Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

The Asymmetric Synthesis of Chiral Cyclic α-Hydroxy Phosphonates and Quaternary Cyclic α-Hydroxy Phosphonates

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SUPPORTING INFORMATION

1. General

Melting points were recorded on a hot-plate microscope apparatus and uncorrected. ^{1}H NMR spectra were measured on Varian-Mercury 600 (600 MHz) spectrometers. Chemical shifts were recorded in δ (ppm) relative to tetramethylsilane (TMS) or residual solvent signals as the internal standard ($CHCl_3$, δ = 7.26, DMSO-d_6, δ = 2.50). Spectra were reported as follows: Chemical shifts (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were collected on Varian-Mercury 600 (150 MHz) spectrometers with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (DMSO-d_6, δ = 39.5). Infrared spectra were obtained as a KBr disc on a Perkin-Elmer PE-983 infrared spectrometer. The X-ray diffraction data were collected on a Bruker SMART AXS CCD diffractometer. Mass spectra were measured on a Finnigan Trace MS spectrometer. Elementary analyses were taken on a Vario EL III elementary analysis instrument. Optical rotations were measured on JASCO P-1020 polarimeter and reported as follows: $[\alpha]_D^T$ (c = g/100 mL, solvent). The enantiomeric excesses (*ee*) of the products were determined by HPLC analysis on chiral DAICEL CHIRALPAK AS-H column at 254 nm unless specially indicated. All reagents are commercial reagents and were used as received. Solvents were purified by standard techniques[1]. The chiral ligands **9a-f** were prepared according to literature reported[2]. The progress of reaction was monitored by TLC.

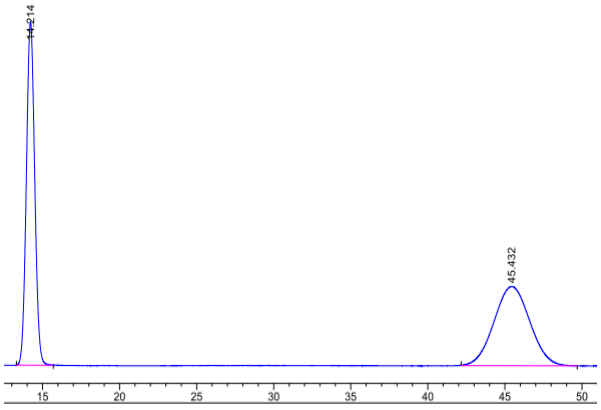
2. Typical Procedure for Asymmetric Hydrophosphonylation of Aldehydes and Ketones

Et_2AlBr (1.0 mmol) was added to a solution of ligand **(*S*)-9f** (1.0 mmol) in CH_2Cl_2 (4 mL) under nitrogen. After stirring at room temperature for 30 minutes, the aldehyde or ketone (10 mmol) in THF (6 mL) and silver carbonate (0.4 mmol) were added and stirred for a further 30 minutes. The cyclic phosphite **6** (12 mmol) was added at -15 °C, and the reaction solution was stirred for 2 hours. The reaction were quenched by diluted hydrochloric acid (v/v = 1/15). The pure α-hydroxy phosphonate **7** or **8** was afforded by column chromatography on silica gel (acetone/petroleum ether = 1/2).

Products: α-hydroxy phosphonates 7

7a: (*S*)-2-[hydroxy(phenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 154.1-155.3°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 14.22 min (*S*), t_r (minor) = 45.43 min (*R*)]; $[\alpha]_D^{20}$ = -78.3° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.80 (s, 3H), 1.11 (s, 3H), 3.97-4.06 (m, 4H), 5.16 (d, *J* = 11.4 Hz, 1H), 7.31-7.38 (m, 3H), 7.50 (d, *J* = 7.2 Hz, 2H). The ^{1}H NMR data were consistent with literature data[3a].



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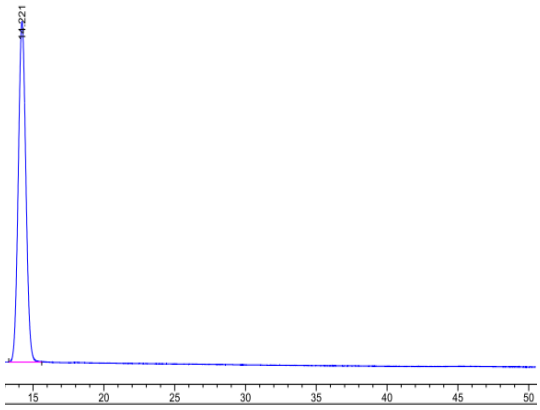
2	45.432	BB	2.2847	3236.24609	19.99057	49.8588



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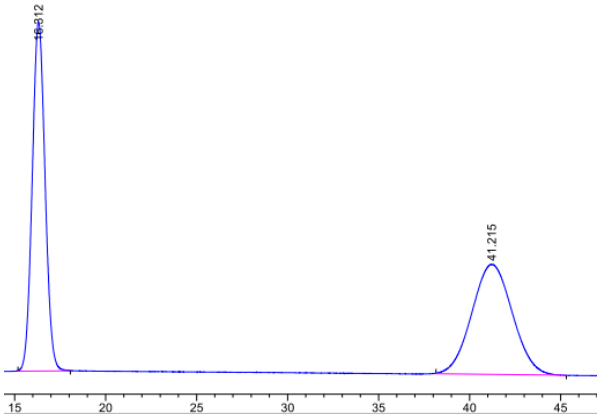
1	14.221	BB	0.5785	2912.93311	78.20595	100.0000

7b: (*S*)-2-[hydroxy(4-methylphenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 170.3-172.1°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 16.24 min (*S*), t_r (minor) = 41.21 min (*R*)]; $[\alpha]_D^{20}$ = -60.7° (*c* = 0.49, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (s, 3H), 1.11 (s, 3H), 2.34 (s, 3H), 3.98-4.05 (m, 4H), 5.12 (d, *J* = 10.8 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 6.6 Hz, 2H). The ^{1}H NMR data were consistent with literature data[3a].



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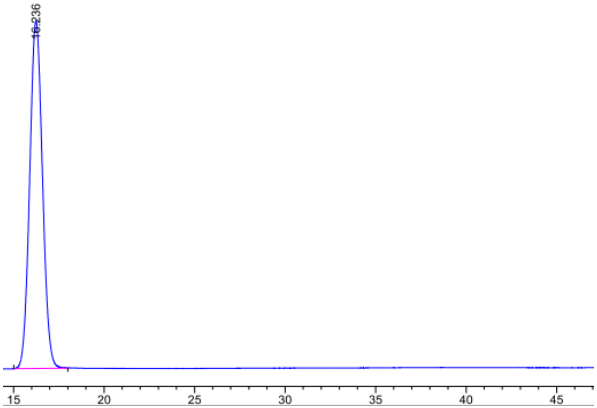
1	16.312	BB	0.7655	3146.98853	64.01596	50.0982
2	41.215	BB	2.2502	3134.64795	20.20313	49.9018



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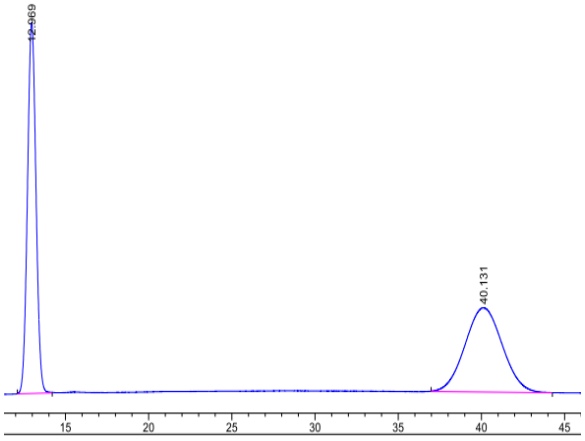
1	16.236	BB	0.7633	6795.99805	138.77852	100.0000

7c: (*S*)-2-[hydroxy(3-methylphenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 175.9-176.9°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 12.97 min (*S*), t_r (minor) = 40.13 min (*R*)]; $[\alpha]_D^{20}$ = -59.2° (*c* = 0.39, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.83 (s, 3H), 1.12 (s, 3H), 2.36 (s, 3H), 3.99- 4.07 (m, 4H), 5.11 (d, *J* = 11.4 Hz, 1H), 7.12(d, *J* = 7.2 Hz, 1H), 7.28 (m, 3H). The ^{1}H NMR data were consistent with literature data[3a].



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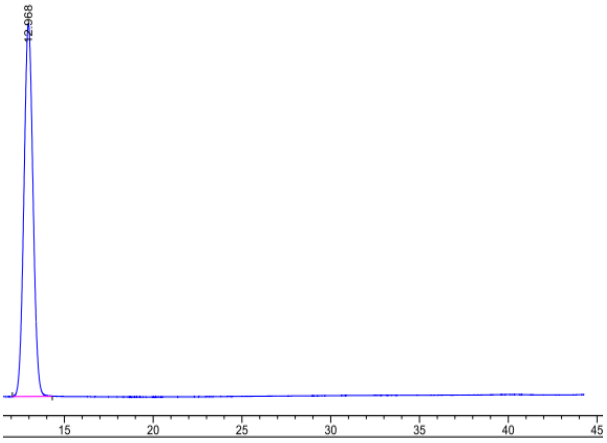

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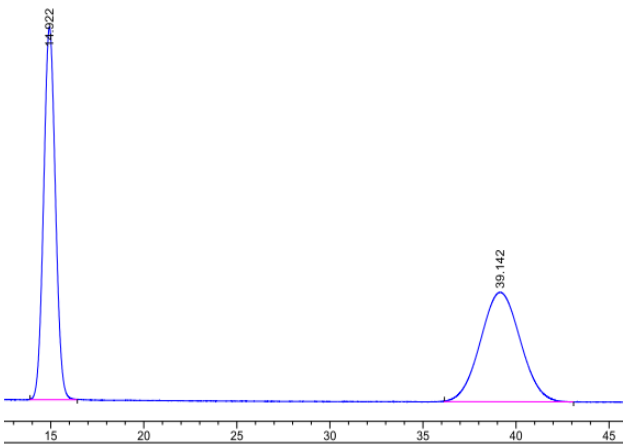
1	12.968	BB	0.5548	3338.90649	93.90493	100.0000

7d: (*S*)-2-[hydroxy(4-chlorophenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 175.3-176.8°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 14.83 min (*S*), t_r (minor) = 39.14 min (*R*)]; $[\alpha]_D^{20}$ = -60.4° (*c* = 0.56, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (s, 3H), 1.10 (s, 3H), 3.99-4.11 (m, 4H), 5.14 (d, *J* = 12.0 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H). The ^{1}H NMR data were consistent with literature data[3a].



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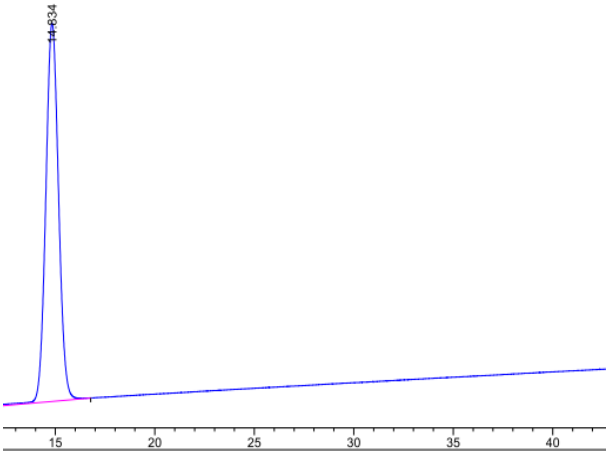
1	14.922	BB	0.6902	2667.19531	60.51818	50.1312
2	39.142	BB	2.0738	2653.23511	17.77153	49.8688



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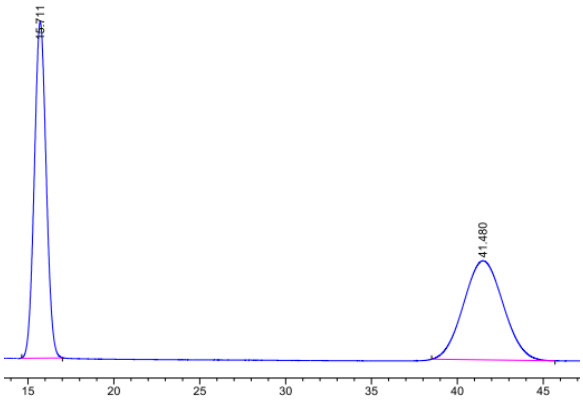
1	14.834	PB	0.7052	4395.84570	96.91525	100.0000

7e: (*S*)-2-[hydroxy(4-bromophenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 189.1-191.6°C; The material was determined to be of 96% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 15.81 min (*S*), t_r (minor) = 42.15 min (*R*)]; $[\alpha]_D^{20}$ = -59.6° (*c* = 0.39, $CHCl_3$); IR (KBr): 3233, 2978, 1483, 1247, 1202, 1180, 826 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.84 (s, 3H), 1.10 (s, 3H), 3.99-4.12 (m, 4H), 5.12 (d, *J* = 12 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.5, 32.1, 68.8, 68.9, 69.9, 77.4, 78.0, 120.8, 129.4, 131.0, 138.1; MS (EI) (m/z): 334 (M^+); Anal. Calcd. for $C_{12}H_{16}BrO_4P$: C 43.01, H 4.81; Found: C 43.20, H 4.67.



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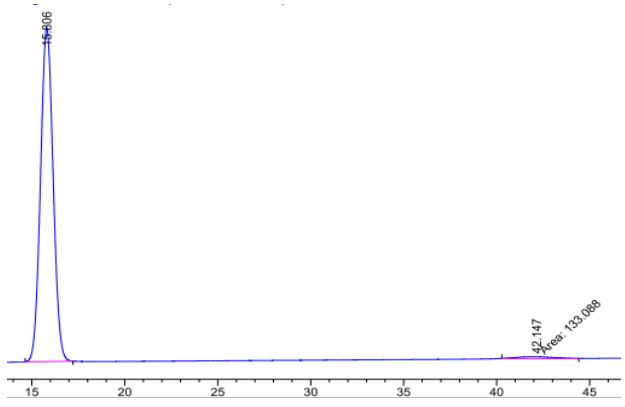

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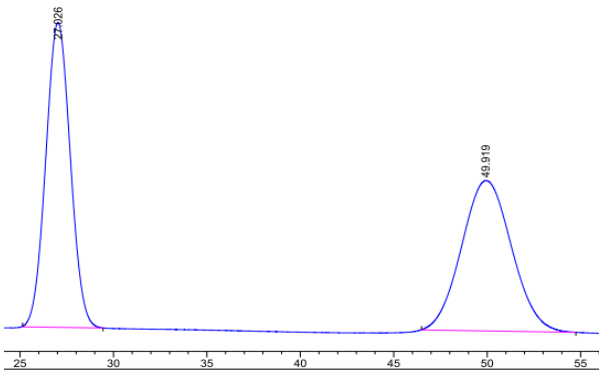
1	15.806	BB	0.7362	6555.02979	138.98593	98.0101
2	42.147	MM	2.5705	133.08813	8.62930e-1	1.9899

7f: (*S*)-2-[hydroxy(4-methoxyphenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 186.4-187.9°C; The material was determined to be of 92% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 27.02 min (*S*), t_r (minor) = 49.84 min (*R*)]; $[\alpha]_D^{20}$ = -59.6° (*c* = 0.42, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 0.86 (s, 3H), 1.12 (s, 3H), 3.81 (s, 3H), 4.03-4.05 (m, 4H), 5.10 (d, *J* = 10.2 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H). The ^1H NMR data were consistent with literature data[3a]



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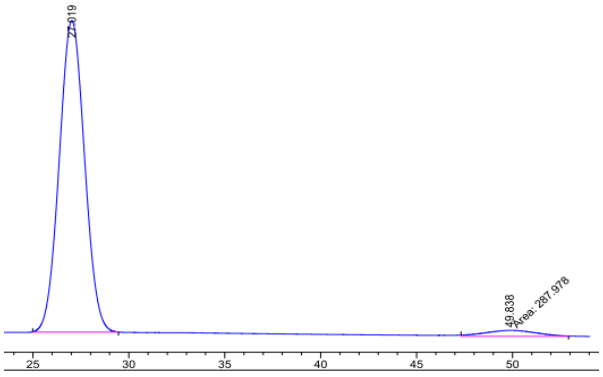
1	27.026	BB	1.3688	2704.04614	29.57046	49.8733
2	49.919	BB	2.1846	2717.78101	14.59456	50.1267



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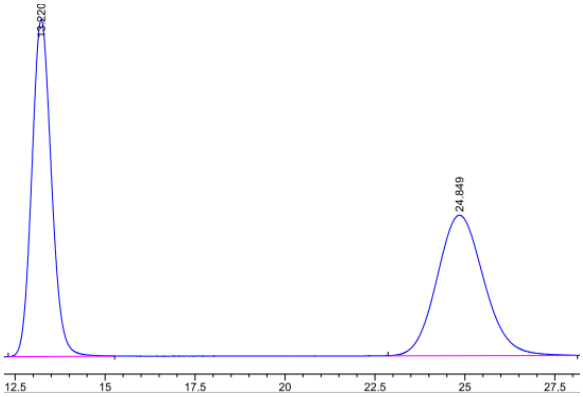
1	27.019	BB	1.3993	7335.66943	79.88567	96.2226
2	49.838	MM	3.1602	287.97803	1.51878	3.7774

7g: (*S*)-2-[hydroxy(2,4-dichlorophenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 188.4-189.2°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 13.22 min (*S*), t_r (minor) = 24.85 min (*R*)]; $[\alpha]_D^{20}$ = -63.1° (*c* = 0.52, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (s, 3H), 1.10 (s, 3H), 3.96-4.10 (m, 4H), 5.62 (d, *J* = 12.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.39 (s, 1H), 7.70 (d, *J* = 7.2 Hz, 1H). The ^1H NMR data were consistent with literature data[3a].



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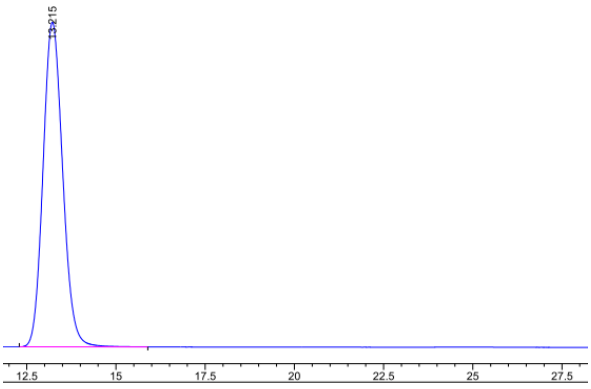
1	13.220	BB	0.5856	6254.34082	165.24513	49.9945
2	24.849	BB	1.4144	6255.71582	68.95677	50.0055



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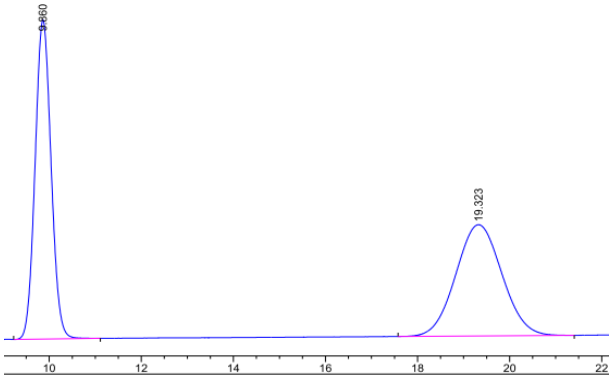
1	13.215	BB	0.5985	1.74550e4	456.11603	100.0000

7h: (*S*)-2-[hydroxy(2,3-dichlorophenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 193.1-194.5°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 9.86 min (*S*), t_r (minor) = 19.32 min (*R*)]; $[\alpha]_D^{20}$ = -61.8° (*c* = 0.51, $CHCl_3$); IR (KBr): 3221, 2970, 1375, 1237, 1185, 749, 683 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (s, 3H), 1.10 (s, 3H), 3.98-4.11 (m, 4H), 5.71 (d, *J* = 12.0 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 19.9, 21.3, 32.0, 67.3, 68.4,77.8, 78.0, 128.0, 128.3, 129.7, 131.4, 138.9, 139.0; MS (EI) (m/z): 324 (M^+); Anal. Calcd. for $C_{12}H_{15}Cl_2O_4P$: C 44.33, H 4.65; Found: C 44.36, H 4.59.



