Supplementary Information

"Phosphine Catalyzed Allylic Substitution of Morita-Baylis Hillman Acetates: Synthesis of *N*-Protected β-Aminophosphonic Acid Esters"

HaeIl Park,[a] Chang-Woo Cho,[b] and Michael J. Krische[b]*

[a]*College of Pharmacy*
Kangwon National University
Chuncheon, 200-701
Republic of Korea

[b]*University of Texas at Austin*
Department of Chemistry and Biochemistry
Austin, TX 78712
USA

Table of Contents

Experimental Section

General. All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. 1,4-Dioxane was distilled from sodium and degassed with Ar prior to use. Chemical reagents were used without further purification, unless otherwise noted.

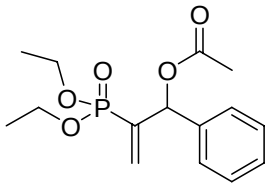
Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates. Preparative column chromatography employing silica gel was performed according to the method of Still.[1] Melting points were determined on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected. High-resolution mass spectra (HRMS) were reported as m/e (relative intensity). Accurate masses are reported for the molecular ion (M+1) or a suitable fragment ion.

Chemical Shifts of proton nuclear magnetic resonance (^{1}H NMR) spectra are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Chemical shifts of carbon-13 nuclear magnetic resonance (^{13}C NMR) are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadbrand decoupling.

General procedure for the preparation of acetates 1b-6b: To an acetonitrile solution (0.2 M) of alcohol **1a** (1 mmol, 100 mol%) at ambient temperature was added acetic anhydride (1.2 mmol, 120 mol%) followed by ferric chloride (0.05 mmol, 5 mol%). The reaction vessel was allowed to stir for 3 h, at which point saturated aqueous $NaHCO_3$ solution was added until bubbling ceased. The reaction mixture was partitioned between diethyl ether and water. The aqueous layer was extracted with diethyl ether and the combined ethereal extracts were dried ($MgSO_4$), filtered and evaporated onto silica gel. Purification by silica gel column chromatography provides allylic acetate **1b**.

General procedure for the preparation of 4,5-dichlorophthalimides 1c-6c: To a reaction vessel charged with acetate **1b** (0.5 mmol, 100 mol%), 4,5-dichlorophthalimide (1.0 mmol, 200 mol%), and PPh_3 (0.1 mmol, 20 mol%) was added a dioxane (0.3 M). The reaction vessel was placed in a heating bath at 110 ^{o}C and was allowed to stir until complete consumption of **1b** was observed by TLC analysis, at which point the reaction mixture was evaporated onto silica gel. Purification by silica gel column chromatography provides phthalimide **1c**.

(1) Still, W. C.; Kahn, M; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



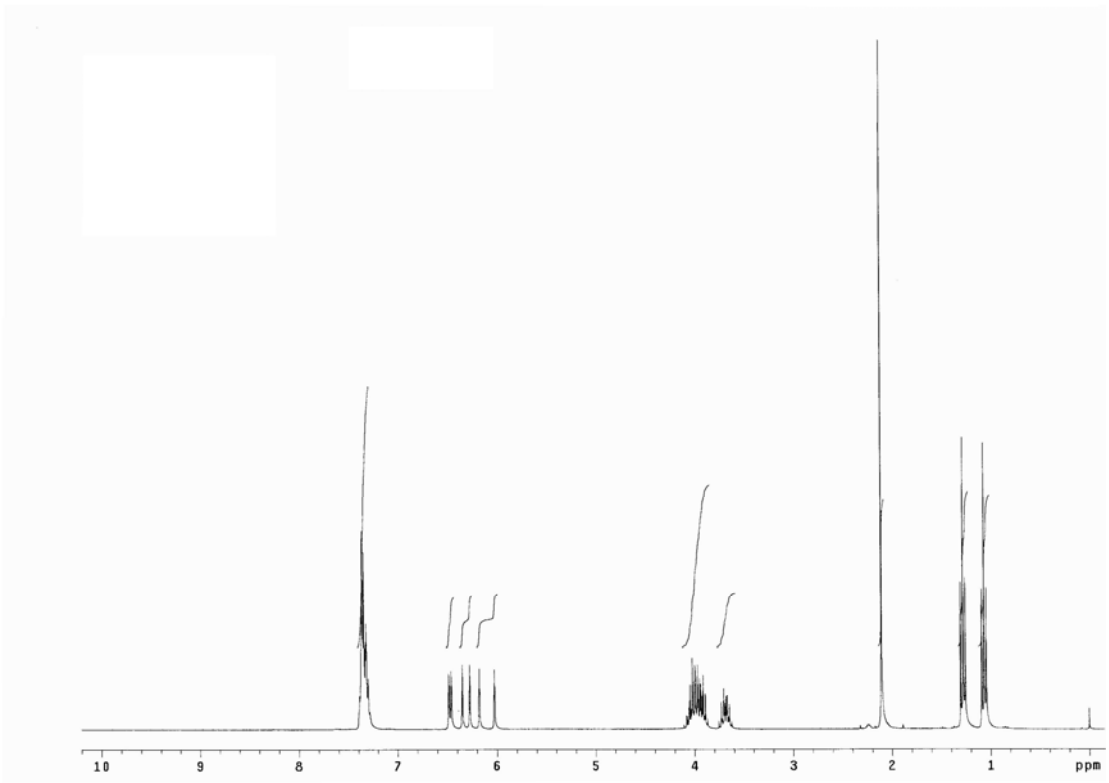
1b

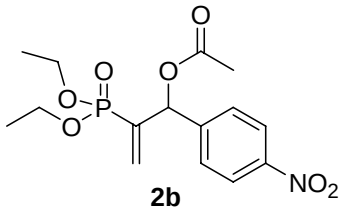
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.47 (d, *J* = 7.2 Hz, 1H), 6.31 (d, *J* = 22.5 Hz, 1H), 6.10 (d, *J* = 45.3 Hz, 1H), 4.04-3.89 (m, 3H), 3.72-3.64 (m, 1H), 2.10 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 140.0, 137.7, 137.2, 130.7, 130.6, 128.3, 128.2, 127.7, 73.9, 61.9, 61.7, 20.9, 16.1, 15.8

