Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Diastereo- and Enantioselective Nitro-Mannich Reaction of α-Substituted Nitroacetates to *N*-Phosphoryl imines Catalyzed by Cinchona Alkaloid Thiourea Organocatalysts

Weidong Fan,[a] Shasha Kong,[a] Yan Cai,[a] Guiping Wu,[a] and Zhiwei Miao[a,]*

[a] *State Key Laboratory and Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P. R. China Fax: (+86)-22-2350-2351; e-mail: miaozhiwei@nankai.edu.cn*

Supporting Information

List of contents (pages)

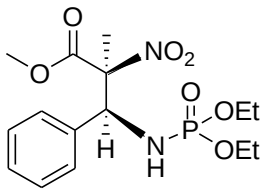
General Comments.

All reactions were carried out under an inert atmosphere and in heat-dried glassware. Solvents were dried and distilled prior to use according to the standard methods. Unless otherwise indicated, all materials were obtained from commercial sources, and used as purchased without dehydration. Chiral thiourea-based organocatalysts were prepared on the base of the literature.[1,2,3] Flash column chromatography was performed on silica gel (particle size 10-40 μm, Ocean Chemical Factory of Qingdao, China). ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were recorded in $CDCl_3$ at Bruker 400 MHz spectrometers, TMS served as internal standard (δ = 0 ppm) for ^{1}H NMR and ^{13}C NMR, H_3PO_4 served as internal standard (δ = 0 ppm) for ^{31}P NMR. HPLC analyses were recorded on a chiral column Daicel Chiralcel AD-H column or a AS-H column, at 220 nm). The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer. Optical rotations were recorded on a Perkin Elemer 241 Polarimeter. Melting points were determined on a T-4 melting point apparatus (uncorrected).

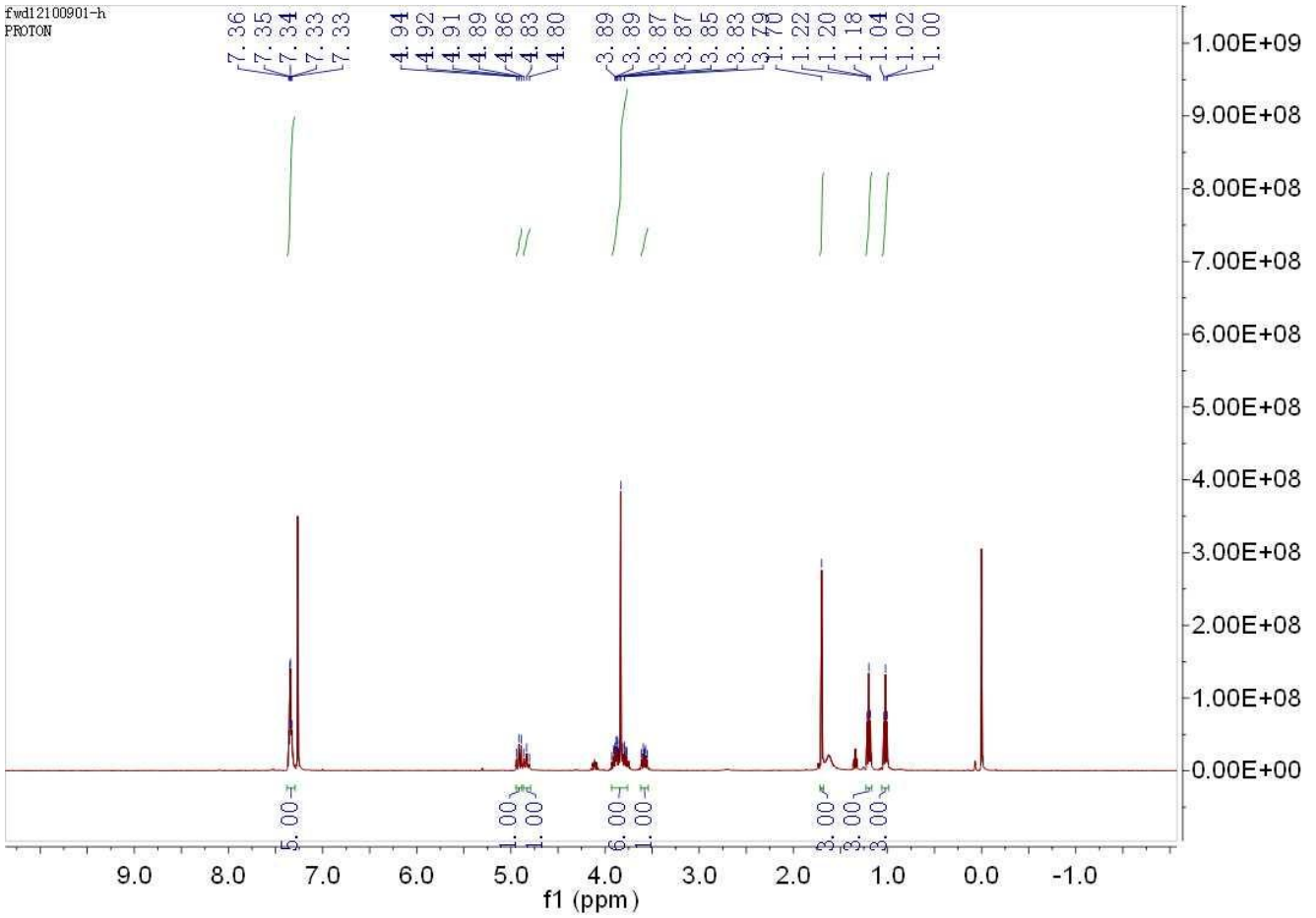
General procedure for the synthesis of β-nitro ethylphosphoramidates 6:

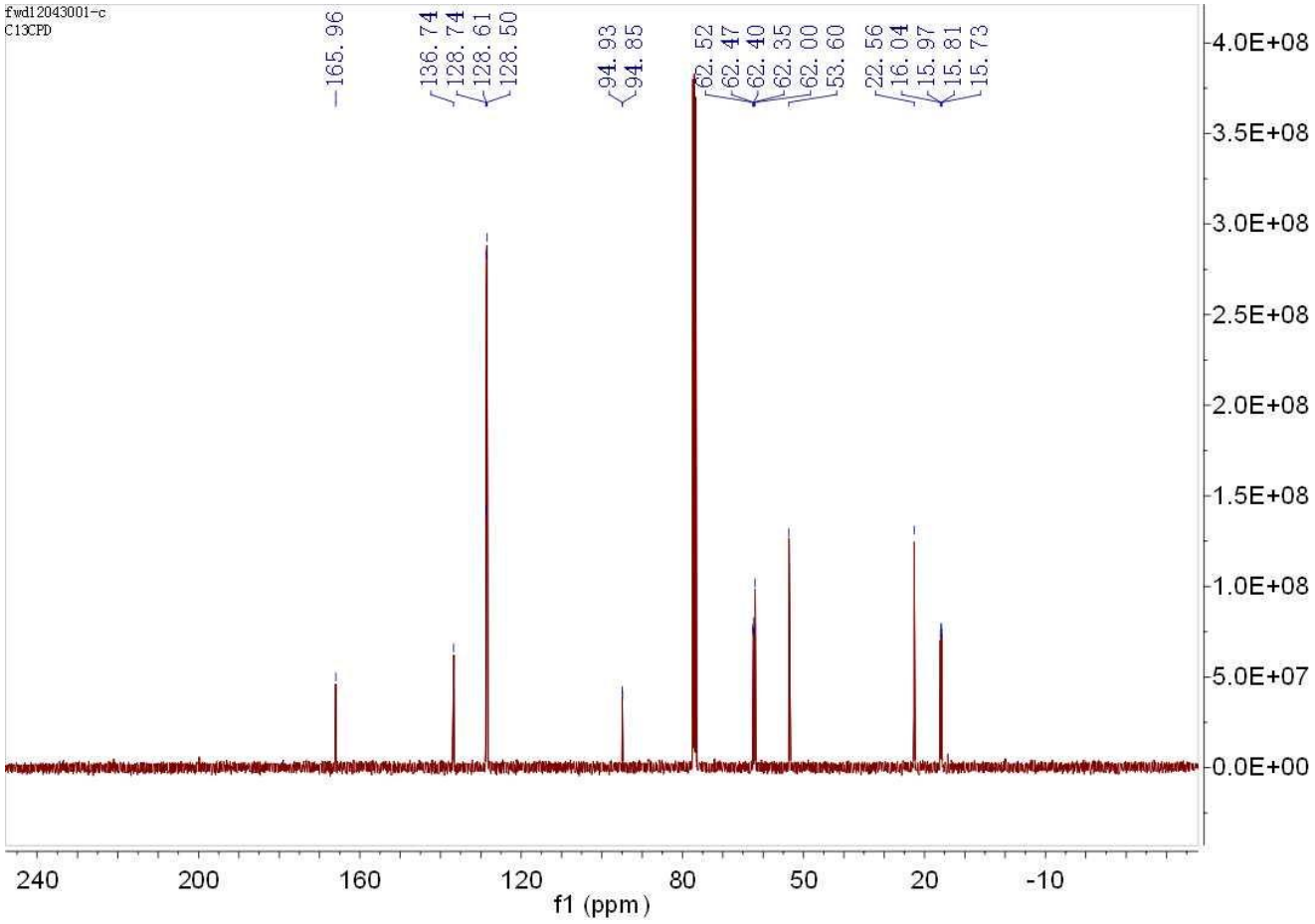
To a solution of *N*-phosphoryl imines **4** (0.3 mmol) and chiral catalyst **3a** (0.015 mmol, 5 mol%) in toluene (3.0 mL) was added 2-nitropropanoate **5** (0.45 mmol, 1.5 equiv) at -20 °C under a nitrogen atmosphere. The mixture was stirred for corresponding time at -20 °C (monitored by TLC). Then saturated NH_4Cl aq (3 mL) was added, and the mixture was extracted with ethyl acetate (3×5 mL). The organic layers were washed with brine solution (2 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude products **6**, which were purified by flash column chromatography on silica gel [petroleum ether/ethyl acetate, 1:1 (v/v)] to provide pure products **6**.

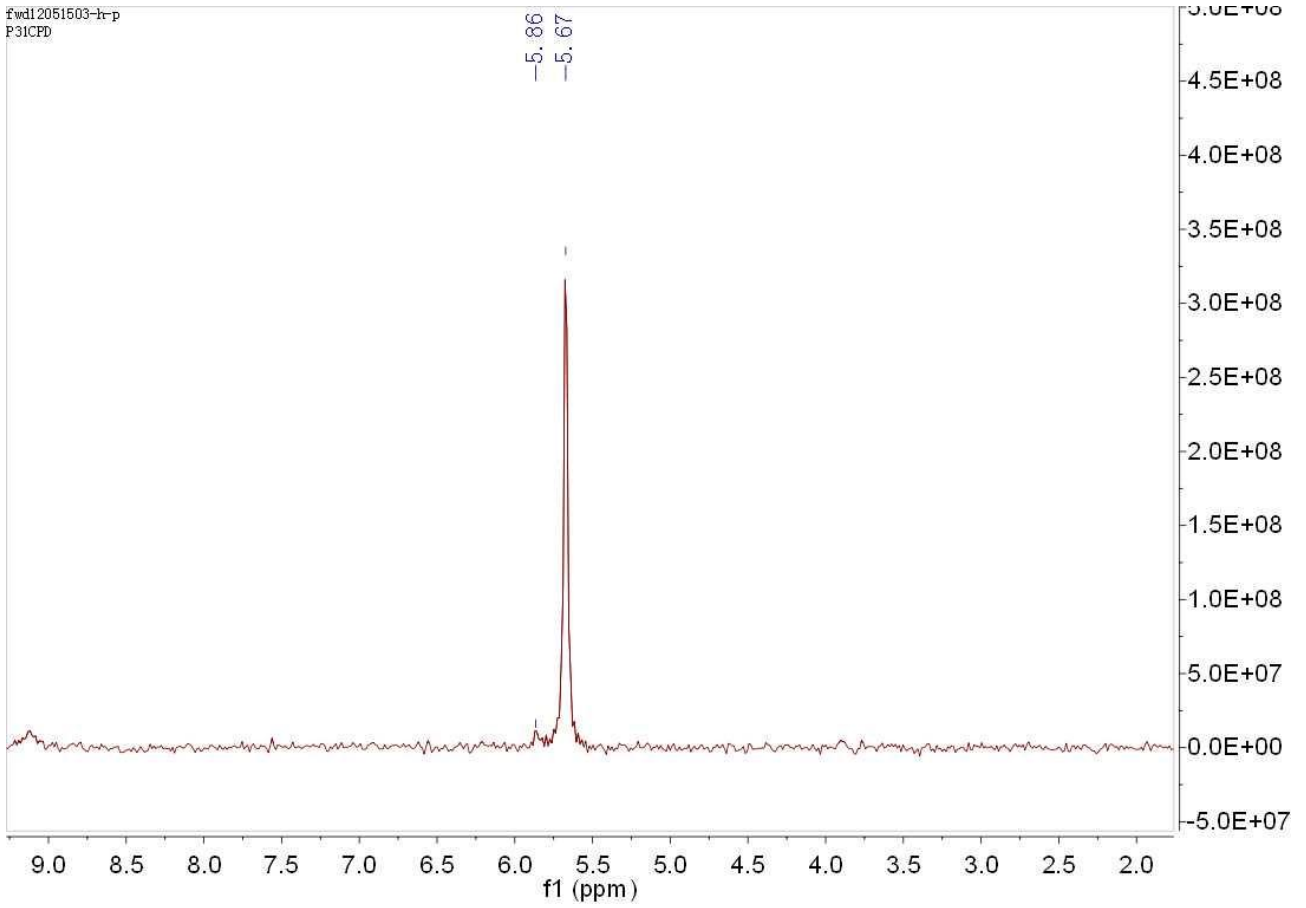
Methyl 3-((diethylphosphoryl)amino)-2-methyl-2-nitro-3-phenylpropanoate (6a):

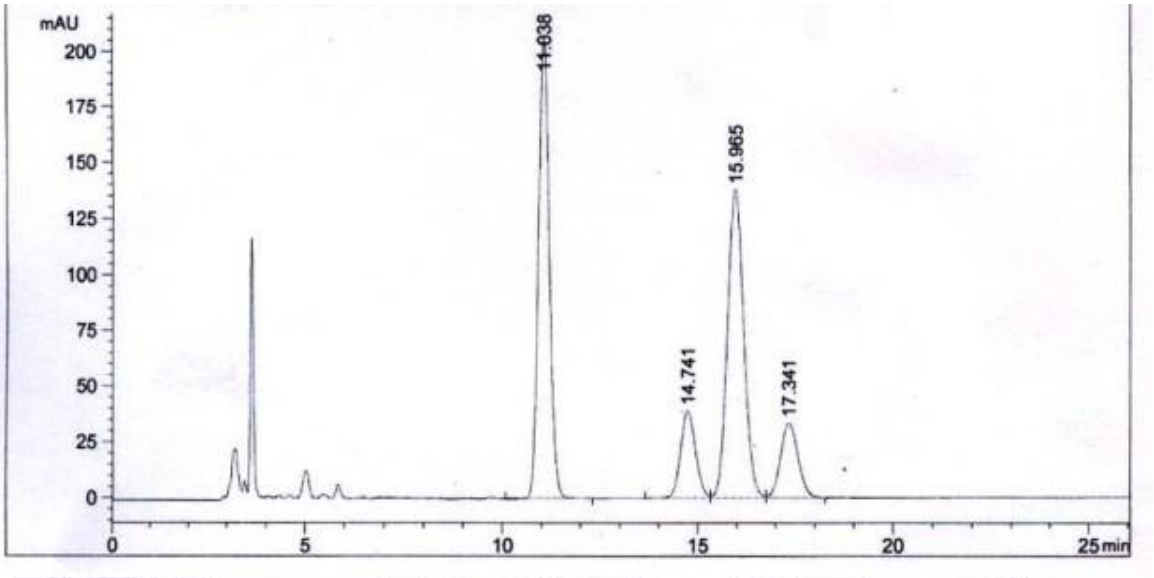


White solid; mp 114-117 °C; $[\alpha]^{20}_{D}$ = 48.8° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.38 (m, 5H), 4.92 (dd, *J* = 11.5, 9.7 Hz, 1H), 4.83 (t, *J* = 11.5 Hz, 1H), 3.73-3.95 (m, 6H), 3.50-3.65 (m, 1H), 1.70 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.96, 136.74, 128.74, 128.61, 128.50, 94.89 (d, *J* = 8.1 Hz), 62.49 (d, *J* = 5.0 Hz), 62.37 (d, *J* = 5.0 Hz), 62.00, 53.60, 22.56, 16.00 (d, *J* = 7.5 Hz), 15.77 (d, *J* = 7.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.86, 5.67; HRMS (MALDI) calculated for $[C_{15}H_{23}N_2O_7P+H]^+$: 375.1321, Found: 375.1315; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 10.848 min, tr (major) = 14.388 min, tr (major) = 15.401 min, tr (major) = 17.012 min.

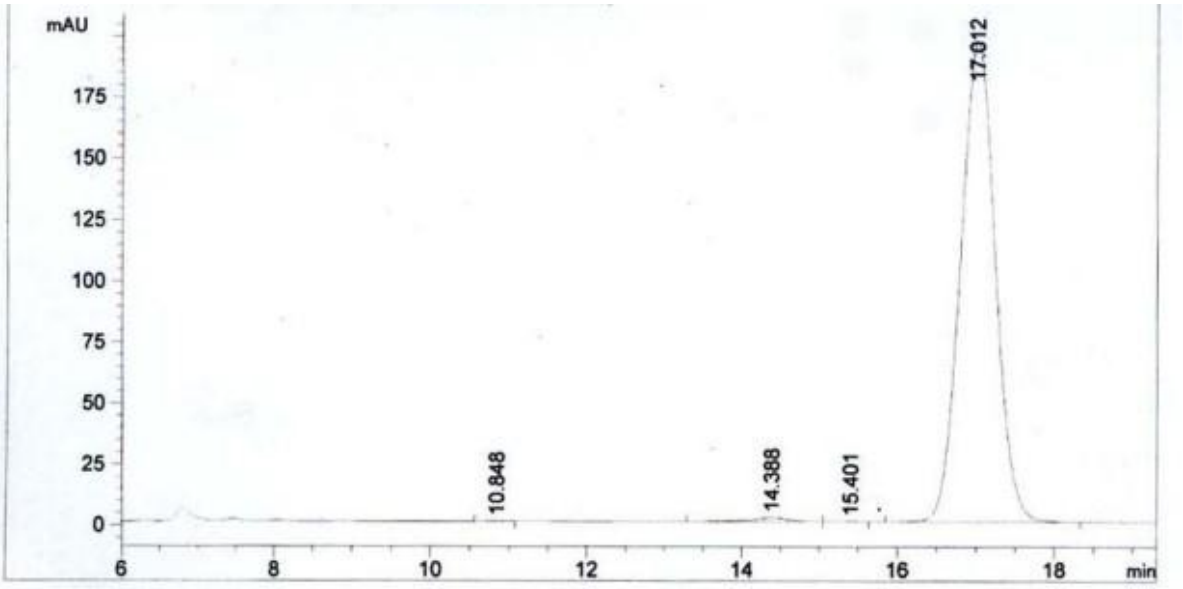






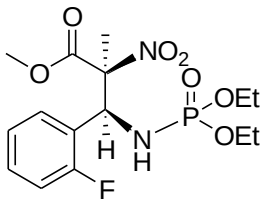


#	[min]		[min]	mAU	*s	[mAU]	%
1	11.038	VB	0.3013	4004.04199		207.03935	39.4843
2	14.741	VV	0.4202	1056.84265		39.09988	10.4216
3	15.965	VV	0.4534	4027.57129		138.26025	39.7163
4	17.341	VV	0.4877	1052.39746		33.60102	10.3778

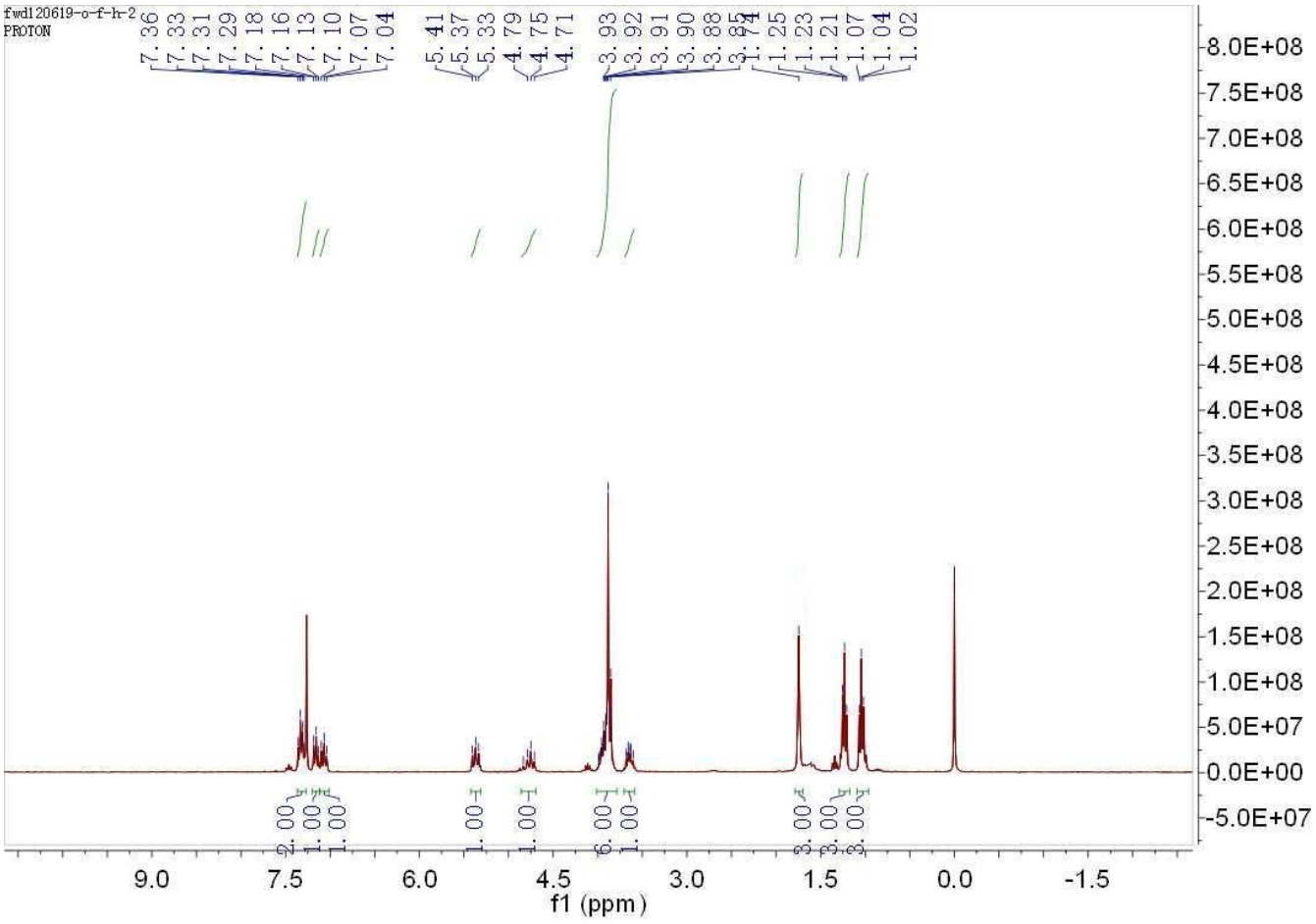


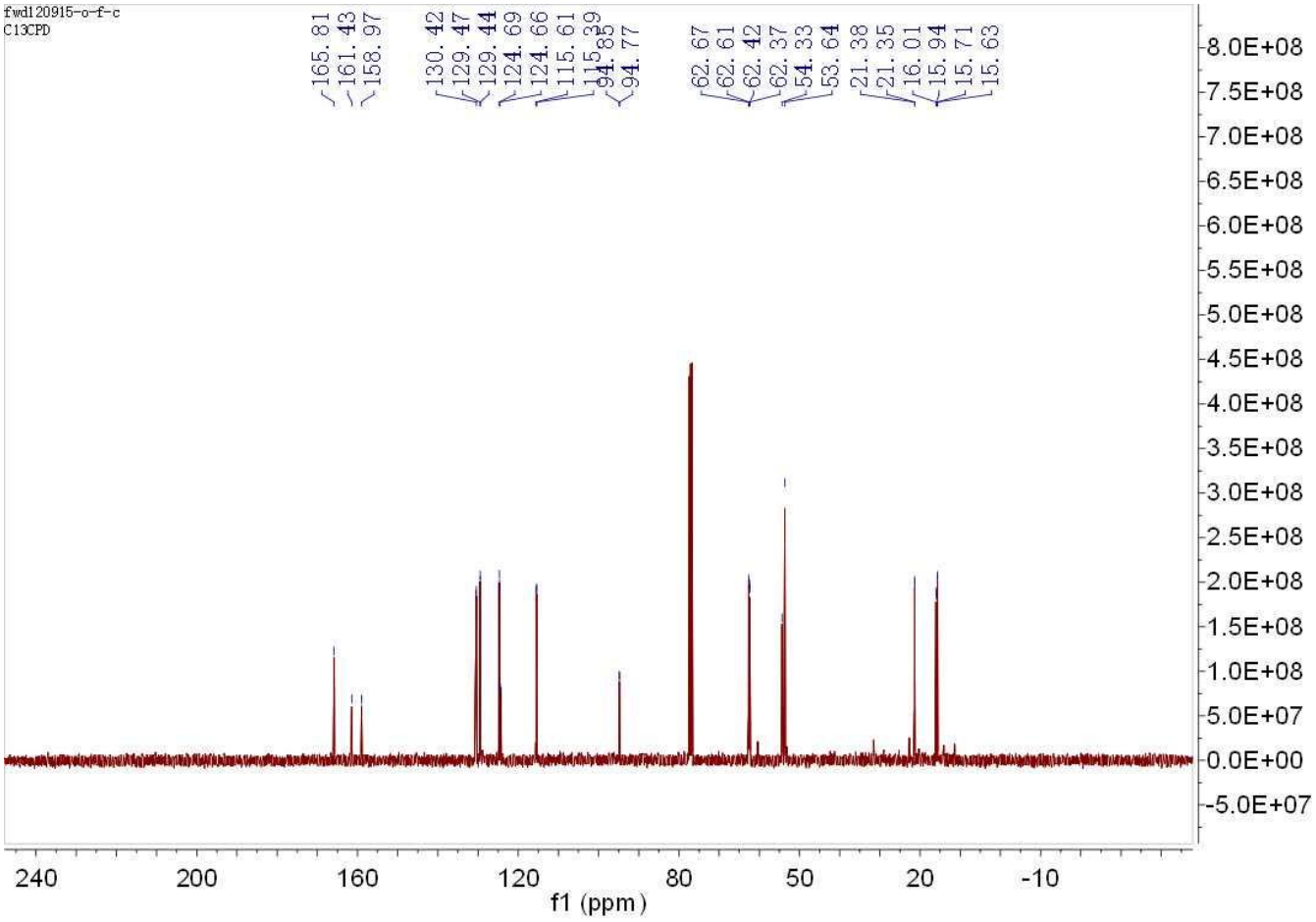
#	[min]		[min]	mAU	*s	[mAU]	%
1	10.848	VV	0.2435	3.99938		2.03771e-1	0.0652
2	14.388	BV	0.4405	54.30903		1.73672	0.8854
3	15.401	VV	0.2538	2.37142		1.14247e-1	0.0387
4	17.012	VV	0.4800	6073.36621		197,26630	99.0108

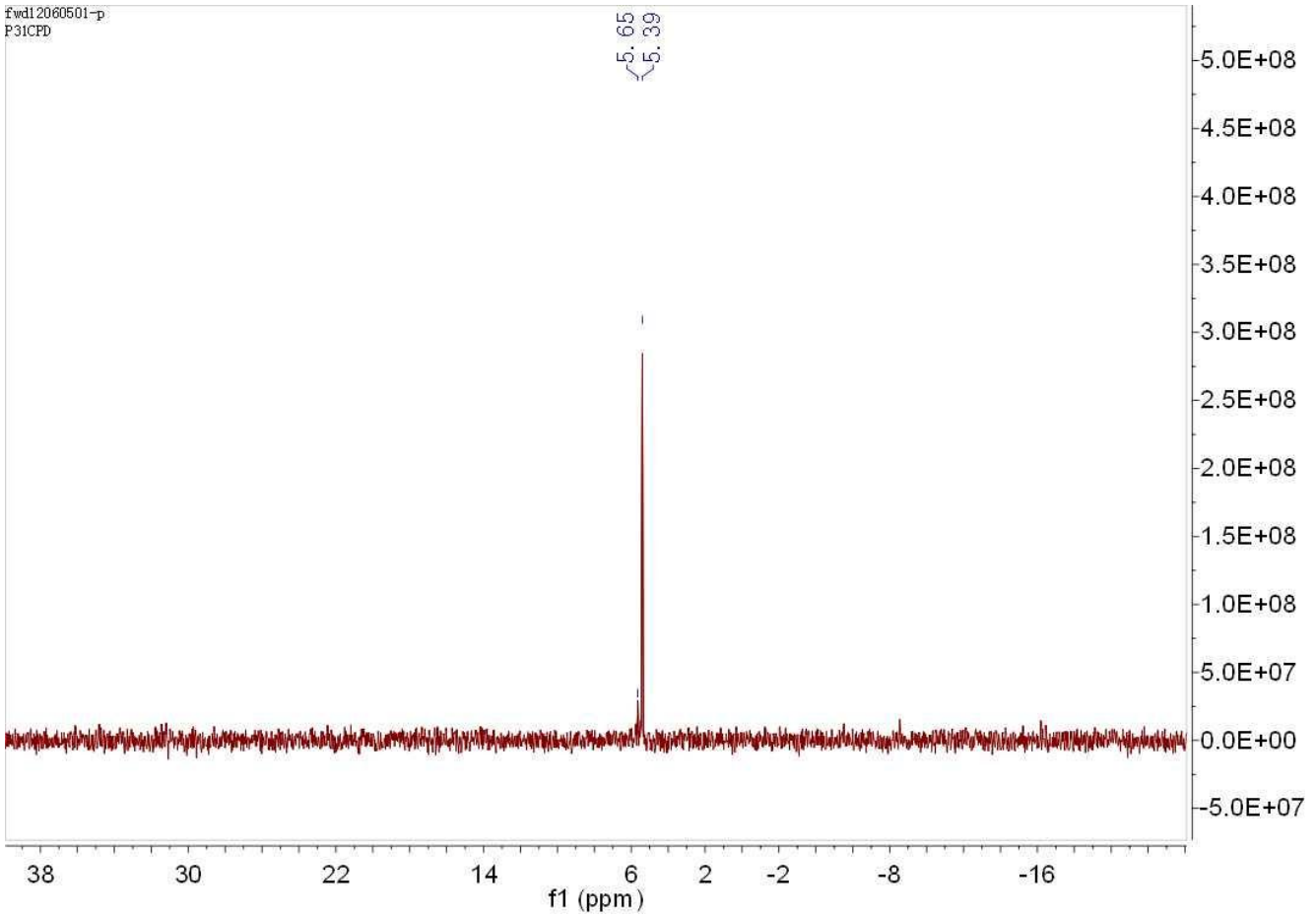
Methyl 3-((diethylphosphoryl)amino)-3-(2-fluorophenyl)-2-methyl-2-nitropropanoate (6b):

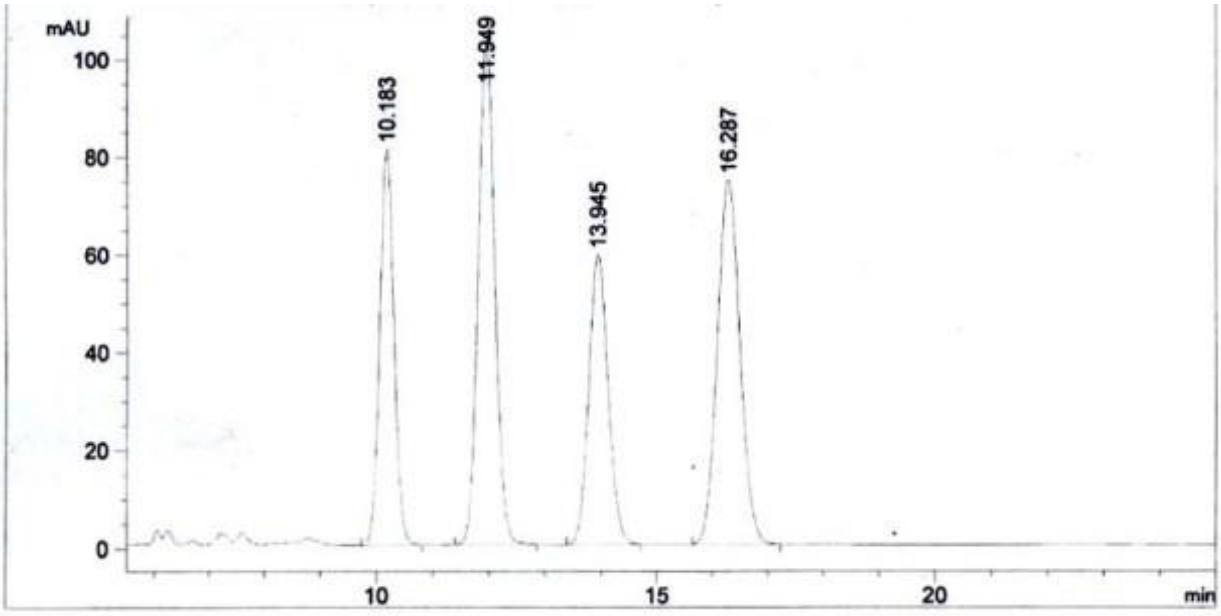


White solid; mp 68-71 °C; $[\alpha]^{20}_{D}$ = 56.4° (c = 0.005, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.39 (m, 2H), 7.12-7.21 (m, 1H), 7.01-7.12 (m, 1H), 5.37 (dd, *J* = 11.4, 10.4 Hz, 1H), 4.75 (t, *J* = 11.4 Hz, 1H), 3.79-4.01 (m, 6H), 3.57-3.71 (m, 1H), 1.74 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.81, 160.20 (d, *J* = 247.2 Hz), 130.46, 129.46, 124.68, 124.36, 115.50 (d, *J* = 22.9 Hz), 94.81 (d, *J* = 7.9 Hz), 62.64 (d, *J* = 5.3 Hz), 62.39 (d, *J* = 5.4 Hz), 54.33 (s), 53.64 (s), 21.36 (d, *J* = 2.6 Hz), 15.98 (d, *J* = 7.4 Hz), 15.67 (d, *J* = 7.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.65, 5.39; HRMS (MALDI) calculated for $[C_{15}H_{22}FN_2O_7P+H]^+$: 415.1046, Found 415.1044; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 10.252 min, tr (major) = 12.068 min, tr (major) = 14.155 min, tr (major) = 16.552 min.