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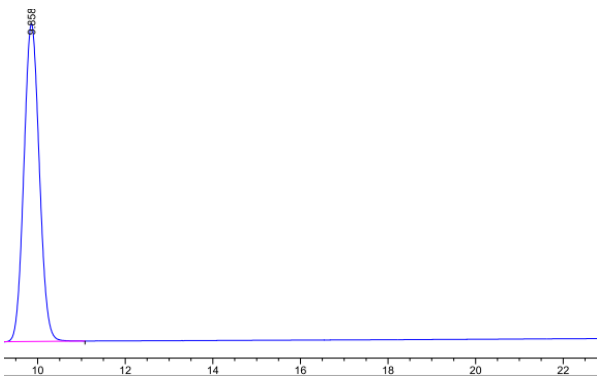
2	19.323	BB	1.0990	5526.02393	79.10829	50.2214



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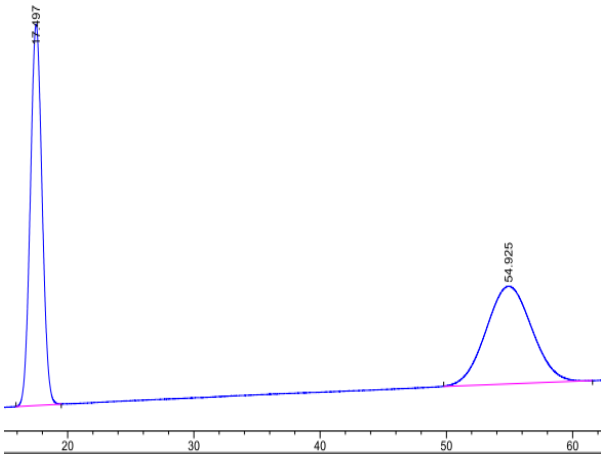
1	9.858	PB	0.3811	1.19391e4	488.48492	100.0000

7i: (*S*)-2-[hydroxy(3,4-dichlorophenyl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 189.8-191.5°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 17.50 min (*S*), t_r (minor) = 54.93 min (*R*)]; $[\alpha]_D^{20}$ = -60.2° (*c* = 0.48, $CHCl_3$); IR (KBr): 3273, 2967, 1466, 1247, 1193, 885, 822 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.88 (s, 3H), 1.12 (s, 3H), 4.04-4.15 (m, 4H), 5.14 (d, *J* = 12.6 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 19.9, 21.5, 32.2, 68.1, 69.2, 77.6, 78.0, 127.5, 129.0, 130.2, 130.3, 130.8, 139.9; MS (EI) (m/z): 324 (M^+); Anal. Calcd. for $C_{12}H_{15}Cl2O_4P$: C 44.33, H 4.65; Found: C 44.56, H 4.68.



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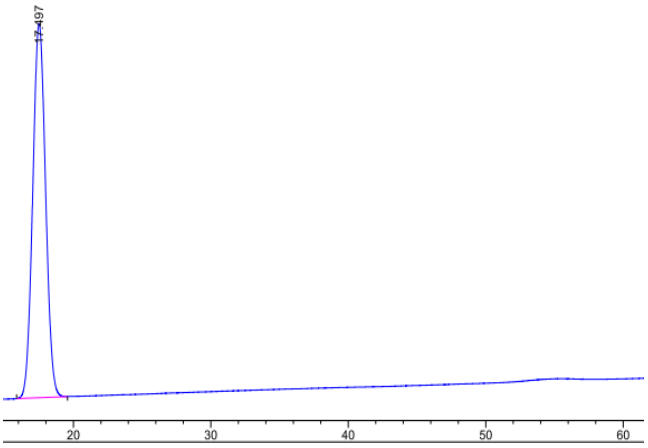
1	17.497	BB	1.0154	5597.28760	86.45017	49.9910
2	54.925	BP	2.9742	5599.30908	22.17241	50.0090



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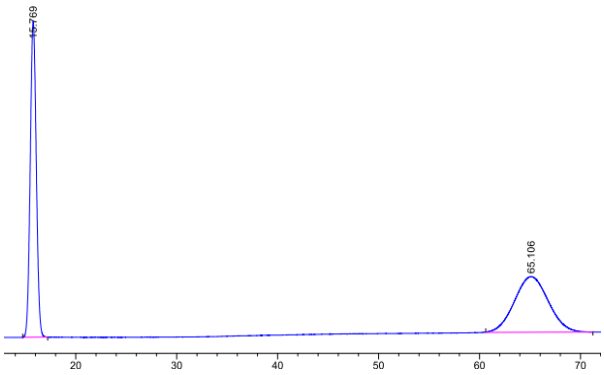
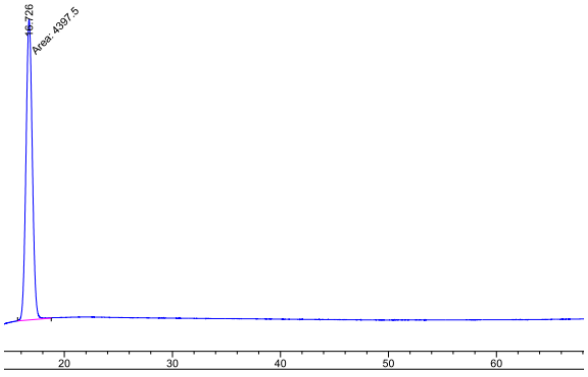
1	17.497	BB	1.0180	9997.98730	153.89265	100.0000

7j: (*S*)-2-[hydroxy(furan-2-yl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 202.4-203.4°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 16.73 min (*S*), t_r (minor) = 65.11 min (*R*)]; $[\alpha]_D^{20}$ = -64.1° (*c* = 0.53, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 0.89 (s, 3H), 1.21(s, 3H), 4.00-4.04 (m, 2H), 4.24-4.25 (m, 2H),5.20 (d, *J* = 13.2 Hz, 1H), 6.38 (s, 1H), 6.52 (s, 1H), 7.43 (s, 1H). The ^1H NMR data were consistent with literature data[3b].



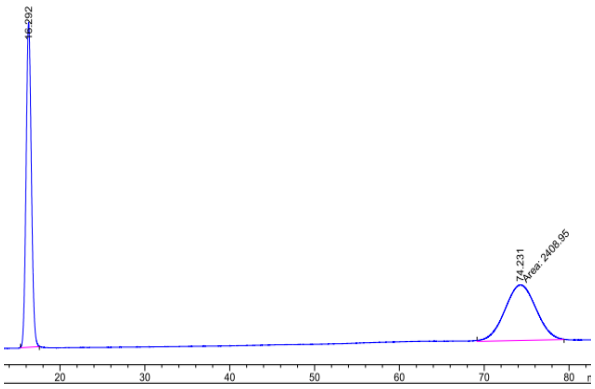
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.769	BB	0.6538	4314.81104	103.62823	50.2354
2	65.106	BB	2.8034	4274.37598	18.28399	49.7646



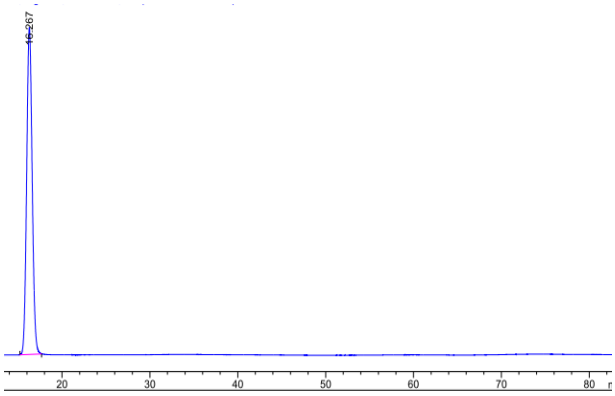
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.726	MM	0.6771	4397.49609	108.25129	100.0000

7k: (S)-2-[hydroxy(thiophen-2-yl)methyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

yellowish solid; mp 226.0-227.4°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 10/90, 0.5 mL/min; t_r (major) = 16.27 min (*S*), t_r (minor) = 74.23 min (*R*)]; $[\alpha]_D^{20}$ = -62.1° (*c* = 0.42, $CHCl_3$); IR (KBr): 3215, 2968, 1469, 1237, 1079, 825, 722 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.88 (s, 3H), 1.19 (s, 3H), 4.02-4.25 (m, 4H), 5.41 (d, *J* = 12.0 Hz, 1H), 7.01 (t, *J* = 4.2 Hz, 1H), 7.20 (s, 1H), 7.32 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.6, 32.1, 65.8, 66.9, 77.6, 78.0, 125.6, 125.9, 126.8, 141.8; MS (EI) (m/z): 262 (M^+); Anal. Calcd. for $C_{10}H_{15}O_4PS$: C 45.80, H 5.76; Found: C 45.61; H 5.72.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.292	BB	0.6745	2383.87695	54.90501	49.7384
2	74.231	MM	4.2759	2408.95483	9.38963	50.2616

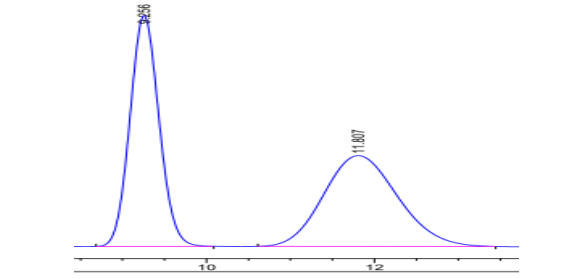


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.267	BB	0.6737	4156.24121	95.88452	100.0000

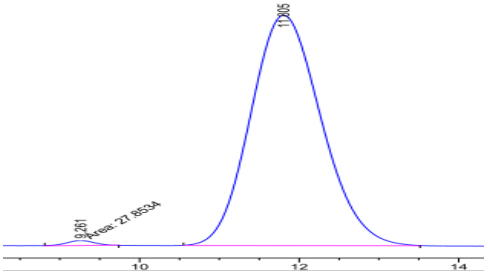
Products: α-hydroxy phosphonates 8

8a: (*S*)-2-[1-hydroxy-1-(4-chlorophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 149.8-151.6°C; The material was determined to be of 98% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 9.26 min (*R*), t_r (major) = 11.81 min (*S*)]; $[\alpha]_D^{20}$ = -53.4° (*c* = 0.54, $CHCl_3$); IR (KBr): 3241, 2970, 1489, 1222, 1138, 829 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.86 (s, 3H), 1.07 (s, 3H), 1.88 (d, *J* = 15.6 Hz, 3H), 3.96-4.09 (m, 4H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.57 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 25.5, 32.0, 74.6, 75.6, 78.0, 78.5, 127.7, 128.1, 131.8, 142.0; MS (EI) (m/z): 304 (M^+); Anal. Calcd. for $C_{13}H_{18}ClO_4P$: C 51.24, H 5.95; Found: C 50.96, H 5.90.



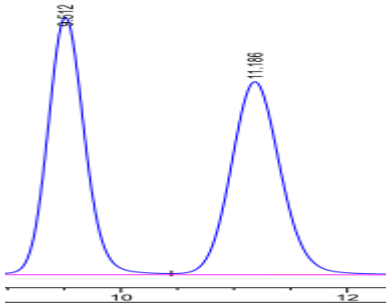
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.256	BB	0.3789	2052.43286	84.63397	49.9721
2	11.807	BB	0.9452	2054.72852	33.33028	50.0279



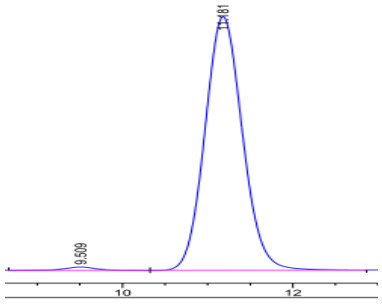
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.261	MM	0.4026	27.85340	1.15303	0.8271
2	11.805	BB	0.9485	3339.91992	54.08178	99.1729

8b: (*S*)-2-[1-hydroxy-1-(3-chlorophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 142.0.3-143.6°C; The material was determined to be of 97% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 9.51 min (*R*), t_r (major) = 11. 18 min (*S*)]; $[\alpha]_D^{20}$ = -53.7° (*c* = 0.51, $CHCl_3$); IR (KBr): 3229, 2969, 1486, 1222, 1138, 787, 691 cm^{-1}; ^1H NMR (600 MHz, DMSO -d_6): δ 0.85 (s, 3H), 1.15 (s, 3H), 1.74 (d, *J* = 15.6 Hz, 3H), 3.89-3.93 (m, 1H), 4.03-4.08 (m, 1H), 4.39-4.40 (m, 1H), 4.47-4.49 (m, 1H), 7.37-7.43 (m, 2H), 7.54-7.60 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 25.6, 32.0, 74.6, 75.6, 78.0, 78.5, 124.9, 125.8, 126.9, 129.7,132.6, 145.5; MS (EI) (m/z): 304 (M^+); Anal. Calcd. for $C_{13}H_{18}ClO_4P$: C 51.24, H 5.95; Found: C 50.98, H 5.91.



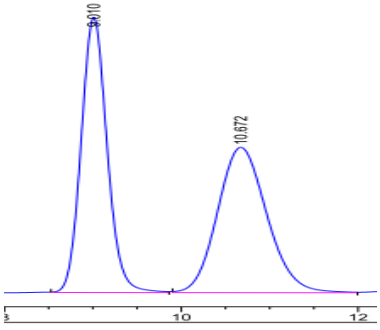
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.512	VV	0.3567	3080.73755	133.75887	49.9206
2	11.186	VV	0.4752	3090.54346	100.36668	50.0794



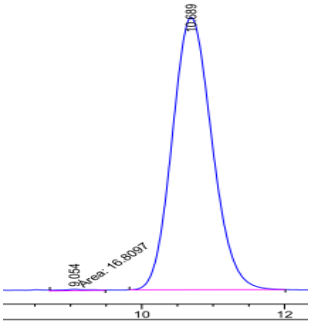
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.509	VV	0.4380	81.21056	2.70687	1.2984
2	11.181	VB	0.4779	6173.24268	201.21259	98.7016

8c: (*S*)-2-[1-hydroxy-1-(2-chlorophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 145.9-147.8°C; The material was determined to be of 99% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 9.05 min (*R*), t_r (major) = 10.69 min (*S*)]; $[\alpha]_D^{20}$ = -58.4° (*c* = 0.52, $CHCl_3$); IR (KBr): 3241, 2970, 1489, 1222, 1138, 768 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ 0.85 (s, 3H), 1.14 (s, 3H), 1.74 (d, *J* = 15.6 Hz, 3H), 3.87-3.92 (m, 1H), 4.03-4.07 (m, 1H), 4.37-4.39 (m, 1H), 4.47-4.48 (m, 1H),7.44 (d, *J* = 7.8 Hz, 2H), 7.59 (m, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 25.5, 32.0, 74.5, 75.6, 77.9, 78.4,127.6, 128.0, 131.8, 141.9; MS (EI) (m/z): 304 (M^+); Anal. Calcd. for $C_{13}H_{18}ClO_4P$: C 51.24, H 5.95; Found: C 51.06, H 5.89.



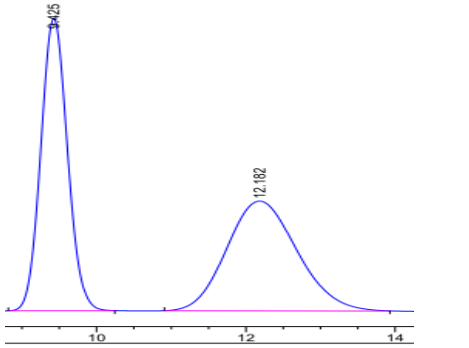
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.010	BB	0.3145	2643.16187	129.28024	49.9377
2	10.672	BB	0.6028	2649.75195	68.27175	50.0623



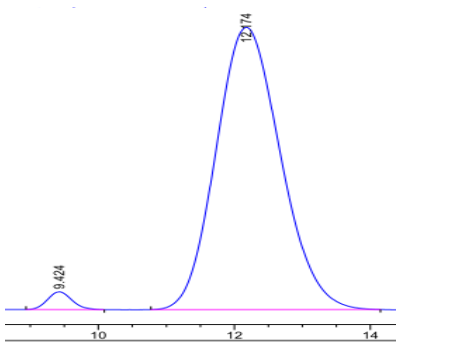
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.054	MM	0.4712	16.80968	5.94560e-1	0.3955
2	10.689	BB	0.6074	4233.41016	108.92749	99.6045

8d: (*S*)-2-[1-hydroxy-1-(4-bromophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 148.5-150.2°C; The material was determined to be of 95% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 9.42 min (*R*), t_r (major) = 12.17 min (*S*)]; $[\alpha]_D^{20}$ = -64.8° (*c* = 0.56, $CHCl_3$); IR (KBr): 3239, 2970, 1486, 1222, 1138, 830 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.84 (s, 3H), 1.06 (s, 3H), 1.85 (d, *J* = 15.6 Hz, 3H), 4.00-4.01 (m, 4H), 7.49 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 19.8, 21.3, 25.4, 31.8, 74.5, 75.5, 77.8, 78.3, 120.3, 128.3, 130.4, 142.2; MS (EI) (m/z): 348 (M^+); Anal. Calcd. for $C_{13}H_{18}BrO_4P$: C 44.72, H 5.20 %; Found: C 44.51; H 5.31.



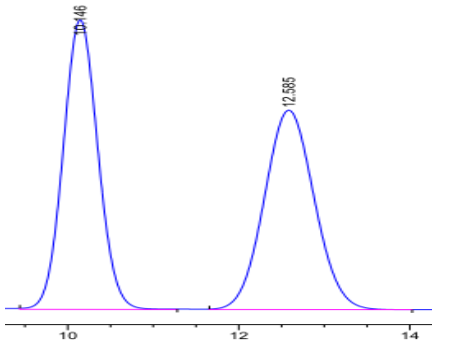
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.425	BB	0.3879	2268.59131	91.28895	50.1443
2	12.182	BB	0.9917	2255.53442	34.27659	49.8557



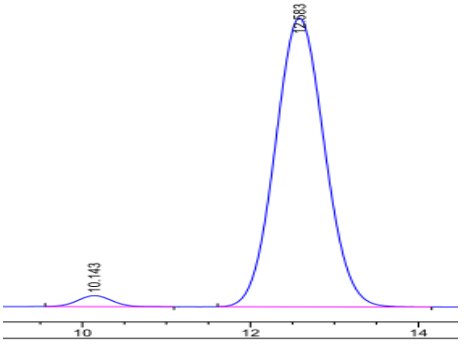
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.424	BB	0.3912	182.54555	7.26401	2.3350
2	12.174	BB	1.0345	7635.13525	115.60606	97.6650

8e: (*S*)-2-[1-hydroxy-1-(3-bromoophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 162.3-163.5°C; The material was determined to be of 95% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 10.14 min (*R*), t_r (major) = 12.58 min (*S*)]; $[\alpha]_D^{20}$ = -74.0° (*c* = 0.41, $CHCl_3$); IR (KBr): 3233, 2969, 1477, 1225, 1139, 777, 690 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (s, 3H), 1.10 (s, 3H), 1.89 (d, *J* = 15.6 Hz, 3H), 3.96-4.11 (m, 4H), 7.27 (m, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 1.8Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 25.7, 32.0 (d, *J* = 8.55Hz,), 74.5, 75.6, 78.0, 78.6, 121.3, 125.2, 128.7, 129.8, 130.0, 145.8; MS (EI) (m/z): 348 (M^+); Anal. Calcd. for $C_{13}H_{18}BrO_4P$: C 44.72, H 5.20; Found: C 44.39, H 5.48.



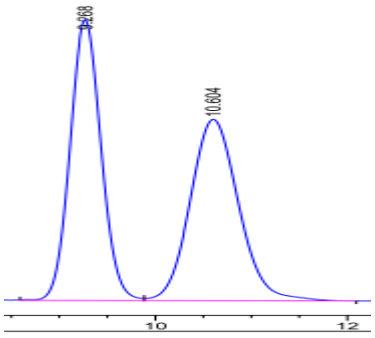
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.146	BB	0.4428	3571.77808	125.96223	50.1654
2	12.585	BB	0.6411	3548.22900	86.77180	49.8346



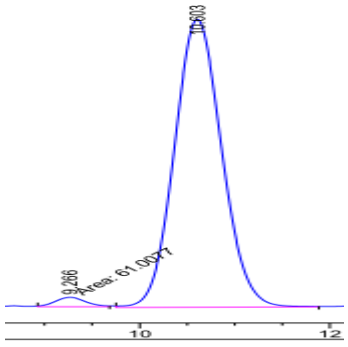
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.143	BB	0.4453	168.77376	5.90750	2.5965
2	12.583	BB	0.6413	6331.33350	154.74683	97.4035

8f: (S)-2-[1-hydroxy-1-(4-fluorophenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 168.7-169.9°C; The material was determined to be of 96% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 9.27 min (*R*), t_r (major) = 10.60 min (*S*)]; $[\alpha]_D^{20}$ = -65.0° (*c* = 0.64, $CHCl_3$); IR (KBr): 3220, 2974, 1510, 1374, 1223, 1135, 828 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.86 (s, 3H), 1.07 (s, 3H), 1.89 (d, *J* = 15.6 Hz, 3H), 3.92-4.10 (m, 4H), 7.06 (m, 2H), 7.61 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 25.6, 31.9, 74.4, 75.5, 78.3(m), 114.4(d, *J* = 6.9 Hz), 128.1, 139.0, 160.5, 162.1; MS (EI) (m/z): 288 (M^+); Anal. Calcd. for $C_{13}H_{18}FO_4P$: C 54.17, H 6.29 ; Found: C 54.19; H 6.51.