HRMS calcd for $C_{15}H_{22}O_5P$ [M+1] 313.1205, found 313.1201

FTIR (neat) 3018, 2399, 1739, 1523, 1424, 1371, 1215, 1025, 975, 928, 769, 669 cm^{-1}





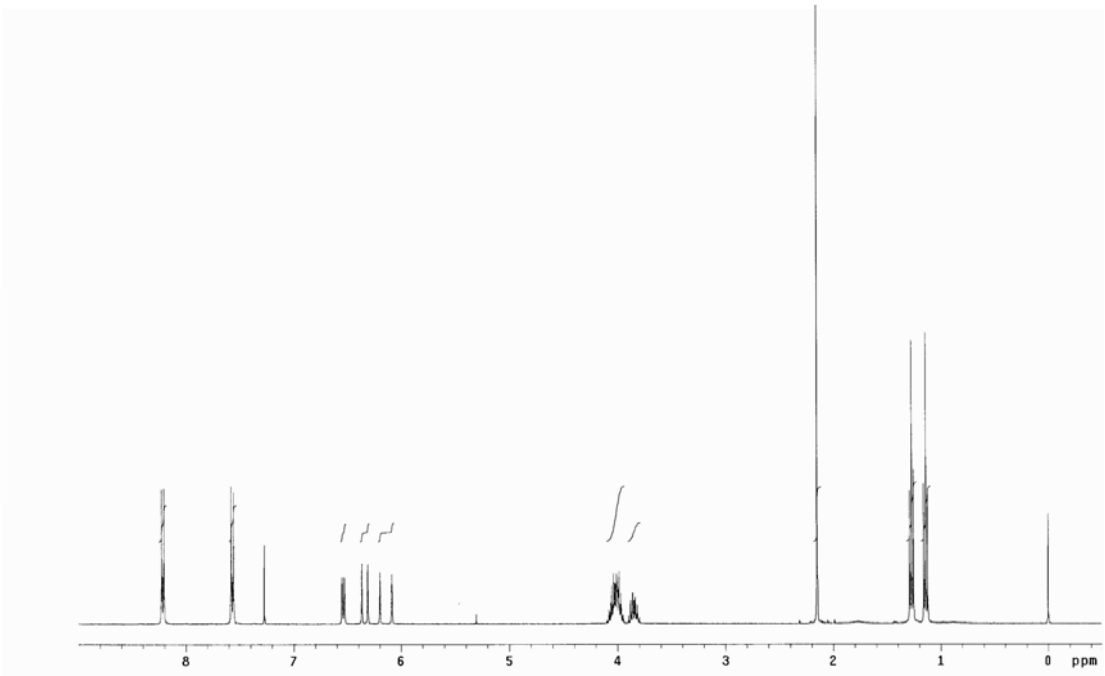
2b

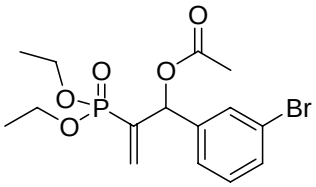
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.20 (m, 2H), 7.58-7.56 (m, 2H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.34 (d, *J* = 22.0 Hz, 1H), 6.14 (d, *J* = 44.8 Hz, 1H), 4.07-3.94 (m, 3H), 3.89-3.79 (m, 1H), 2.15 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 147.7, 144.6, 139.3, 136.9, 131.5, 131.4, 128.5, 123.5, 73.0, 62.2, 62.1, 20.8, 16.1, 16.0

