Supporting Information

Dramatic effect of modified boranes in diastereoselective reduction of chiral cyclic α-ketophosphinates

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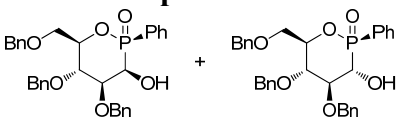
I. General Considerations

Melting points were measured on a Büchi B-540 apparatus and are uncorrected. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR and ^{31}P NMR using a Bruker DRX 400 MHz NMR spectrometer or a Bruker Avance 250 MHz NMR spectrometer. All NMR experiments performed on phosphorus are indicated uncoupling of hydrogen and all studies led during processing were done with a DMSO-D_6 probe. High resolution mass spectra were measured on JEOL JMS–SX 102A spectrometer. Analytical HPLC (Column: Waters SunFire^{TM} C18 5µ 4.6X250mm, Eluent: Acetonitrile/water (63:34), Flow: 1 mL.min^{-1})

Materials: Before use, commercial reagents were purified by distillation or sublimation. 2,3,5-tri-*O*-benzyl-D-arabinofuranose was purchased from Carbosynth and dried under vacuum before use. All manipulations were carried out using standard Schlenck Techniques. Solvents were dried according to current methods, distilled and stored under nitrogen atmosphere. All reactions involving air or moisture sensitive reagents or intermediates were carried out under dry nitrogen in flame-dried glassware.

II. General procedure for the synthesis of 3 and 4



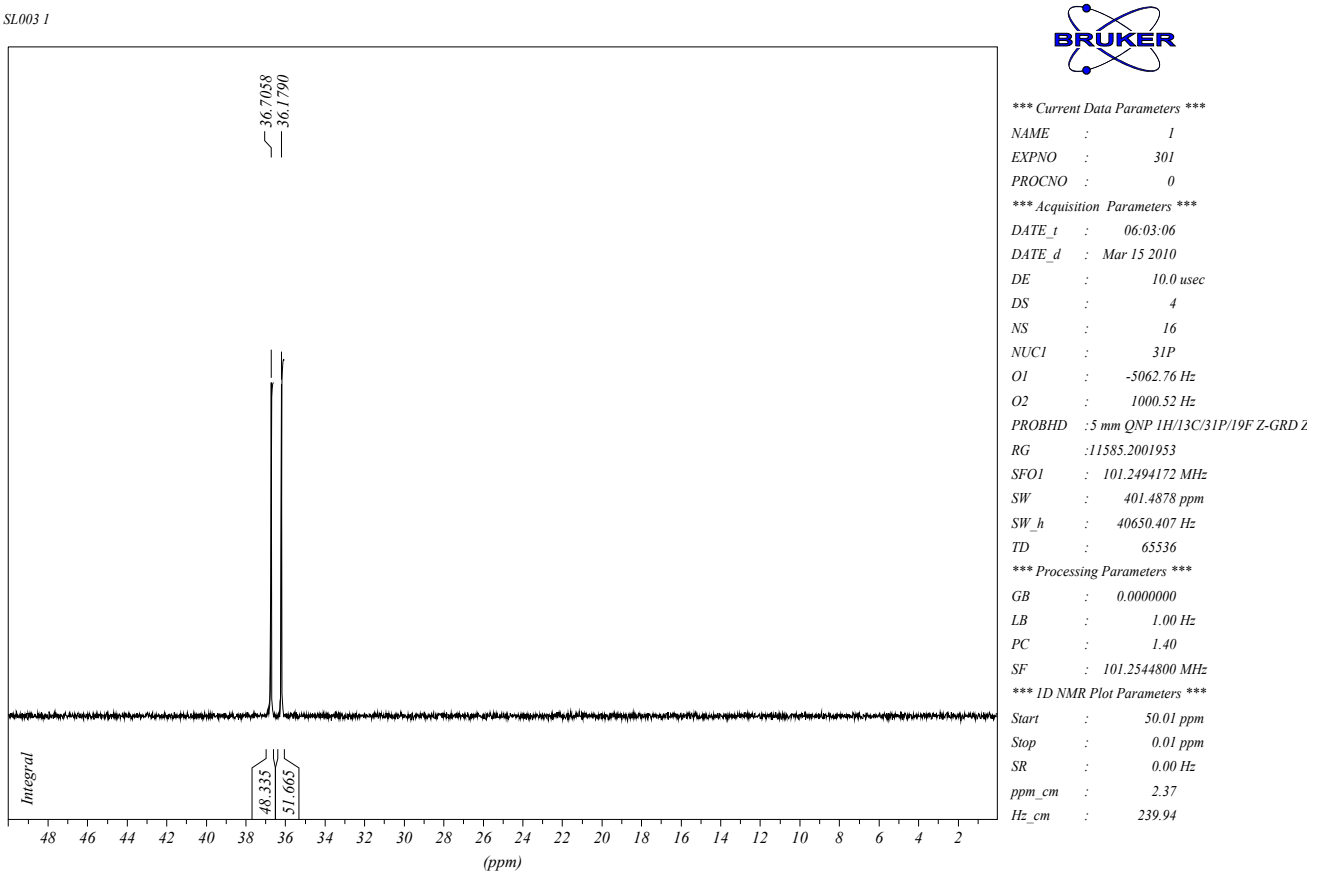
3 **4**

4,5-bis-benzyloxy-6-benzyloxymethyl-2-phenyl-2-oxo-2λ^{5}-[1,2]oxaphosphinan-3-ol (3) and (4). Ethyl phenylphosphinate (**1**) was prepared by a known literature method (esterification of commercial phenylphosphinic acid).[1] 2,3,5-tri-*O*-benzyl-*D*-arabinofuranose **2** (21.00 g, 49 mmol) was added under nitrogen to a solution of ethyl phenylphosphinate (**1**, 8.50 g, 50 mmol) in THF (70 mL). Freshly sublimated potassium *tert*-butoxide (1.12 g 12 mmol) was added to the solution. Reaction mixture was stirred at room temperature for 15 h. After solvent evaporation under vacuum, chloroform (160 mL) was added to the crude oil. The organic solution was washed with a saturated solution of ammonium chloride (3 × 50 mL). The organic layer was dried over sodium sulfate, filtered off and solvent was evaporated under vacuum. The yellow oil residue containing a mixture of four diastereomers (25.7 g, 26/28/19/27) was dissolved in diethyl ether and a white precipitate was formed and filtered to give a mixture of **3**/**4** (6.35g, 48/52) as a white powder. After purification on Water Prep LC (Column: Waters SunFire^{TM} C18, 8µm, 50×250 mm; Eluent: Acetonitrile/water (60:40); Flow: 17 mL.min^{-1}), compounds **3** and **4** were recovered pure, respectively.

The two diastereomers (**3** and **4**), after separation were fully characterized allowing the attribution of the complete stereochemistry of all the stereogenic centers. Compounds **3** and **4** are respectively epimer at the carbon center.

