Supporting Information

Temporary Phosphate Tethers: A Metathesis Strategy to Differentiated Polyol Subunits

Joshua D. Waetzig and Paul R. Hanson*
Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive,
Lawrence, KS 66045-7582 *phanson@KU.edu*

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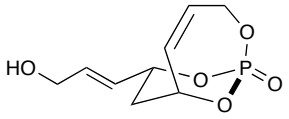
General Experimental Methods

All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon atmosphere using standard gastight syringes, cannulaes, and septa. Stirring was achieved with oven-dried magnetic stir bars. Et_2O, toluene, THF and CH_2Cl_2 were purified by passage through the Solv-Tek purification system employing activated Al_2O_3 (Grubbs, R.H.; Rosen, R.K.; Timmers, F.J.; *Organometallics* **1996**, *15*, 1518-1520). Et_3N was purified by passage over basic alumina and stored over KOH. Butyl Lithium was purchased from Aldrich and titrated prior to use. Grubb's first and second-generation as well as the Hoveyda-Grubb's olefin metathesis catalysts were acquired from Materia and used without further purification. Glycidol ether was acquired from Daiso Co., Ltd., Fine Chemical Department and used without further purifiction. Flash column chromatography was performed with Merck silica gel (EM-9385-9, 230-400 mesh). Thin layer chromatography was performed on silica gel 60F254 plates (EM-5717, Merck). Deuterated solvents were purchased from Cambridge Isotope Isotope laboratories. 1H, 13C and 31P NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz, 100 MHz, and 162 MHz respectively; or a Bruker Avance operating at 500 MHz and 125 MHz respectively. High-resolution mass spectrometry (HRMS) and FAB spectra were obtained on a VG Instrument ZAB double-focusing mass spectrometer.

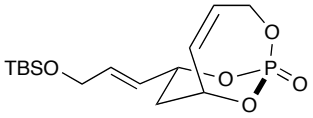
General Procedure for Cross Metathesis of Type I Olefins: A flask or pressure tube containing **5** (20 mg, 0.099 mmol) was charged with CH_2Cl_2 (2 mL) that had been degassed 15 minutes with argon. The Type I olefin partner (1.1 equiv. relative to compound **5**) followed by Hoveyda-Grubbs II catalyst (6.2 mg, 0.009 mmol) were added and the reaction mixture was refluxed for 3-6 hours. Upon completion (monitored by TLC) the reaction was cooled to rt and concentrated under reduced pressure.

2,9,10-Trioxa-1-phosphabicyclo[4.3.1]dec-4-ene, 8-*E*-(3-hydroxy-propenyl)-, 1-oxide, (1R,6R, 8R) : 9



Purification via flash chromatography (9:1 EtOAc/MeOH) supplied 19 mg (86% yield) of **9** as a viscous oil. $[\propto]_D$ -78.83 (c = 0.60, CH_2Cl_2); IR (neat) 3402, 2923, 2358, 1286, 1064, 973 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.92-6.03 (m, 2H), 5.72 (ddd, J_{HH} = 15.48, 3.81, 1.52 Hz, 1H), 5.55 (ddd, J_{HH} = 11.83, 3.63, 2.74 Hz, 1H), 5.10-5.19 (m, 1H), 5.01 (dd, J_{HH} = 11.78, 5.58 Hz, 1H), 4.91-4.98 (m, 1H), 4.38 (ddd, J = 27.78, 14.79, 6.71 Hz, 1H), 4.14 (d, J_{HH} = 4.32 Hz, 2H), 2.20 (ddd, J_{HH} = 18.28, 12.16, 6.21 Hz, 1H), 1.73 (d, J_{HH} = 14.70 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.6, 130.1, 128.5, 127.2 (d, J_{CP} = 10.3 Hz), 77.6, 76.4 (d, J_{CP} = 6.1 Hz), 63.5 (d, J_{CP} = 6.4 Hz), 62.5, 35.6 (d, J_{CP} = 5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.70; Exact Mass: calculate for $C_9H_{13}O_5P$ $(M+Na)^+$ 255.0398; found 255.0403 (ESI)

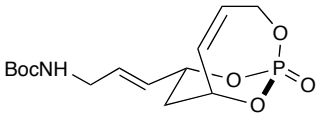
2,9,10-Trioxa-1-phosphabicyclo[4.3.1]dec-4-ene, 8-*E*-[3-[(*tert*-butyl)dimethylsilyl]]oxy-propenyl)-, 1-oxide, (1R,6R,8R) : 10



Purification via flash chromatography (1:1 Hexane/EtOAc) supplied 29 mg (87% yield) of **10** as a oil. $[\propto]_D$ -44.20 (c = 0.24, CH_2Cl_2); IR (neat) 2954, 2927, 2856, 2348, 1299, 1068 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.98 (dddd, J_{HH} = 11.98, 6.62, 2.83, 2.81 Hz, 1H), 5.88 (dddd, J_{HH} = 15.45, 8.20. 4.10, 1.58 Hz, 1H), 5.67-5.71 (m, 1H), 5.63 (ddd, J_{HH} = 11.82, 3.80, 2.76 Hz, 1H), 5.18-5.25 (m, 1H), 5.00 (dd, J_{HH} = 11.49, 5.44 Hz, 1H), 4.95 (m, 1H), 4.37 (ddd, J = 27.73, 14.77, 6.71 Hz, 1H), 4.13 (t, J_{HH} = 1.94 Hz, 2H), 2.19 (ddd, J_{HH} = 18.23, 12.08, 6.21 Hz, 1H), 1.70-1.74 (m, 1H), 0.84 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 129.7, 128.4, 125.8 (d, J_{CP} = 10.0

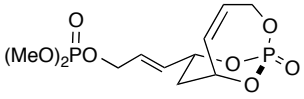
Hz), 76.0 (d, J_{CP} = 6.3 Hz), 63.0 (d, J_{CP} = 6.4 Hz), 62.5, 35.3 (d, J_{CP} = 6.3 Hz), 25.9, 18.4, -5.31, -5.29; ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.75; Exact Mass: calculate for $C_{15}H_{27}O_5PSi$ $(M+Na)^+$ 369.1263; found 369.1263 (ESI)

Boc-Protected Allyl Amine derived Bicyclo[4.3.1]phosphate Triester: 11



Purification via flash chromatography (1:1 Hexane/EtOAc) supplied 22 mg (69% yield) of **11** as a oil. $[\propto]_D$ -49.37 (c = 0.16, CH_2Cl_2); IR (neat) 3330, 2962, 2358, 1712, 1515, 1292 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.98-6.02 (m, 1H), 5.81 (app dt, J_{HH} = 15.33, 5.28 Hz, 1H), 5.59 (dd, J_{HH} = 15.47, 5.06 Hz, 1H), 5.53 (app dt, J_{HH} = 10.91, 3.24 Hz, 1H), 5.13 (app d, J = 24.48 Hz, 1H), 4.90-5.01 (m, 2H), 4.40 (ddd, J = 28.75, 14.79, 6.72 Hz, 1H), 3.71 (s, 2H), 2.17 (ddd, J_{HH} = 18.41, 12.32, 6.26 Hz, 1H), 1.71 (d, J_{HH} = 14.53, 1H) 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 130.9, 129.6, 128.2, 127.9 (d, J_{CP} = 9.6 Hz), 76.9, 75.8 (d, J_{CP} = 6.1 Hz), 63.0 (d, J_{CP} = 6.3 Hz), 41.6, 35.1 (d, J_{CP} = 6.0 Hz), 29.7, 28.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.96; Exact Mass: calculate for $C_{14}H_{22}NO_6P$ $(M+H)^+$ 332.1263; found 332.1277 (ESI)

2,9,10-Trioxa-1-phosphabicyclo[4.3.1]dec-4-ene, 8-*E*-[3-(dimethyl-phosphate)-propenyl]-, 1-oxide, (1R,6R, 8R): 12

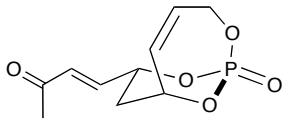


Purification via flash chromatography (9:1 EtOAc/MeOH) supplied 27 mg (80% yield) of **12** as a oil. $[\propto]_D$ -48.3 (c = 0.48, CH_2Cl_2); IR (neat) 2956, 2358, 1296 1037, 955 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) trans isomer δ 5.98-6.03 (m, 1H), 5.94 (app dt, J_{HH} = 15.47, 5.27 Hz, 1H), 5.78 (dd, J_{HH} = 15.48, 3.49 Hz, 1H), 5.55 (app dt, J_{HH} = 11.81, 3.68 Hz, 1H), 5.15 (d, J_{HH} = 24.30 Hz, 1H), 5.00-5.06 (m, 1H), 4.91-4.99 (m, 1H), 4.51 (dd, J = 7.80, 4.66 Hz, 2H), 4.33 (ddd, J = 27.74, 14.77, 6.66 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.17 (app ddd, J_{HH} = 18.31, 12.35, 6.11 Hz, 1H), 1.75 (app d, J_{HH} = 14.17 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) trans isomer δ 130.0 (d, J_{CP} = 10.3 Hz), 129.5, 128.3, 127.4 (d, J_{CP} = 6.6 Hz), 77.0, 76.9, 75.1 (d, J_{CP} = 6.0 Hz), 66.5 (d, J_{CP} = 5.2 Hz), 54.5, 54.4, 35.0 (d, J_{CP} = 5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) trans isomer δ 2.66, -3.04; cis

isomer δ 2.74, 2.89; Exact Mass: calculate for $C_{11}H_{18}O_8P_2$ $(M+Na)^+$ 363.0375; found 363.0386 (ESI)

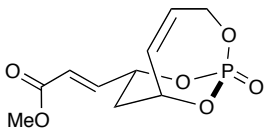
General Procedure for Cross Metathesis of Type II Olefins: A flask or pressure tube containing **5** (20 mg, 0.099 mmol) was charged with CH_2Cl_2 (2 mL) that had been degassed 15 minutes with argon. The Type II olefin partner (4-5 equiv. relative to compound **5**) followed by Hoveyda-Grubbs II catalyst (6.2 mg, 0.009 mmol) were added and the reaction mixture was refluxed for 3-6 hours. Upon completion (monitored by TLC) the reaction was cooled to rt and concentrated under reduced pressure.

2,9,10-Trioxa-1-phosphabicyclo[4.3.1]dec-4-ene, 8-*E*-[3-(oxo)-butenyl]-, 1-oxide, (1R,6R, 8R): 8



Purification via flash chromatography (9:1 EtOAc/MeOH) supplied 18 mg (75% yield) of **8** as a oil. $[\propto]_D$ -56.7 (c = 0.33, CH_2Cl_2); IR (neat) 2958, 2362, 1701, 1677, 1275, 973 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.61 (app dt, J_{HH} = 20.34, 3.53Hz, 1H), 6.50 (dd, J_{HH} = 15.71, 1.66 Hz, 1H), 6.12 (ddd, J_{HH} = 11.87, 3.81, 2.75 Hz, 1H), 5.57 (dddd, J_{HH} = 11.83, 6.62, 2.79, 2.40 Hz, 1H), 5.20-5.24 (m, 1H), 5.14-5.19 (m, 1H), 4.94-5.00 (m, 1H), 4.35 (ddd, J = 27.97, 14.85, 6.71 Hz, 1H), 2.22 (s, 3H), 2.13-2.23 (m, 1H), 1.82 (app dd, J_{HH} = 14.62, 1.46 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 140.4 (d, J_{CP} = 10.4 Hz), 129.9, 129.2, 128.7, 76.9 (d, J_{CP} = 5.7 Hz), 74.2 (d, J_{CP} = 5.9 Hz), 63.2 (d, J_{CP} = 6.3 Hz), 34.5 (d, J_{CP} = 6.0 Hz), 28.67; ^{31}P NMR (162 MHz, $CDCl_3$) δ -3.39; Exact Mass: calculate for $C_{10}H_{13}O_5P$ $(M+Na)^+$ 267.0398; found 267.0409 (ESI)

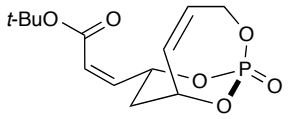
Methyl acrylate derived Bicyclo[4.3.1]phosphate Triester: 14



Purification via flash chromatography (1:2 Hexane/EtOAc) supplied 20 mg (78% yield) of **14** as a oil. $[\propto]_D$ -42.75 (c = 0.40, CH_2Cl_2); IR (neat) 2954, 2852, 1724, 1300, 973 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.87 (app dt, J_{HH} = 15.55, 3.73 Hz, 1H), 6.27 (dd, J_{HH} = 15.54, 1.85 Hz, 1H), 6.12

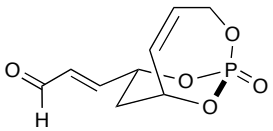
(dddd, J_{HH} = 11.89, 6.61, 2.81, 2.40 Hz, 1H), 5.66 (ddd, J_{HH} = 11.86, 3.83, 2.66 Hz, 1H), 5.28-5.32 (m, 1H), 5.22-5.28 (m, 1H), 5.03-5.09 (m, 1H), 4.44 (ddd, J = 27.93, 14.84, 6.71 Hz, 1H), 3.79 (s, 3H), 2.25 (ddd, J_{HH} = 18.35, 12.28, 6.23 Hz, 1H), 1.90 (app dd, J_{HH} = 14.66, 1.25 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 142.6 (d, J_{CP} = 10.3 Hz), 129.2, 128.7, 122.1, 76.8, 74.1 (d, J_{CP} = 5.8 Hz), 52.0, 34.4 (d, J_{CP} = 5.9 Hz) 29.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ -3.36; Exact Mass: calculate for $C_{10}H_{13}O_6P$ $(M+H)^+$ 261.0528; found 261.0533 (ESI)

_t_-Butyl acrylate derived Bicyclo[4.3.1]phosphate Triester: 15



Purification via flash chromatography (1.5:1 Hexane/EtOAc) supplied 3 mg of the minor *cis*-**15** isomer of methyl acrylate derived bicyclic phosphate as a oil. The *trans* isomer was inseparable from starting material (5:1 *E/Z)*. $[\propto]_D$ -65.50 (*c* = 0.20, CH_2Cl_2); IR (neat) 3010, 2923, 1710, 1301, 1242, 1159, 973 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.21 (dd, J_{HH} = 11.66, 6.68 Hz, 1H), 6.04-4.14 (m, 2H), 5.77 (dd, J_{HH} = 11.67, 1.06 Hz, 1H), 5.72 (ddd, J_{HH} = 11.90, 3.86, 2.67 Hz, 1H), 5.16-5.27 (m, 1H), 4.98-5.08 (m, 1H), 4.44 (ddd, J = 27.95, 14.62, 6.78 Hz, 1H), 2.14-2.24 (m, 1H), 2.06 (ddd, J_{HH} = 14.38, 3.87, 2.38 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 144.5 (d, J_{CP} = 12.5 Hz), 129.8, 128.0, 122.7, 81.2, 74.3 (d, J_{CP} = 5.0 Hz), 63.1, 33.4 (d, J_{CP} = 6.3 Hz) 29.7, 28.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ -3.33 *trans*, -3.29 *cis*; Exact Mass: calculate for $C_{13}H_{19}O_6P$ $(M+Na)^+$ 325.0817; found 325.0825 (ESI)

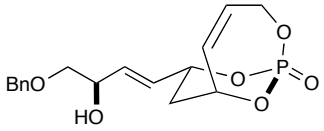
2,9,10-Trioxa-1-phosphabicyclo[4.3.1]dec-4-ene, 8-*E*-[3-(oxo)-propenyl]-, 1-oxide, (1R,6R, 8R): 16



Purification via flash chromatography (9:1 EtOAc/MeOH) supplied 18 mg (78% yield) of **16** as a oil. $[\propto]_D$ -34.4 (*c* = 0.45, CH_2Cl_2); IR (neat) 3150, 2930, 1698, 1300, 975 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (d, J_{HH} = 7.44 Hz, 1H), 6.76 (ddd, J_{HH} = 15.73, 3.93, 3.13 Hz, 1H), 6.47 (ddd, J_{HH} = 16.33, 7.42, 1.64 Hz, 1H), 6.12-6.18 (m, 1H), 5.68 (ddd, J_{HH} = 11.88, 3.88, 2.67 Hz, 1H), 5.36 (ddd, J = 12.30, 3.81, 1.82 Hz, 1H), 5.26-5.33 (m, 1H), 5.04-5.11 (m, 1H), 4.46 (ddd, *J*

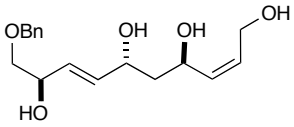
= 27.99, 14.87, 6.71 Hz, 1H), 2.33 (ddd, J_{HH} = 18.36, 12.23, 2.10 Hz, 1H), 1.95 (ddd, J_{HH} = 14.53, 3.35, 2.10 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 149.8 (d, J_{CP} = 10.8 Hz), 132.1, 129.1, 128.9, 76.7, 74.0 (d, J_{CP} = 5.7 Hz), 63.2 (d, J_{CP} = 6.3 Hz), 34.2 (d, J_{CP} = 6.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ -3.65; Exact Mass: calculate for $C_9H_{11}O_5P$ $(M+H)^+$ 231.0422; found 231.0447 (ESI)