HRMS calcd for $C_{15}H_{21}NO_7P$ [M+1] 358.1056, found 358.1057

FTIR (neat) 2983, 2927, 1747, 1523, 1348, 1225, 1024, 970, 856, 835 cm^{-1}





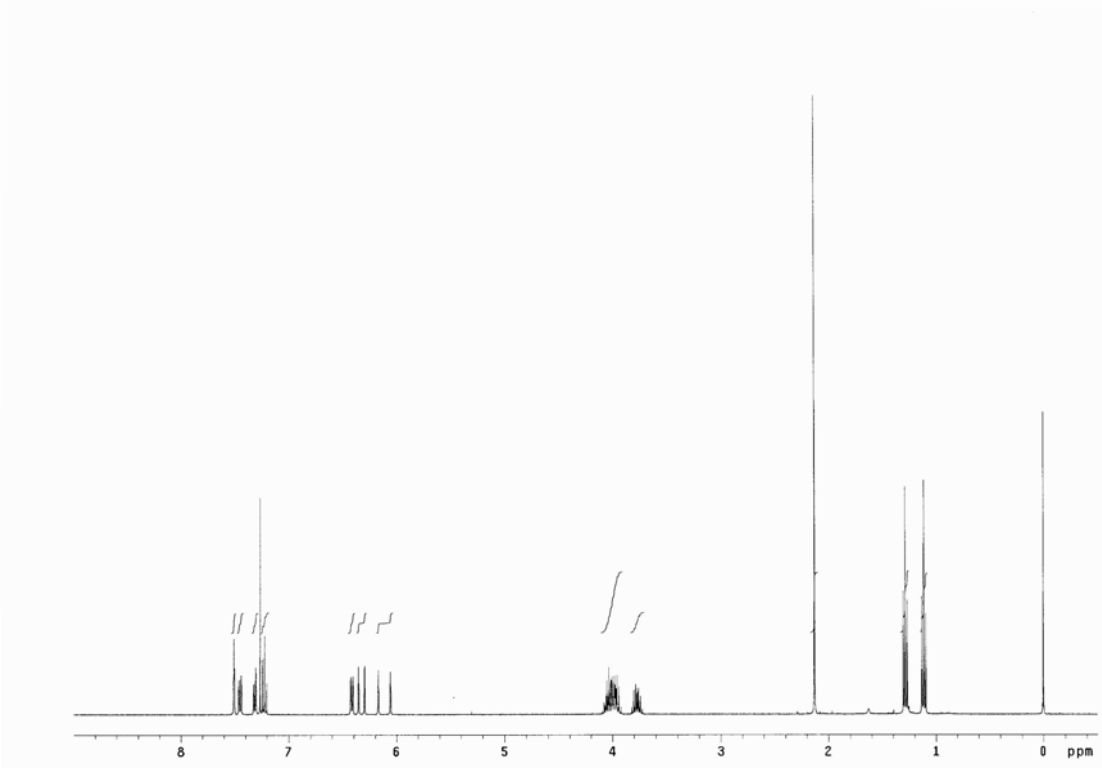
3b

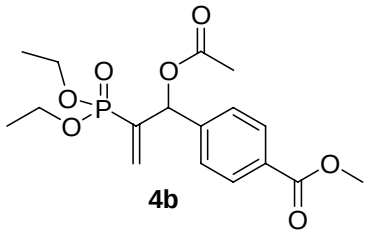
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.50 (m, 1H), 7.46-7.43 (m, 1H), 7.32-7.30 (m, 1H), 7.24-7.20 (m, 1H), 6.41 (d, *J* = 7.6 Hz, 1H), 6.0432 (d, *J* = 22.4 Hz, 1H), 6.11 (dt, *J* = 45.2, 1.2 Hz, 1H), 4.09-3.92 (m, 3H), 3.81-3.72 (m, 1H), 2.12 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 139.8, 137.4, 131.6, 131.3, 130.8, 130.0, 126.7, 122.4, 73.4, 62.3, 62.1, 21.0, 16.3, 16.1

HRMS calcd for $C_{15}H_{21}O_5PBr$ [M+1] 391.0310, found 391.0317

FTIR (neat): 2982, 2929, 1747, 1572, 1476, 1429, 1370, 1227, 1194, 1024, 971, 802, 693 cm^{-1}





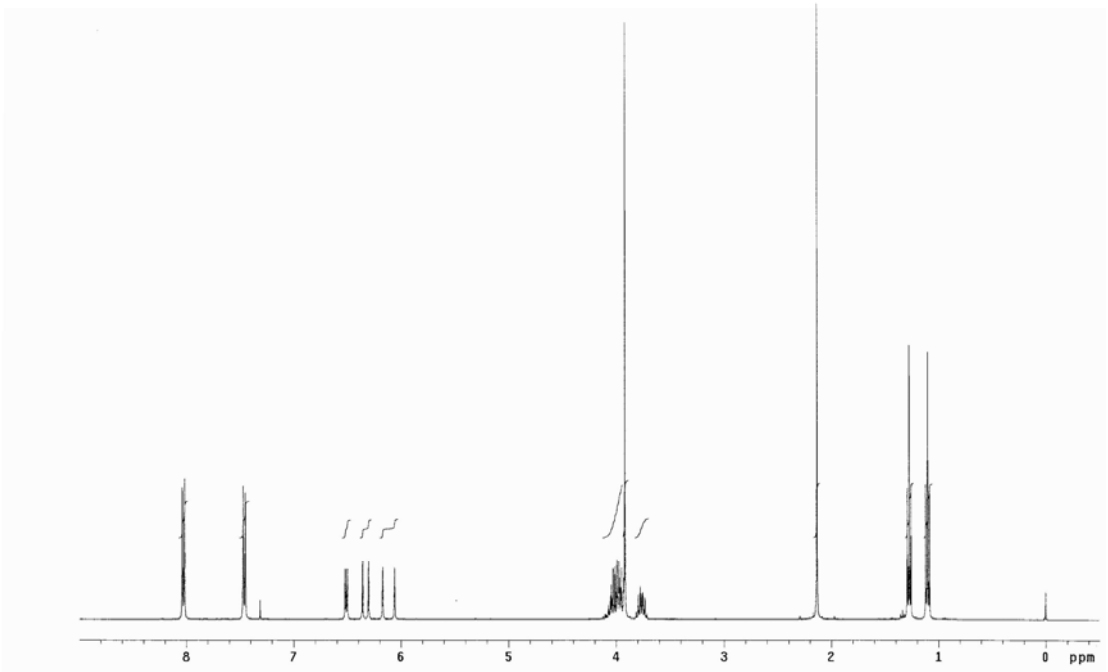
4b

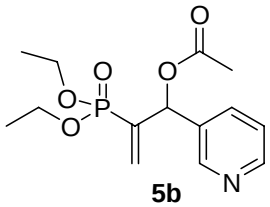
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 7.6 Hz, 1H), 6.33 (d, *J* = 22.4 Hz, 1H), 6.11 (d, *J* = 44.8 Hz, 1H), 4.07-3.93 (m, 3H), 3.91 (s, 3H), 3.81-3.71 (m, 1H), 2.13 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.871.10 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 166.8, 142.6, 139.9, 137.6, 131.6, 131.5, 130.4, 129.8, 128.0, 73.8, 62.4, 62.2, 52.4, 21.2, 16.4, 16.3

HRMS calcd for $C_{17}H_{24}O_7P$ [M+1] 371.1260, found 371.1264

FTIR (neat) 2984, 2929, 1746, 1723, 1612, 1437, 1371, 1282, 1228, 1110, 1021, 970, 810, 798, 769, 705 cm^{-1}