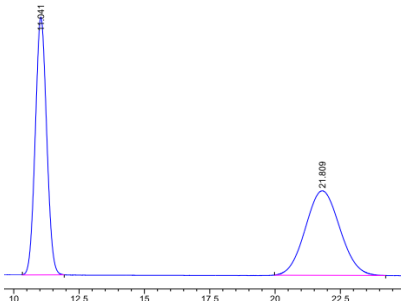
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.268	BV	0.3561	1156.59949	51.09824	49.9818
2	10.604	VB	0.5451	1157.44324	33.00841	50.0182



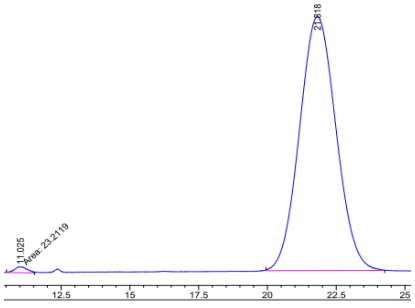
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.266	MM	0.3787	61.00770	2.68522	2.1232
2	10.603	VB	0.5407	2812.41968	81.08451	97.8768

8g: (S)-2-[1-hydroxy-1-(4-methoxyphenyl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 155.6-156.3°C; The material was determined to be of 98% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 85/15, 0.5 mL/min; t_r (minor) = 11.03 min (*R*), t_r (major) = 21.82 min (*S*)]; $[\alpha]_D^{20}$ = -48.1° (*c* = 0.48, $CHCl_3$); IR (KBr): 3329, 2969, 1513, 1251, 1230, 1137, 830 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.88 (s, 3H), 1.10 (s, 3H), 1.90 (d, *J* = 15.6 Hz, 3H), 3.82 (s, 3H), 3.90-4.08 (m, 4H), 6.93 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.1, 21.5, 25.6, 32.0 (d, *J* = 7.05 Hz), 55.1, 74.4, 75.5, 77.7, 78.2, 113.1, 127.4, 134.7, 158.3; MS (EI) (m/z): 300(M^+); Anal. Calcd. for $C_{14}H_{21}O_5P$: C 56.00, H 7.05 %; Found: C 55.72, H 7.28.



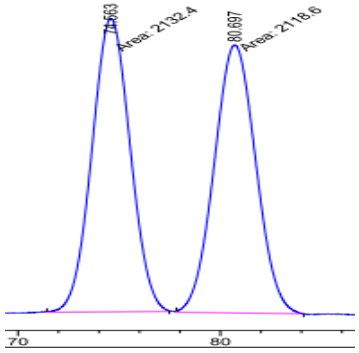
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.041	BB	0.4710	2268.95776	74.98581	50.0911
2	21.809	BB	1.2979	2260.70044	24.60513	49.9089



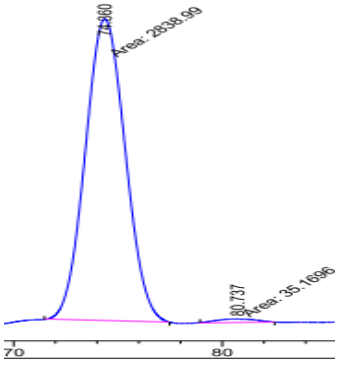
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.025	MM	0.5361	23.21194	7.21586e-1	0.8180
2	21.818	BB	1.3721	2814.53809	30.45821	99.1820

8h: (S)-2-[1-hydroxy-1-(thiophen-2-yl)ethyl]-5,5-dimethyl-1,3,2-dioxaphosphinane-2-one

white solid; mp 152.0-153.8°C; The material was determined to be of 97% *ee* by chiral HPLC analysis [Daicel Chiralpak AS-H, *n*-hexane/*i*-PrOH = 80/20, 0.5 mL/min; t_r (major) = 74.36 min (*S*), t_r (minor) = 80.74 min (*R*)]; $[\alpha]_D^{20}$ = -63.0^o (*c* = 0.57, $CHCl_3$); IR (KBr): 3234, 2967, 1468, 1372, 1224, 1128, 1064, 836 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ 0.84 (s, 3H), 1.17 (s, 3H), 1.78 (d, *J* = 15.6Hz, 3H), 3.92-4.05 (m, 2H), 4.43-4.45 (m, 2H), 6.70 (d, *J* = 18Hz ,1H), 7.04 (d, *J* = 18Hz, 2H), 7.47(s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 20.0, 21.4, 26.3, 32.0, 73.9, 75.0, 78.1, 78.5, 124.4, 125.2, 126.9, 147.8; MS (EI) (m/z): 276 (M^+); Anal. Calcd. for $C_{11}H_{17}O_4PS$: C 47.82, H 6.20; Found: C 47.72, H 6.02.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	74.563	MM	2.1914	2132.40112	16.21831	50.1624
2	80.697	MM	2.3823	2118.59619	14.82198	49.8376



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	74.360	MM	2.2233	2838.99146	21.28217	98.7764
2	80.737	MM	2.2923	35.16958	2.55711e-1	1.2236

References

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2 (a) D. A. Cogan, G.-C. Liu, K. J. Kim, B. J. Backes and J. A. Ellman, *J. Am. Chem. Soc*., 1998, **120**, 8011; (b) J. Hartung, S. Drees, M. Greb, P. Schmidt, I. Svoboda, H.t Fuess, A. Murso and D. Stalke, *Eur. J. Org. Chem.*, 2003, **13**, 2388.

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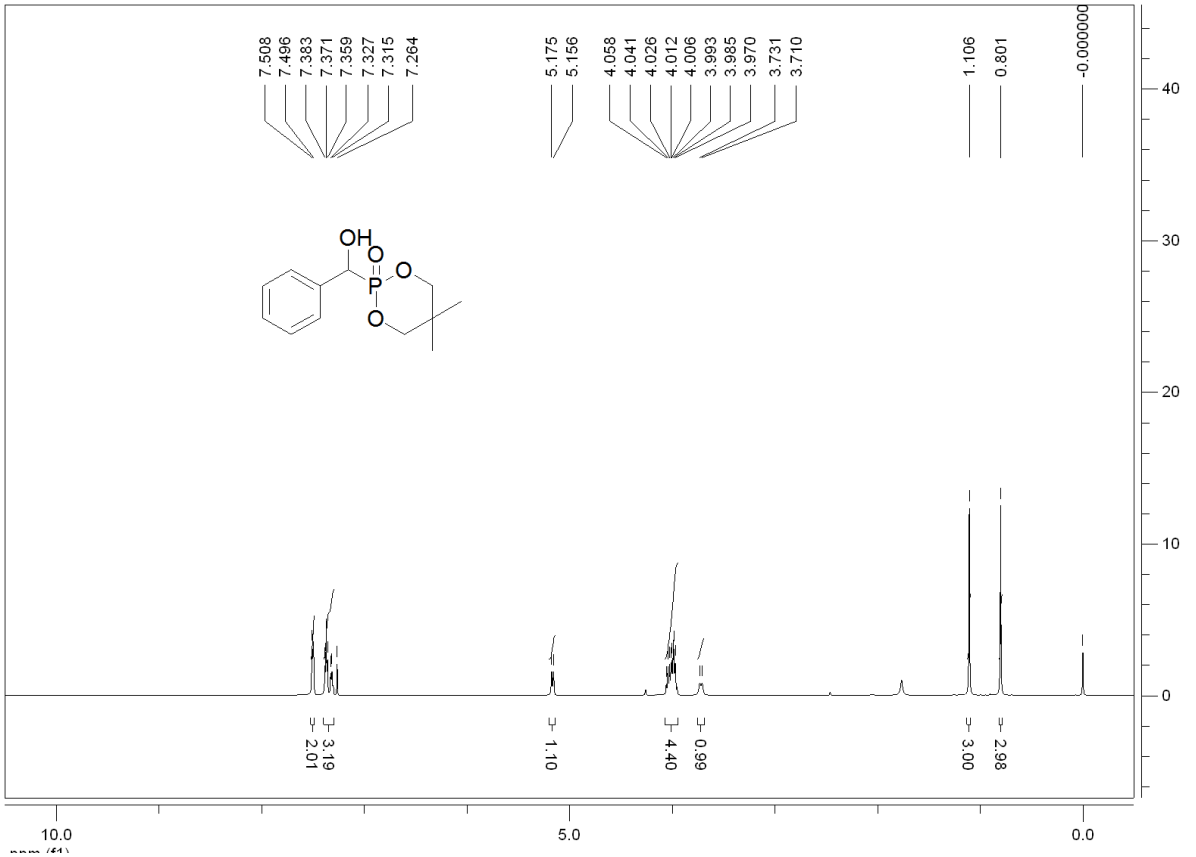
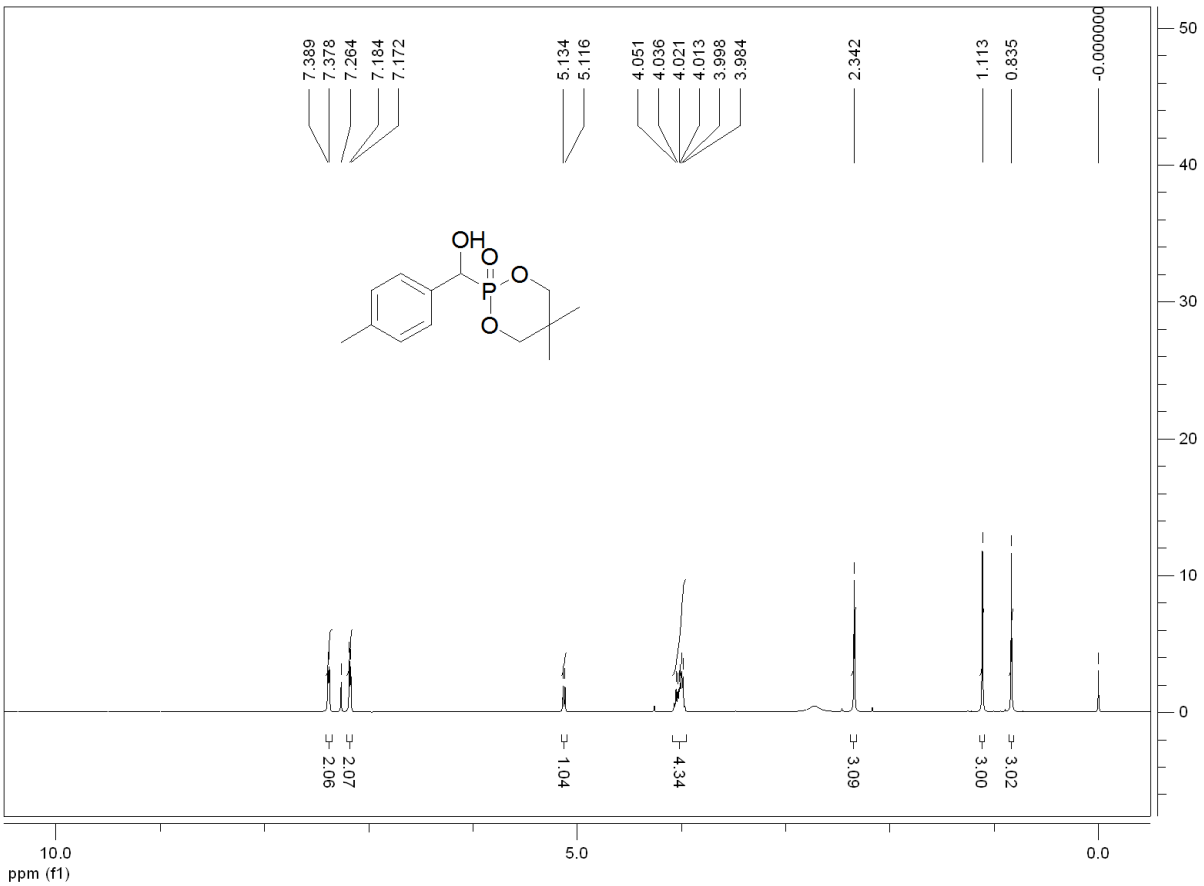
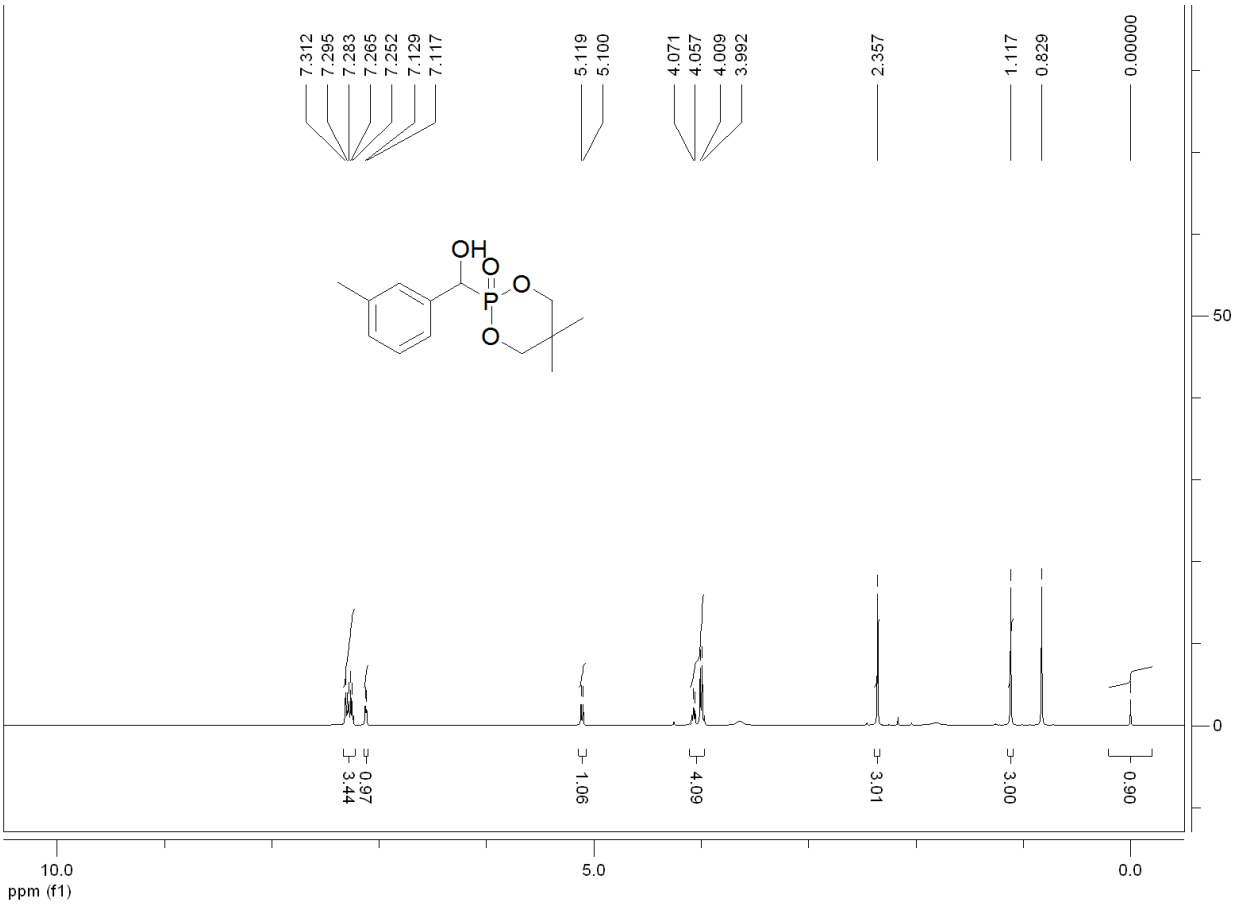
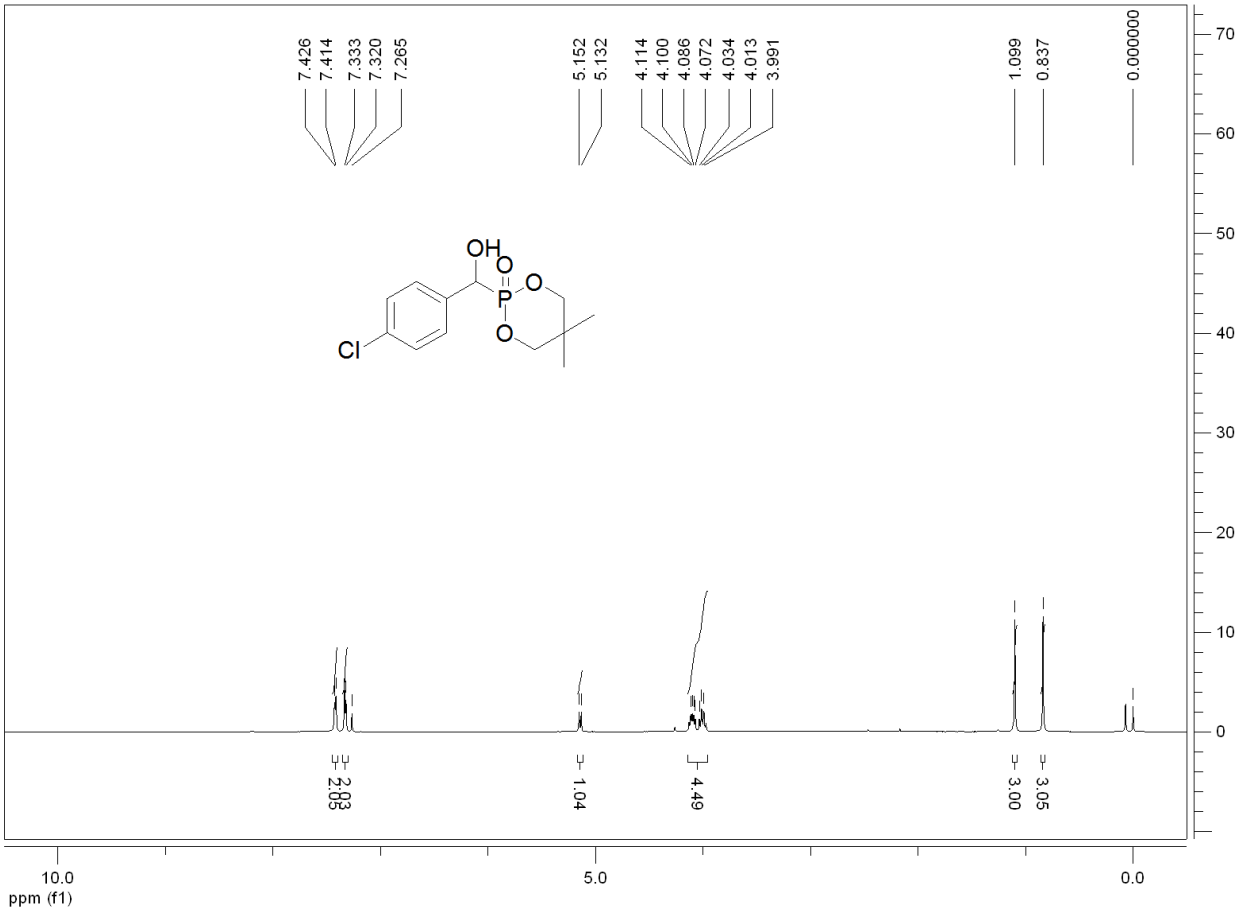
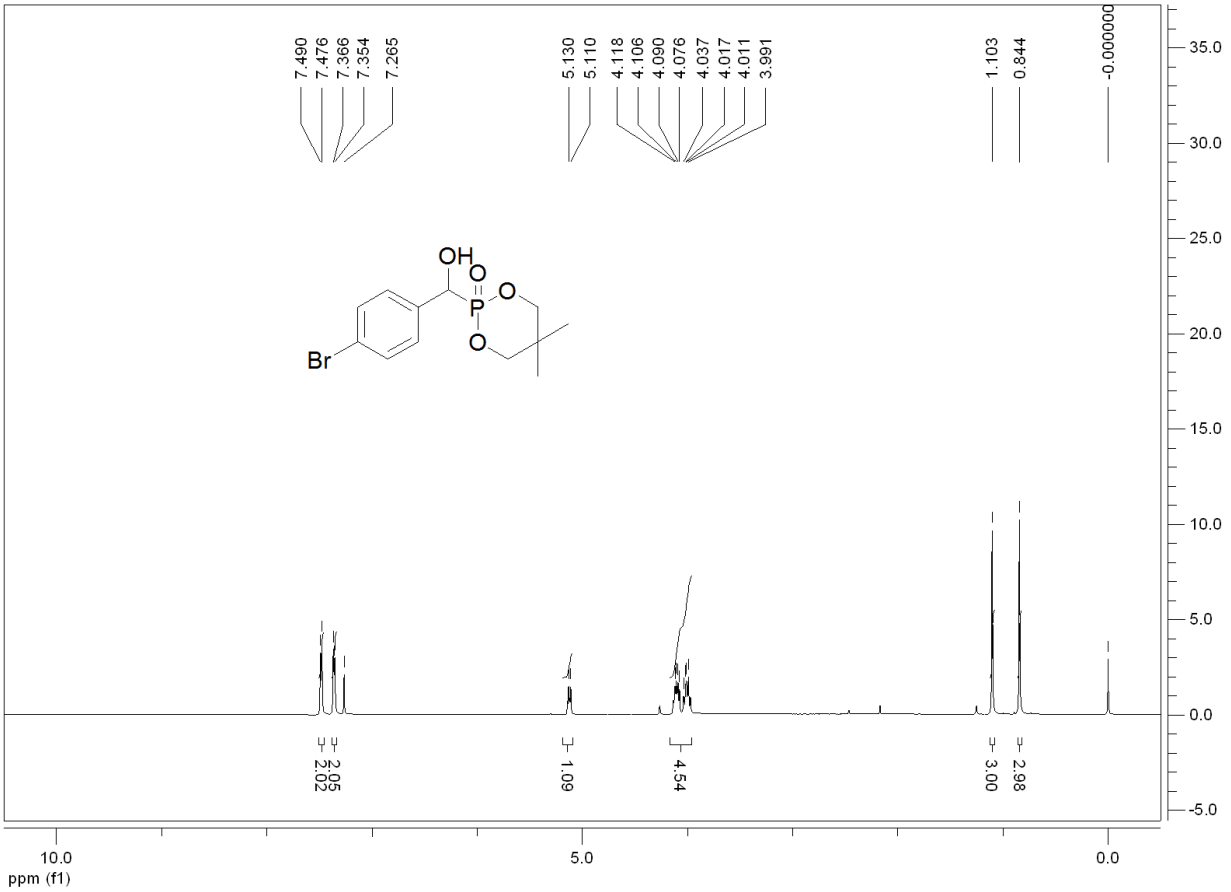
3. Copy of ^{1}H NMR and ^{13}C NMR Spectra

