Supporting Information

Efficient Syntheses of Phosphonylated Isochromenes by Regioselective 6-*Endo-dig* Addition to Carbon-Carbon Triple Bond Catalyzed by $Pd(OAc)_2$

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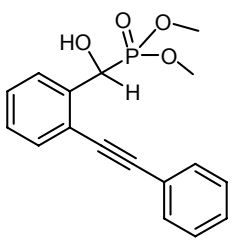
General Comments.

All reactions were carried out under an inert atmosphere and in heat-dried glassware. Anhydrous THF were obtained by distillation from sodium. Column chromatography was performed on silica gel (particle size 10-40 μm, Ocean Chemical Factory of Qingdao, China). ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on Brucker-400 (400 MHz for ^{1}H, 162 MHz for ^{13}C, 121 MHz for ^{31}P) and Brucker-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C, 100 MHz for ^{31}P) spectrometers. Chemical shifts were reported in ppm downfield from internal $Si(CH_3)_4$ and external 85% H_3PO_4, respectively. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer.

General Procedure for the Synthesis of Dialkyl (2-(2-ethynyl)phenyl)(hydroxyl)methylphosphonate 6

o-Alkynyl benzaldehyde **5** (0.5 mmol) in THF (5 ml) was added dropwise to a stirred mixture of dialkyl phosphite **4** (1.0 mmol) and Et_3N (0.101 g, 1.0 mmol) in THF (5 ml) at room temperature. After 20h stirring at r.t. (TLC (silica gel) monitoring), the mixture was cooled and work-up with water (5 ml) below 0°C. The result mixture was then extracted by AcOEt and dried with anhydrous sodium sulfate. After concentrated the residue **6** was obtained (yield>95%) and used directly without further purification.

Dimethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methylphosphonate (6a)



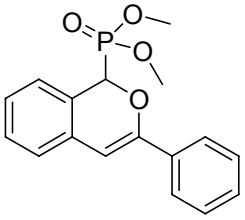
Colorless crystal (AcOEt); mp 124-125ºC; ^{31}P-NMR (100 MHz, $CDCl_3$): δ24.06; ^{1}H-NMR (300 MHz, $CDCl_3$): δ3.66 (d, 3H, $J_{P\text{-}H}$ = 10.3 Hz, 3H, P(OCH_3)$_2$), 3.76 (d, 3H, $J_{P\text{-}H}$ = 10.6 Hz, 3H,

P(OCH_3)$_2$), 5.14 (s, 1H, O*H*), 5.78 (d, $J_{P\text{-}H}$ = 11.2Hz, 1H, *H*COH), 7.27-7.41 (m, 5H, *Ph*), 7.52-7.56 (m, 3H, *Ph*), 7.78-7.80 (d, 1H, *Ph*); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 53.70 (d, $^2J_{C,P}$ = 7.2 Hz, P(O*C*H$_3$)$_2$), 54.10 (d, $^2J_{C,P}$ = 7.1 Hz, P(O*C*H$_3$)$_2$), 68.59 (d, $^1J_{C,P}$ = 159.5 Hz, H*C*P(OCH$_3$)$_2$), 86.94 (s, C*C*Ph), 94.45 (s, *C*CPh), 122.00, 122.10, 122.96, 127.58, 127.63, 127.98, 128.47, 128.57, 128.72, 131.53, 131.96, 138.49 (*Ph*); Ms-ESI: 339.35 ([M+Na]$^+$).

General Procedure for the Synthesis of Phosphonylated Isochromenes 7

Dialkyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6** (0.5 mmol) in THF (5 ml) was stirred at room temperature for half an hour. Pd(OAc)$_2$ (10 mol%, 0.011 g) was added to the mixture and the mixture was kept stirring for 5 h (TLC (silica gel) monitoring). The result mixture was filtered through silica column and concentrated. The residue was purified by flash CC (silica gel, AcOEt/petroleum ether (b.p. 60-90°C) 1:3) to afford the product **7**.

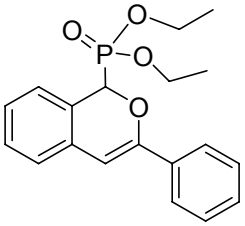
Dimethyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7a)



Dimethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6a** (0.158 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), five hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7a** (0.142 g, 90%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 16.57; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.61 (d, $J_{P\text{-}H}$ = 10.3 Hz, 3H, P(OC*H*$_3$)$_2$), 3.90 (d, $J_{P\text{-}H}$ = 10.6 Hz, 3H, P(OC*H*$_3$)$_2$), 5.96 (d, $J_{P\text{-}H}$ = 6.4 Hz, 1H, *H*CP(OCH$_3$)$_2$), 6.02 (s, 1H, *H*CCPh), 7.18-7.41 (m, 5H, *Ph*), 7.58-7.76 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 54.07 (d, $^2J_{C,P}$ = 7.0 Hz, P(O*C*H$_3$)$_2$), 54.32

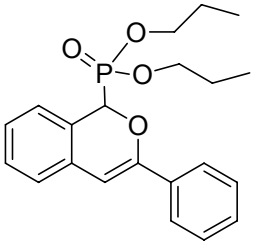
(d, $^{2}J_{C,P}$ = 7.0 Hz, P(O*C*H$_3$)$_2$), 80.56 (d, $^{1}J_{C,P}$ = 166.2 Hz, H*C*P(OCH$_3$)$_2$), 97.87 (d, $^{4}J_{C,P}$ = 4.7 Hz, H*C*CPh), 119.97, 122.87, 125.81, 127.98, 128.45, 128.83, 129.10, 130.91, 134.82, 135.54 (*Ph*), 154.81 (s, O*C*Ph); Ms-ESI: 317.09 ([M+H]$^{+}$); HRMS calcd for $C_{17}H_{17}O_4P$: 339.0757 (M+Na)$^{+}$, found: 339.0755

Diethyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7b)



Diethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6b** (0.172 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), five hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7b** (0.148 g, 86%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.54; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.10 (t, $J_{H\text{-}H}$ = 7.0 Hz, 3H, P(OCH$_2$C*H*$_3$)$_2$), 1.37 (t, $J_{H\text{-}H}$ = 7.0 Hz, 3H, P(OCH$_2$C*H*$_3$)$_2$), 3.87-4.30 (m, 4H, P(OC*H*$_2$CH$_3$)$_2$), 5.92 (d, $J_{P\text{-}H}$ = 7.2 Hz, 1H, *H*CP(OCH$_2$CH$_3$)$_2$), 6.00 (d, $J_{H\text{-}H}$ = 1.9 Hz, 1H, *H*CCPh), 7.15-7.43 (m, 5H, *Ph*), 7.56-7.76 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 15.20 (d, $^{3}J_{C,P}$ = 5.4 Hz, P(OCH$_2$*C*H$_3$)$_2$), 15.45 (d, $^{3}J_{C,P}$ = 5.6 Hz, P(OCH$_2$*C*H$_3$)$_2$), 62.57 (d, $^{2}J_{C,P}$ = 7.1 Hz, P(O*C*H$_2$CH$_3$)$_2$), 62.82 (d, $^{2}J_{C,P}$ = 7.1 Hz, P(O*C*H$_2$CH$_3$)$_2$), 79.79 (d, $^{1}J_{C,P}$ = 165.9 Hz, H*C*P(OCH$_2$CH$_3$)$_2$), 96.53 (d, $^{4}J_{C,P}$ = 4.6 Hz, H*C*CPh), 118.85, 121.85, 124.66, 126.95, 127.36, 127.95, 128.03, 133.92, 134.71, 134.84 (*Ph*), 153.99 (s, O*C*Ph); Ms-ESI: 345.13 ([M+H]$^{+}$); HRMS calcd for $C_{19}H_{21}O_4P$: 367.1070 (M+Na)$^{+}$, found: 367.1071

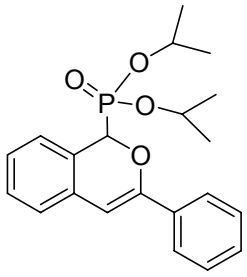
Di-(*n*)-propyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7c)



Di-(*n*)-propyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6c** (0.186 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$

(0.011 g, 10 mol%), five hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7c** (0.158 g, 85%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.46; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.74 (t, $J_{H\text{-}H}$ = 7.4 Hz, 3H, $P(OCH_2CH_2CH_3)_2$), 0.98 (t, $J_{H\text{-}H}$ = 7.4 Hz, 3H, $P(OCH_2CH_2CH_3)_2$), 1.40-1.49 (m, 2H, $P(OCH_2CH_2CH_3)_2$), 1.71-1.79 (m, 2H, $P(OCH_2CH_2CH_3)_2$), 3.73-4.21 (m, 4H, $P(OCH_2CH_2CH_3)_2$), 5.93 (d, $J_{P\text{-}H}$ = 7.2 Hz, 1H, $HCP(OCH_2CH_2CH_3)_2$), 6.00 (d, $J_{H\text{-}H}$ = 1.5 Hz, 1H, *H*CCPh), 7.15-7.43 (m, 5H, *Ph*), 7.56-7.76 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 9.73 (s, $P(OCH_2CH_2CH_3)_2$), 9.98 (s, $P(OCH_2CH_2CH_3)_2$), 23.70 (d, $^{3}J_{C,P}$ = 5.7 Hz, $P(OCH_2CH_2CH_3)_2$), 23.93 (d, $^{3}J_{C,P}$ = 5.9 Hz, $P(OCH_2CH_2CH_3)_2$), 68.94 (d, $^{2}J_{C,P}$ = 7.3 Hz, $P(OCH_2CH_2CH_3)_2$), 69.23 (d, $^{2}J_{C,P}$ = 7.4 Hz, $P(OCH_2CH_2CH_3)_2$), 80.77 (d, $^{1}J_{C,P}$ = 165.8 Hz, $HCP(OCH_2CH_2CH_3)_2$), 97.54 (d, $^{4}J_{C,P}$ = 4.6 Hz, H*C*CPh), 119.85, 122.89, 125.67, 127.98, 128.34, 128.94, 129.03, 134.96, 135.76, 135.93 (*Ph*), 155.05 (s, O*C*Ph); Ms-ESI: 373.17 ($[M+H]^+$); HRMS calcd for $C_{21}H_{25}O_4P$: 395.1383 $(M+Na)^+$, found: 395.1390

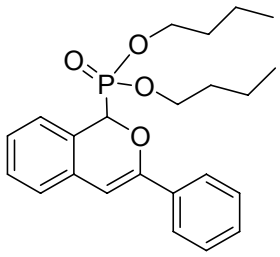
Di-(*i*)-propyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7d)



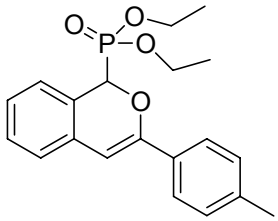
Di-(*i*)-propyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6d** (0.186 g, 0.5 mmol) in THF (5 ml), $Pd(OAc)_2$ (0.011 g, 10 mol%), five hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7d** (0.149 g, 80%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 12.78; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.94 (d, $J_{P\text{-}H}$ = 6.2 Hz, 3H, $P(OCH(CH_3)_2)_2$), 1.22 (d, $J_{H\text{-}H}$ = 6.2 Hz, 3H, $P(OCH(CH_3)_2)_2$), 1.36 (d, $J_{H\text{-}H}$ = 6.2 Hz, 3H, $P(OCH(CH_3)_2)_2$), 1.42 (d, $J_{H\text{-}H}$ = 6.2 Hz,

3H, P(OCH(CH_3)$_2$)$_2$), 4.47-4.54 (m, 1H, P(OCH(CH$_3$)$_2$)$_2$), 4.81-4.89 (m, 1H, P(OCH(CH$_3$)$_2$)$_2$), 5.88 (d, $J_{P\text{-}H}$ = 7.4 Hz, 1H, HCP(OCH(CH$_3$)$_2$)$_2$), 6.00 (d, $J_{P\text{-}H}$ = 1.6 Hz, 1H, HCCPh), 7.15-7.43 (m, 5H, *Ph*), 7.56-7.77 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 23.96 (d, $^3J_{C,P}$ = 4.2 Hz, P(OCH(*C*H$_3$)$_2$)$_2$), 24.11 (d, $^3J_{C,P}$ = 4.6 Hz, P(OCH(*C*H$_3$)$_2$)$_2$), 72.30 (d, $^2J_{C,P}$ = 7.4 Hz, P(O*C*H(CH$_3$)$_2$)$_2$), 72.71 (d, $^2J_{C,P}$ = 7.2 Hz, P(O*C*H(CH$_3$)$_2$)$_2$), 81.12 (d, $^1J_{C,P}$ = 167.2 Hz, H*C*P(OCH(CH$_3$)$_2$)$_2$), 97.28 (d, $^4J_{C,P}$ = 4.5 Hz, H*C*CPh), 119.78, 122.97, 125.57, 128.00, 128.30, 128.85, 128.96, 135.17, 135.89, 136.19 (*Ph*), 155.20 (s, O*C*Ph); Ms-ESI: 373.08 ([M+H]$^+$); HRMS calcd for $C_{21}H_{25}O_4P$: 373.1563 (M+H)$^+$, found: 373.1565

Di-(*n*)-butyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7e)



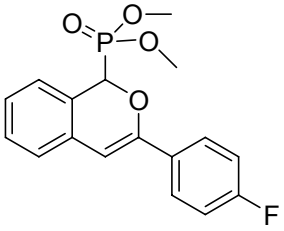
Di-(*n*)-butyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6e** (0.200 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7e** (0.164 g, 82%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.54; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.77 (t, $J_{H\text{-}H}$ = 7.4 Hz, 3H, P(OCH$_2$CH$_2$CH$_2$CH_3)$_2$), 0.94 (t, $J_{H\text{-}H}$ = 7.4 Hz, 3H, P(OCH$_2$CH$_2$CH$_2$CH_3)$_2$), 1.12-1.76 (m, 8H, P(OCH$_2$CH_2CH_2CH$_3$)$_2$), 3.77-4.25 (m, 4H, P(OCH_2CH$_2$CH$_2$CH$_3$)$_2$), 5.92 (d, $J_{P\text{-}H}$ = 7.1 Hz, 1H, HCP(OCH$_2$CH$_2$CH$_2$CH$_3$)$_2$), 6.00 (s, 1H, HCCPh), 7.15-7.42 (m, 5H, *Ph*), 7.56-7.76 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 13.44 (s, P(OCH$_2$CH$_2$CH$_2$*C*H$_3$)$_2$), 13.60 (s, P(OCH$_2$CH$_2$CH$_2$*C*H$_3$)$_2$), 18.41 (s, P(OCH$_2$CH$_2$*C*H$_2$CH$_3$)$_2$), 18.68 (s, P(OCH$_2$CH$_2$*C*H$_2$CH$_3$)$_2$), 32.32 (d, $^3J_{C,P}$ = 5.6 Hz, P(OCH$_2$*C*H$_2$CH$_2$CH$_3$)$_2$), 32.55 (d, $^3J_{C,P}$ = 5.8 Hz, P(OCH$_2$*C*H$_2$CH$_2$CH$_3$)$_2$),