(*R*)-1-(Benzyloxy)buten-2-ol derived Bicyclo[4.3.1]phosphate Triester: 17



Purification via flash chromatography (1:2 Hexane/EtOAc) supplied 25 mg (72% yield) of **17** as a oil. $[\propto]_D$ -45.00 (c = 0.60, CH_2Cl_2); IR (neat) 3404, 2923, 2854, 1272, 1114 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22-7.33 (m, 5H), 5.94-6.01 (m, 1H), 5.75-5.85 (m, 2H), 5.53 (ddd, J_{HH} = 11.85, 3.84, 2.61 Hz, 1H), 5.13 (app d, J = 24.47 Hz, 1H), 4.91-5.02 (m, 2H), 4.50 (s, 2H), 4.33 (m, 1H), 4.31 (ddd, J = 27.78, 14.79, 6.71 Hz, 1H), 3.48 (dd, J_{HH} = 9.56, 3.30 Hz, 1H), 3.27 (dd, J_{HH} = 9.56, 7.95 Hz, 1H), 2.47 (s, 1H), 2.16 (ddd, J_{HH} = 18.21, 12.05, 6.19 Hz, 1H), 1.72 (dd, J_{HH} = 14.71, 1.16 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 131.6, 129.6, 128.5, 128.3 (d, J_{CP} = 10.1 Hz), 128.2, 128.0, 127.9, 77.0, 75.6 (d, J_{CP} = 6.1 Hz), 73.7, 73.5, 70.2, 63.0 (d, J_{CP} = 6.3 Hz), 35.2 (d, J_{CP} = 5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.88

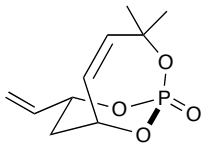
(2*Z*,4*R*,6*R*,7*E*,9*R*)-10-(benzyloxy)deca-2,7-diene-1,4,6,9-tetraol: 18



17 (0.033 g, 0.090 mmol) was taken up in THF (2.0 mL) and lowered to 0 ºC. $LiAlH_4$ (17 mg, 0.45 mmol) was slowly added. Upon complete addition of $LiAlH_4$, the reaction was warmed to rt and stirred for one hour. The reaction was quenched under non-aqueous conditions (0.017 mL H_2O slowly, 0.017 mL 15% NaOH slowly, and 0.051 mL H_2O). Salts were filtered and washed (5x with ether) and reaction was concentrated. The concentrated reaction mixture was purified by flash chromotagraphy (9:1 EtOAc) to supply 23 mg of **18** (70% yield) as an oil. $[\propto]_D$ -24.28 (c = 0.034, CH_2Cl_2); IR (neat) 3404, 2923, 2856, 1452, 1272, 1110 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.39 (m, 5H), 5.85 (dd, J_{HH} = 15.29, 5.23 Hz, 1H), 5.54-5.76 (m, 3H), 4.68-4.77 (m, 1H), 4.56 (s, 2H), 4.33-4.44 (m, 2H), 4.24 (dd, J_{HH} = 12.52, 6.56 Hz, 1H), 4.02-4.10 (m, 1H), 3.51

(dd, J_{HH} = 9.50, 3.19 Hz, 1H), 3.38 (app t, J_{HH} = 7.98 Hz, 1H), 3.13-3.33 (broad s, 4H), 1.75-1.85 (m, 1H), 1.68-1.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7, 134.6, 134.6, 130.2, 128.9, 128.5, 128.0, 127.9, 74.0, 73.4, 70.7, 69.8, 65.7, 58.7, 42.6; Exact Mass: calculate for $C_{17}H_{24}O_5$ $(M+NH_4)^+$ 326.1968; found 326.1942 (FAB)

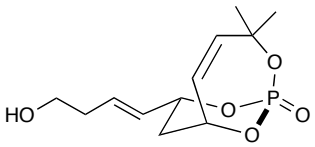
Second Generation Bicyclic Phosphate: 19



A flask was charged with diol **1** (0.60 g, 4.69 mmol), NEt_3 (1.444 g, 14.3 mmol), and DMAP (0.057 g, 0.47 mmol) in DCM (23 mL). The solution was cooled to 0 ^oC, and freshly distilled $POCl_3$ (0.789 g, 5.16 mmol) was added dropwise. After 25 minutes stirring in the ice bath, 20 mL of ether was added, and the salts filtered off. The concentrated reaction mixture was purified by flash chromotagraphy (1:1 Hexane/EtOAc) to supply 0.682 g (70% yield) of the (3*R*,5*R*)-phosphate monochloride as a clear oil. A solution of 2-methylbut-3-en-2-ol (0.310 g, 3.60 mmol) in THF (18.0 mL) was cooled to -30 ^oC. BuLi (2.47 M, 3.60 mmol) was slowly added, followed by one hour of stirring. A solution of phosphate monochloride (0.682 g, 3.27 mmol) in THF (6.0 mL) was slowly cannulated into the reaction vessel containing the alkoxide. The reaction was stirred at rt for 24 hours and was quenched with 1 mL of $NH_4^+Cl^-$ (sat'd aq) and diluted with 20 ml distilled water. The separated aqueous layer was extracted EtOAc (3x), and the combined organic layers were washed with $Na^+HCO_3^-$ (sat'd aq.), brine, and dried (Na_2SO_4). A flask containing triene phosphate was charged with CH_2Cl_2 (360 mL) that had been degassed 15 minutes with argon. Grubbs Second Generation catalyst was added (122 mg, 0.144 mmol) and the reaction mixture was refluxed for 3-3.5 hours. Upon completion (monitored by TLC) the reaction was cooled to rt and concentrated under reduced pressure. Purification via flash chromatography (1:1 Hexanes/EtOAc) supplied 377 mg (50% yield over two steps) of the **19**. $[\propto]_D$ -93.20 (*c* = 0.72, CH_2Cl_2); IR (neat) 3197, 2933, 2383, 1384, 1299, 999 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83-5.94 (m, 1H), 5.87 (dd, J_{HH} = 12.17, 1.37 Hz, 1H), 5.45 (d, J_{HH} = 16.46 Hz, 1H), 5.42 (dd, J_{HH} = 12.31, 4.71 Hz, 1H), 5.27 (d, J_{HH} = 10.63 Hz, 1H), 5.14 (ddd, *J* = 24.56, 5.91, 4.63 Hz, 1H), 4.99 (ddd, *J* = 11.85, 3.40, 1.54 Hz, 1H), 2.20 (ddd, J_{HH} = 18.22, 12.06, 6.20 Hz, 1H), 1.84 (s, 3H), 1.79 (app dd, J_{HH} = 14.58, 1.19 Hz, 1H), 1.52 (d, J_{HP} = 2.59 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 135.0 (d, J_{CP} = 10.4 Hz), 125.6, 117.1 (d, J_{CP} = 1.1 Hz), 80.9 (d, J_{CP} = 7.6 Hz), 75.9 (d, J_{CP} = 6.5 Hz), 75.8 (d, J_{CP} = 6.0 Hz), 34.6 (d, J_{CP} = 5.8 Hz), 31.5 (d, J_{CP} = 12.2 Hz), 28.7;

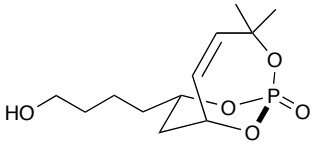
^{31}P NMR (162 MHz, $CDCl_3$) δ -6.86; Exact Mass: calculate for $C_{10}H_{15}O_4P$ $(M+H)^+$ 231.0786; found 231.0793 (ESI)

Homoallyl Alcohol Derived Second Generation Bicyclic Phosphate: 20



A flask or pressure tube containing **19** (20 mg, 0.087 mmol) was charged with CH_2Cl_2 (2 mL) that had been degassed 15 minutes with argon. Homo-allyl alcohol (12.5 mg, 0.173 mmol) followed by Hoveyda-Grubbs II catalyst (6.2 mg, 0.009 mmol) was added and the reaction mixture was refluxed for 3-6 hours. Upon completion (monitored by TLC) the reaction was cooled to rt and concentrated under reduced pressure. Purification via flash chromatography (9:1 EtOAc/MeOH) supplied 17 mg (71% yield) of **20** as an oil. $[\propto]_D$ -99.33 (c = 0.30, CH_2Cl_2); IR (neat) 3404, 2923, 1384, 1288, 1271, 1002 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (dd, J_{HH} = 15.13, 6.94 Hz, 1H), 5.77 (dd, J_{HH} = 12.33, 1.58 Hz, 1H), 5.56 (ddd, J_{HH} = 15.13, 5.67, 0.63 Hz, 1H), 5.32 (dd, J_{HH} = 12.31, 4.59 Hz, 1H), 4.98-5.08 (m, 1H), 4.90 (q, J = 11.66, 5.67 Hz, 1H), 3.63 (t, J_{HH} = 6.86 Hz, 2H), 2.27 (q, J_{HH} = 12.59, 6.20 Hz, 2H), 2.17 (ddd, J_{HH} = 18.97, 11.95, 6.30 Hz, 1H), 1.75 (s, 3H), 1.68 (ddd, J_{HH} = 14.50, 3.21, 2.20 Hz, 1H), 1.44 (d, J_{HP} = 2.47 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 130.5, 129.8 (d, J_{CP} = 10.1 Hz), 125.6, 80.9 (d, J_{CP} = 7.7 Hz), 75.9 (d, J_{CP} = 6.4 Hz), 75.8 (d, J_{CP} = 5.9 Hz), 61.6, 35.4, 34.9 (d, J_{CP} = 5.8 Hz), 31.5 (d, J_{CP} = 12.3 Hz), 28.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ -6.89; Exact Mass: calculate for $C_{12}H_{19}O_5P$ $(M+H)^+$ 275.1048; found 275.1059 (ESI)

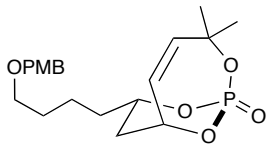
Partial Hydrogenation Alcohol-derived Second Generation Phosphate: 21



CH_2Cl_2 (14 mL) was added to a flask containing the **20** (0.019 g, 0.069 mmol). Grubbs second generation catalyst (0.06 g, 0.007 mmol) was added along with Et_3N (0.004 g, 0.03 mmol). The solution was then canulated into a H_2 Parr bomb apparatus. The solution was purged with H_2 and the bomb sealed. The mixture was heated at 37 ^{o}C and 300 psi H_2 for 2 hours. Concentration under reduced pressure and purification of the mixture via flash chromatography (9:1

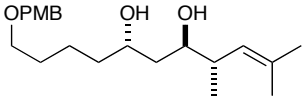
EtOAc/MeOH) supplied 15 mg of the **21** (76% yield) as a oil. $[\propto]_D$ -68.90 (c = 0.14, CH_2Cl_2); IR (neat) 3407, 2927, 2854, 1384, 1290, 1271, 1095, 1002 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.73 (dd, J_{HH} = 10.30, 1.89 Hz, 1H), 5.28 (dd, J_{HH} = 12.29, 4.73 Hz, 1H), 4.96-5.02 (m, 1H), 4.38-4.45 (m, 1H), 3.57 (t, J_{HH} = 6.30, 2H), 2.08 (ddd, J_{HH} = 17.97, 11.98, 5.99 Hz, 1H), 1.73 (s, 3H), 1.40-173 (m, 7H), 1.41 (d, J_{HP} = 2.51 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 125.5, 80.4 (d, J_{CP} = 7.5 Hz), 75.9 (d, J_{CP} = 3.8 Hz), 75.8 (d, J_{CP} = 3.8 Hz), 62.3, 35.1 (d, J_{CP} = 8.8 Hz), 34.0 (d, J_{CP} = 6.3 Hz), 31.9, 31.2 (d, J_{CP} = 12.5 Hz), 28.3, 20.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ -6.37; Exact Mass: calculate for $C_{12}H_{21}O_5P$ $(M+H)^+$ 277.1205; found 277.1213 (ESI)

PMB-Protected Alcohol derived Second Generation Phosphate: 22



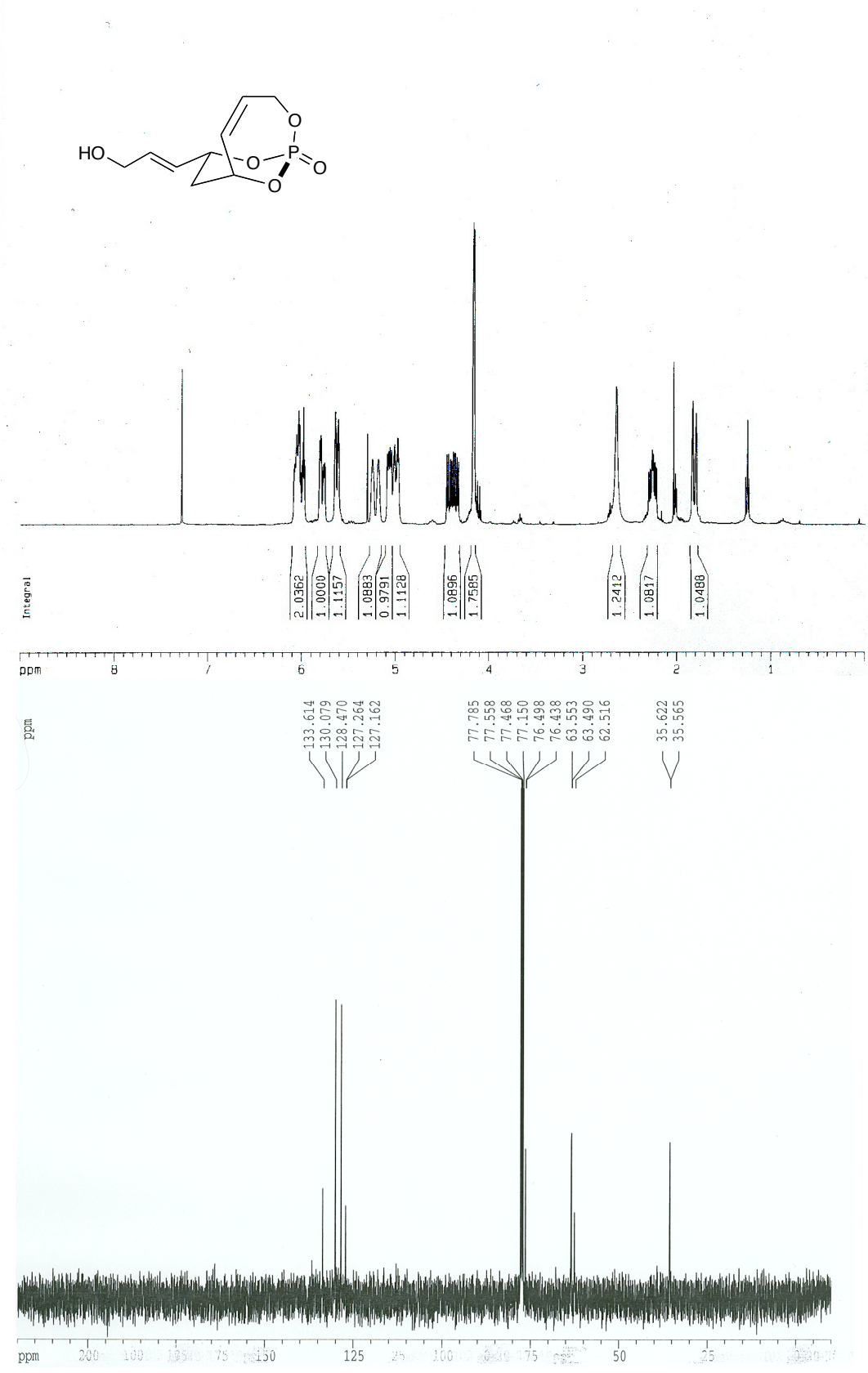
The PMB-imidate was prepared via previous method (Organ, M. G.; Wang, J. *J. Org. Chem.* **2002**, *67*, 7847-7851). The crude PMB-imidate (86 mg, 0.306 mmol) was dissolved in CH_2Cl_2 (1.0 mL) at rt and **21** (28 mg, 0.102 mmol) and PPTS (3 mg, 0.0119 mmol) were added. The mixture was stirred for 22 h during which time a white solid formed. After washing with saturated $NaHCO_3$ and brine, the solution was dried over anhydrous Na_2SO_4 and subsequently filtered. Concentration under reduced pressure and purification of the mixture via flash chromatography (1:1 EtOAc/MeOH) supplied 37 mg of the **22** (94% yield) as an oil. $[\propto]_D$ -65.70 (c = 0.525, CH_2Cl_2); IR (neat) 2931, 2858, 1612, 1512 1367, 1290, 1271, 1095, 1000 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (app d, J_{HH} = 6.49 Hz, 2H), δ 6.87 (app d, J_{HH} = 8.61 Hz, 2H), δ 5.81 (dd, J_{HH} = 12.32, 1.74 Hz, 1H), 5.35 (dd, J_{HH} = 12.33, 4.51 Hz, 1H), 5.08 (app dt, J = 24.56, 5.19 Hz, 1H), 4.45-4.53 (m, 1H), 4.42 (s, 2H), 3.81 (s, 3H), 3.43 (t, J_{HH} = 6.15 Hz, 2H), 2.13 (ddd, J_{HH} = 18.11, 11.91, 6.31 Hz, 1H), 1.81 (s, 3H), 1.45-179 (m, 7H), 1.49 (d, J_{HP} = 6.00 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.1, 136.6, 129.5, 128.3, 124.8, 112.8, 79.7 (d, J_{CP} = 7.7 Hz), 75.2 (d, J_{CP} = 3.1 Hz), 75.1 (d, J_{CP} = 2.7 Hz), 71.6, 68.7, 54.3, 34.5 (d, J_{CP} = 9.3 Hz), 33.3 (d, J_{CP} = 5.9 Hz), 30.5 (d, J_{CP} = 12.1 Hz), 28.3, 27.6, 20.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ -6.34; Exact Mass: calculate for $C_{20}H_{29}O_6P$ $(M+H)^+$ 397.1780; found 397.1782 (ESI)