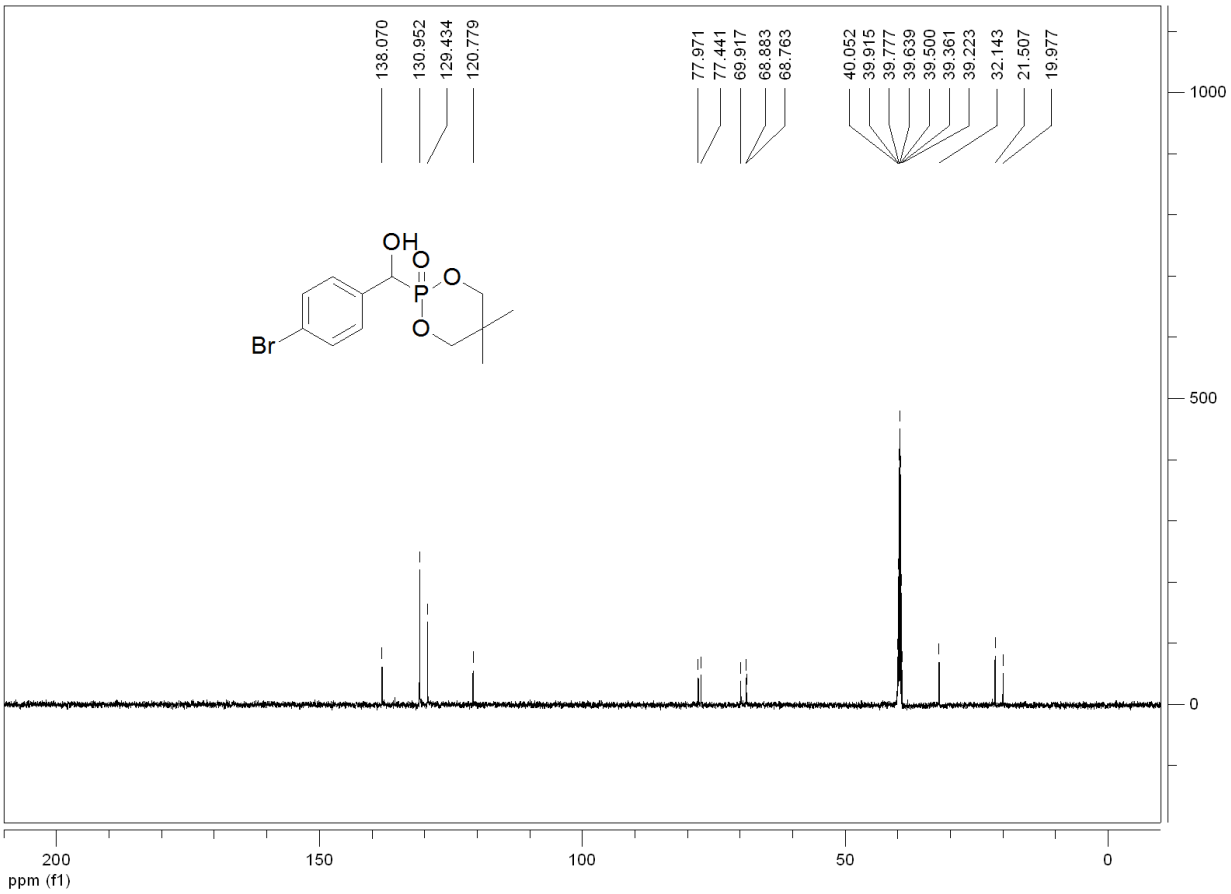


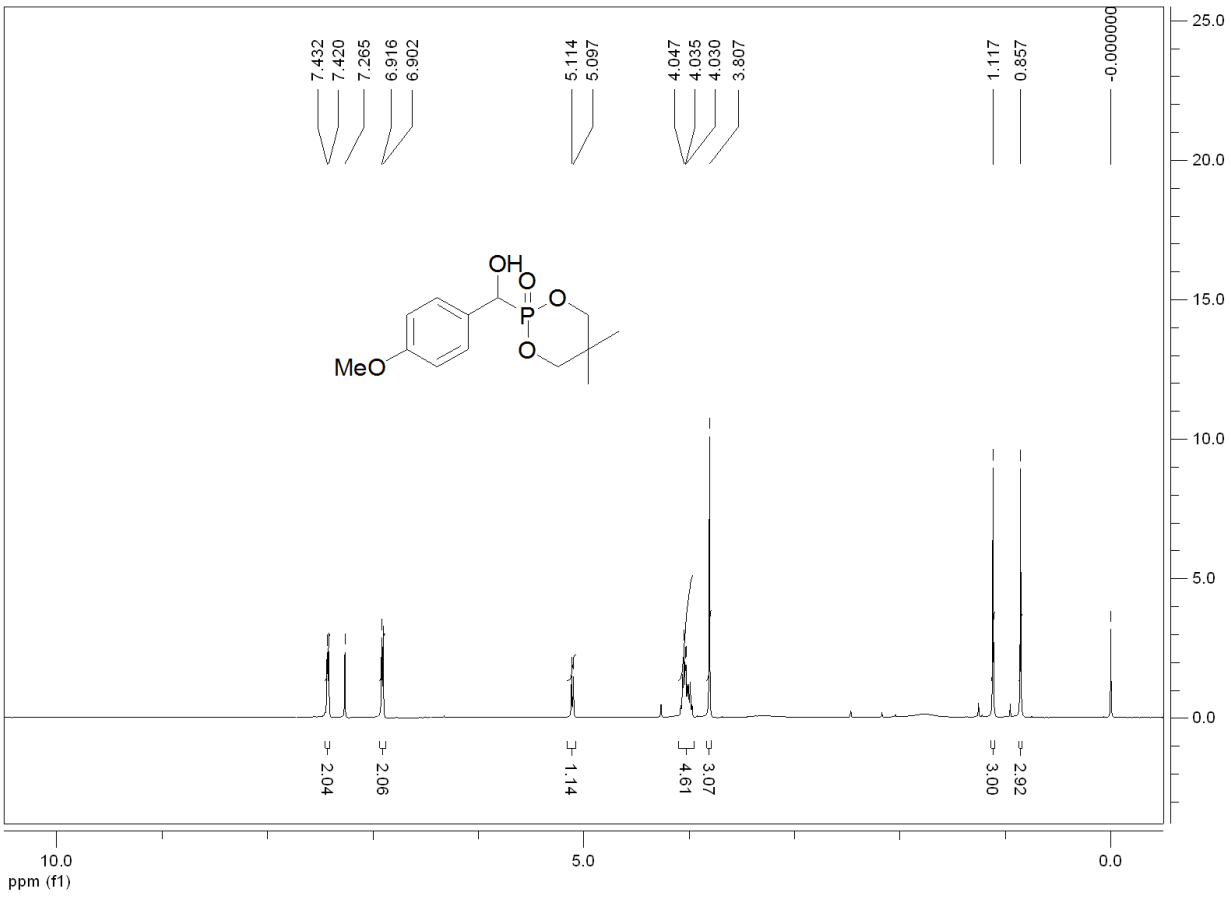








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4.030
3.807
1.117
0.857
-0.000000
OH
O
O
P
O
MeO
2.04
2.06
1.14
4.61
3.07
3.00
2.92
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20.0
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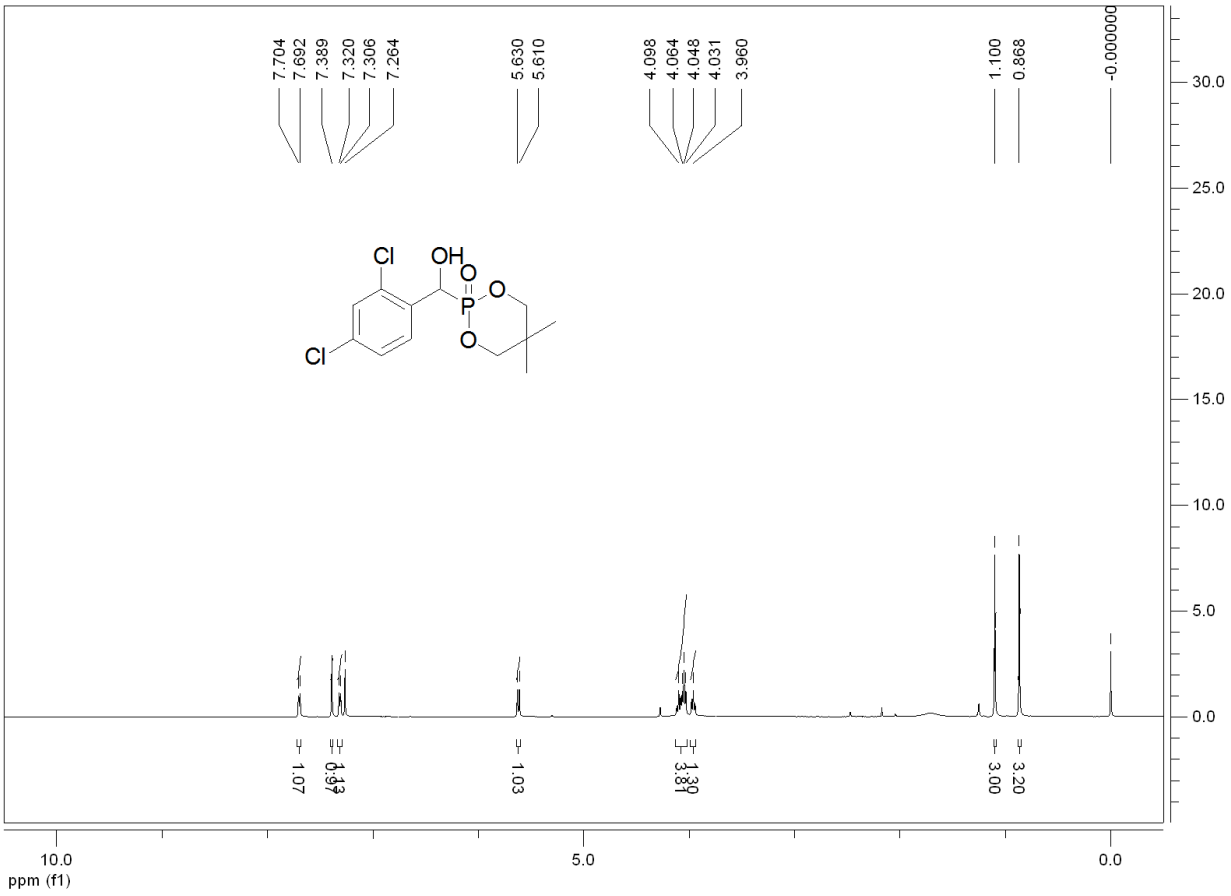
10.0
5.0
0.0
10.0
5.0
0.0
ppm (f1)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4.064
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3.960