AcOEt/petroleum ether (1:3) to afford product **7g** (0.145 g, 81%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.57; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.06 (t, $J_{H\text{-}H}$ = 7.0 Hz, 3H, $P(OCH_2CH_3)_2$), 1.21 (t, $J_{H\text{-}H}$ = 7.1 Hz, 3H, $P(OCH_2CH_3)_2$), 2.30 (s, 3H, $PhCH_3$), 4.05-4.10 (m, 4H, $P(OCH_2CH_3)_2$), 5.88 (d, $J_{P\text{-}H}$ = 6.9 Hz, 1H, $HCP(OCH_2CH_3)_2$), 5.94 (s, 1H, *H*CCPh), 7.10-7.37 (m, 4H, *Ph*); 7.50-7.62 (m, 4H, *Ph*); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 16.16 (d, $^{3}J_{C,P}$ = 5.5 Hz, $P(OCH_2CH_3)_2$), 16.41 (d, $^{3}J_{C,P}$ = 5.5 Hz, $P(OCH_2CH_3)_2$), 21.17 (s, CH_3Ph), 63.61 (d, $^{2}J_{C,P}$ = 6.9 Hz, $P(OCH_2CH_3)_2$), 63.86 (d, $^{2}J_{C,P}$ = 7.2 Hz, $P(OCH_2CH_3)_2$), 80.64 (d, $^{1}J_{C,P}$ = 166.0 Hz, $HCP(OCH_2CH_3)_2$), 97.54 (d, $^{4}J_{C,P}$ = 4.7 Hz, H*C*CPh), 119.70, 122.80, 125.18, 127.90, 128.80, 128.92, 129.05, 135.03, 135.33, 135.62 (*Ph*), 154.29 (s, O*C*Ph); Ms-ESI: 359.30 ($[M+H]^+$); HRMS calcd for $C_{20}H_{23}O_4P$: 381.1226 $(M+Na)^+$, found: 381.1231

Dimethyl 3-(4-fluorophenyl)-1*H*-isochromen-1-ylphosphonate (7h)

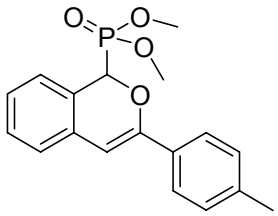
Dimethyl (2-(2-(4-fluorophenyl)ethynyl)phenyl)(hydroxyl)methyl phosphonate **6h**



(0.167 g, 0.5 mmol) in THF (5 ml), $Pd(OAc)_2$ (0.011 g, 10 mol%), 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7h** (0.139 g, 83%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 16.83; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.62 (d, $J_{P\text{-}H}$ = 10.4 Hz, 3H, $P(OCH_3)_2$), 3.89 (d, $J_{P\text{-}H}$ = 10.4 Hz, 3H, $P(OCH_3)_2$), 5.94 (d, $J_{P\text{-}H}$ = 7.0 Hz, 1H, $HCP(OCH_3)_2$), 5.98 (d, $J_{P\text{-}H}$ = 1.9 Hz, 1H, *H*CCPh), 7.02-7.06 (m, 2H, *Ph*), 7.38-7.44 (m, 2H, *Ph*), 7.56-7.60 (m, 2H, *Ph*), 7.69-7.73 (m, 2H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 52.99 (d, $^{2}J_{C,P}$ = 7.0 Hz, $P(OCH_3)_2$), 53.28 (d, $^{2}J_{C,P}$ = 7.1 Hz,

67.18 (d, $^{2}J_{C,P}$ = 7.3 Hz, P(O*C*H_2CH$_2$CH$_2$CH$_3$)$_2$), 67.50 (d, $^{2}J_{C,P}$ = 7.4 Hz, P(O*C*H_2CH$_2$CH$_2$CH$_3$)$_2$), 80.72 (d, $^{1}J_{C,P}$ = 165.7 Hz, H*C*P(OCH$_2$CH$_2$CH$_2$CH$_3$)$_2$), 97.54 (d, $^{4}J_{C,P}$ = 4.6 Hz, H*C*CPh), 119.84, 122.89, 125.66, 127.99, 128.34, 128.94, 129.03, 134.96, 135.76, 135.92 (*Ph*), 155.04 (s, O*C*Ph); Ms-ESI: 401.21 ([M+H]$^{+}$); HRMS calcd for $C_{23}H_{29}O_4P$: 423.1696 (M+Na)$^{+}$, found: 423.1688

Dimethyl 3-*p*-tolyl-1*H*-isochromen-1-ylphosphonate (7f)



Dimethyl (2-(2-*p*-tolylethynyl)phenyl)(hydroxyl)methyl phosphonate **6f** (0.165 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7f** (0.140 g, 85%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 16.74; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, PhC*H*$_3$), 3.60 (d, $J_{P\text{-}H}$ = 10.4 Hz, 3H, P(OC*H*$_3$)$_2$), 3.89 (d, $J_{P\text{-}H}$ = 10.6 Hz, 3H, P(OC*H*$_3$)$_2$), 5.94 (d, $J_{P\text{-}H}$ = 6.9 Hz, 1H, *H*CP(OCH$_3$)$_2$), 5.99 (s, 1H, *H*CCPh), 7.15-7.42 (m, 4H, *Ph*), 7.55-7.65 (m, 4H, *Ph*); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 21.21 (s, *C*H$_3$Ph), 54.06 (d, $^{2}J_{C,P}$ = 7.1 Hz, P(O*C*H$_3$)$_2$), 54.29 (d, $^{2}J_{C,P}$ = 7.3 Hz, P(O*C*H$_3$)$_2$), 80.45 (d, $^{1}J_{C,P}$ = 166.1 Hz, H*C*P(OCH$_3$)$_2$), 97.87 (d, $^{4}J_{C,P}$ = 4.5 Hz, H*C*CPh), 119.80, 122.84, 125.21, 127.92, 128.90, 129.03, 129.16, 134.94, 135.38, 135.52 (*Ph*), 154.13 (s, O*C*Ph); Ms-ESI: 331.26 ([M+H]$^{+}$); HRMS calcd for $C_{18}H_{19}O_4P$: 353.0953 (M+Na)$^{+}$, found: 353.0922

Diethyl 3-*p*-tolyl-1*H*-isochromen-1-ylphosphonate (7g)

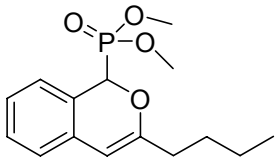
Diethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6g** (0.179 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), 5 hours at room temperature.

P(O*C*H$_3$)$_2$), 79.46 (d, $^1J_{C,P}$ = 166.4 Hz, H*C*P(OCH$_3$)$_2$), 95.75 (d, $^4J_{C,P}$ = 4.6 Hz, H*C*CPh), 114.28, 118.85, 121.86, 128.10, 128.13, 128.41, 130.73, 133.64, 134.40 (*Ph*), 153.32 (s, O*C*Ph), 158.69, 161.14, 170.12 (*Ph*); Ms-ESI: 357.32 ([M+Na]$^+$); HRMS calcd for $C_{17}H_{16}FO_4P$: 357.0662 (M+Na)$^+$, found: 357.0664

Diethyl 3-(4-fluorophenyl)-1*H*-isochromen-1-ylphosphonate (7i)

Diethyl (2-(2-(4-fluorophenyl)ethynyl)phenyl)(hydroxyl)methyl phosphonate **6i** (0.181 g, 0.5 mmol) in THF (5 ml), Pd(OAc)$_2$ (0.011 g, 10 mol%), 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7i** (0.148 g, 82%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.62; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.35 (dt, J_{P-H} = 1.4 Hz, J_{H-H} = 7.1 Hz, 6H, P(OCH$_2$C*H*$_3$)$_2$), 4.08-4.16 (m, 4H, P(OC*H*$_2$CH$_3$)$_2$), 5.90 (d, J_{P-H} = 7.1 Hz, 1H, *H*CP(OCH$_2$CH$_3$)$_2$), 5.95 (d, J_{P-H} = 1.6 Hz, 1H, *H*CCPh), 6.90-7.03 (m, 2H, *Ph*), 7.35-7.42 (m, 2H, *Ph*), 7.54-7.58 (m, 2H, *Ph*), 7.67-7.72 (m, 2H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ 15.22 (d, $^3J_{C,P}$ = 5.8 Hz, P(OCH$_2$*C*H$_3$)$_2$), 15.45 (d, $^3J_{C,P}$ = 5.6 Hz, P(OCH$_2$*C*H$_3$)$_2$), 62.52 (d, $^2J_{C,P}$ = 7.0 Hz, P(O*C*H$_2$CH$_3$)$_2$), 62.81 (d, $^2J_{C,P}$ = 7.1 Hz, P(O*C*H$_2$CH$_3$)$_2$), 79.74 (d, $^1J_{C,P}$ = 166.4 Hz, H*C*P(OCH$_2$CH$_3$)$_2$), 95.44 (d, $^4J_{C,P}$ = 4.7 Hz, H*C*CPh), 114.20, 118.77, 121.87, 127.99, 128.07, 128.39, 130.88, 133.78, 134.74 (*Ph*), 153.53 (s, O*C*Ph), 158.64, 161.08, 170.13 (*Ph*); Ms-ESI: 363.32 ([M+H]$^+$); HRMS calcd for $C_{19}H_{20}FO_4P$: 385.0975 (M+Na)$^+$, found: 385.0974

Dimethyl 3-butyl-1*H*-isochromen-1-ylphosphonate (7j)



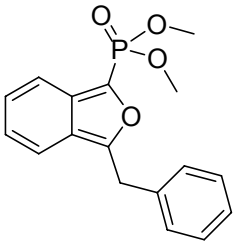
Dimethyl (2-(hex-1-ynyl)phenyl)(hydroxyl)methyl phosphonate **6j** (0.148 g, 0.5 mmol) in THF (5 ml), $Pd(OAc)_2$ (0.011 g, 10 mol%), 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **7j** (0.093g, 63%), yellow liquid; ^{31}P-NMR (121 MHz, $CDCl_3$): δ19.89; ^{1}H-NMR (400 MHz, $CDCl_3$): δ0.85 (t, $J_{H\text{-}H}$ = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 1.27-1.36 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.45-1.53 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.12 (t, $J_{H\text{-}H}$ = 7.4 Hz, 2H, $CH_2CH_2CH_2CH_3$), 3.53 (d, $J_{P\text{-}H}$ = 10.4 Hz, 3H, $P(OCH_3)_2$), 3.66 (d, $J_{P\text{-}H}$ = 10.6 Hz, 3H, $P(OCH_3)_2$), 5.48 (s, 1H, $HCCCH_2CH_2CH_2CH_3$), 5.54 (d, $J_{P\text{-}H}$ = 11.7 Hz, 1H, $HCP(OCH_3)_2$), 6.80-7.13 (m, 4H, *Ph*); ^{13}C-NMR (162 MHz, $CDCl_3$): δ12.86 (s, $CH_2CH_2CH_2CH_3$), 21.25 (s, $CH_2CH_2CH_2CH_3$), 27.63 (s, $CH_2CH_2CH_2CH_3$), 32.24 (s, $CH_2CH_2CH_2CH_3$), 52.17 (d, $^{2}J_{C,P}$ = 7.0 Hz, $HCP(OCH_3)_2$), 52.79 (d, $^{2}J_{C,P}$ = 6.8 Hz, $HCP(OCH_3)_2$), 73.06 (d, $^{1}J_{C,P}$ = 160.1 Hz, $HCP(OCH_3)_2$), 99.01 (s, $HCCCH_2CH_2CH_2CH_3$), 121.77, 122.14, 124.73, 125.19, 127.94, 130.12 (*Ph*), 155.52 (s, $OCCH_2CH_2CH_2CH_3$); Ms-ESI: 297.18 ($[M+H]^+$); HRMS calcd for $C_{15}H_{21}O_4P$: 319.1070 $(M+Na)^+$, found: 319.1079

General Procedure for the Synthesis of Phosphonylate Isobenzopyran 8

Dimethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methylphosphonate **6a** (0.158 g, 0.5 mmol) in THF (5 ml) was stirred at room temperature for half an hour. DBU (1 mmol,

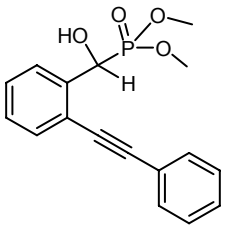
0.153 g) was added to the mixture and the mixture was kept stirring for 5h (TLC (silica gel) monitoring). The result mixture was work-up with water (5 ml) below 0°C. Then the mixture was extracted by AcOEt and dried with anhydrous sodium sulfate. After concentrated the residue was purified by CC (silica gel, AcOEt/petroleum ether (b.p. 60-90°C) 1:3) to afford the product **8**.

Dimethyl 3-benzylisobenzofuran-1-ylphosphonate (8)

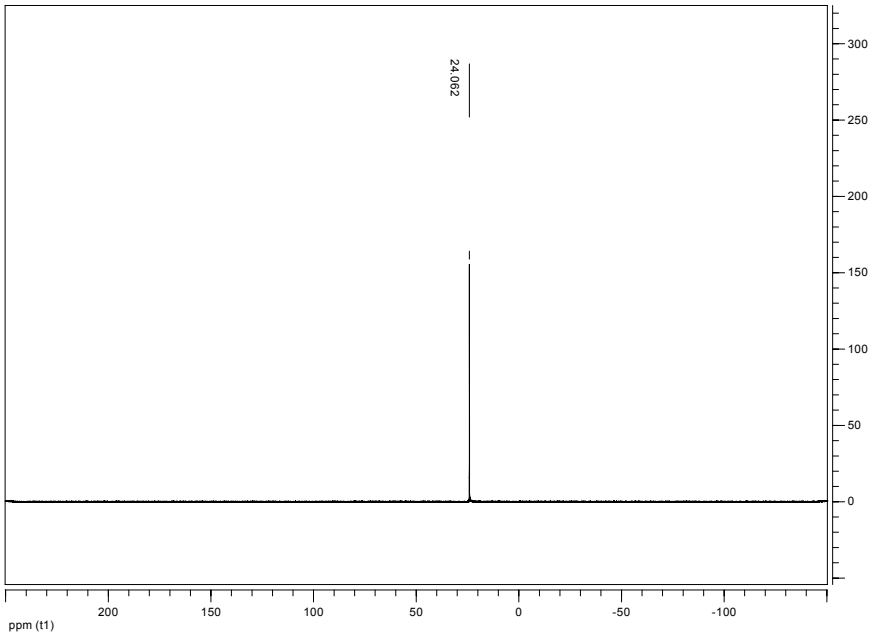


Dimethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methyl phosphonate **6a** (0.158 g, 0.5 mmol) in THF (5 ml), DBU (0.153 g, 1.0 mmol) 5 hours at room temperature. AcOEt/petroleum ether (1:3) to afford product **8** (0.149 g, 94%), yellow liquid; ^{31}P-NMR (100 MHz, $CDCl_3$): δ 1.35; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.67 (d, $J_{P\text{-}H}$ = 11.1 Hz, 6H, P(OCH_3)$_2$), 5.25 (d, $J_{P\text{-}H}$ = 7.1 Hz, 2H, CH_2Ph), 7.22-7.31 (m, 5H, *Ph*), 7.43-7.50 (m, 4H, *Ph*); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 54.35 (d, $^{2}J_{C,P}$ = 5.9 Hz, P(O*C*H$_3$)$_2$), 67.55 (d, $^{5}J_{C,P}$ = 5.0 Hz, *C*H$_2$Ph), 90.39 (d, $^{1}J_{C,P}$ = 629.9 Hz, O*C*P(OCH$_3$)$_2$), 122.57 (d, $^{4}J_{C,P}$ = 50.6 Hz, O*C*CH$_2$Ph), 128.12, 128.42, 128.61, 131.64, 132.23, 137.28, 137.38 (*Ph*); Ms-ESI: 339.36 ([M+Na]$^+$); HRMS calcd for $C_{17}H_{17}O_4P$: 317.0937 (M+H)$^+$, found: 317.0938

