Supporting Information

Experimental

General Experimental Methods

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware. Solutions or liquids were introduced to the round bottom flask using oven dried Hamilton syringes through rubber septa. Reactions performed using magnetic stirring were performed using Teflon-coated stirrer bars. Removal of solvents was achieved using a rotary evaporator at water aspirator pressure or under high vacuum (0.01 mm Hg).

Dichloromethane was distilled over calcium hydride.

Chemicals were purchased from Sigma-Aldrich Chemical Company. Phosphorodiamidite **11** and phosphoramidite **12** were synthesised in-house. Solvents for extractions and chromatography were of technical grade. Purification was carried out *via* flash chromatography using the Biotage purification system. Analytical TLC was performed with Merck Silica gel 60 F_{254} plates. Visualisation was accomplished by UV-light (λ= 254 nm) and/or staining with an anisaldehyde or ninhydrin solution, followed by heating. ^{1}H, ^{13}C, ^{31}P and 2D (H-COSY, HMQC) NMR spectra were recorded on Brüker advance DPX 400. TMS (0 ppm, ^{1}H NMR) and $CDCl_3$ (77 ppm, ^{13}C NMR) were used as internal references. The chemical shifts (δ) are reported in p.p.m (parts per million). High resolution mass spectrometry (HRMS) was recorded on a VG Quattro Triple Quadropole Mass Spectrometer (ES). The names of the compounds have been named according to standard IUPAC.

Experimental Data

*Synthesis of **11***: To a stirred solution of PCl_3 (1.37 g, 10.00 mmol, 1 eq) in dried $[C_4mpyrr][NTf_2]$ (8.44 g, 20.00 mmol, 2 eq) under an inert atmosphere of N_2, Hünig's Base (1.29 g, 10.00 mmol, 1 eq) was added. After vigorous stirring for 5 min, 2-cyanoethanol (0.71 g, 10.00 mmol, 1 eq) was added and the reaction mixture stirred for a further 30 min. Diisopropylamine (4.05 g, 40.00 mmol, 4 eq) was then added and the reaction mixture stirred for a further 120 min after which the reaction was complete as shown by ^{31}P NMR. The desired product was distilled from the crude reaction mixture at 71 °C at 0.01 mmHg to give a colourless liquid (0.93 g, 31%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.17 (app. t, 24H,

NCH(CH_3)$_2$), 2.61 (t, *J*= 6.4 Hz, 2H, OCH$_2$CH_2CN), 3.49-3.58 (m, 4H, NC*H*(CH$_3$)$_2$), 3.77 (dt, *J*= 7.3, *J*= 6.4 Hz, 2H, OCH_2CH$_2$CN,). **^{13}C NMR** (125 MHz, CDCl$_3$) δ ppm 20.6 (d, *J*= 8.9 Hz, OCH$_2$*C*H$_2$CN), 23.8 (d, *J*= 5.8 Hz, NCH(*C*H$_3$)$_2$), 24.6 (d, *J*= 8.2 Hz, NCH(*C*H$_3$)$_2$), 44.6 (d, *J*= 12.4 Hz, N*C*H(CH$_3$)$_2$), 59.3 (d, *J*= 24.9 Hz, O*C*H$_2$*C*H$_2$CN), 118.0 (CN). **^{31}P NMR** (162 MHz, CDCl$_3$) δ ppm 123.7. **HRMS** (ES, M+H$^+$) calculated for $C_{15}H_{33}N_3OP$ 302.2361, found 302.2363.

*Synthesis of **12***: To a stirred solution of PCl$_3$ (1.37 g, 20.00 mmol, 1 eq) in [C$_4$dmim][NTf$_2$] (8.44 g, 20.00 mmol, 2 eq) under an inert atmosphere of N$_2$, Hünig's base (2.58 g, 20.00 mmol, 2 eq) was added. After 5 min, 2-cyanoethanol (1.42 g, 20.00 mmol, 2 eq) was added and the solution stirred for a further 30 min. Diisopropylamine (2.02 g, 20.00 mmol, 2 eq) was added and the solution stirred for a further 40 min. The solution was extracted with diethyl ether (3 x 30 ml) and concentrated to give a colourless oil (1.57 g, 58 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 1.20 (app. t, 12H, NCH(*CH$_3$)$_2$*), 2.66 (t, *J*= 6.2 Hz, 4H, OCH$_2$CH_2CN) 3.60-3.65 (m, 2H, NC*H*(*CH$_3$)$_2$*), 3.78-3.94 (m, 4H, OCH_2CH$_2$CN). **^{13}C NMR** (125 MHz, CDCl$_3$) δ 20.4 (d, *J*= 6.9 Hz, OCH$_2$*C*H$_2$CN), 24.6 (d, *J* = 7.2 Hz, NCH(*C*H$_3$)$_2$), 43.3 (d, *J*= 12.4 Hz, N*C*H(*CH$_3$)$_2$*), 58.5 (d, *J*= 15.8Hz, O*C*H$_2$CH$_2$CN), 117.6 (*C*N). **^{31}P NMR** (162 MHz, CDCl$_3$) δ 149.0. **HRMS** (ES, M+H$^+$) calculated for $C_{12}H_{21}N_3O_2P$ 272.1528, found 272.1570.