1.100
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O
O
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O
Cl
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1.03
3.00
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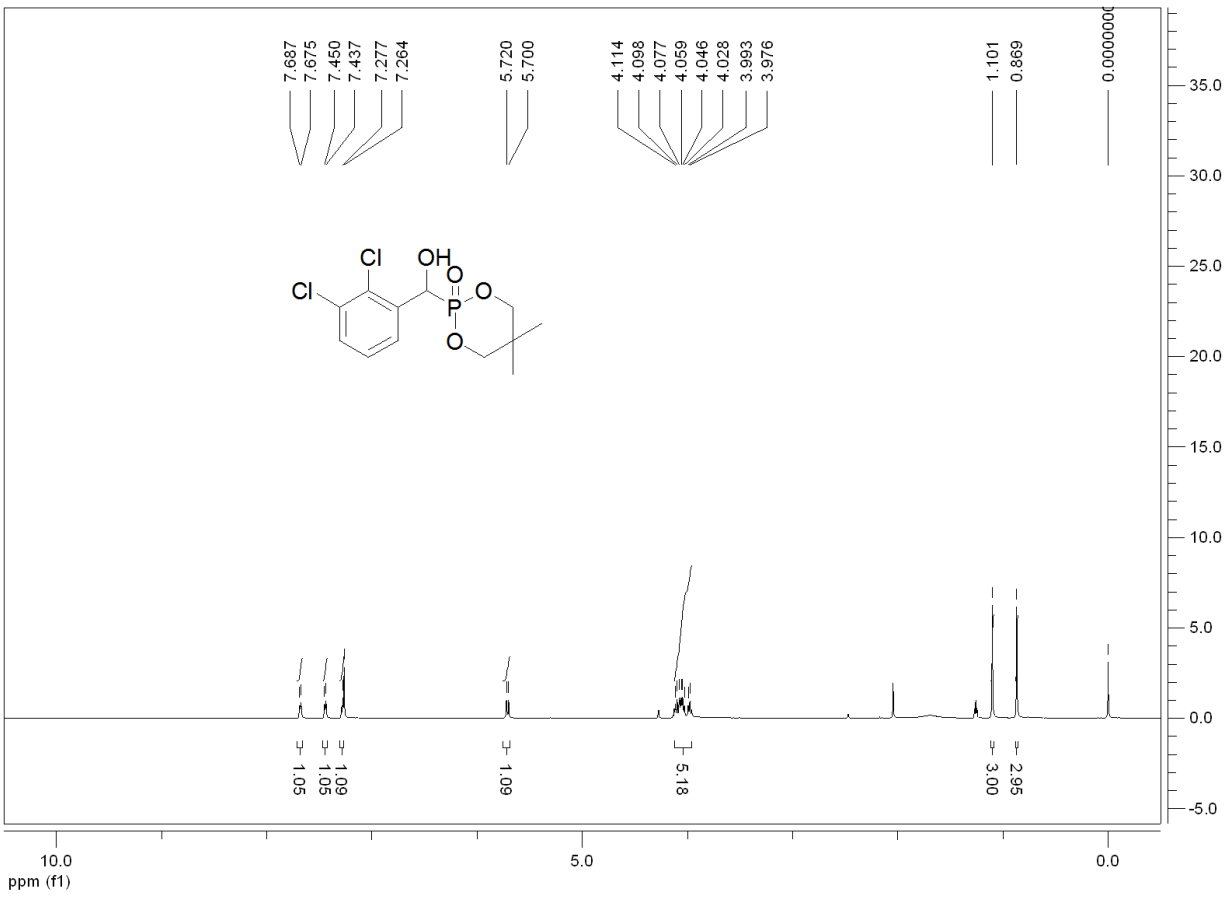
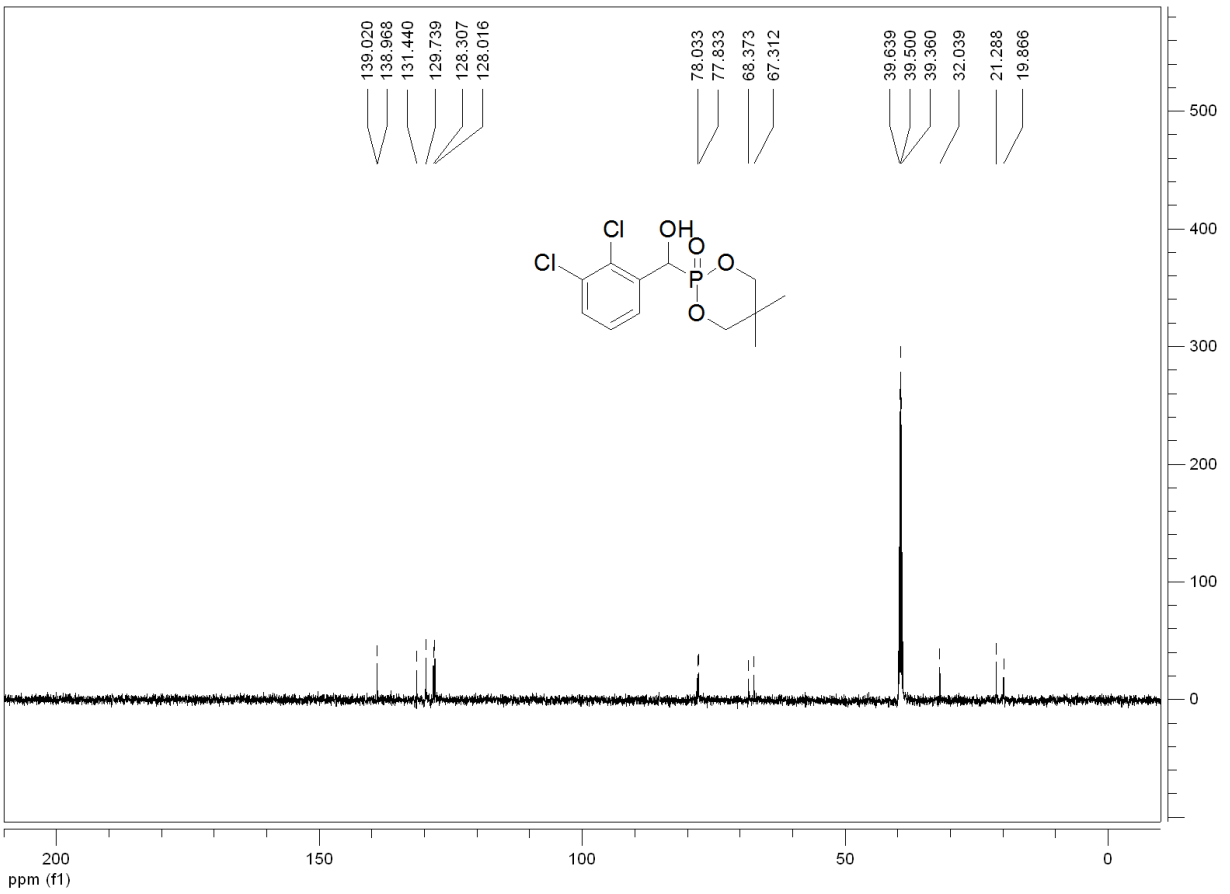
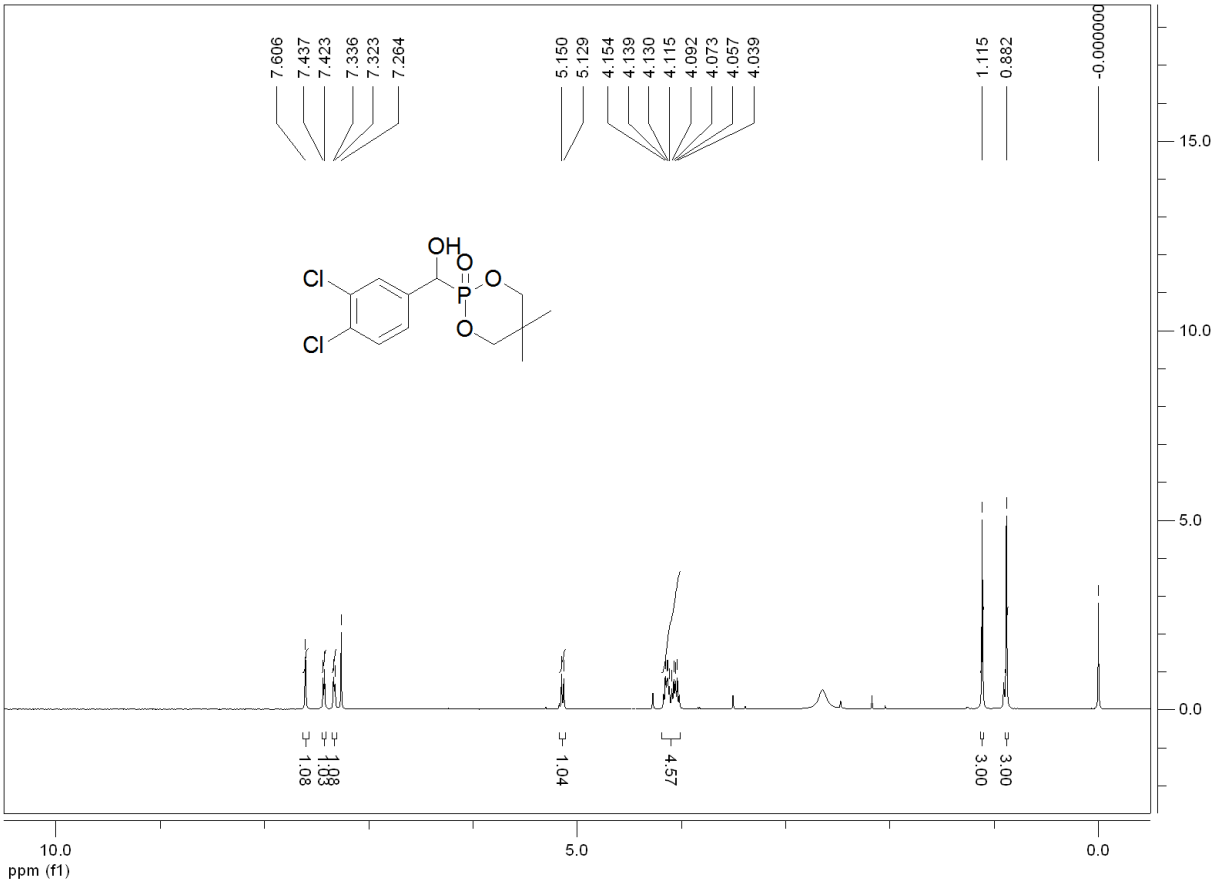
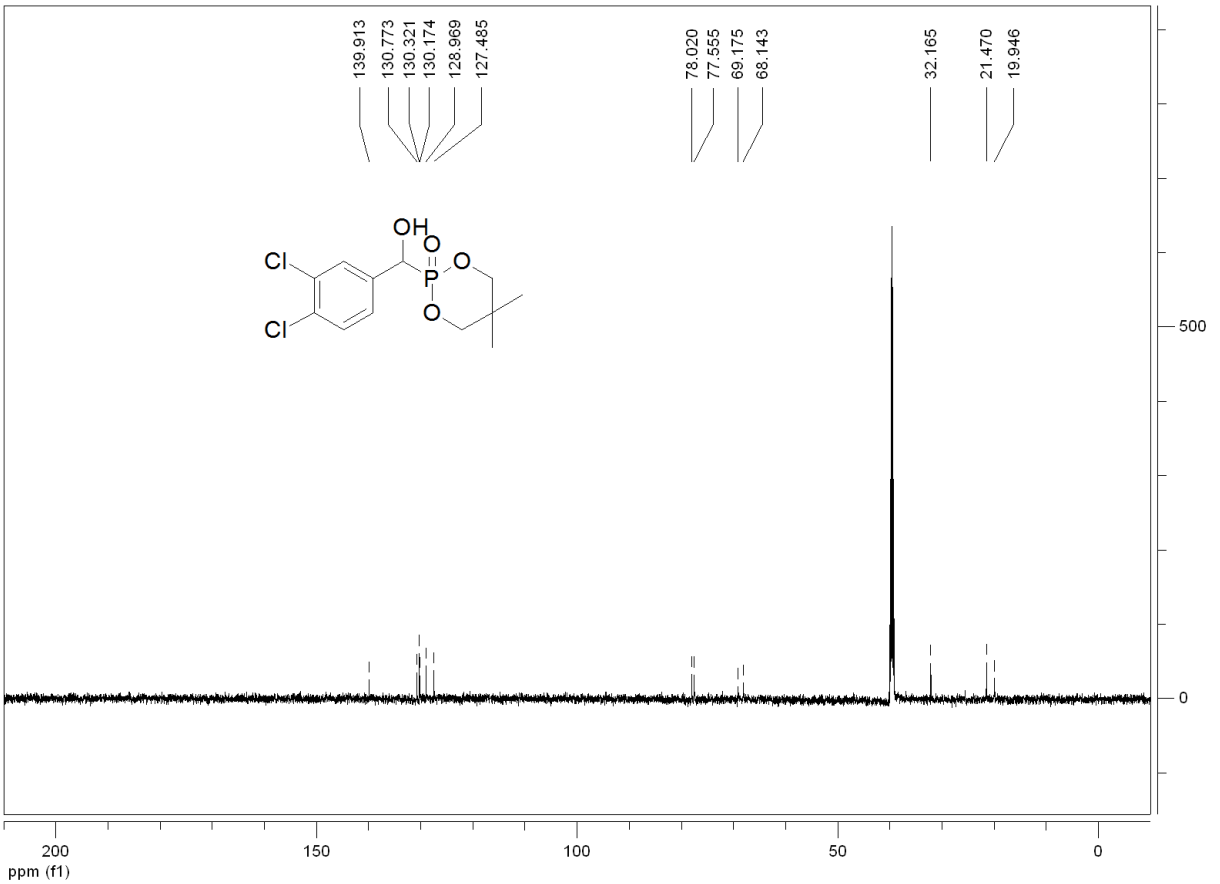
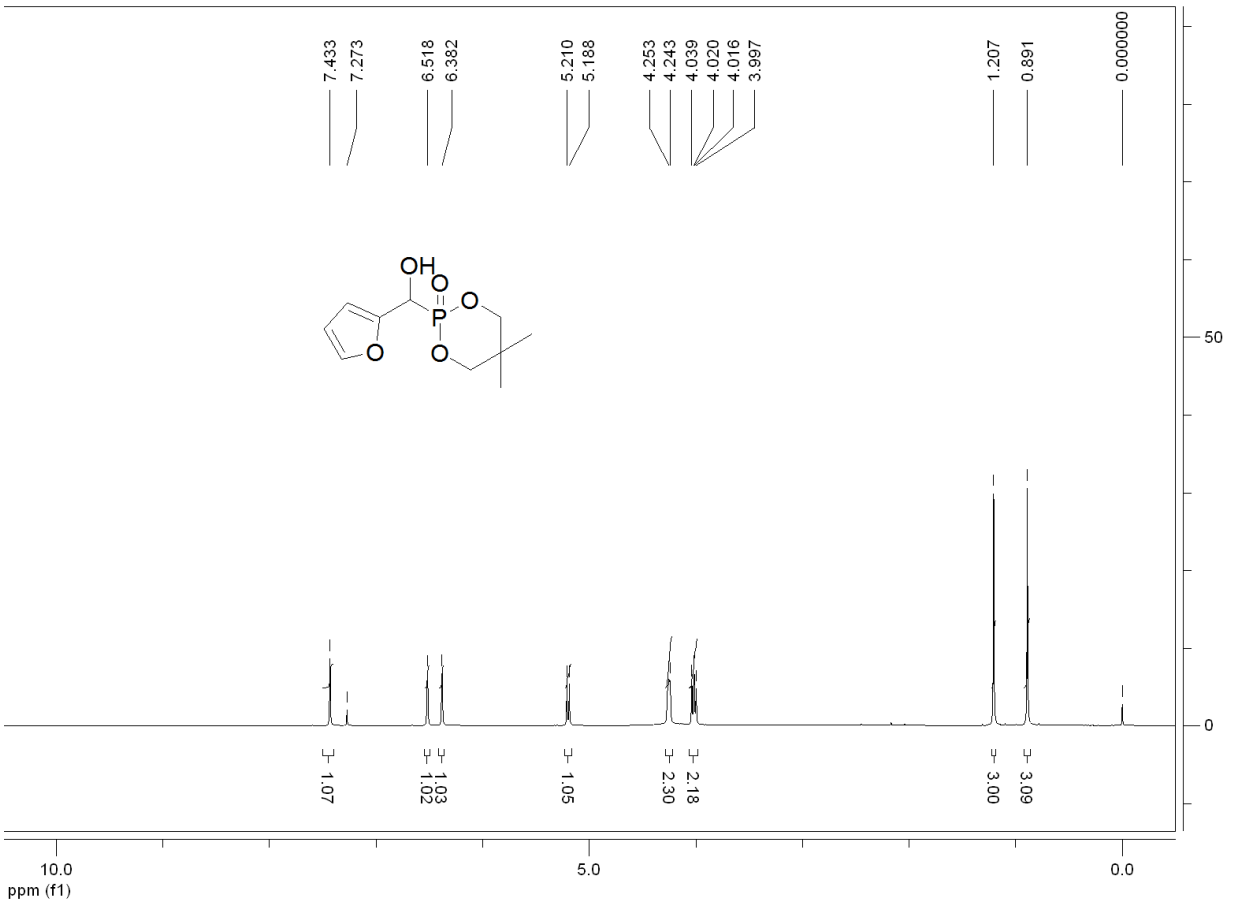
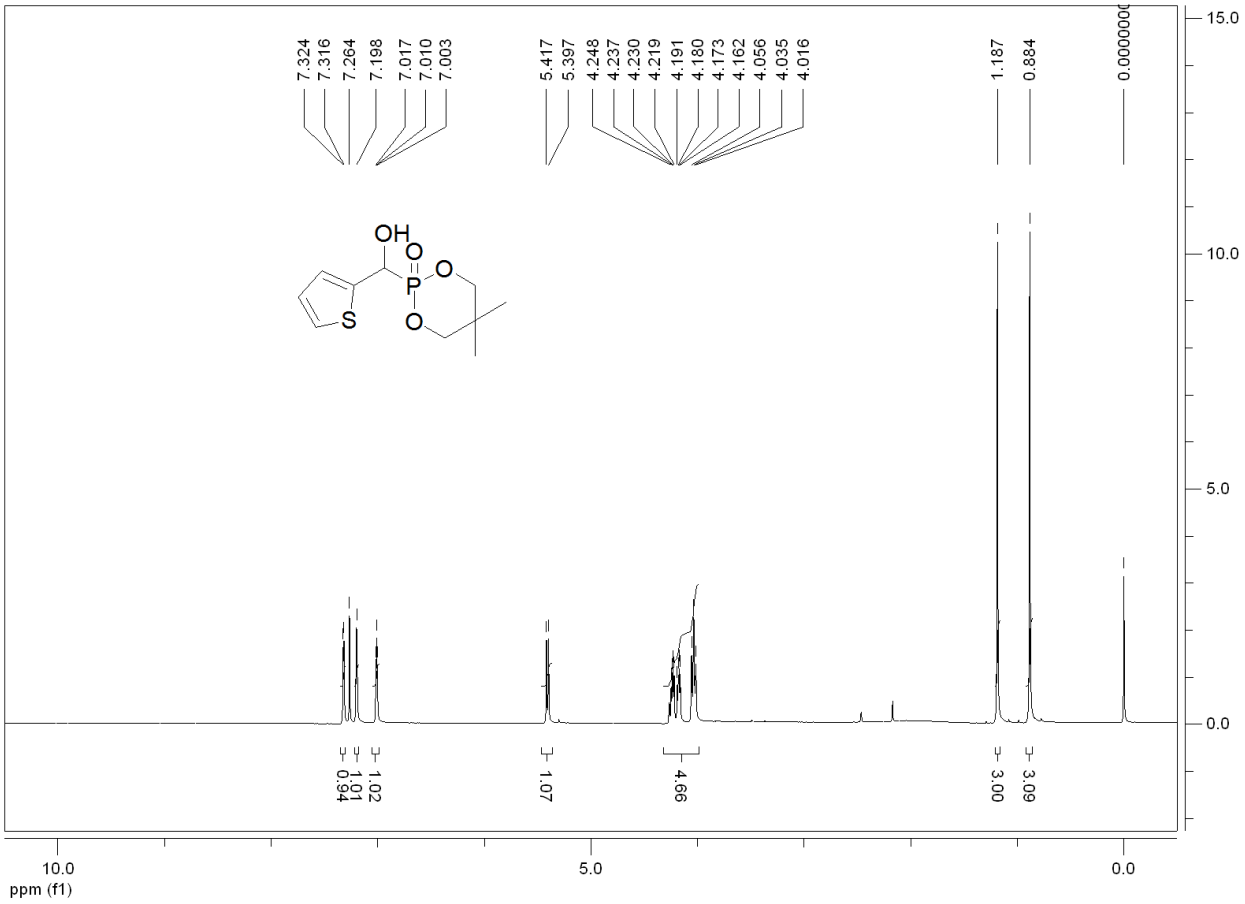