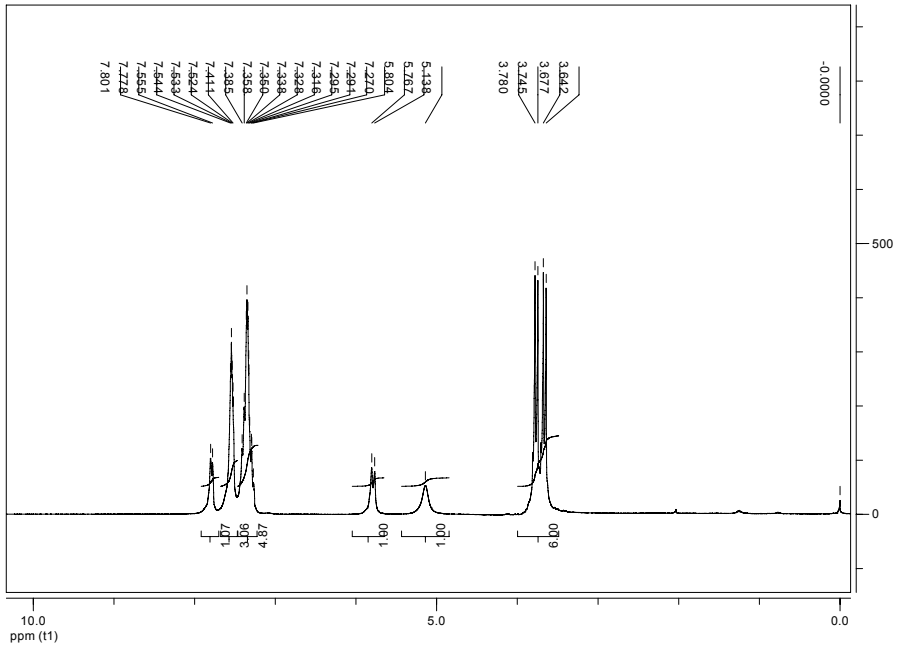
Dimethyl (2-(2-phenylethynyl)phenyl)(hydroxyl)methylphosphonate (6a)



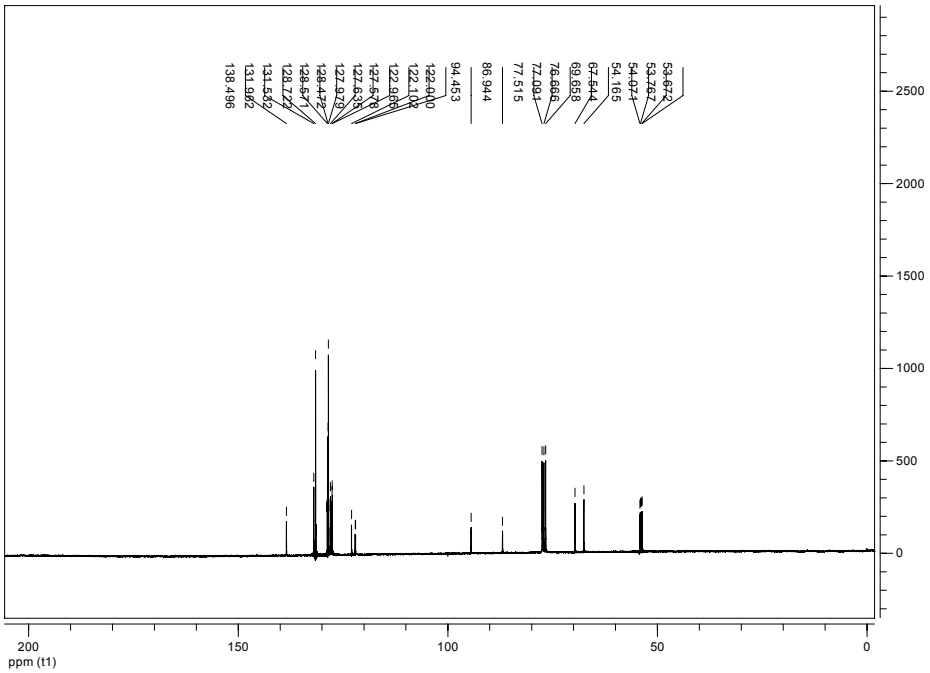
^{31}P-NMR (100 MHz, $CDCl_3$)



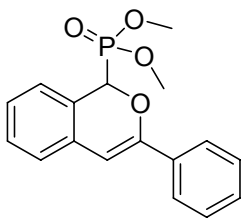
^{1}H-NMR (300 MHz, $CDCl_3$)



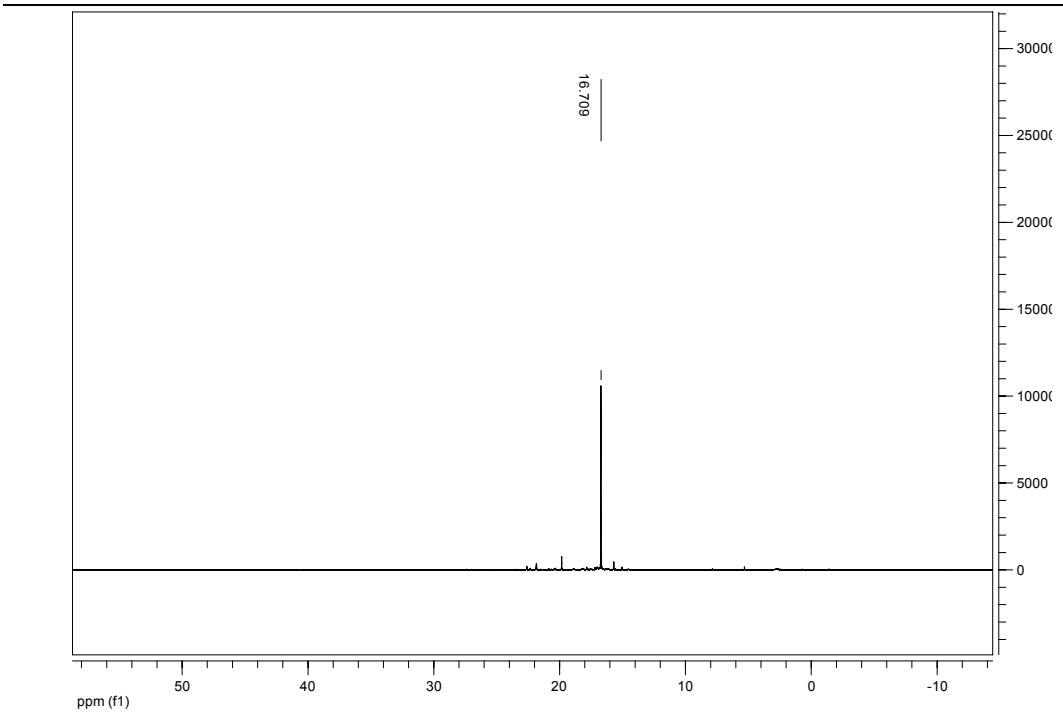
^{13}C-NMR (75 MHz, $CDCl_3$)



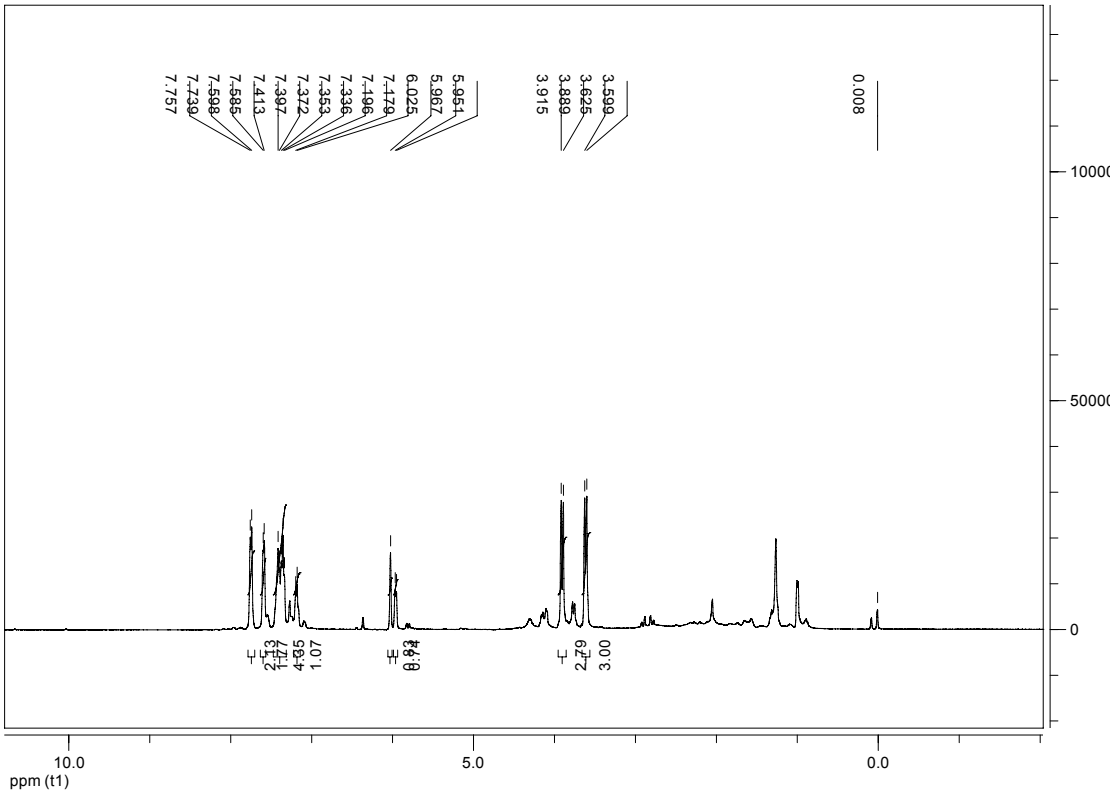
Dimethyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7a)



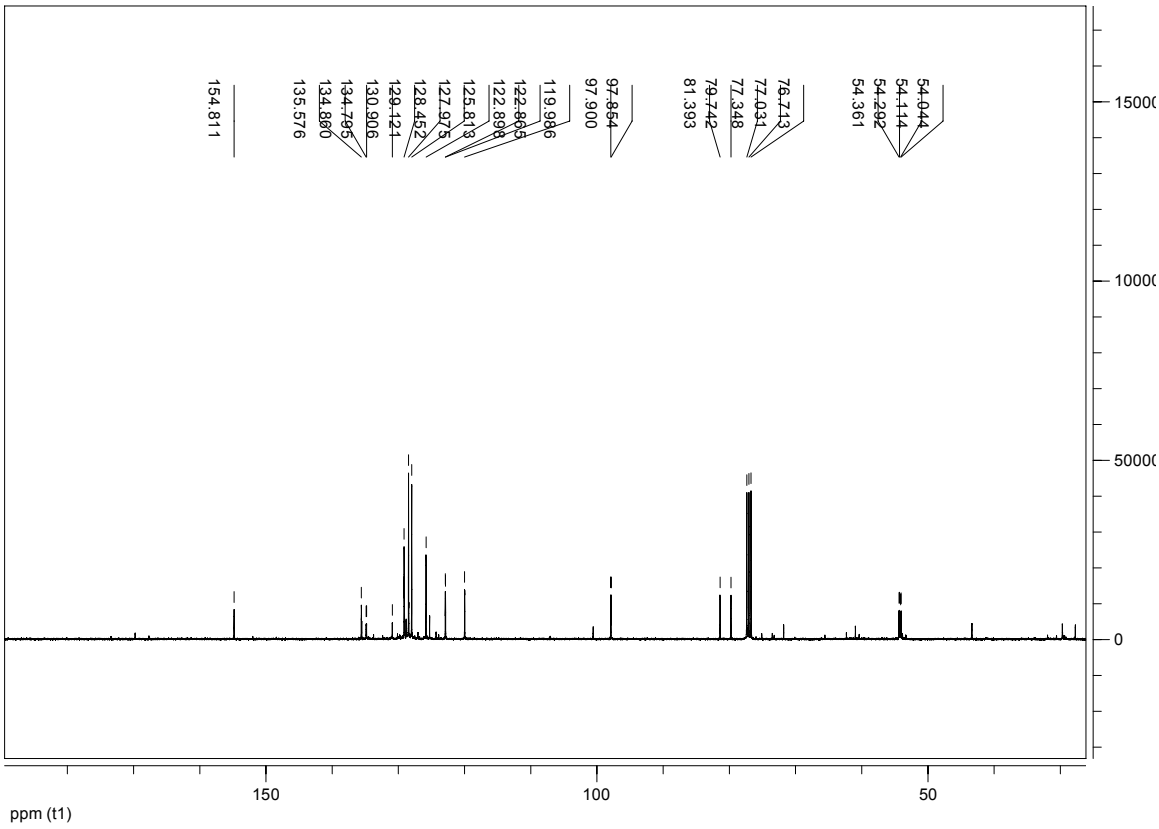
^{31}P-NMR (121 MHz, $CDCl_3$)



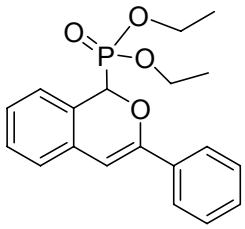
^{1}H-NMR (400 MHz, $CDCl_3$)



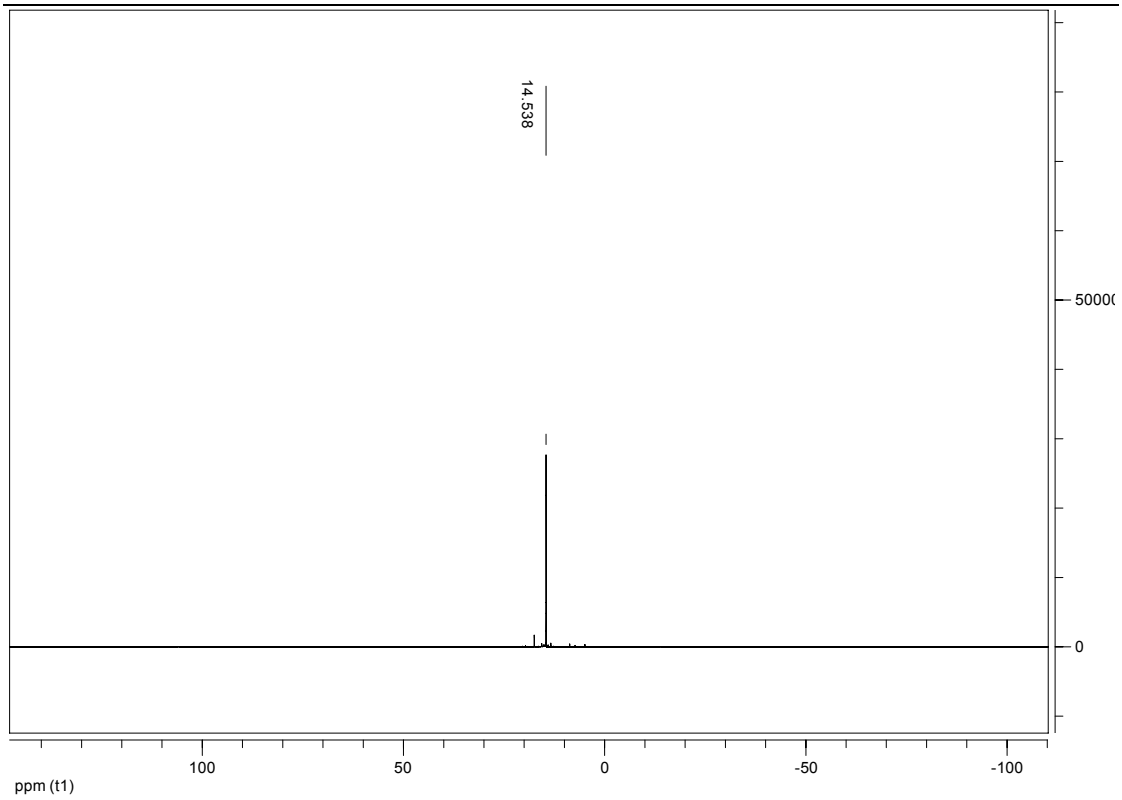
^{13}C-NMR (162 MHz, $CDCl_3$)