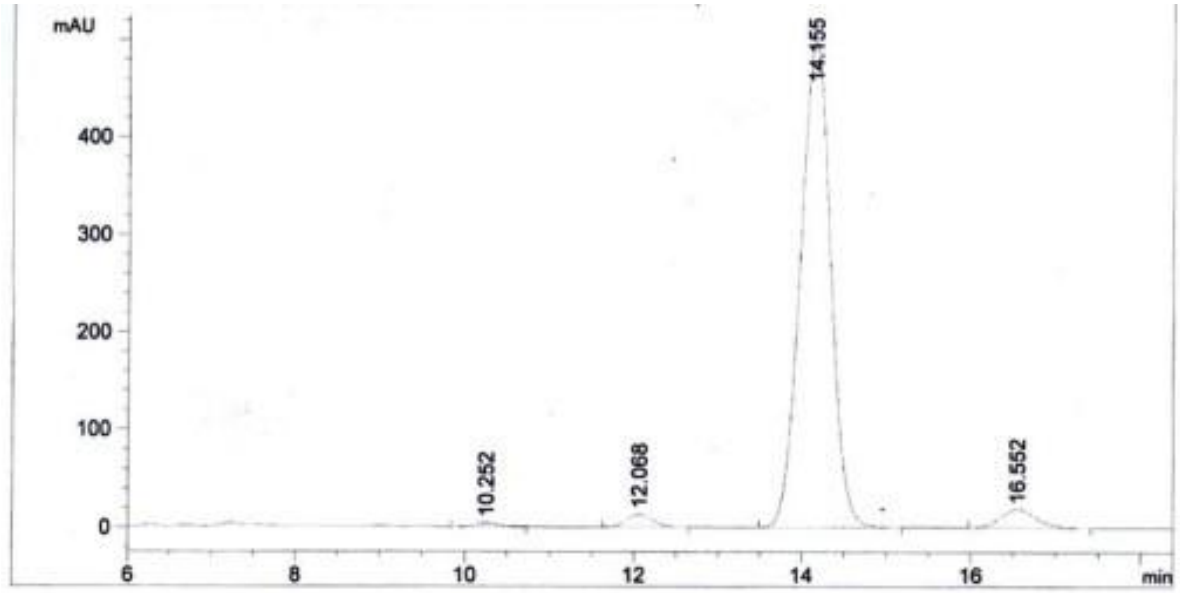






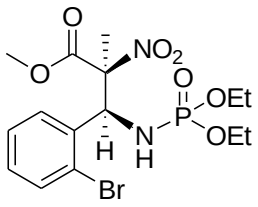


#	[min]		[min]	mAU	*s	[mAU]	%
1	10.183	BB	0.2701	1420.37500		81.01555	20.0056
2	11.949	BB	0.3196	2130.50952		103.14367	30.0077
3	13.945	BB	0.3732	1423.87988		59.33326	20.0550
4	16.287	BB	0.4426	2125.10742		74.68053	29.9316

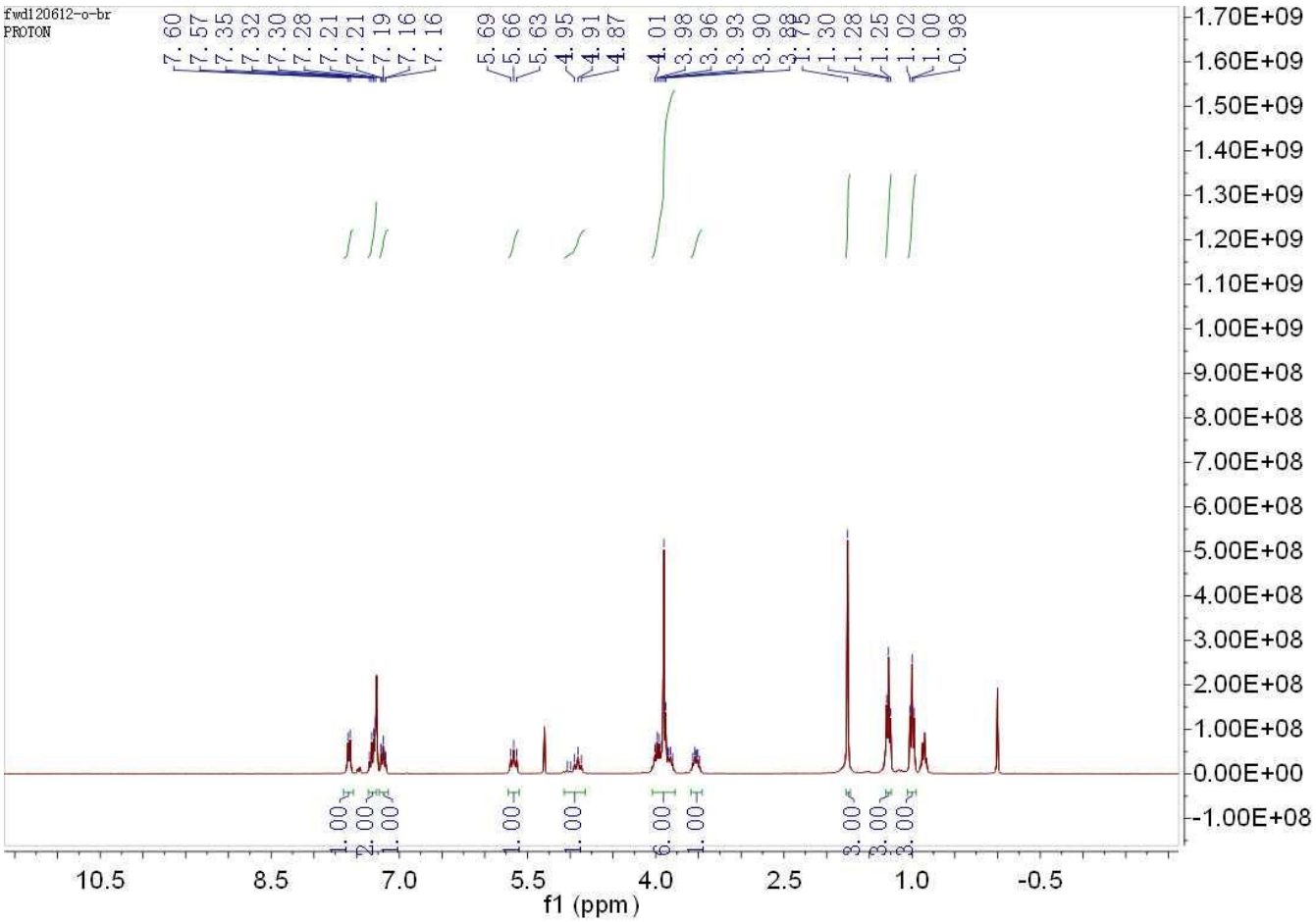


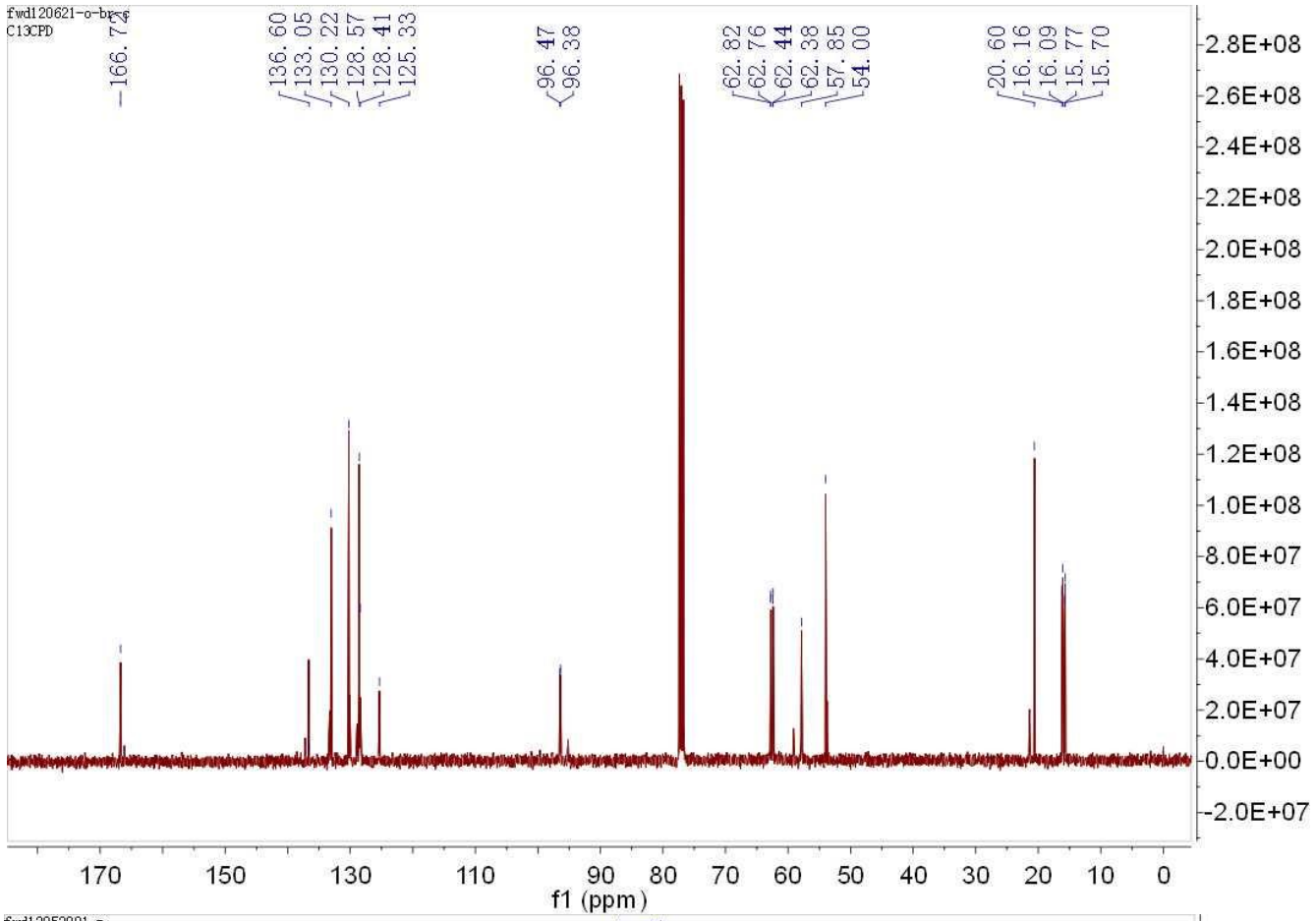
#	[min]		[min]	mAU	*s	[mAU]	%
1	10.252	VB	0.2803	72.35455		4.01229	0.5399
2	12.068	BB	0.3283	277.97662		13.14114	2.0743
3	14.155	BB	0.3908	1.24993e4		499.74579	93.2717
4	16.552	BB	0.4525	551.32843		18.97832	4.1141

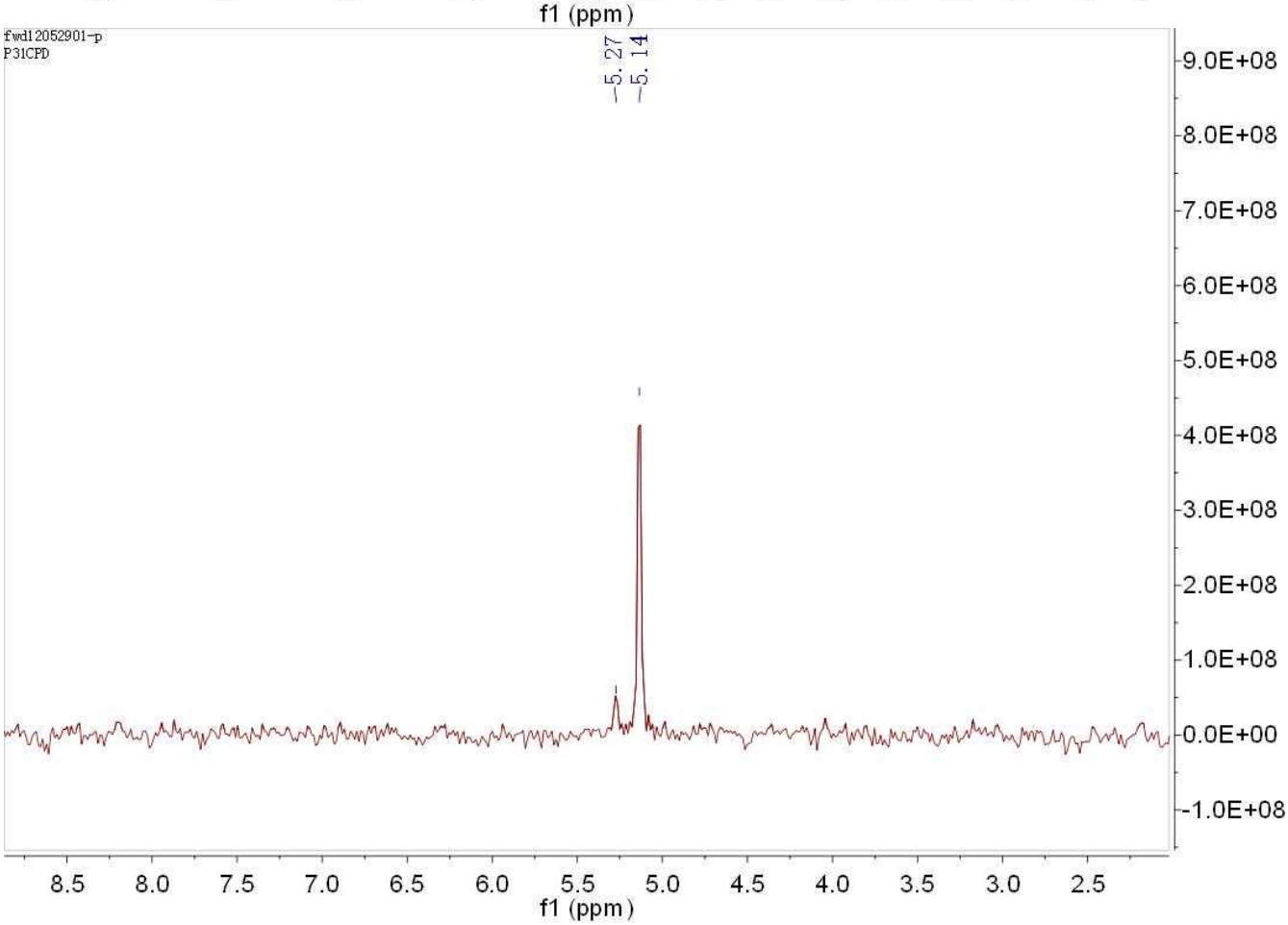
Methyl 3-((diethylphosphoryl)amino)-3-(2-bromophenyl)-2-methyl-2-nitropropanoate (6c):

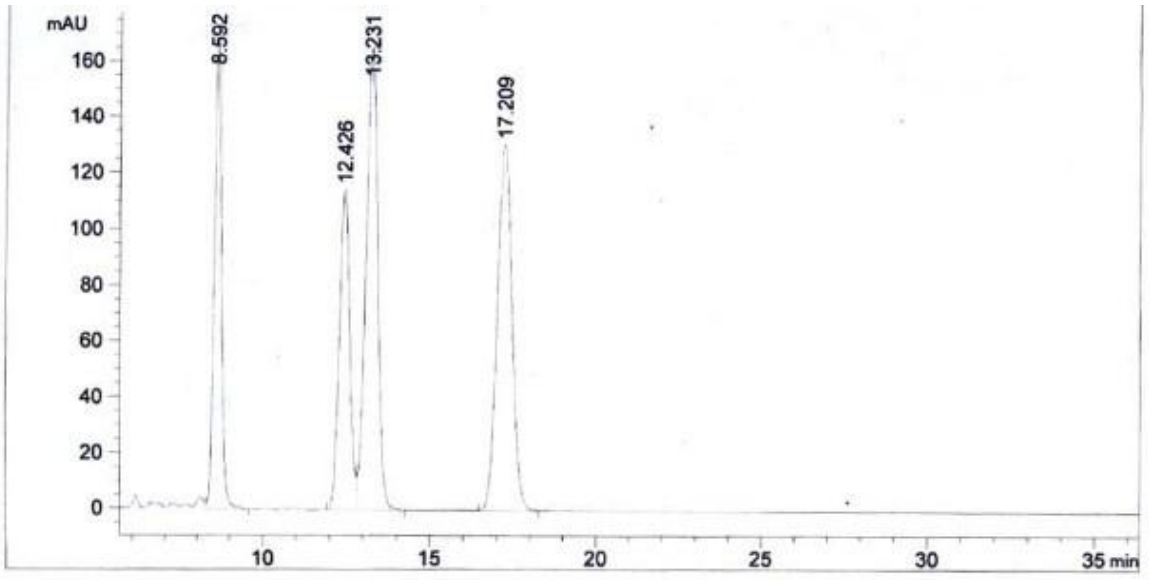


White solid; mp 80-83 °C; $[\alpha]^{20}_{D}$ = 9.8° (c = 0.01, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.65 (m, 1H), 7.25-7.38 (m, 2H), 7.11-7.24 (m, 1H), 5.66 (t, *J* = 10.3 Hz, 1H), 4.91 (t, *J* = 11.6 Hz, 1H), 3.76-4.07 (m, 6H), 3.44-3.61 (m, 1H), 1.75 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.00 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.72, 136.60, 133.05, 130.22, 128.57, 128.41, 125.33, 96.43 (d, *J* = 8.8 Hz), 62.79 (d, *J* = 5.6 Hz), 62.41 (d, *J* = 5.5 Hz), 57.85, 54.00, 20.60, 16.12 (d, *J* = 7.7 Hz), 15.74 (d, *J* = 7.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.27, 5.14; HRMS (MALDI) calculated for $[C_{15}H_{22}BrN_2O_7P+Na]^+$: 475.0246, Found 475.0242; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.617min, tr (major) = 12.468 min, tr (major) = 13.262 min, tr (major) = 17.233 min.

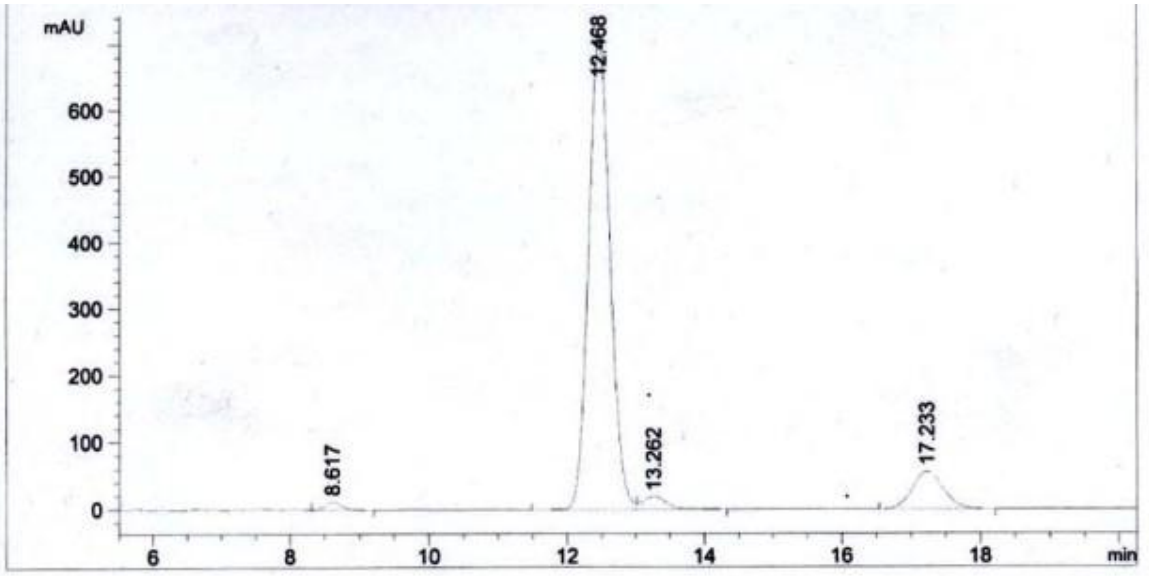






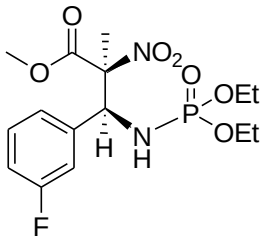


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.592	VB	0.2361	2600.24365		169.14220	19.6698
2	12.426	BV	0.3379	2491.85205		114.72330	18.8498
3	13.231	VB	0.3803	4078.69800		165.71559	30.8536
4	17.209	BB	0.4795	4048.70557		131.16098	30.6268

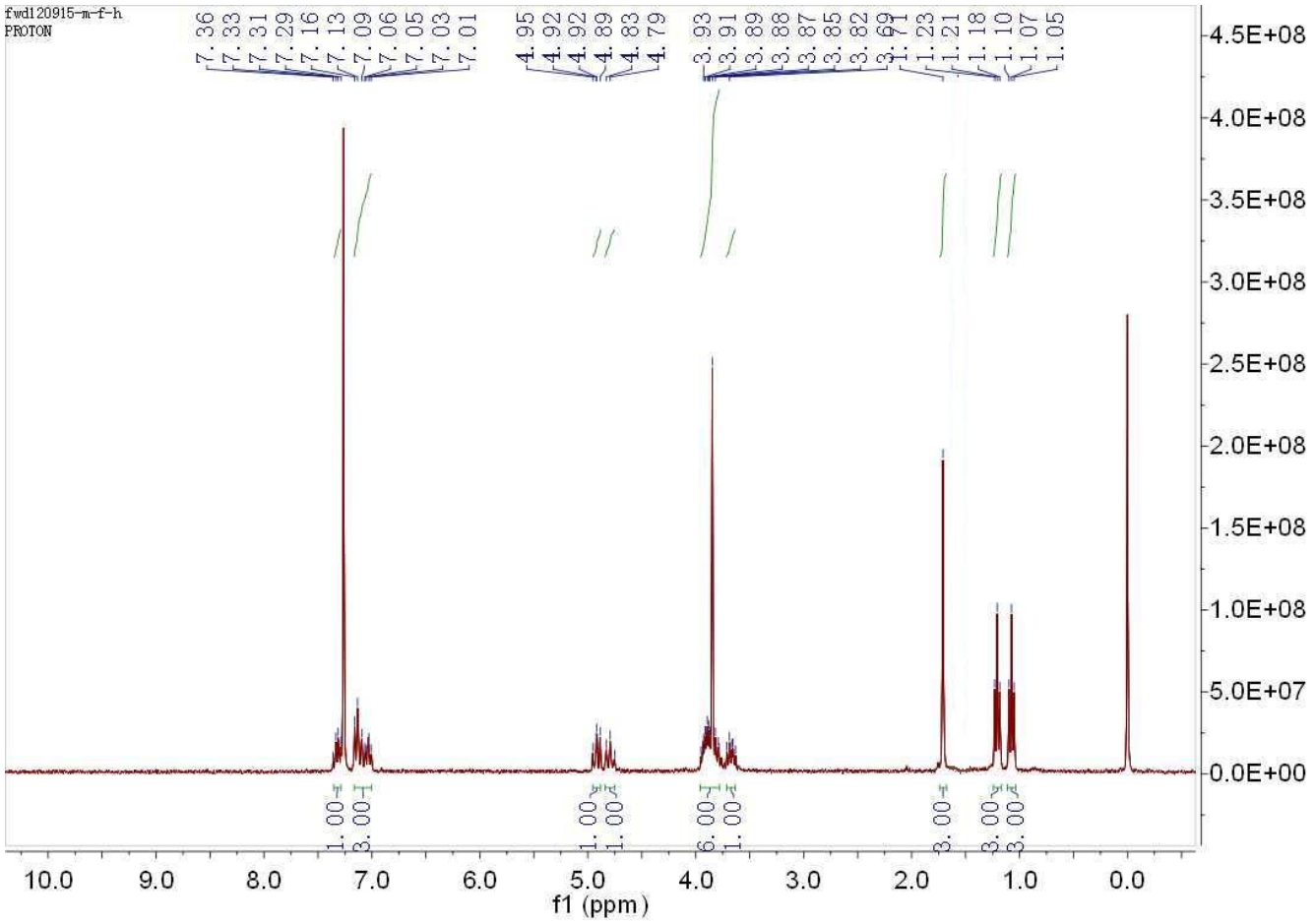


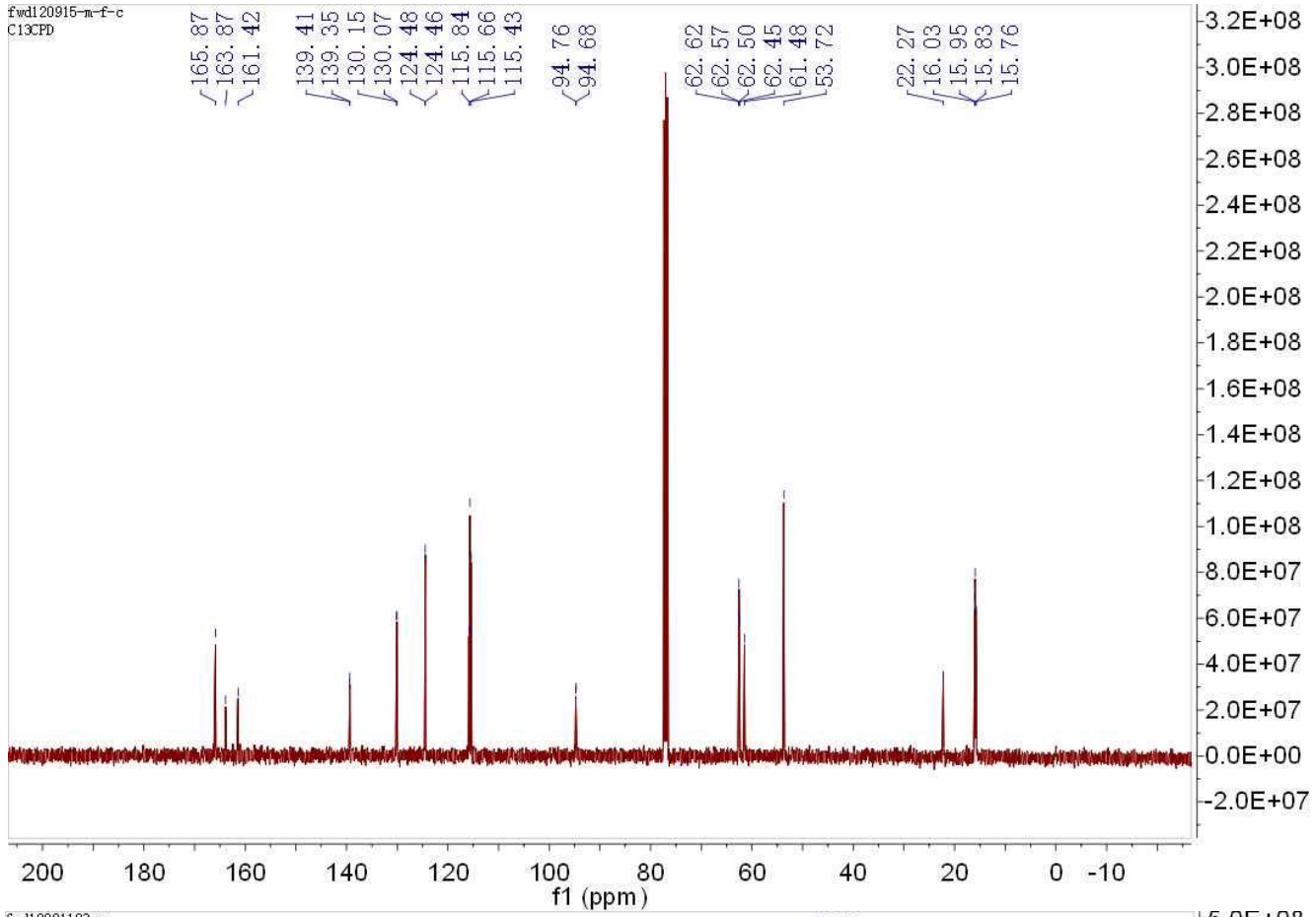
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.617	VB	0.2440	201.84937		12.67476	1.1273
2	12.468	VV	0.3400	1.54767e4		710.59247	86.4351
3	13.262	VB	0.3730	476.15884		19.34979	2.6593
4	17.233	BB	0.4815	1750.85071		56.40494	9.7783

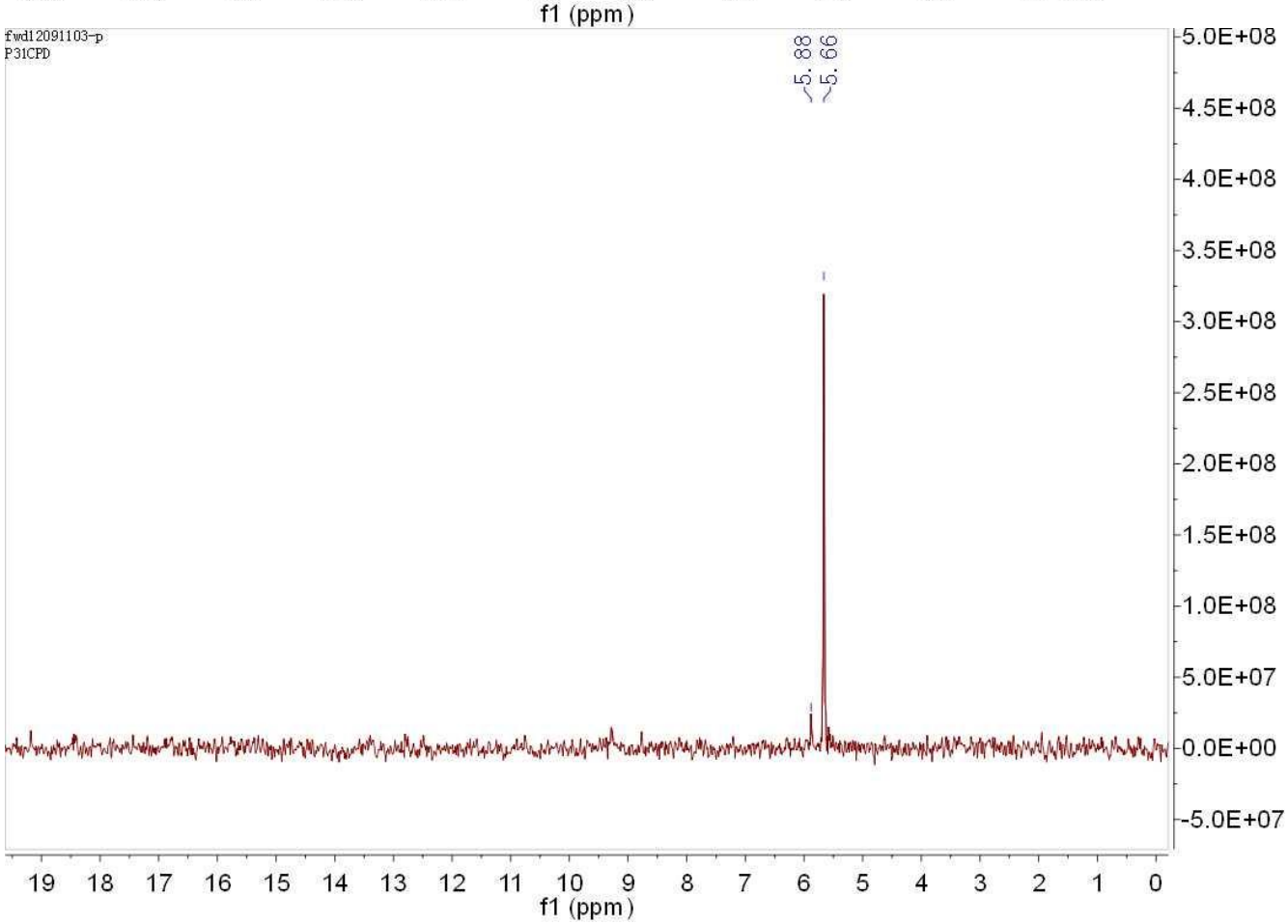
Methyl 3-((diethylphosphoryl)amino)-3-(3-fluorophenyl)-2-methyl-2-nitropropanoate (6d):

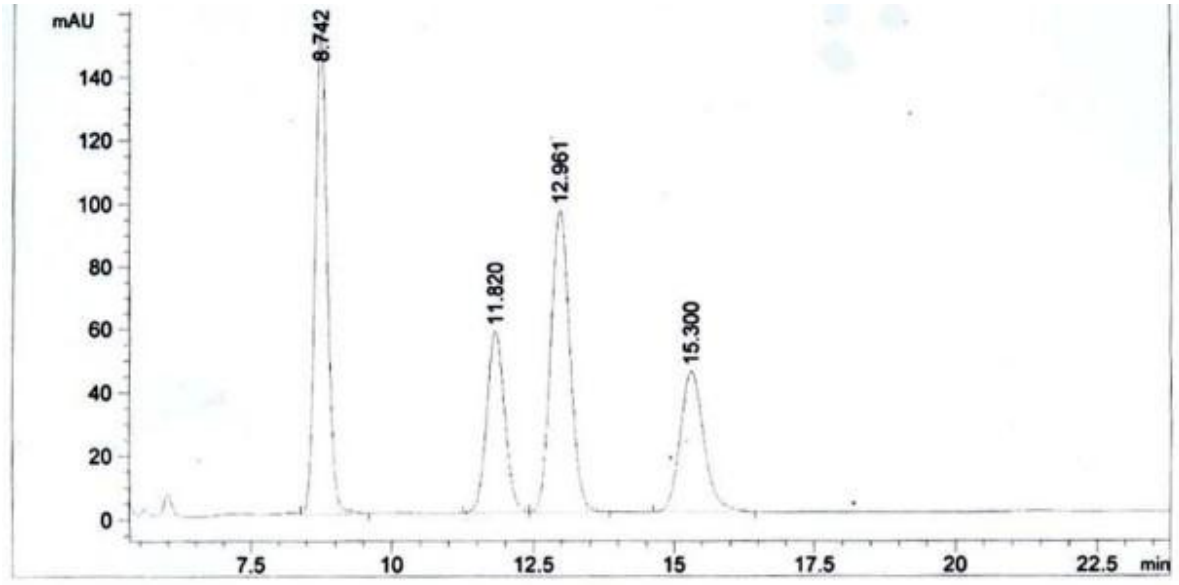


White solid; mp 90-93 °C; $[\alpha]^{20}_{D}$ = 51.2° (c = 0.005, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27-7.38 (m, 1H), 6.97-7.20 (m, 3H), 4.92 (dd, *J* = 11.5, 9.4 Hz, 1H), 4.79 (t, *J* = 11.5 Hz, 1H), 3.75-3.99 (m, 6H), 3.51-3.75 (m, 1H), 1.71 (s, 3H),1.21 (t, *J* = 7.1 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.87, 162.64 (d, *J* = 247.3 Hz), 139.38, 130.11, 124.47, 115.75, 115.43, 94.72 (d, *J* = 7.9 Hz), 62.59 (d, *J* = 5.3 Hz), 62.48 (d, *J* = 5.2 Hz), 61.48, 53.72, 22.27, 15.99 (d, *J* = 7.4 Hz), 15.79 (d, *J* = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.88, 5.66; HRMS (MALDI) calculated for $[C_{15}H_{22}FN_2O_7P+Na]^+$: 415.1046, Found 415.1043; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.831 min, tr (major) = 12.005 min, tr (major) = 13.113 min, tr (major) = 15.505 min.