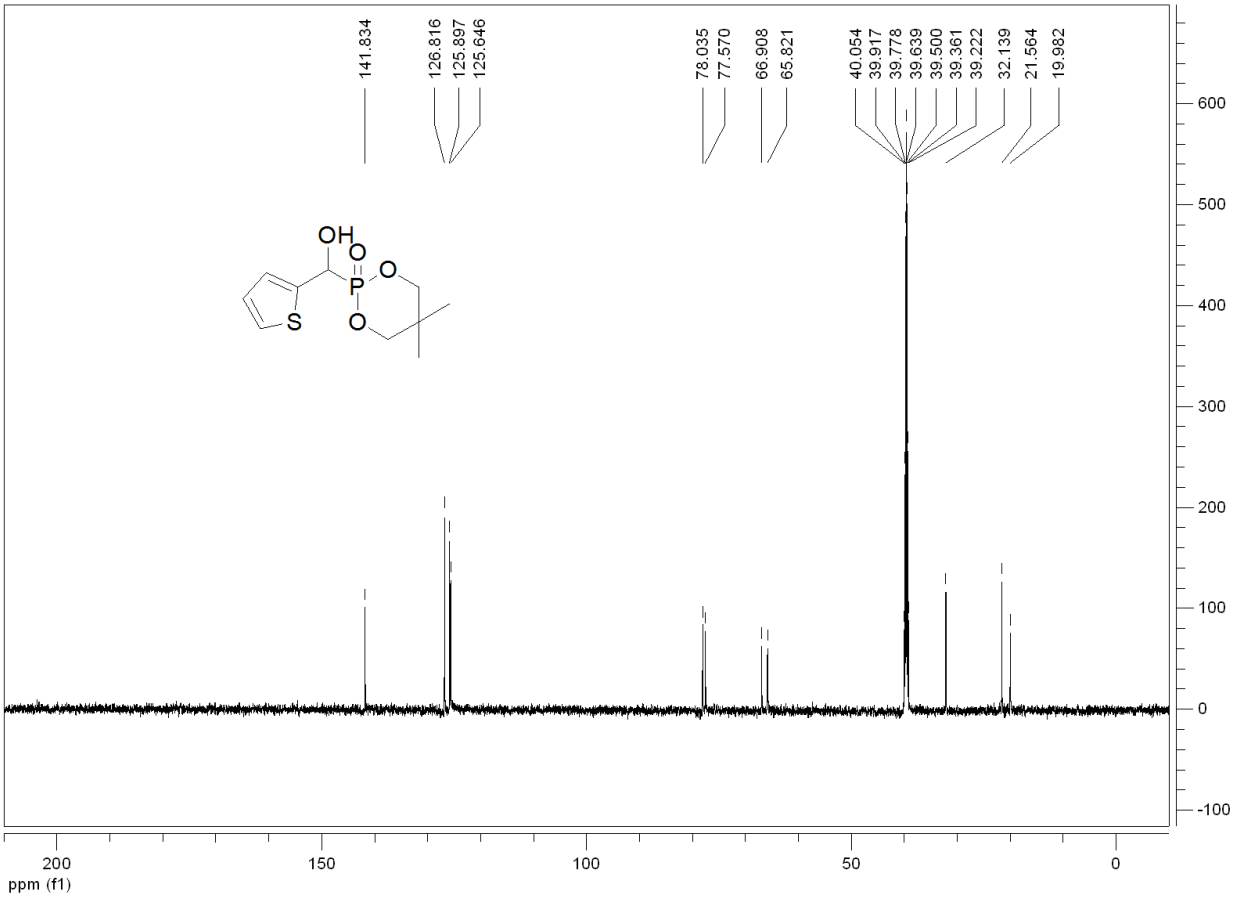


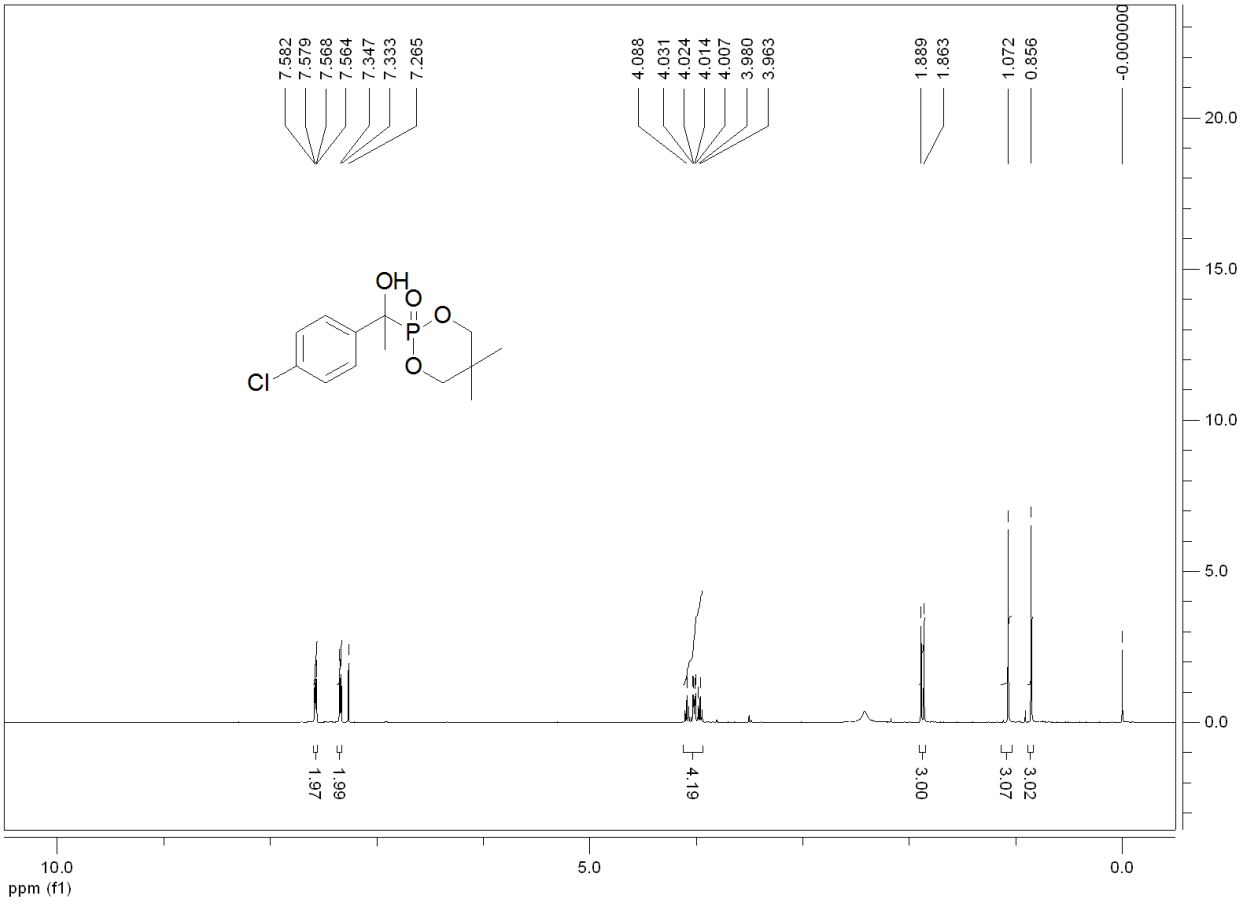


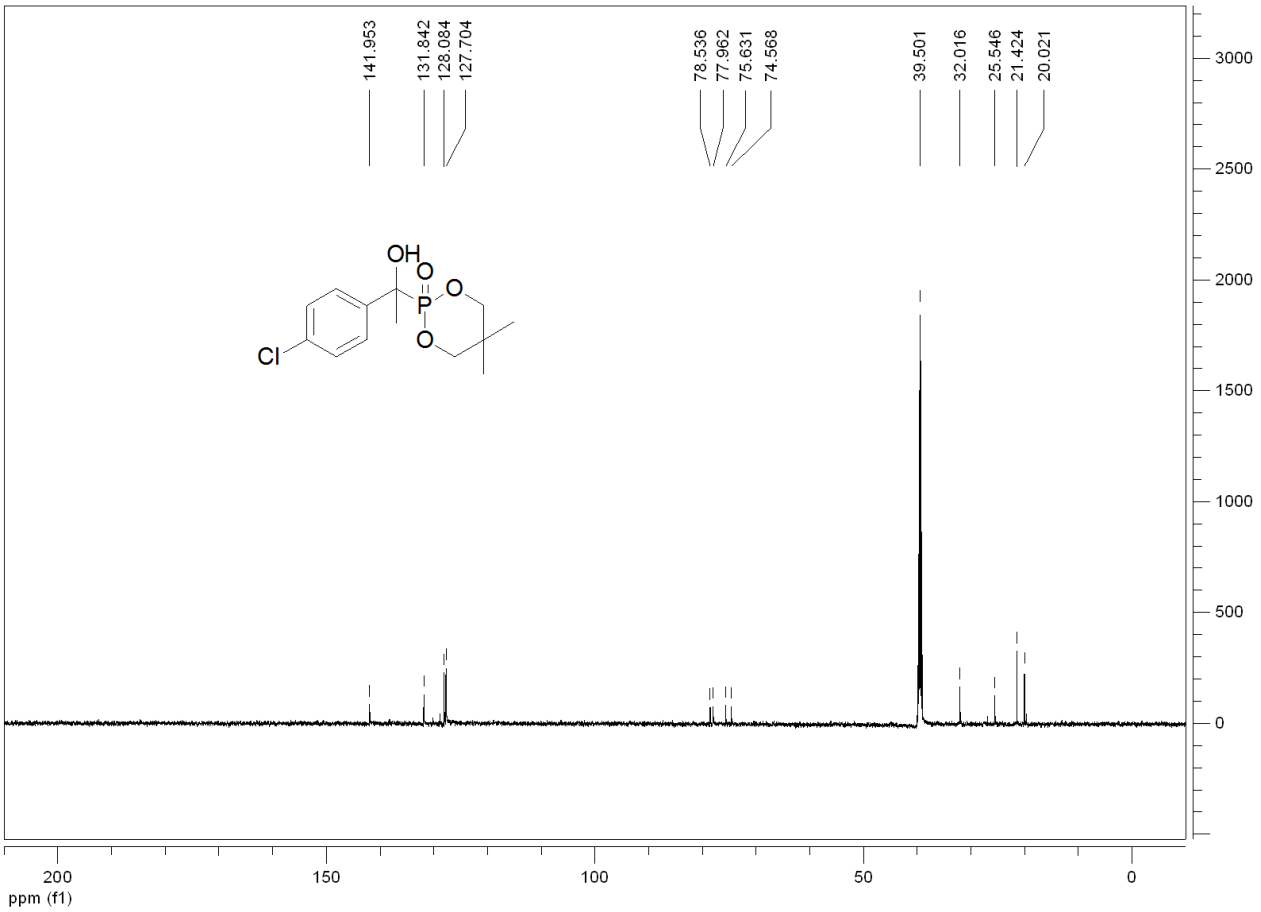


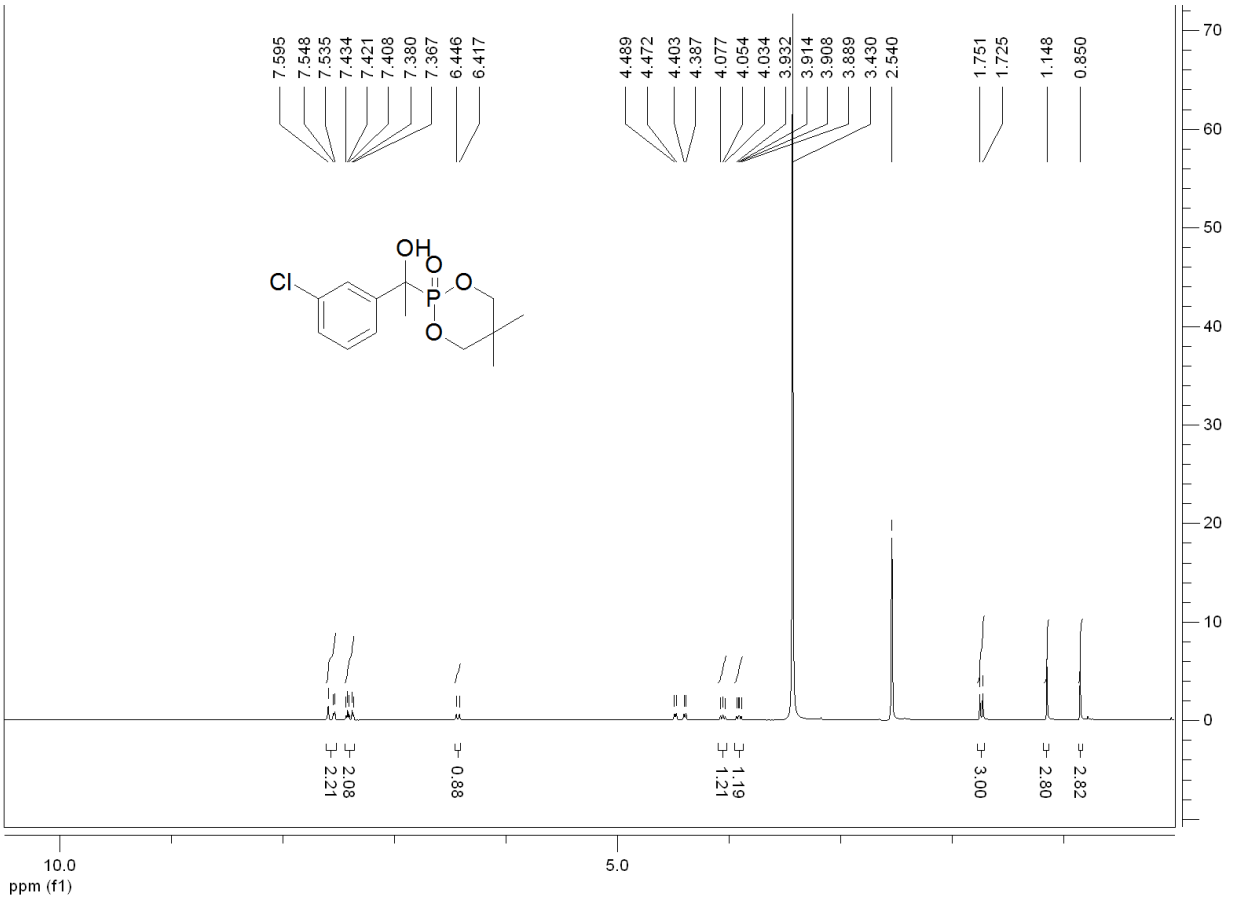


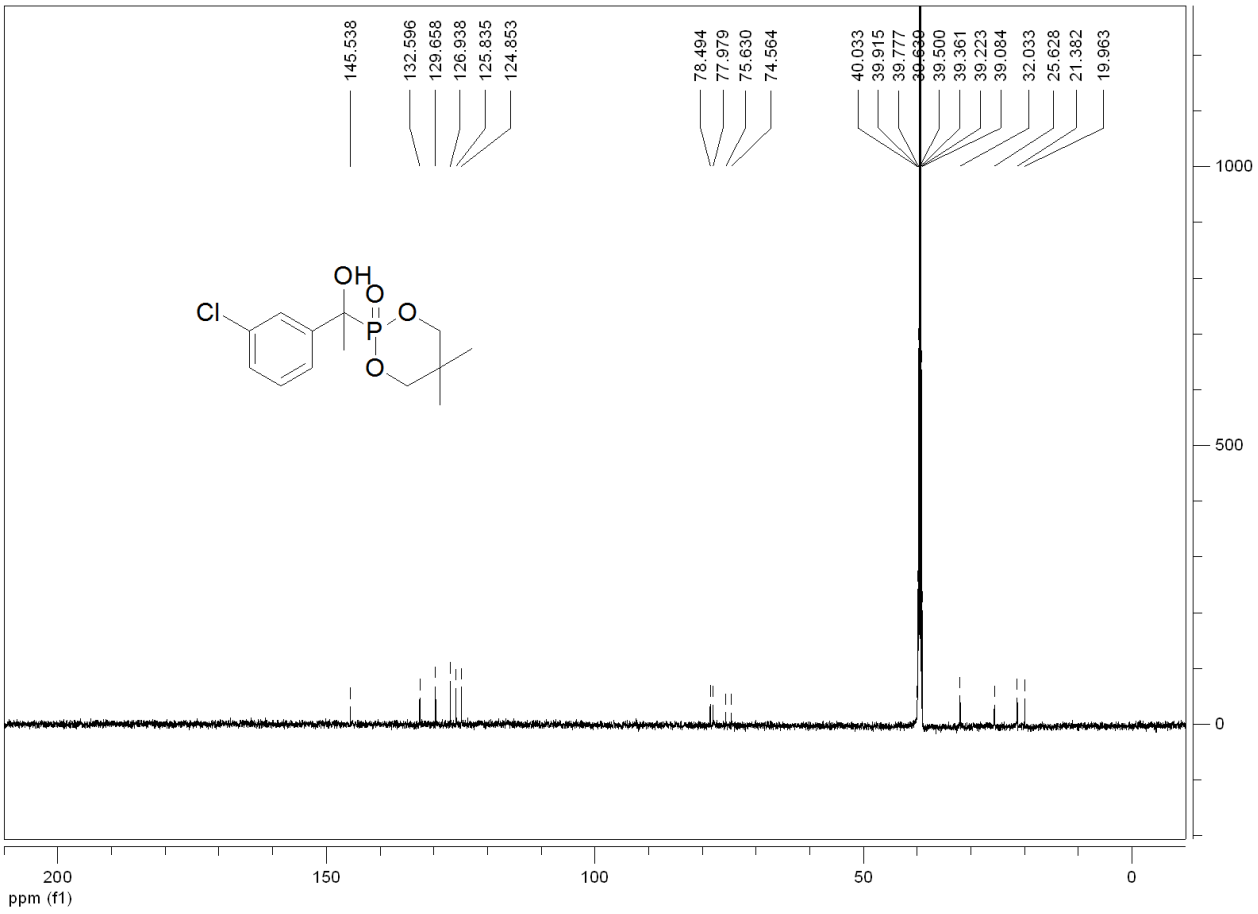


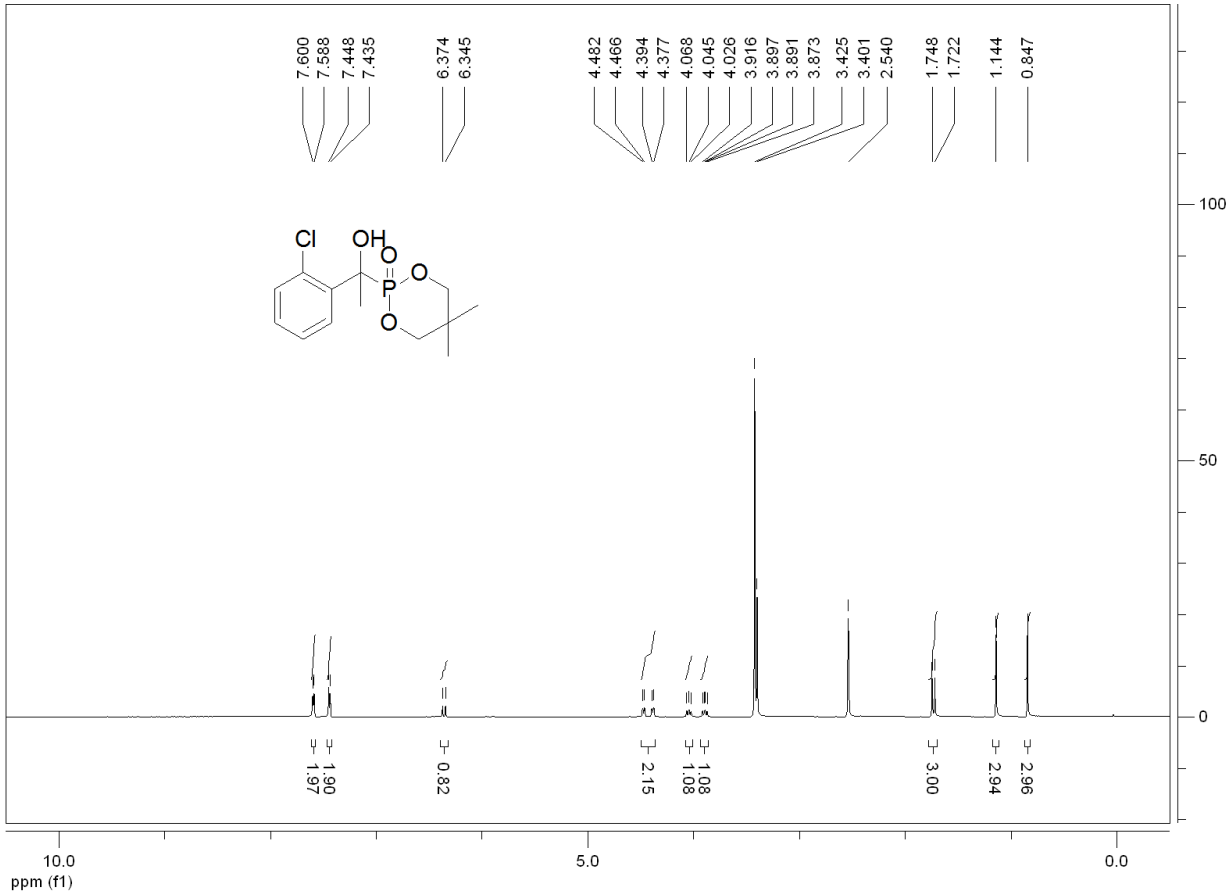


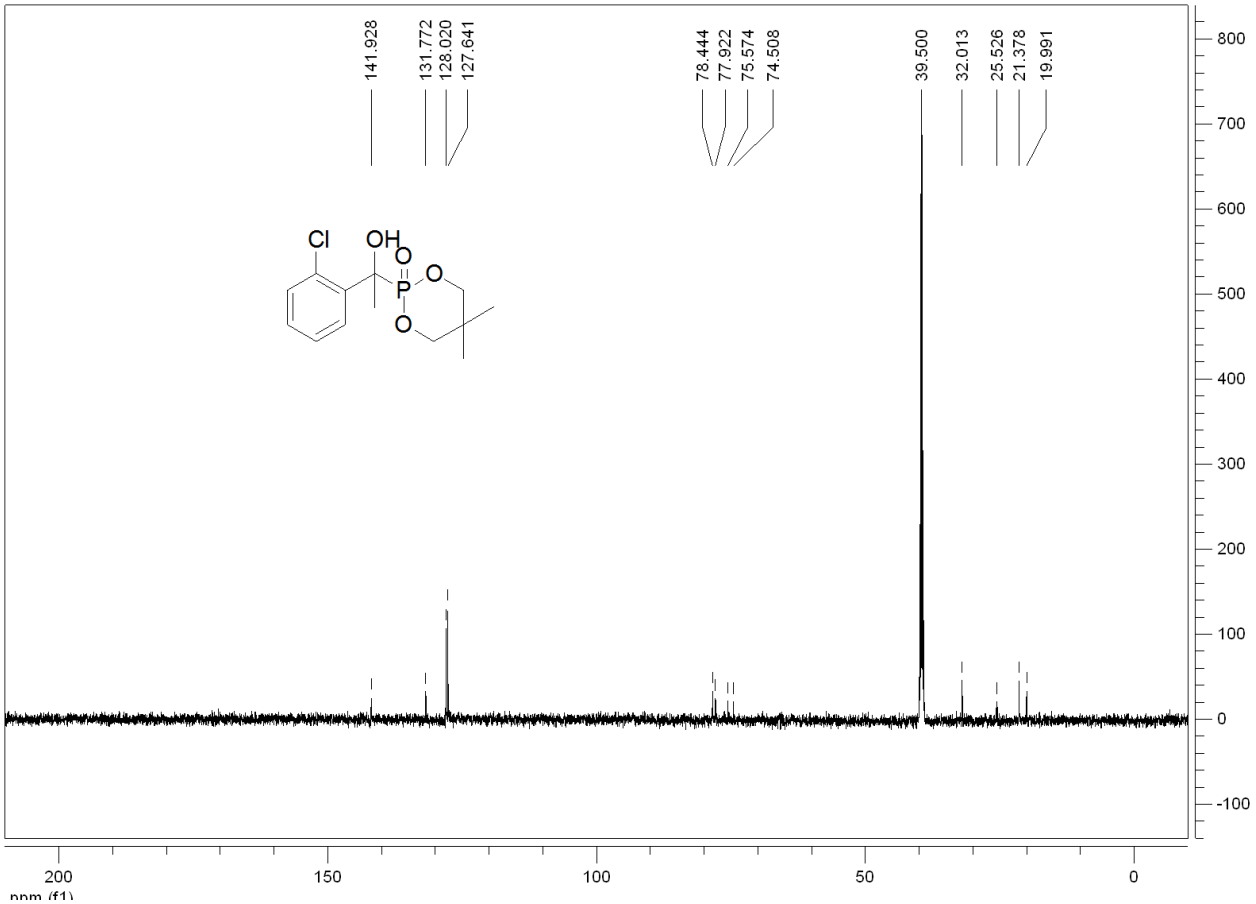


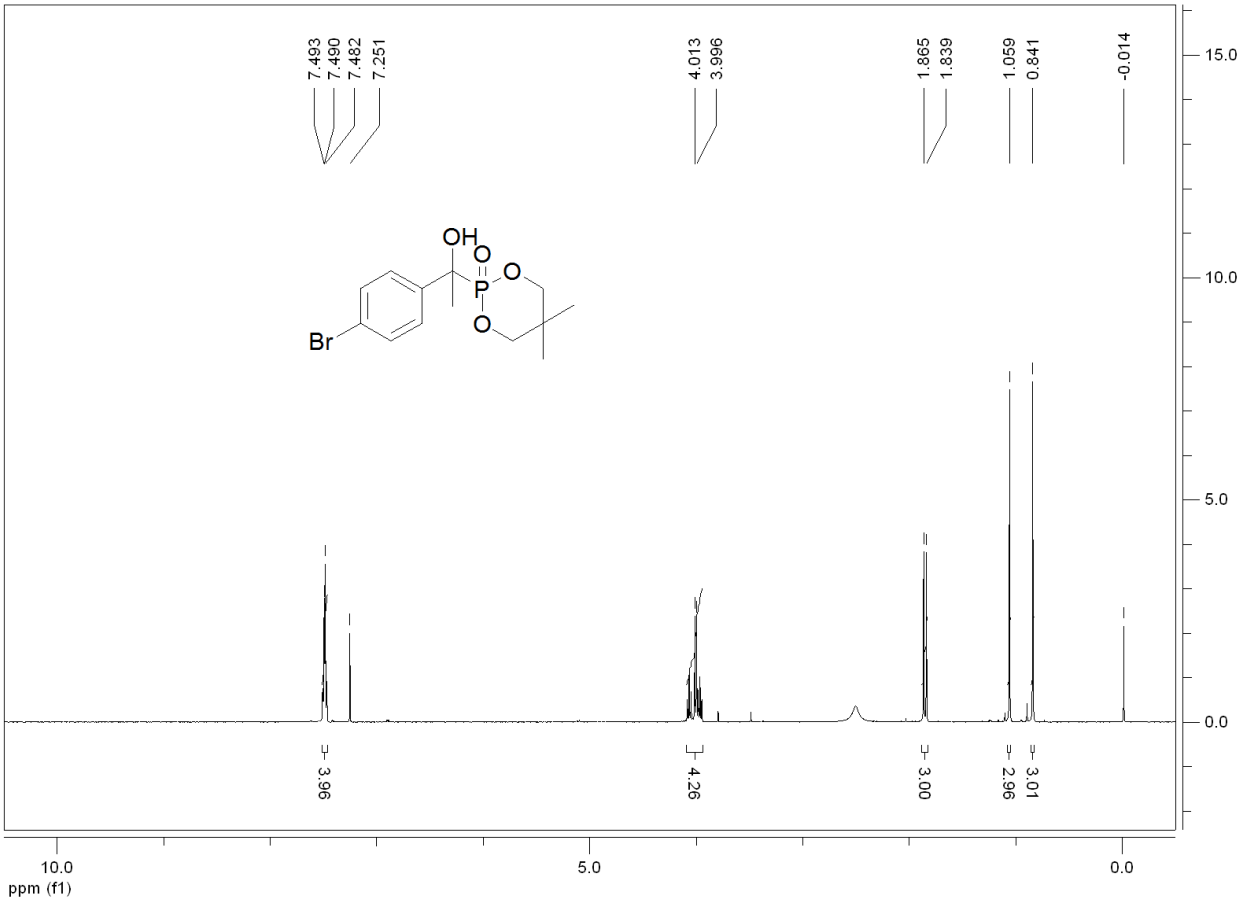


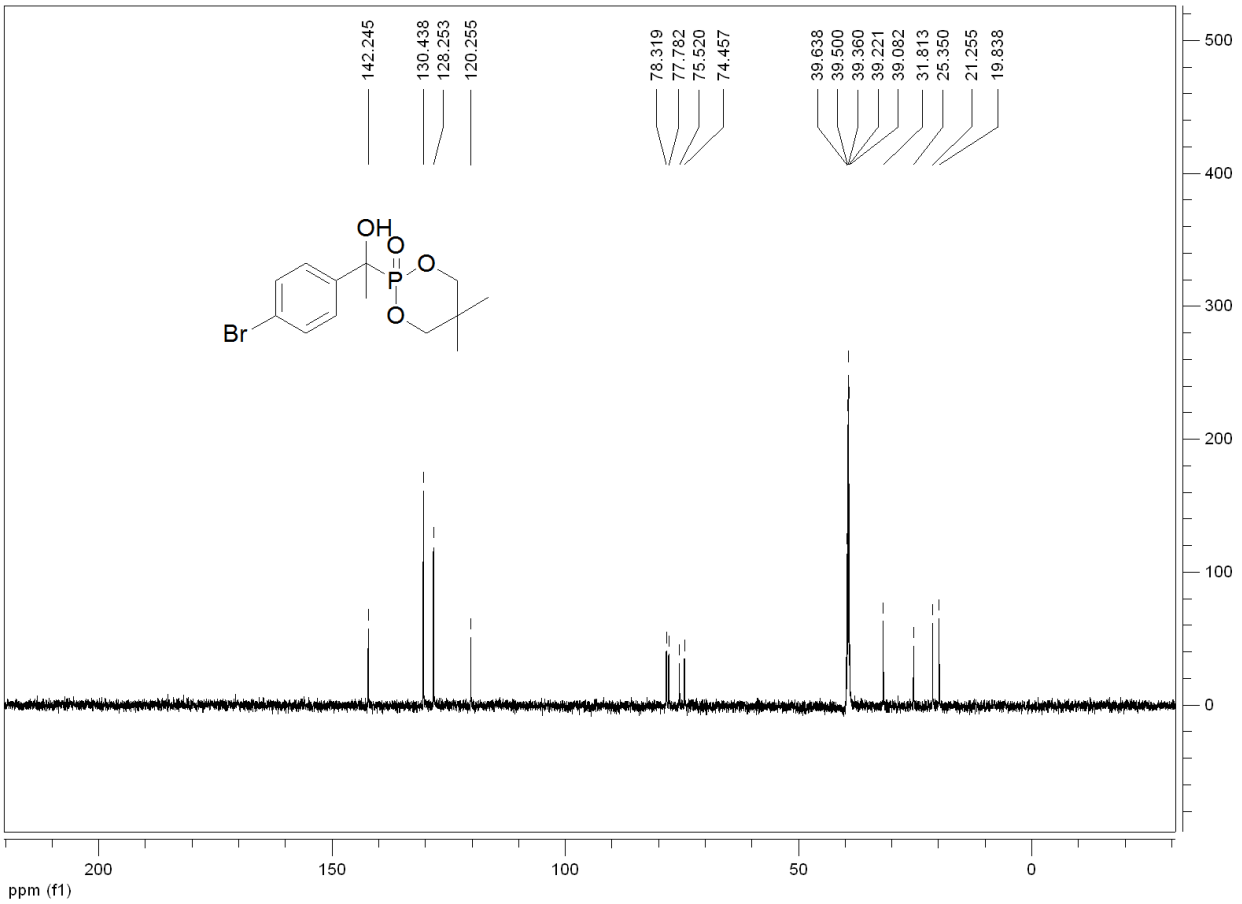


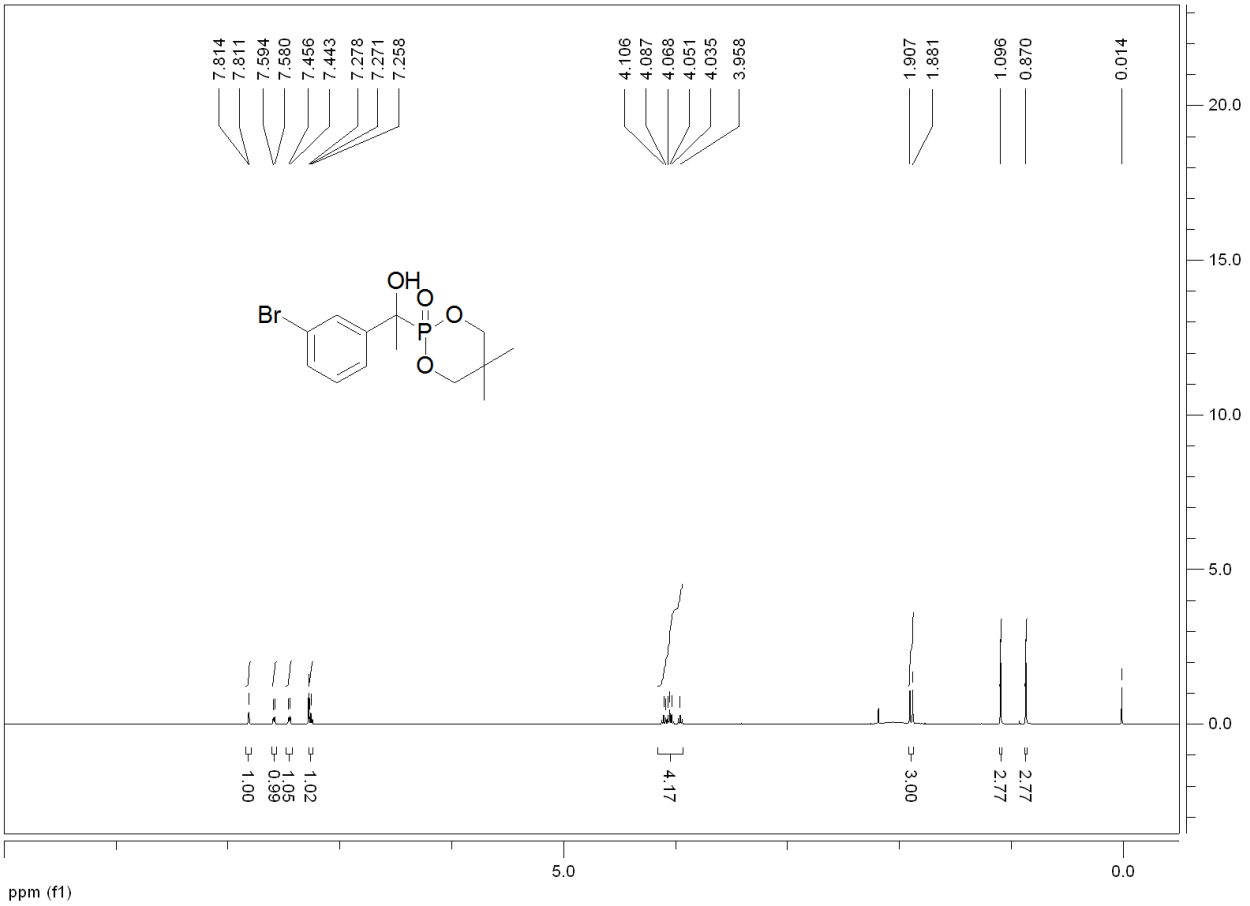


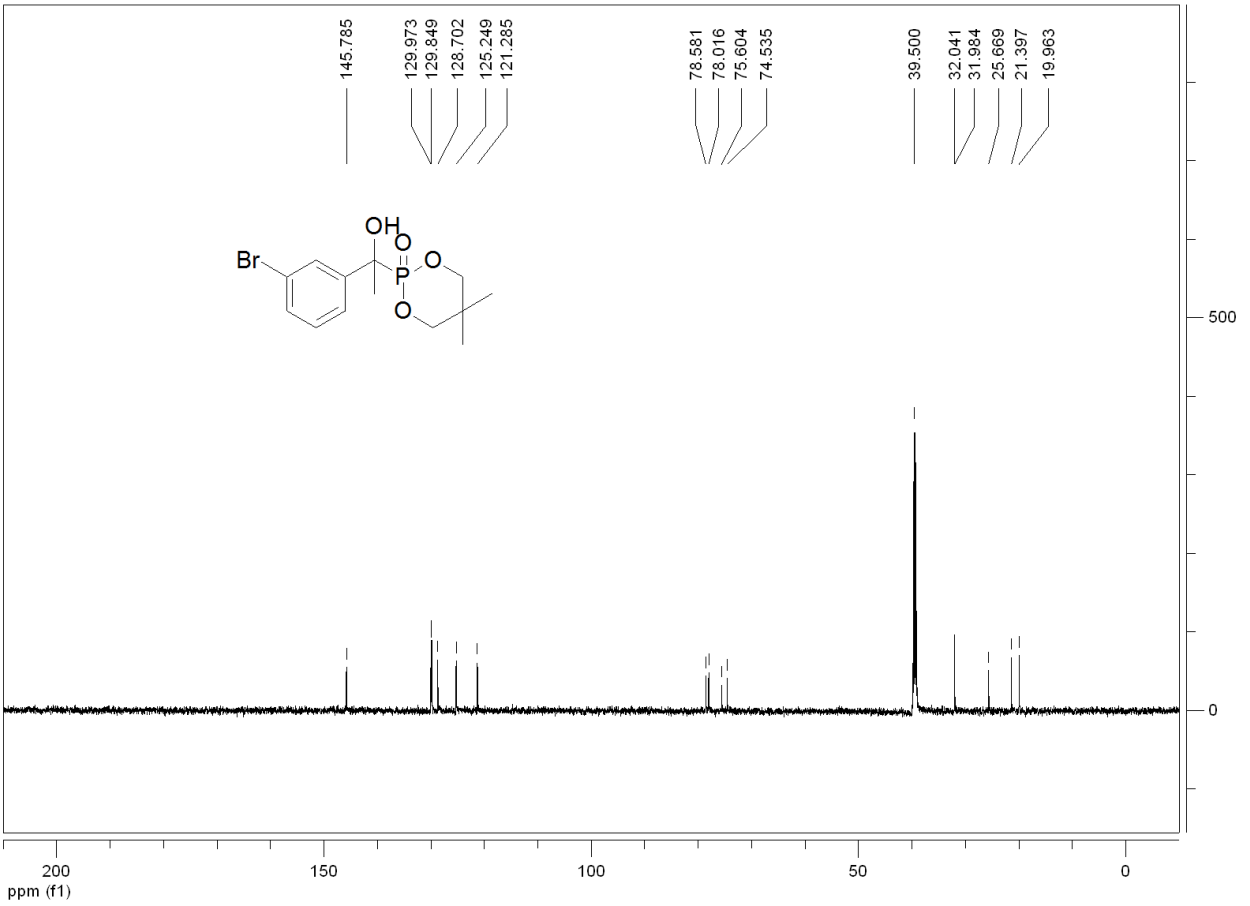


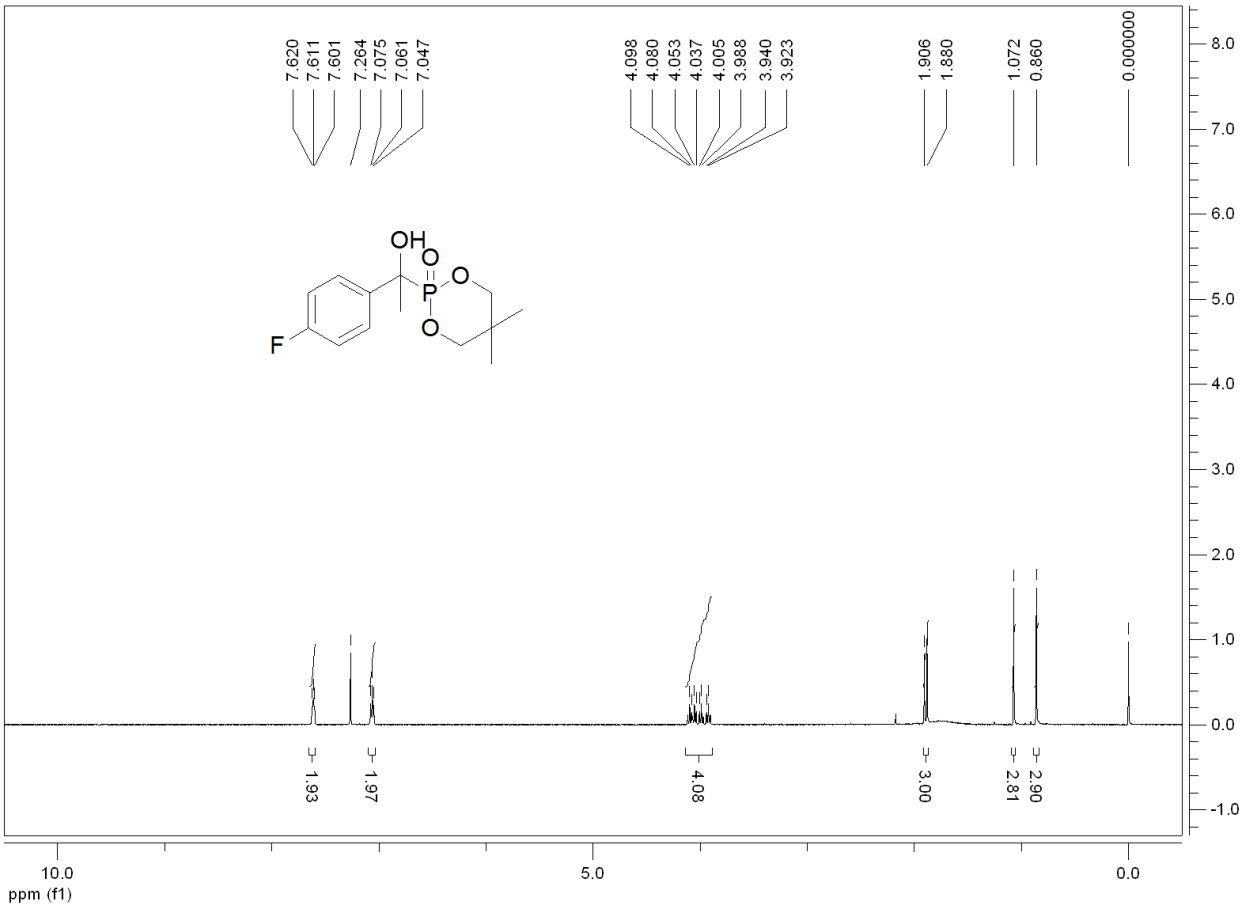


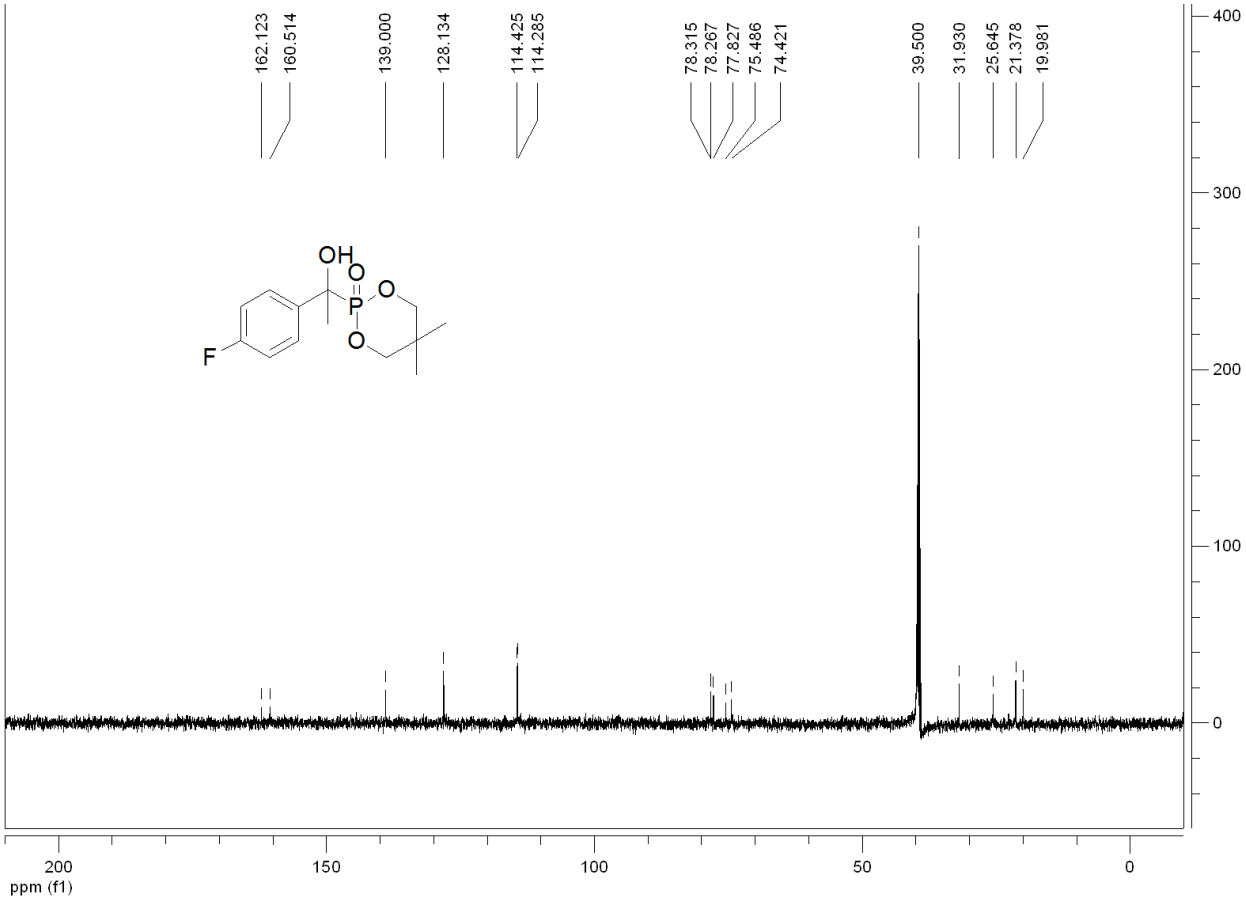


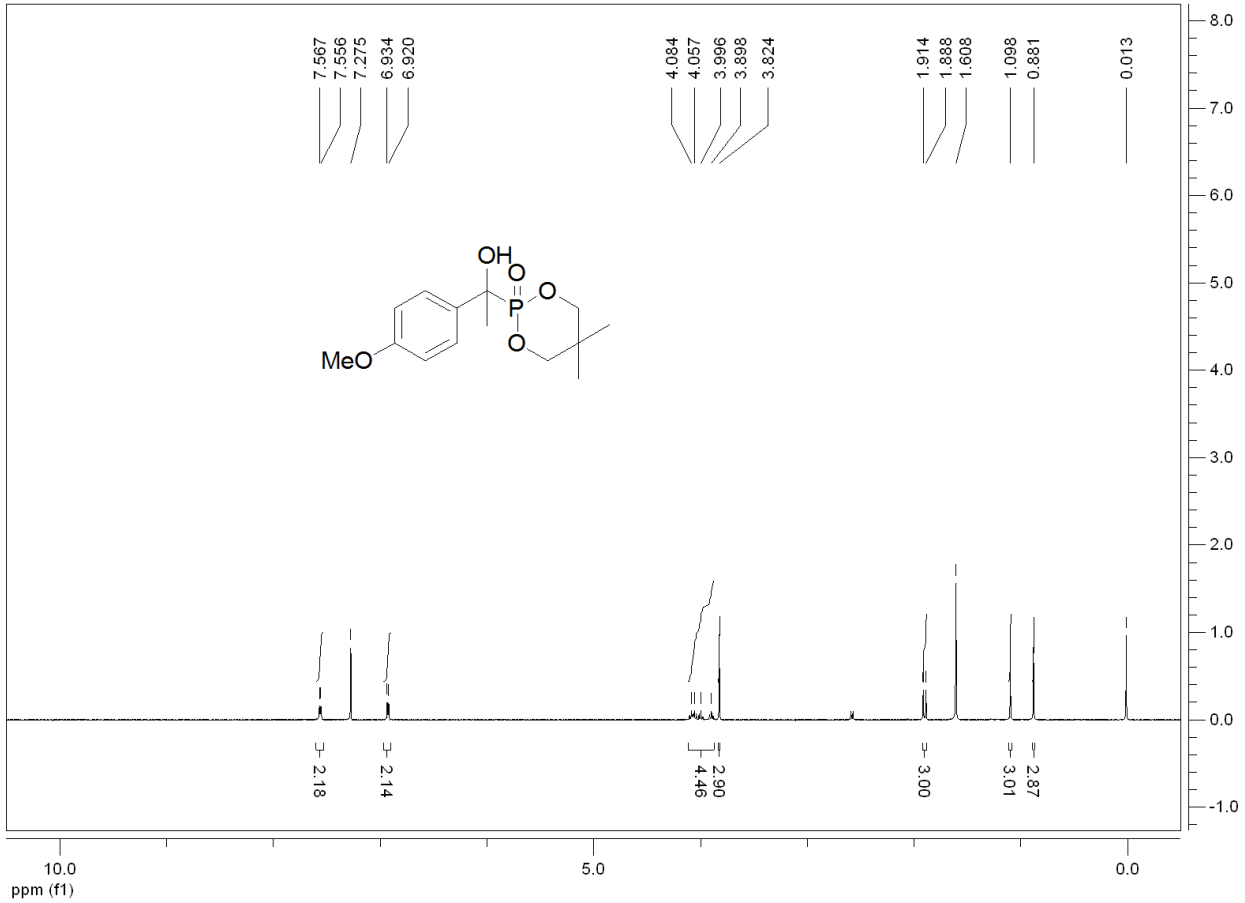


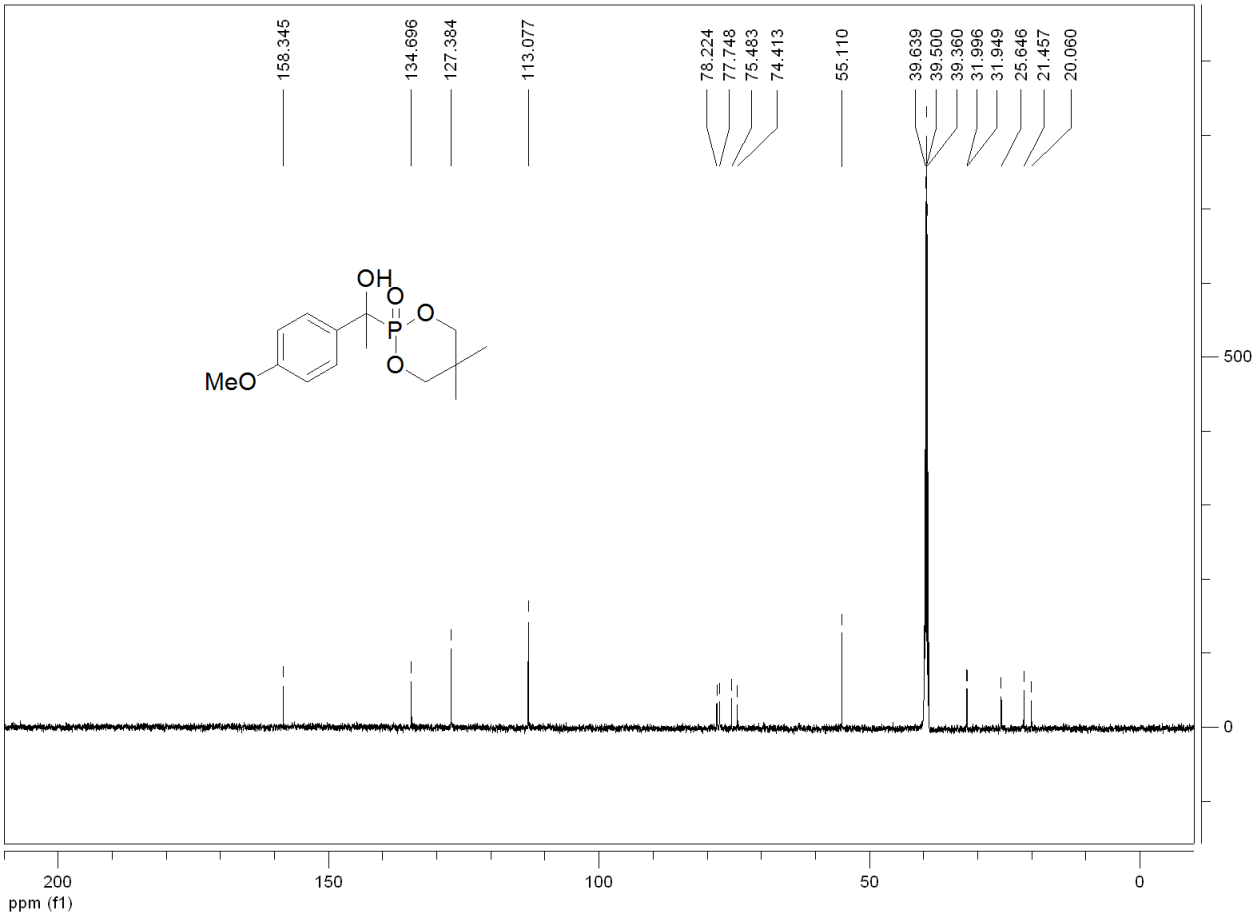


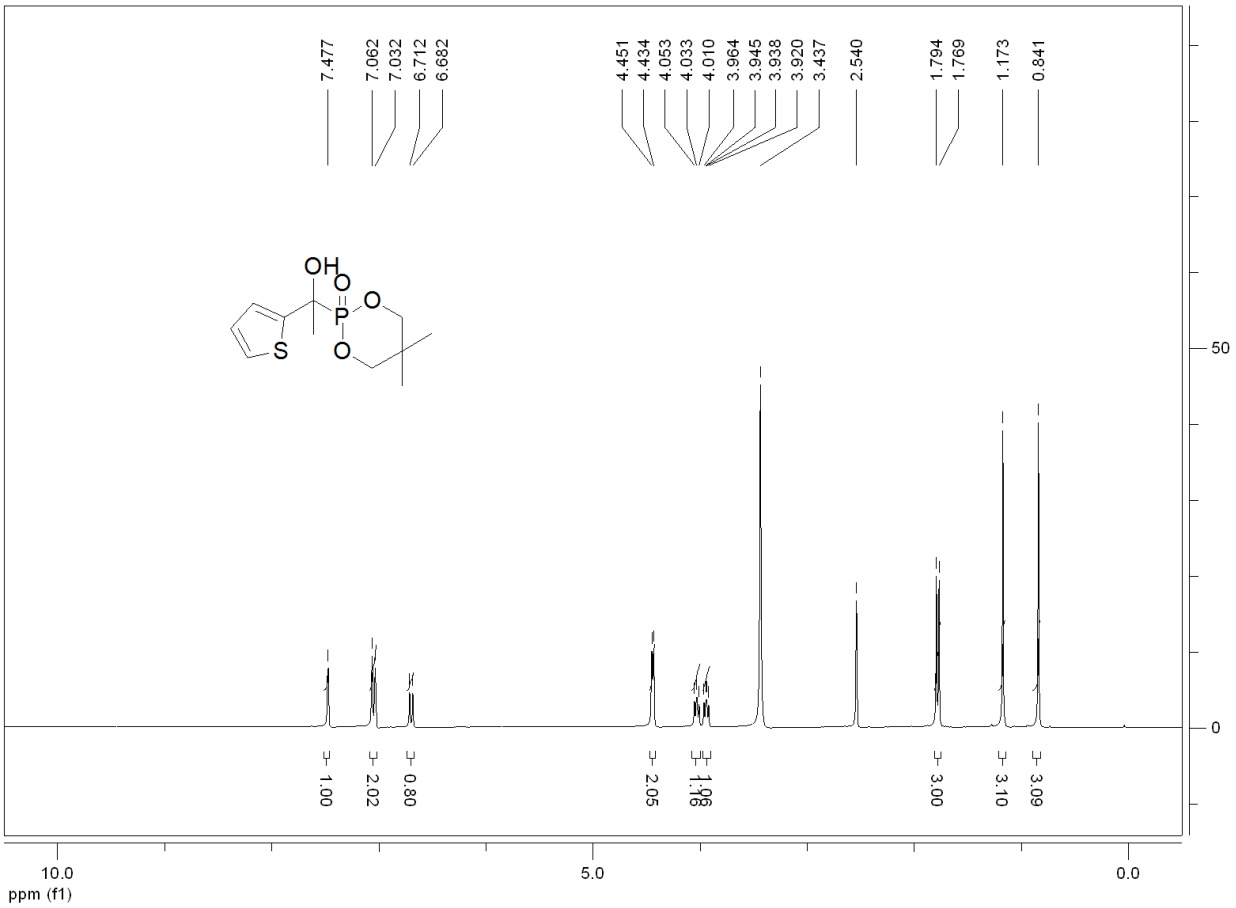


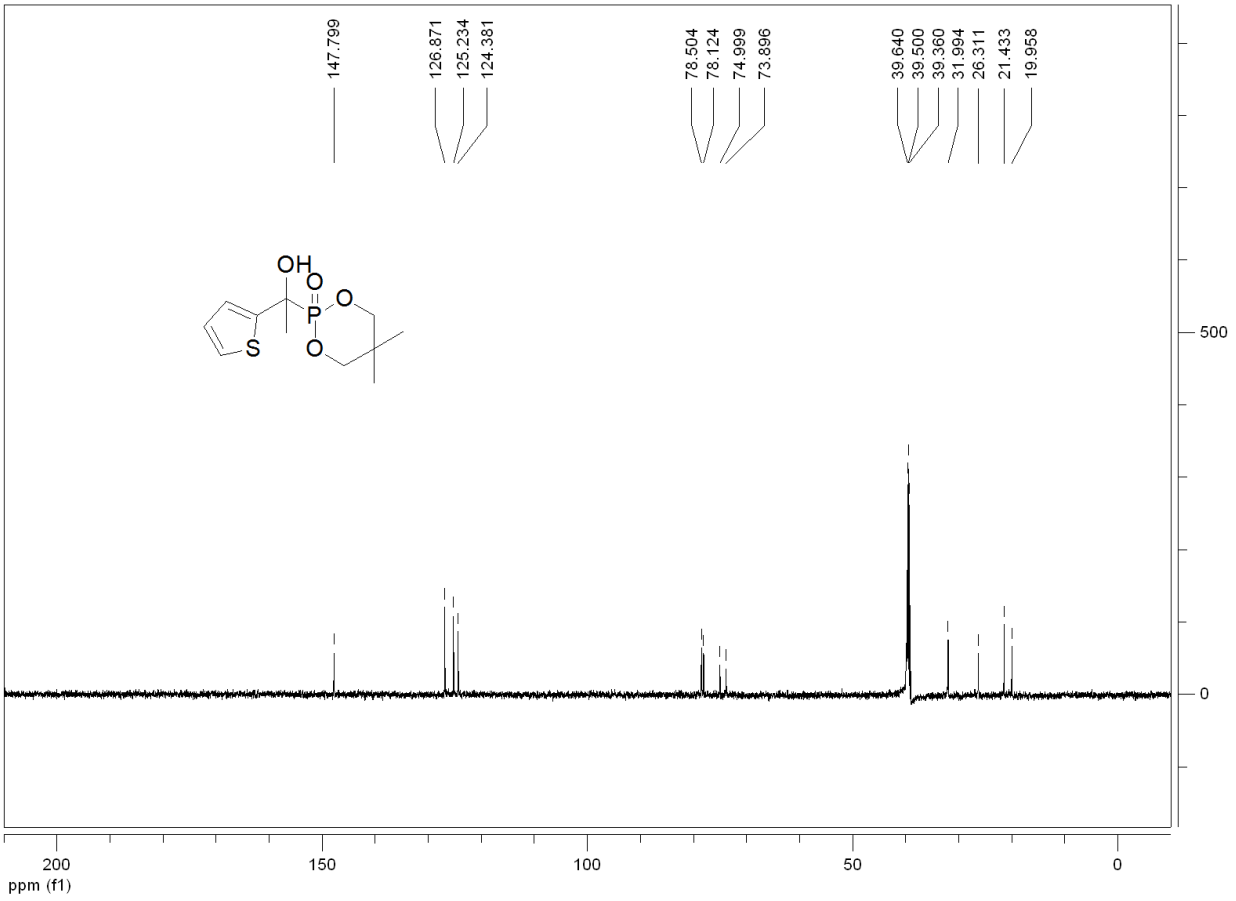












4. The Crystal Structures of 7g, 8d and (*S*)-10d

Crystal data of 7g: CCDC 806530

Crystal data

$C_{12}H_{15}Cl_2O_4P$	V = 742.08 (17) Å^3
M_r = 325.11	Z = 2
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
a = 7.0263 (9) Å	μ = 0.55 mm^{-1}
b = 9.9443 (13) Å	T = 298 K
c = 10.6462 (14) Å	0.16 × 0.12 × 0.10 mm
β = 93.975 (2)°	

Data collection

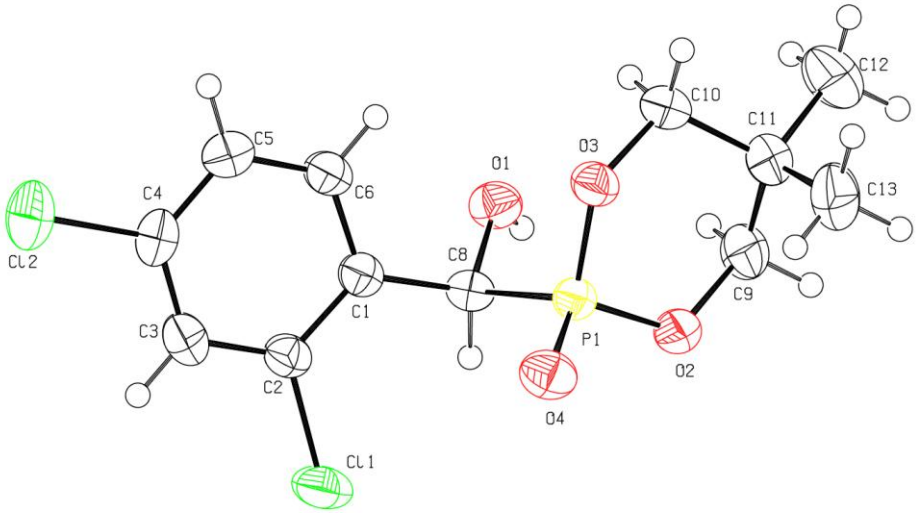
Bruker SMART APEX CCD area detector diffractometer	2478 reflections with $I > 2\sigma(I)$
4069 measured reflections	R_{int} = 0.067
2597 independent reflections	θ_{max} = 25.5°

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.042	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2)$ = 0.105	$\Delta\rho_{max}$ = 0.39 e Å^{-3}