[1] K. Afarinkia, H.-W. Yu, Hewitt reaction revisited, *Tetrahedron Letters*, **2003**, *44* (4), 781-783.

^{31}P NMR spectrum of a mixture of **3** and **4**.



Preparative HPLC analysis of a mixture of compounds **3** and

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Injection Volume:	1000,00 ul	Processing Method:	severine01_18052010
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Sample Set Name:		Proc. Chnl. Descr.:	W2489 ChB 254nm

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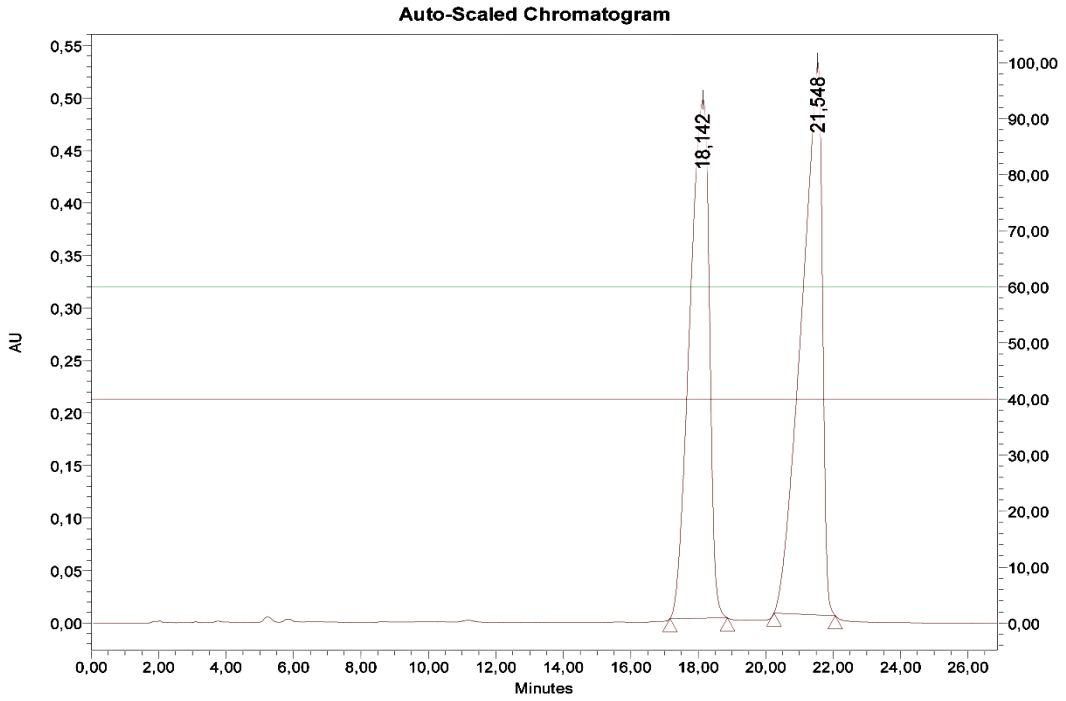

Processed Channel: W2489 ChB 254nm

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SampleName
DEE055(mel)2_flow17iso60_2152010

4.

SAMPLE INFORMATION

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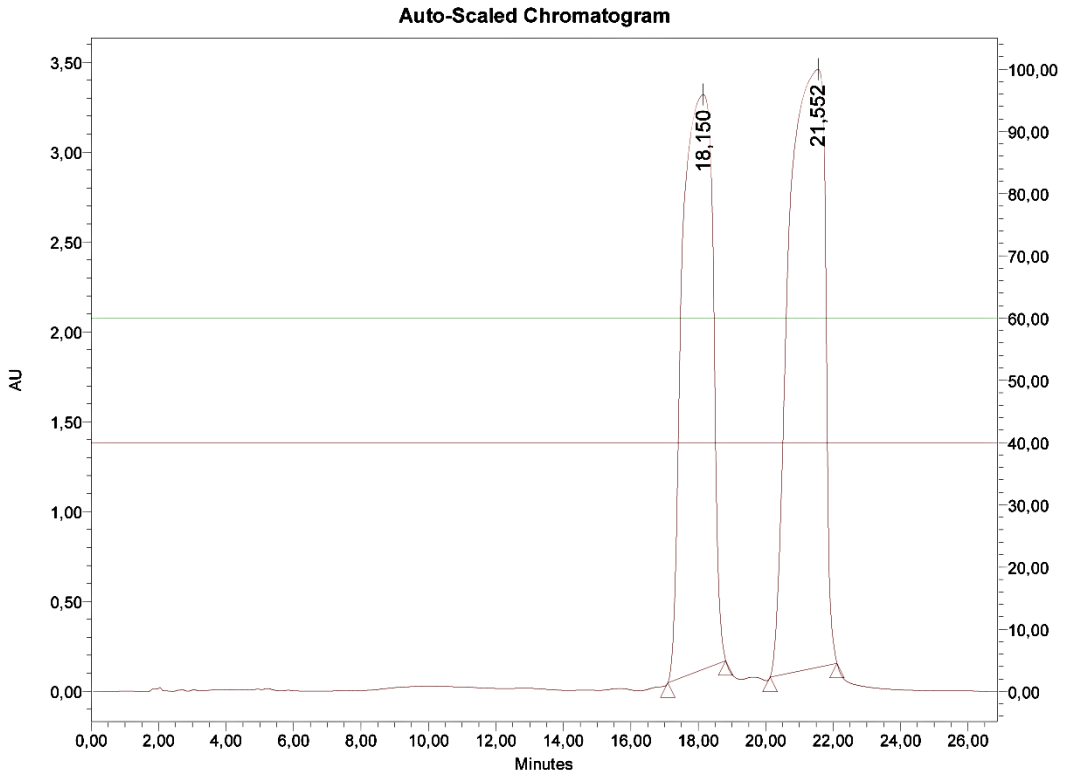

Processed Channel: W2489 ChA 214nm

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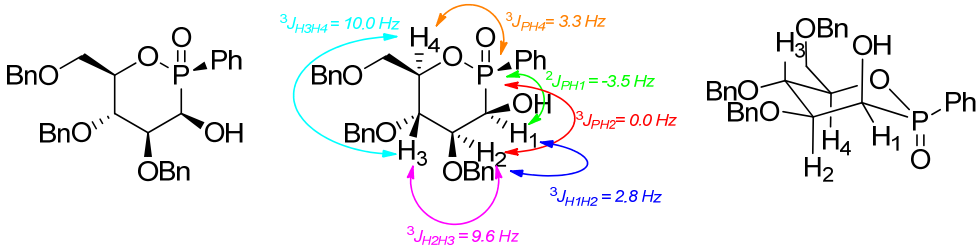
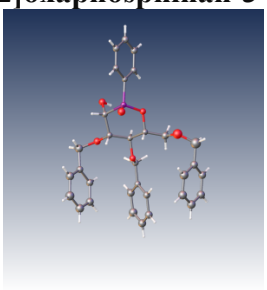
2	W2489 ChA 214nm	21,552	244200199	55,16	3327480