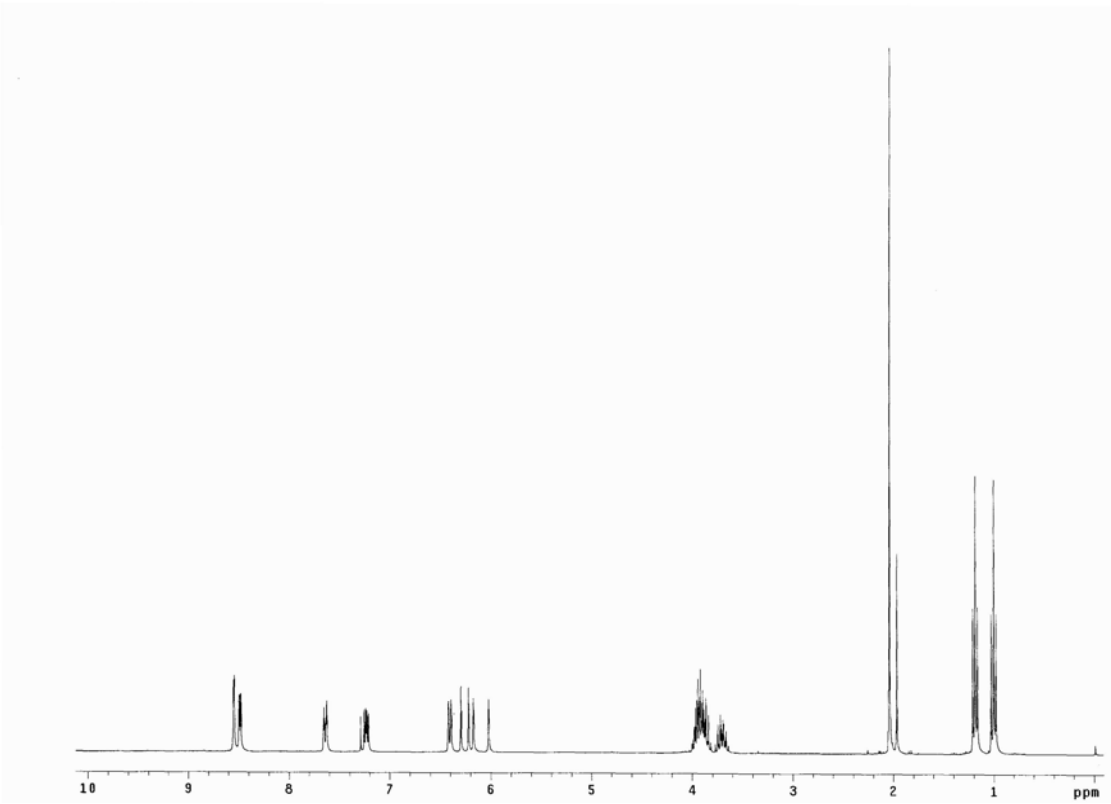
5b

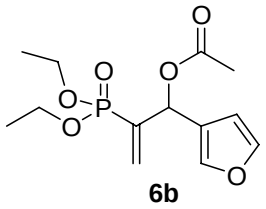
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55-8.47 (m, 2H), 7.66-7.62 (m, 1H), 7.25-7.21 (m, 1H), 6.40 (d, *J* = 7.8 Hz, 1H), 6.26 (d, *J* = 22.2 Hz, 1H), 6.10 (d, *J* = 45.0 Hz, 1H), 3.97-3.84 (m, 3H), 3.74-3.66 (m, 1H), 2.04 (s, 3H), 1.18 (t, *J* = 6.9 Hz, 3H), 1.00 (t, *J* = 6.9 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 149.1, 148.8, 139.1, 136.7, 135.5, 130.7, 123.1, 71.7, 62.0, 61.8, 20.6, 15.9, 15.7