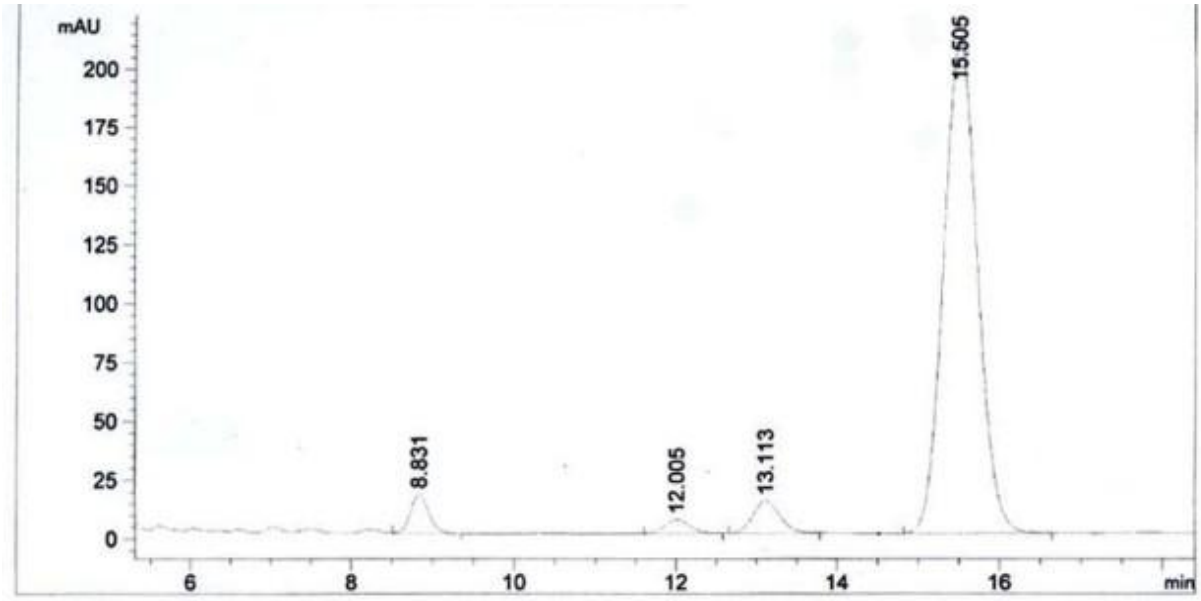






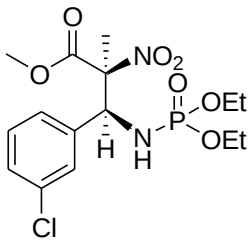


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.742	VB	0.2353	2311.87158		152.30722	32.3189
2	11.820	BV	0.3420	1262.78503		57.20149	17.6531
3	12.961	VB	0.3656	2261.33594		95.80389	31.6124
4	15.300	BB	0.4577	1317.32996		44.28624	18.4156

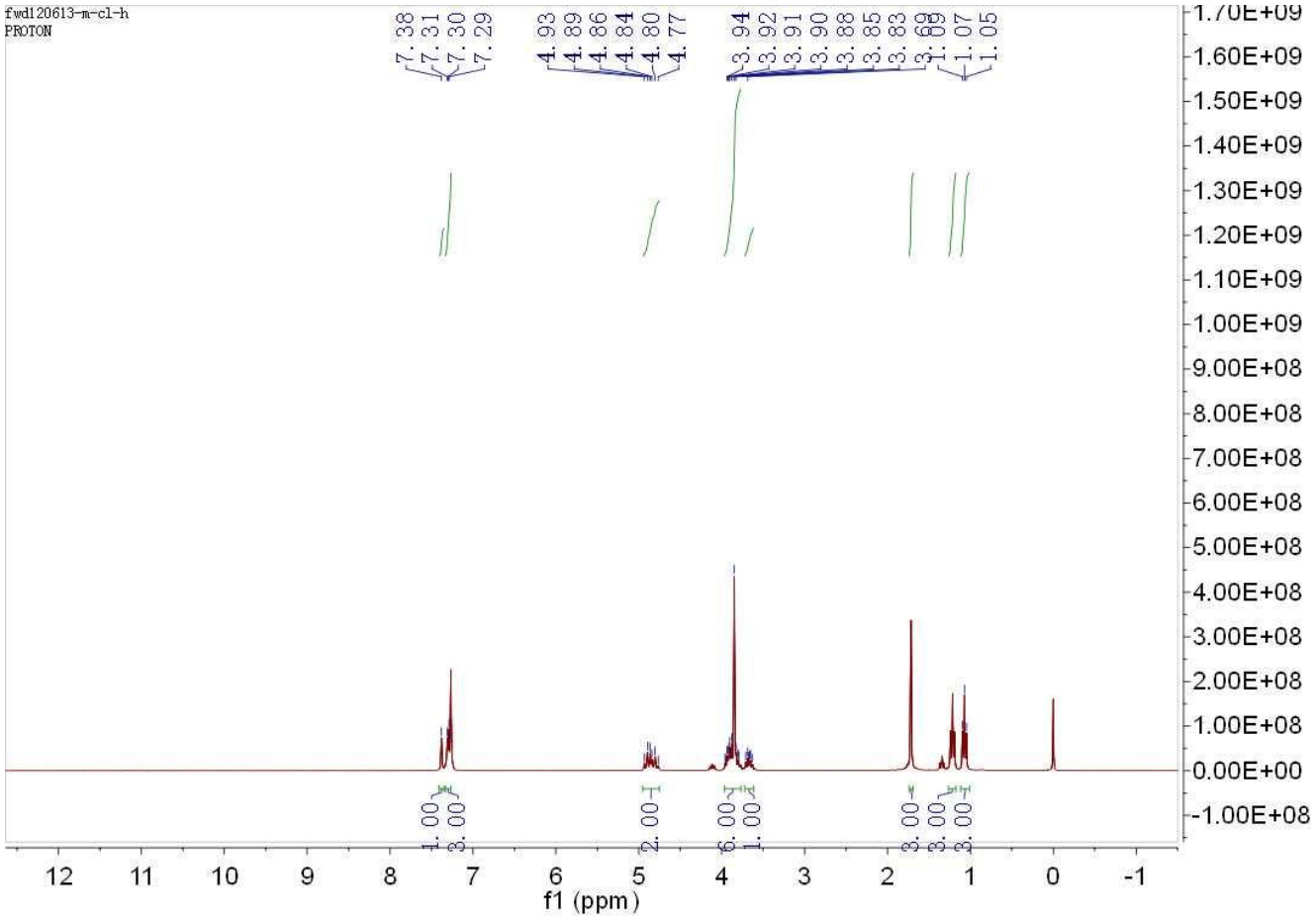


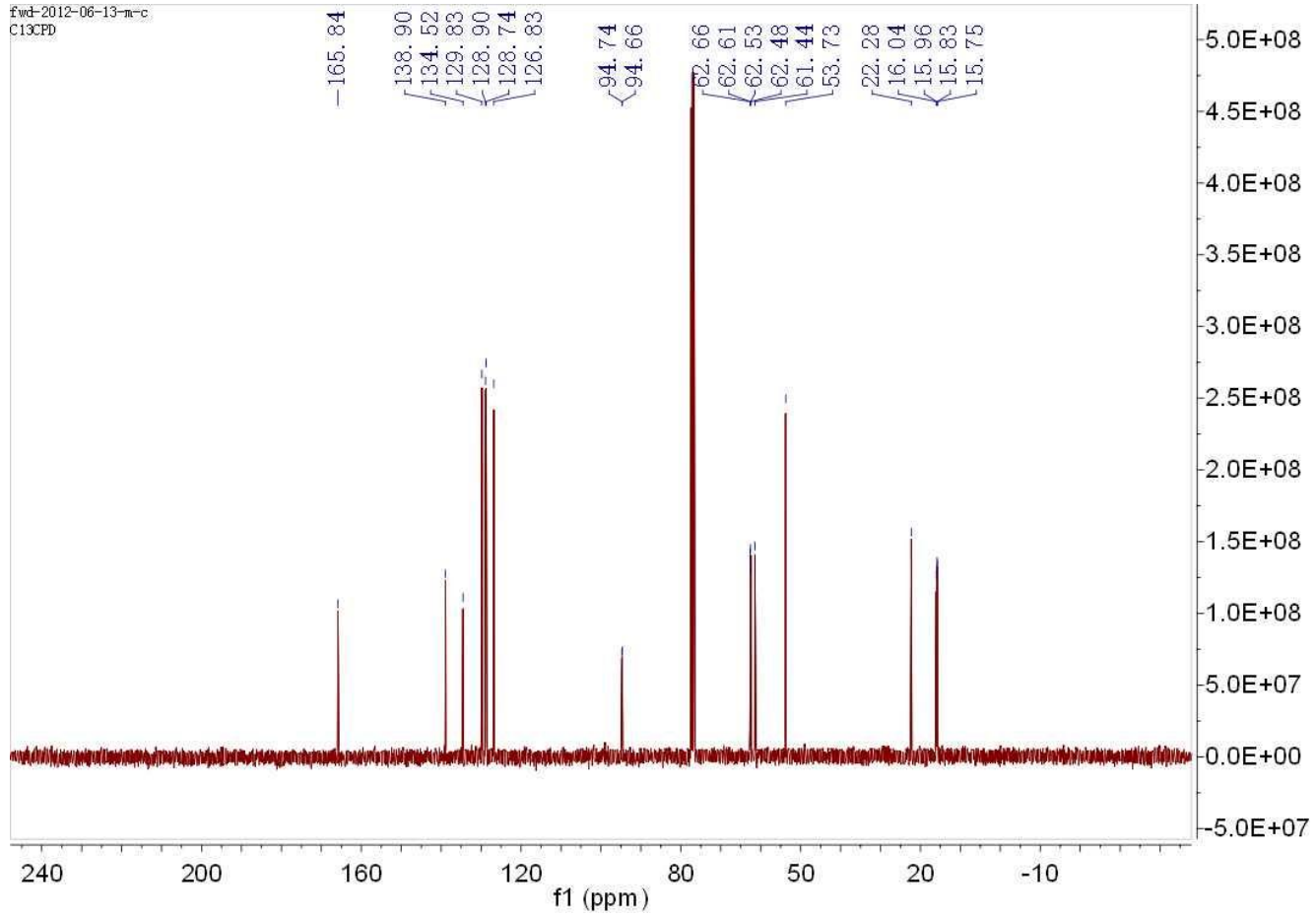
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.831	VB	0.2413	260.33157		16.58973	3.8231
2	12.005	BB	0.3415	133.20288		6.04572	1.9562
3	13.113	BB	0.3701	331.46655		13.96321	4.8678
4	15.505	BB	0.4505	6084.39600		210.66946	89.3529

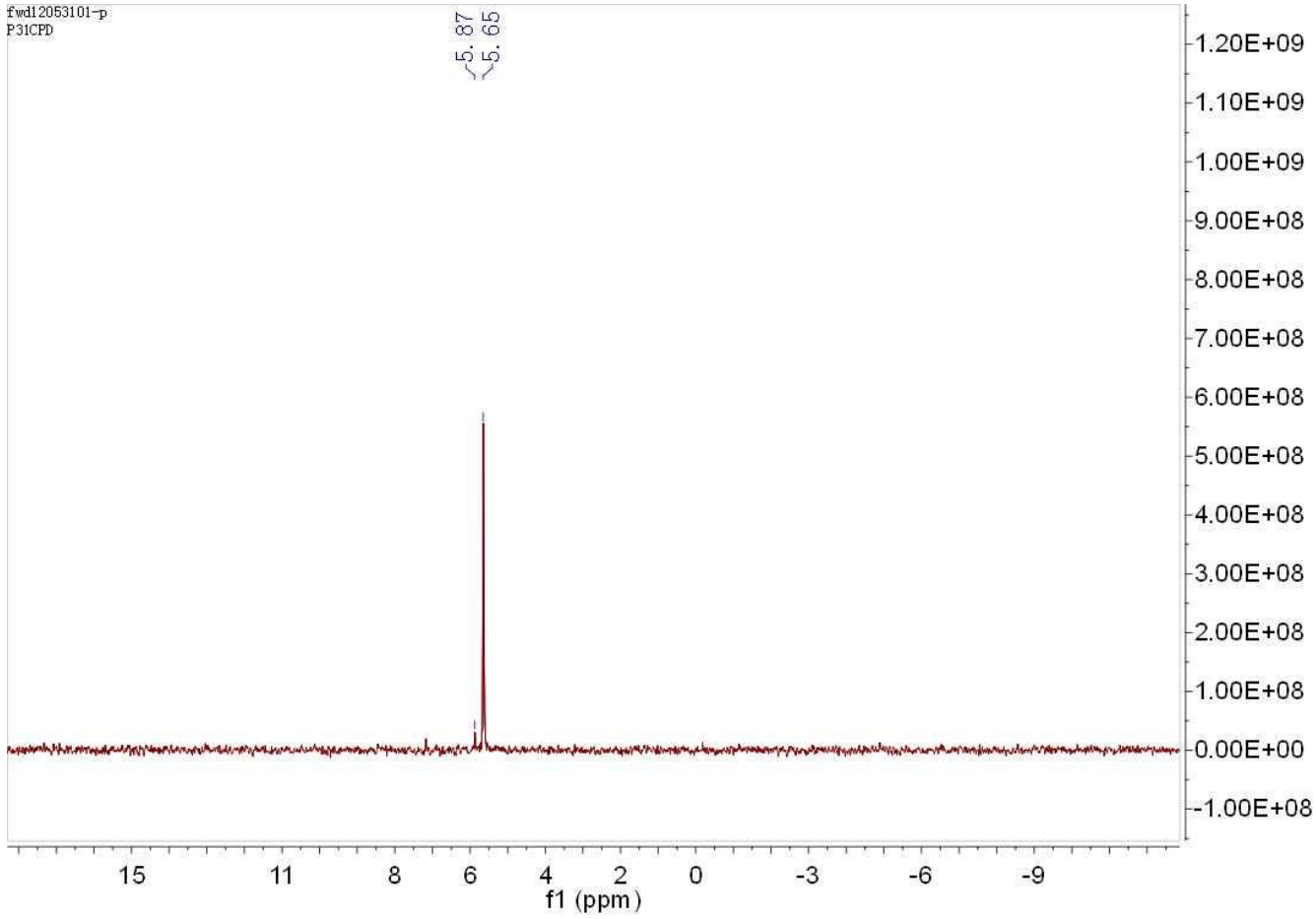
Methyl 3-((diethoxyphosphoryl)amino)-3-(3-chlorophenyl)-2-methyl-2-nitropropanoate (6e):

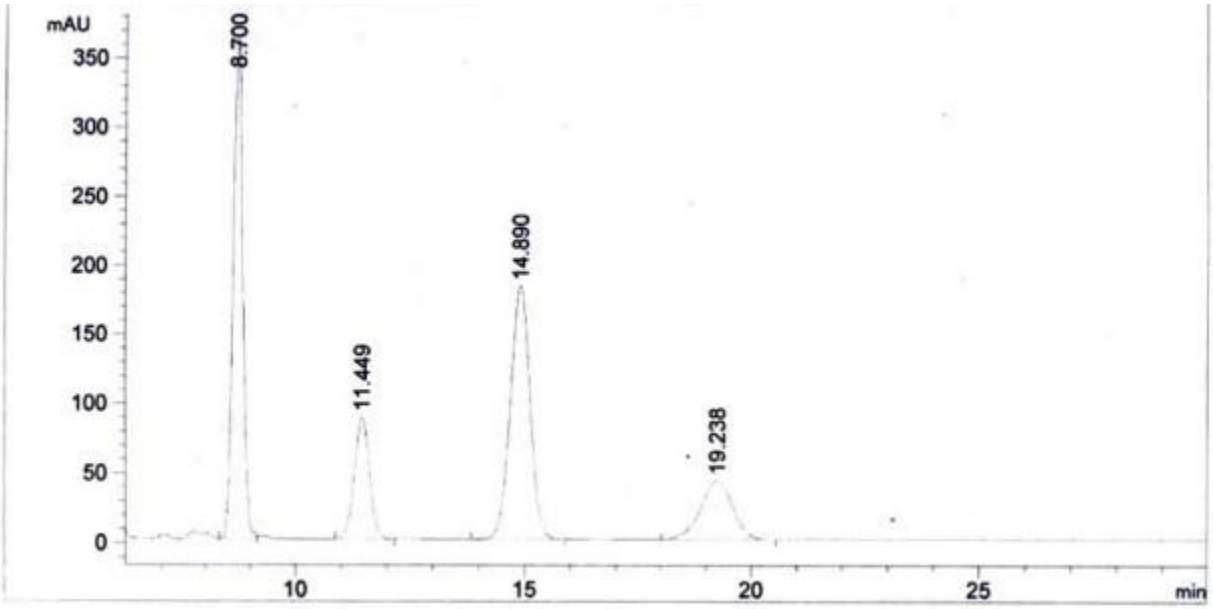


White solid; mp 89-92 °C; $[\alpha]^{20}_{D}$ = 50.8° (c = 0.005, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.43 (m, 1H), 7.28-7.35 (m, 3H), 4.66-4.99 (m, 2H), 3.75-3.99 (m, 6H), 3.58-3.74 (m, 1H), 1.72 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.84, 138.90, 134.52, 129.83, 128.90, 128.74, 126.83, 94.70 (d, *J* = 8.1 Hz), 62.63 (d, *J* = 5.3 Hz), 62.50 (d, *J* = 5.2 Hz), 61.44, 53.73, 22.28, 16.00 (d, *J* = 7.4 Hz), 15.79 (d, *J* = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.87 (s), 5.65 (s); HRMS (MALDI) calculated for $[C_{15}H_{22}ClN_2O_7P+Na]^+$: 431.0751, Found 431.0748; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.626 min, tr (major) = 11.287 min, tr (major) = 14.668 min, tr (major) = 18.758 min.

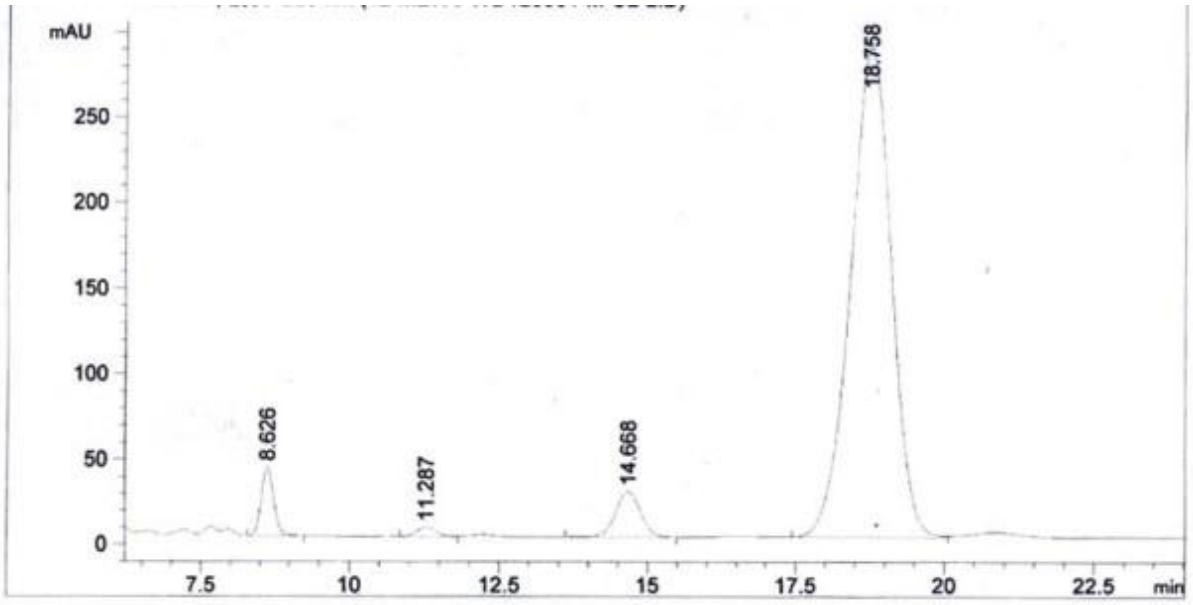






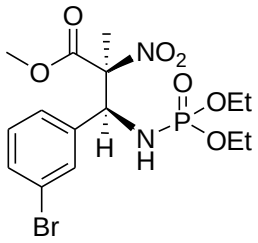


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.700	VV	0.2319	5386.86914		361.85449	36.0214
2	11.449	BB	0.3571	2010.90027		87.43375	13.4467
3	14.890	BB	0.4638	5466.33447		182.86984	36.5528
4	19.238	BB	0.7664	2090.53931		42.47835	13.9792

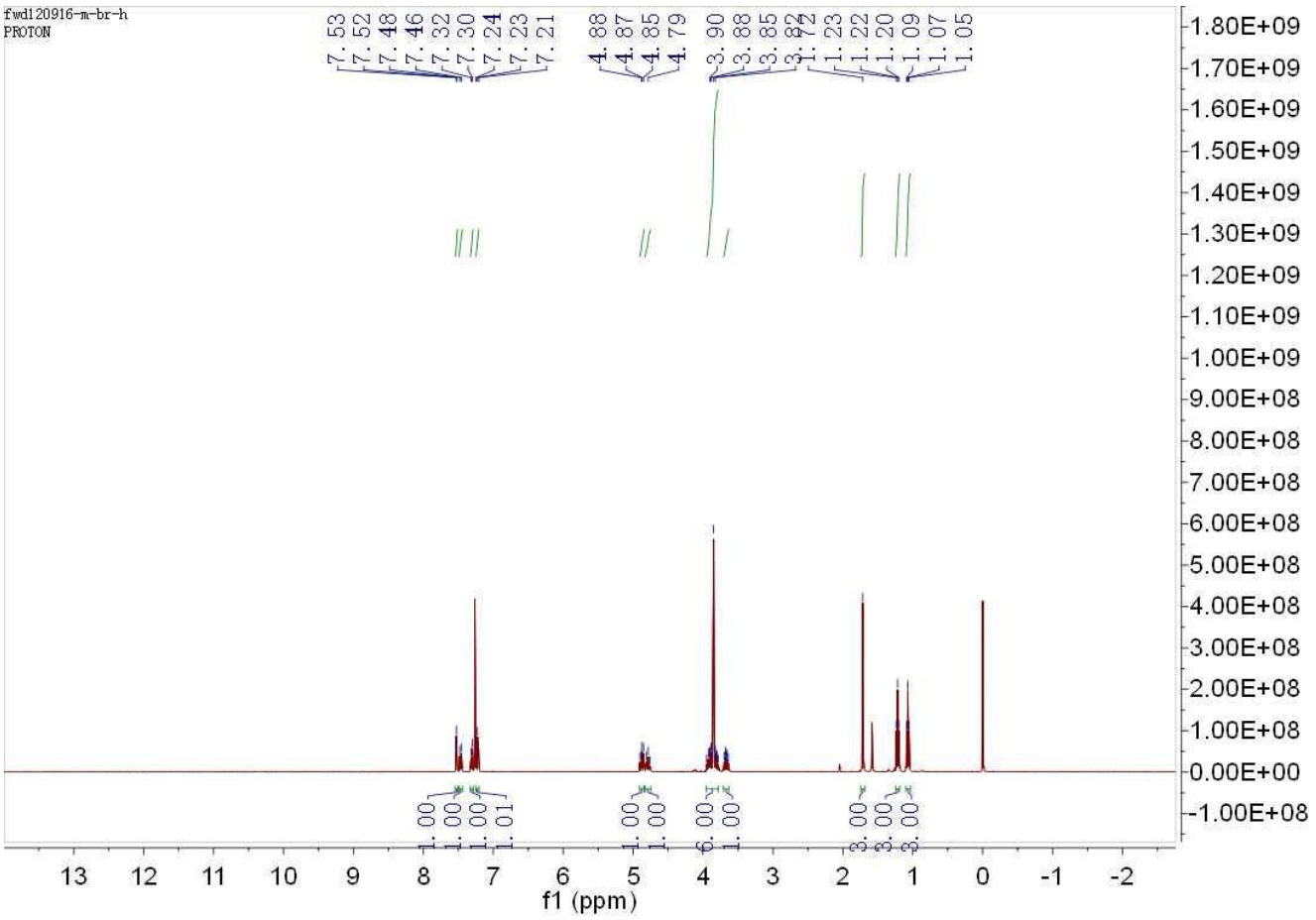


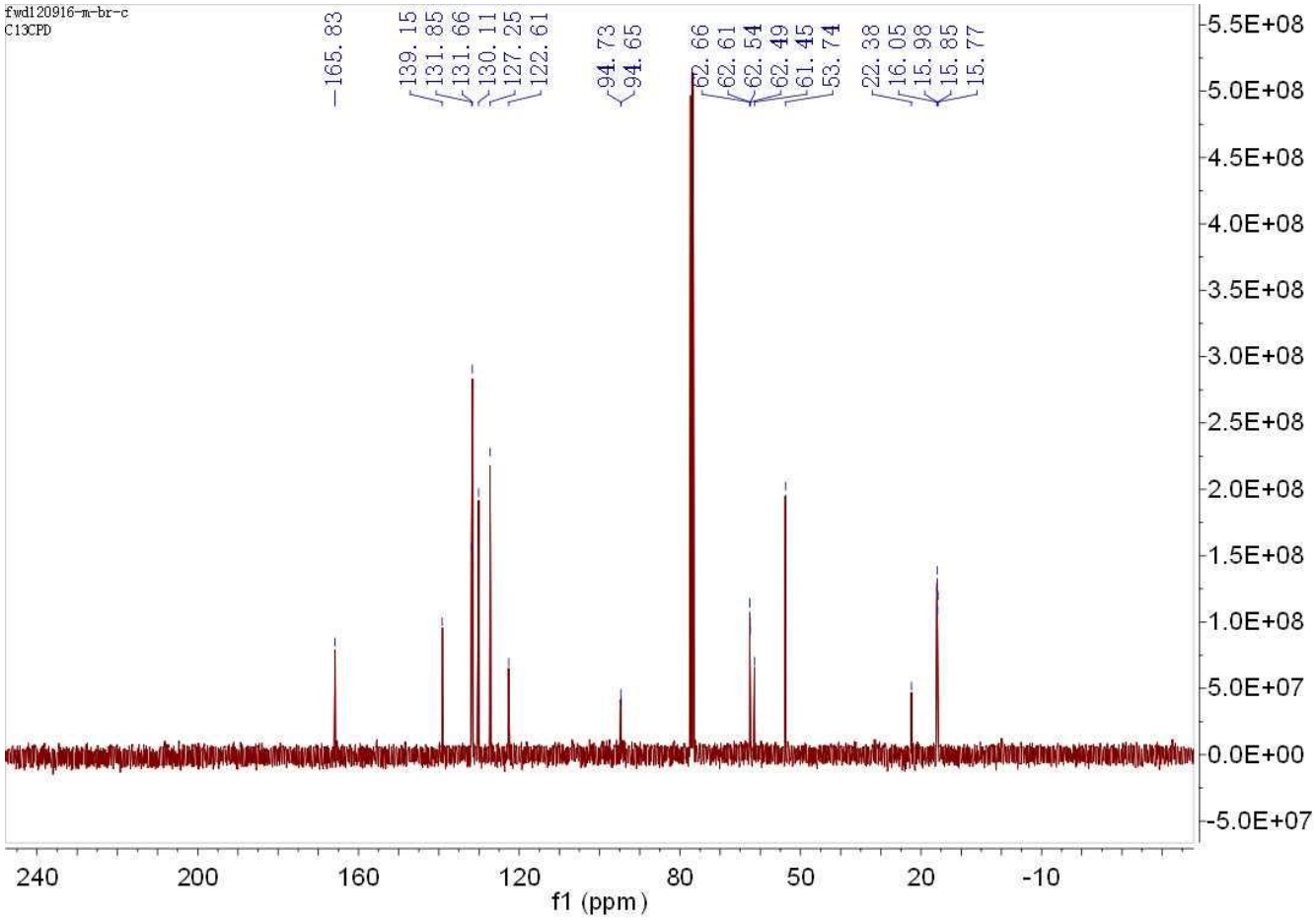
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.626	VB	0.2284	599.02533		40.73059	3.9190
2	11.287	VV	0.3470	128.95047		5.76222	0.8436
3	14.668	BB	0.4560	805.46228		27.43838	5.2696
4	18.758	BB	0.7377	1.37516e4		287.93399	89.9677

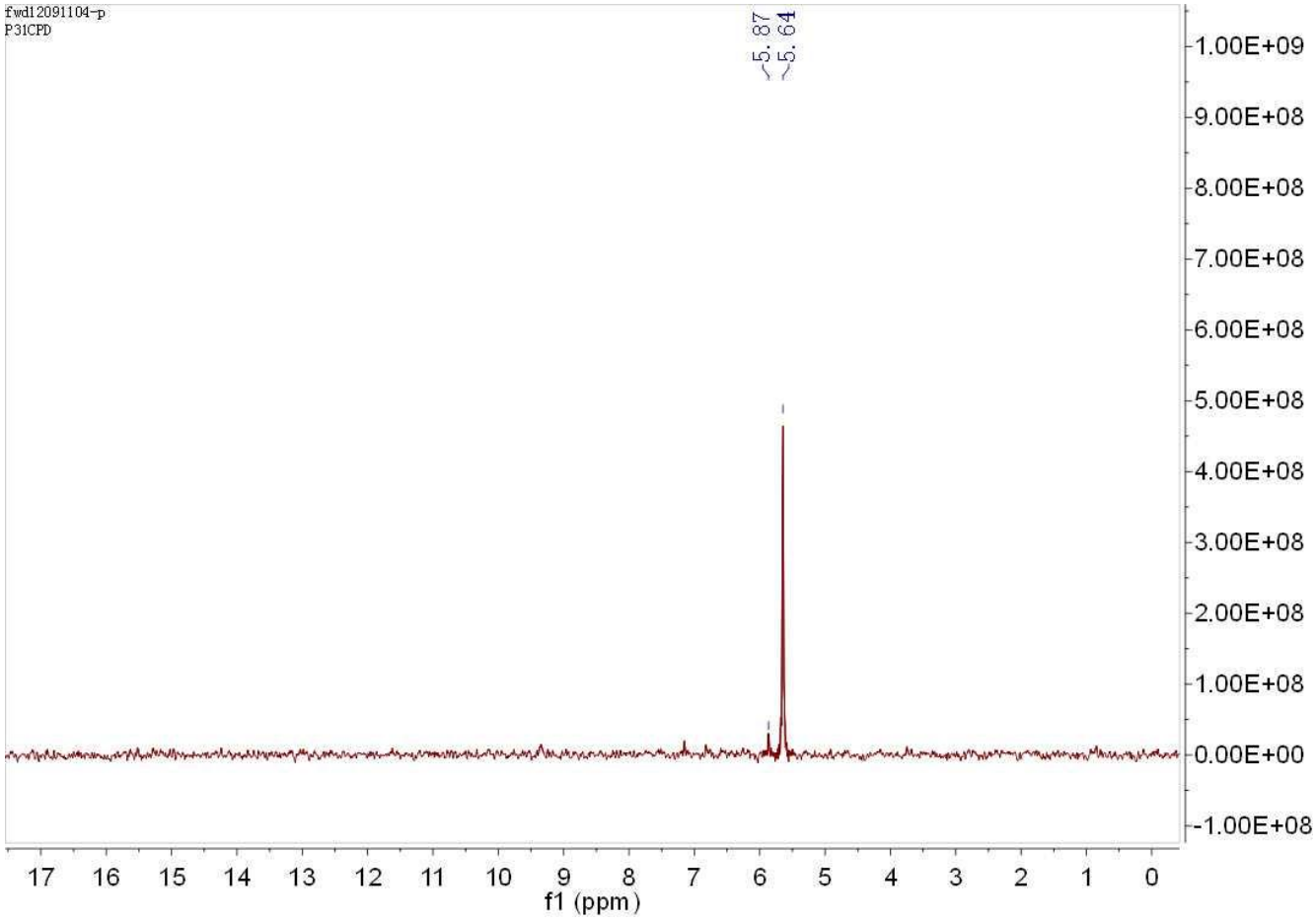
Methyl 3-((diethoxyphosphoryl)amino)-3-(3-bromophenyl)-2-methyl-2-nitropropanoate (6f):