*Synthesis of **14***: To a 10 ml round bottom flask equipped with a magnetic stirrer, 2-cyanoethyl-*N,N,N',N'*-tetraisopropylphosphoramide **11** (0.30 g, 0.96 mmol, 1 eq) was added under an atmosphere of N$_2$. To the reaction vessel was added benzoyl chloride (0.15 g, 0.96 mmol, 1 eq) drop wise at room temperature. The crude mixture was purified on a Biotage system using 9:1 hexane: EtOAc to afford the product as a bright yellow solid (0.31 g, 92 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ ppm 1.18 (d, *J*= 6.8 Hz, 12H, NCH(CH_3)$_2$), 1.31 (d, *J*= 6.8 Hz, 12H, NCH(CH_3)$_2$), 3.56 (septet, *J*= 6.7 Hz, 4H, NC*H*(CH$_3$)$_2$), 7.45 (t, *J*= 8.2 Hz, 2H, aromatic), 7.56 (t, *J*= 7.3 Hz, 1H, aromatic), 8.58 (d, *J*= 7.0 Hz, 2H, aromatic). **^{13}C NMR** (125 MHz, CDCl$_3$) δ ppm 22.7 (d, *J*= 1.25 Hz, NCH(*C*H$_3$)$_2$), 23.3 (d, *J*= 1.25 Hz, NCH(*C*H$_3$)$_2$), 46.5 (d, *J*= 5.0 Hz, N*C*H(CH$_3$)$_2$), 128.3, 130.5, 133.5 (aromatic), 137.8 (d, *J*= 67.5 Hz, C=O-*C*), 207.6 (d, *J*= 168.8 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, CDCl$_3$) δ ppm 14.4. **HRMS** (ES, M+H$^+$) calculated for $C_{19}H_{34}N_2OP$ 353.2358, found 353.2368.

*Synthesis of **13e***: To a stirred solution of 4-pentynoic acid (0.10 g, 1.02 mmol, 1 eq) under an atmosphere of N$_2$, oxalyl chloride (0.65 g, 5.10 mmol, 5 eq) was added. The reaction was

stirred overnight where completion of the reaction was determined by ^{1}H NMR. The oxalyl chloride was removed under high vacuum to yield the titled compound as a pale yellow liquid in quantitative yield without the need for further purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 2.04 (t, *J*= 2.6 Hz, 1H), 2.57 (td, *J*= 7.1 Hz, 2.7 Hz, 2H), 3.14 (t, *J*= 7.1 Hz, 2H). **^{13}C-NMR** (125 MHz, $CDCl_3$) δ ppm 172.1 (*C*=$OCH_2CH_2C \equiv CH$), 80.5 (C=$OCH_2CH_2C \equiv CH$), 70.3 (C=$OCH_2CH_2C \equiv C$H), 45.6 (C=O*C*$H_2CH_2C \equiv CH$), 14.6 (C=$OCH_2CH_2C \equiv CH$).

*Synthesis of **13f***: To a stirred solution of 5-hexynoic acid (0.10 g, 0.89 mmol, 1 eq) under an atmosphere of N_2, oxalyl chloride (0.57 g, 4.46 mmol, 5 eq) was added. The reaction was stirred overnight where completion of the reaction was determined by ^{1}H NMR. The excess oxalyl chloride was removed under reduced pressure to yield the titled compound as a pale yellow liquid in quantitative yield without the need for further purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.91 (quintet, *J*= 7.3 Hz, 2H), 2.02 (t, *J*= 2.7 Hz, 1H), 2.31 (td, *J*= 6.8 Hz, 2.7 Hz, 2H), 3.08 (t, *J*= 7.3 Hz, 2H). **^{13}C-NMR** (125MHz, $CDCl_3$) δ ppm 172.5 (*C*=$OCH_2CH_2CH_2C \equiv CH$), 81.1 (C=$OCH_2CH_2CH_2C \equiv CH$), 72.0 (C=$OCH_2CH_2CH_2C \equiv C$H), 45.9 (C=$OCH_2CH_2CH_2C \equiv CH$), 23.7 C=$OCH_2CH_2CH_2C \equiv CH$, 17.2 C=O*C*$H_2CH_2CH_2C \equiv CH$).