***(2S,3R,4S,5S,6R)*-4,5-bis-benzyloxy-6-benzyloxymethyl-2-phenyl-2-oxo-2λ^5-[1,2]oxaphosphinan-3-ol 3**:





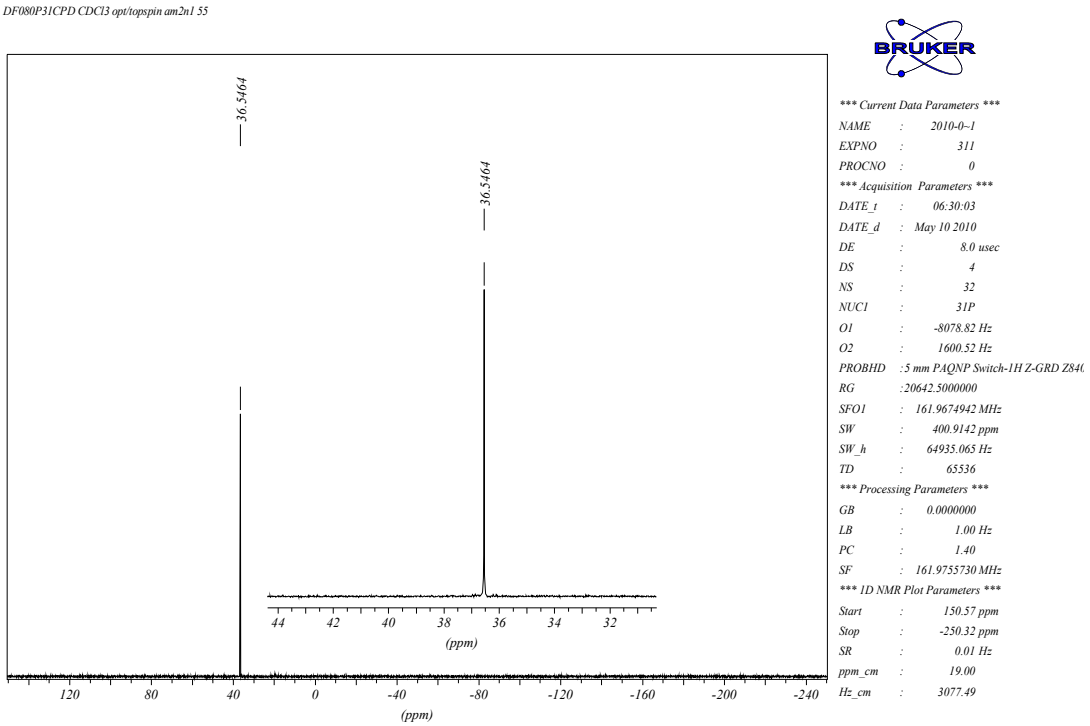
ORTEP structure of compound **3**.

White powder
^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm) = 36.55 (s); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ (ppm) = 2.67 (s, 1H, O*H*), 3.80 (dd, $^2J_{HH}$ = -11.3 Hz, $^3J_{HH}$ = 2.0 Hz, 1H, OCH_2), 4.00 (ddd, $^2J_{HH}$ = 11.3 Hz, $^4J_{PH}$ = 3.3 Hz, $^3J_{HH}$ = 3.2 Hz, 1H, CH_2), 4.30 (dd, $^3J_{HH}$ = 10.0 Hz, $^3J_{HH}$ = 9.6 Hz, 1H, PCCC*H*), 4.36 (dd, $^3J_{HH}$ = 9.6 Hz, $^3J_{HH}$ = 2.8 Hz, 1H, PCC*H*), 4.43 (dd, $^2J_{HP}$ = -3.5 Hz, $^3J_{HH}$ = 2.8 Hz, 1H, PC*H*), 4.56 (dddd, $^3J_{HH}$ = 10.0 Hz, $^3J_{HH}$ = 3.3 Hz, $^3J_{HP}$ = 3.2 Hz, $^3J_{HH}$ = 2.0 Hz, 1H, POC*H*), 7.24-7.38 (m, 15H, CH_{Ar}), 7.48-7.54 (m, 2H, CH_{Ar}), 7.62-7.68 (m, 1H, CH_{Ar}), 7.96-8.03 (m, 2H, CH_{Ar}); ^{13}C NMR (400,13 MHz, $CDCl_3$): δ (ppm) = 66.81 (d, $^1J_{CP}$ = 105.1 Hz, P*C*H), 68.91 (d, $^3J_{CP}$ = 8.8 Hz, OC*C*H$_2$), 72.48 (s, Ph*C*H$_2$), 73.43 (s, Ph*C*H$_2$), 73.74 (d, J_{CP} = 2.2 Hz, *C*H), 75.46 (d, J_{CP} = 5.6 Hz, *C*H), 75.64 (s, Ph*C*H$_2$), 81.38 (d, $^2J_{CP}$ = 2.9 Hz, PC*C*H), 126.53 (d, $^1J_{CP}$ = 138.8 Hz, P*C*$_{Ph}$), 127.68, 127.80, 127.84, 127.98, 128.19 (s, *C*H$_{Bn}$), 128.31 (d, $^3J_{CP}$ = 13.4 Hz, *C*H$_{Ph}$), 128.42, 128.66 (s, *C*H$_{Bn}$), 132.99 (d, $^2J_{CP}$ = 9.9 Hz, *C*H$_{Ph}$), 133.34 (d, $^4J_{CP}$ = 2.8 Hz, *C*H$_{Ph}$), 137.32, 138.07, 138.09 (s, *C*$_{Bn}$); HRMS m/z (MH^+) 545.2092 (calcd for $C_{32}H_{34}O_6P$: 545.2093); Analytical HPLC (Column: Waters SunFire™ C18, 5 µm 4.6×250 mm; Eluent: acetonitrile/water (63:37), Flow: 1 mL.min^{-1}): Retention time = 15.97. $[\alpha]_D^{25}$ = +13.48 (*c* 0.0445, $CHCl_3$). HRMS m/z (MH^+) 545.2091 (calcd for $C_{32}H_{34}O_6P$: 545.2093); Analytical HPLC (Column: Waters SunFire™ C18, 5 µm 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 15.97.