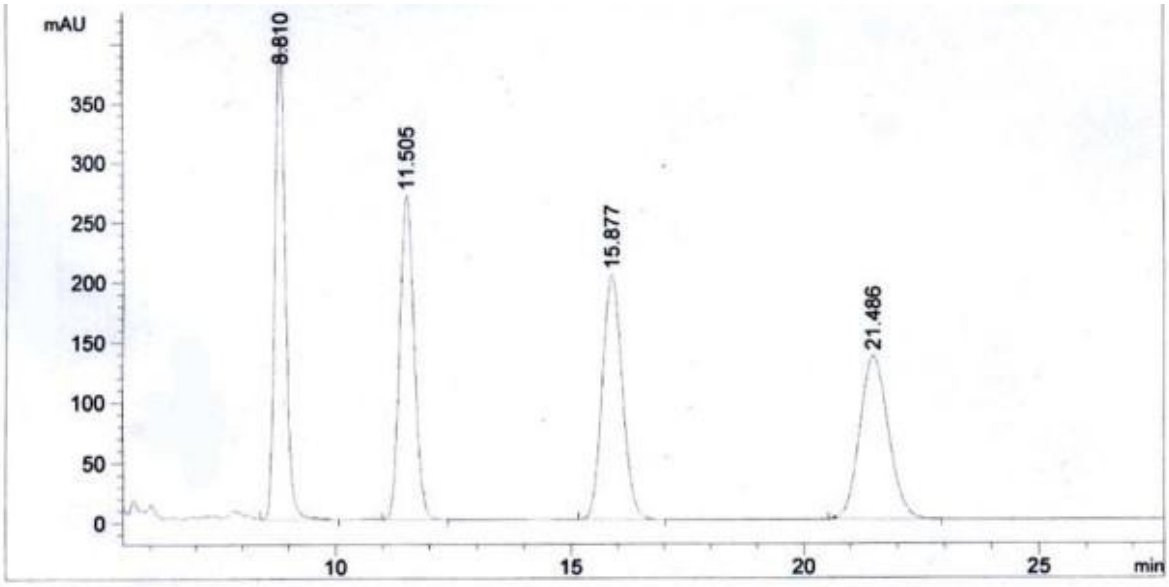


White solid; mp 73-75 °C; $[\alpha]^{20}_{D}$ = 50.8° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.56 (m, 1H), 7.43-7.50 (m, 1H), 7.28-7.34 (m, 1H), 7.19-7.25 (m, 1H), 4.88 (dd, *J* = 11.5, 9.2 Hz, 1H), 4.79 (t, *J* = 11.5 Hz, 1H), 3.76-3.97 (m, 6H), 3.62-3.72 (m, 1H), 1.72 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.83, 139.15, 131.85, 131.66, 130.11, 127.25, 122.61, 94.69 (d, *J* = 7.8 Hz), 62.64 (d, *J* = 5.2 Hz), 62.52 (d, *J* = 5.2 Hz), 61.45, 53.74, 22.38, 16.02 (d, *J* = 7.5 Hz), 15.81 (d, *J* = 7.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.87, 5.64; HRMS (MALDI) calculated for $[C_{15}H_{22}BrN_2O_7P+Na]^+$: 475.0246, Found 475.0243; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) =8.888 min, tr (major) = 11.594 min, tr (major) = 15.833 min, tr (major) = 21.252 min.

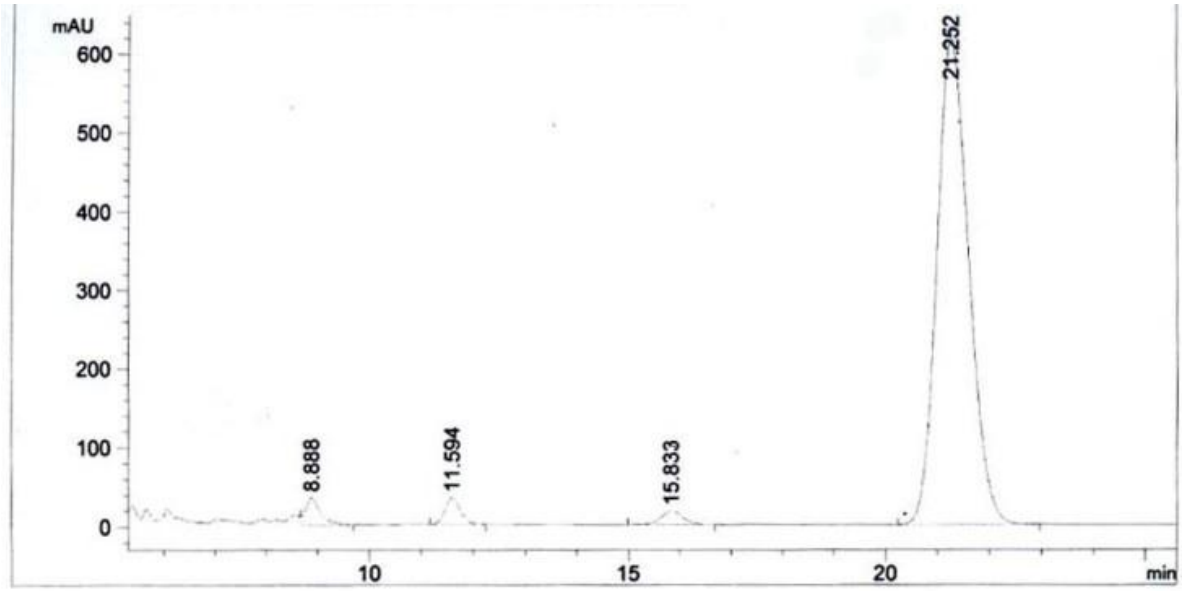






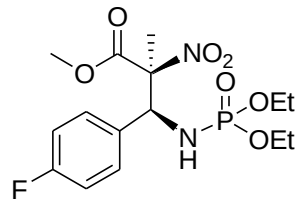


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.810	VB	0.2400	6290.82178		403.71979	26.2784
2	11.505	VB	0.3342	5760.04395		269.01837	24.0612
3	15.877	BB	0.4656	6099.05176		203.81094	25.4773
4	21.486	BB	0.6606	5789.20752		135.75108	24.1830

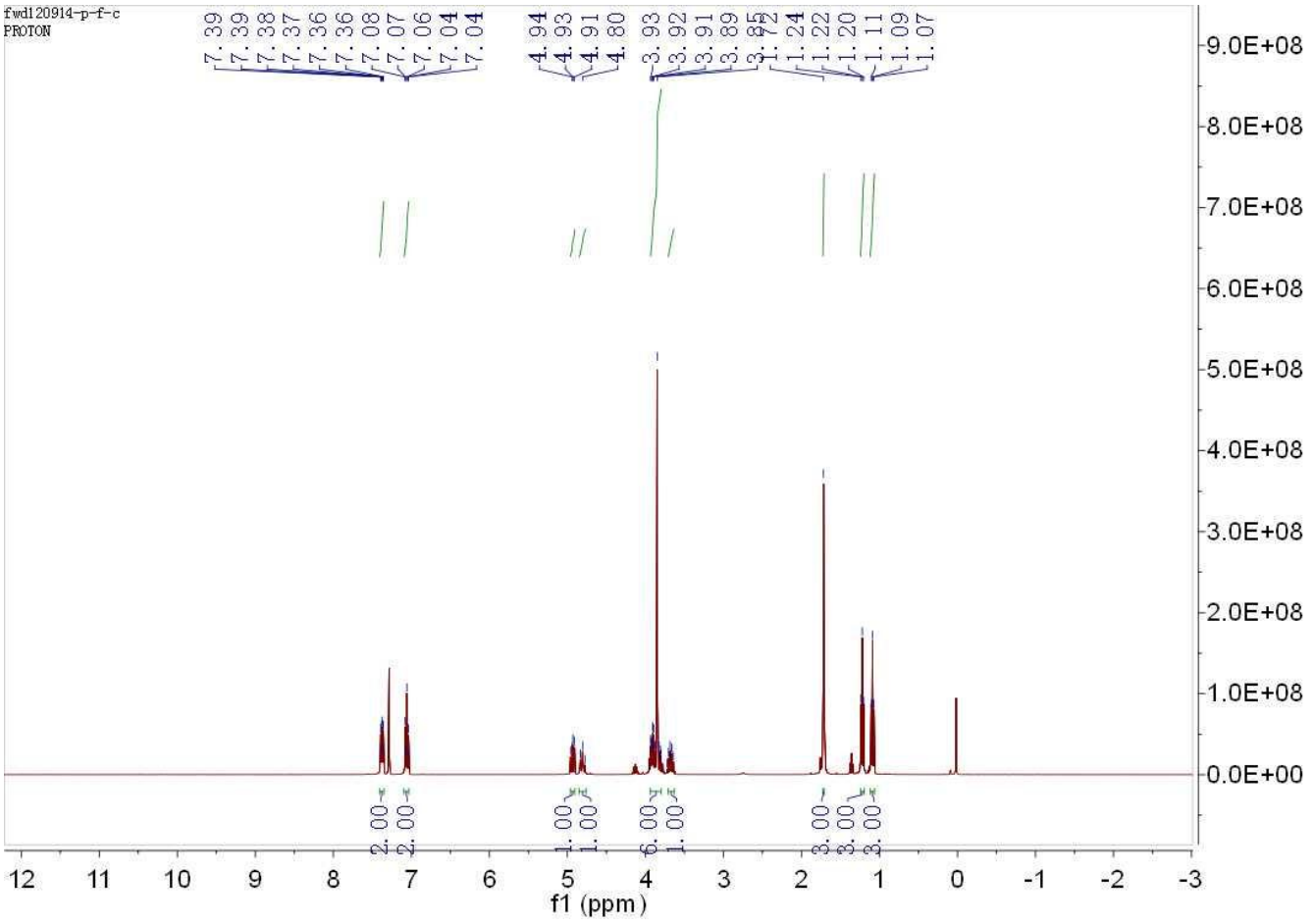


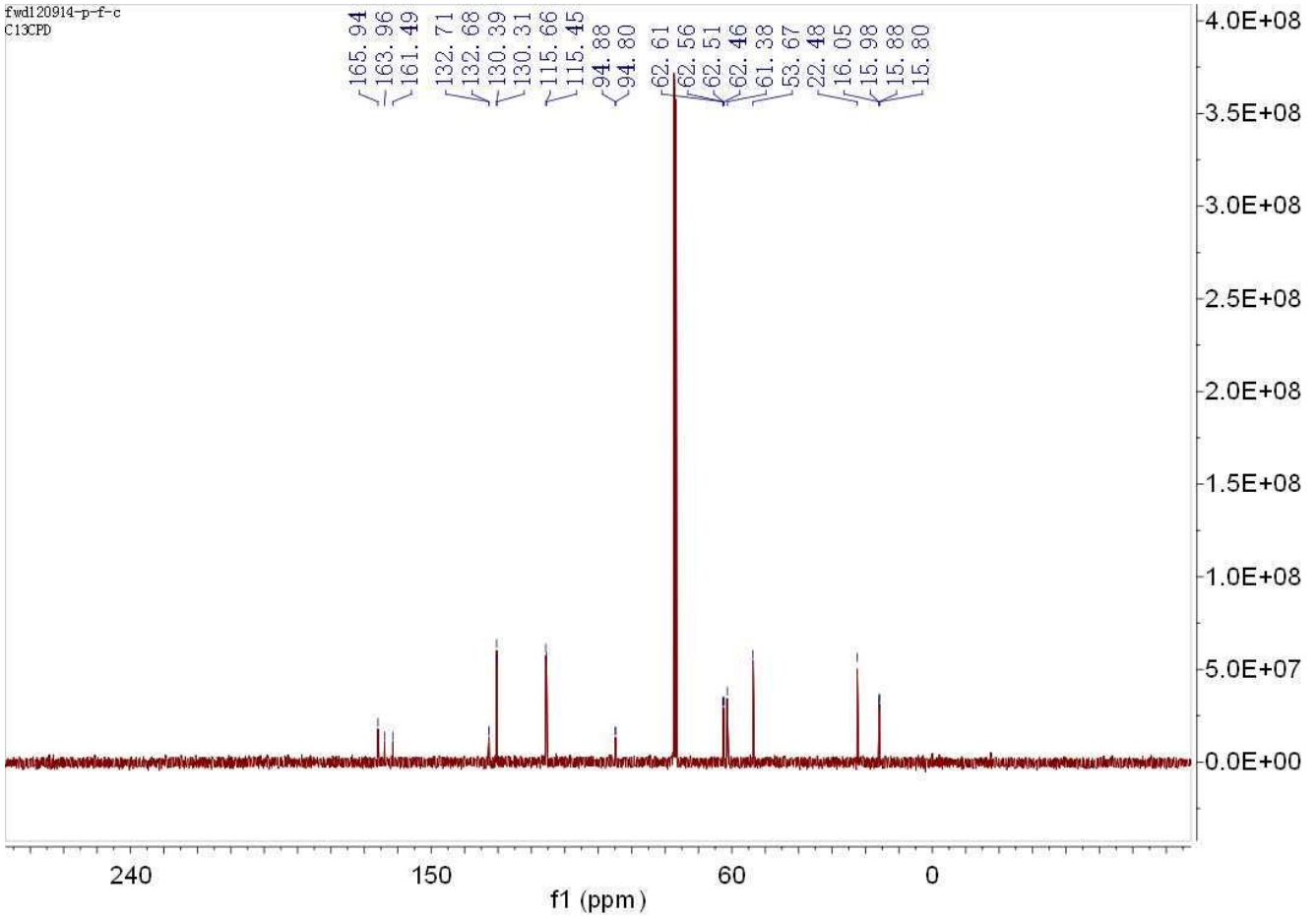
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.888	VB	0.2864	674.85675		34.07043	2.3926
2	11.594	BB	0.3223	689.35284		33.40004	2.4440
3	15.833	BB	0.4633	519.30255		17.18209	1.8411
4	21.252	BB	0.6634	2.63221e4		617.34601	93.3222

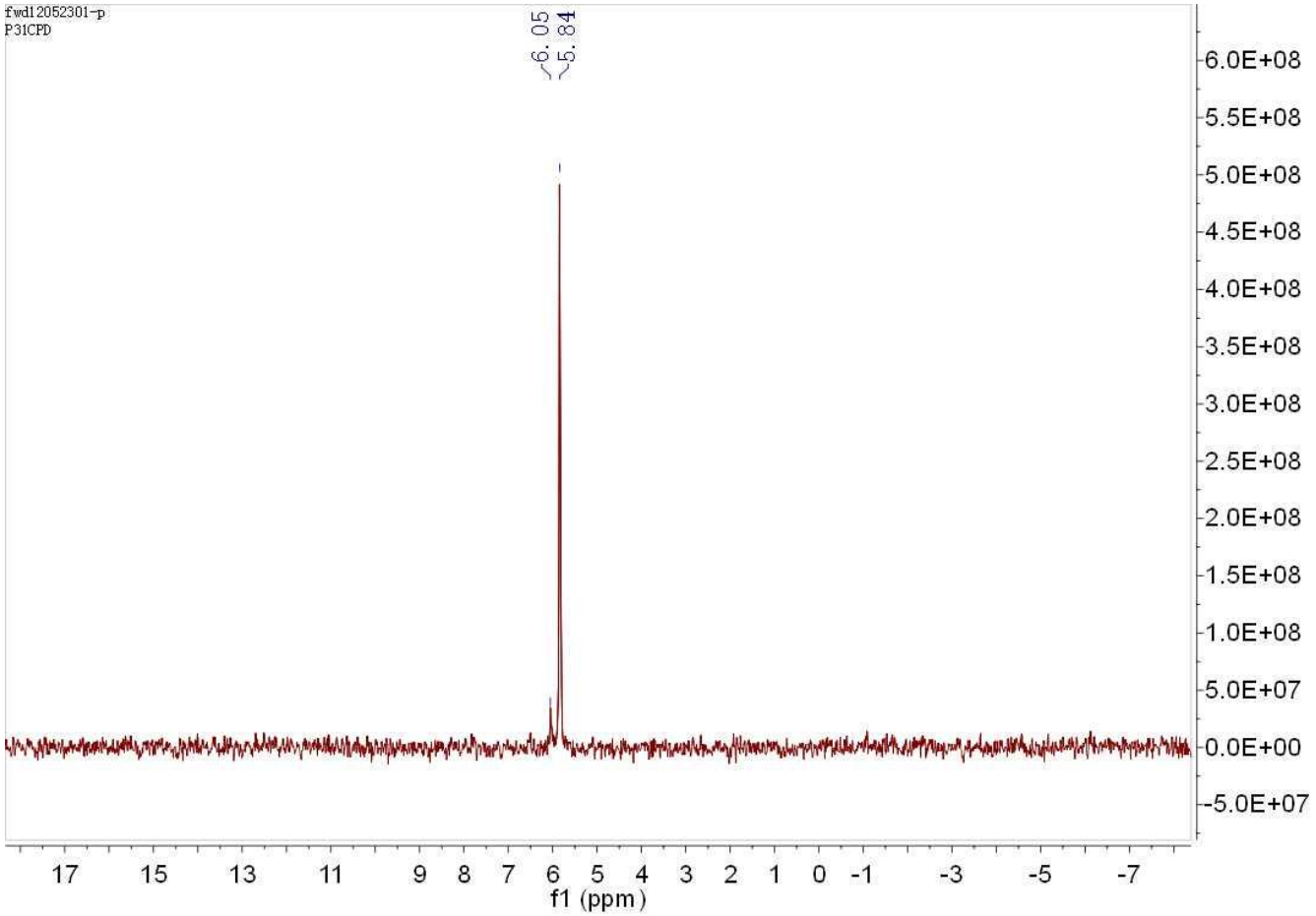
Methyl 3-((diethylphosphoryl)amino)-3-(4-fluorophenyl)-2-methyl-2-nitropropanoate (6g):

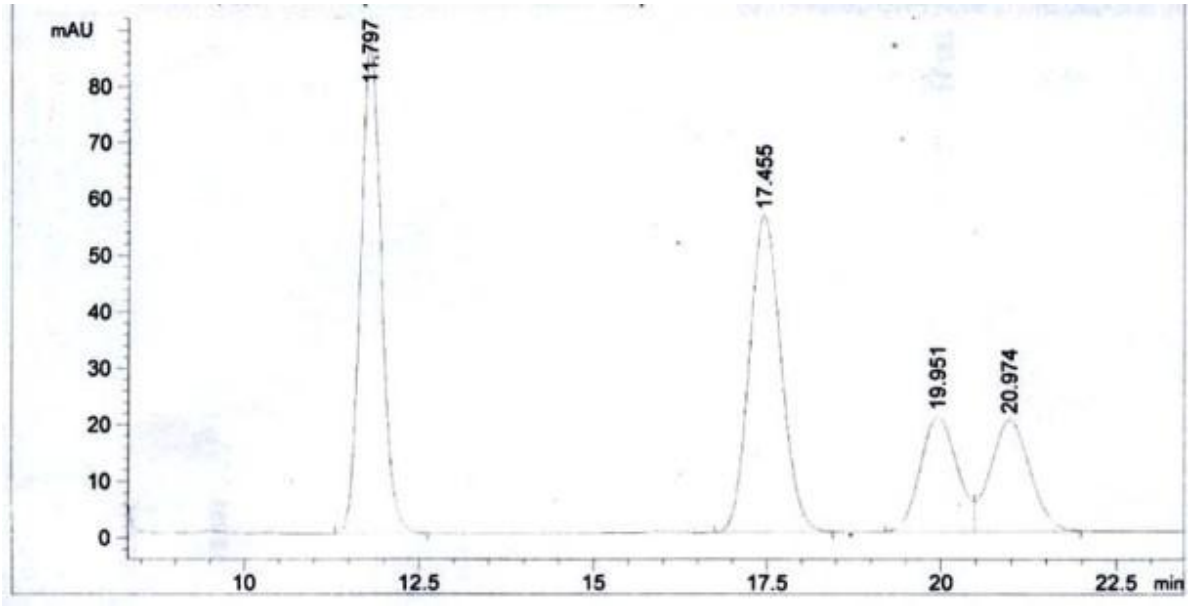


White solid; mp 99-102 °C; $[\alpha]^{20}_{D}$ = 28.0° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.42 (m, 2H), 7.01-7.11 (m, 2H), 4.93 (dd, *J* = 11.5, 9.2 Hz, 1H), 4.80 (t, *J* = 11.5 Hz, 1H), 3.77-3.98 (m, 6H), 3.62-3.73 (m, 1H), 1.72 (s, 3H), 1.22 (3, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.94, 162.73 (d, *J* = 248.6 Hz), 132.70, 130.35, 115.55, 94.84 (d, *J* = 8.1 Hz), 62.58 (d, *J* = 5.3 Hz), 62.49 (d, *J* = 5.3 Hz), 61.38, 53.67, 22.48, 16.02 (d, *J* = 7.4 Hz), 15.84 (d, *J* = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.05, 5.84; HRMS (MALDI) calculated for $[C_{15}H_{22}FN_2O_7P+Na]^+$: 415.1046, Found 415.1044; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) =11.789 min, tr (major) = 17.388 min, tr (major) = 19.970 min, tr (major) = 21.001 min.

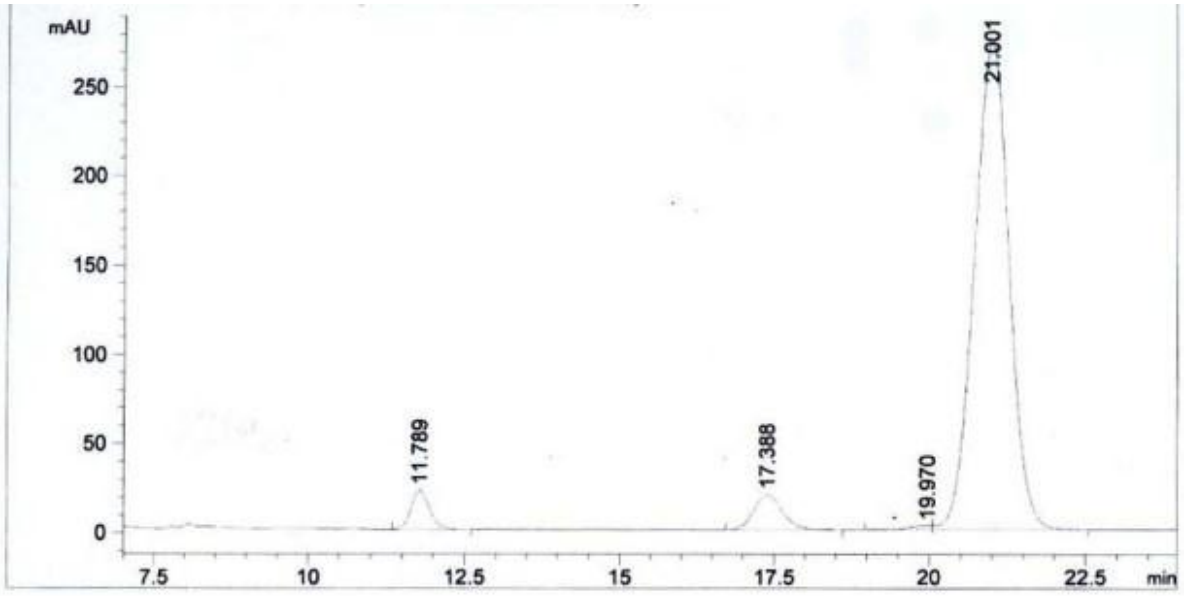






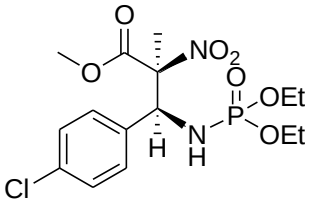


#	[min]		[min]	mAU	*s	[mAU]	%
1	11.797	BB	0.3210	1808.09448		87.03419	35.2042
2	17.455	BB	0.4988	1797.73145		56.13455	35.0024
3	19.951	BV	0.5674	749.71240		20.52518	14.5972
4	20.974	VB	0.6012	780.47931		19.85799	15.1962

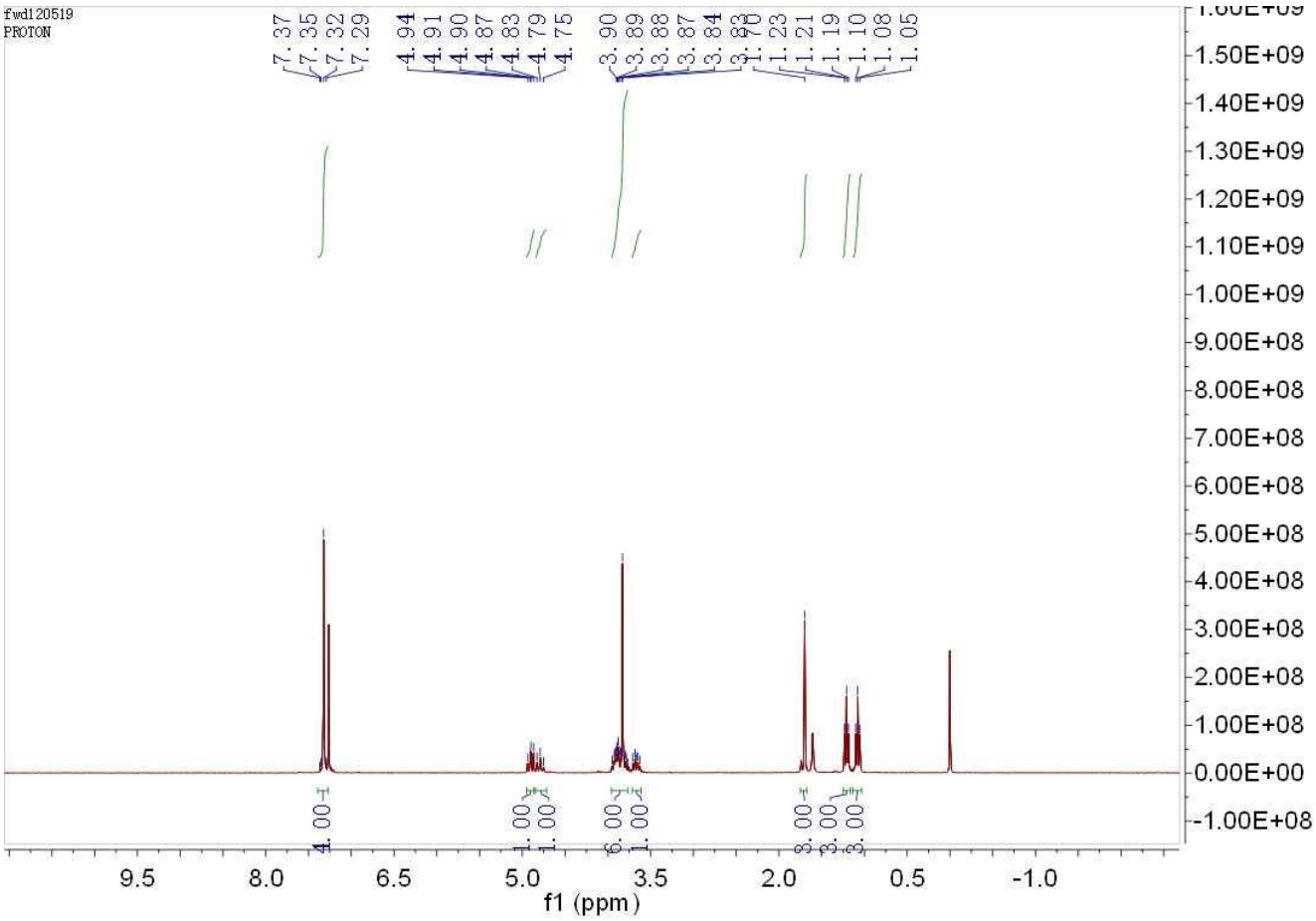


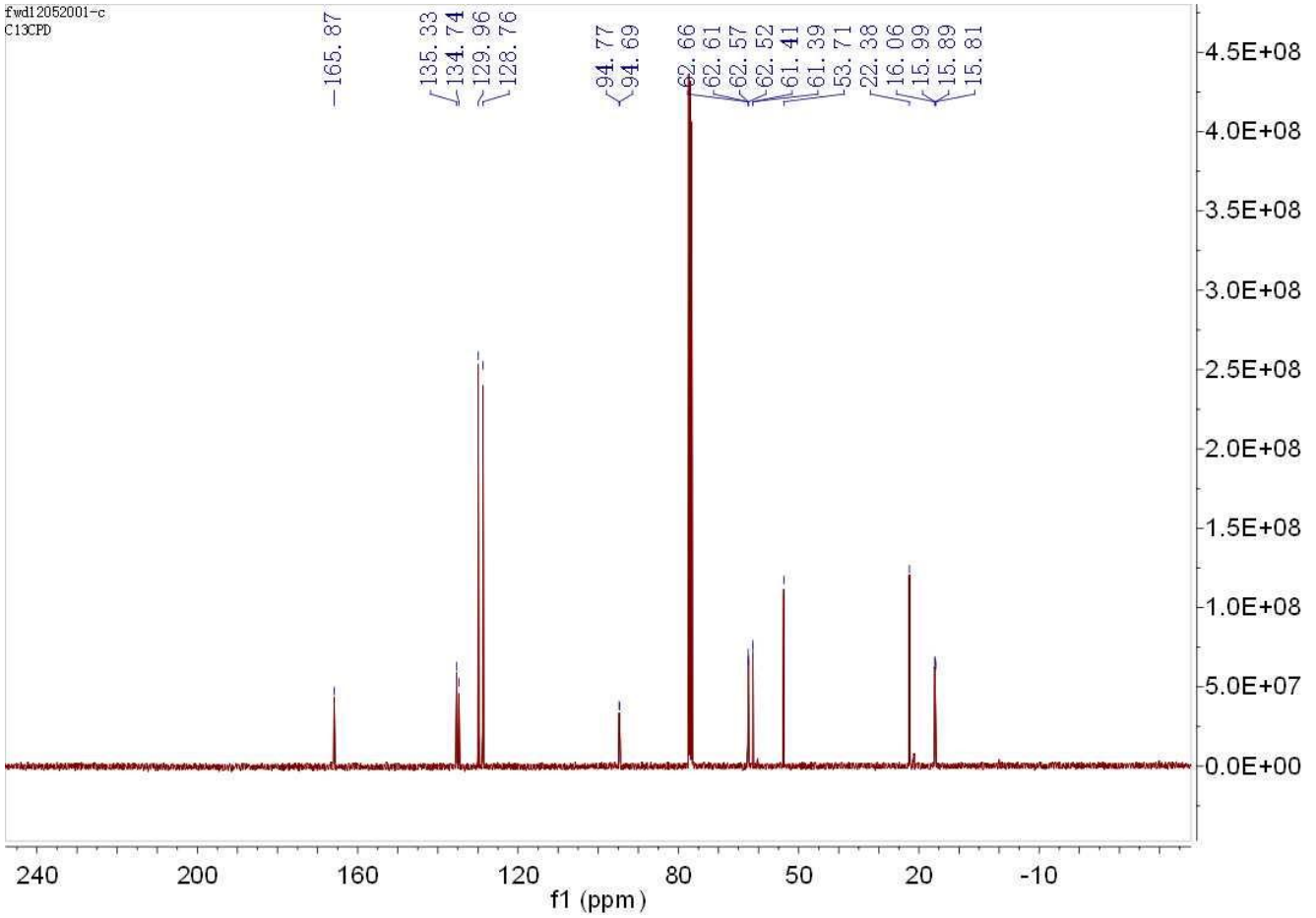
#	[min]		[min]	mAU	*s	[mAU]	%
1	11.789	BB	0.3199	457.33142		22.11229	3.8728
2	17.388	BB	0.5012	642.14392		19.92486	5.4379
3	19.970	BV	0.3864	56.67465		2.23300	0.4799
4	21.001	VB	0.6044	1.06526e4		274.34323	90.2094