HRMS calcd for $C_{14}H_{21}NO_5P$ [M+1] 314.1157, found 314.1157

FTIR (neat): 3019, 2399, 1743, 1522, 1425, 1215, 1025, 929, 766, 669 cm^{-1}





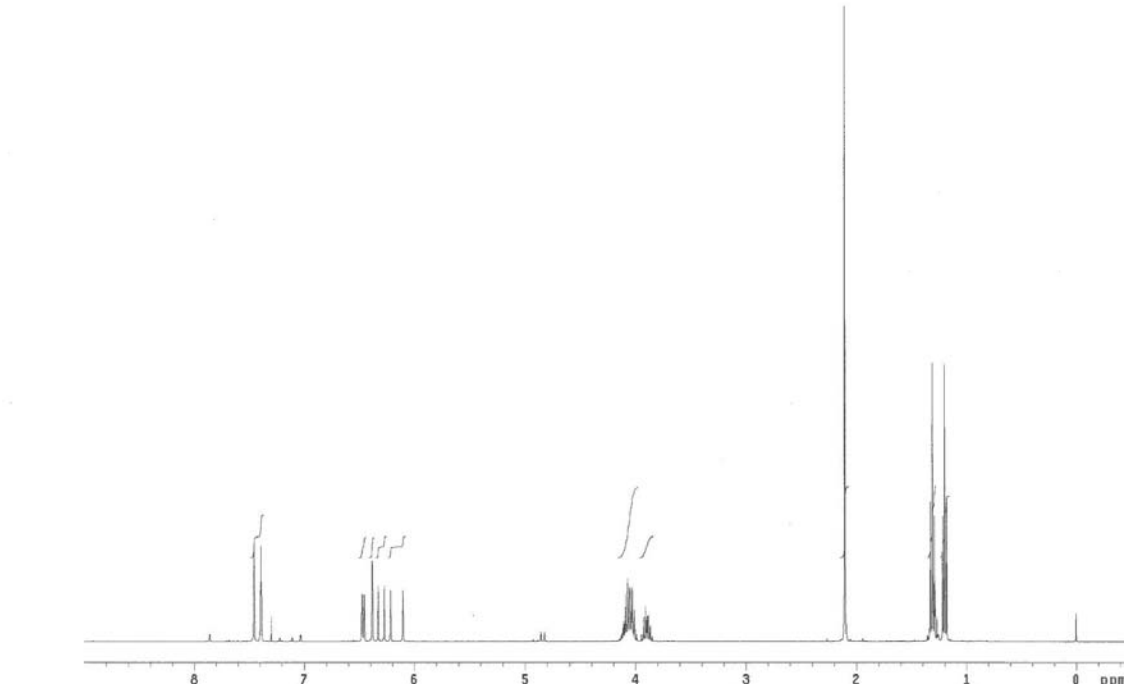
6b

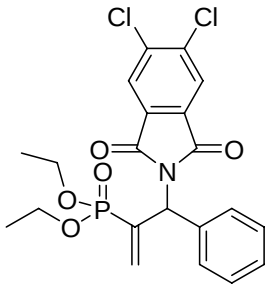
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.45 (m, 1H), 7.40-7.38 (m, 1H), 6.47 (d, *J* = 7.5 Hz, 1H), 6.39-6.38 (m, 1H), 6.30 (d, *J* = 22.2 Hz, 1H), 6.16 (d, *J* = 45.3 Hz, 1H), 4.13-3.99 (m, 3H), 3.95-3.85 (m, 1H), 2.10 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 143.1, 141.3, 139.6, 137.2, 130.7, 122.6, 66.5, 62.0, 61.9, 20.8, 16.0, 15.8

HRMS calcd for $C_{13}H_{20}O_6P$ [M+1] 303.0998, found 303.0995

FTIR (neat): 2984, 2932, 1746, 1503, 1370, 1160, 1023, 971, 798 cm^{-1}





1c

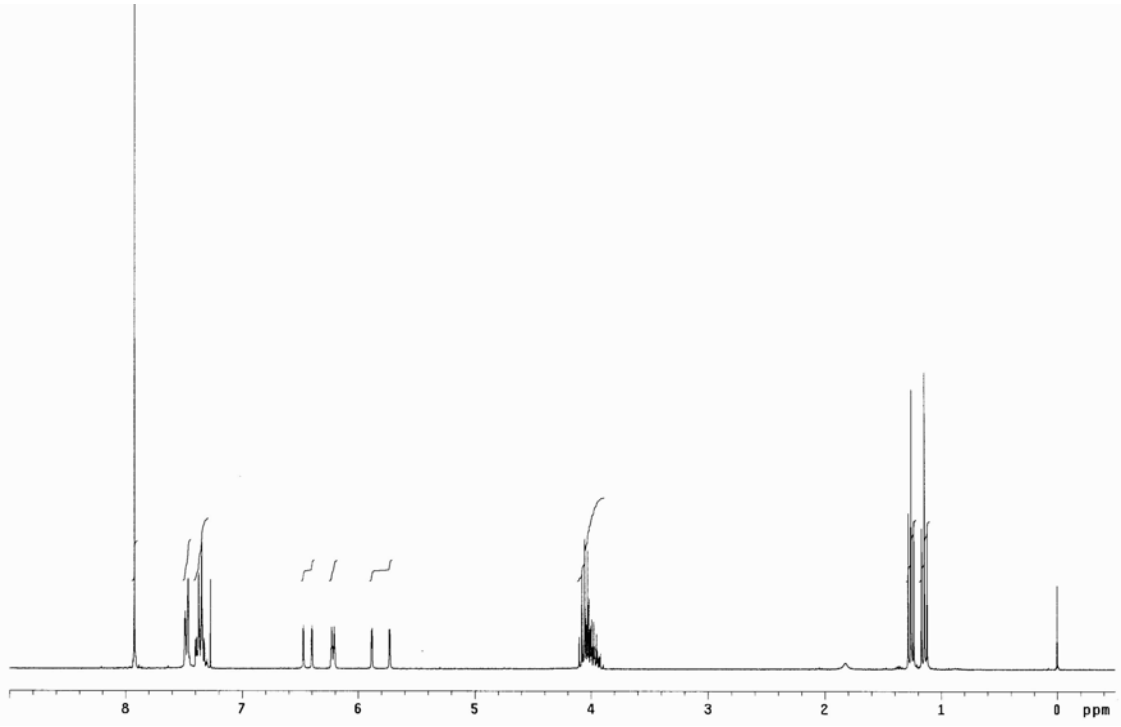
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 2H), 7.50-7.46 (m, 2H), 7.40-7.29 (m, 3H), 6.44 (dd, *J* = 22.2, 1.5 Hz, 1H), 6.22 (d, *J* = 6.3 Hz, 1H), 5.79 (dd, *J* = 45.9, 1.8 Hz, 1H), 4.11-3.92 (m, 4H), 1.26 (t, *J* = 6.9 Hz, 3H), 1.15 (t, *J* = 6.9 Hz, 3H)

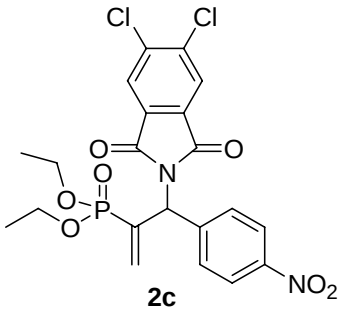
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 138.9, 137.2, 135.7, 135.6, 134.9, 134.8, 131.0, 129.0, 128.7, 128.4, 125.3, 62.3, 62.2, 55.3, 16.2, 16.1