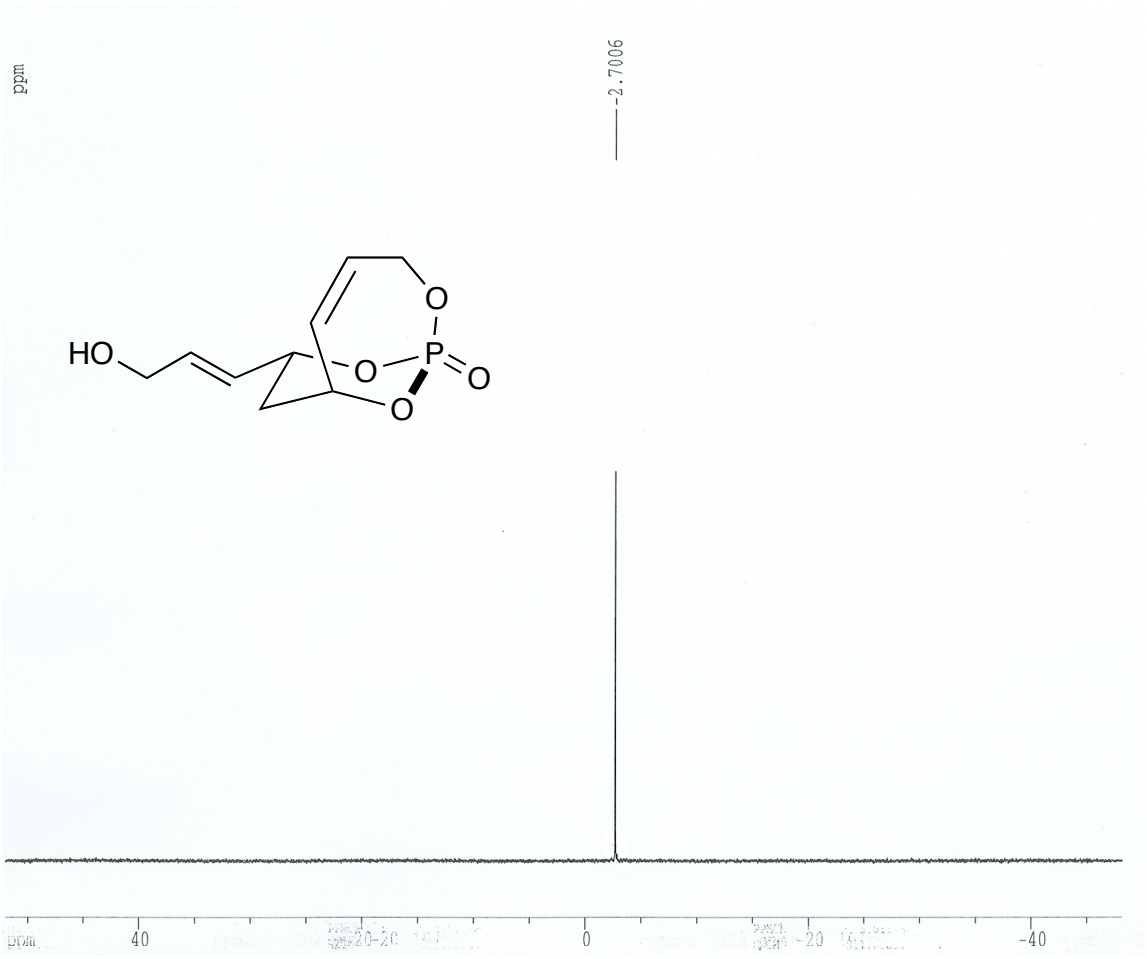
(4*S*,5*R*,7*S*)-11-(4-methoxybenzyloxy)-2,4-dimethylundec-2-ene-5,7-diol: 23



A thoroughly dried flask was charged with a solution of CuCN·2LiCl in THF (0.342 mL, 1.0 M solution) and lowered to –30 ºC. Me_2Zn in THF (0.171 mL, 2.0 M solution) was slowly added. Upon addition, the mixture was stirred for 30 minutes at –30 ºC (mossy green color). A solution of **22** (27 mg, 0.069 mmol) in THF (0.069 mL) was cannulated slowly into the cuprate solution (at –30 ºC). The reaction was stirred for 3 hrs and quenched with 10% HCl (5 mL, the reaction was stirred until copper solids dissolved). The two layers were separated, and the aqueous layer was washed with CH_2Cl_2 (4x). The combined organic layers were washed with H_2O (1x) and concentrated under reduced pressure to provide the crude phosphonic acid (one product peak by ^{31}P analysis) as an oil. The acid was taken up in methanol and $TMSCHN_2$ was added at rt until the yellow solution persisted. A drop of acetic acid was added and the solution was evaporated under reduced pressure. The phosphate was taken up in toluene (0.685 mL) and cooled to 0 ºC. Red-Al (0.083 mL of 65% solution in toluene) was slowly added. Upon addition of Red-Al, the flask was warmed to rt and stirred for 3 hrs. The reaction was quenched with 3 mL of $NH_4^+Cl^-$ (sat'd, aq.). The layers were separated and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were washed with brine (1x), dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (1:1 EtOAc/hexane) provided 15 mg of **23** (65% yield over three steps). $[\propto]_D$ -13.72 (*c* = 0.510, CH_2Cl_2); IR (neat) 3392, 2927, 2856, 1612, 1512 1363, 1247, 1209, 1097, 1035 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (app d, J_{HH} = 8.39 Hz, 2H), δ 6.87 (app d, J_{HH} = 8.51 Hz, 2H), δ 4.97 (d, J_{HH} = 9.78 Hz, 1H), 4.42 (s, 2H), 3.90-3.96 (m, 1H), 3.81 (s, 3H), 3.58 (ddd, J_{HH} = 7.94, 7.87, 2.97 Hz, 1H), 3.44 (t, J_{HH} = 6.53 Hz, 2H), 2.80 (broad s, 2H), 2.44-2.51 (m, 1H), 1.76 (s, 3H), 1.67-173 (m, 1H), 1.66 (s, 3H), 1.35-1.65 (m, 9H), 0.92 (d, J_{HH} = 6.70 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 135.2, 130.7, 129.3, 126.7, 113.8, 73.4, 72.6, 70.0, 69.1, 55.3, 39.0, 38.9, 37.2, 29.8, 26.1, 22.6, 18.4, 17.0; Exact Mass: calculate for $C_{21}H_{34}O_4$ $(M+H)^+$ 351.2535; found 351.2538 (ESI)

Allyl Alcohol derived Bicyclo[4.3.1]phosphate Triester: 9

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P
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O
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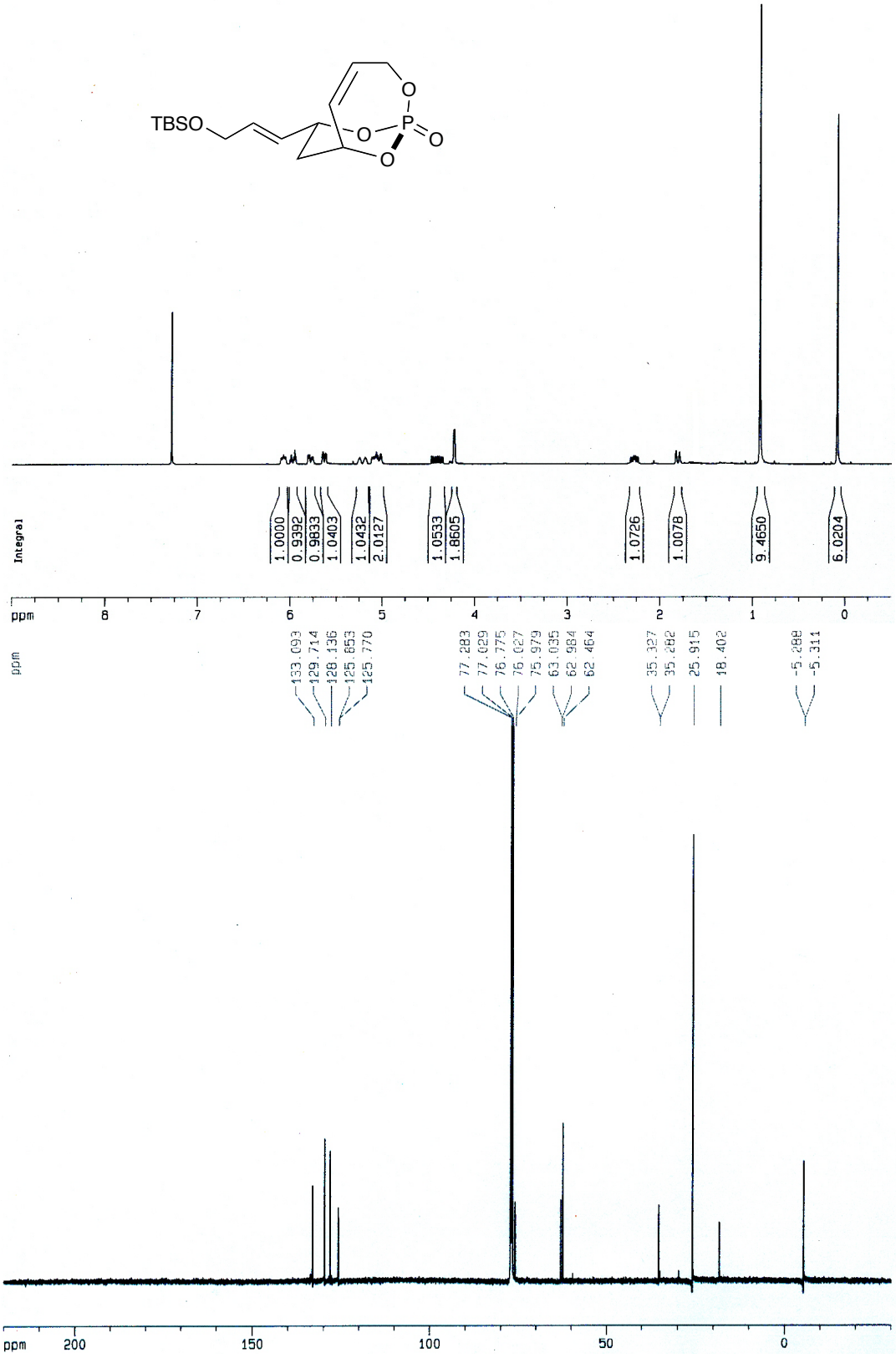
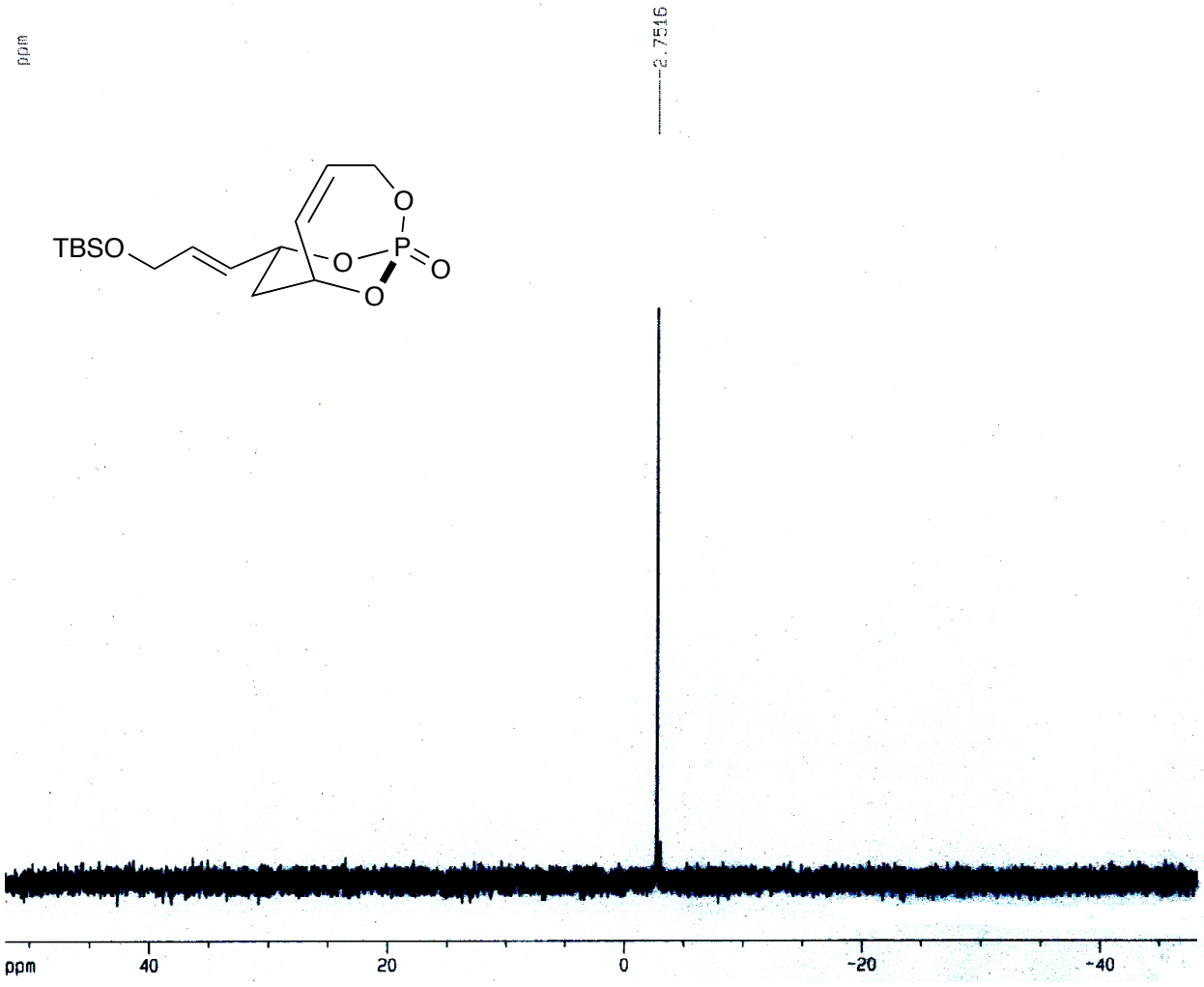
-40