*Synthesis of **16a***: To a 10 ml round bottom flask equipped with a magnetic stirrer, bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.30 g, 1.10 mmol, 1 eq) was added under an atmosphere of N_2. The reaction vessel was cooled to -78°C and benzoyl chloride (1.10 mmol, 0.16 g, 1 eq) was added drop-wise. The vessel was allowed to warm to room temperature and the crude mixture was purified on a Biotage system using 4:6 hexane: EtOAc to afford the product as a viscous bright yellow oil (0.32 g, 90 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.28 (d, *J*= 6.7 Hz, 6H, NCH(CH_3)$_2$), 1.31 (d, *J*= 6.7 Hz, 6H, NCH(CH_3)$_2$), 2.82-2.91 (m, 2H, OCH_2CH_2CN), 3.39-3.50 (m, 2H, NC*H*(CH_3)$_2$), 4.26-4.40 (m, 2H, OCH_2CH_2CN), 7.49 (t, *J*= 7.3 Hz, 2H, aromatic), 7.61 (t, *J*= 7.4 Hz, 1H, aromatic), 8.33 (d, *J*= 7.2 Hz, 2H, aromatic). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 20.1 (d, *J*= 7.3 Hz, OCH_2CH_2CN), 22.2 (d, *J*= 2.7 Hz, NCH(CH_3)$_2$), 22.9 (d, *J*= 1.8 Hz, NCH(CH_3)$_2$), 46.7 (d, *J*= 5.5 Hz, N*C*H(CH_3)$_2$), 59.9 (d, *J*= 8.2 Hz, O*C*H_2CH_2CN), 116.8 (CN), 128.7, 129.8, 134.4 (aromatic), 136.1 (d, *J*= 73.8 Hz, C=O-C), 202.1 (d, *J*= 196.9 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 9.69. **HRMS** (ES, $M+H^+$) calculated for $C_{16}H_{24}N_2O_3P$ 323.1535, found 323.1587.

Synthesis of ***16b***: To a 10 ml round bottom flask equipped with a magnetic stirrer, bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.10 g, 0.37 mmol, 1 eq) was added under an atmosphere of N_2. The reaction vessel was cooled to -78°C and acetyl chloride (0.37 mmol, 0.03 g, 1 eq) was added drop-wise. The vessel was allowed to warm to room temperature and the crude mixture was purified on a Biotage system using 3:7 hexane: EtOAc to afford the product as a pale yellow oil (0.17 g, 87 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.27 (d, *J*= 7.0 Hz, 6H, NCH(CH_3)$_2$), 1.30 (d, *J*= 7.0 Hz, 6H, NCH(CH_3)$_2$), 2.51 (d, 3H, *J*= 4.8 Hz, P(O)CH_3), 2.70-2.94 (m, 2H, OCH$_2$CH_2CN), 3.35-3.46 (m, 2H, NC*H*(CH$_3$)$_2$), 4.14-4.17 (m, 1H, OCH_2CH$_2$CN), 4.19-4.27 (m, 1H, OCH_2CH$_2$CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 20.1 (d, *J*= 7.3 Hz, OCH$_2$*C*H$_2$CN), 22.3 (d, *J*= 12.7 Hz, NCH(*C*H$_3$)$_2$), 23.3 (d, *J*= 2.7 Hz, NCH(*C*H$_3$)$_2$), 29.5 (d, *J*= 75.1 Hz, P(O)*C*H$_3$), 46.2 (d, *J*= 5.5 Hz, N*C*H(CH$_3$)$_2$), 59.3 (d, *J*= 8.2 Hz, O*C*H$_2$CH$_2$CN), 116.6 (CN), 211.9 (d, *J*= 192.3 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 7.88 **HRMS** (ES, M+H$^+$) calculated for $C_{11}H_{22}N_2O_3P$ 261.1368, found 261.1360.