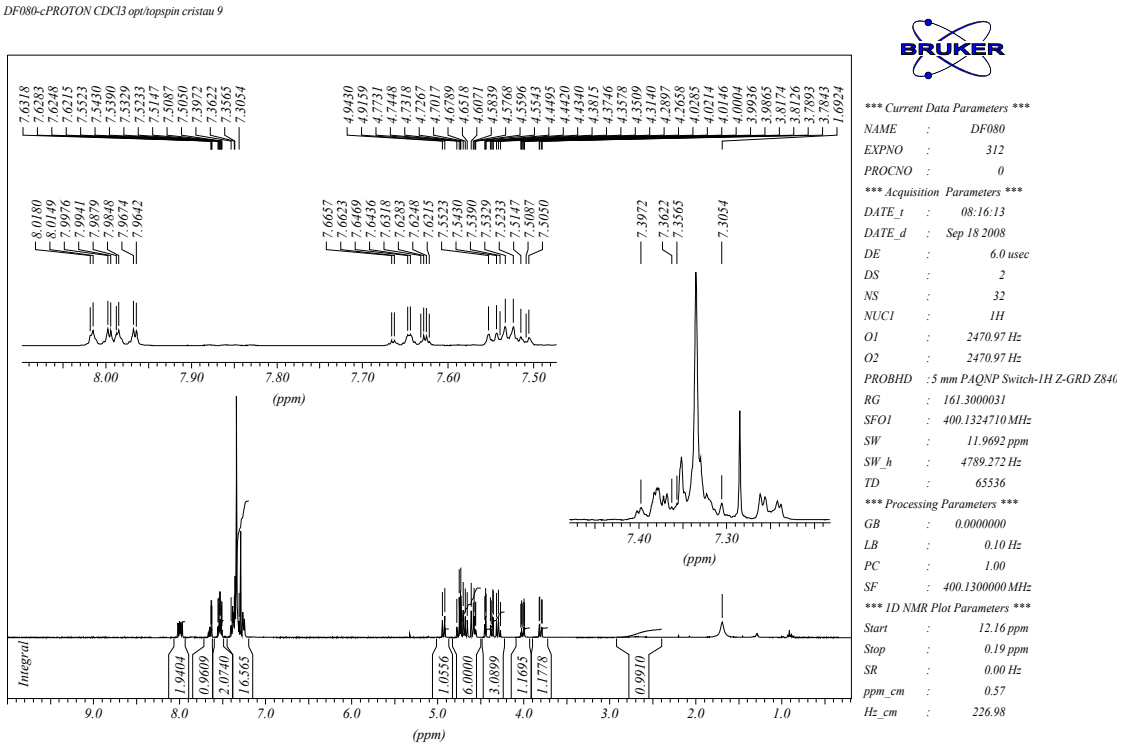
Suitable crystals for X-ray analysis were obtained in Et_2O/CH_2Cl_2 for compound **3** (CCDC 848920). According to the ORTEP structure, we were able to assign the absolute configuration of the newly created asymmetric centers of the diastereomer **3**. Compound **3** shows a chair structure with P_2(*S*) and C_3(*R*) configuration [Crystal data for compound **3**: Formula=$C_{32}H_{33}O_6P$, T = 175 K, M_r = 544.55 gmol^{-1}, crystal size = 0.100x0.500x0.500 mm^3, monoclinic, space group *P*21, a = 15.6590(3), b = 5.6930(1), c = 15.8108(3) Å, α = 90°, β = 91.3777(16)°, γ = 90°, V = 1409.07(5) Å^3, Z = 2, ρ_{cald}= 1.283 gcm^{-3}, µ= 1.221 mm^{-1}, θ_{max}= 66.187°, 13913 reflections measured, 4543 unique, 4074 with I>2σ(I), R_{int} = 0.031, <σ(I)/I> = 0.0384, refined parameters = 353, R_1 (I>2σ(I)) = 0.0388, wR_2 (I>2σ(I)) = 0.1001 R_1 (all data) = 0.0436, wR_2 (all data) = 0.1049, GOF = 0.9297, Δρ(min/max)= -0.26/0.25 eÅ^{-3}. Cu radiation was used in order to have a more reliable estimate of the Flack and Hooft parameters. Charge flipping as implemented in *Superflip* (Palatinus, L.; Chapuis, G. J. Appl. Cryst. 2007, 40, 786-790) was used to solve the structure and least-squares from *CRYSTALS* (Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. J. Appl. Crystallogr., 2003, 36, 1487) to refine the structure. The Flack parameter was refined to 0.07(2) and the Hooft parameter determined to be 0.08(1). The chance that the correct hand was assigned in the two-hypotheses model of an enantiopure material is 100%. (R. W. W. Hooft, L. H. Straver, A. L. Spek, J. Appl. Cryst. 41 2008, 96-103)].

The oxidation of the two diastereomers **3** and **4**, with Dess-Martin reagent afforded the same stereoisomer of α-ketophosphinate **7**, demonstrating that compounds **3** and **4** are epimers at the carbon atom, α to the phosphorus atom. Furthermore, the vicinal coupling constant ^{1}H NMR data showed: a trans di-axial vicinal coupling constants between protons H_2/H_3 (J_{H2-H3} = 9.6 Hz) and protons H_3/H_4 (J_{H3-H4} = 10.0 Hz) and a cis axial-equatorial vicinal coupling constant between protons H_1/H_2 (J_{H1-H2} = 2.8 Hz) confirming that in solution the major conformer is similar to those observed by X-ray.