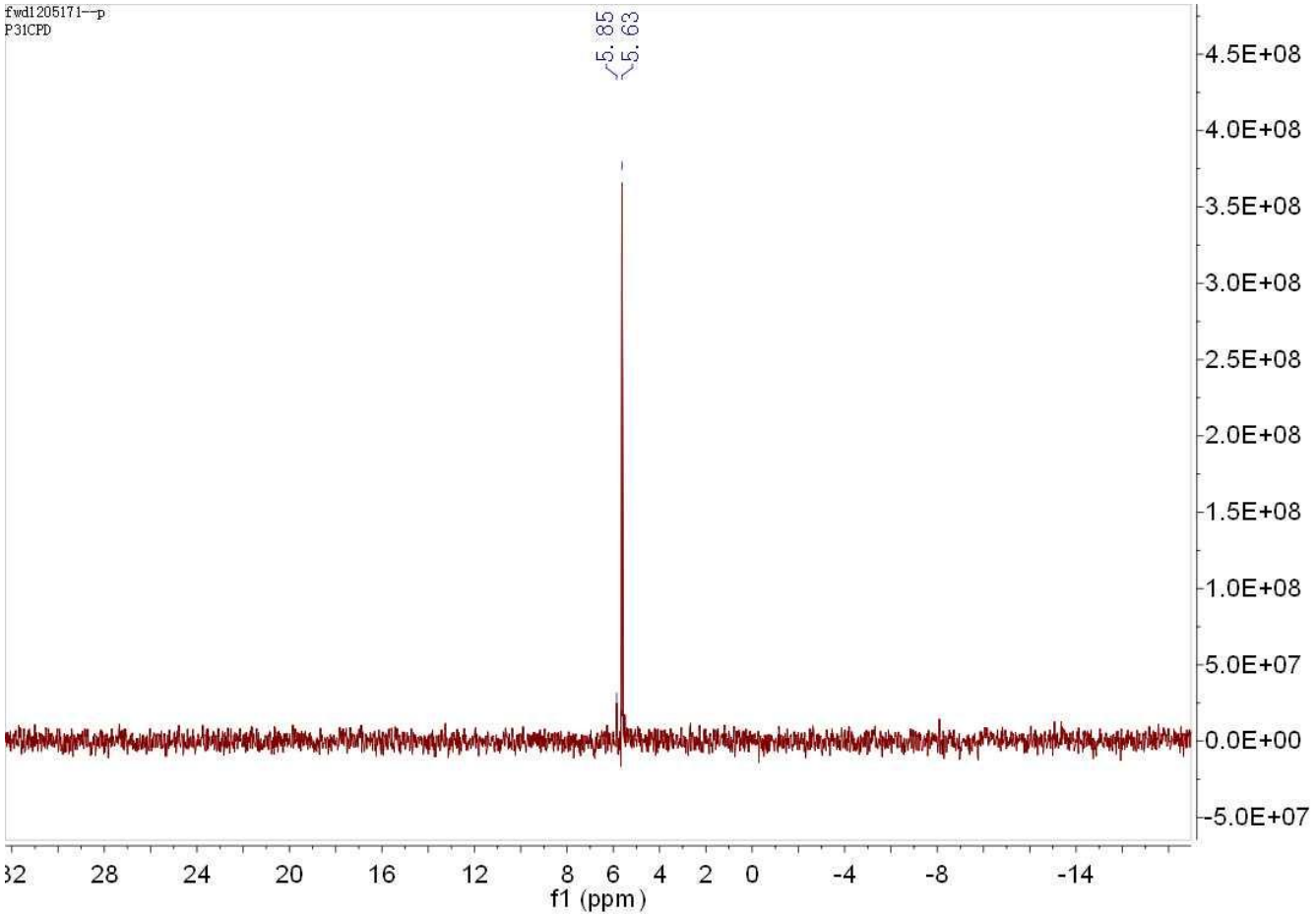
Methyl 3-((diethylphosphoryl)amino)-3-(4-chlorophenyl)-2-methyl-2-nitropropanoate (6h):

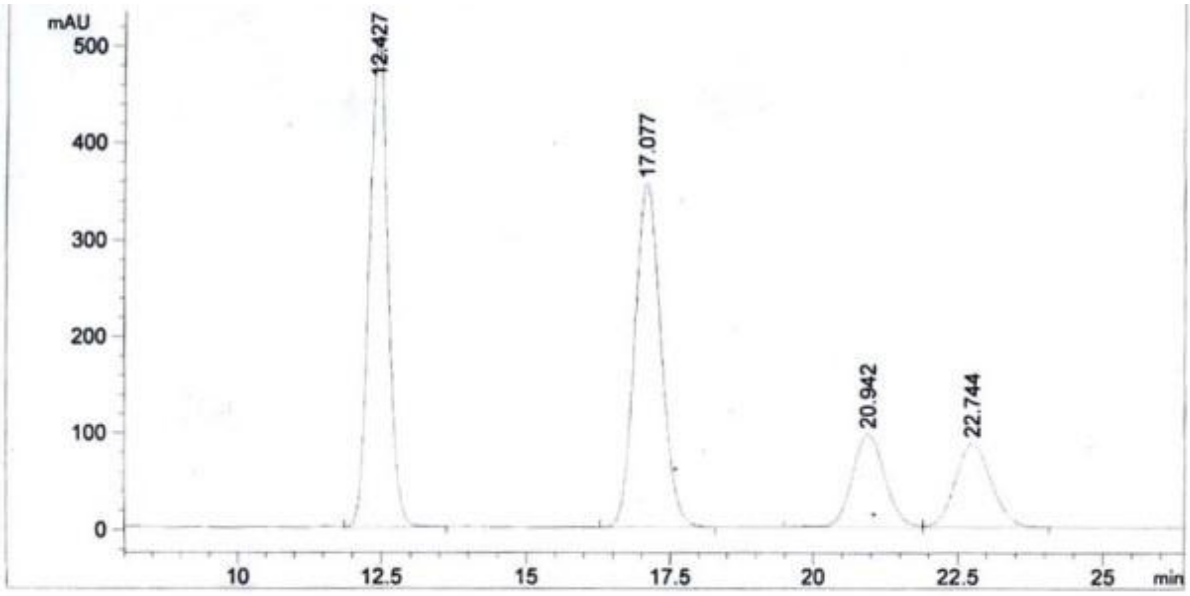


White solid; mp 103-105 °C; $[\alpha]^{20}_{D}$ = 48.0° (c = 0.005, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.38 (m, 4H), 4.90 (dd, *J* = 11.5, 9.3 Hz, 1H), 4.79 (t, *J* = 11.5 Hz, 1H), 3.75-3.98 (m, 6H), 3.61-3.73 (m, 1H), 1.70 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.87, 135.33, 134.74, 129.96, 128.76, 94.73 (d, *J* = 7.9 Hz), 62.64 (d, *J* = 5.3 Hz), 62.54 (d, *J* = 5.3 Hz), 61.40 (d, *J* = 2.2 Hz), 53.71, 22.38, 16.02 (d, *J* = 7.4 Hz), 15.85 (d, *J* = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.85, 5.63; HRMS (MALDI) calculated for $[C_{15}H_{22}ClN_2O_7P+Na]^+$: 431.0751, Found 431.0747; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 12.390 min, tr (major) = 17.051 min, tr (major) = 21.081 min, tr(major) = 23.011 min.

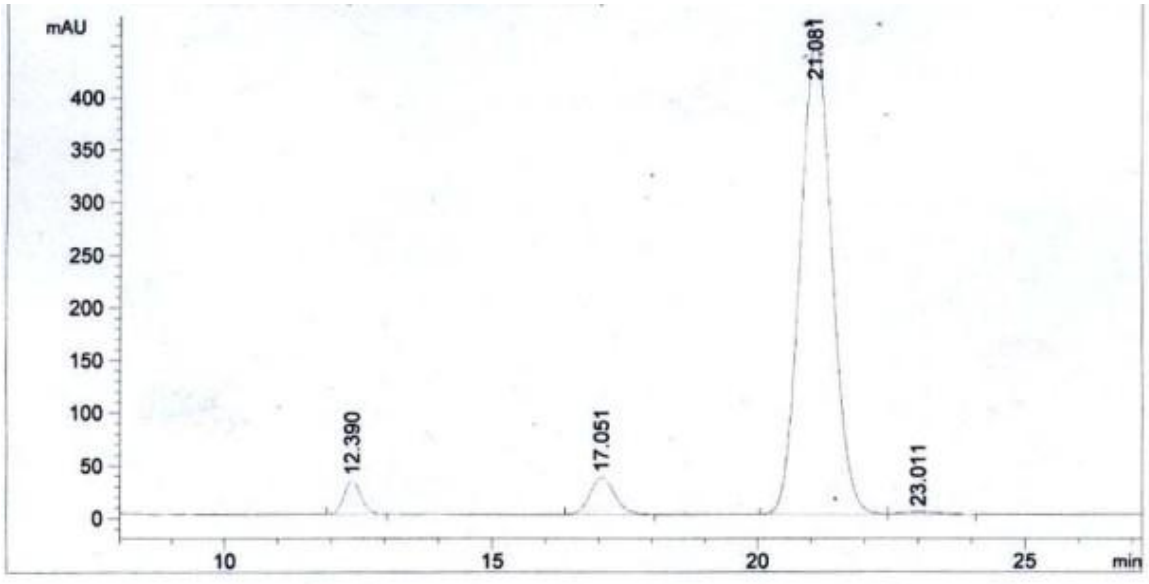






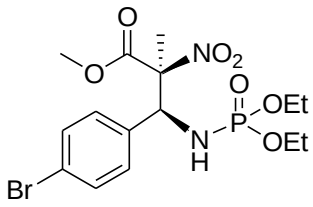


#	[min]		[min]	mAU	*s	[mAU]	%
1	12.427	VB	0.3476	1.14037e4		508.34262	37.6240
2	17.077	BB	0.4974	1.13861e4		355.56967	37.5659
3	20.942	BV	0.6097	3773.66455		96.07207	12.4503
4	22.744	VB	0.6720	3746.22656		86.62969	12.3598

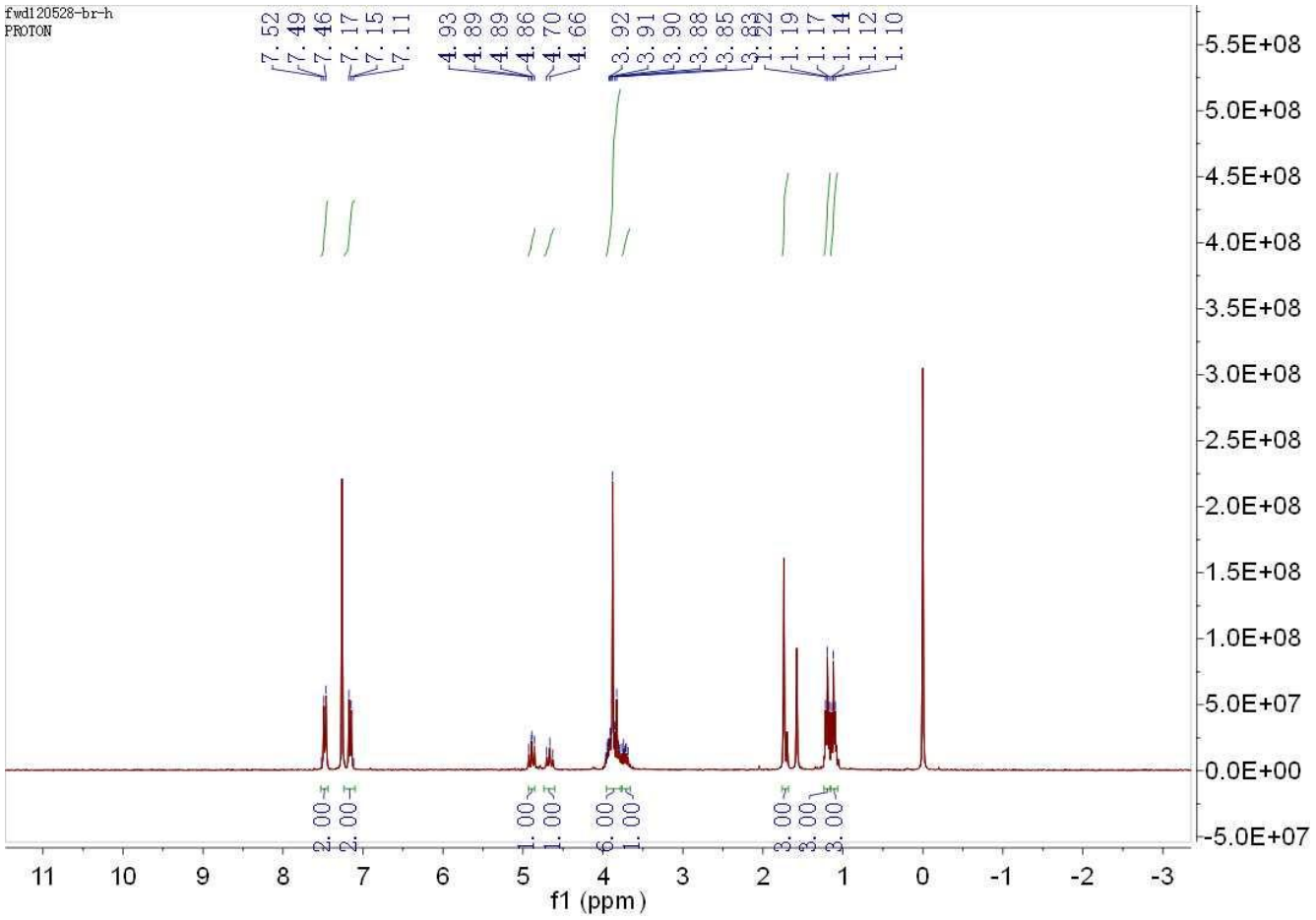


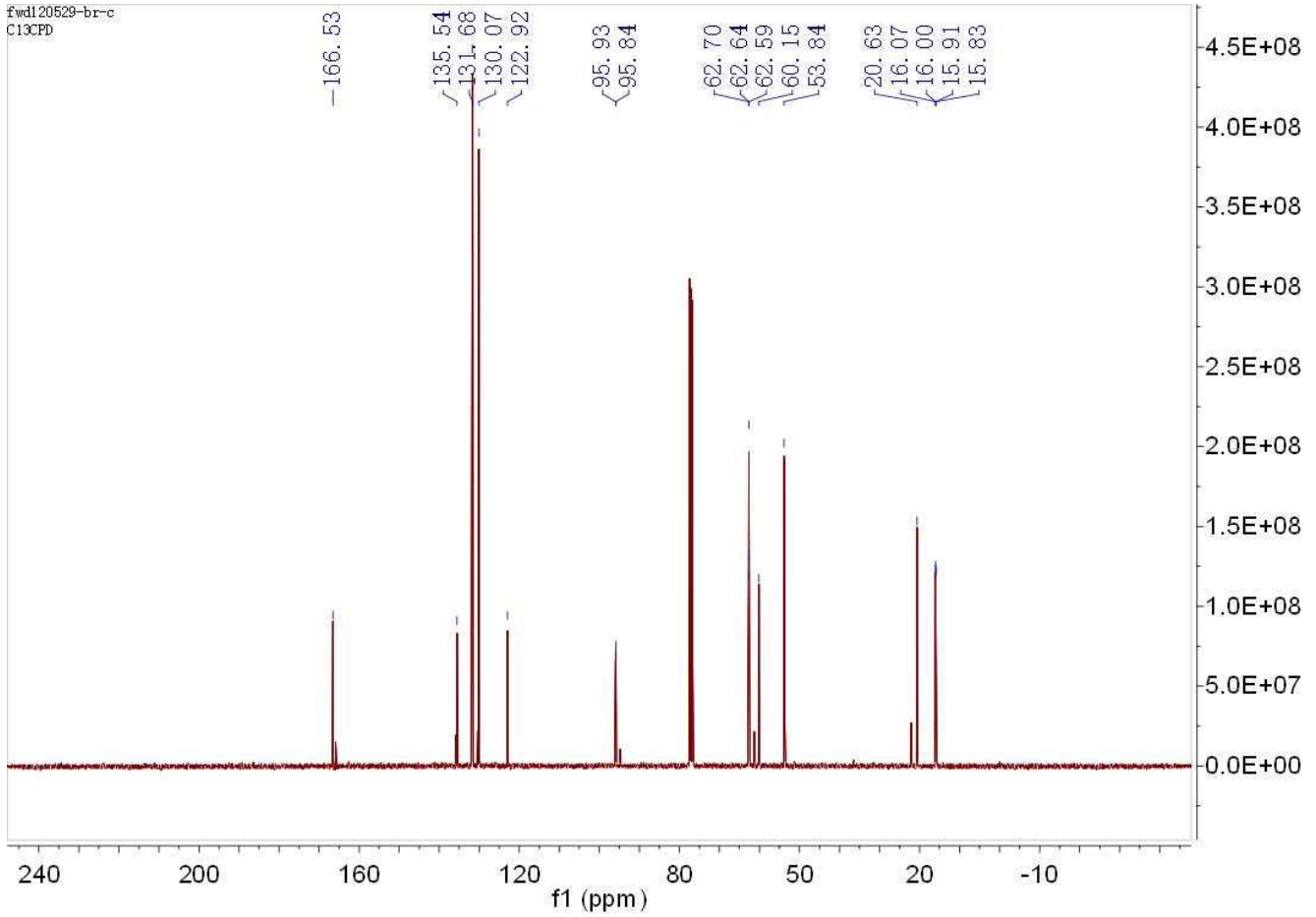
#	[min]		[min]	mAU	*s	[mAU]	%
1	12.390	BB	0.3444	699.04413		31.55050	3.3673
2	17.051	BB	0.5038	1138.90894		35.09845	5.4861
3	21.081	BB	0.6466	1.88088e4		452.44757	90.6016
4	23.011	BB	0.6723	113.14812		2.44524	0.5450

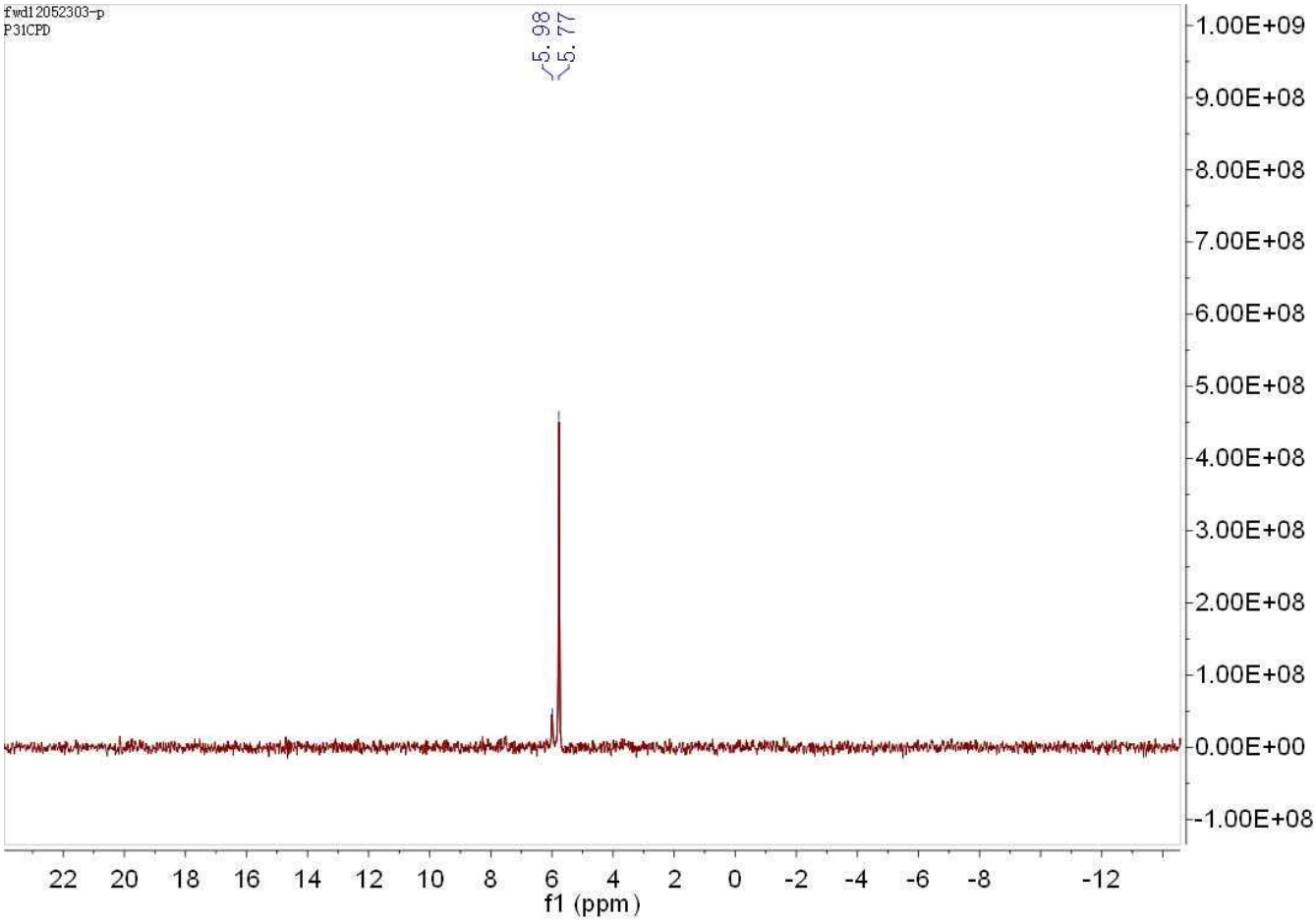
Methyl 3-((diethylphosphoryl)amino)-3-(4-bromophenyl)-2-methyl-2-nitropropanoate (6i):

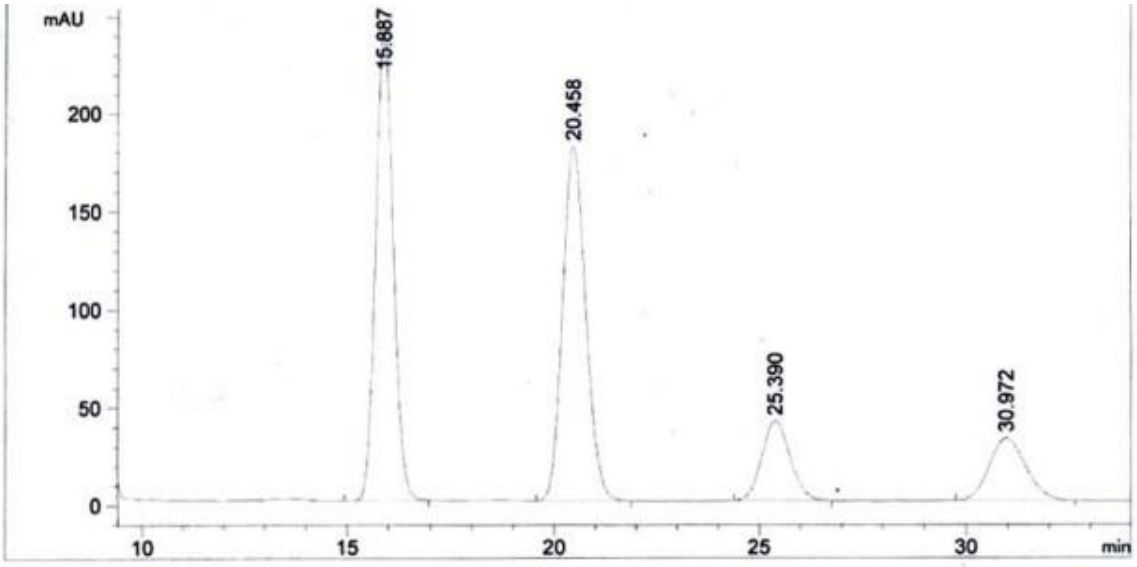


White solid; mp 104-107 °C; $[\alpha]^{20}_{D}$ = 26.2° (c = 0.01, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.57 (m, 2H), 7.08-7.21 (m, 2H), 4.89 (dd, *J* = 11.4, 10.0 Hz, 1H), 4.66 (t, *J* = 11.4 Hz, 1H), 3.78-4.00 (m, 6H), 3.64-3.78 (m, 1H), 1.74 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.53, 135.54, 131.68, 130.07, 122.92, 95.88 (d, *J* = 8.5 Hz), 62.70, 62.62 (d, *J* = 5.8 Hz), 60.15, 53.84, 20.63, 16.03 (d, *J* = 7.2 Hz), 15.87 (d, *J* = 7.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.98, 5.77; HRMS (MALDI) calculated for $[C_{15}H_{22}BrN_2O_7P+Na]^+$: 475.0246, Found 475.0244; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 15.881 min, tr (major) = 20.424 min, tr (major) = 25.370 min, tr (major) = 31.095 min.

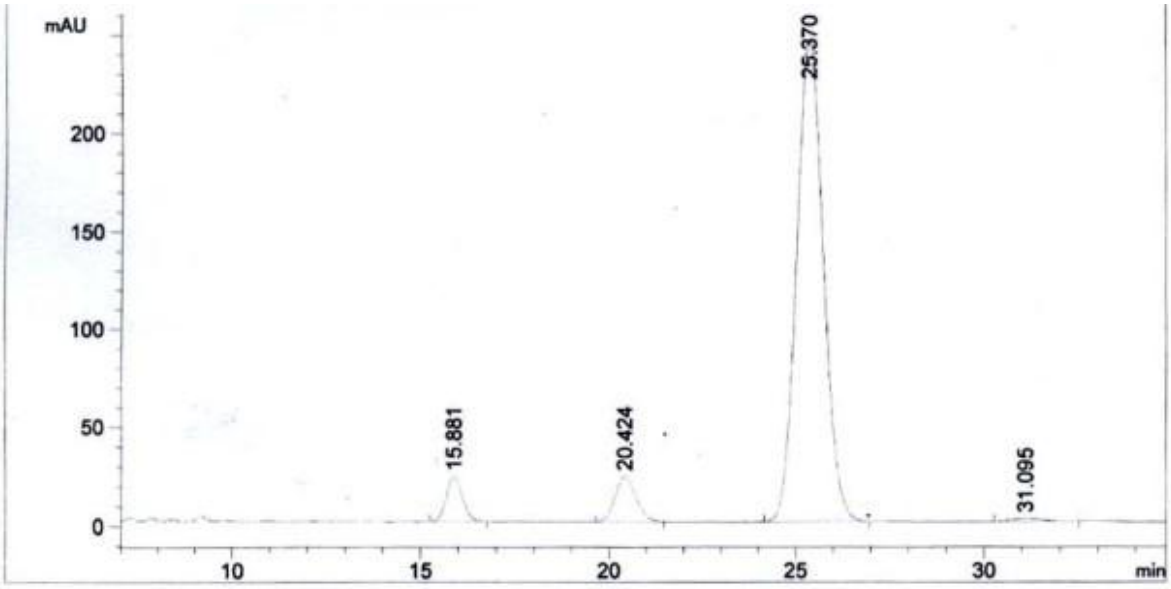






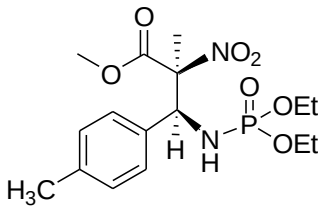


#	[min]		[min]	mAU	*s	[mAU]	%
1	15.887	VB	0.4616	7147.87402		240.61142	39.0839
2	20.458	BB	0.6094	7138.79443		181.27058	39.0342
3	25.390	BB	0.7590	1997.45386		41.00712	10.9219
4	30.972	BB	0.9628	2004.43896		32.36461	10.9601

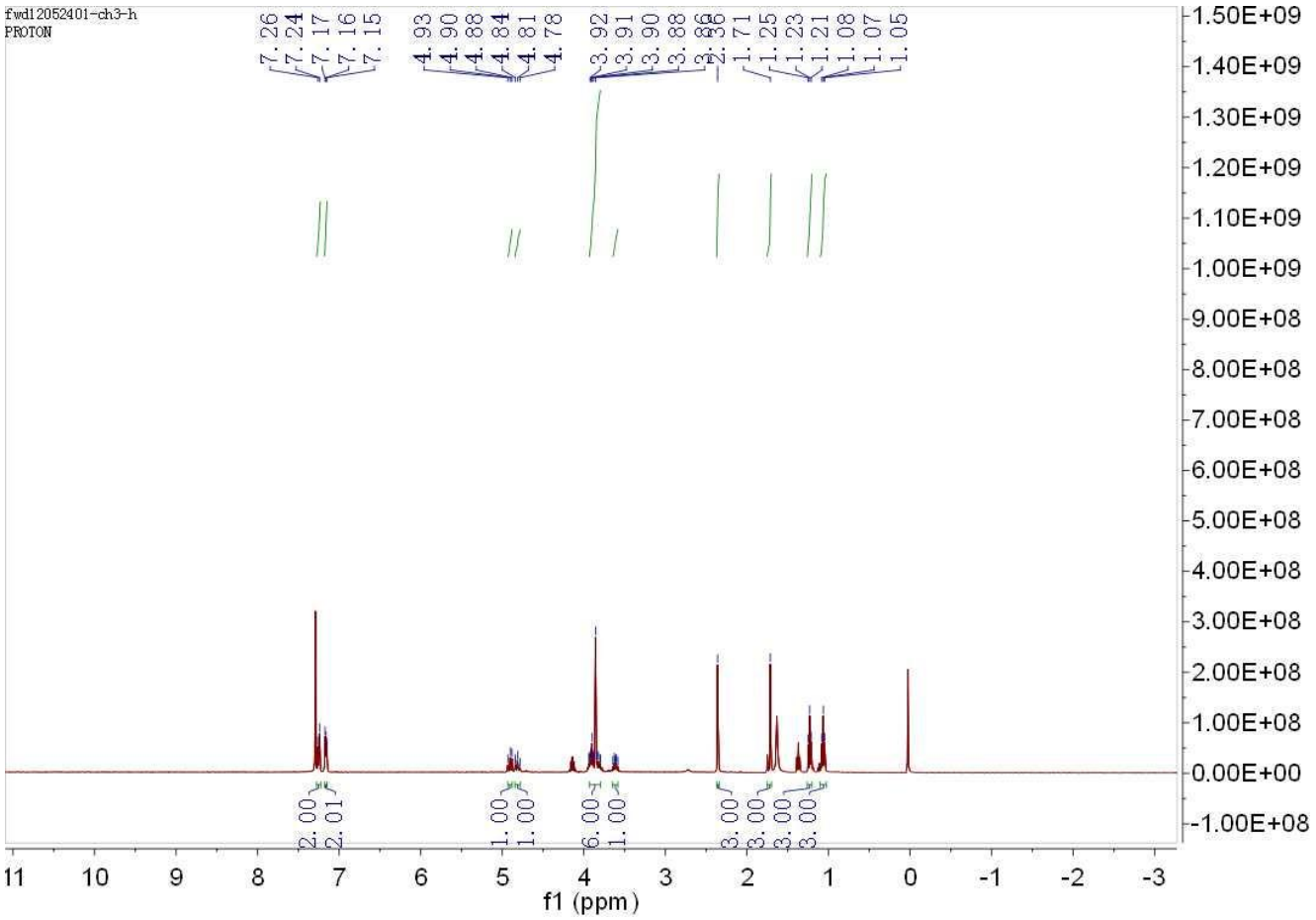


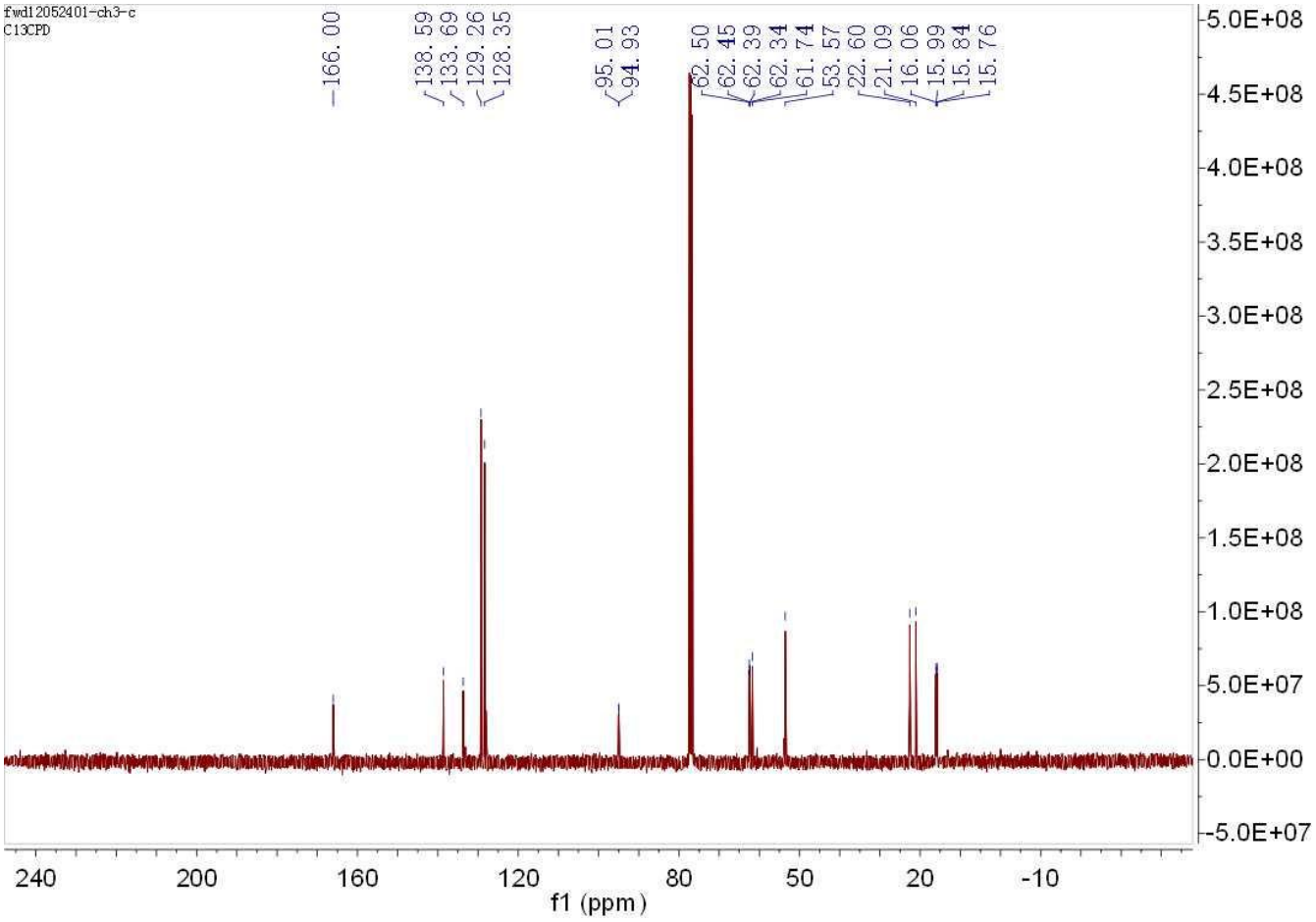
#	[min]		[min]	mAU	*s	[mAU]	%
1	15.881	BB	0.4571	673.04498		22.76204	4.8610
2	20.424	BB	0.6090	889.49597		22.74982	6.4242
3	25.370	BB	0.7702	1.22108e4		246.47144	88.1902
4	31.095	BB	0.6341	72.63612		1.37420	0.5246