Synthesis of ***16c*****:** To a 10 ml round bottom flask equipped with a magnetic stirrer, bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.10 g, 0.37 mmol, 1 eq) was added under an atmosphere of N_2. The reaction vessel was cooled to -78°C and hydrocinnamoylchloride (0.06 g, 0.37 mmol, 1 eq) was added drop-wise. The vessel was allowed to warm to room temperature and the crude mixture was purified on a Biotage system using 3:7 hexane: EtOAc to afford the product as a colourless oil (0.25 g, 80 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.19 (d, *J*= 6.8 Hz, 6H, NCH(CH_3)$_2$), 1.26 (d, *J*= 6.8 Hz, 6H, NCH(CH_3)$_2$), 2.69-2.88 (m, 2H, OCH$_2$CH_2CN), 2.94 (t, *J*= 7.4 Hz, 2H, CH$_2$CH_2Ph), 3.21-3.26 (m, 2H, P(O)-CH_2CH$_2$Ph), 3.30-3.42 (m, 2H, NC*H*(CH$_3$)$_2$), 4.09-4.17 (m, 1H, OCH_2CH$_2$CN), 4.22-4.28 (m, 1H, OCH_2CH$_2$CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 20.1 (d, *J*= 7.2 Hz, OCH$_2$*C*H$_2$CN), 22.2 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 23.4 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 28.6 (d, *J*= 5.5 Hz, CH$_2$*C*H$_2$Ph), 43.8 (d, *J*= 64.7 Hz, P(O)-*C*H$_2$CH$_2$Ph), 46.4 (d, *J*= 5.5 Hz, N*C*H(CH$_3$)$_2$), 59.2 (d, *J*= 8.2 Hz, O*C*H$_2$CH$_2$CN), 116.6 (CN) 126.3, 128.4, 128.5 (aromatic), 213.1 (d, *J*= 193.8 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 7.81. **HRMS** (ES, M+H$^+$) calculated for $C_{18}H_{28}N_2O_3P$ 350.1759, found 350.1761.

Synthesis of ***16d***: To a 10 ml round bottom flask equipped with a magnetic stirrer, bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.10 g, 0.37 mmol, 1 eq) was added under an atmosphere of N_2. The reaction vessel was cooled to -78°C and butyryl chloride (0.04 g, 0.37 mmol, 1 eq) was added drop-wise. The vessel was allowed to warm to room

temperature and the crude mixture was purified on a Biotage system using 3:7 hexane: EtOAc to afford the product as a colourless oil (0.09 g, 82 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 0.94 (t, *J*= 7.4 Hz, 3H, P(O)$CH_2CH_2CH_3$), 1.26 (d, *J*=6.8 Hz, 6H, NCH(CH_3)$_2$), 1.29 (d, *J*=6.8 Hz, 6H, NCH(CH_3)$_2$), 1.56-1.73 (m, 2H, P(O)$CH_2CH_2CH_3$), 2.68-2.95 (m, 4H, OCH_2CH_2CN, P(O)$CH_2CH_2CH_3$), 3.35-3.43 (m, 2H, NCH(CH_3)$_2$), 4.11-4.16 (m, 1H, OCH_2CH_2CN), 4.26-4.33 (m, 1H, OCH_2CH_2CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 13.6 (P(O)$CH_2CH_2CH_3$), 16.2 (d, *J*= 6.3 Hz, P(O)$CH_2CH_2CH_3$), 20.1 (d, *J*= 8.2 Hz, OCH_2CH_2CN), 22.3 (d, *J*= 1.6 Hz, NCH(CH_3)$_2$), 23.4 (d, *J*= 1.6 Hz, NCH(CH_3)$_2$), 44.1 (d, *J*= 61.4 Hz, P(O)$CH_2CH_2CH_3$), 46.3 (d, *J*= 5.5 Hz, NCH(CH_3)$_2$), 59.2 (d, *J*= 8.3 Hz, OCH_2CH_2CN), 116.6 (CN), 214.1 (d, *J*= 194.6 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 8.03. **HRMS** (ES, M+Na^+) calculated for $C_{13}H_{25}N_2O_3PNa$ 311.1501, found. 311.1490