HRMS calcd for $C_{21}H_{21}NO_5PCl_2$ [M] 468.0534, found 468.0535

FTIR (neat) 3018, 2927, 1779, 1720, 1603, 1380, 1354, 1215, 1101, 1050, 1023, 971, 756, 668 cm^{-1}

M.P. 114~115 ºC





2c

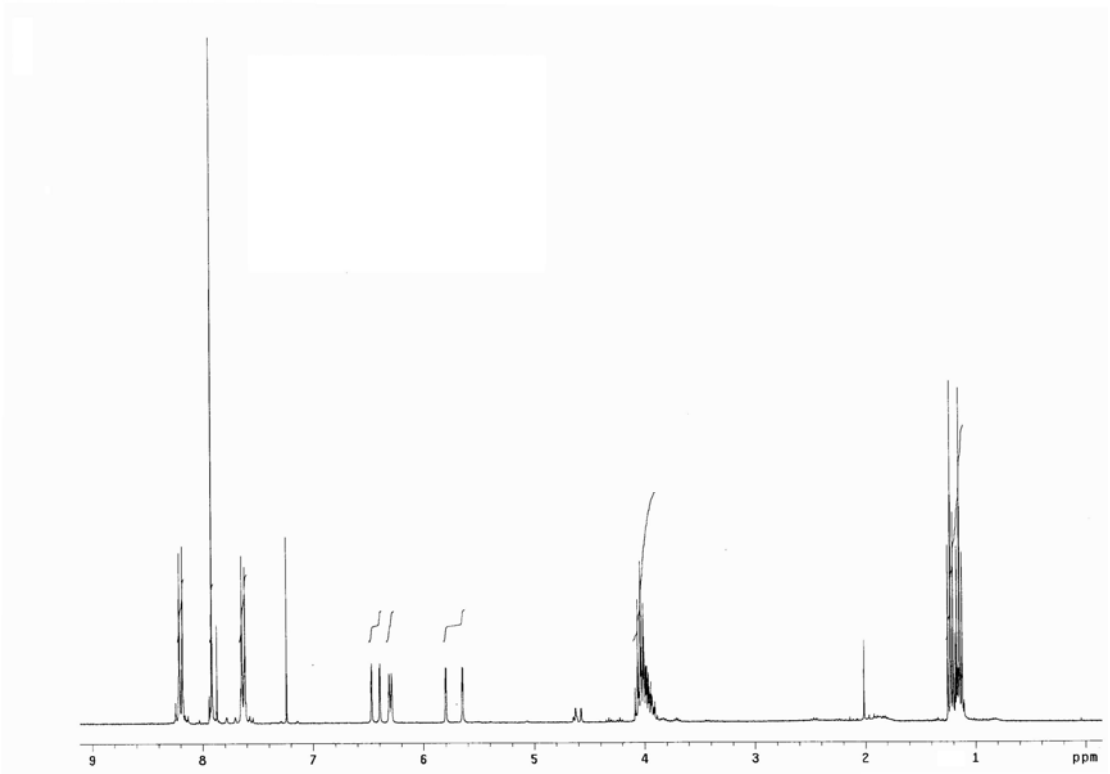
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.7 Hz, 2H), 7.91 (s, 2H), 7.63 (d, *J* = 9.0 Hz, 2H), 6.43 (dd, *J* = 22.2, 1.5 Hz, 1H), 6.30 (d, *J* = 6.9 Hz, 1H), 5.72 (dd, *J* = 45.3, 1.8 Hz, 1H), 4.09-3.89 (m, 4H), 1.22 (t, *J* = 6.9 Hz, 3H), 1.14 (t, *J* = 6.9 Hz, 3H)

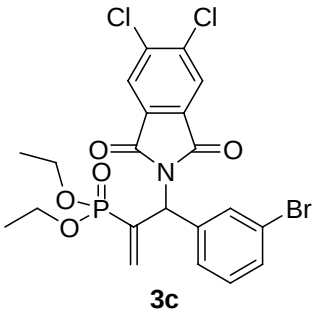
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 147.6, 142.7, 139.2, 136.6, 134.7, 134.2, 130.6, 130.0, 125.5, 123.7, 62.5, 62.4, 54.4, 16.1, 16.0

HRMS calcd for $C_{21}H_{20}N_2O_7PCl_2$ [M+1] 513.0385, found 513.0381

FTIR (neat) 2984, 2924, 1781, 1721, 1523, 1385, 1344, 1251, 1101, 1048, 1020, 969, 742 cm^{-1}