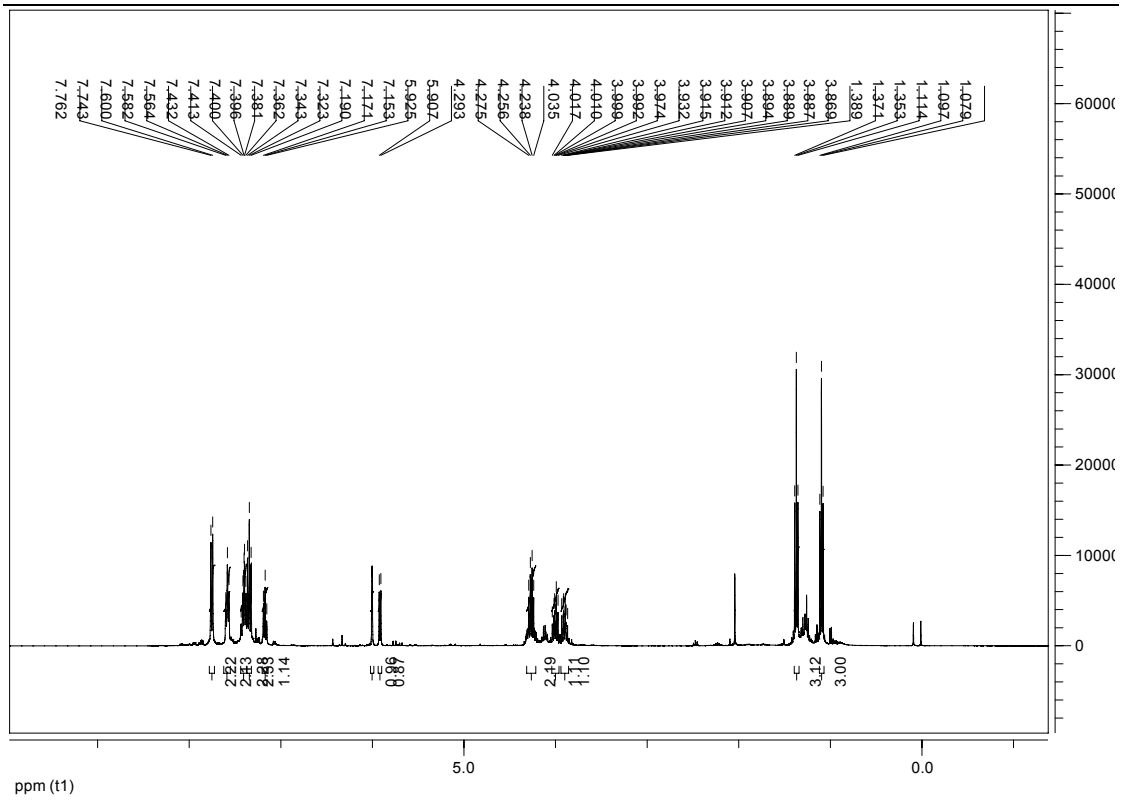
Diethyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7b)



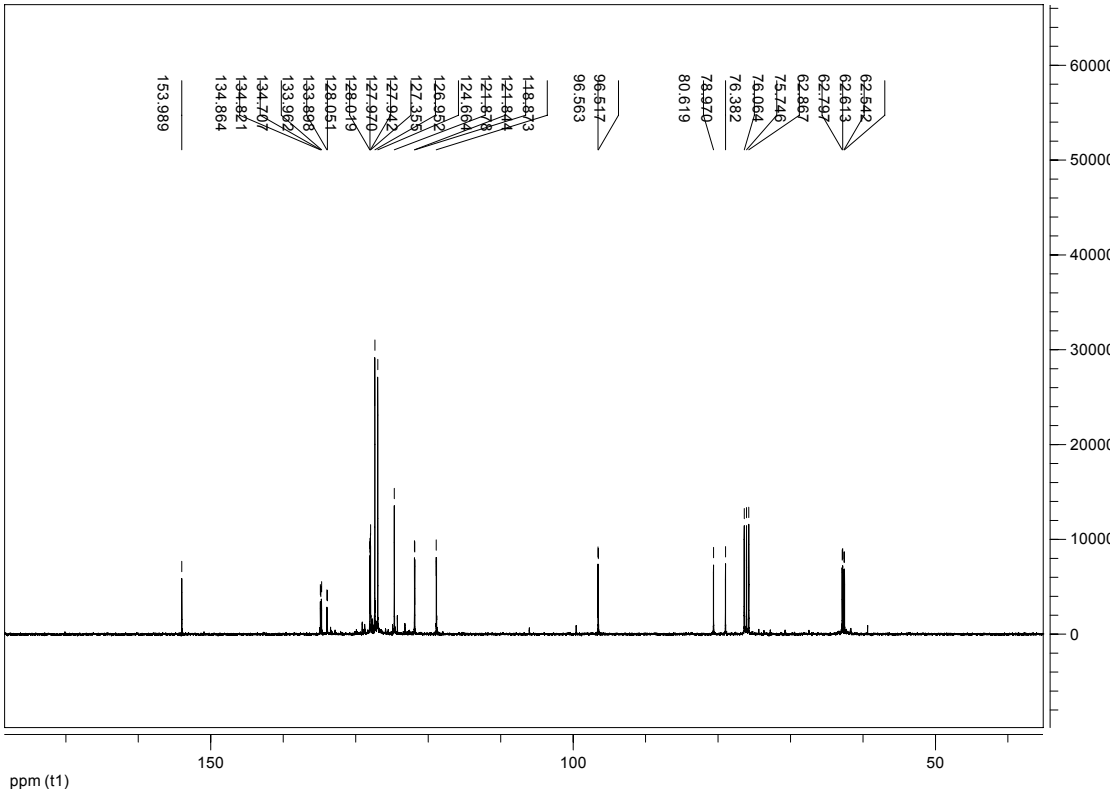
^{31}P-NMR (121 MHz, $CDCl_3$)



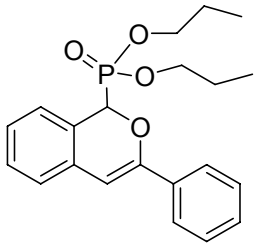
^{1}H-NMR (400 MHz, $CDCl_3$)



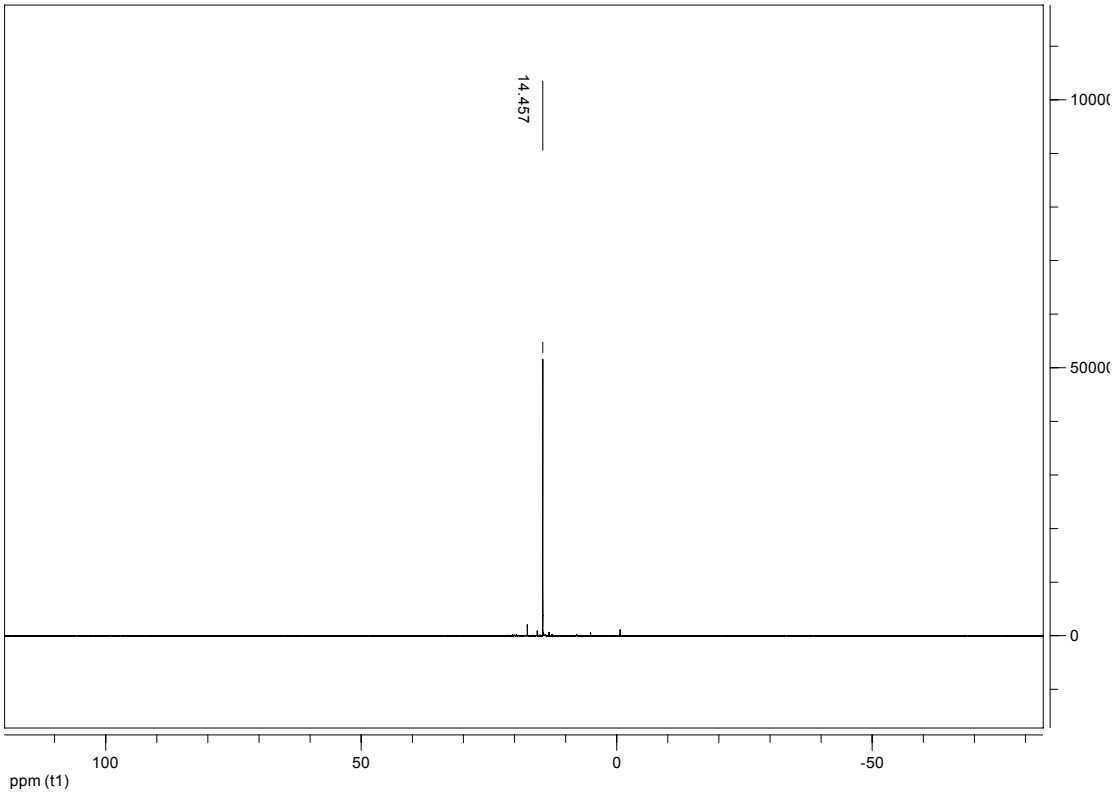
^{13}C-NMR (162 MHz, $CDCl_3$)



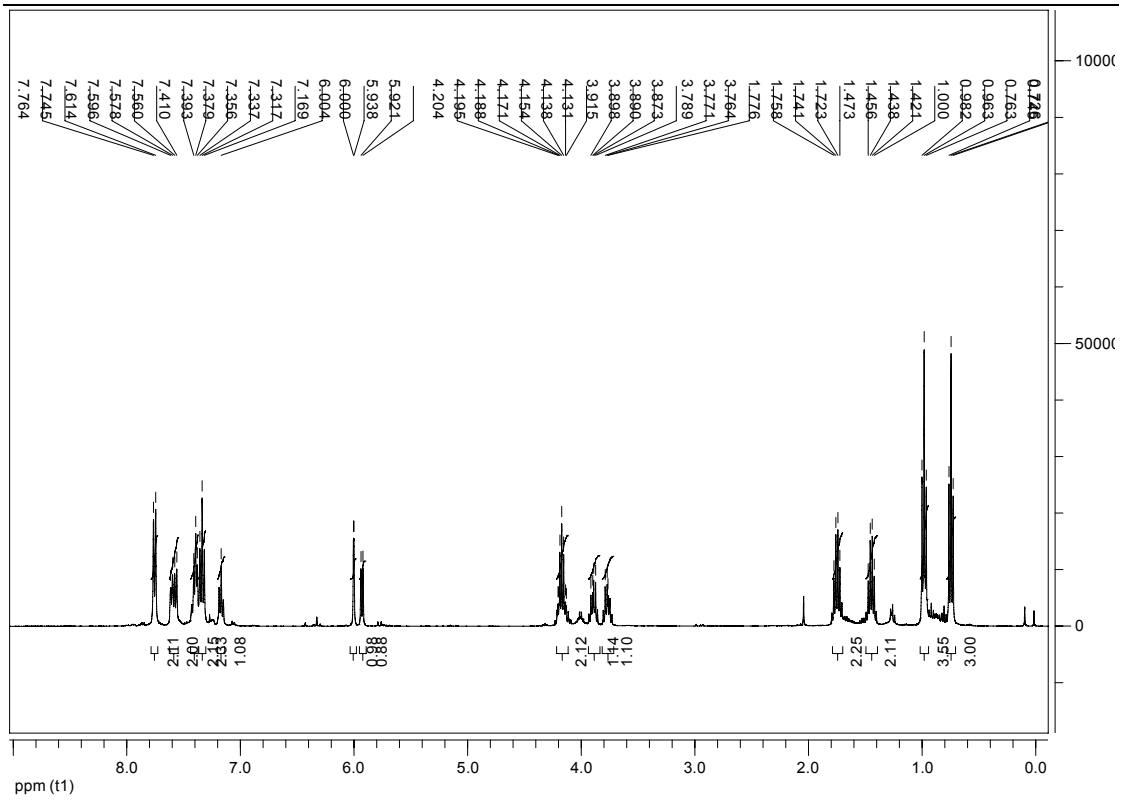
Di-(*n*)-propyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7c)



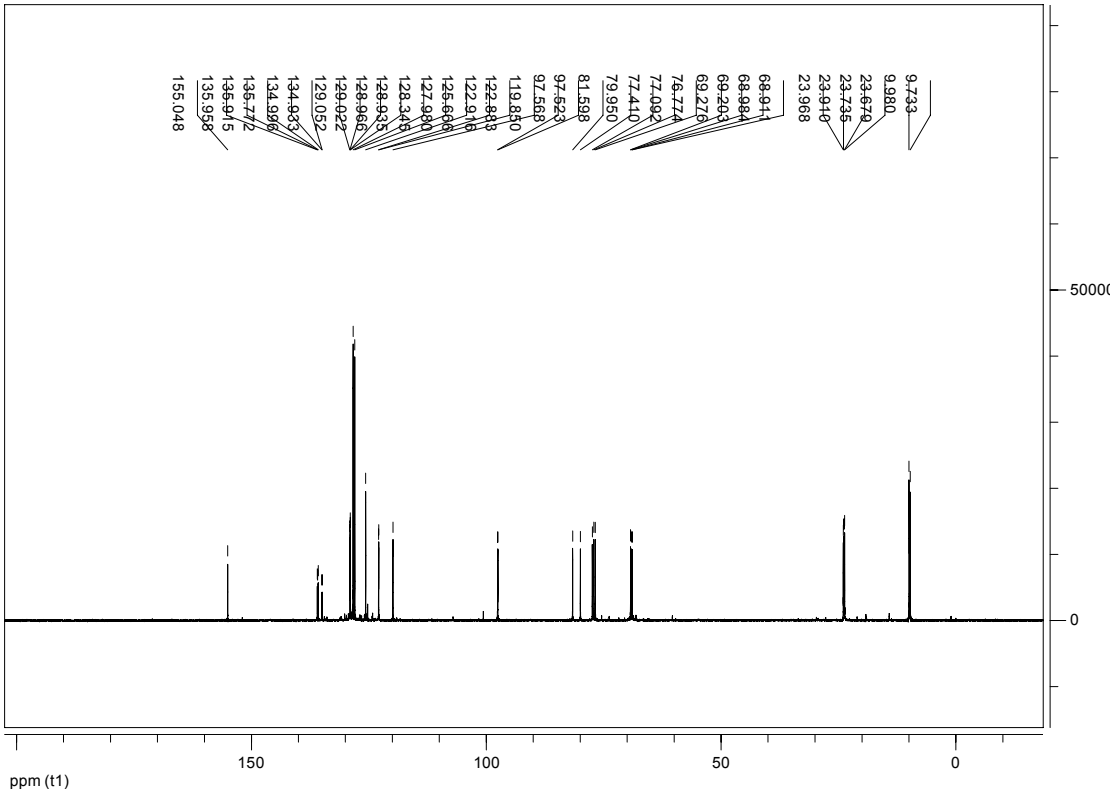
^{31}P-NMR (121 MHz, $CDCl_3$)