*Synthesis of **16e***: To a 10 ml round bottom flask equipped with a magnetic stirrer 4-pentyonic acid chloride (0.04g, 0.37 mmol, 1 eq) was added under an atmosphere of N_2 and the reaction vessel was cooled to -78°C. To this was added bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.10 g, 0.37 mmol, 1 eq) and the vessel was allowed to warm to room temperature. The crude mixture was purified on a Biotage system using 3:7 hexane: EtOAc to afford the product as a brown oil (0.08 g, 71 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.22 (d, *J*=6.7 Hz, 6H, NCH(CH_3)$_2$), 1.32 (d, *J*= 6.7 Hz, 6H, NCH(CH_3)$_2$), 2.09 (t, *J*= 2.8 Hz, 1H, P(O)CH_2CH_2CCH), 2.53-2.57 (m, 2H, P(O)CH_2CH_2CCH), 2.64-2.70 (m, 2H, OCH_2CH_2CN) 3.17 (dt, *J*= 7.4, 1.5 Hz, 2H, P(O)CH_2CH_2CCH), 3.32-3.51 (m, 2H, NCH(CH_3)$_2$), 4.06-4.15 (m, 1H, OCH_2CH_2CN), 4.25-4.32 (m, 1H, OCH_2CH_2CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 15.8 (P(O)CH_2CH_2CCH), 20.3 (d, *J*= 7.2 Hz, OCH_2CH_2CN), 22.4 (d, *J*= 1.8 Hz, NCH(CH_3)$_2$), 23.6 (d, *J*= 1.8 Hz, NCH(CH_3)$_2$), 34.7 (d, *J*= 61.9 Hz, P(O)CH_2CH_2CCH), 46.2 (d, *J*= 5.5 Hz, NCH(CH_3)$_2$), 59.1 (d, *J*= 8.2 Hz, OCH_2CH_2CN), 72.9 (P(O)CH_2CH_2CCH), 84.3 (P(O)CH_2CH_2CCH) 116.9 (CN), 214.2 (d, *J*= 195.5 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 7.72. **HRMS** (ES, M+H^+) calculated for $C_{14}H_{24}N_2O_3P$, 299.1446 found, 299.1440.

*Synthesis of **16f***: To a 10 ml round bottom flask equipped with a magnetic stirrer 5-hexanoyic acid chloride (0.04 g, 0.37 mmol, 1 eq) was added under an atmosphere of N_2 and the reaction vessel was cooled to -78°C. To this was added bis-(2-cyanoethyl)-*N*, *N*-diisopropylphosphoramidite **12** (0.10 g, 0.37 mmol, 1 eq) and the vessel was allowed to warm to room temperature. The crude mixture was purified on a Biotage system using 3:7 hexane: EtOAc to afford the product as a brown oil (0.08 g, 74 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ

ppm 1.25 (d, *J*= 6.9 Hz, 6H, NCH(CH_3)$_2$), 1.30 (d, *J*= 6.9 Hz, 6H, NCH(CH_3)$_2$), 1.84 (quintet, *J*= 7.0 Hz, 2H, P(O)CH$_2$CH_2CH$_2$CCH), 1.99 (t, *J*= 2.7 Hz, 1H, P(O)CH$_2$CH$_2$CH$_2$CC*H*), 2.24-2.34 (m, 2H, P(O)CH$_2$CH$_2$CH_2CCH), 2.68-2.75 (m, 2H, OCH$_2$CH_2CN), 3.06 (dt, *J*= 7.2, 1.3 Hz, 2H, P(O)CH_2CH$_2$CH$_2$CCH), 3.36-3.54 (m, 2H, NC*H*(CH$_3$)$_2$), 4.09-4.18 (m, 1H, OCH_2CH$_2$CN), 4.28-4.35 (m, 1H, OCH_2CH$_2$CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 15.8 (P(O)CH$_2$CH$_2$*C*H$_2$CCH), 17.4 (P(O)CH$_2$*C*H$_2$CH$_2$CCH), 20.3 (d, *J*= 7.3 Hz, OCH$_2$*CH*$_2$CN), 22.4 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 23.6 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 36.7 (d, *J*= 61.3 Hz, P(O)*C*H$_2$CH$_2$CH$_2$CCH), 46.9 (d, *J*= 5.5 Hz, N*C*H(CH$_3$)$_2$), 59.7 (d, *J*= 8.4 Hz, O*C*H$_2$CH$_2$CN), 73.6 (P(O)CH$_2$CH$_2$CH$_2$C*C*H), 82.9 (P(O)CH$_2$CH$_2$CH$_2$*C*CH), 116.6 (CN), 213.7 (d, *J*= 195.3 Hz, P-*C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 7.72. **HRMS** (ES, M+H$^+$) calculated for $C_{15}H_{26}N_2O_3P$ 313.1602 found, 313.1610

