}$P NMR Spectrum of (3c).

$^{19}$F NMR Spectrum of (3c).
$^{13}$C NMR Spectrum of (3c).
The spectrum is a 96:4 mixture of both diastereoisomers.

\(^1\)H NMR Spectrum of Methyl 5-(3,4-dichlorophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3d).
$^{31}$P NMR Spectrum of (3d).

$^{31}$C NMR Spectrum of (3d).
The spectrum is a 94:6 mixture of both diastereoisomers.

$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(4-(methoxycarbonyl)phenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3e).
$^{19}$P NMR Spectrum of (3e).

$^{13}$C NMR Spectrum of (3e).
The spectrum is a 95:5 mixture of both diastereoisomers.

$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(3-nitrophenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3f).
$^{31}\text{P} \text{NMR Spectrum of (3f).}$

$^{13}\text{C} \text{NMR Spectrum of (3f).}$
The spectrum is a 95:5 mixture of both diastereoisomers.

$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(4-(trifluoromethyl)-phenyl)-1,4,5,6-tetrahydro- 1,2,4-triazine-3-carboxylate (3g).
$^{31}$P NMR Spectrum of (3g).

$^{19}$F NMR Spectrum of (3g).
$^{31}$C NMR Spectrum of (3g).
The spectrum is a 80:20 mixture of both diastereoisomers.

$^1$H NMR Spectrum of Methyl 5-(4-cyanophenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3h).
$^{31}$P NMR Spectrum of (3h).

$^{13}$C NMR Spectrum of (3h).
\(^1\text{H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(4-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3i).}\)
$^{31}\text{P NMR Spectrum of (3i).}$

$^{13}\text{C NMR Spectrum of (3i).}$
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(3-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3j).
$^{31}$P NMR Spectrum of (3j).

$^{13}$C NMR Spectrum of (3j).
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(2-methoxyphenyl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3k).
$^{31}P$ NMR Spectrum of (3k).

$^{13}C$ NMR Spectrum of (3k).
$^1$H NMR Spectrum of Methyl 5-(3-(dibenzylamino)phenyl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3l).
$^{31}$P NMR Spectrum of (3l).

$^{13}$C NMR Spectrum of (3l).

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$^{1}$H NMR Spectrum of Methyl 5-([1,1'-biphenyl]-4-yl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3m).
$^{31}$P NMR Spectrum of (3m).

$^{13}$C NMR Spectrum of (3m).
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3n):
$^{31}$P NMR Spectrum of (3n).

$^{13}$C NMR Spectrum of (3n).
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(naphthalen-2-yl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3o).
$^{31}$P NMR Spectrum of (3o).

$^{13}$C NMR Spectrum of (3o).
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(naphthalen-1-yl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3p).
$^{31}$P NMR Spectrum of (3p).

$^{13}$C NMR Spectrum of (3r).
$^1$H NMR Spectrum of Methyl 5-(anthracen-9-yl)-6-(diethoxyphosphoryl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (3q).
$^{31}$P NMR Spectrum of (3q).

$^{13}$C NMR Spectrum of (3q).
$^1$H NMR Spectrum of Methyl 6-(diethoxyphosphoryl)-5-(thiophen-2-yl)-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (4).
$^{31}$P NMR of (4).

$^{13}$C NMR of (4).
X-Ray Crystallographic Data of 3b

The X-ray crystallographic structures for 3b. ORTEP representation with 50% probability thermal ellipsoids. Crystal data have been deposited to CCDC with number 1977600. A racemic mixture of 3b existed in the X-ray crystallographic analysis.

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