S = 1.01	$\Delta\rho_{min}$ = −0.25 e Å^{-3}
2597 reflections	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
177 parameters	Flack parameter: −0.15 (8)
1 restraints	

Computing details

Data collection: Bruker *SMART*; cell refinement: Bruker *SMART*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*



The Crystal Structures of **7g**, showing the atom-labeling scheme for the non-H atoms and 50% probability displacement ellipsoids

Crystal data of 8d: CCDC 806531

Crystal data

$C_{13}H_{18}BrO_4P$	V = 1497.7 (4) Å^3
M_r = 349.15	Z = 4
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
a = 11.0662 (17) Å	μ = 2.86 mm^{-1}
b = 11.3149 (18) Å	T = 298 K
c = 11.9609 (19) Å	0.20 × 0.12 × 0.10 mm

Data collection

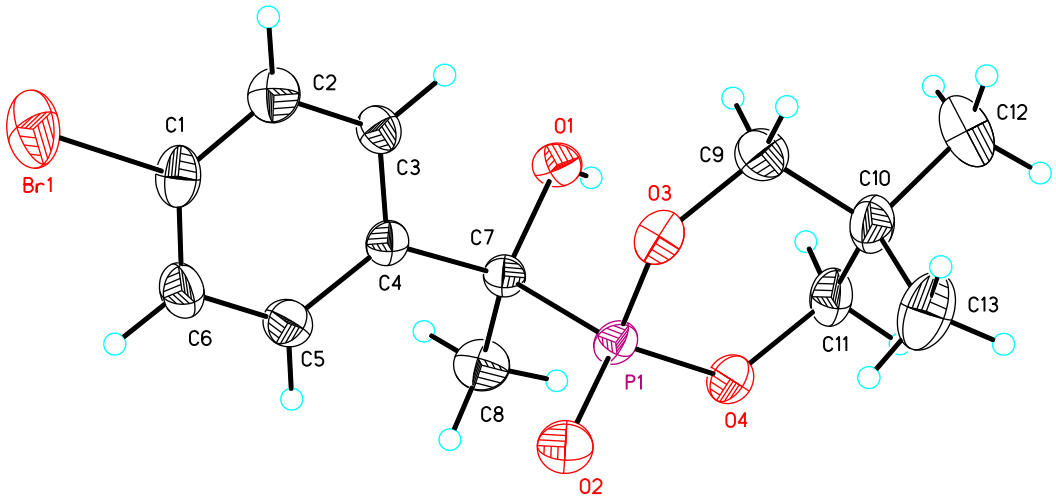
Bruker SMART APEX CCD area detector diffractometer	2691 reflections with $I > 2\sigma(I)$
10072 measured reflections	R_{int} = 0.114
3627 independent reflections	θ_{max} = 28.3°

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.045	H-atom parameters constrained
$wR(F^2)$ = 0.105	$\Delta\rho_{max}$ = 0.46 e Å^{-3}
S = 0.93	$\Delta\rho_{min}$ = −0.45 e Å^{-3}
3627 reflections	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
176 parameters	Flack parameter: −0.011 (10)
0 restraints	

Computing details