M.P. 144~145 °C





3c

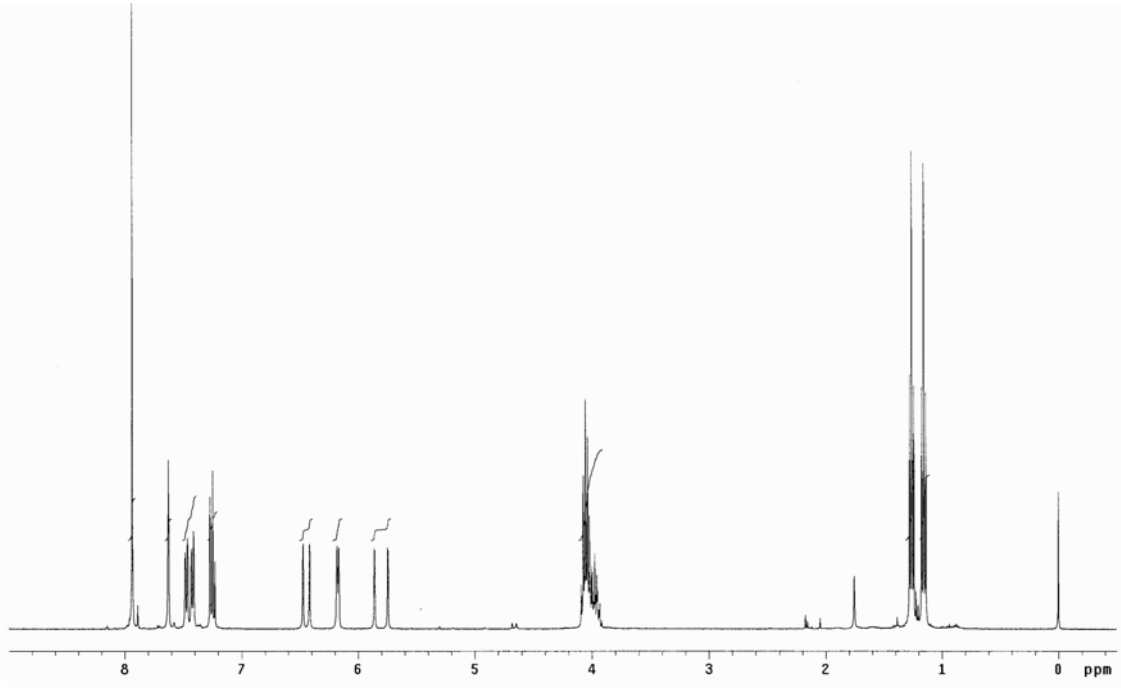
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 2H), 7.63-7.62 (m, 1H), 7.48-7.45 (m, 1H), 7.43-7.41 (m, 1H), 7.26-7.22 (m, 1H), 6.44 (dd, *J* = 22.0, 1.6 Hz, 1H), 6.18 (dt, *J* = 6.4, 2.0 Hz, 1H), 5.80 (dd, *J* = 46.0, 2.0 Hz, 1H), 4.08-3.93 (m, 4H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H)

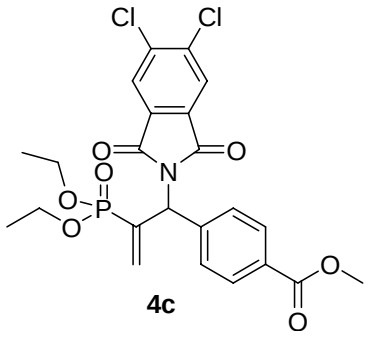
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 139.1, 138.0, 136.9, 134.8, 134.6, 132.0, 131.6, 130.9, 130.2, 127.7, 125.4, 122.7, 62.4, 62.3, 54.7, 16.1, 16.0

HRMS calcd for $C_{21}H_{20}NO_5PCl_2Br$ [M+1] 545.9640, found 545.9639

FTIR (neat) 2982, 2926, 1780, 1721, 1570, 1475, 1375, 1350, 1252, 1101, 1050, 1021, 968, 772, 744 cm^{-1}

M.P. 119~120 ^{o}C





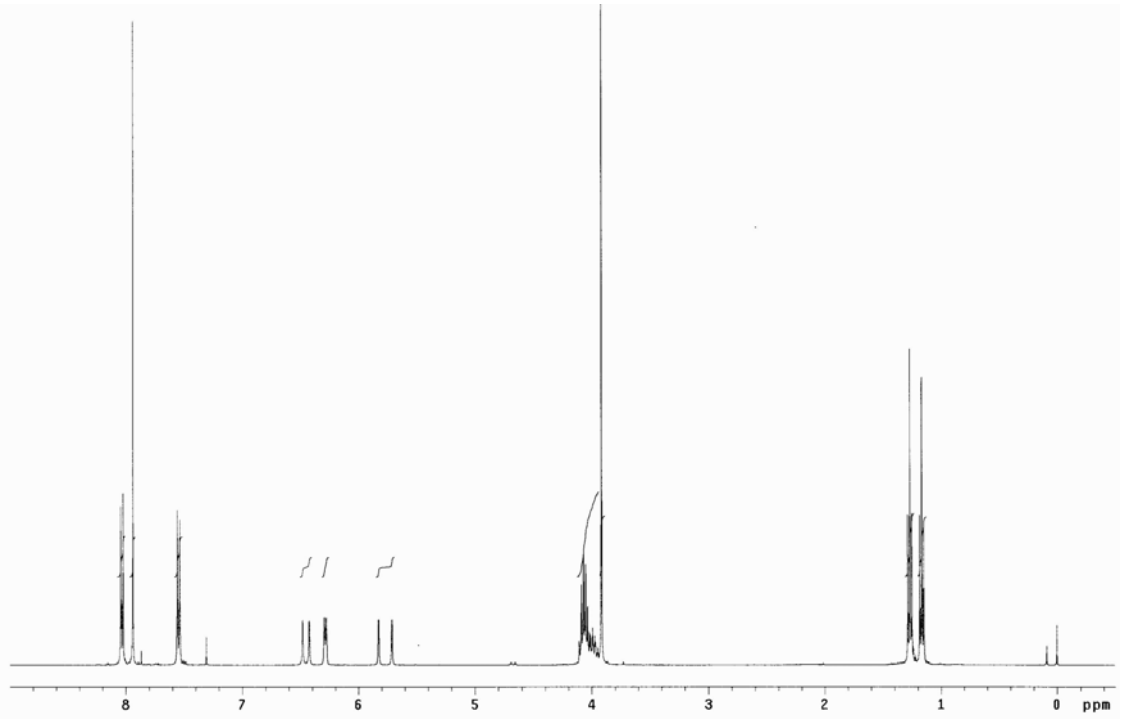
4c

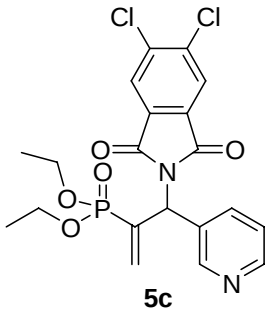
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 6.45 (d, *J* = 22.0, 1H), 6.29 (d, *J* = 6.4 Hz, 1H), 5.77 (dt, *J* = 45.6, 1.6 Hz, 1H), 4.10-3.94 (m, 4H), 3.91 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 165.6, 140.5, 139.0, 136.8, 134.8, 134.4, 130.8, 130.0, 129.8, 128.9, 125.3, 62.3, 62.2, 54.8, 52.0, 16.1, 16.0