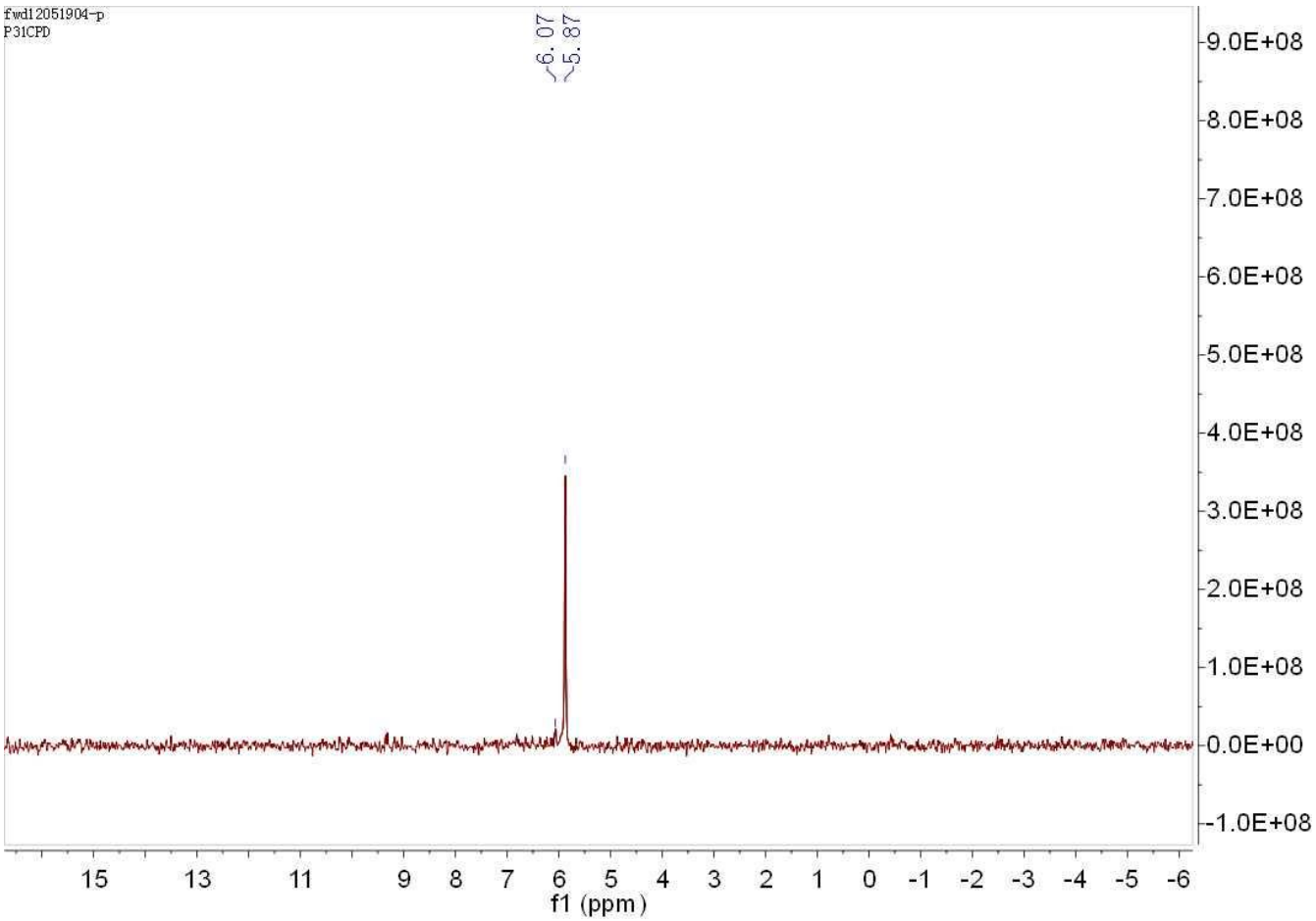
Methyl 3-((diethylphosphoryl)amino)-2-methyl-2-nitro-3-(*p*-tolyl)propanoate (6j):

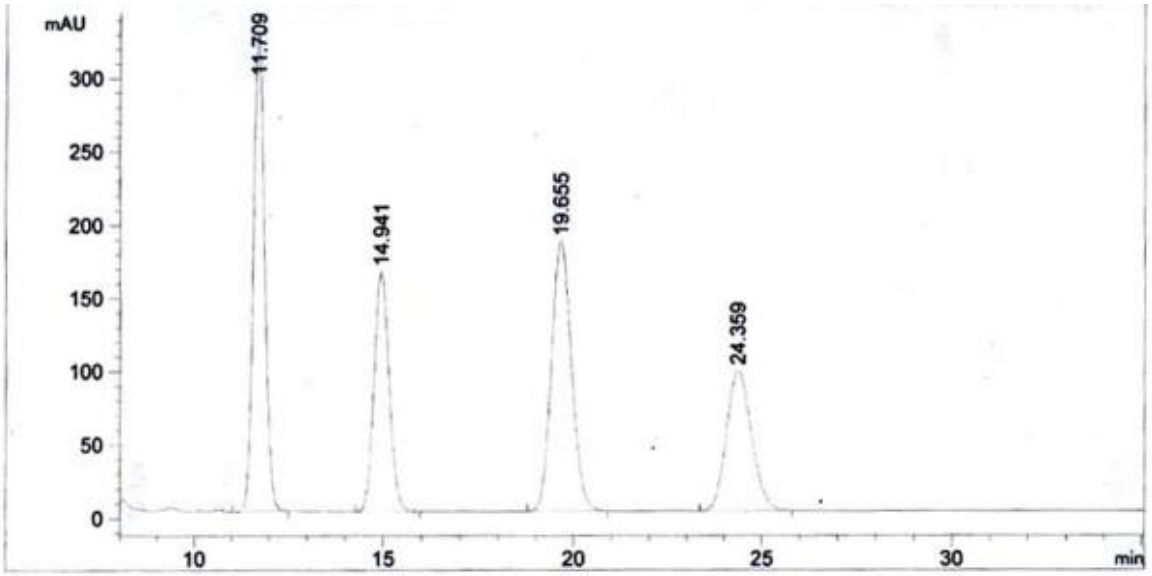


White solid; mp 100-103 °C; $[\alpha]^{20}_{D}$ = 44.0° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.27 (m, 2H), 7.14-7.19 (m, 2H), 4.87-4.95 (m, 1H), 4.81 (t, *J* = 11.4 Hz, 1H), 3.77-3.99 (m, 6H), 3.57-3.66 (m, 1H), 2.36 (s, 3H), 1.71 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.00, 138.59, 133.69, 129.26, 128.35, 94.97 (d, *J* = 8.1 Hz), 62.47 (d, *J* = 5.1 Hz), 62.37 (d, *J* = 4.9 Hz), 61.74, 53.57, 22.60, 21.09, 16.03 (d, *J* = 7.4 Hz), 15.80 (d, *J* = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.07, 5.87; HRMS (MALDI) calculated for $[C_{16}H_{25}N_2O_7P+Na]^+$: 411.1297, Found 411.1293; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 11.737 min, tr (major) = 14.974 min, tr (major) = 19.705 min, tr (major) = 24.333 min.

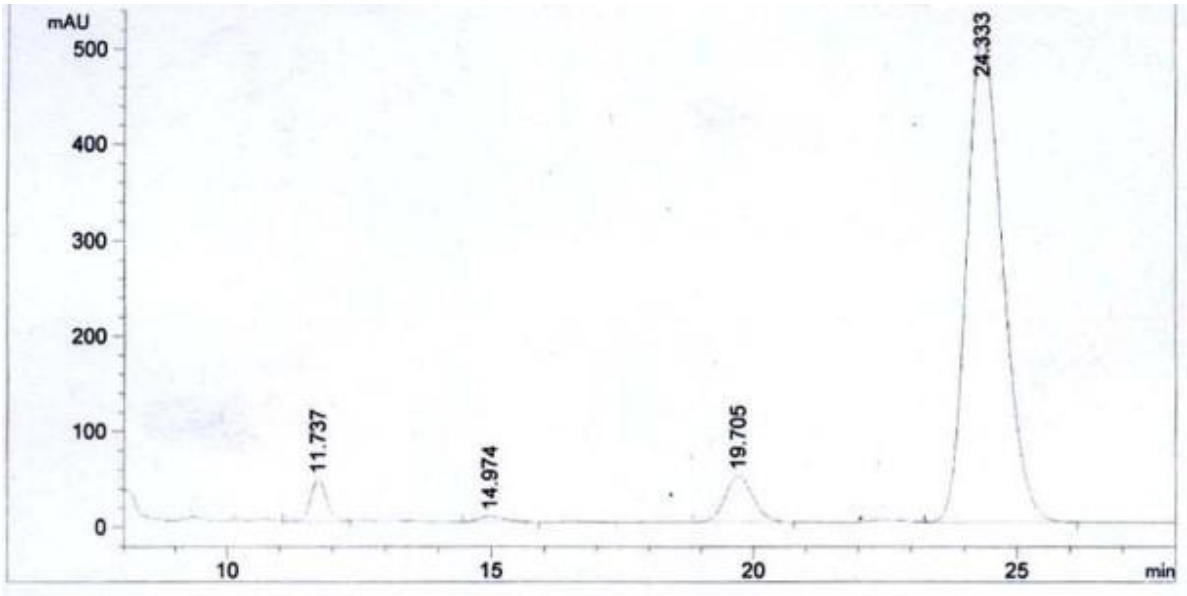






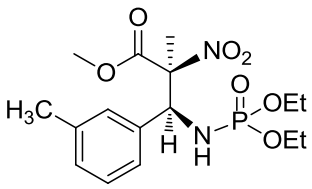


#	[min]		[min]	mAU	*s	[mAU]	%
1	11.709	VB	0.3240	6776.40967		324.16849	30.1468
2	14.941	VB	0.4234	4474.20410		163.84016	19.9048
3	19.655	BB	0.5707	6777.65186		184.12691	30.1523
4	24.359	BB	0.7223	4449.79639		95.56572	19.7962

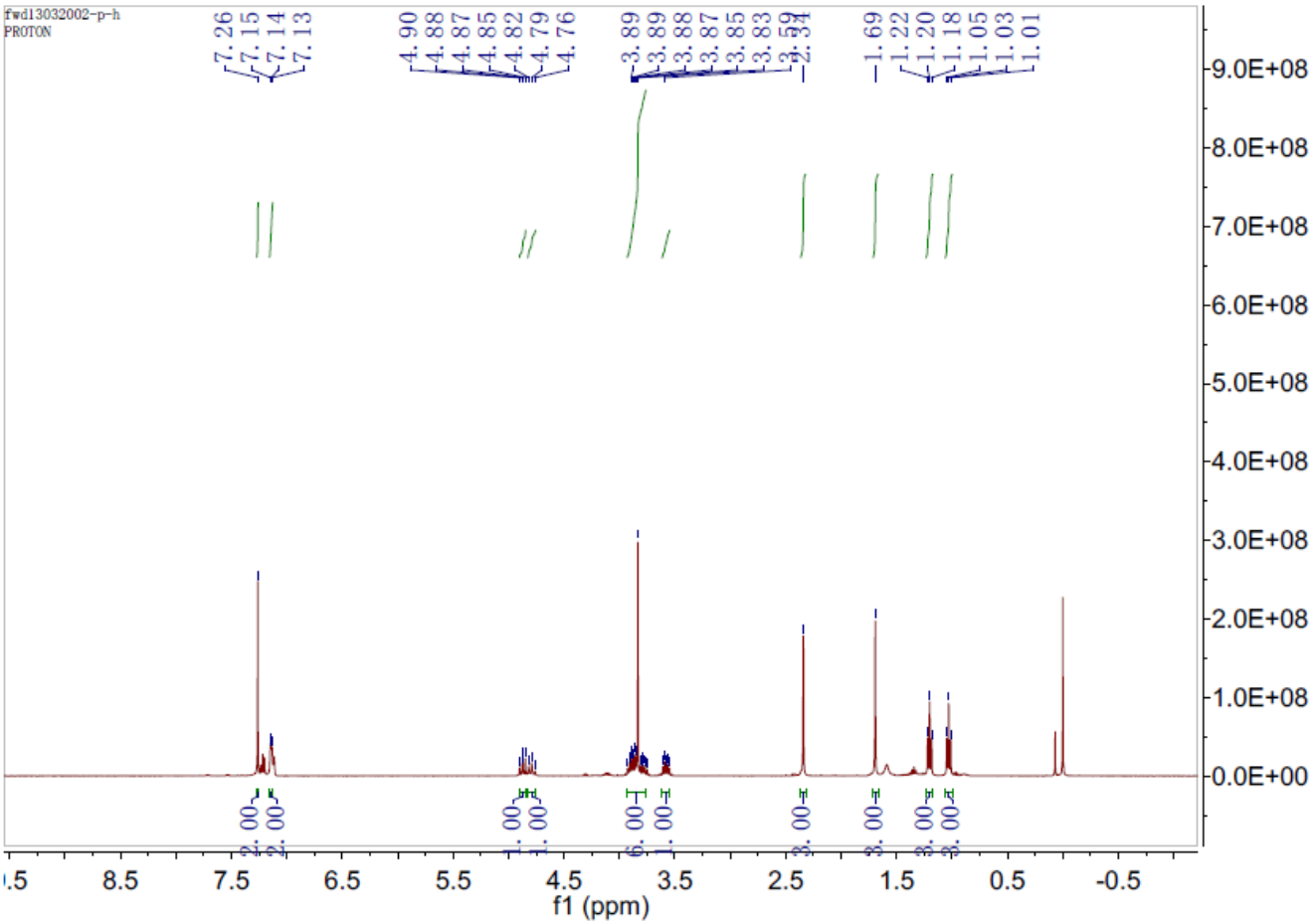


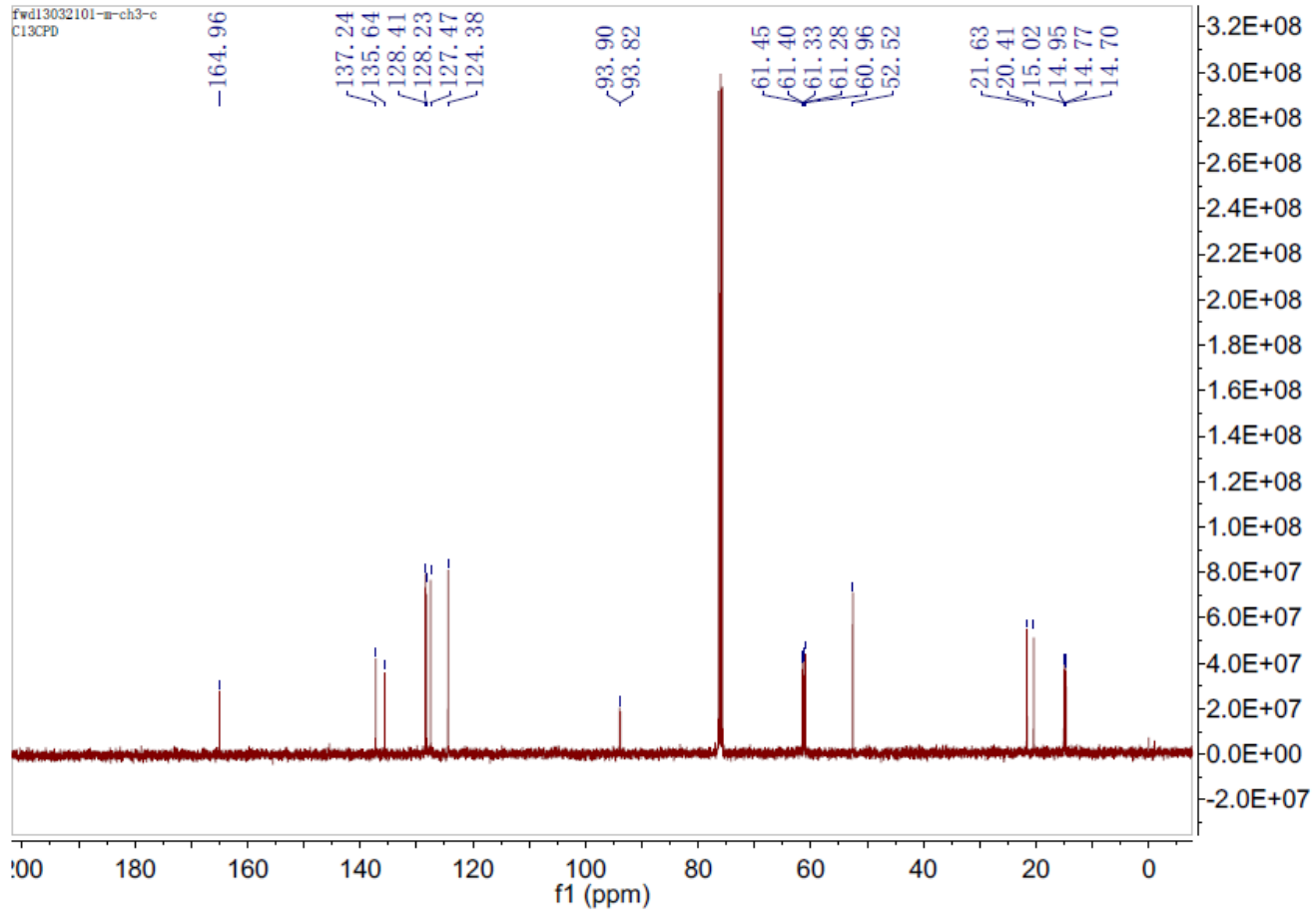
#	[min]		[min]	mAU	*s	[mAU]	%
1	11.737	VB	0.3400	1000.22113		44.90058	3.6811
2	14.974	VB	0.4743	202.23769		6.38663	0.7443
3	19.705	BB	0.5742	1797.81714		48.60213	6.6165
4	24.333	VB	0.7341	2.41716e4		509.39432	88.9582

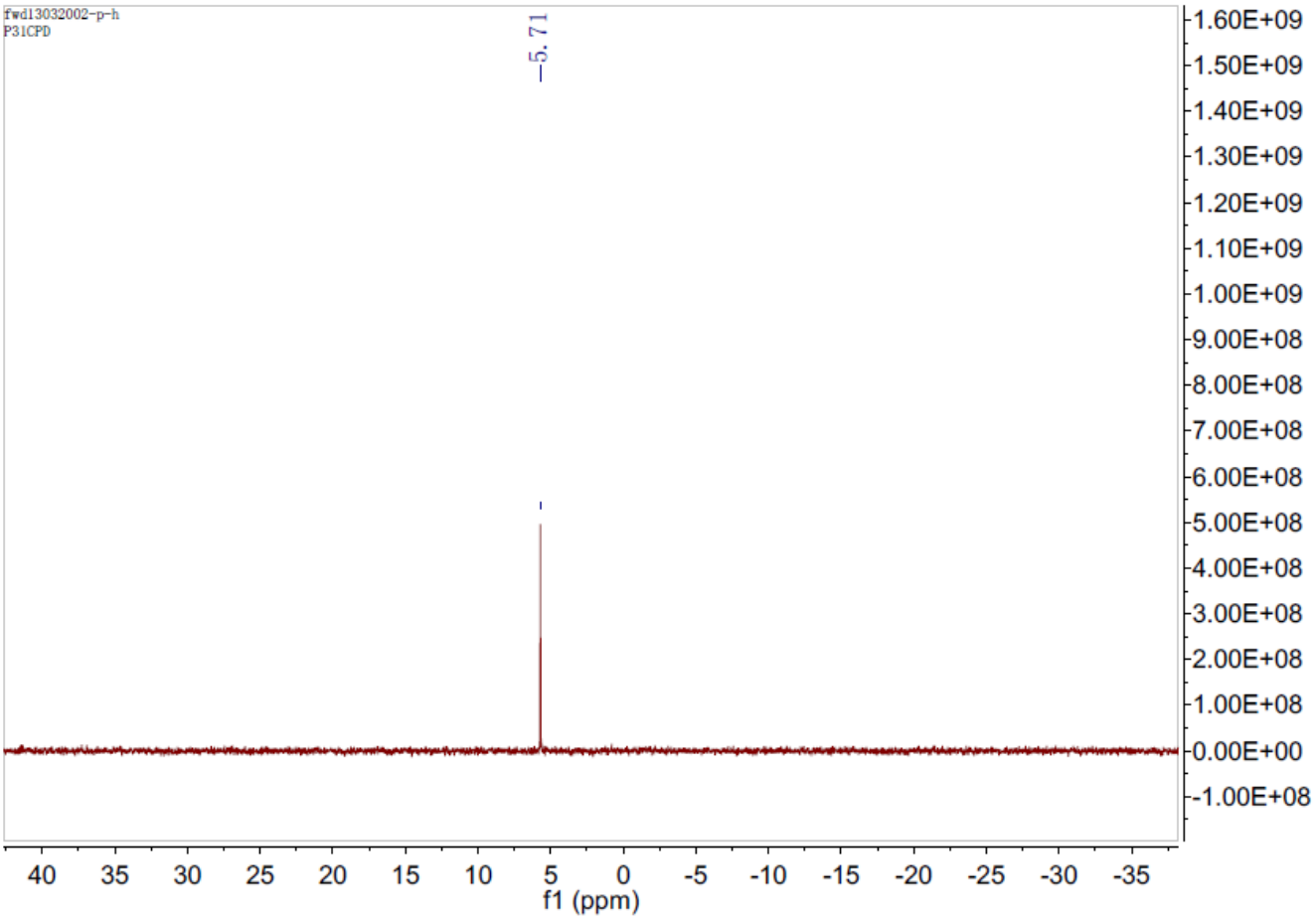
Methyl 3-((diethoxyphosphoryl)amino)-2-methyl-2-nitro-3-(m-tolyl)propanoate (6k):

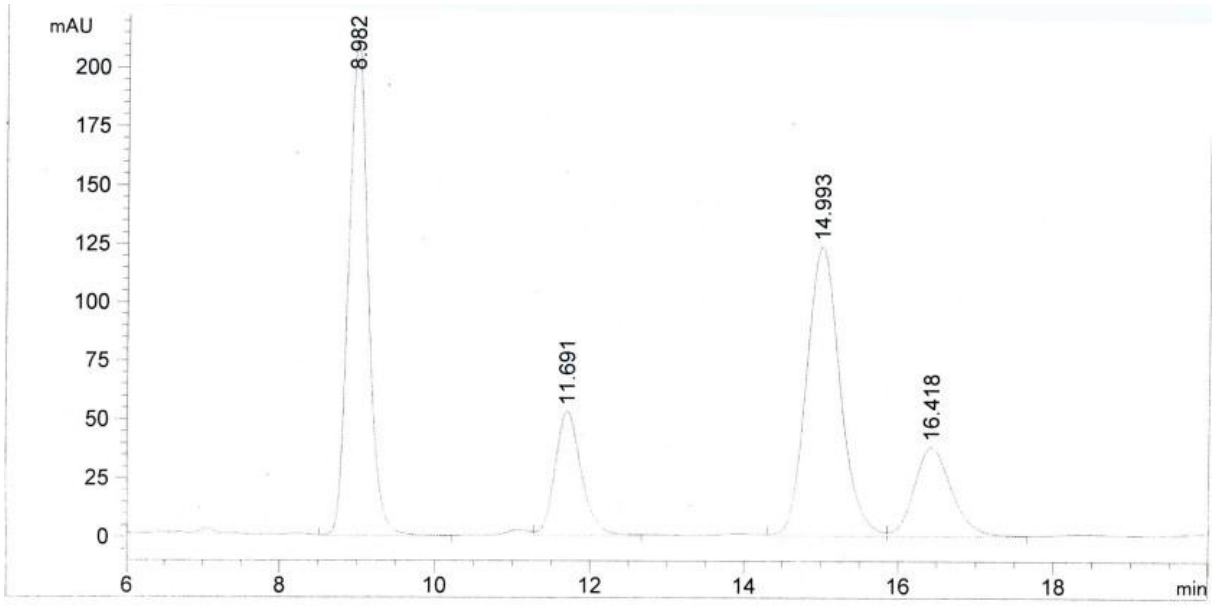


White solid; mp 102-105 °C; $[\alpha]^{20}_{D}$ = 50.9° (c = 0.005, CH_2Cl_2); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.24-7.29 (m, 2H), 7.12-7.17 (m, 2H), 4.84-4.92 (m, 1H), 4.75-4.83 (m, 1H), 3.74-3.96 (m, 6H), 3.54-3.63 (m, 1H), 2.34 (s, 3H), 1.69 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 164.96, 137.24, 135.64, 128.41, 128.23, 127.47, 124.38, 93.86 (d, *J* = 8.0 Hz), 61.43 (d, *J* = 5.0 Hz), 61.30 (d, *J* = 5.1 Hz), 60.96, 52.52, 21.63, 20.41, 14.98 (d, *J* = 7.6 Hz), 14.74 (d, *J* = 7.6 Hz); ^{31}P-NMR (162 MHz, $CDCl_3$): δ 5.71; HRMS (MALDI) calculated for $[C_{16}H_{25}N_2O_7P+Na]^+$: 411.1297, Found 411.1293; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.982 min, tr (major) = 11.691 min, tr (major) = 14.993 min, tr (major) = 16.418 min.

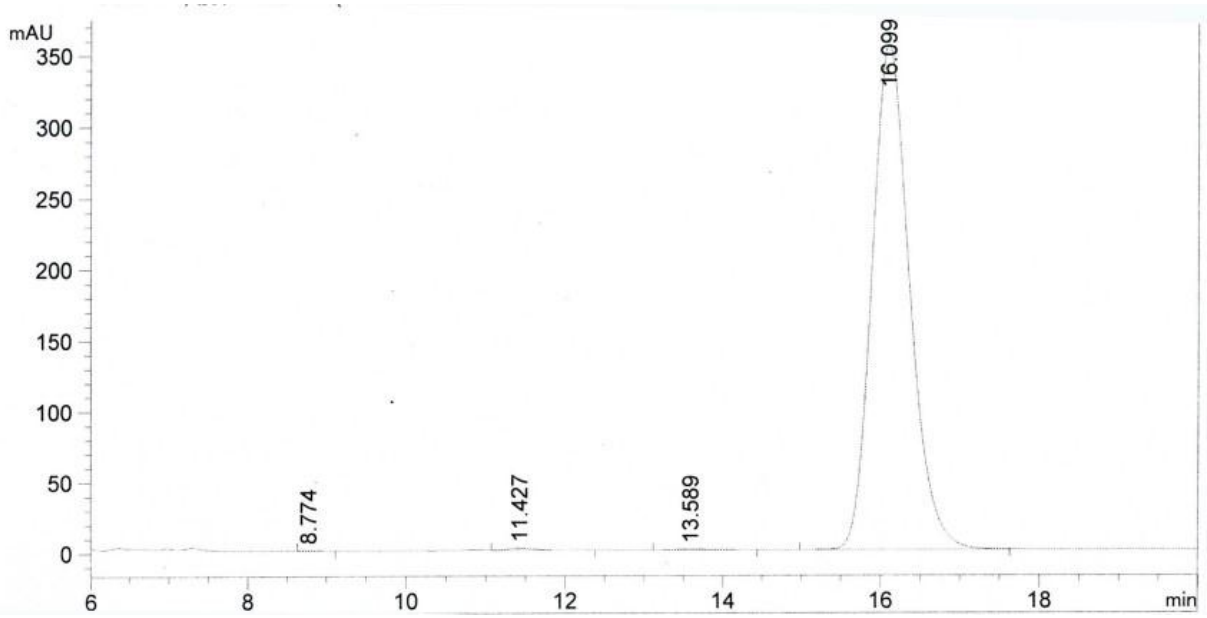






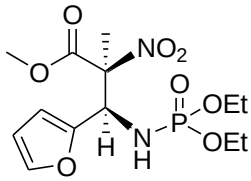


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.982	VB	0.2709	3744.64185		211.25081	37.3204
2	11.691	VB	0.3662	1264.89343		52.91571	12.6064
3	14.993	VV	0.4646	3753.94092		123.73191	37.4130
4	16.418	VV	0.5120	1270.30371		38.02853	12.6603