*Synthesis of **18***: To a 10 ml round bottom flask equipped with a magnetic stirrer, *N*-dibenzyloxyphosphanyl-*N*-isopropyl-propan-2-amine **17** (0.20 g, 0.56 mmol, 1 eq) was added under an atmosphere of N_2. The reaction vessel was cooled to -78°C and acetyl chloride (0.04 g, 0.56 mmol, 1 eq) was added drop-wise. The vessel was allowed to warm to room temperature and the crude mixture was purified on a Biotage system using 100 % hexane and increasing to 1:1 hexane: EtOAc to afford the product as a colourless oil (0.12 g, 73 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.25 (d, *J*= 2.8 Hz, 6H, NCH(CH_3)$_2$), 1.27 (d, *J*= 2.8 Hz, 6H, NCH(CH_3)$_2$), 2.46 (d, *J*= 4.0 Hz, 3H, P(O)CH_3), 3.38-3.39 (m, 2H, , NC*H*(CH$_3$)$_2$), 5.00 (dd, *J*= 11.8 Hz, *J*=7.3 Hz, 1H, OCH_2Ph), 5.16 (dd, *J*= 11.8 Hz, *J*=7.3 Hz, 1H, OCH_2Ph), 7.32-7.43 (m, 5H, OCH$_2$*Ph*). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 22.2 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 23.5 (d, *J*= 1.8 Hz, NCH(*C*H$_3$)$_2$), 30.0 (d, *J*= 70.1 Hz, P(O)*C*H3), 46.3 (d, *J*= 5.5 Hz, N*C*H(CH$_3$)$_2$), 66.0 (d, *J*= 8.2 Hz, O*C*H$_2$Ph), 127.8 (OCH$_2$*Ph*), 128.3 (OCH$_2$*Ph*), 128.6 (OCH$_2$*Ph*), 136.4 (d, *J*= 9.1 Hz, OCH$_2$*Ph*), 213.0 (d, *J*= 119.1 Hz, *C*=O). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 6.85 **HRMS** (ES, M+H$^+$) calculated for $C_{15}H_{25}NO_3P$ 298.1438 found, 298.1435.

Synthesis of **20**: To a stirred solution of *N*,*N*-diisopropyl-*O*-cyanoethoxy(acetyl)phosphonicdiamide **16b** (0.19 g, 0.73 mmol, 1 eq) in DCM (1 ml) under an N_2 atmosphere, triethyl phosphite (0.25 ml, 1.46 mmol, 2 eq) and pyridinium perchlorate (0.26 g, 1.46 mmol, 2eq) were added. The reaction was followed by TLC and ^{31}P NMR analysis where completion of the reaction was determined by the disappearance of the acyl phosphonamidate. 5 ml of DCM was then added and the reaction mixture filtered to remove

the pyridinium perchlorate. The sample was concentrated and placed under high vacuum to in order to remove the *H*- phosphonate (H-P(O)(OEt)$_2$). The crude mixture was purified on a Biotage system using a gradient of 100 % DCM to 9:1 DCM: MeOH to afford the product as a colourless oil (0.20 g, 71 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.30 (m, 12H, NCH(C*H*$_3$)$_2$), 1.36 (td, *J*= 7.1 Hz, *J*= 2.2 Hz, 6H, OCH$_2$C*H*$_3$), 1.66 (t, *J*= 16.0 Hz, 3H, Me), 2.84-2.77 (m, 1H, OCH$_2$C*H*$_2$CN), 2.97-2.89 (m, 1H, OCH$_2$C*H*$_2$CN), 3.67-3.56 (m, 2H, NC*H*(CH$_3$)$_2$), 4.30-4.18 (m, 5H, OC*H*$_2$CH$_3$, OC*H*$_2$CH$_2$CN), 4.51-4.47 (m, 1H, OC*H*$_2$CH$_2$CN). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 16.5 (app. t, OCH$_2$*C*H$_3$), 19.6 (d, *J*= 2.7 Hz, Me), 20.0 (d, *J*= 7.3 Hz, OCH$_2$*C*H$_2$CN), 22.5 (NCH(*C*H$_3$)$_2$), 23.9 (NCH(*C*H$_3$)$_2$), 46.9 (d, *J*= 4.6 Hz, N*C*H(CH$_3$)$_2$), 59.6 (d, *J*= 7.3 Hz, O*C*H$_2$CH$_2$CN), 63.7 (dd, *J*= 58.5 Hz, *J*= 9.2 Hz, O*C*H$_2$CH$_3$), 74.1 (dd, *J*= 181.4 Hz, *J*= 175.4 Hz, P-*C*-P), 117.2 (CN). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 21.4-21.1 (m) 25.1 (d, *J*= 33.9 Hz), 28.2 (d, *J*= 30.3 Hz). **HRMS** (ES, M+H$^+$) calculated for $C_{15}H_{33}N_2O_6P_2$ 399.1799, found 399.1801