TBS-Protected Allyl Alcohol derived Bicyclo[4.3.1]phosphate Triester: 10

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P
O
O
ppm
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20
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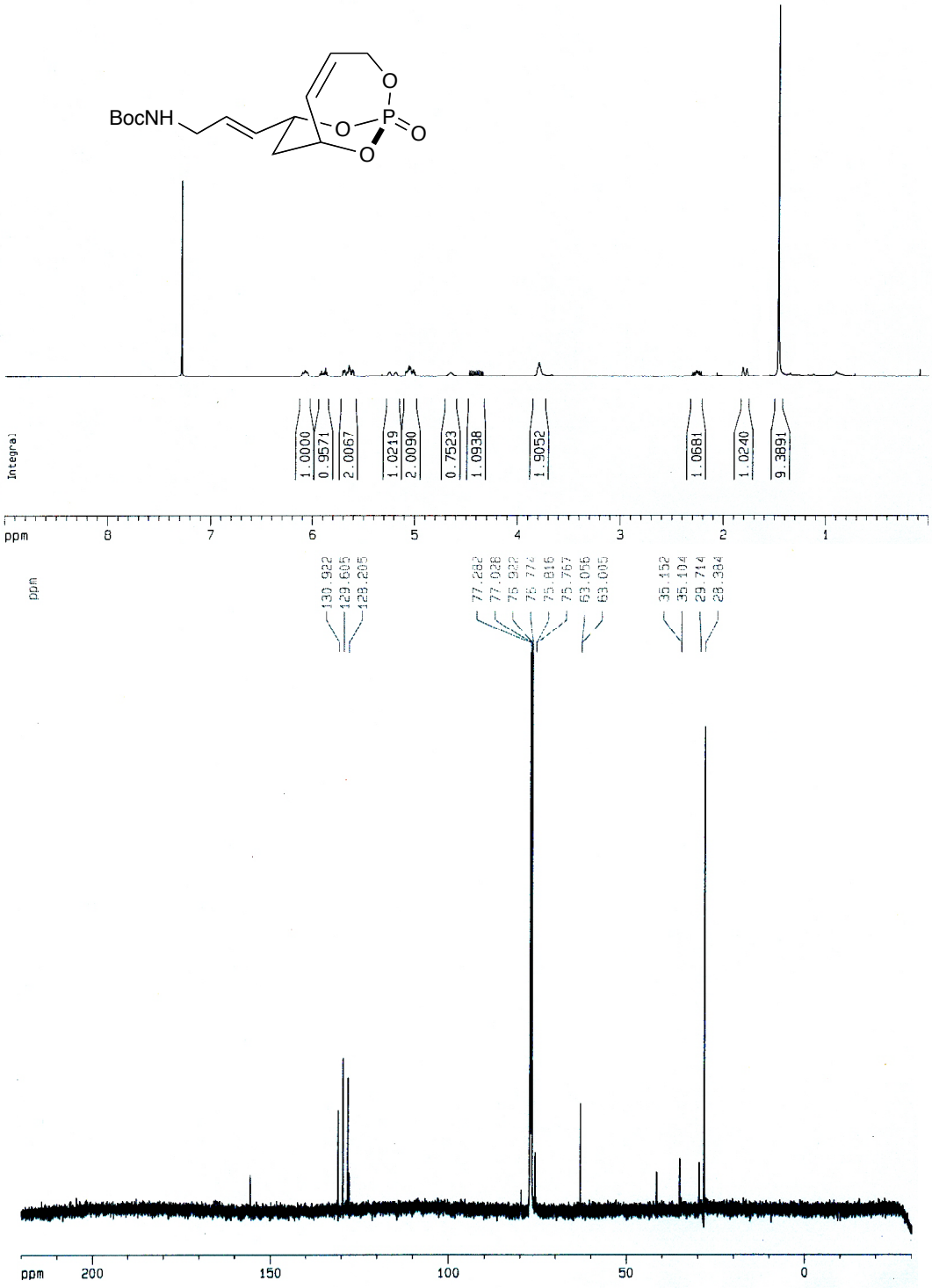
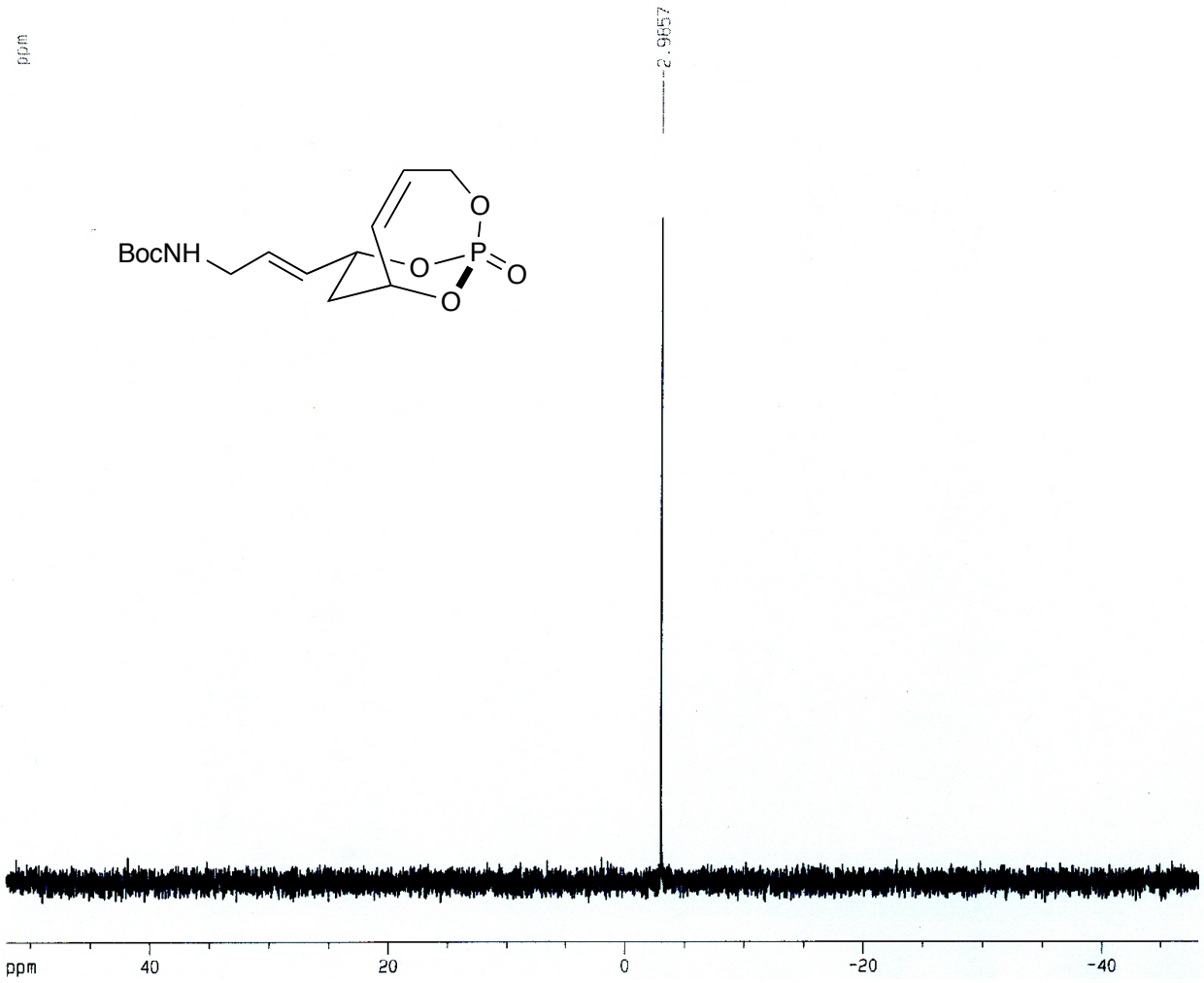
-40

Boc-Protected Allyl Amine derived Bicyclo[4.3.1]phosphate Triester: 11

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BocNH
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O
P
O
O
ppm
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20
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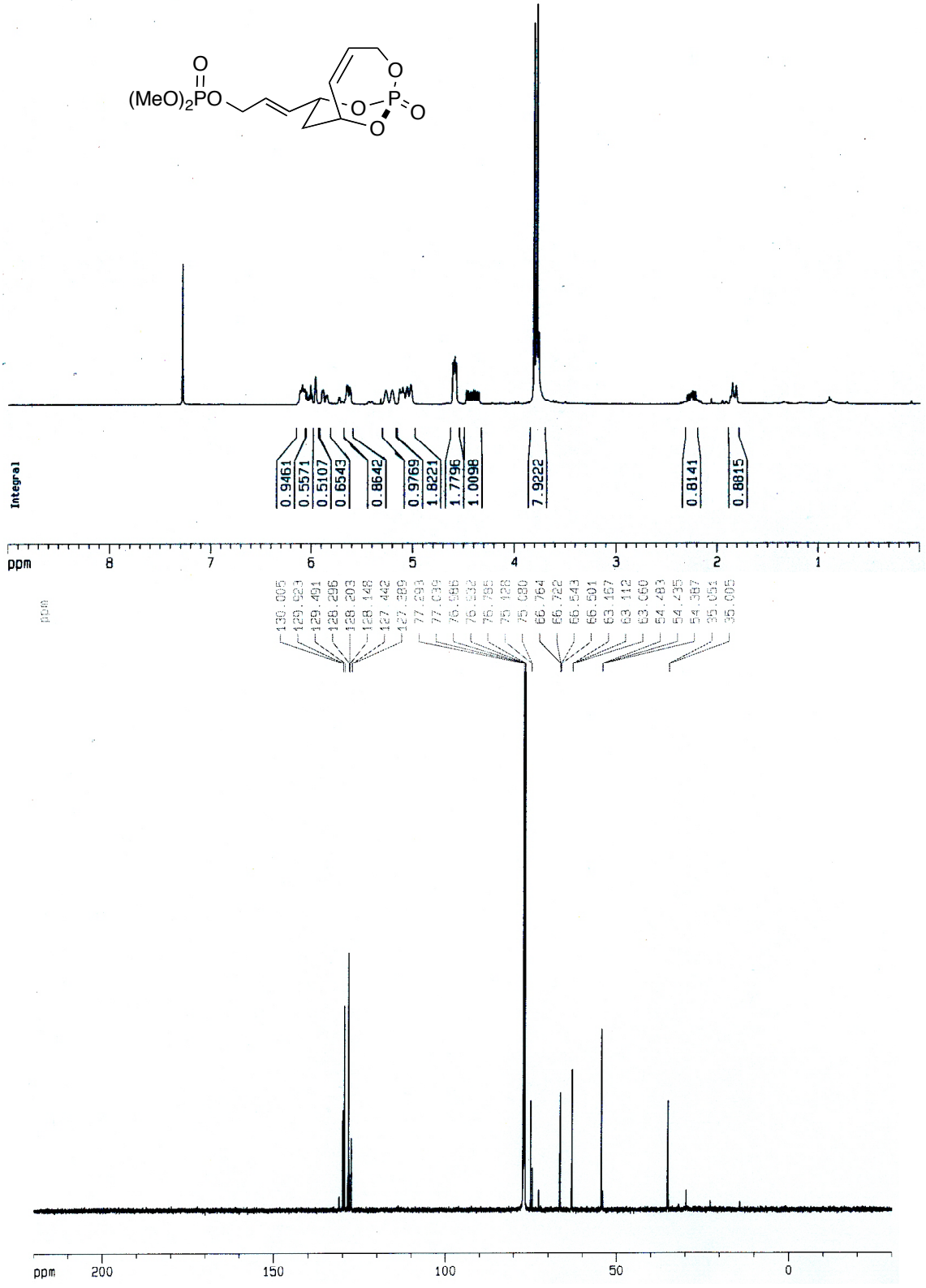
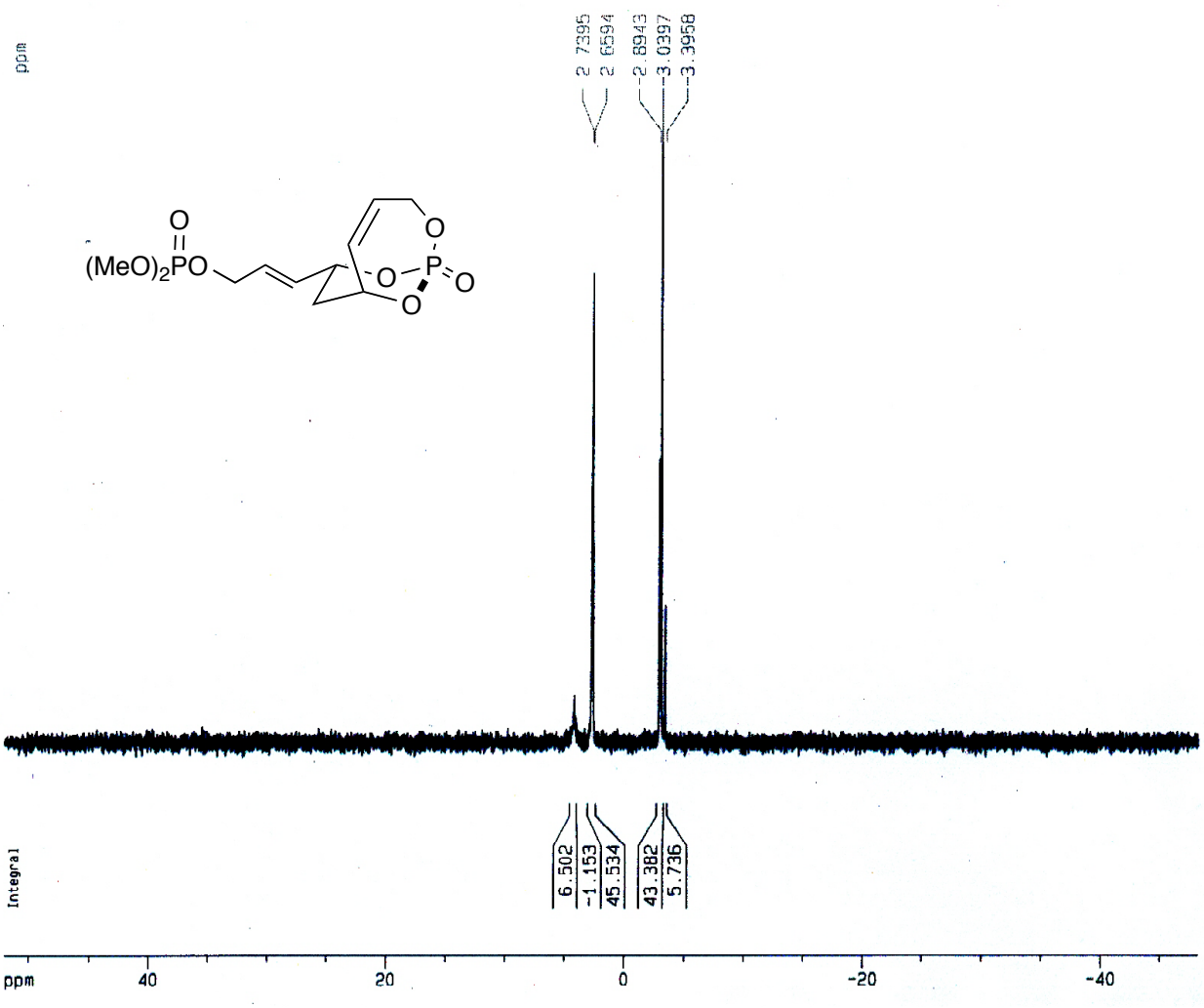
-40

Allyl Phosphate derived Bicyclo[4.3.1]phosphate Triester: 12

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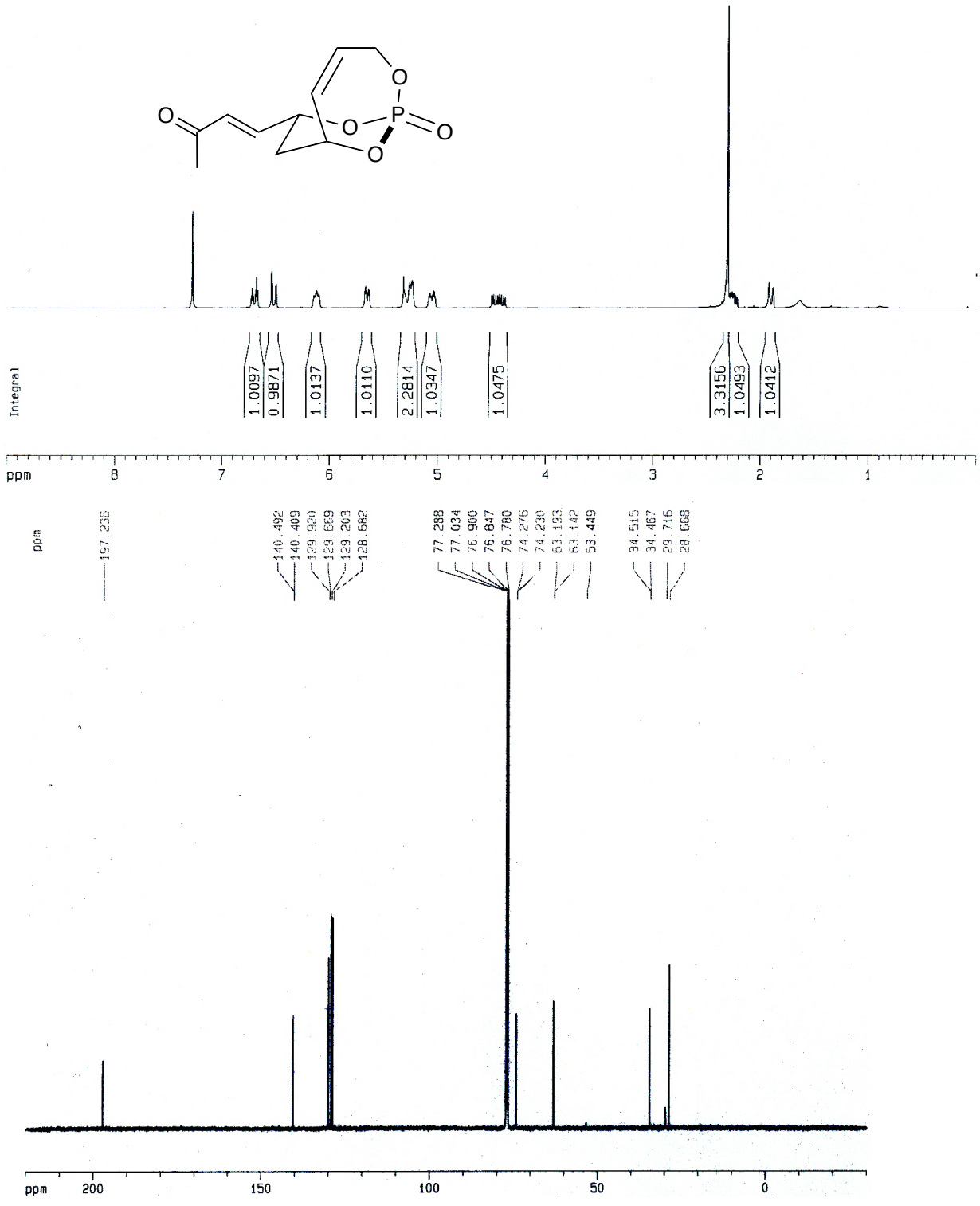
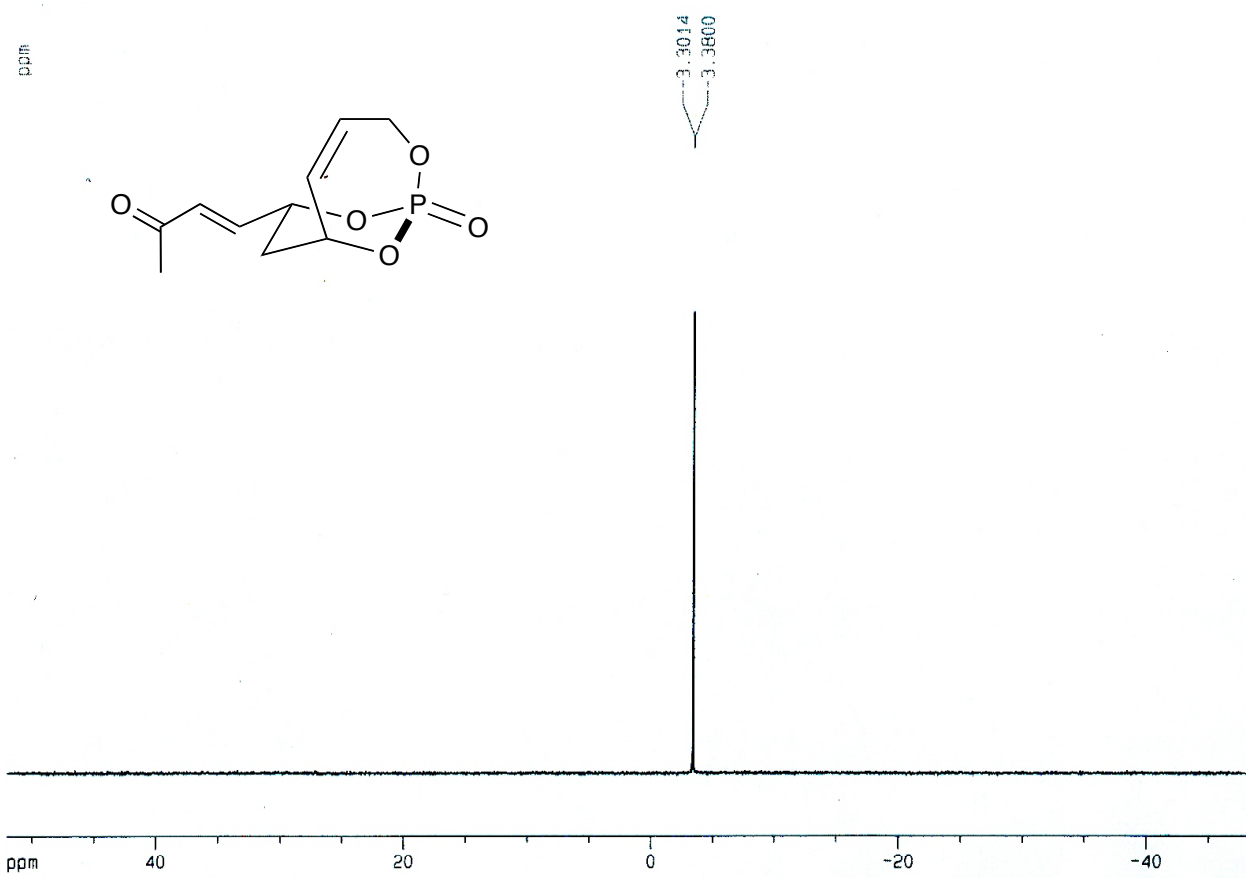
Methyl Vinyl Ketone derived Bicyclo[4.3.1]phosphate Triester: 8