HRMS calcd for $C_{23}H_{23}NO_7PCl_2$ [M+1] 526.0589, found 526.0591

FTIR (neat) 2984, 2925, 1780, 1721, 1612, 1436, 1375, 1351, 1280, 1253, 1102, 1049, 1020, 966, 743 cm^{-1}





5c

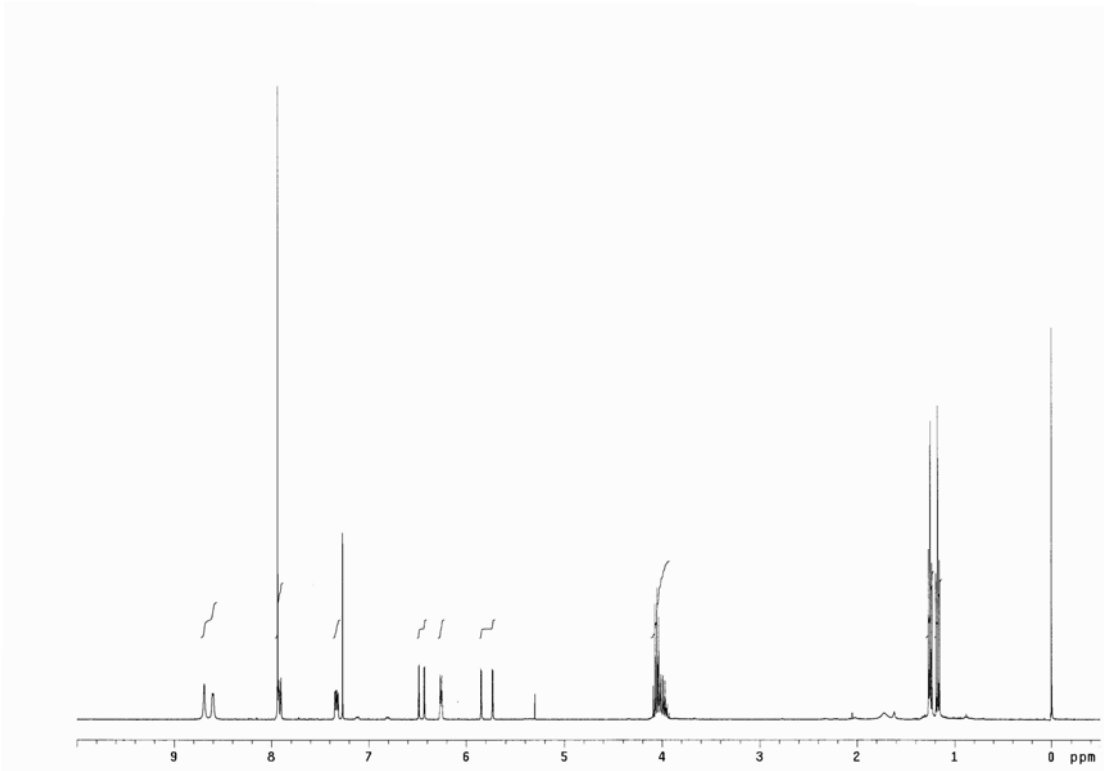
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69-8.59 (m, 2H), 7.93 (s, 2H), 7.92-7.90 (m, 1H), 7.34-7.31 (m, 1H), 6.45 (dd, *J* = 22.0, 1.6 Hz, 1H), 6.26 (d, *J* = 6.4 Hz, 1H), 5.79 (dd, *J* = 45.2, 1.6 Hz, 1H), 4.08-3.92 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H)

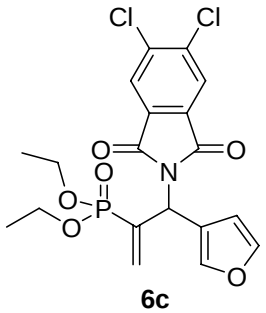
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 150.0, 149.5, 139.2, 137.2, 136.8, 134.5, 134.3, 130.7, 125.4, 123.5, 62.5, 62.4, 53.0, 16.1, 16.0

HRMS calcd. for $C_{20}H_{20}N_2O_5PCl_2$ [M+1] 469.0487, found 469.0487

FTIR (neat) 3018, 2399, 1781, 1722, 1520, 1429, 1378, 1355, 1214, 1100, 1049, 1025, 973, 929, 758, 669 cm^{-1}

M.P. 128~129 ^{o}C





6c

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 2H), 7.53 (s, 1H), 7.42 (t, *J* = 1.6 Hz, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 6.41 (dd, *J* = 21.6, 1.6 Hz, 1H), 6.17-6.15 (m, 1H), 6.04 (dd, *J* = 45.2, 2.0 Hz, 1H), 4.13-3.88 (m, 4H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 143.1, 141.3, 139.6, 137.2, 130.7, 122.6, 109.3, 66.5, 66.3, 62.0, 61.9, 20.8, 16.0, 15.8

HRMS calcd. for $C_{19}H_{19}NO_6PCl_2$ [M+1] 458.0327, found 458.0323

FTIR (neat) 2982, 2925, 1780, 1720, 1614, 1386, 1365, 1349, 1253, 1161, 1101, 1050, 1022, 967, 778, 742 cm^{-1}

M.P. 124~126 ^{o}C