Synthesis of **21**: To a stirred solution of 1-[benzyloxy-(diisopropylamino)phosphoryl]ethanone **18** (0.11 mg, 0.37 mmol) in DCM (1 ml) under N_2, triethyl phosphite (0.13 ml, 0.74 mmol) and pyridinium perchlorate (0.13 g, 0.74 mmol) were added. The reaction was followed by TLC and ^{31}P NMR analysis where completion of the reaction was determined by the disappearance of the acyl phosphonamidate. 5 ml of DCM were then added and the reaction mixture filtered to remove the pyridinium perchlorate. The sample was concentrated and placed under high vacuum to in order to remove the *H*- phosphonate (H-P(O)(OEt)$_2$). The crude mixture was purified on a Biotage system using 100 % DCM and slowly increasing to 95:5 DCM: MeOH to afford the product as a white powder (0.09 g, 70 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.23-1.33(m, 18H, NCH(C*H*$_3$)$_2$, OCH$_2$C*H*$_3$), 1.70 (t, *J*=16.0 Hz, 3H, Me), 3.56-3.67 (m, 2H, NC*H*(CH$_3$)$_2$), 4.41-4.25 (m, 4H, OC*H*$_2$CH$_3$), 5.03 (dd, *J*= 11.7 Hz, *J*= 6.8 Hz, 1H, OC*H*$_2$Ph), 5.24 (dd, *J*= 11.7 Hz, *J*= 6.8 Hz, 1H, OC*H*$_2$Ph), 7.49-7.29 (m, 5H, OCH$_2$*Ph*)). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 16.4 (br. s, OCH$_2$*C*H$_3$), 16.5 (br. s, OCH$_2$*C*H$_3$), 19.6 (br.s, Me), 22.7 (br. s, NCH(*C*H$_3$)$_2$), 23.6 (br. s, NCH(*C*H$_3$)$_2$), 44.9 (d, *J*= 4.4 Hz, N*C*H(CH$_3$)$_2$), 63.6 (dd, *J*= 46.0 Hz, *J*= 9.1 Hz) O*C*H$_2$CH$_3$), 66.2 (d, *J*= 8.2 Hz, O*C*H$_2$Ph), 73.6 (dd, *J*= 182.5 Hz, *J*= 175.6 Hz, P-*C*-P), 127.7, 128.2, 128.6, 136.3 (Ph). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 21.7 (d, *J*= 31.5 Hz), 21.8 (d, *J*= 31.5 Hz), 24.6 (*J*= 31.5 Hz), 27.4 (*J*= 30.0 Hz). **HRMS** (ES, M+H$^+$) calculated for $C_{19}H_{35}NO_6P_2$ 436.1862, found 436.1867.

Synthesis of **1**: 1-[benzyloxy-(diisopropylamino)phosphoryl]-1-diethoxyphosphoryl-ethanol

(0.04 g, 0.09 mmol) was dissolved in trimethylsilyl bromide (1 ml) and stirred at room temperature overnight. The mixture was evaporated *in vacuo* and the residue was dissolved in MeOH (1 ml) and stirred for 60 min at room temperature. The mixture was again evaporated *in vacuo* and the residue was dissolved in H_2O (1 ml) and stirred for 60 min at room temperature. The resultant mixture was washed with EtOAc, the water layer was separated and freeze dried to afford **1** quantitatively as a white powder. **^{1}H NMR** (400 MHz, D_2O) δ ppm 1.22 (br. s, 6H, NCH(CH_3)$_2$), 1.23 (br.s, 6H, NCH(CH_3)$_2$), 1.53 (t, *J*= 12.0 Hz, 3H, Me), 3.41-3.47 (m, 2H, NC*H*(CH$_3$)$_2$). **^{13}C NMR** (125 MHz, D_2O) δ ppm 18.1 (NCH(*C*H$_3$)$_2$), 19.2 (Me), 47.1 (N*C*H(CH$_3$)$_2$). **^{31}P NMR** (162 MHz, D_2O) δ ppm 15.2 (d, *J*= 20.6 Hz), 19.0 (br. s), 24.1 (d, *J*= 20.6 Hz).