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O
P
O
O
O
ppm
40
20
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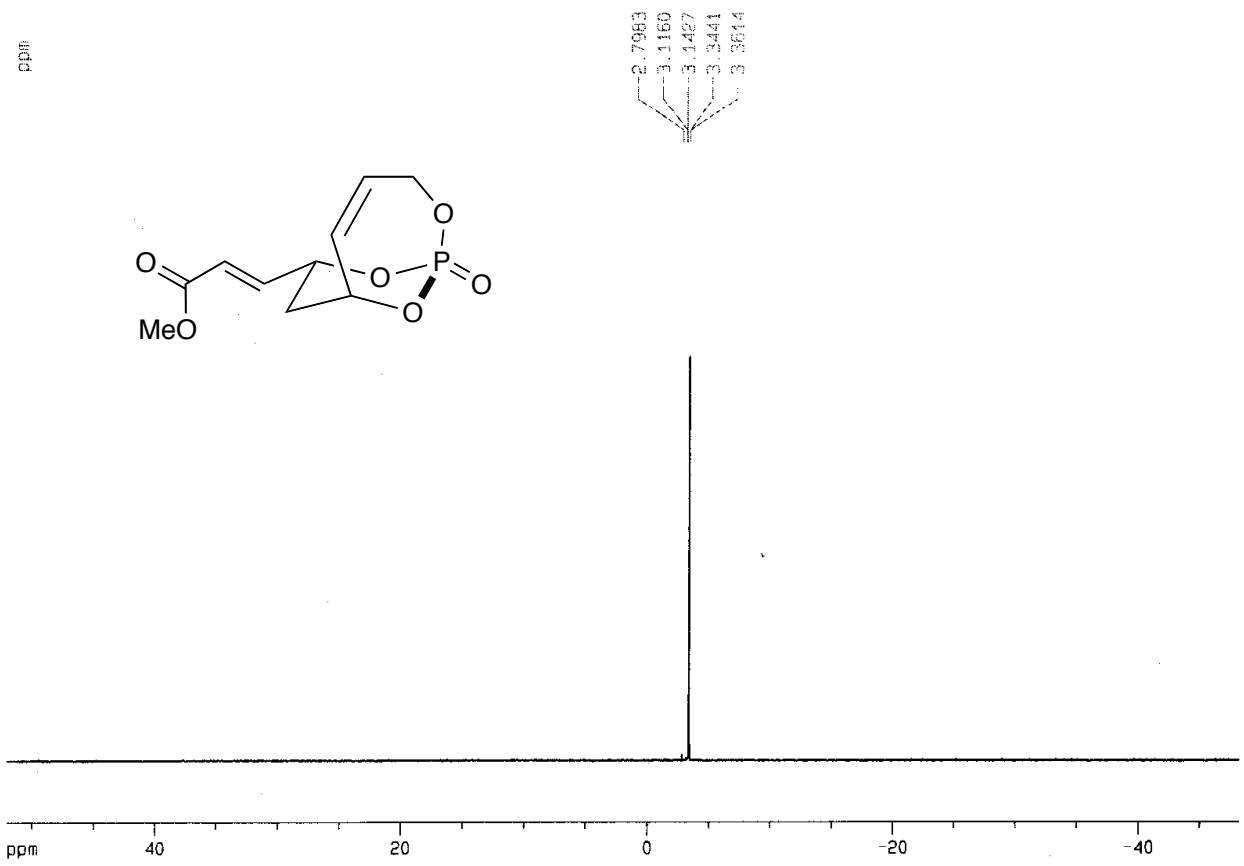
-20
-40

Methyl acrylate derived Bicyclo[4.3.1]phosphate Triester: 14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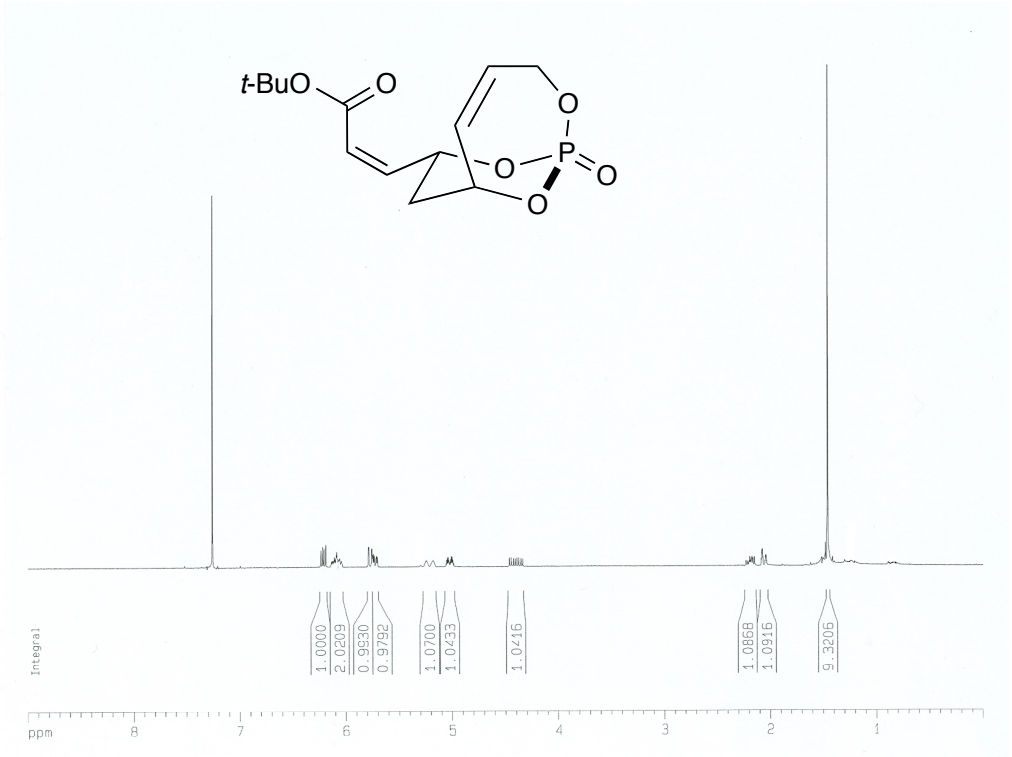
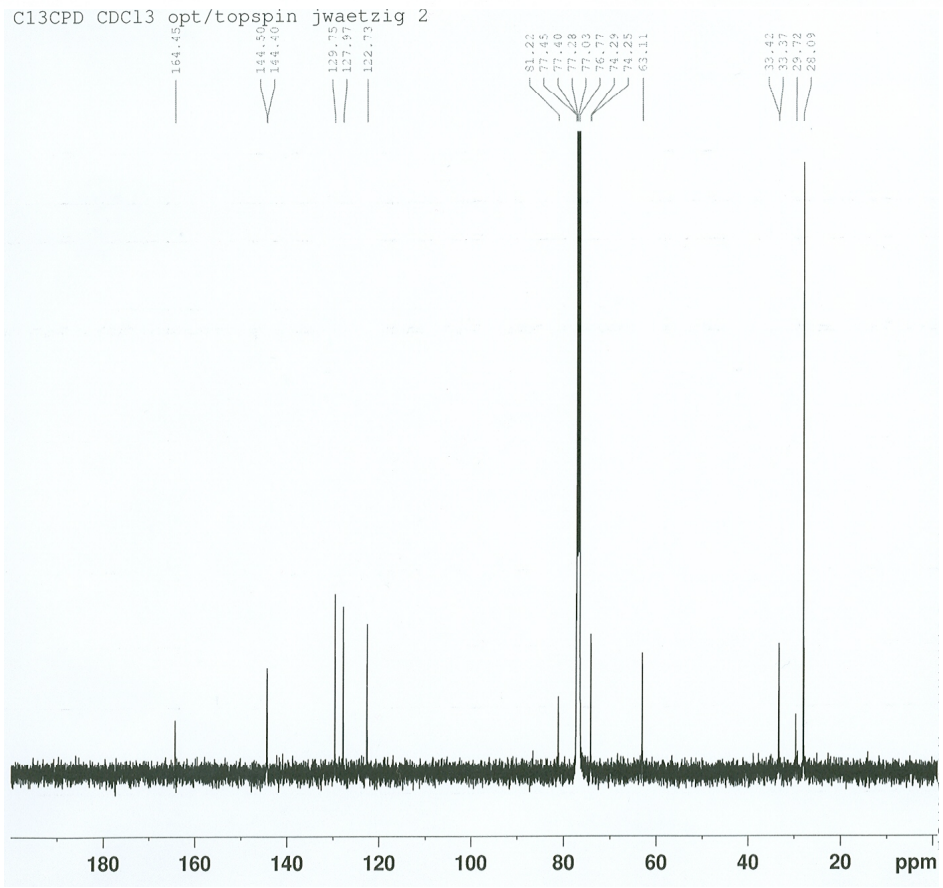
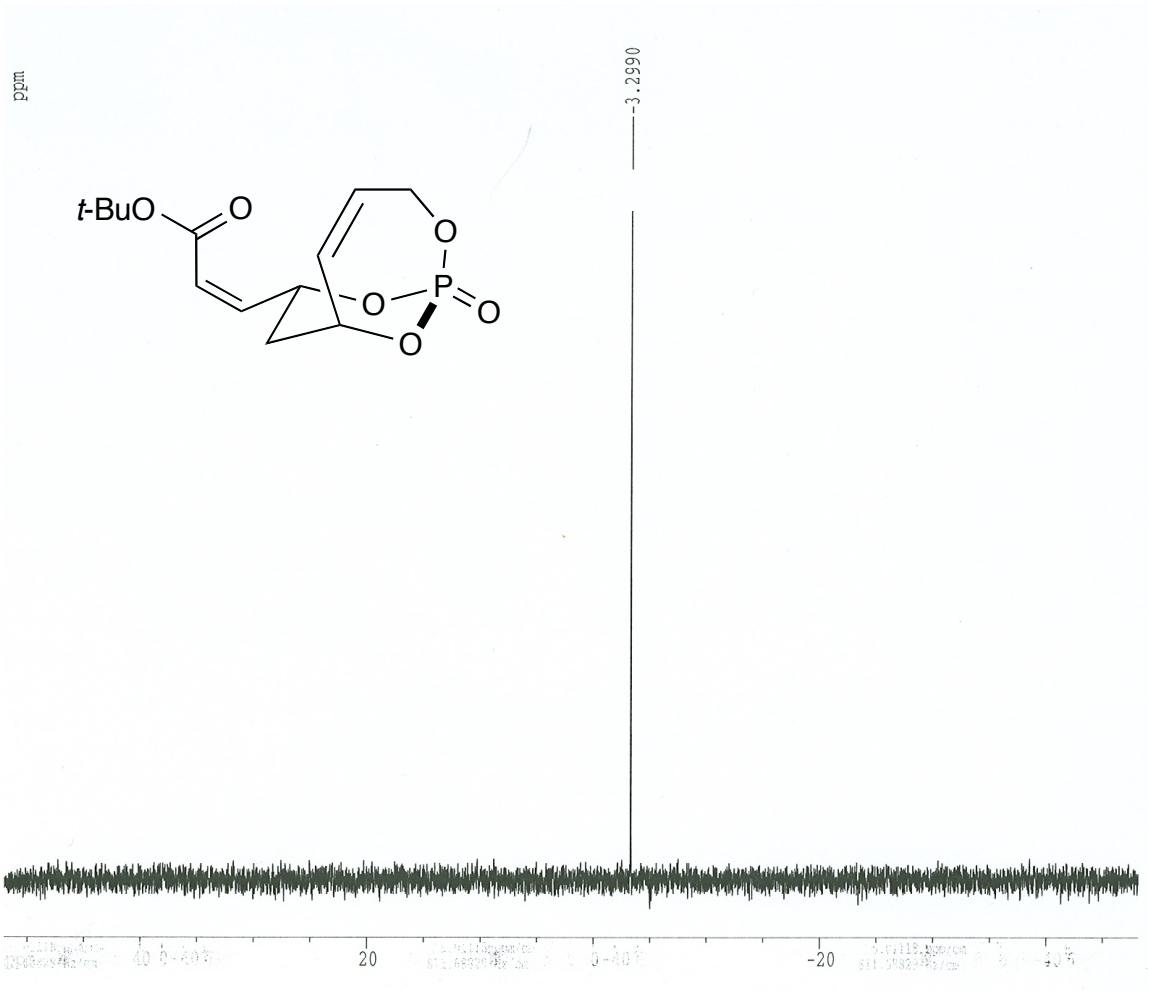
3.3644
O
O
O
P
O
O
O
MeO
ppm
40
20
0
-20
-40