Data collection: Bruker *SMART*; cell refinement: Bruker *SMART*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*



The Crystal Structures of **8d**, showing the atom-labeling scheme for the non-H atoms and 50% probability displacement ellipsoids

Crystal data of (*S*)-10d: CCDC 806532

Crystal data

$C_{44}H_{70}Al_2Br_2Cl_4N_2O_4$	V = 5394.2 (11) Å^3
M_r = 1046.60	Z = 4
Orthorhombic, $C2_22_1$	Mo $K\alpha$ radiation
a = 12.9848 (17) Å	μ = 1.77 mm^{-1}
b = 17.0304 (17) Å	T = 298 K
c = 24.393 (3) Å	0.26 × 0.20 × 0.10 mm

Data collection

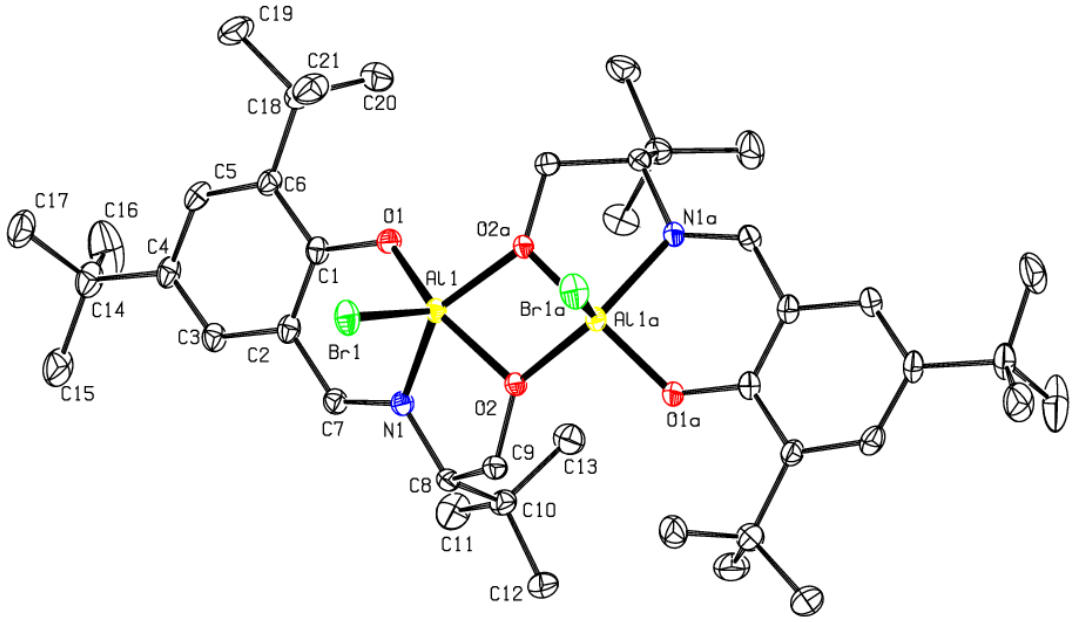
Bruker SMART APEX CCD area detector diffractometer	6666 independent reflections
Absorption correction: ψ scan ?	4745 reflections with $I > 2\sigma(I)$
T_{min} = 0.656, T_{max} = 0.843	R_{int} = 0.083
18710 measured reflections	θ_{max} = 28.3°

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.042	H-atom parameters constrained
$wR(F^2)$ = 0.100	$\Delta\rho_{max}$ = 0.55 e Å^{-3}
S = 0.93	$\Delta\rho_{min}$ = −0.25 e Å^{-3}
6666 reflections	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
271 parameters	Flack parameter: 0.004 (8)
0 restraints	

Computing details

Data collection: Bruker *SMART*; cell refinement: Bruker *SMART*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*



The Crystal Structures of **(*S*)-10d**, showing the atom-labeling scheme for the non-H atoms and 50% probability displacement ellipsoids