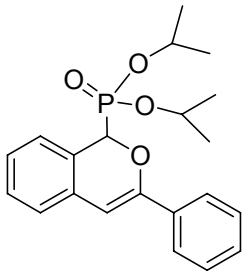
^{1}H-NMR (400 MHz, $CDCl_3$)



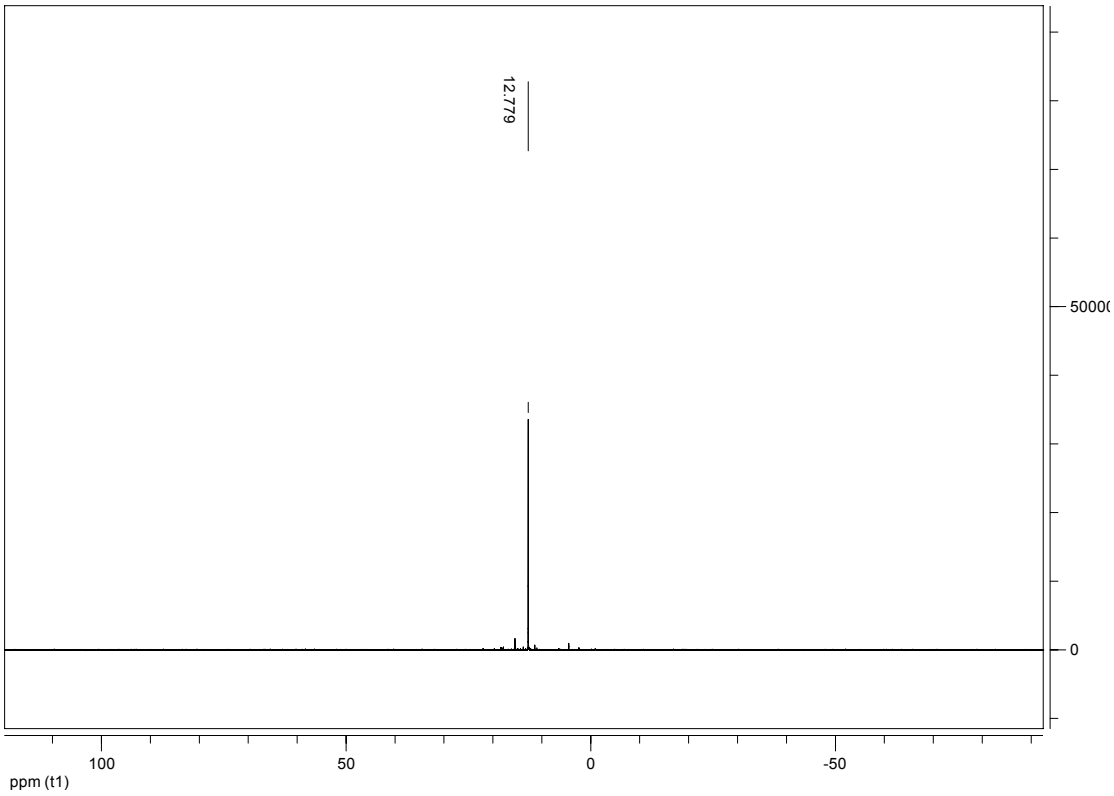
^{13}C-NMR (162 MHz, $CDCl_3$)



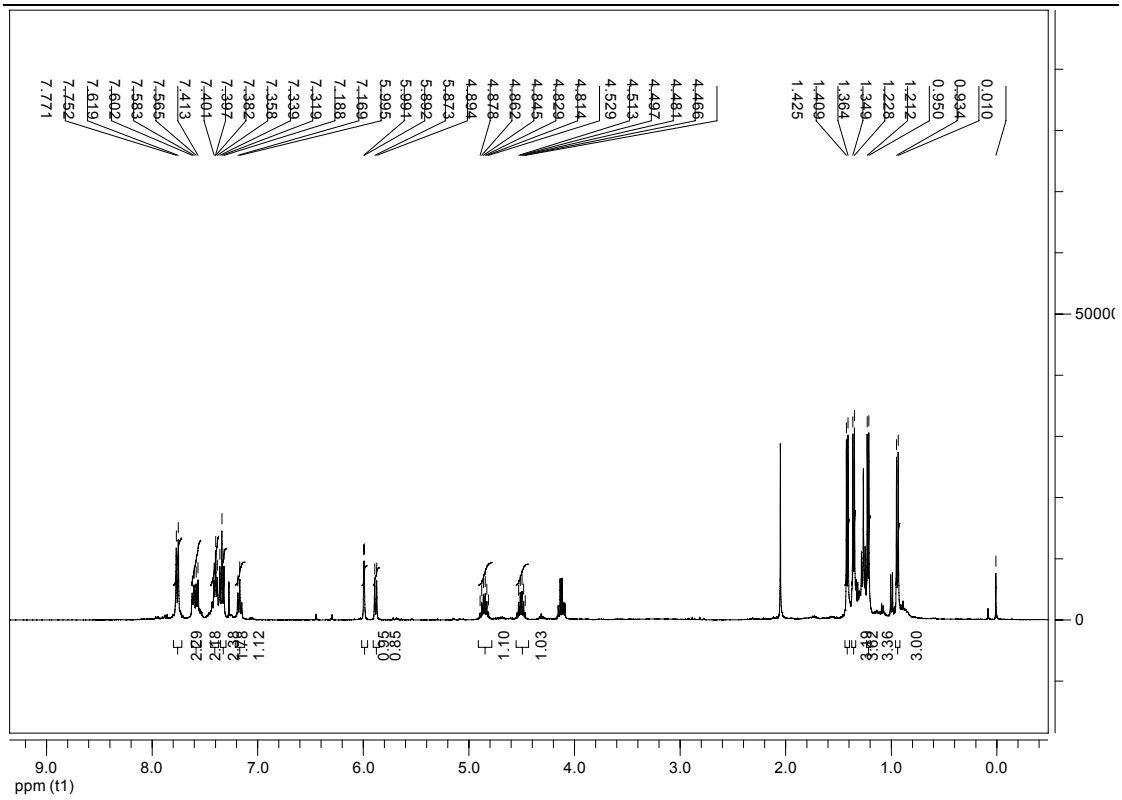
Di-(*i*)-propyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7d)



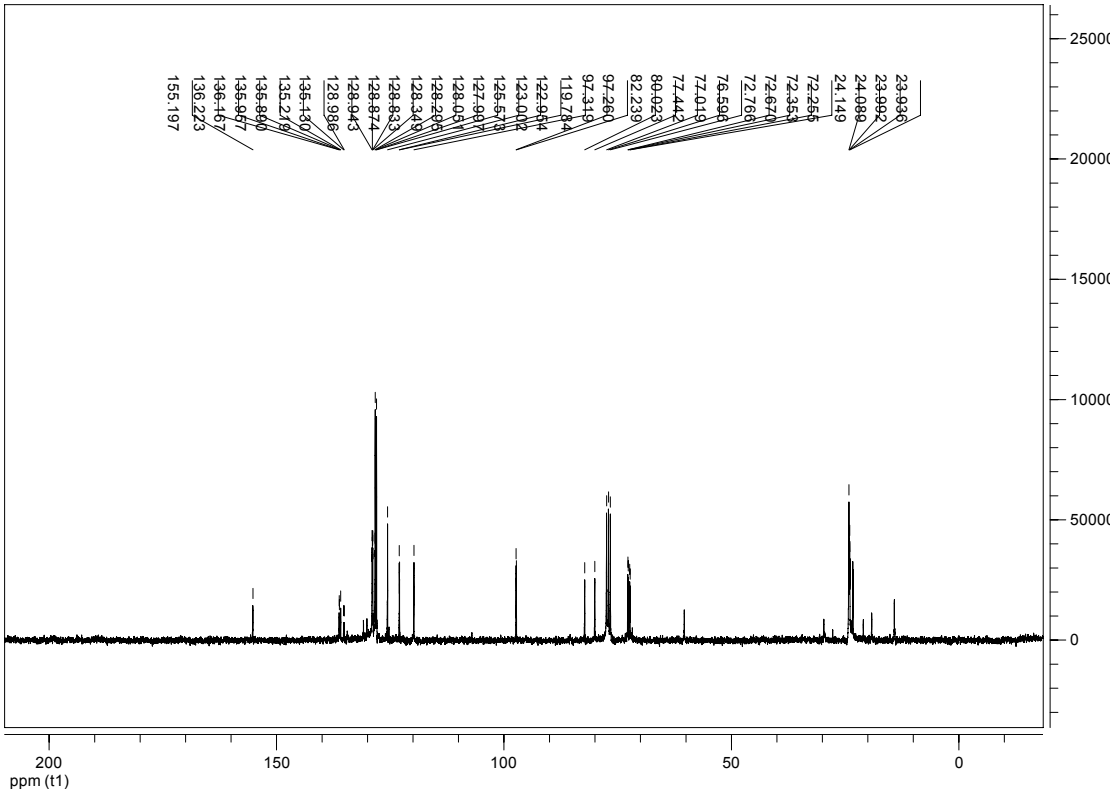
^{31}P-NMR (121 MHz, $CDCl_3$)



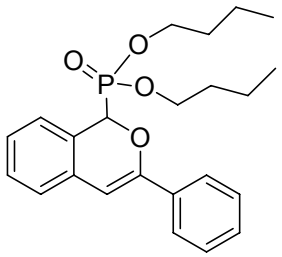
^{1}H-NMR (400 MHz, $CDCl_3$)



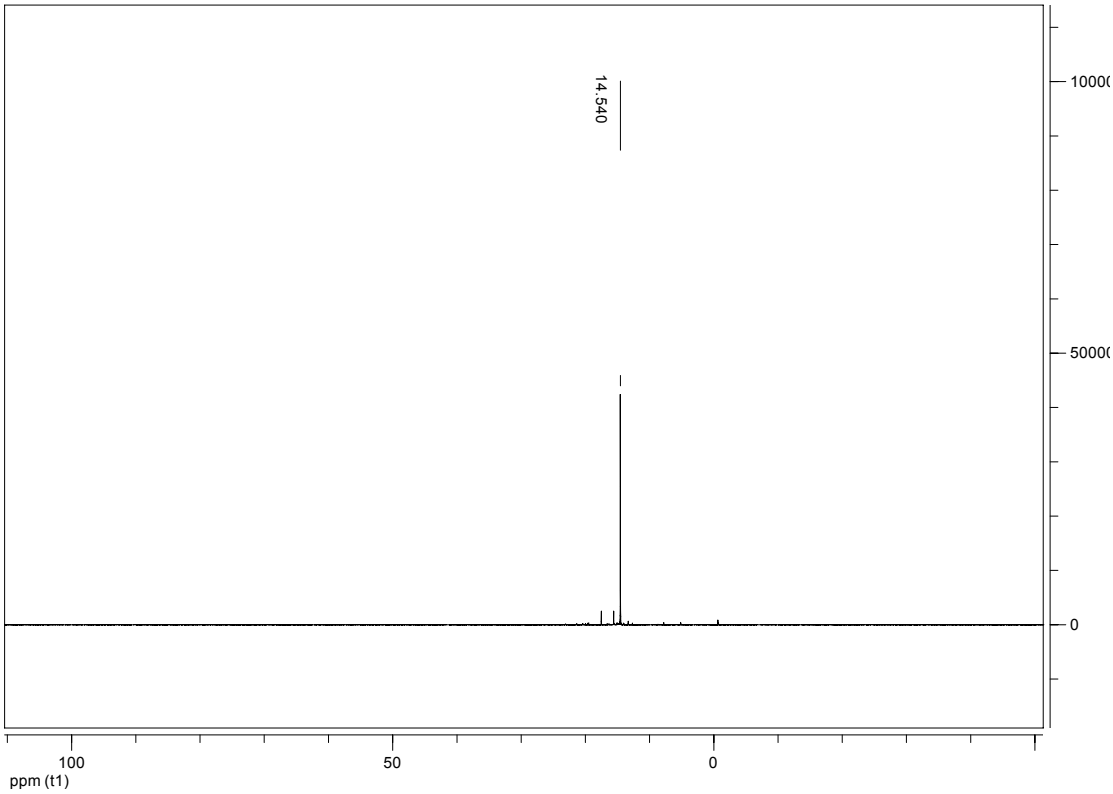
^{13}C-NMR (162 MHz, $CDCl_3$)



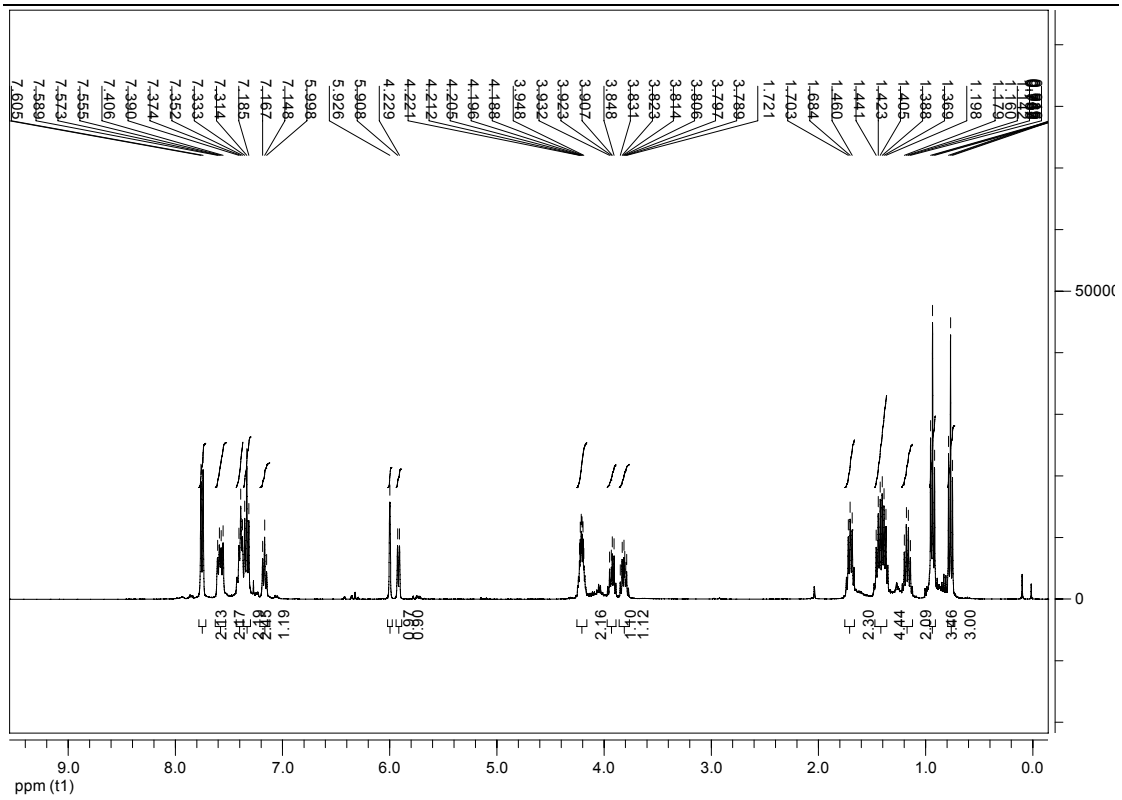
Di-(*n*)-butyl 3-phenyl-1*H*-isochromen-1-ylphosphonate (7e)