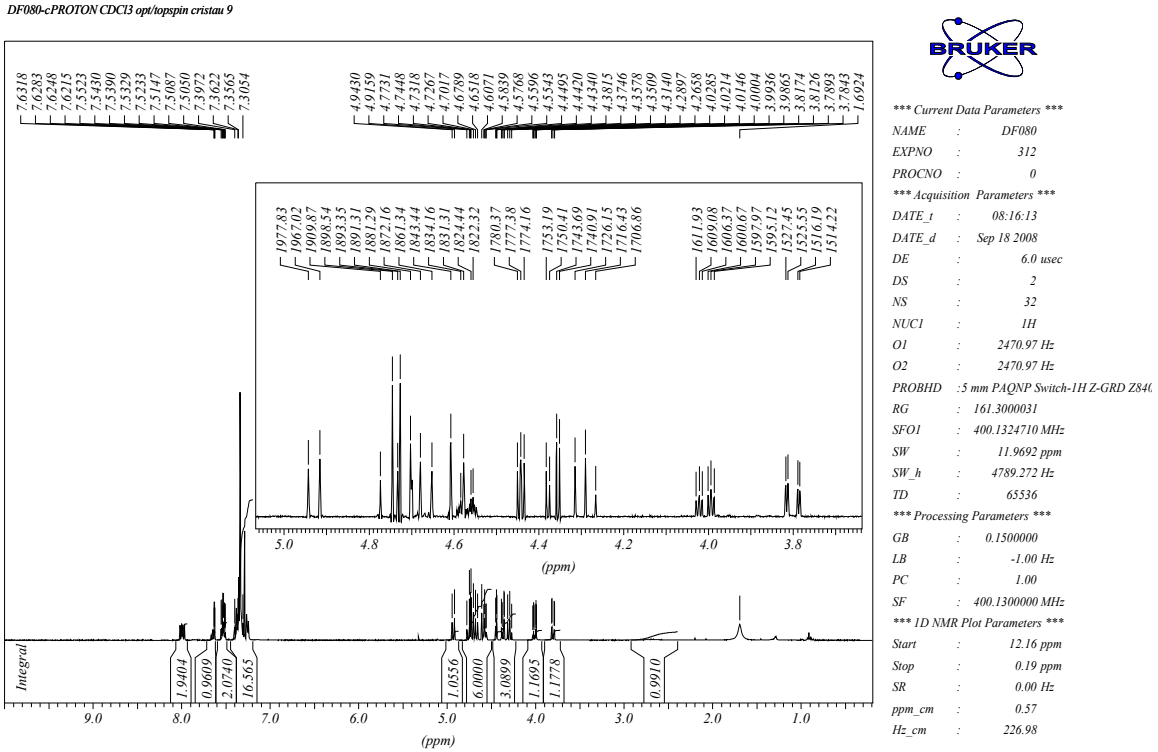
^{31}P NMR – $CDCl_3$



^{1}H NMR – $CDCl_3$



Zoom in proton NMR with Gaussian Fourrier transformation (LB = -1 and GB = 10%)



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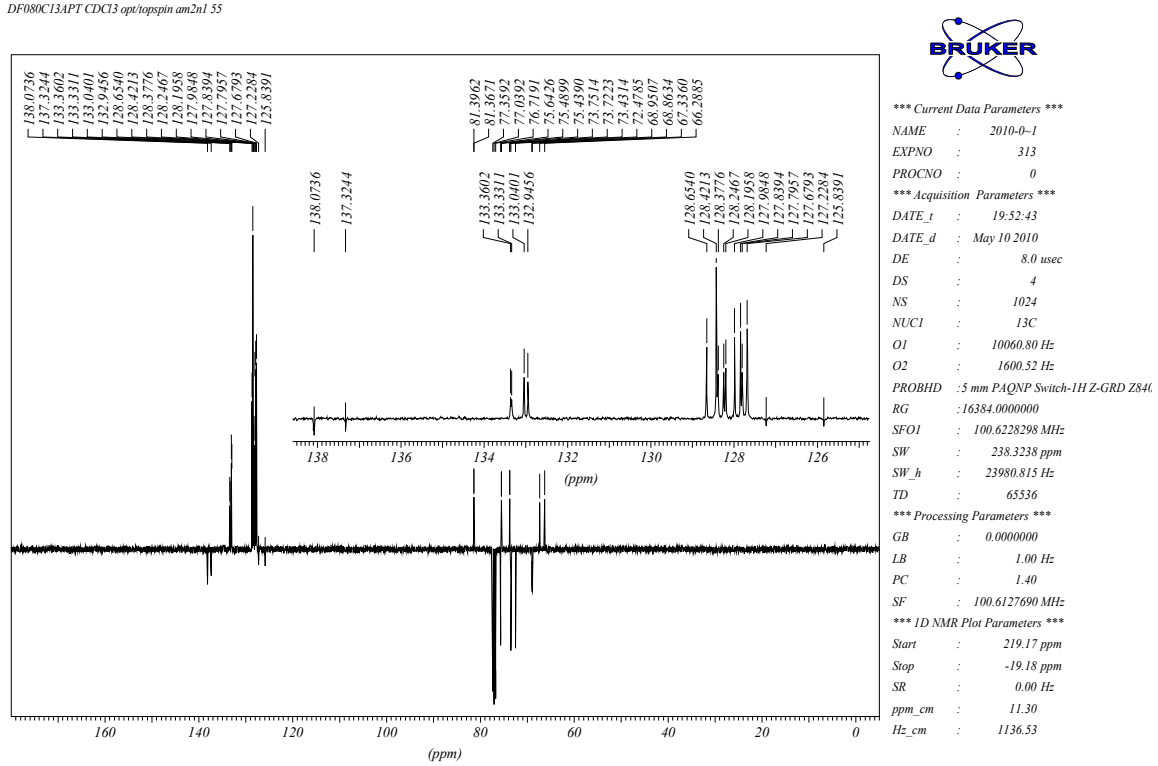