***t*-Butyl acrylate derived Bicyclo[4.3.1]phosphate Triester: 15**



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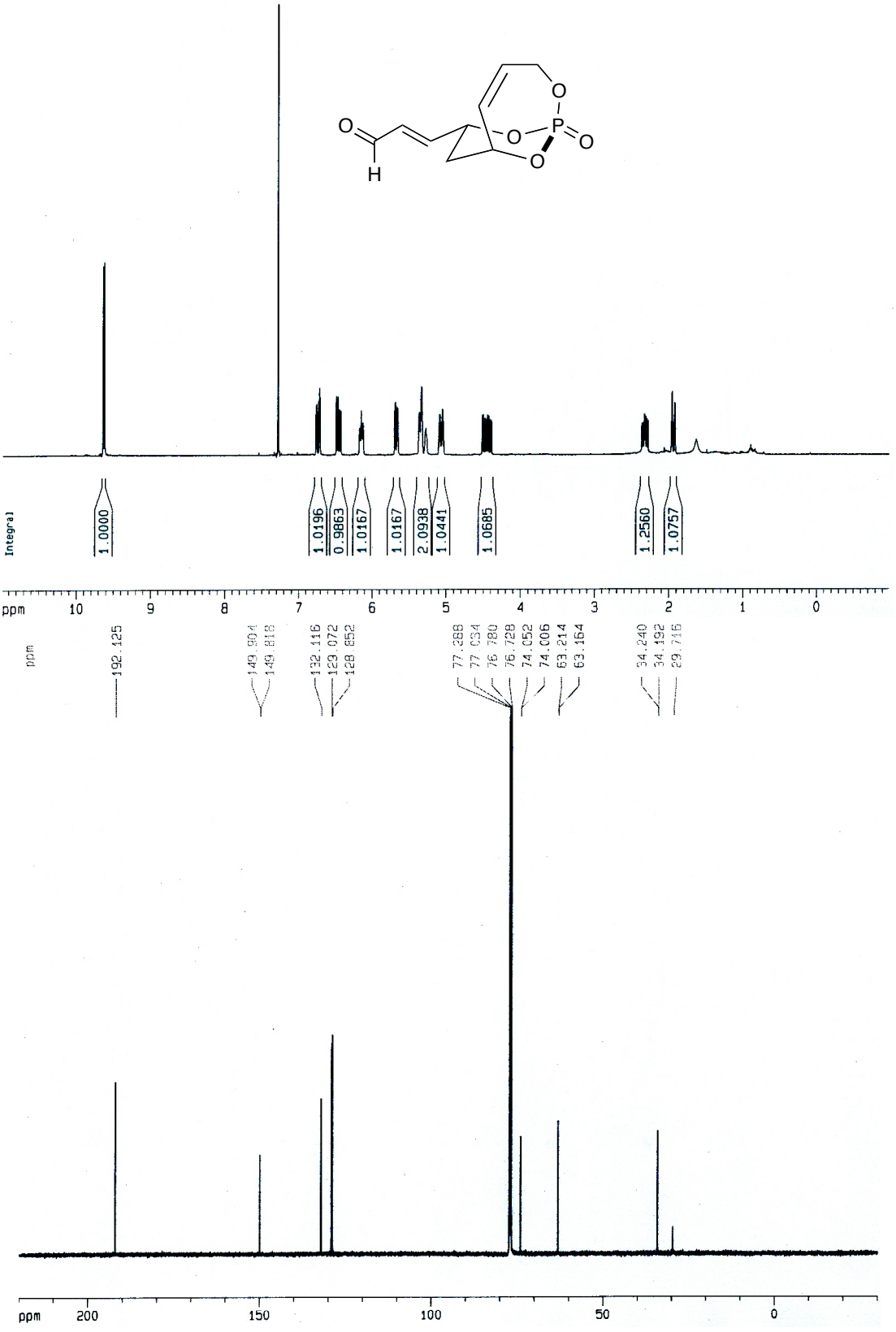
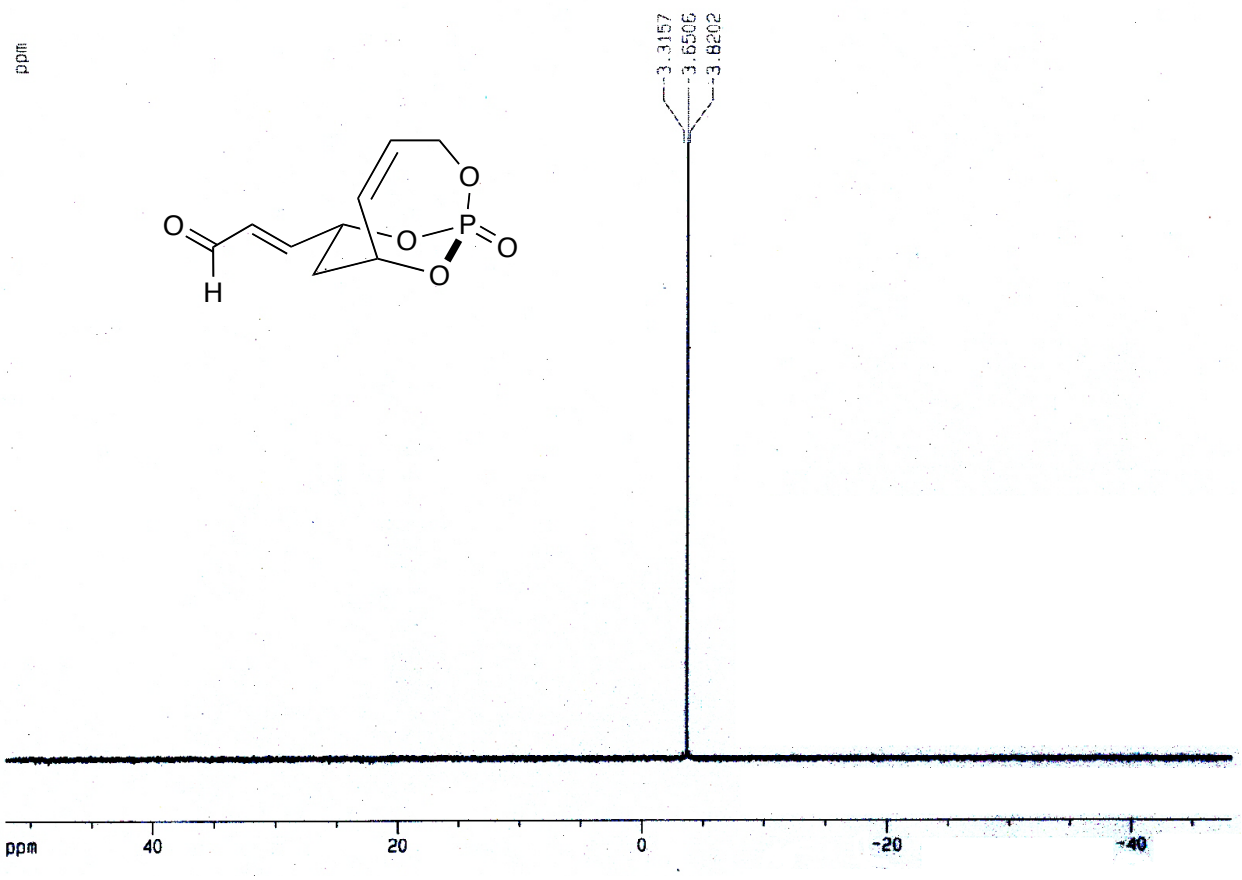
O
O
P
O
O
20
-20

Acrolein derived Bicyclo[4.3.1]phosphate Triester: 16

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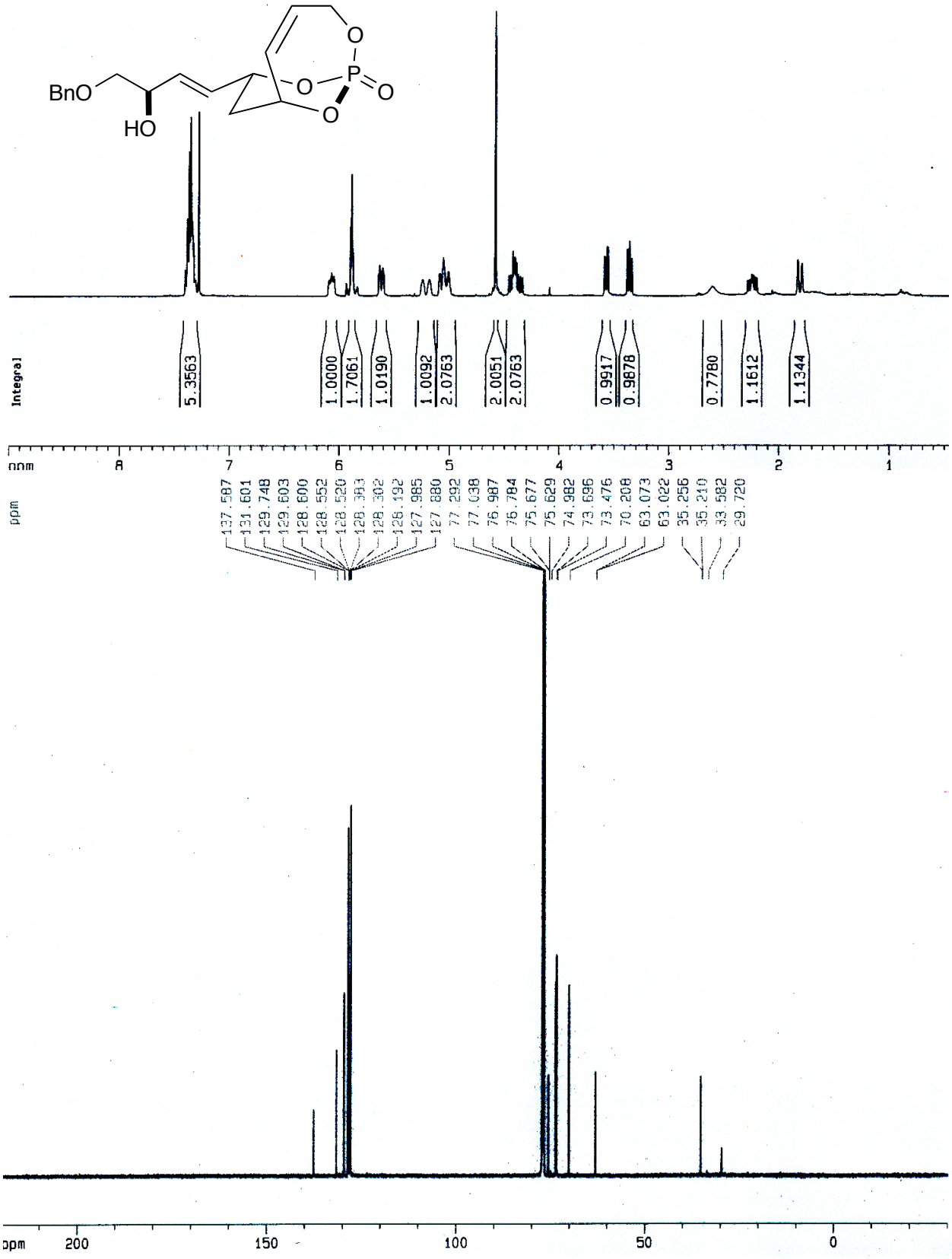
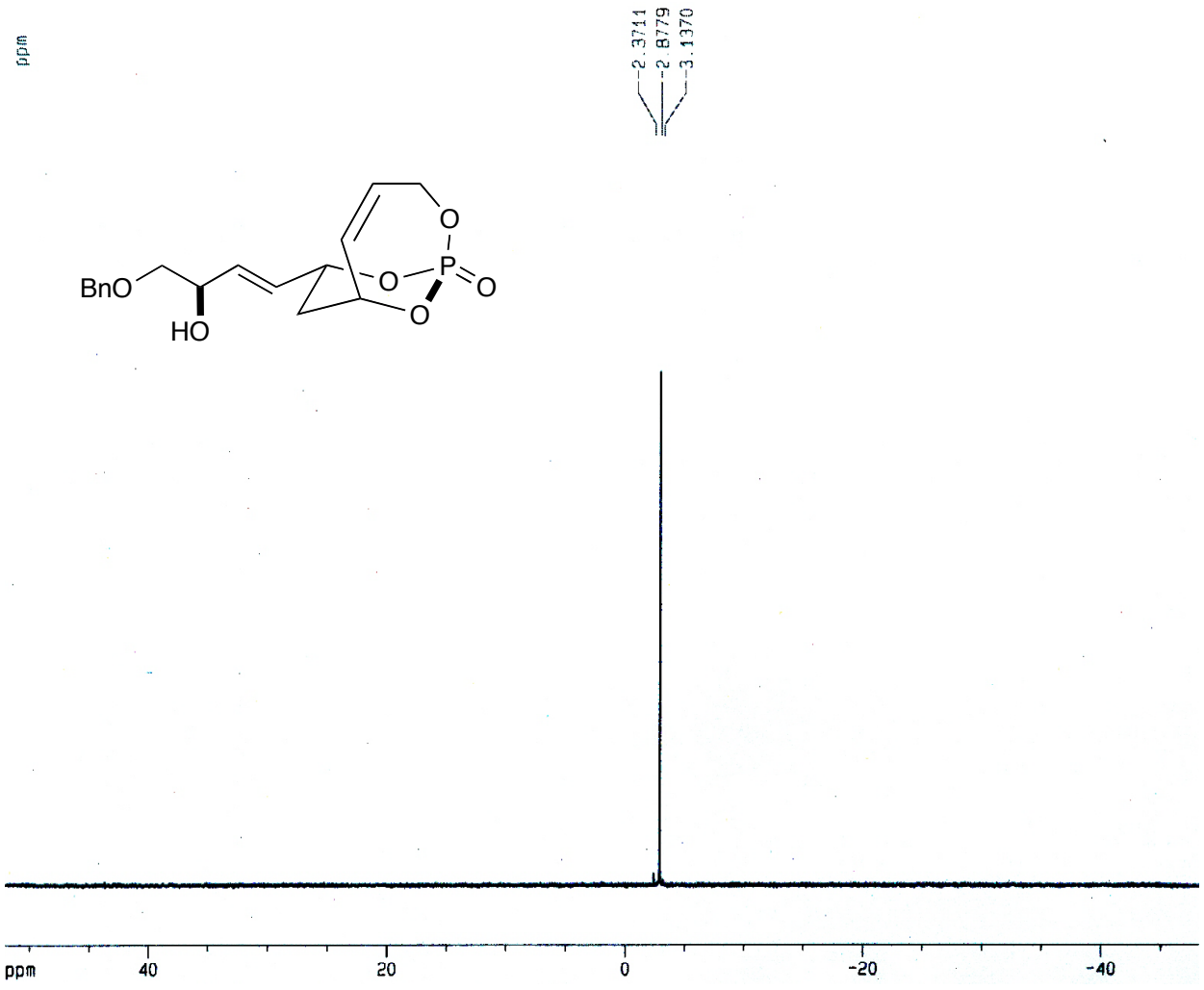
O
O
O
P
O
O
H
ppm
40
20
0
-20
-40