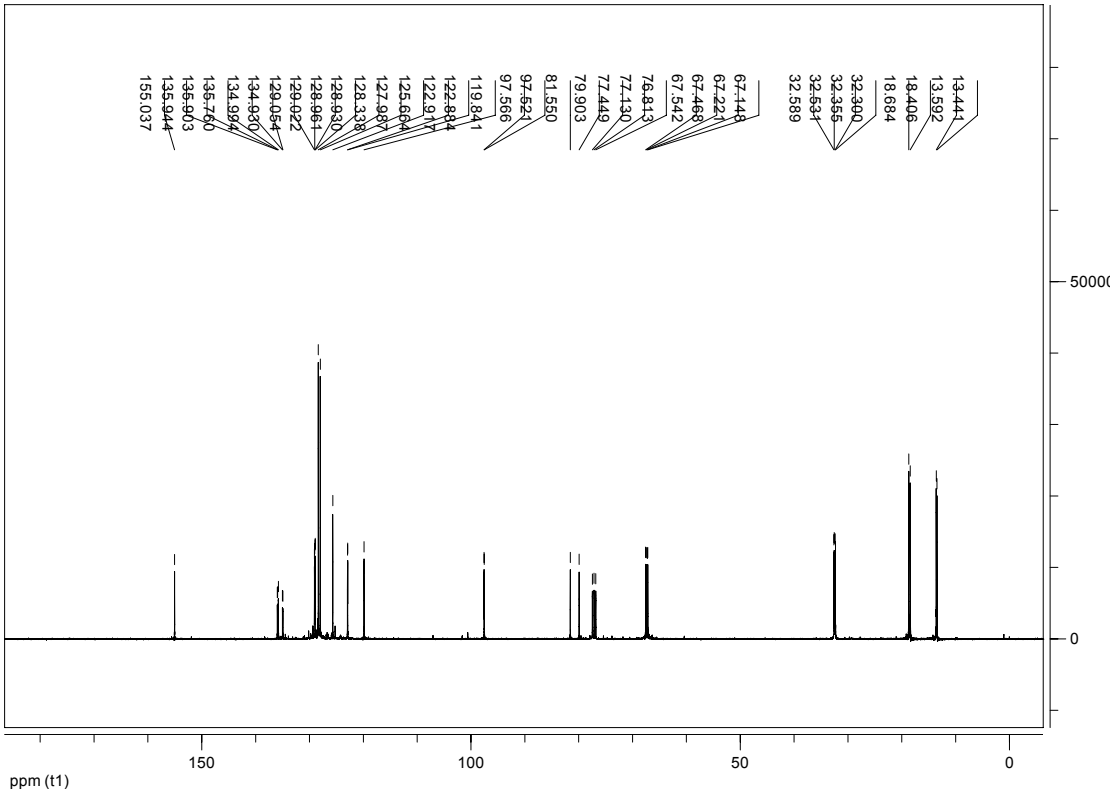
^{31}P-NMR (121 MHz, $CDCl_3$)



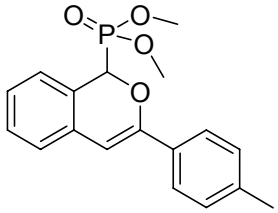
^{1}H-NMR (400 MHz, $CDCl_3$)



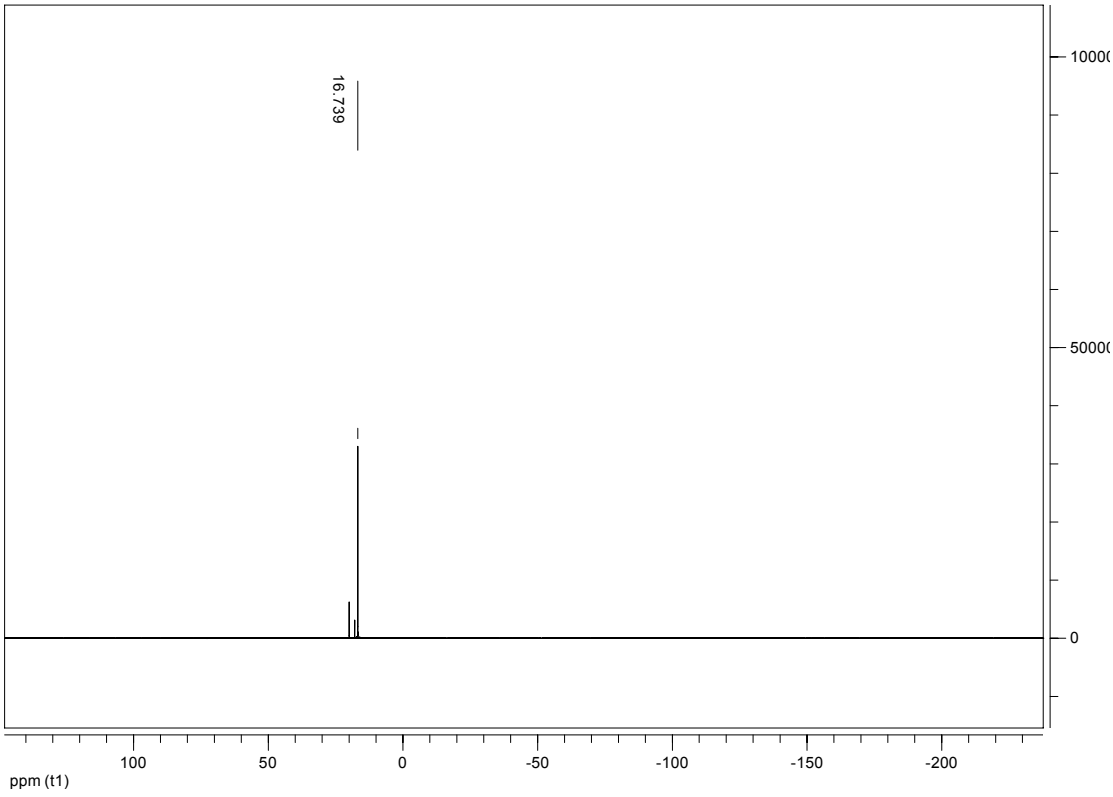
^{13}C-NMR (162 MHz, $CDCl_3$)



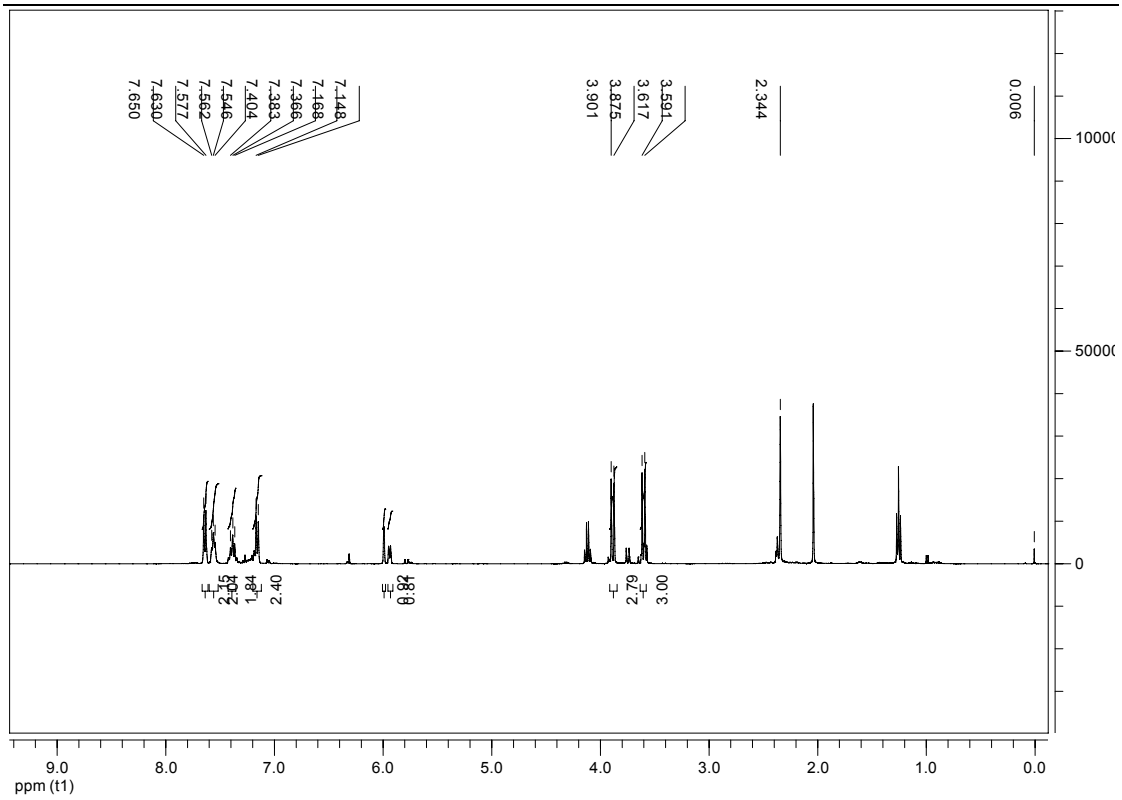
Dimethyl 3-*p*-tolyl-1*H*-isochromen-1-ylphosphonate (7f)



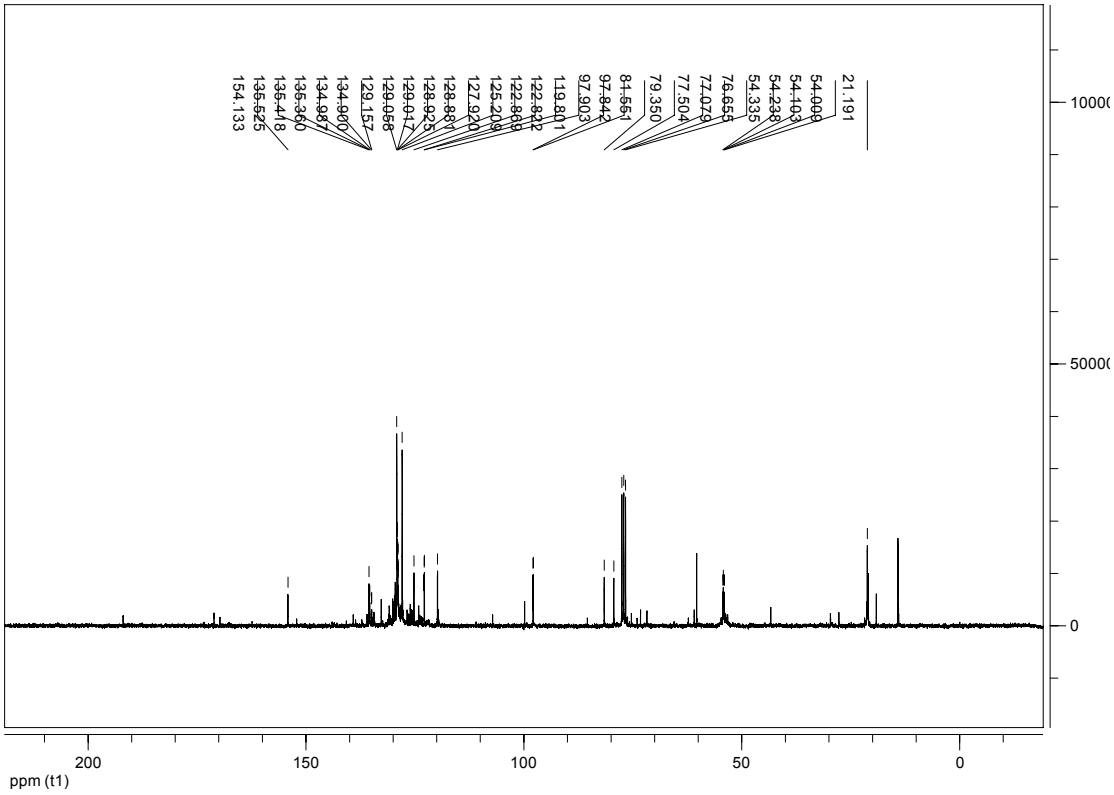
^{31}P-NMR (121 MHz, $CDCl_3$)



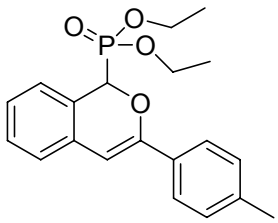
^{1}H-NMR (400 MHz, $CDCl_3$)



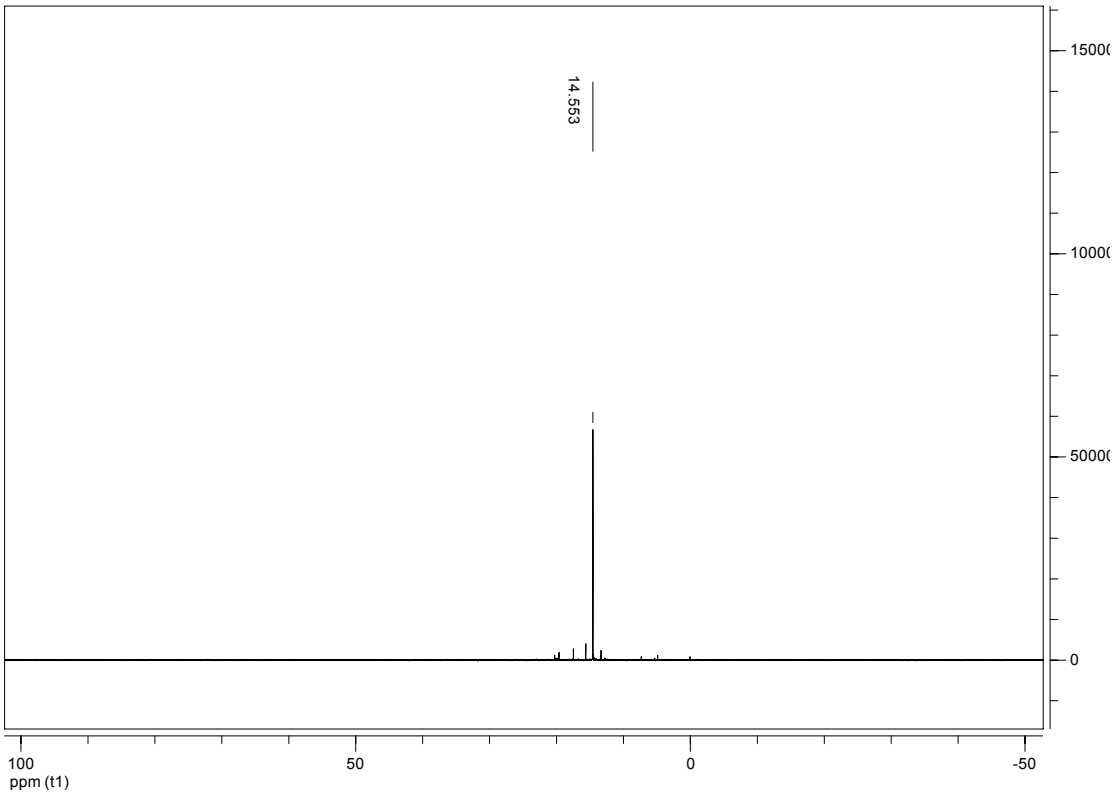
^{13}C-NMR (162 MHz, $CDCl_3$)