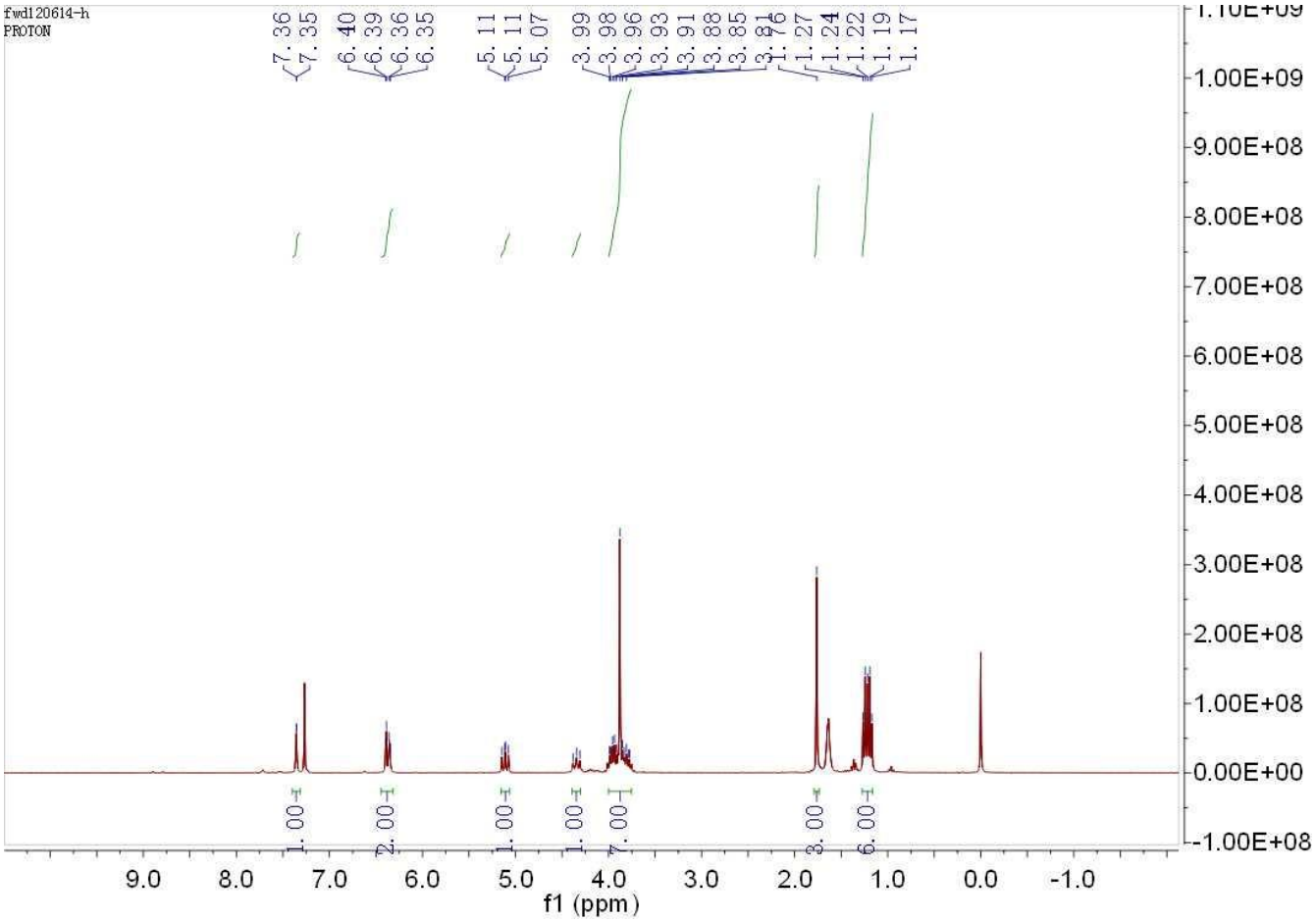


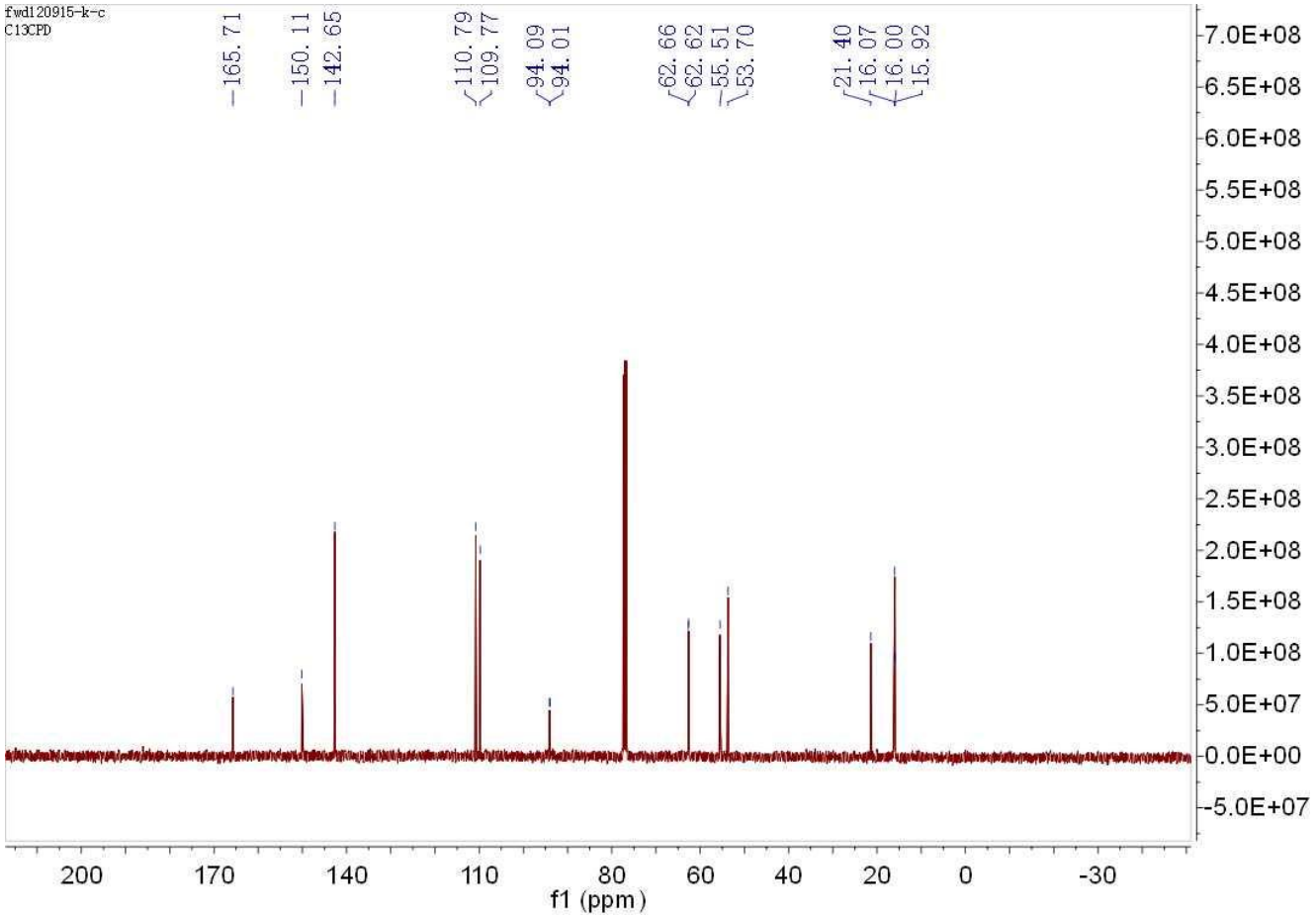
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.774	BB	0.2647	7.31082		3.55415e-1	0.0618
2	11.427	VB	0.3687	37.00798		1.50350	0.3127
3	13.589	VB	0.4432	16.59977		5.01151e-1	0.1403
4	16.099	BB	0.5099	1.17742e4		355.71262	99.4853

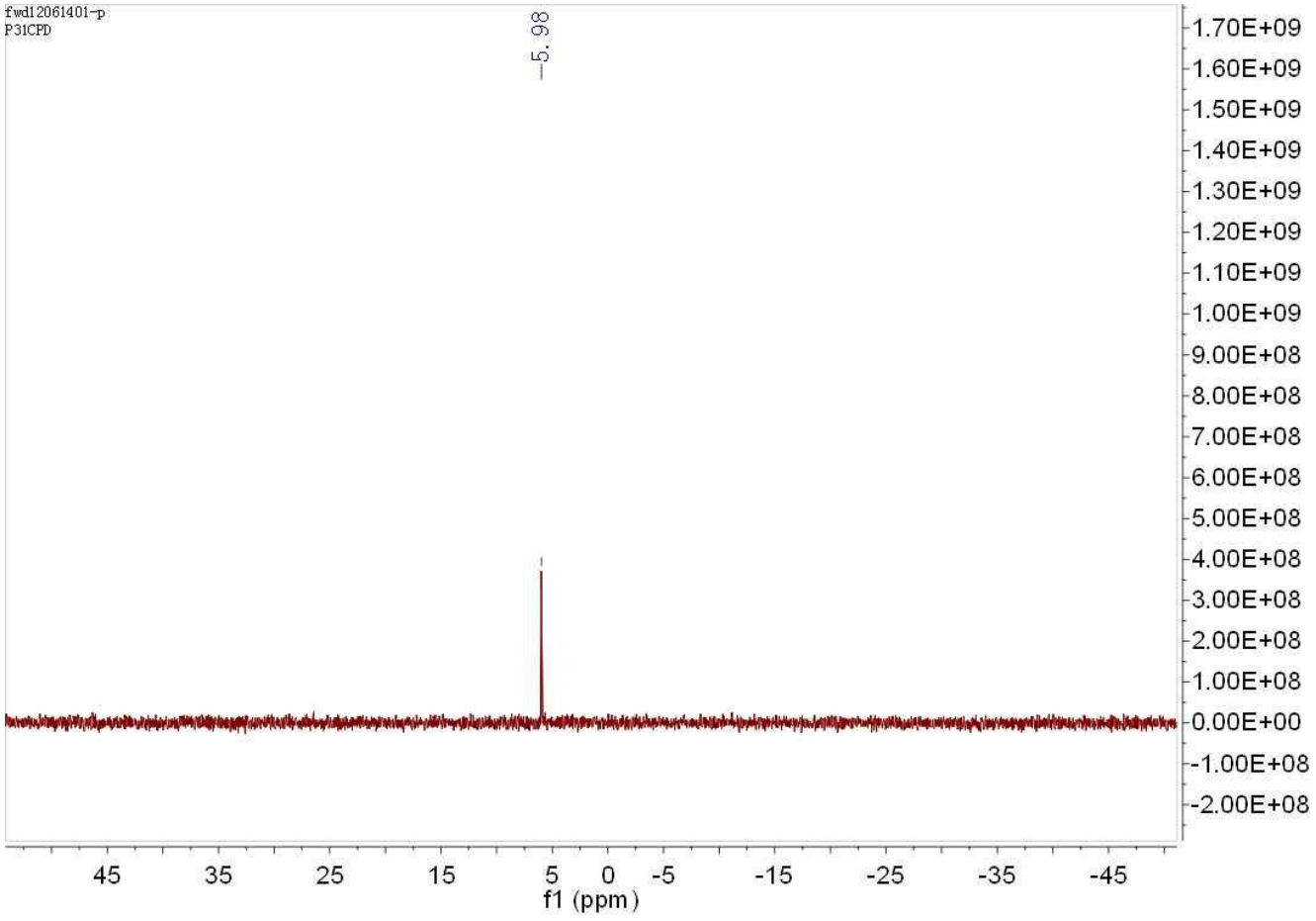
Methyl 3-((diethylphosphoryl)amino)-3-(furan-2-yl)-2-methyl-2-nitropropanoate (6l):

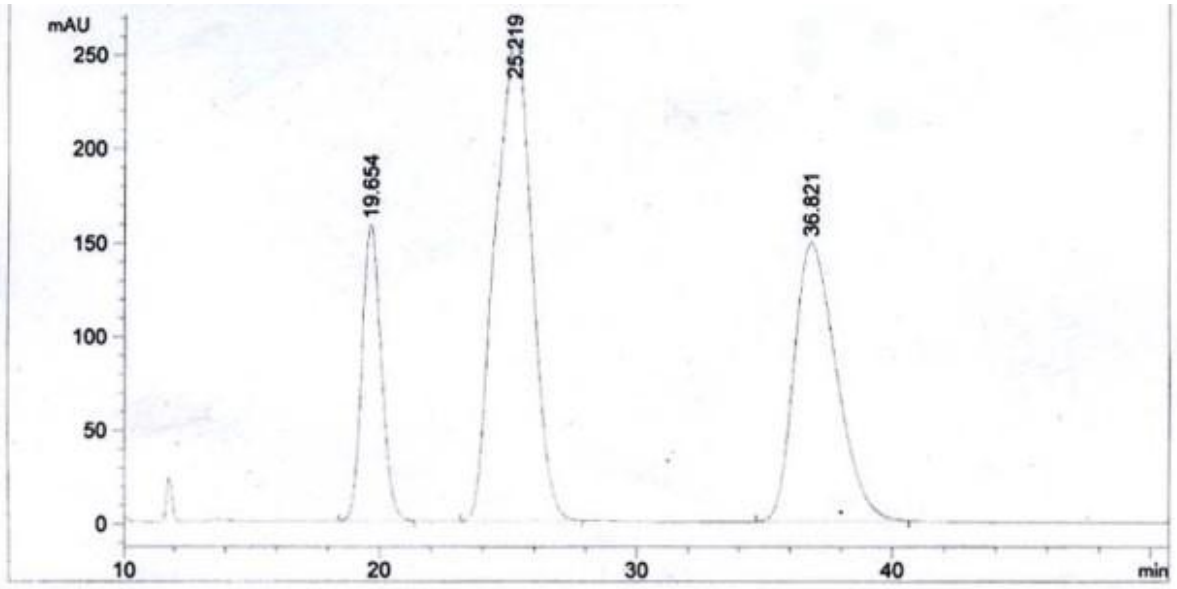


White solid; mp 84-87 °C; $[\alpha]^{20}_{D}$ = 74.0° (c = 0.005, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.37 (m, 1H), 6.28-6.46 (m, 2H), 5.11 (dd, *J* = 11.8, 9.9 Hz, 1H), 4.34 (t, *J* = 11.8 Hz, 1H), 3.70-4.02 (m, 7H), 1.76 (s, 3H), 1.11-1.29 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.71, 150.11, 142.65, 110.79, 109.77, 94.05 (d, *J* = 7.8 Hz), 62.66, 62.62, 55.51, 53.70, 21.40, 16.07, 15.96 (d, *J* = 7.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.98; HRMS (MALDI) calculated for $[C_{13}H_{21}N_2O_8P+Na]^+$: 387.0933, Found: 387.0935; HPLC (Chiralcel AS-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 22.310 min.

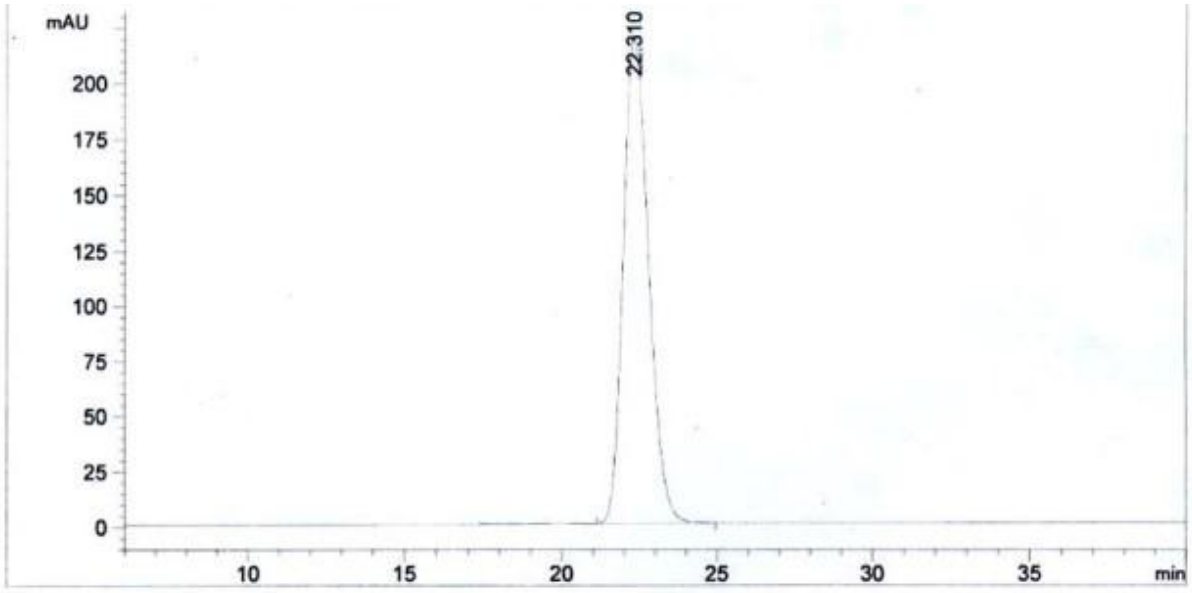






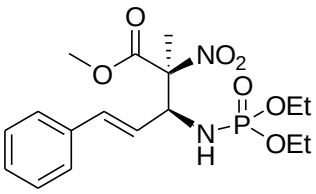


#	[min]		[min]	mAU *s	[mAU]	%
1	19.654	BB	0.8077	8231.20117	158.27026	16.1271
2	25.219	BB	1.4541	2.55519e4	257.62704	50.0629
3	36.821	BB	1.7540	1.72565e4	149.37294	33.8100

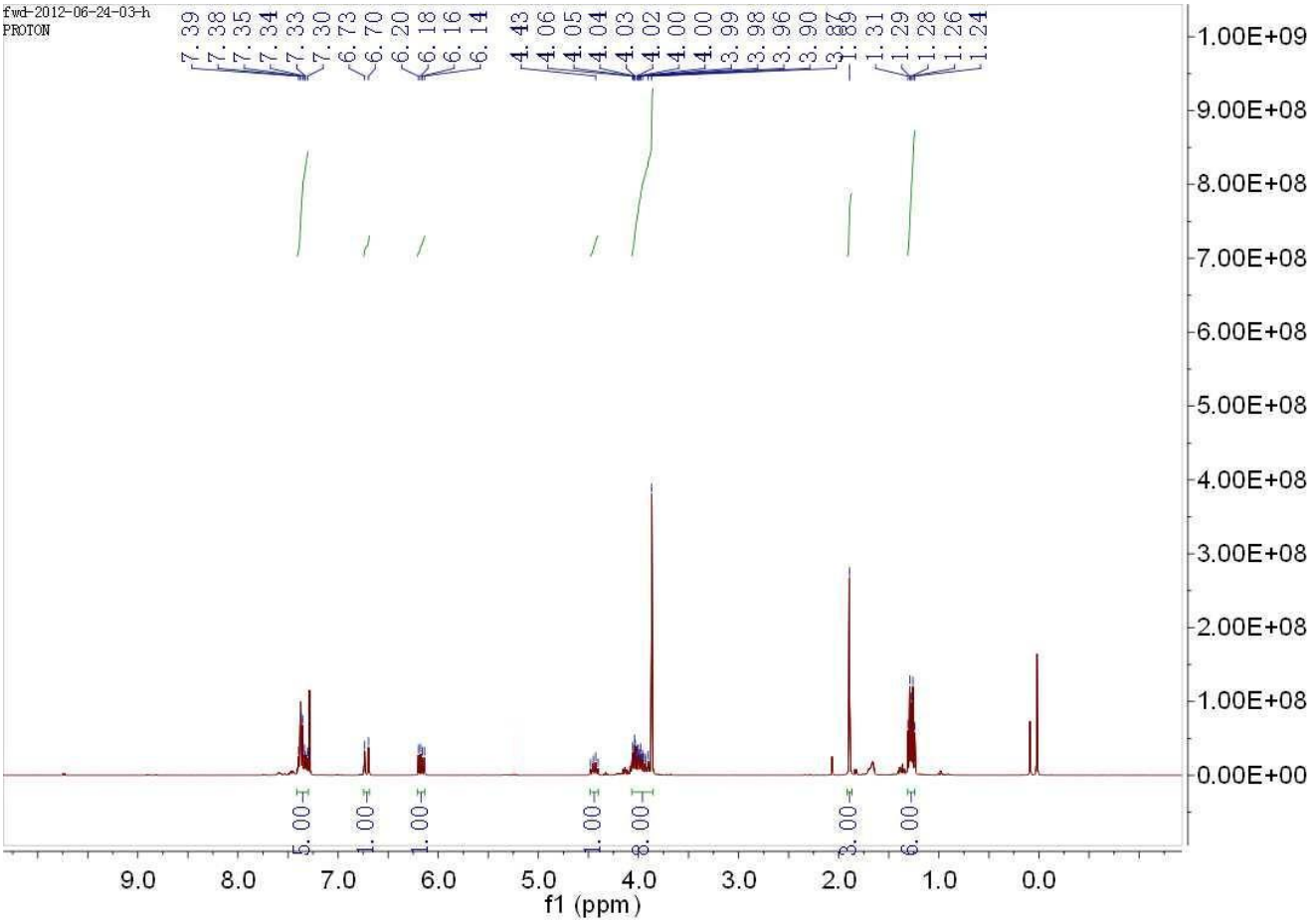


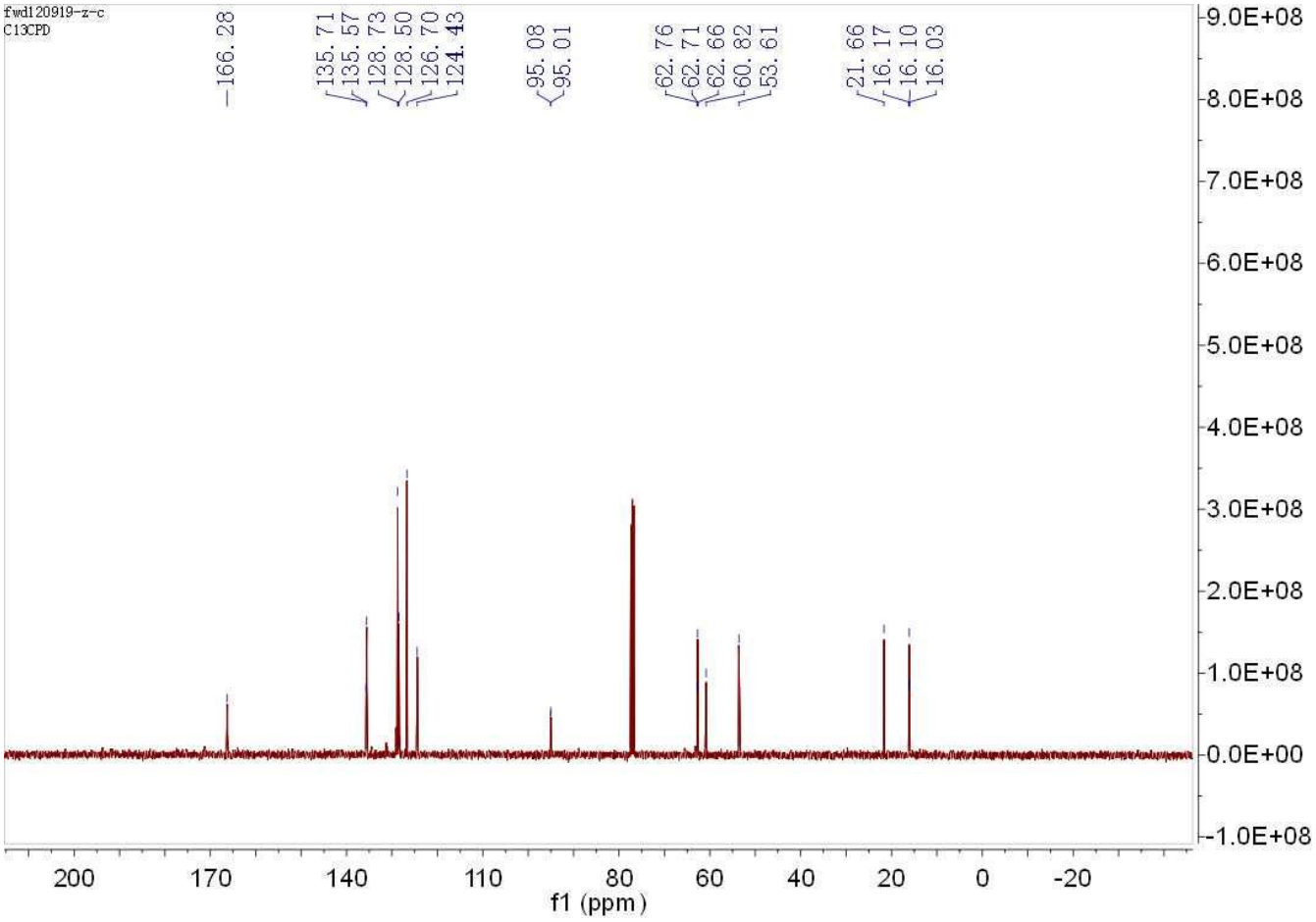
#	[min]		[min]	mAU *s	[mAU]	%
1	22.310	BB	0.8902	1.25131e4	220.15718	100.0000

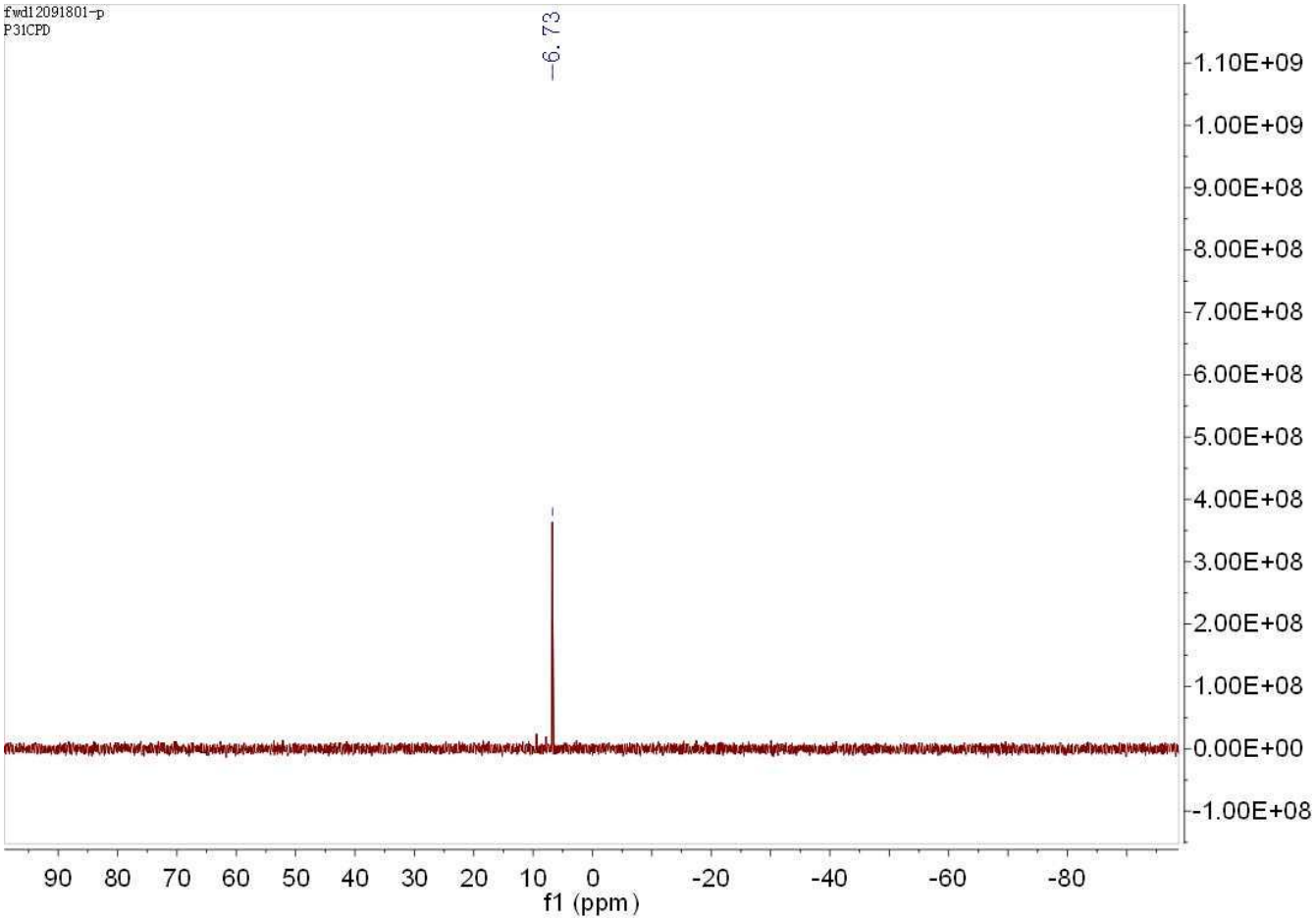
Methyl 3-((diethylphosphoryl)amino)-2-methyl-2-nitro-5-phenylpent-4-enoate (6m):

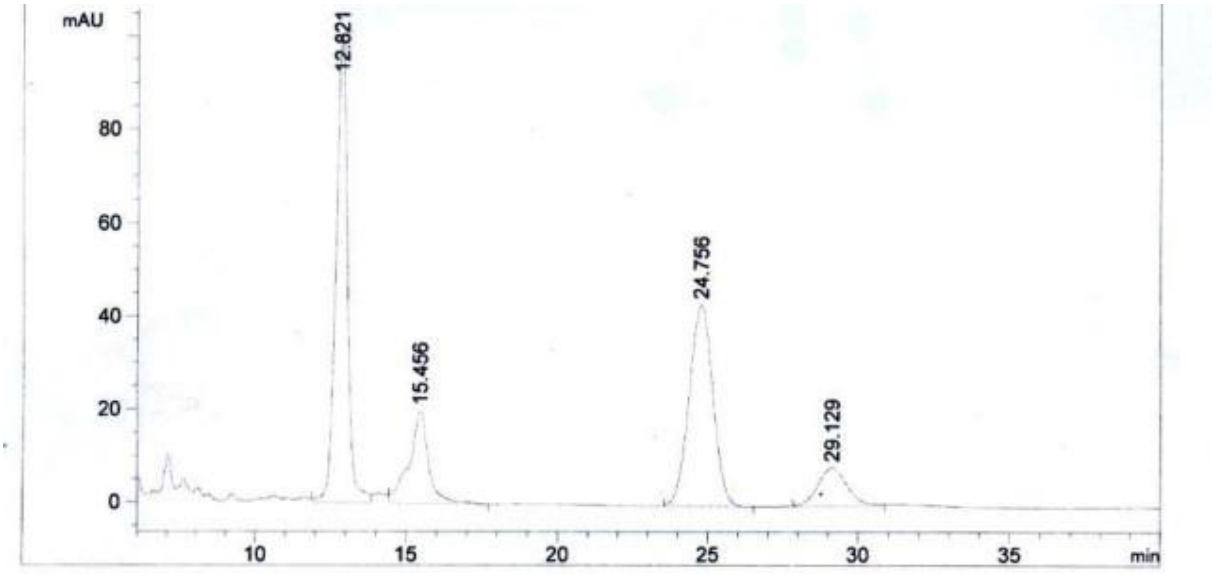


White solid; mp 57-60 °C; $[\alpha]^{20}_{D}$ = 6.4° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.47 (m, 5H), 6.71 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 8.5 Hz, 1H), 4.44 (dd, *J* = 20.4, 9.0 Hz, 1H), 3.81-4.11 (m, 8H), 1.89 (s, 3H), 1.22-1.33 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.28, 135.71, 135.57, 128.73, 128.50, 126.70, 124.43, 95.05 (d, *J* = 7.3 Hz), 62.76, 62.69 (d, *J* = 4.7 Hz), 60.82, 53.61, 21.66, 16.17, 16.07 (d, *J* = 7.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.73; HRMS (MALDI) calculated for $[C_{17}H_{25}N_2O_7P+Na]^+$: 423.1297, Found: 423.1295; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (major) = 12.620 min, tr (major) = 24.532 min.

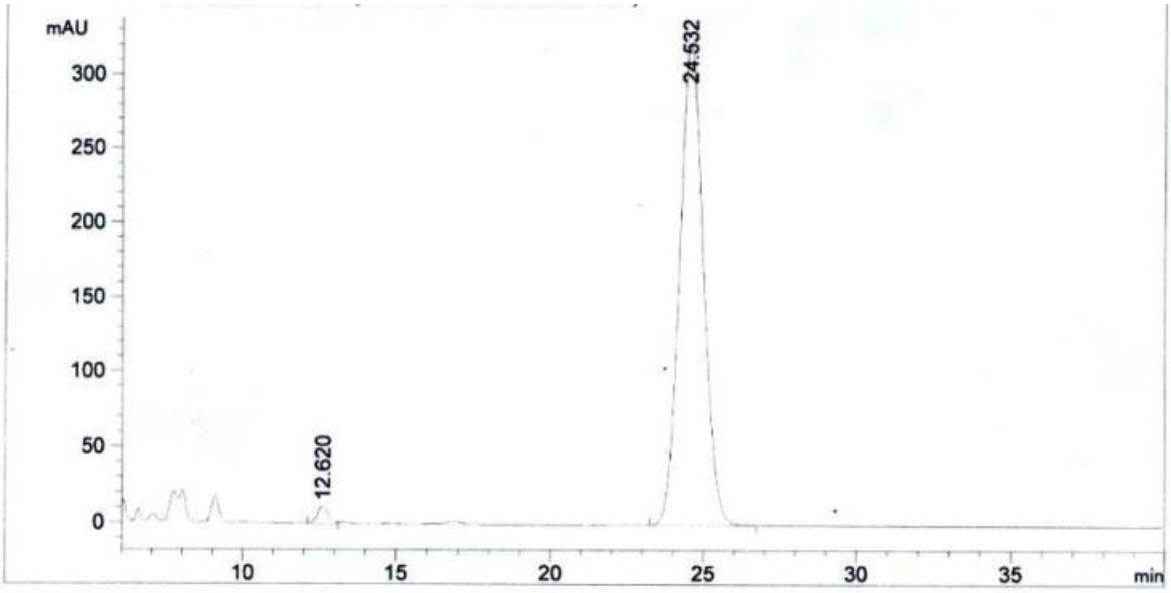






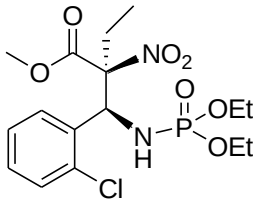


#	[min]		[min]	mAU	*s	[mAU]	%
1	12.821	VV	0.4134	2712.45605		100.66216	41.3371
2	15.456	VB	0.6313	891.24524		19.97224	13.5823
3	24.756	BB	0.8536	2402.01685		43.51958	36.6061
4	29.129	BB	1.0297	556.08356		8.32577	8.4746