(*R*)-1-(Benzyloxy)buten-2-ol derived Bicyclo[4.3.1]phosphate Triester: 17

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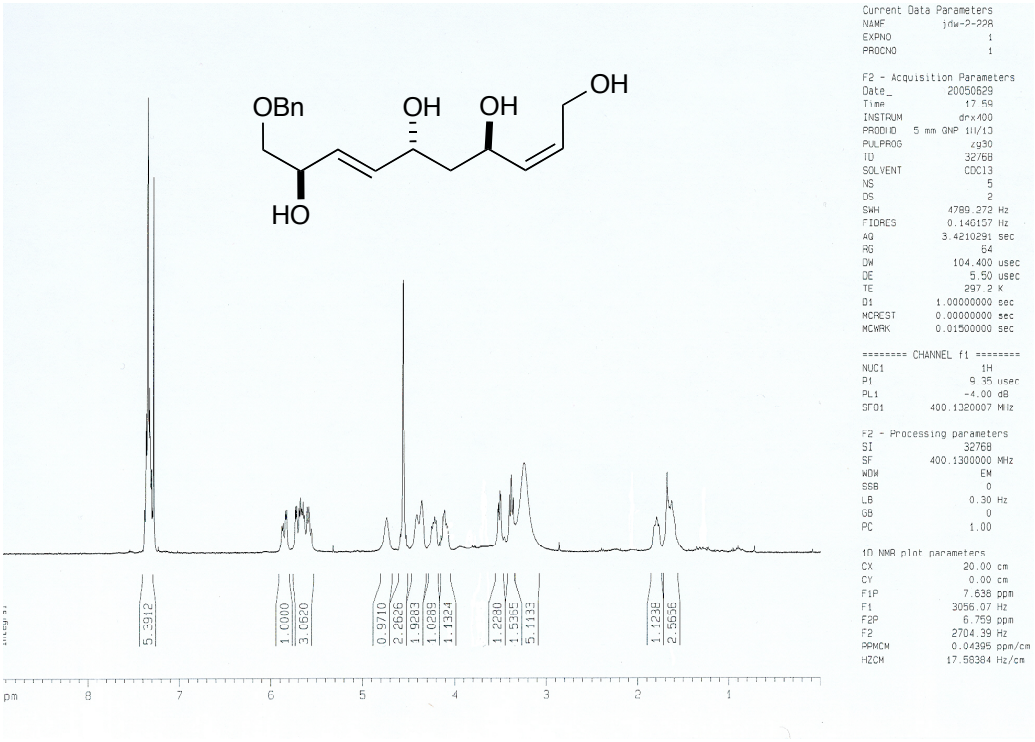
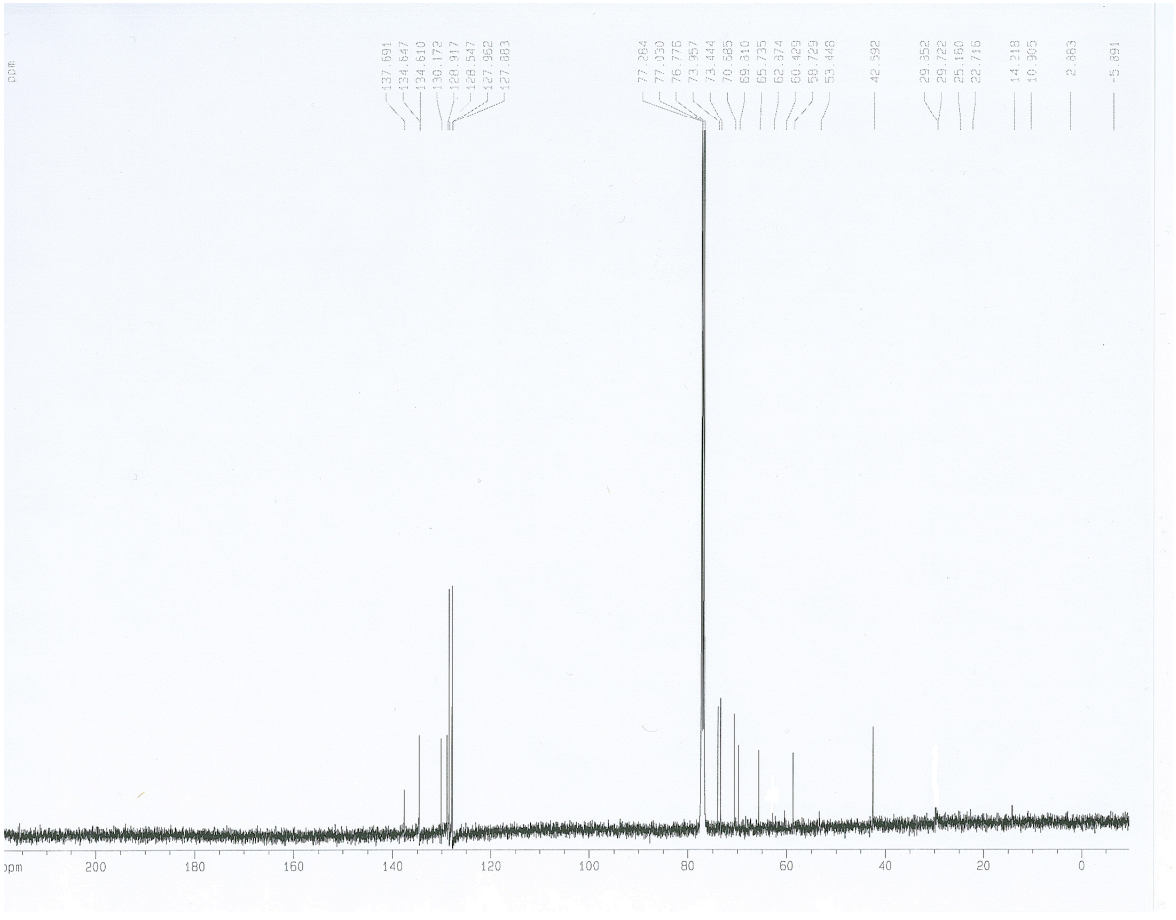
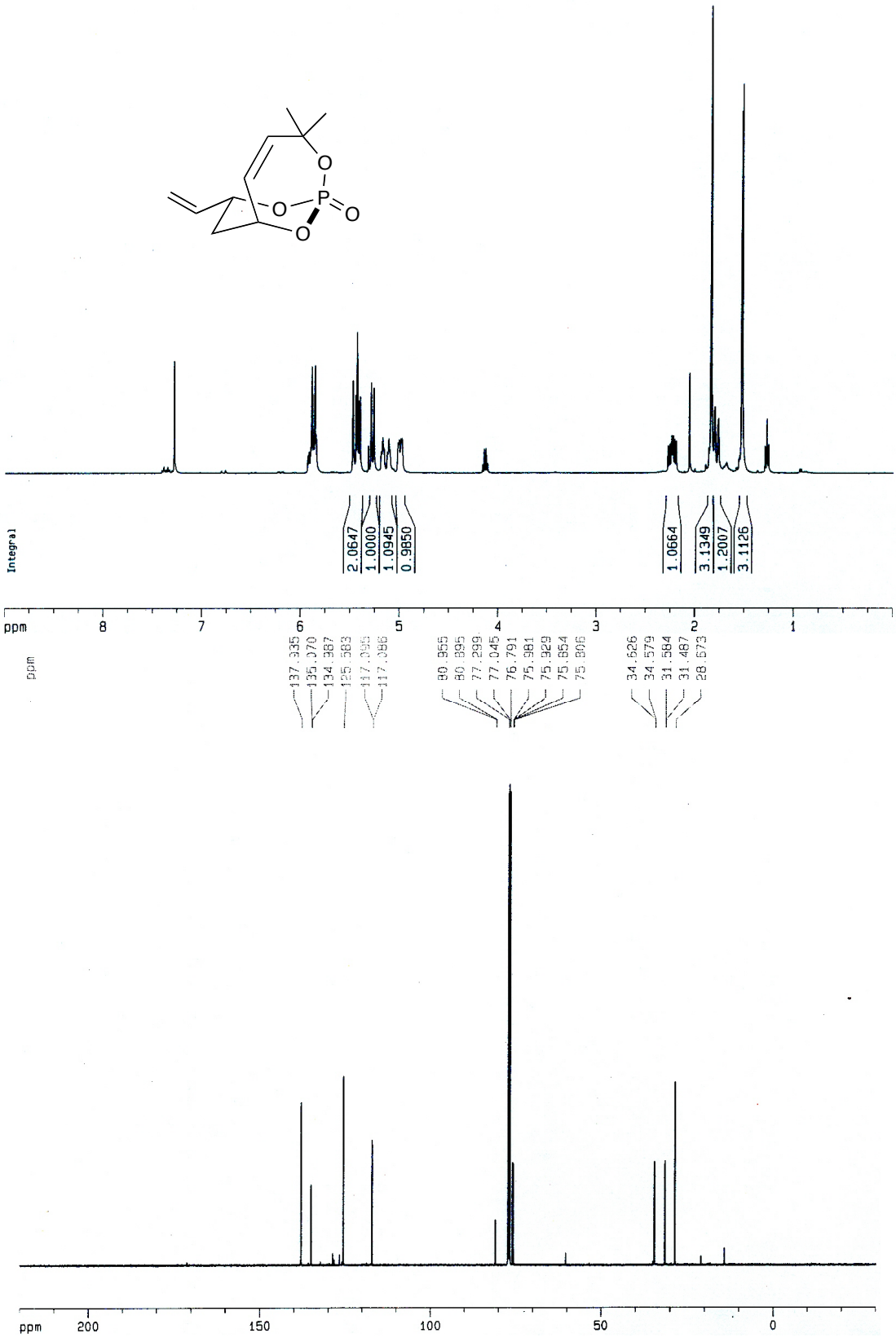
BnO
HO
O
O
P
O
O
ppm
40
20
0
-20
-40

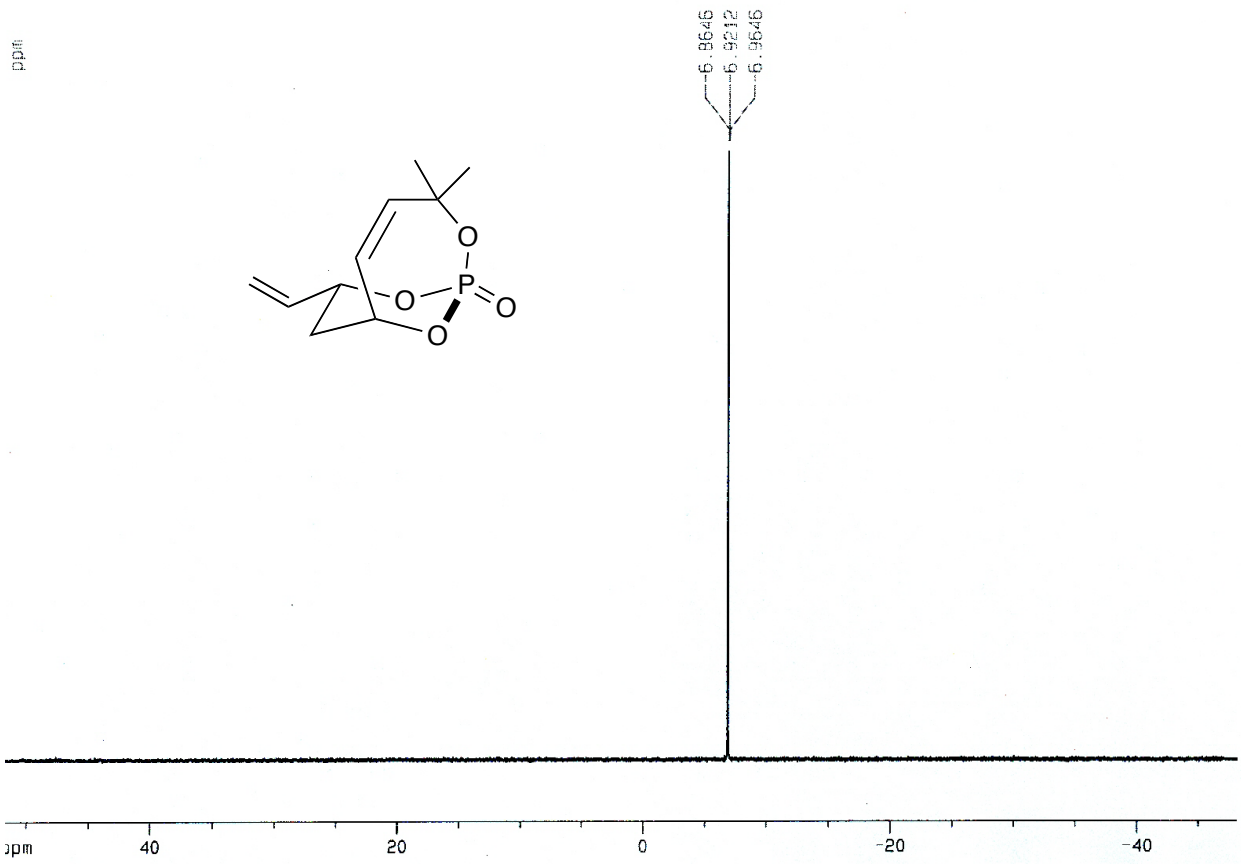
(2*Z*,4*R*,6*R*,7*E*,9*R*)-10-(benzyloxy)deca-2,7-diene-1,4,6,9-tetraol: 18



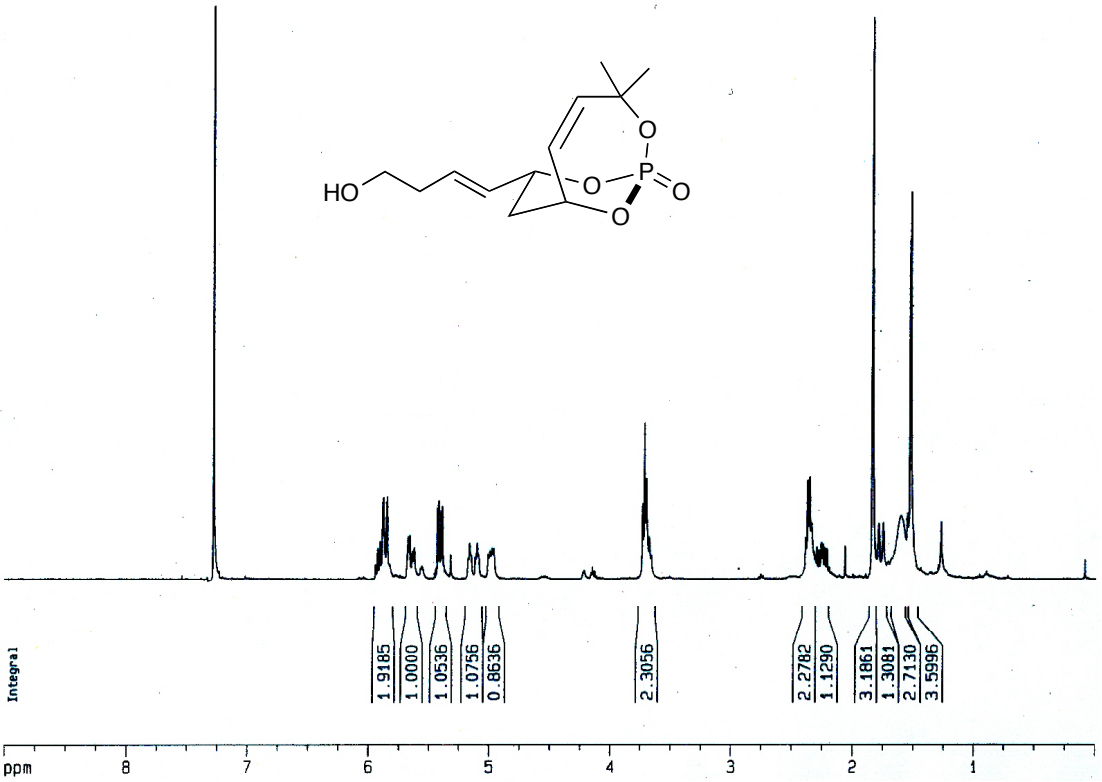


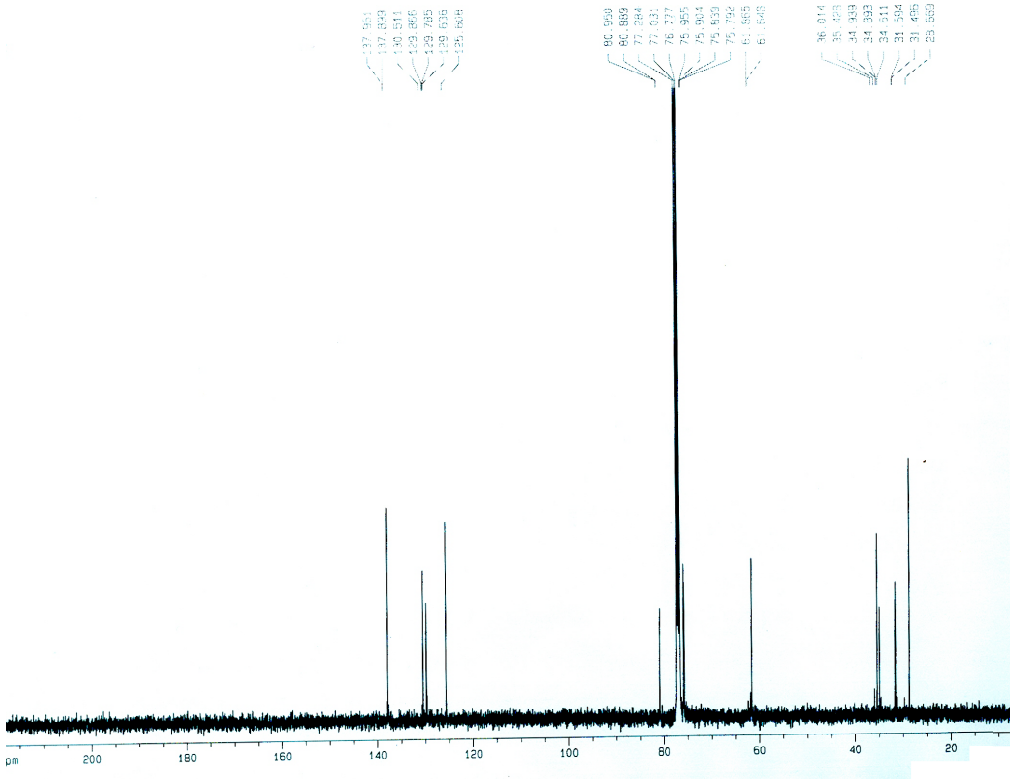
Second Generation Bicyclic Phosphate: 19