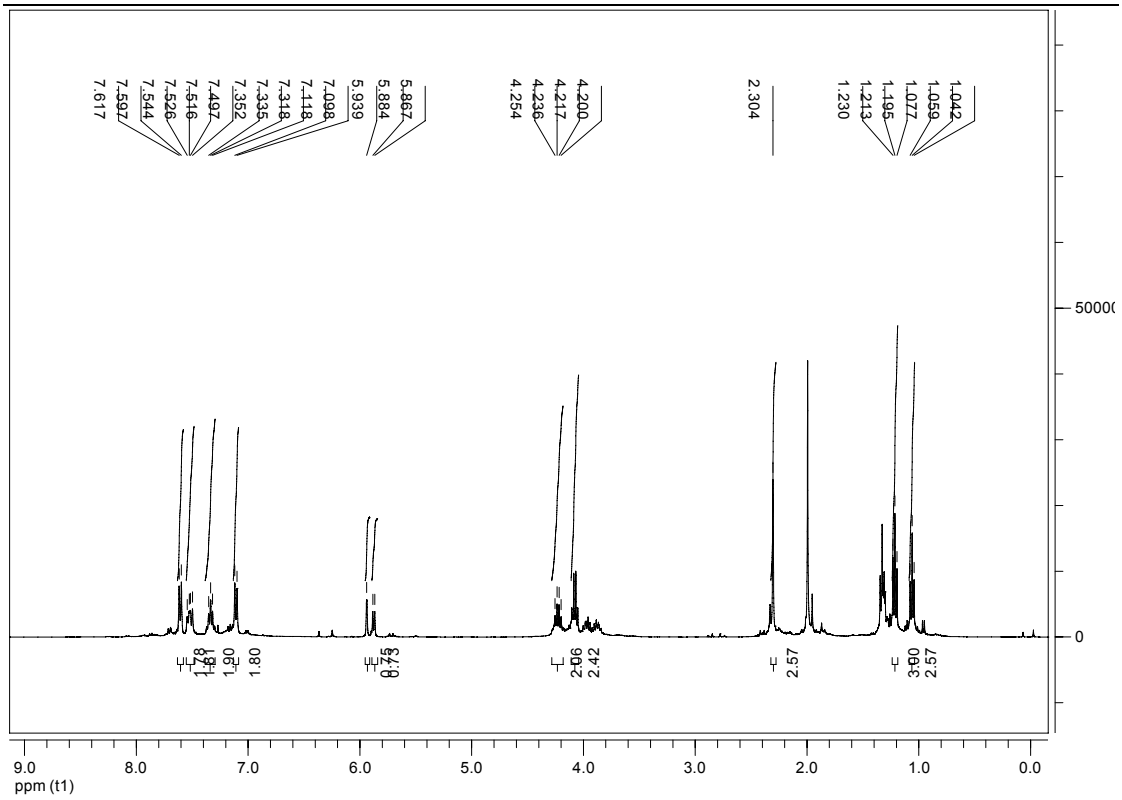
Diethyl 3-*p*-tolyl-1*H*-isochromen-1-ylphosphonate (7g)



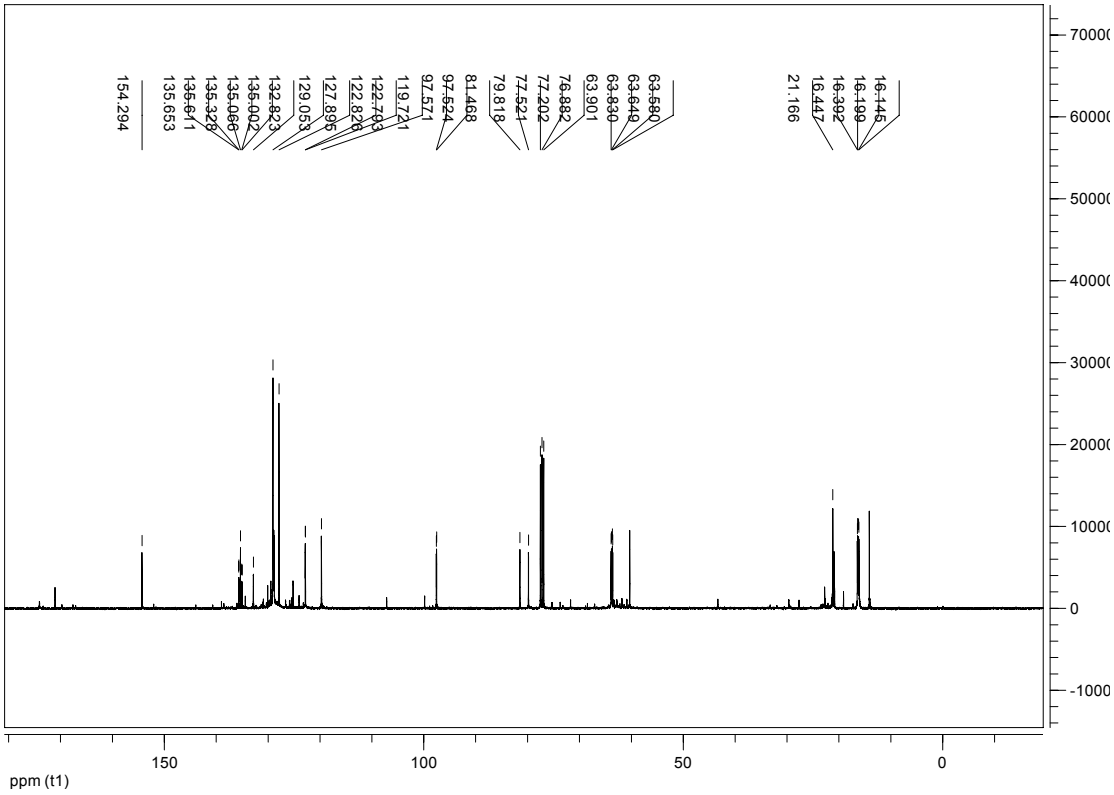
^{31}P-NMR (121 MHz, $CDCl_3$)



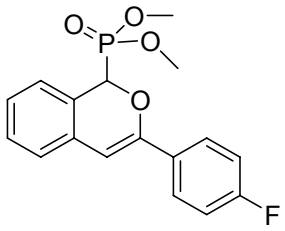
^{1}H-NMR (400 MHz, $CDCl_3$)



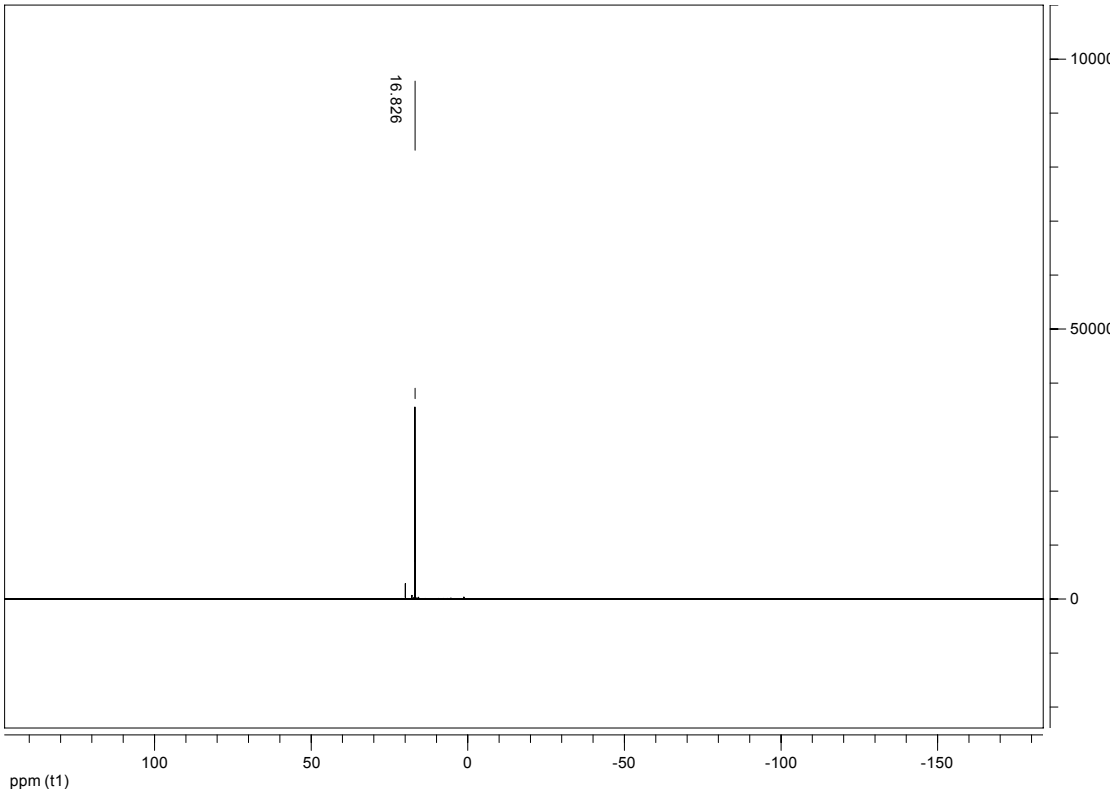
^{13}C-NMR (162 MHz, $CDCl_3$)



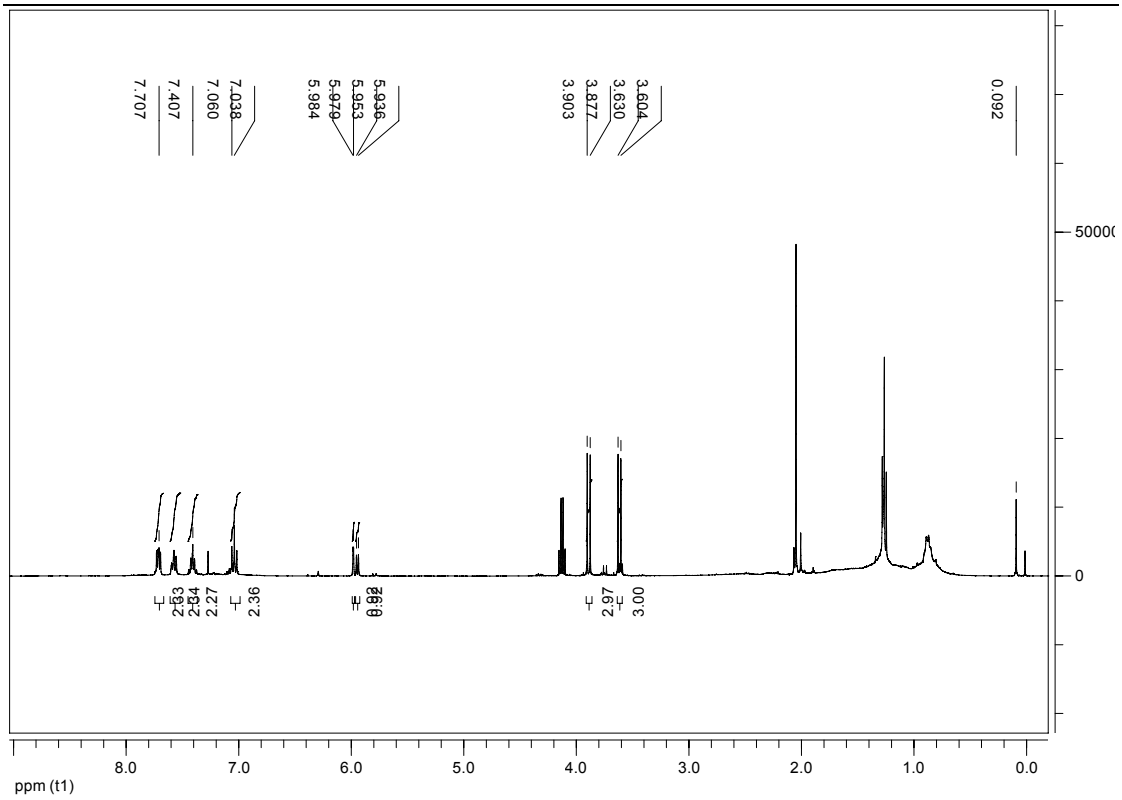
Dimethyl 3-(4-fluorophenyl)-1*H*-isochromen-1-ylphosphonate (7h)



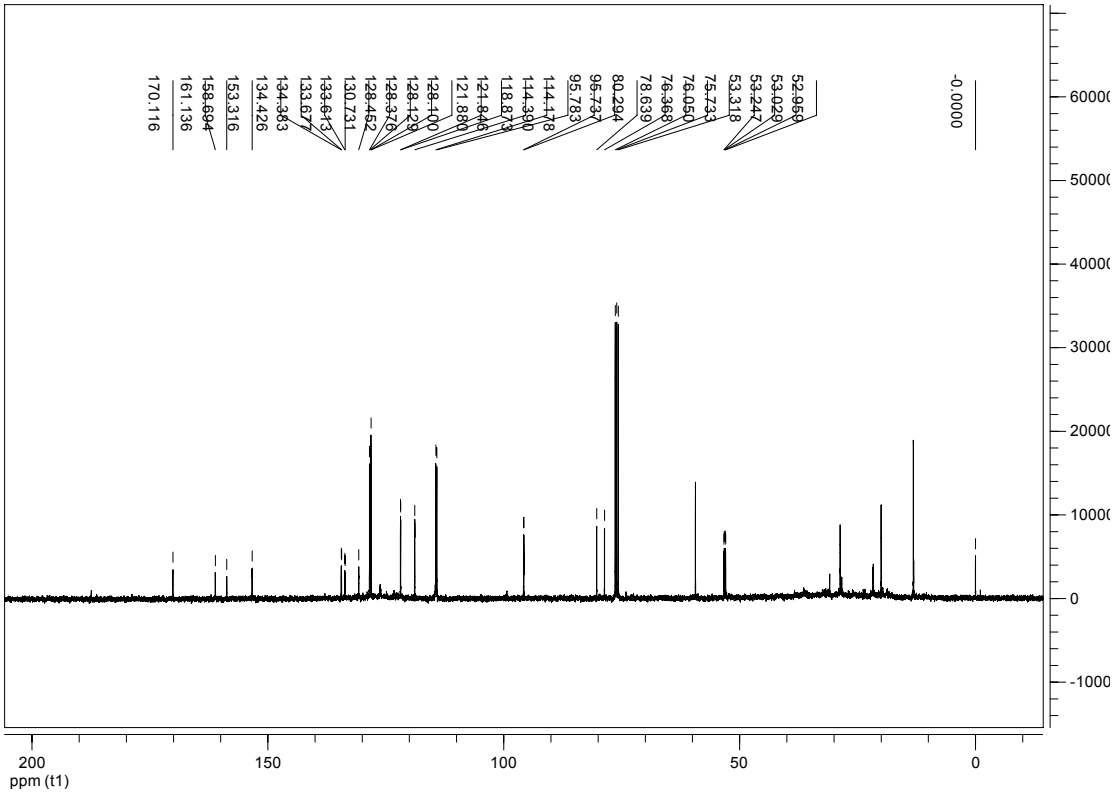
^{31}P-NMR (121 MHz, $CDCl_3$)



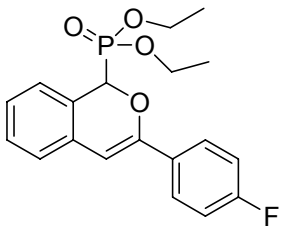
^{1}H-NMR (400 MHz, $CDCl_3$)