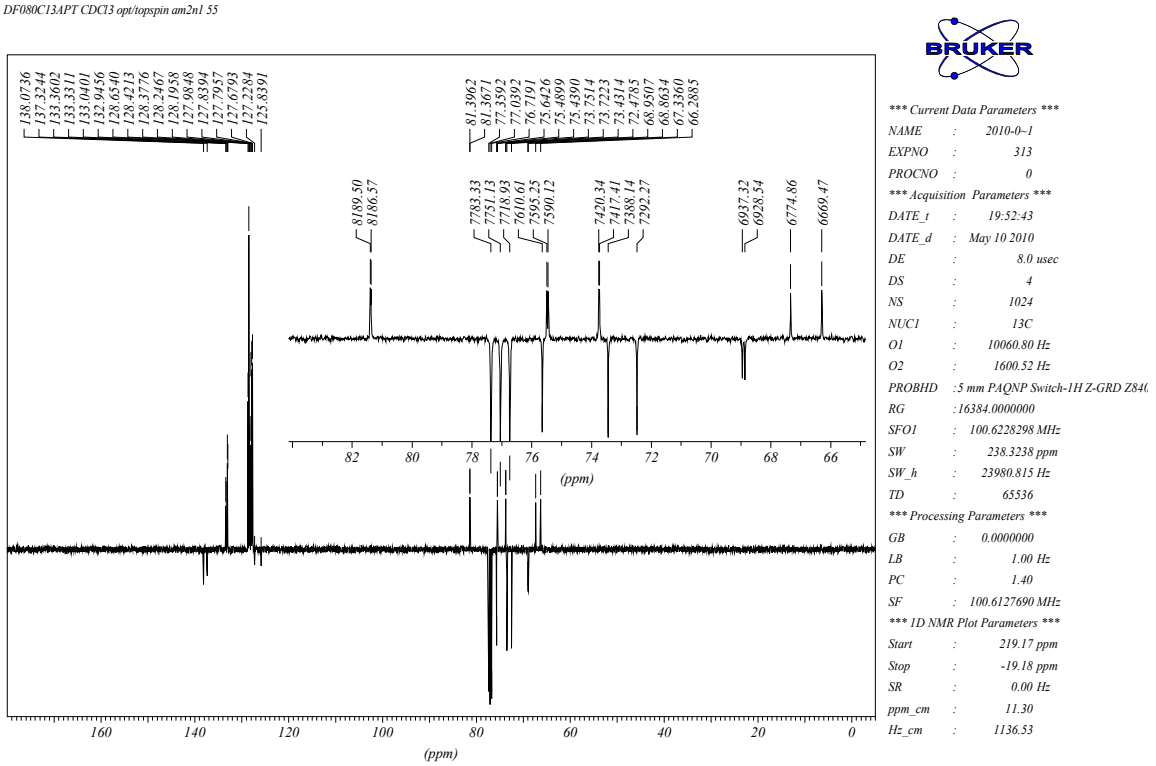

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Analytical HPLC

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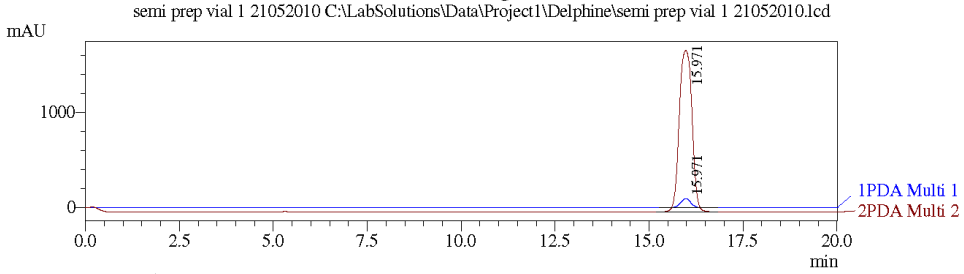

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2 PDA Multi 2 / 214nm 4nm

Chromatogram

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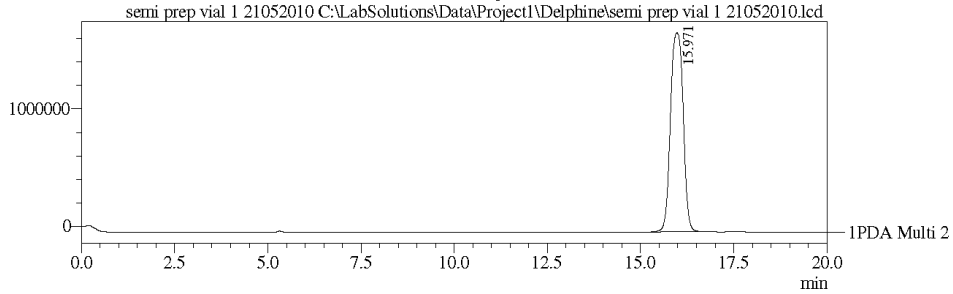

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PDA Ch2 214nm 4nm

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PeakTable

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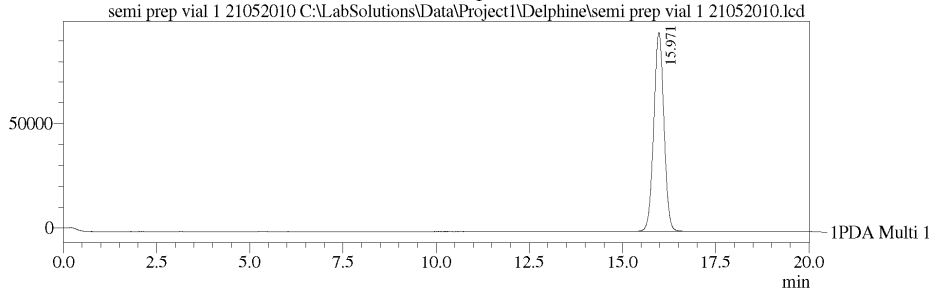
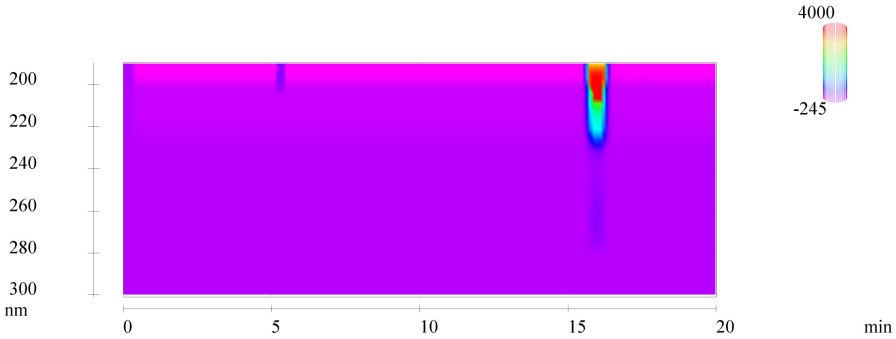


1 PDA Multi 1 / 254nm 4nm

Contour



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Elemental Composition Report

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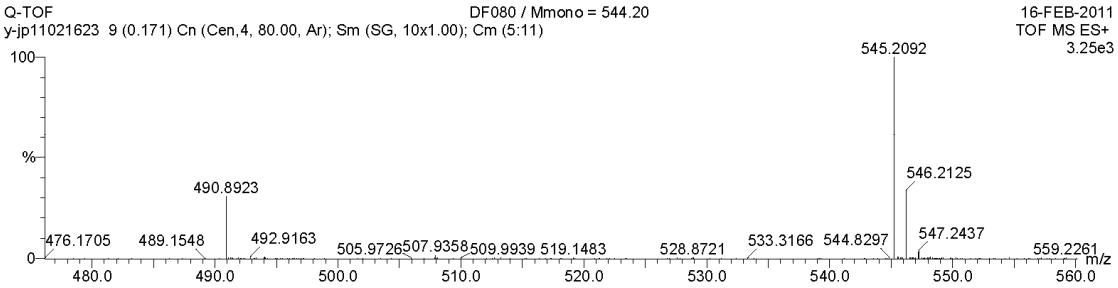
Monoisotopic Mass, Odd and Even Electron Ions
59 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)