*Synthesis of **26***: To a 25 ml RBF under an atmosphere of N_2 triethyl phosphite (0.50 g, 3.01 mmol, 1 eq) was added. The flask was cooled to -78°C and acetyl chloride (0.24 g, 3.01 mmol, 1 eq) was added. The reaction was allowed to warm slowly to room temperature and ^{31}P NMR analysis confirmed complete conversion to the desired product. The reaction mixture was concentrated under high vacuum to remove the EtCl by-product. The crude material (0.51 g, 2.85 mmol, 1 eq) was re-dissolved in anhydrous DCM (5 ml) under an atmosphere of N_2. Pyridinium perchlorate (1.02 g, 5.70 mmol, 2 eq) and *N*-dibenzyloxyphosphanyl-*N*-methyl-methanamine **22** (1.65 g, 5.70 mmol, 2 eq) were added. The reaction was followed by TLC and ^{31}P NMR analysis where completion of the reaction was determined by the disappearance of the acyl phosphonamidate. The sample was filtered to remove the pyridinium perchlorate and placed under high vacuum to in order to remove the *H*- phosphonate (H-P(O)(OEt)$_2$). The crude mixture was purified on a Biotage system using 100 % DCM and slowly increasing to 2% MeOH in DCM to afford the product as a colourless oil (0.89 g, 82 %) as an inseparable mixture. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 1.22-1.35 (m, 6H OCH$_2$CH_3), 1.94-2.08 (m, 3H, Me), 2.74, (d, *J*= 8.0 Hz, 3H, NCH_3), 2.78 (d, *J*= 8.0 Hz, 3H, NCH_3), 4.10-4.28 (m, 4H, OCH_2CH$_3$), 4.98-5.01 (m, 1H, OCH_2Ph), 5.10.5.15 (m, 1H, OCH_2Ph), 7.35-7.43 (m, 5H, OCH$_2$*Ph*). **^{13}C NMR** (125 MHz, $CDCl_3$) δ ppm 16.4-16.6 (m, OCH$_2$*C*H$_3$), 20.6-20.9 (m, Me), 37.5 (d, *J*= 3.8 Hz, N*C*H$_3$), 37.6 (d, *J*= 3.8 Hz, N*C*H$_3$), 63.0-64.2 (m, OCH$_2$*C*H$_3$, O*C*H$_2$Ph), 78.4 (m, P-*C*-P), 127.2-128.5 (m, Ph), 136.2 (Ph). **^{31}P NMR** (162 MHz, $CDCl_3$) δ ppm 18.8 (dd, *J*= 27.5 Hz, 4.9 Hz), 19.0 (d, *J*= 34.0 Hz), 23.1 (d, *J*= 34.0 Hz), 24.0 (d, *J*= 27.5 Hz). **HRMS** (ES, M+H$^+$) calculated for $C_{15}H_{28}NO_6P_2$ 380.1392, found 380.1389.

*Synthesis of **27***: To a 25 ml RBF was added **26** (0.34 g, 0.90 mmol, 1 eq) under an

atmosphere of N_2. Trimethylsilyl bromide (2 ml) was added and the reaction left to stir overnight. The resultant mixture was evaporated *in vacuo* and the residue was dissolved in MeOH (5 ml) and stirred for 60 min at room temperature. The mixture was again evaporated *in vacuo* and the residue was dissolved in H_2O (5 ml) and stirred for 60 min at room temperature. The MeOH was removed under vacuum and the resultant water layer was freeze dried. The resultant residue was then purified on a Biotage system using reverse phase C-18 column chromatography using 100 % H_2O to afford the pure product as a crystalline solid (0.11 g, 53 %). **^{1}H NMR** (400 MHz, D_2O) δ ppm 1.42 (t, *J*= 16.0 Hz, Me), 2.53 (6H, NC*H*$_3$). **^{13}C NMR** (125 MHz, D_2O) δ ppm 19.2, 34.4, 70.3 (t, *J*= 191.4 Hz). **^{31}P NMR** (162 MHz, D_2O) δ ppm 16.2 (br.s), 19.8 (br.s).

Proposed mechanism for the formation alkylvinyloxyphosphonic diamide when phosphoramidite **12** is reacted with acetyl chloride **13b** at room temperature