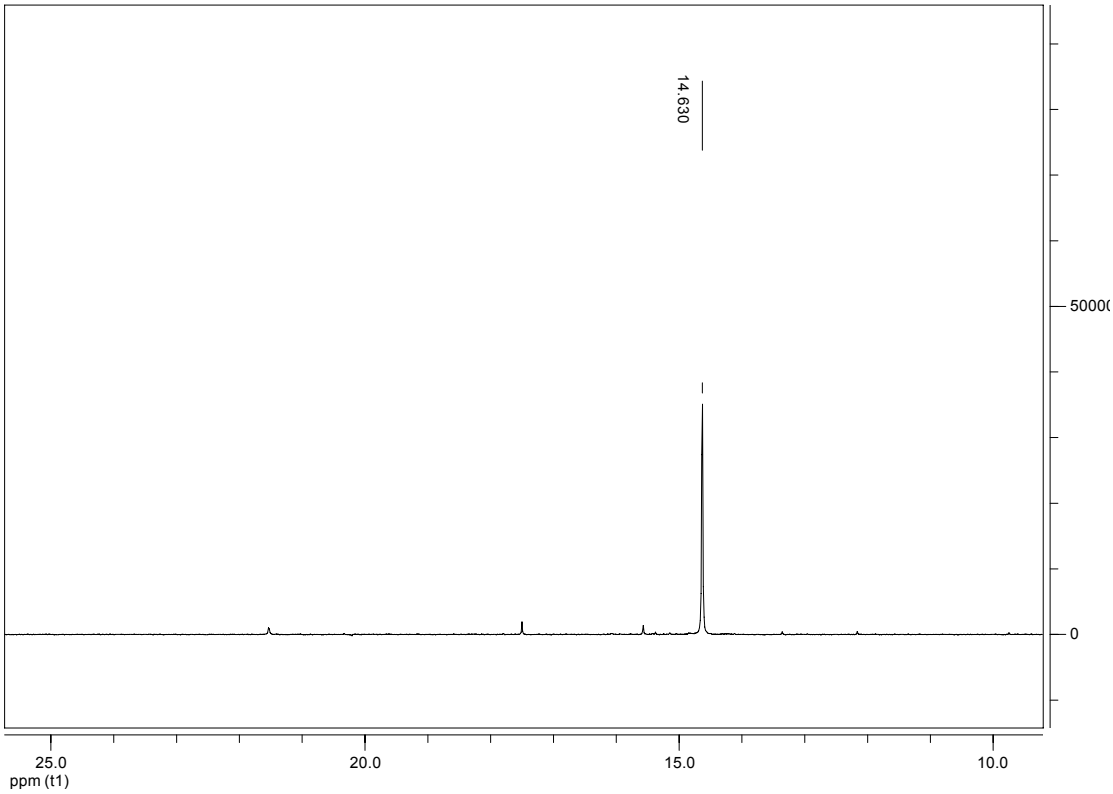
^{13}C-NMR (162 MHz, $CDCl_3$)



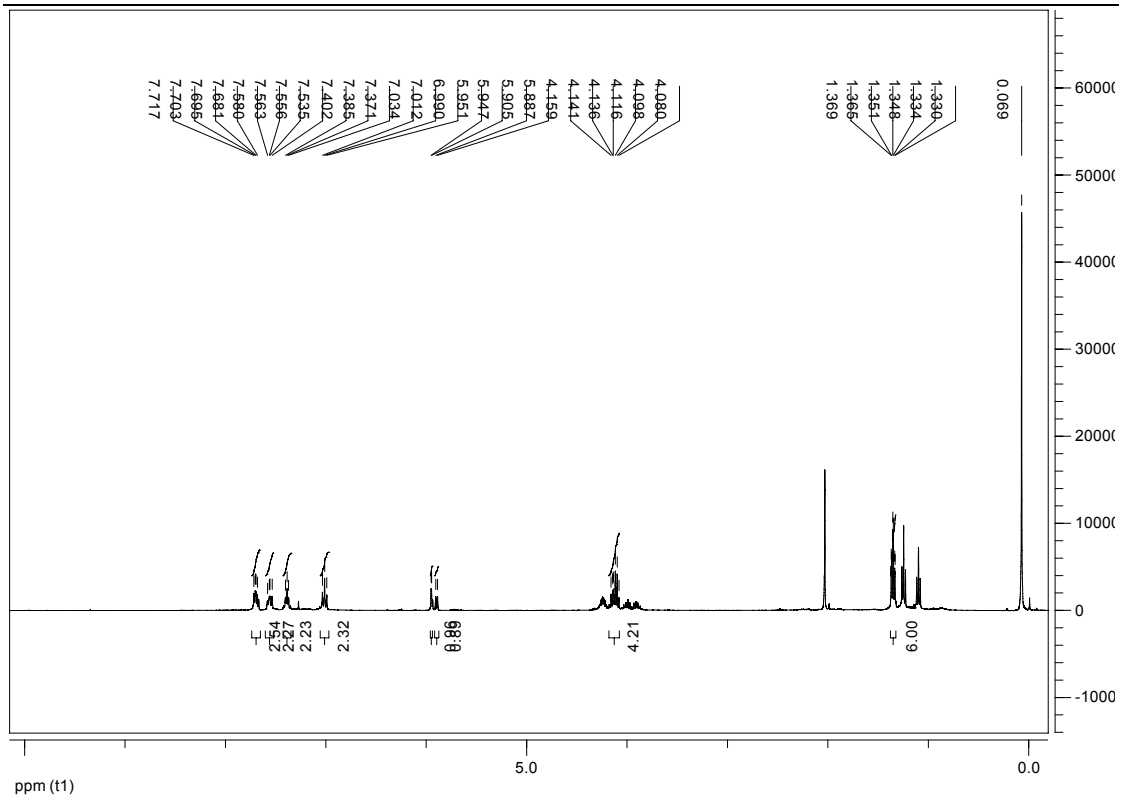
Diethyl 3-(4-fluorophenyl)-1*H*-isochromen-1-ylphosphonate (7i)



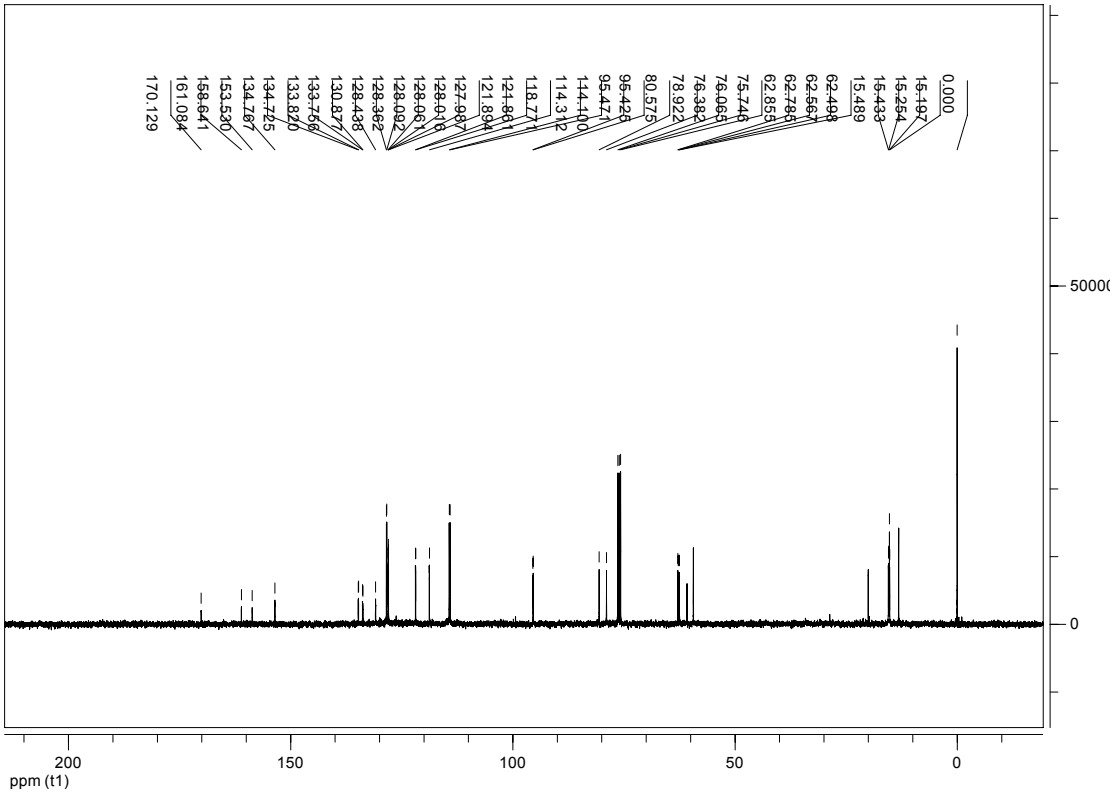
^{31}P-NMR (121 MHz, $CDCl_3$)



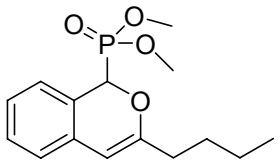
^{1}H-NMR (400 MHz, $CDCl_3$)



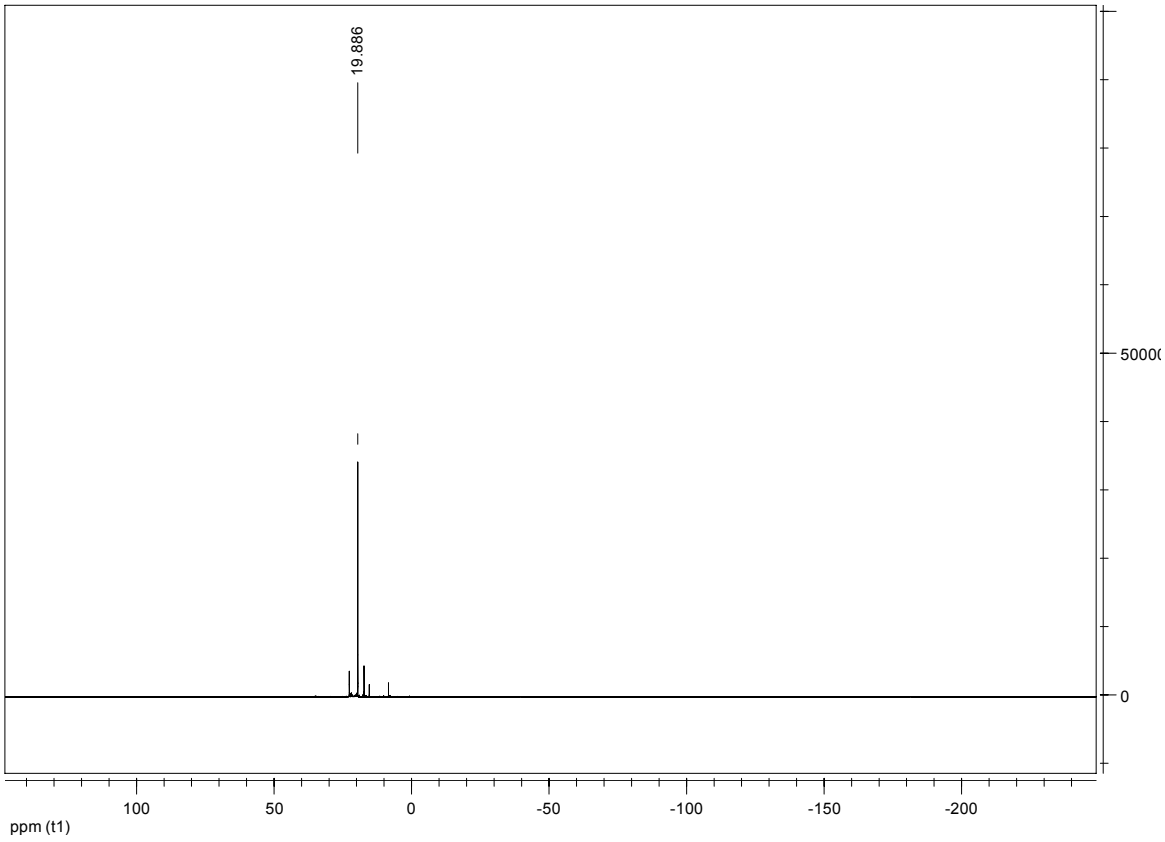
^{13}C-NMR (162 MHz, $CDCl_3$)



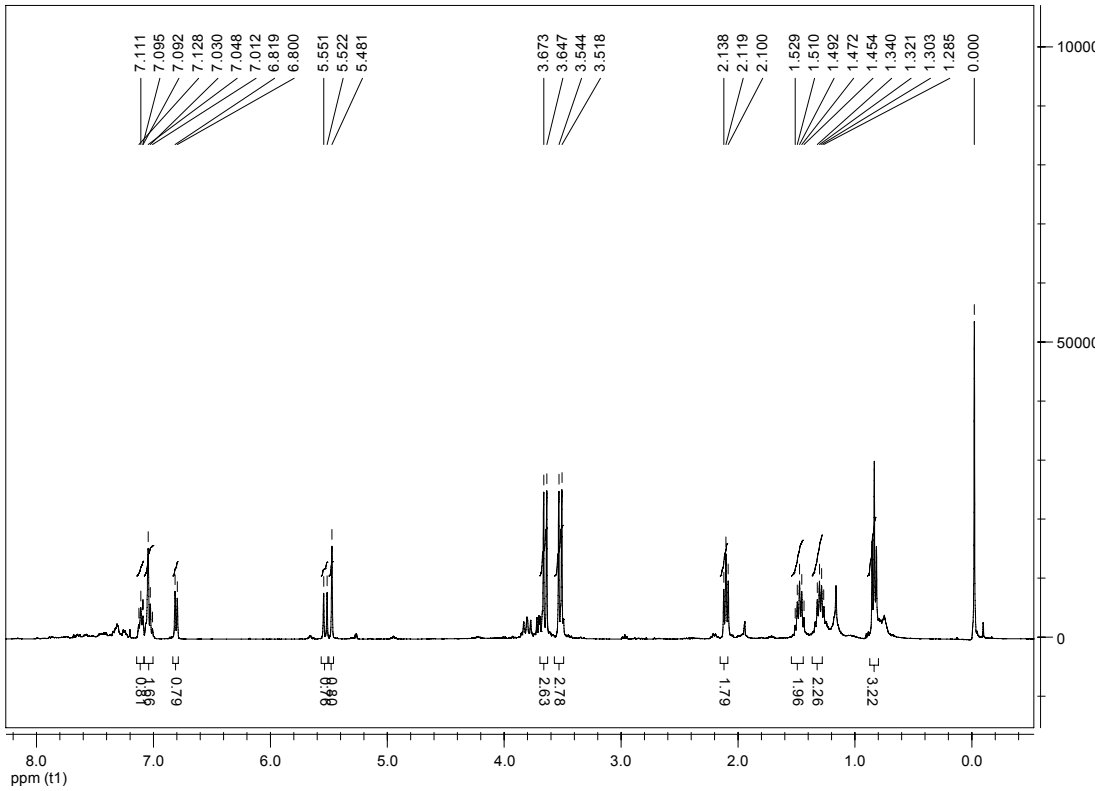
Dimethyl 3-butyl-1*H*-isochromen-1-ylphosphonate (7j)



^{31}P-NMR (121 MHz, $CDCl_3$):



^{1}H-NMR (400 MHz, $CDCl_3$):



^{13}C-NMR (162 MHz, $CDCl_3$):