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Maximum:		3.0	5.0	100.0		
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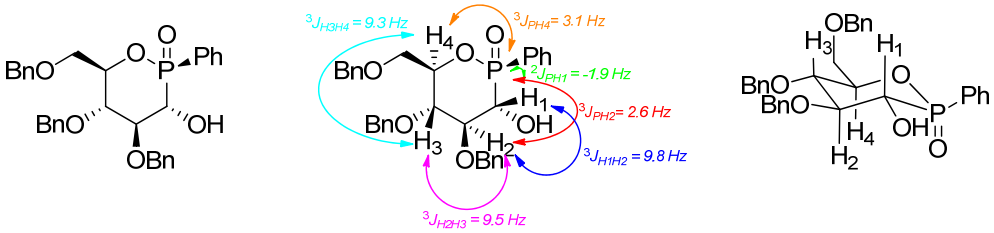
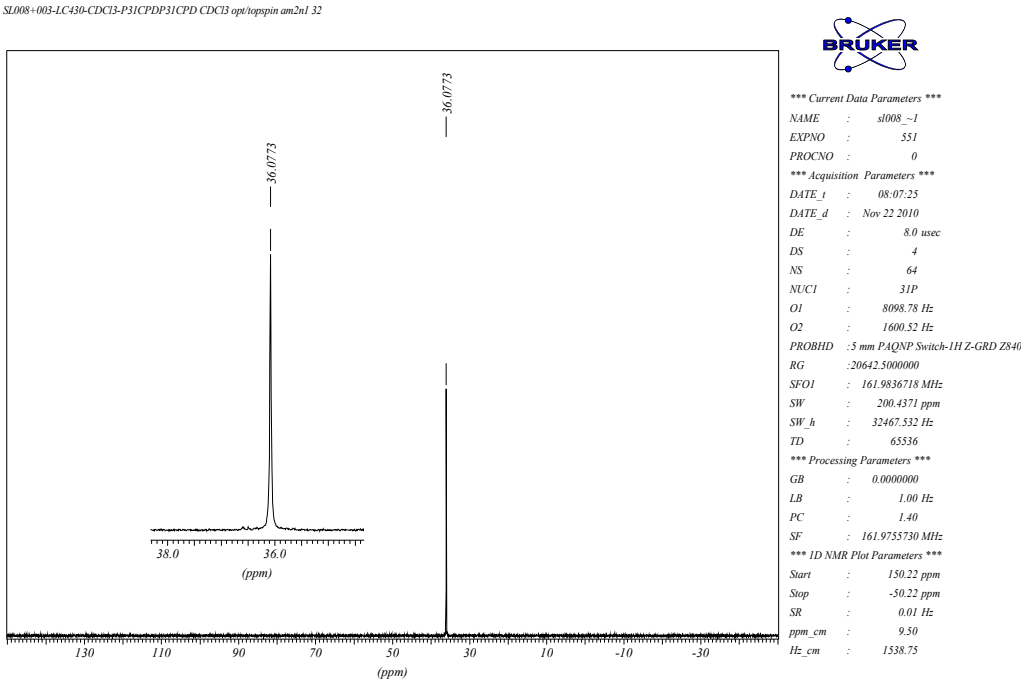


White powder

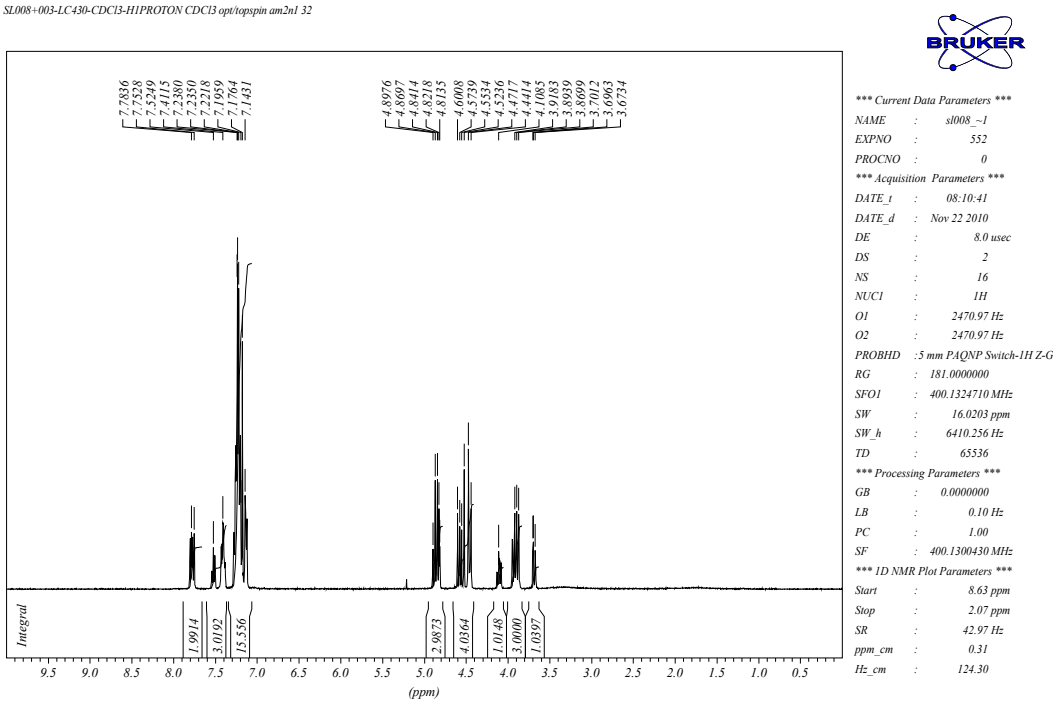
^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm) = 36.08 (s); ^{1}H NMR (400.13 MHz, $CDCl_3$): 3.69 (dd, $^2J_{HH}$ = -11.1 Hz, $^3J_{HH}$ = 2.3 Hz, 1H, C$\underline{H}_2$); 3.88 (ddd, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 2.74 Hz, $^4J_{PH}$ = 2.6 Hz, 1H, C$\underline{H}_2$); 3.90 (dd, $^3J_{HH}$ = 9.5 Hz, $^3J_{HH}$ = 9.3 Hz, 1H, PCCC$\underline{H}$); 3.93 (dd, ^{3}J$_{HH}$ = 9.8 Hz, $^2J_{PH}$ = -1.9 Hz, 1H, PC$\underline{H}$); 4.10 (ddd, ^{3}J$_{HH}$ = 9.8 Hz, $^3J_{HH}$ = 9.5 Hz, $^3J_{PH}$ = 2.6 Hz, 1H, PCC$\underline{H}$); 4.46 (dddd, $^3J_{HH}$ = 9.3 Hz, $^3J_{PH}$ = 3.1 Hz, J_{HH} = 2.7 Hz, $^3J_{HH}$ = 2.3 Hz, 1H, POC$\underline{H}$); 4.46 (d, $^2J_{HH}$ = -12.1 Hz, 1H, PhC$\underline{H}_2$); 4.54 (d, $^2J_{HH}$ = -12.1 Hz, 1H, PhC$\underline{H}_2$); 4.59 (d, $^2J_{HH}$ = -10.8 Hz, 1H, PhC$\underline{H}_2$); 4.83 (d, $^2J_{HH}$ = -11.1 Hz, 1H, PhC$\underline{H}_2$); 4.84 (d, $^2J_{HH}$ = -10.8 Hz, 1H, PhC$\underline{H}_2$); 4.88 (d, $^2J_{HH}$ = -11.1 Hz, 1H, PhC$\underline{H}_2$); 7.38-7.43 (m, 15H, CH_{Ar}); 7.50-7.55 (m, 3H, CH_{Ar}); 7.75-7.80 (m, 2H, CH_{Ar}); ^{13}C NMR (400,13 MHz, $CDCl_3$): δ (ppm) = 68.64 (d, $^3J_{CP}$ = 9.2 Hz, OC$\underline{C}H_2$), 72.19 (d, $^1J_{CP}$ = 97.3 Hz, P$\underline{C}$H), 73.45 (s, Ph$\underline{C}H_2$), 75.24 (d, $^2J_{CP}$ = 5.2 Hz, PO$\underline{C}$H), 75.50 (s, Ph$\underline{C}H_2$), 76.25 (s, Ph$\underline{C}H_2$), 77.65 (s, PCC$\underline{C}$H), 84.34 (d, $^2J_{CP}$ = 6.9 Hz, PC$\underline{C}$H), 127.65, 127.76, 127.82, 127.84, 128.15,128.45 (s, CH_{Bn}), 127.49 (d, $^1J_{CP}$ = 135.8 Hz, P$\underline{C}_{Ph}$), 128.71 (d, $^3J_{CP}$ = 13.4 Hz, $\underline{C}H_{Ph}$), 131.91 (d, $^2J_{CP}$ = 10.4 Hz, $\underline{C}H_{Ph}$), 133.30 (d, $^4J_{CP}$ = 2.8 Hz, $\underline{C}H_{Ph}$), 137.92 (s, C_{Bn}), 137.98 (s, C_{Bn}), 138.37 (s, C_{Bn}); HRMS m/z (MH^+) 545.2091 (calcd for $C_{32}H_{34}O_6P$: 545.2093); Analytical HPLC (Column: Waters SunFire^{TM} C18, 5 µm, 4.6×250 mm; Eluent: acetonitrile / water (63:37), Flow: 1 mL.min^{-1}): Retention time = 18.53. $[\alpha]_D^{25}$ = +26.18 (*c* 0.055, $CHCl_3$). HRMS m/z (MH+) 545.2091 (calcd for $C_{32}H_{34}O_6P$: 545.2093); Analytical HPLC (Column: Waters SunFireTM, C18, 5 µm, 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 mL.min-1): Retention time = 18.53.