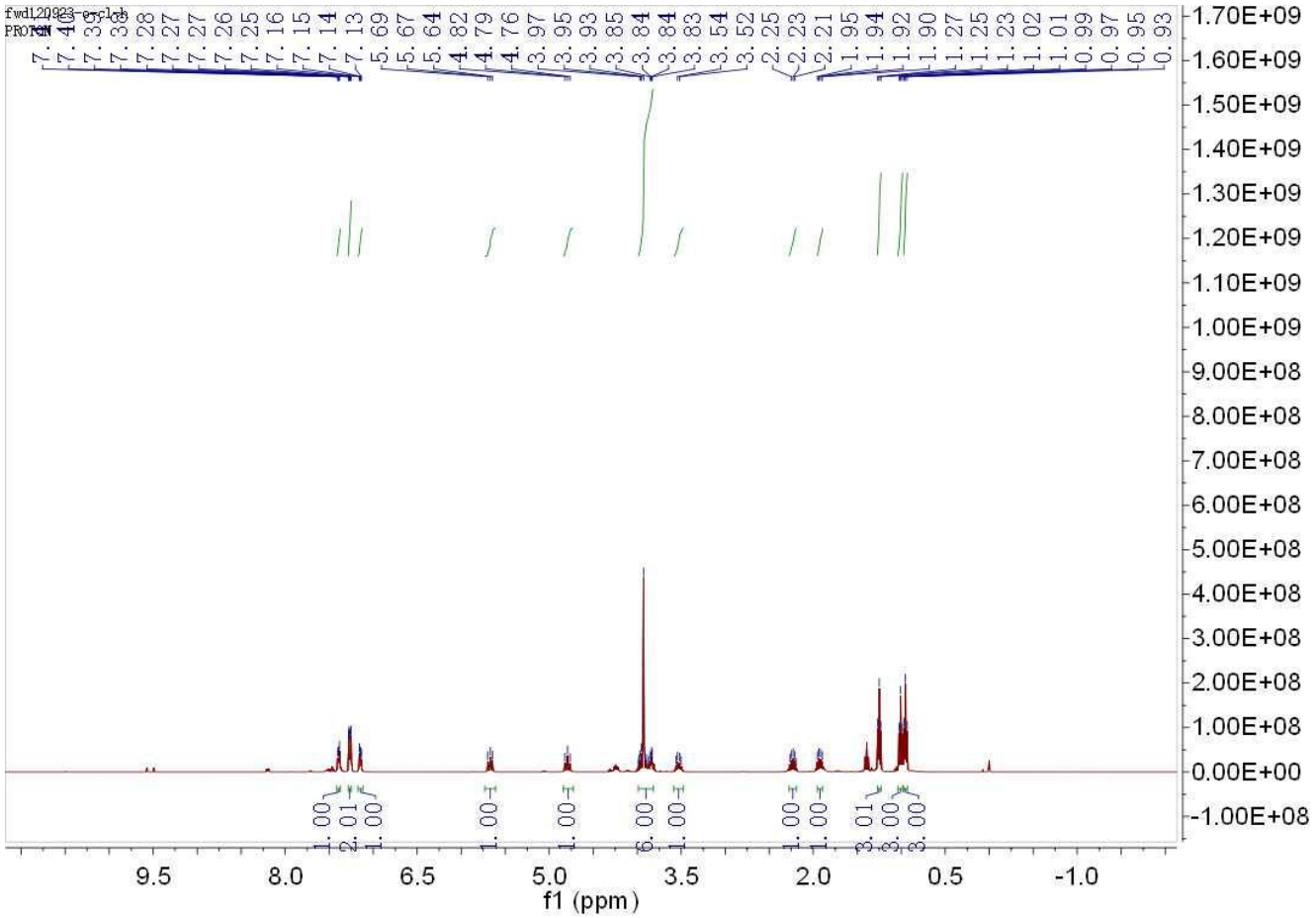


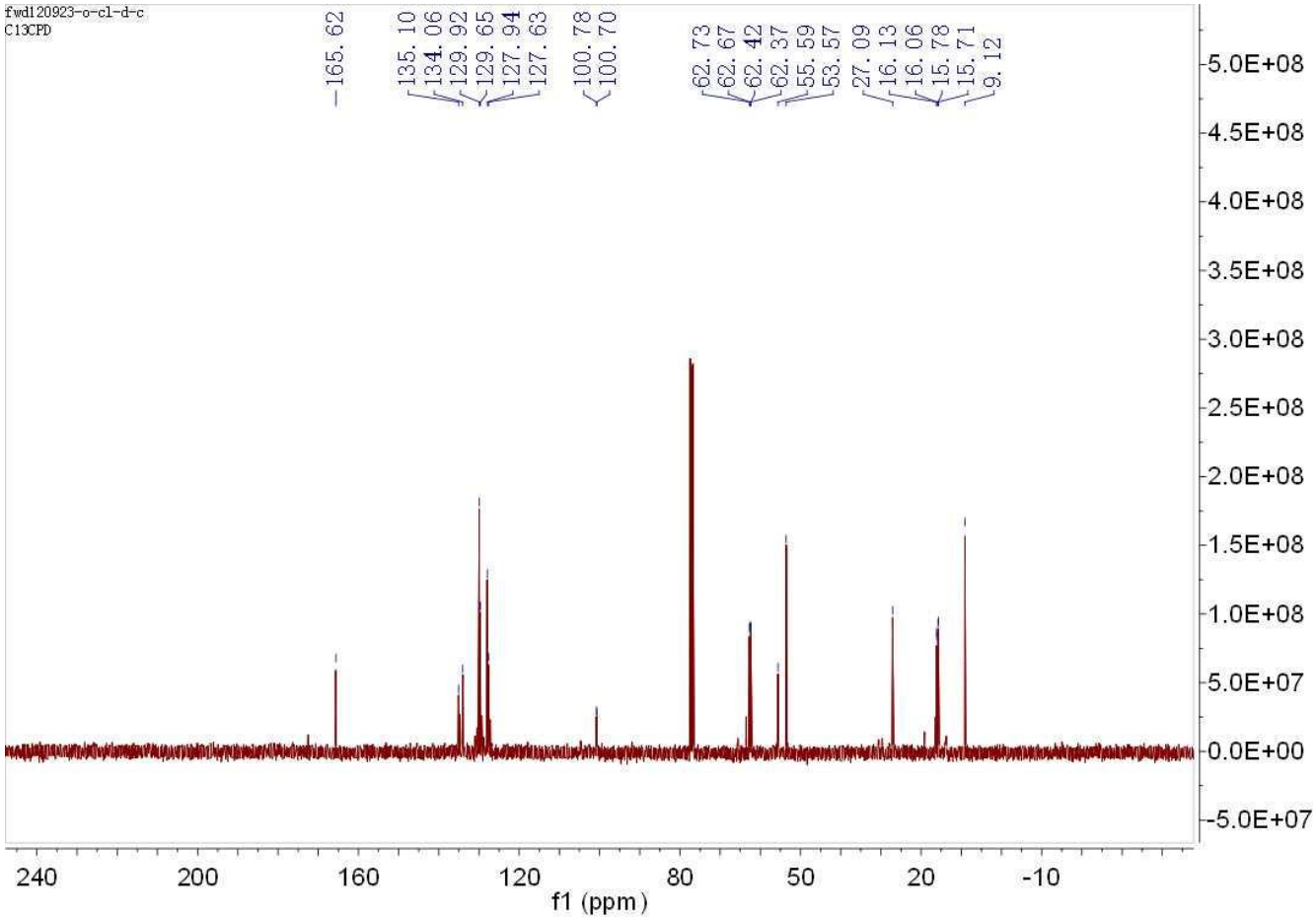
#	[min]		[min]	mAU	*s	[mAU]	%
1	12.620	VV	0.4011	318.33316		12.06316	1.7938
2	24.532	BB	0.8328	1.74277e4		323.25488	98.2062

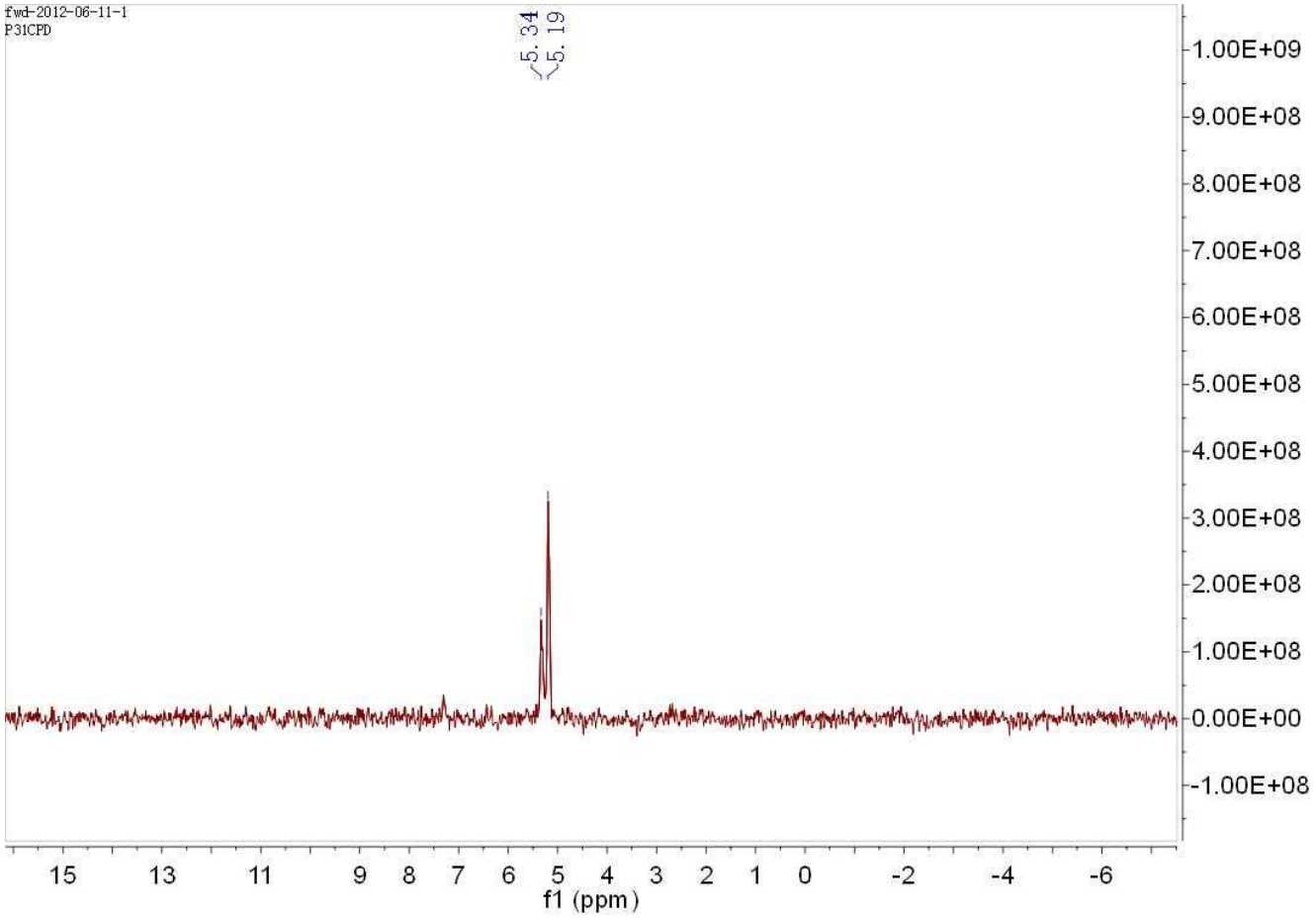
Methyl 2-((2-chlorophenyl)((diethylphosphoryl)amino)methyl)-2-nitrobutanoate (6n):

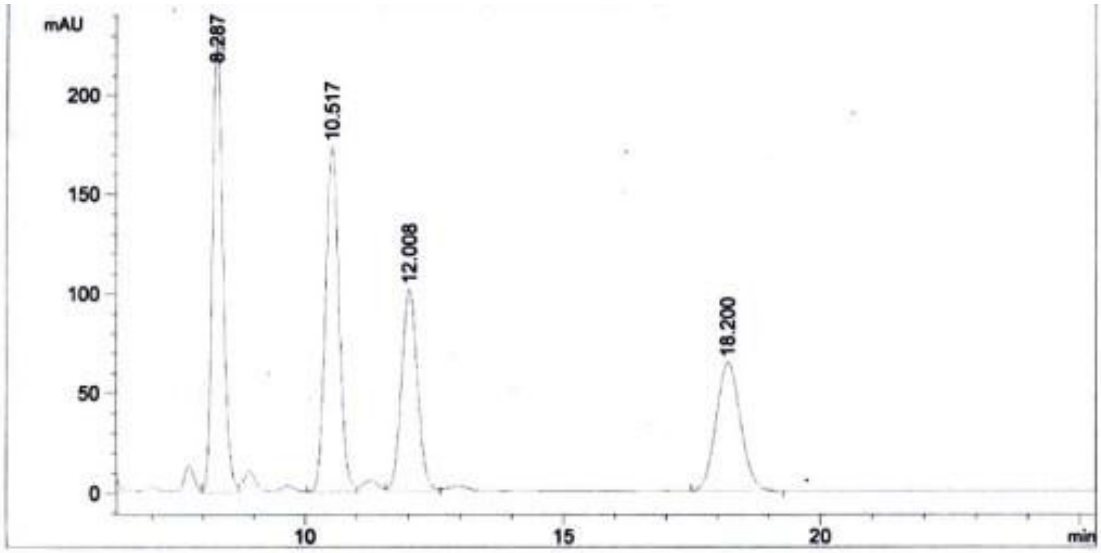


White solid; mp 59-62 °C; $[\alpha]^{20}_{D}$ = 7.0° (c = 0.01, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.41 (m, 1H), 7.23-7.31 (m, 2H), 7.12-7.18 (m, 1H), 5.57-5.75 (m, 1H), 4.65-4.85 (m, 1H), 3.77-4.03 (m, 6H), 3.43-3.62 (m, 1H), 2.16-2.30 (m, 1H), 1.82-1.99 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.01 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.62, 135.10, 134.06, 129.92, 129.65, 127.94, 127.63, 100.74 (d, *J* = 8.4 Hz), 62.70 (d, *J* = 5.5 Hz), 62.40 (d, *J* = 5.5 Hz), 55.59, 53.57, 27.09, 16.09 (d, *J* = 7.5 Hz), 15.75 (d, *J* = 7.5 Hz), 9.12; ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.34, 5.19; HRMS (MALDI) calculated for $[C_{16}H_{24}ClN_2O_7P+Na]^+$: 445.0907, Found 445.0905; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.184 min, tr (major) = 10.391 min, tr (major) = 11.817 min, tr (major) = 17.838 min.

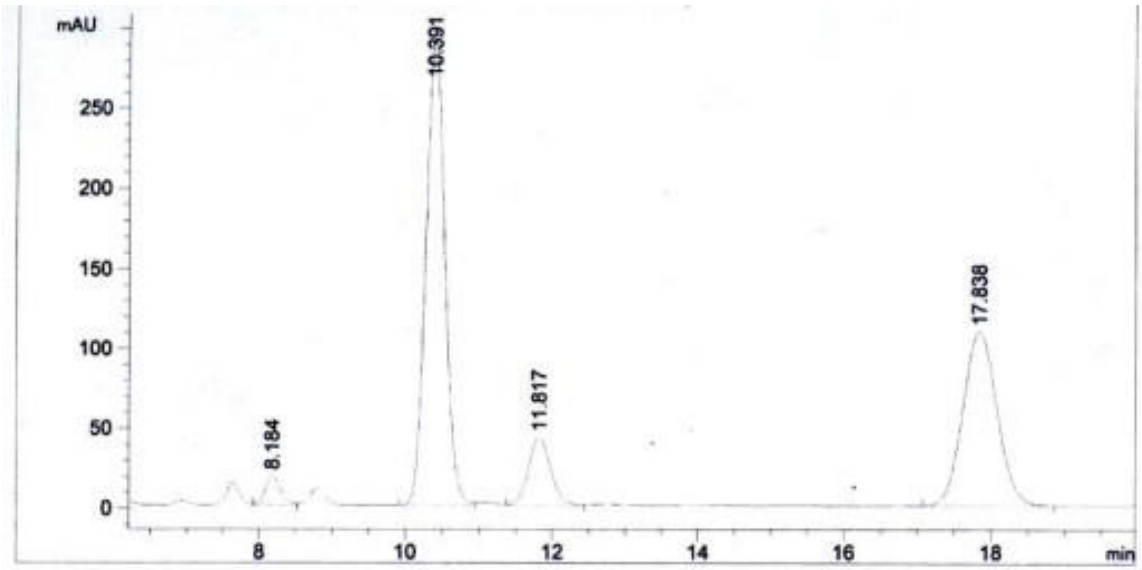






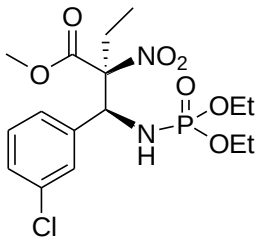


#	[min]		[min]	mAU	*s	[mAU]	%
1	8.287	VV	0.2216	3299.70435		229.57248	30.6022
2	10.517	VV	0.2839	3181.72681		173.45546	29.5080
3	12.008	VV	0.3322	2180.84033		101.50092	20.2256
4	18.200	BB	0.5141	2120.31421		64.09477	19.6642

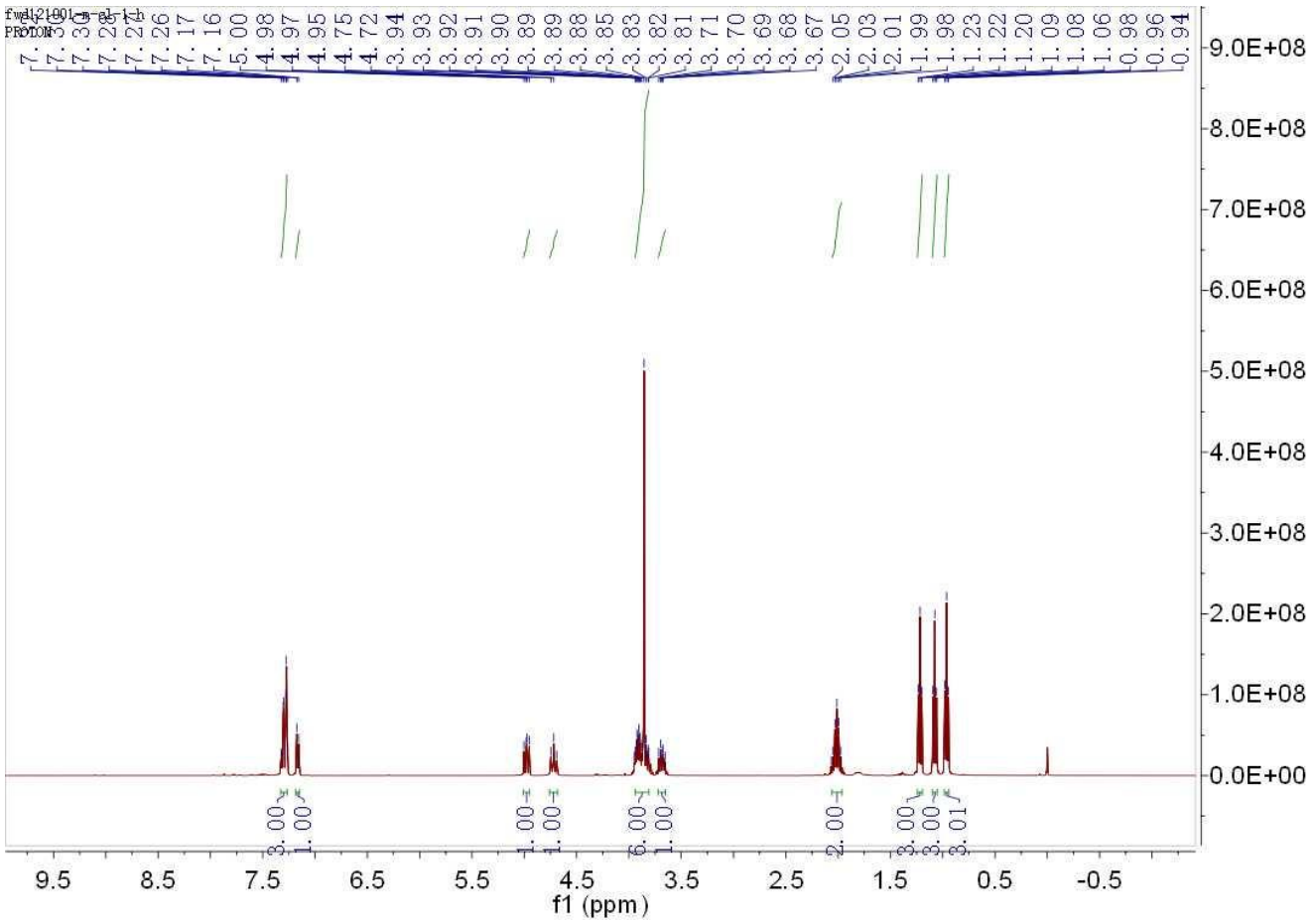


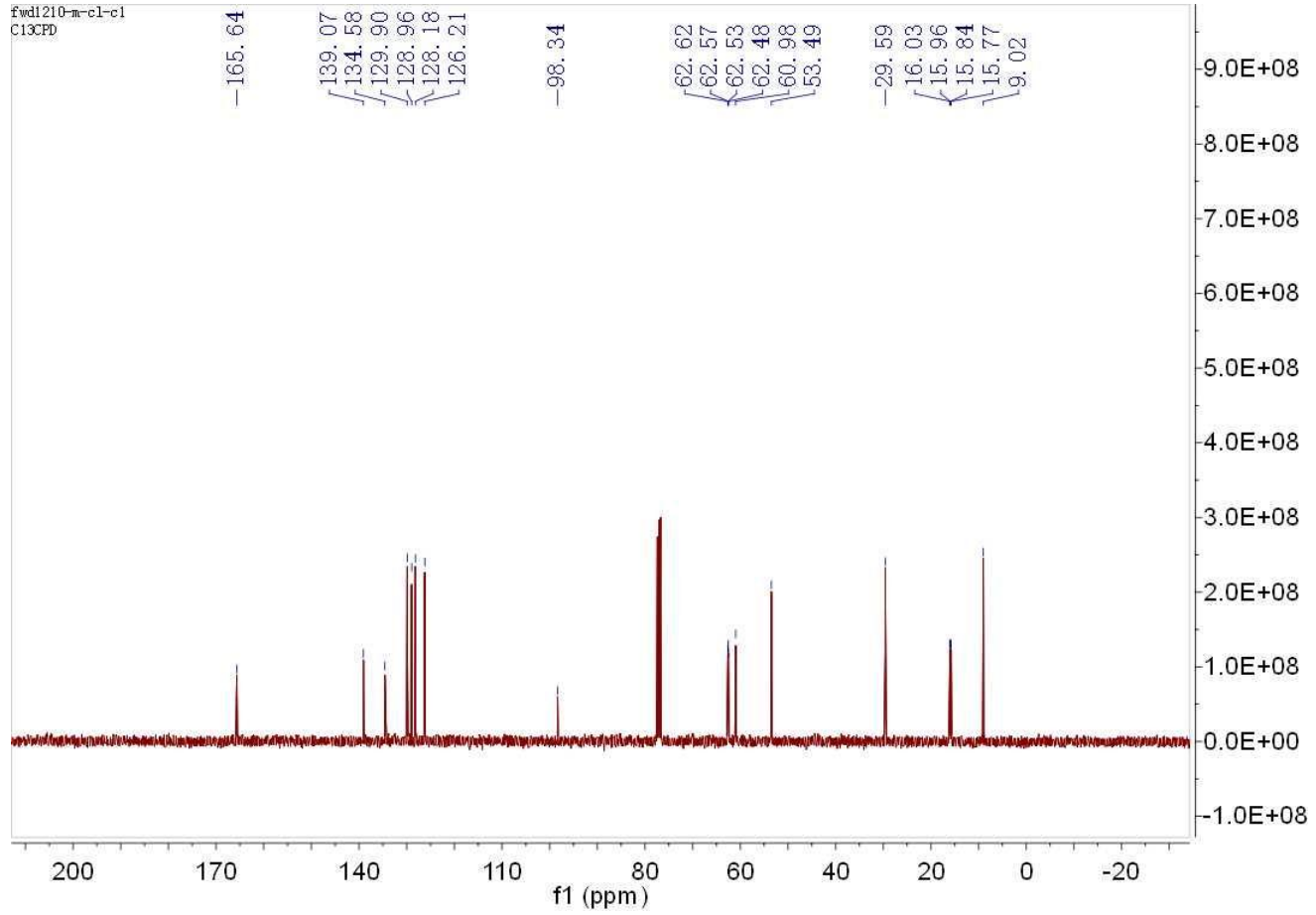
#	[min]		[min]	mAU	*s	[mAU]	%
1	8.184	VV	0.2166	261.67789		18.43349	2.6288
2	10.391	BV	0.2797	5258.64355		292.45578	52.8277
3	11.817	VB	0.3262	905.06299		42.89463	9.0922
4	17.838	BB	0.4991	3528.94531		109.69804	35.4514

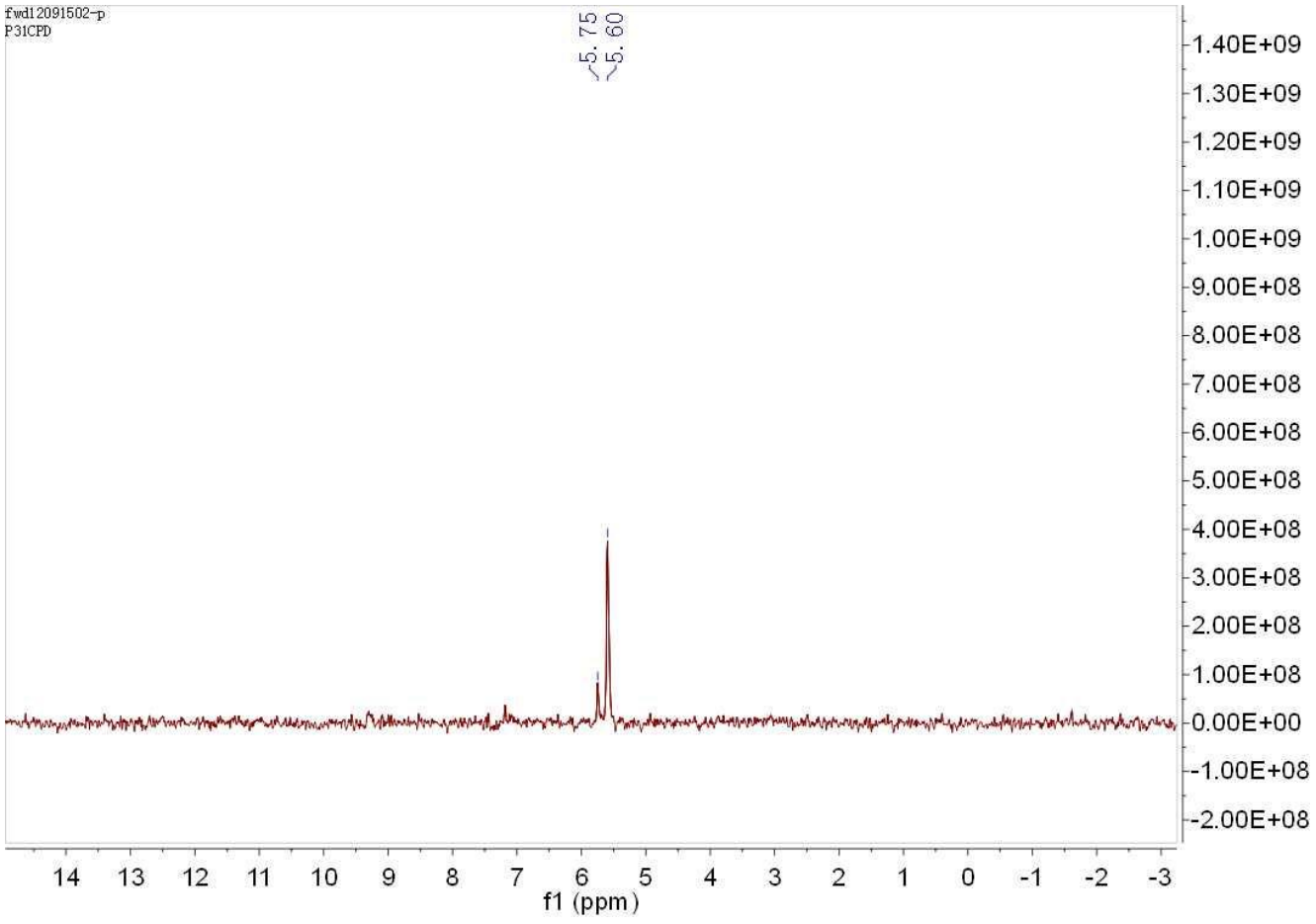
Methyl 2-((3-chlorophenyl)((diethylphosphoryl)amino)methyl)-2-nitrobutanoate (6o):

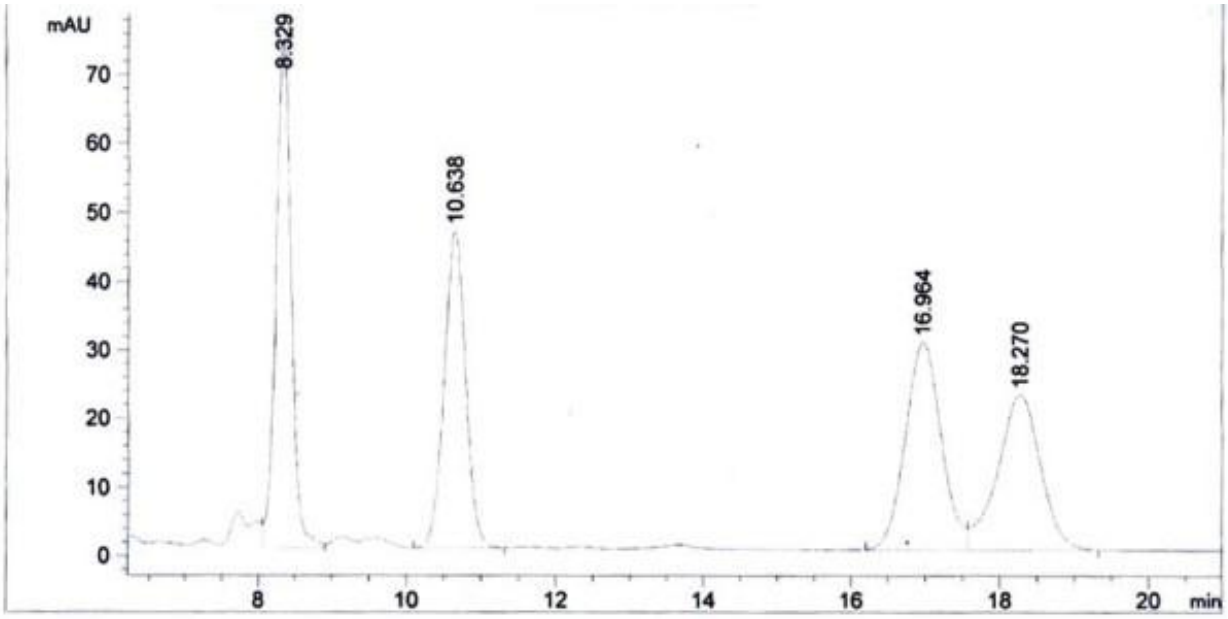


White solid; mp 58-60 °C; $[\alpha]^{20}_{D}$ = 27.6° (c = 0.005, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.35 (m, 3H), 7.13-7.20 (m, 1H), 4.93-5.03 (m, 1H), 4.67-4.78 (m,1H), 3.79-3.97 (m, 6H), 3.63-3.74 (m, 1H), 1.95-2.09 (m, 2H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.08 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.64, 139.07, 134.58, 129.90, 128.96, 128.18, 126.21, 98.34, 62.60 (d, *J* = 5.3 Hz), 62.50 (d, *J* = 5.1 Hz), 60.98, 53.49, 29.59, 15.99 (d, *J* = 7.5 Hz), 15.81 (d, *J* = 7.5 Hz), 9.02; ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.75, 5.60; HRMS (MALDI) calculated for $[C_{16}H_{24}ClN_2O_7P+H]^+$: 423.1088, Found: 423.1086; HPLC (Chiralcel AD-H, hexane/*i*PrOH, 85:15 v/v, 1.0mL/min, 23°C, UV 220 nm): tr (minor) = 8.483 min, tr (major) = 10.905 min, tr (major) = 17.385 min, tr (major) = 18.813 min.

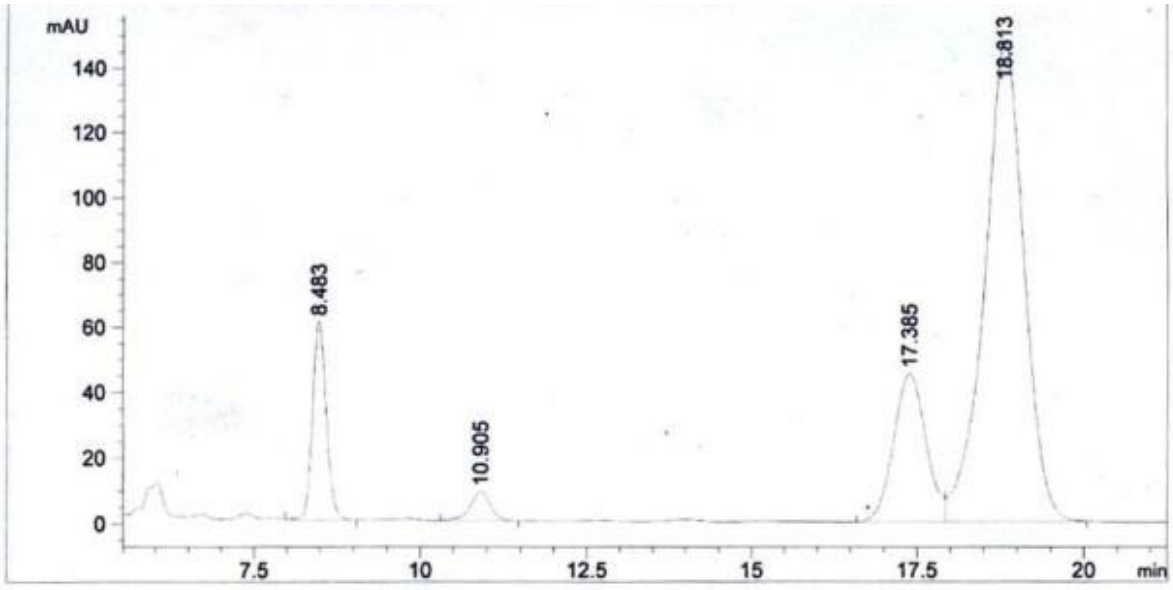








#	[min]		[min]	mAU	*s	[mAU]	%
1	8.329	VV	0.2230	1074.57056		74.11059	27.3074
2	10.638	VB	0.3070	924.48511		46.34566	23.4934
3	16.964	BV	0.5183	1025.83069		30.44744	26.0688
4	18.270	VB	0.6036	910.20184		22.75321	23.1304



#	[min]		[min]	mAU	*s	[mAU]	%
1	8.483	VB	0.2230	879.33209		60.66296	10.1061
2	10.905	BB	0.3242	191.10847		8.91939	2.1964
3	17.385	BV	0.5209	1530.18567		45.28720	17.5863
4	18.813	VB	0.6174	6100.37109		148.56720	70.1112

Reference:

[1] L. Jiang, H. T. Zheng, T. Y. Liu, L. Yue, Y. C. Chen, *Tetrahedron* **2007**, *63*, 5123.

[2] B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967.

[3] K. Liu, H. F. Cui, J. Nie, K. Y. Dong, X. J. Li, J. A. Ma, *Org. Lett.* **2007**, *9*, 923.