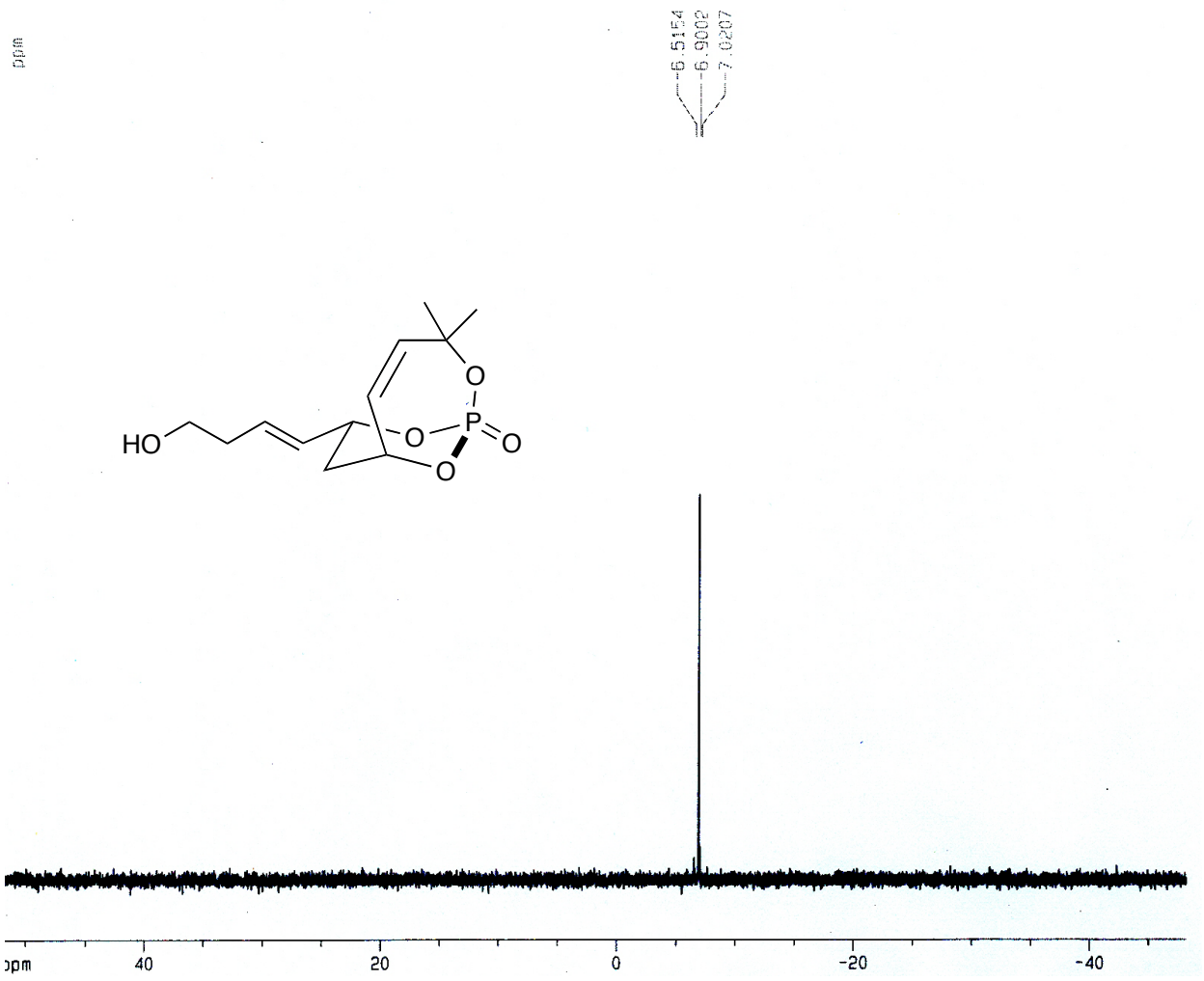



ppm
6.9646
6.9212
6.9646
O
O
P
O
O
O
ppm
40
20
0
-20
-40

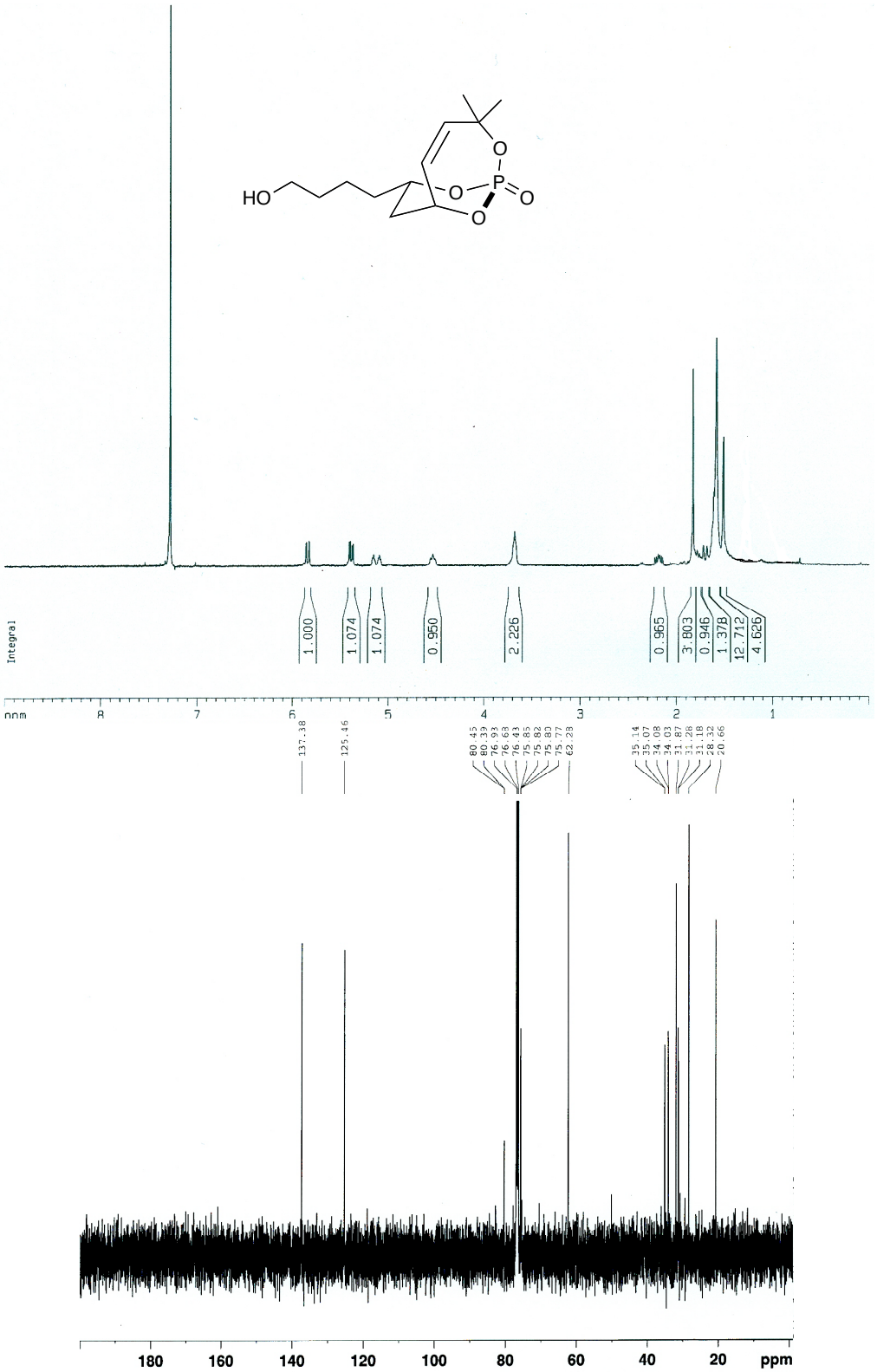
Allyl Alcohol Derive Second Generation Bicyclic Phosphate: 20

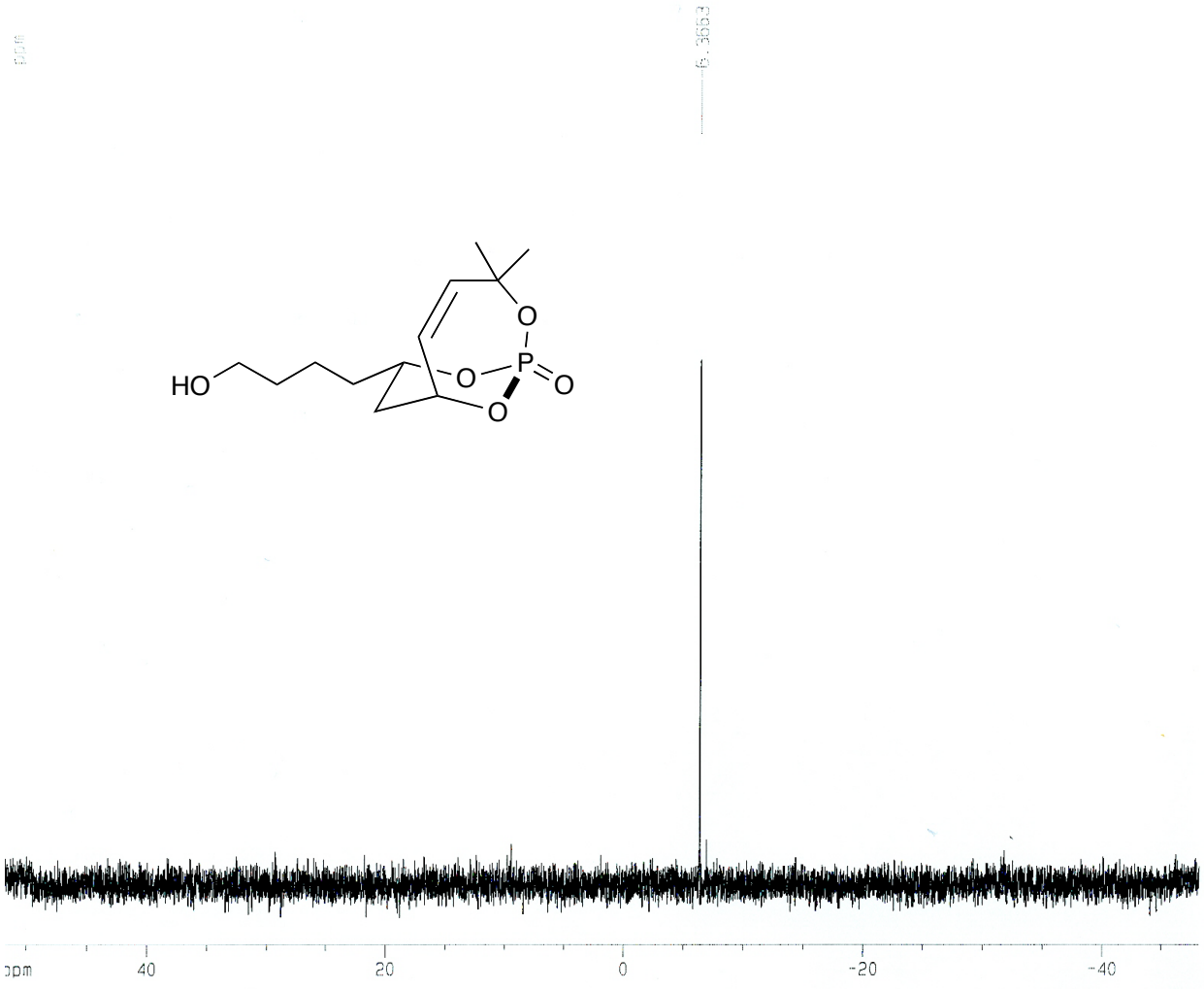




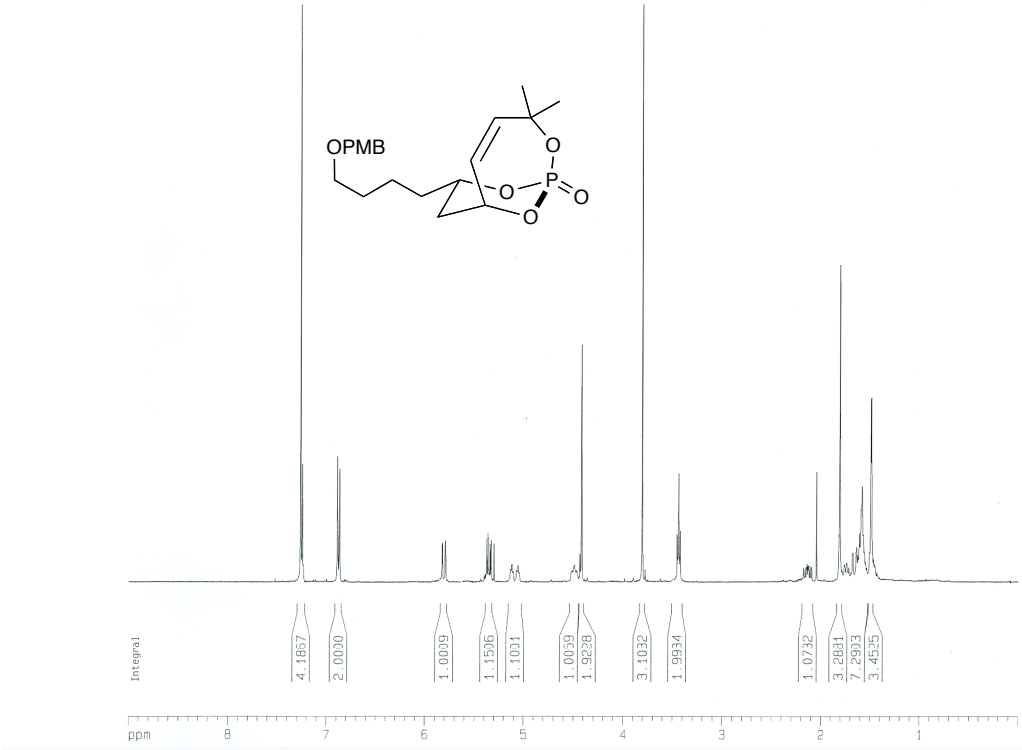

ppm
6.5154
6.9002
7.0207
HO
O
O
P
O
O
ppm
40
20
0
-20
-40

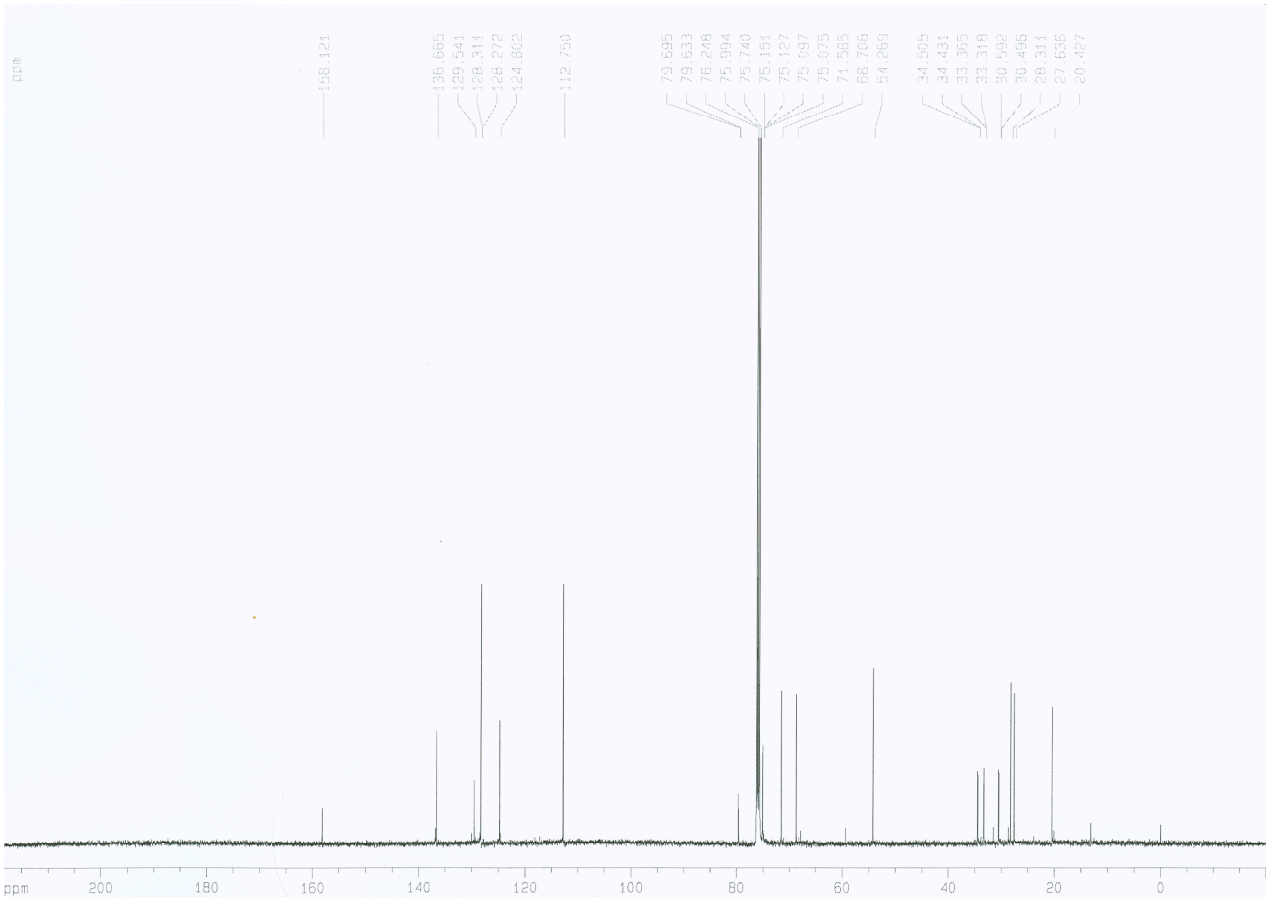
Partially Hydrogenation Alcohol derive Second Generation Phosphate: 21

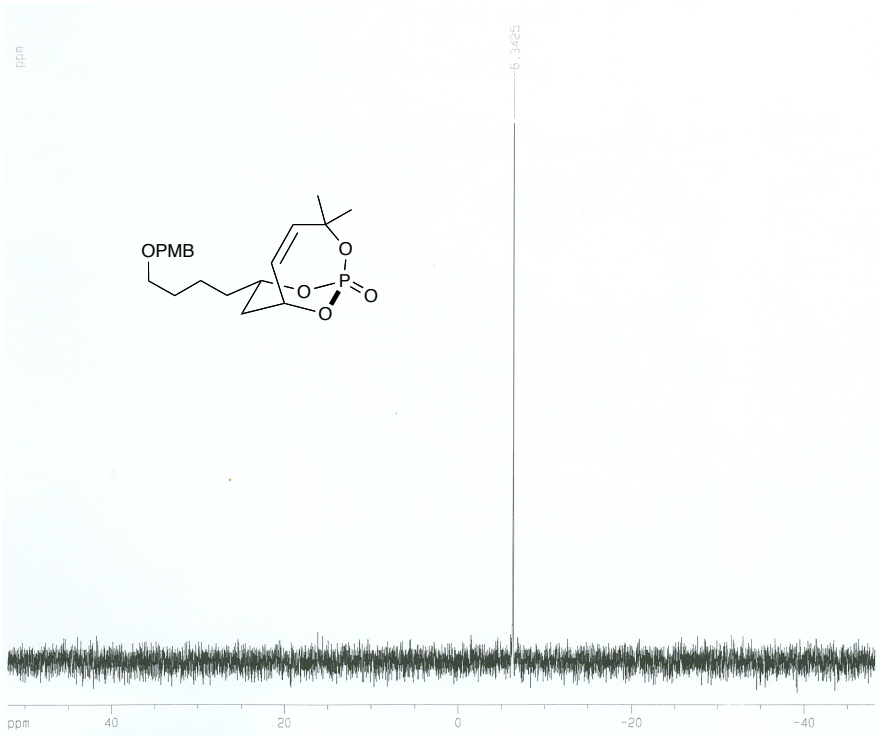



HO
O
P
O
O
O
ppm
40
20
0
-20
-40

PMB-Protected Hydrogenated Second Generation Phosphate: 22






ppm
6.3425
OPMB
O
P
O
O
O
ppm
40
20
0
-20
-40

(4*S*,5*R*,7*S*)-11-(4-methoxybenzyloxy)-2,4-dimethylundec-2-ene-5,7-diol: 23