The ^{1}H NMR data of compound **4**, epimer of compound **3**, showed trans di-axial vicinal coupling constants between protons H_2/H_3 (J_{H2-H3} = 9.5 Hz), protons H_3/H_4 (J_{H3-H4} = 9.3 Hz) and protons H_1/H_2 (J_{H1-H2} = 9.8 Hz) who confirmed a chair structure with P_2(*S*) and C_3(*S*) configuration for compound **4**.

^{31}P NMR – $CDCl_3$



^{1}H NMR – $CDCl_3$


SL008+003-LC430-CDCl3-H1PROTON CDCl3 opt/topspin am2n1 32
7.7836
7.7528
7.7349
7.4115
7.2380
7.2350
7.2218
7.1959
7.1764
7.1431
4.8976
4.8697
4.8414
4.8218
4.8135
4.6008
4.5739
4.5534
4.5236
4.4717
4.4414
4.1085
3.9183
3.8939
3.8699
3.7012
3.6963
3.6734
Integral
1.9914
3.0192
15.536
2.9873
4.0364
1.0148
3.0000
1.0397
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)
*** Current Data Parameters ***
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PROCNO : 0
*** Acquisition Parameters ***
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DATE_d : Nov 22 2010
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NS : 16
NUC1 : 1H
O1 : 2470.97 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-G
RG : 181.0000000
SFO1 : 400.1324710 MHz
SW : 16.0203 ppm
SW_h : 6410.256 Hz
TD : 65536
*** Processing Parameters ***
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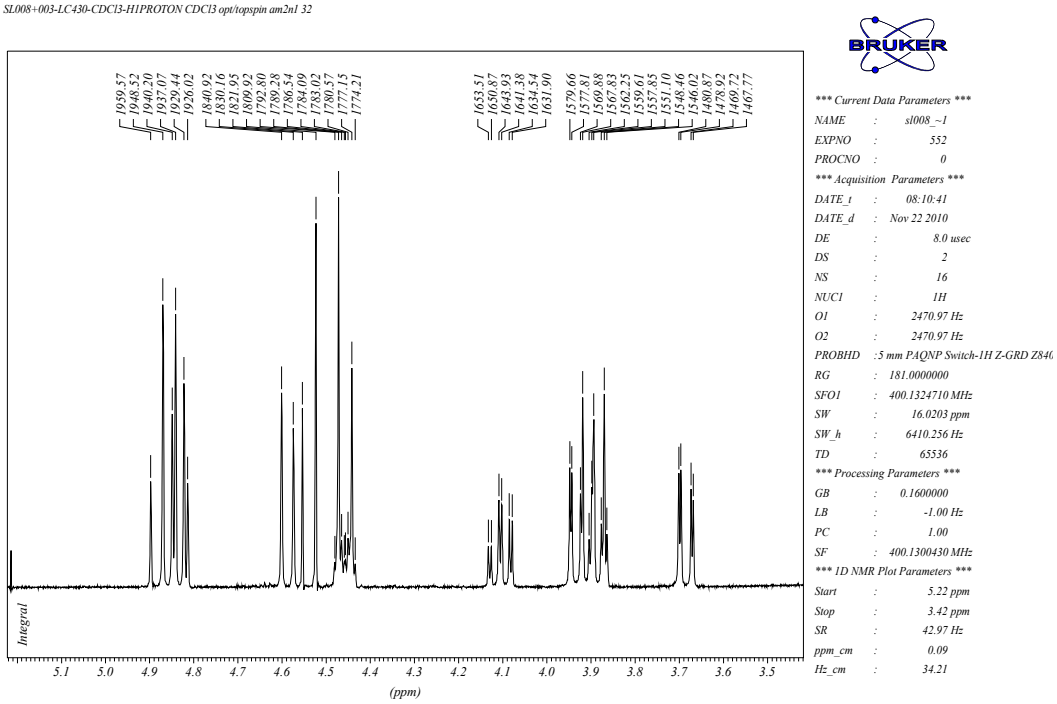
LB : 0.10 Hz
PC : 1.00
SF : 400.1300430 MHz
*** 1D NMR Plot Parameters ***
Start : 8.63 ppm
Stop : 2.07 ppm
SR : 42.97 Hz
ppm_cm : 0.31
Hz_cm : 124.30


SL008+003-LC430-CDCl3-H1PROTON CDCl3 opt/topspin am2n1 32
1959.57
1948.52
1940.20
1937.07
1929.44
1926.02
1840.92
1830.16
1821.95
1809.92
1792.80
1789.28
1786.54
1784.09
1783.02
1780.57
1777.15
1774.21
1653.51
1650.87
1643.93
1641.38
1634.54
1631.90
1579.66
1577.81
1569.88
1567.83
1562.23
1559.61
1557.85
1551.10
1548.46
1546.02
1480.87
1478.92
1469.72
1467.77
Integral
5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5
(ppm)
*** Current Data Parameters ***
NAME : sl008_~1
EXPNO : 552
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 08:10:41
DATE_d : Nov 22 2010
DE : 8.0 usec
DS : 2
NS : 16
NUC1 : 1H
O1 : 2470.97 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z846
RG : 181.0000000
SFO1 : 400.1324710 MHz
SW : 16.0203 ppm
SW_h : 6410.256 Hz
TD : 65536
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GB : 0.1600000
LB : -1.00 Hz
PC : 1.00
SF : 400.1300430 MHz
*** 1D NMR Plot Parameters ***
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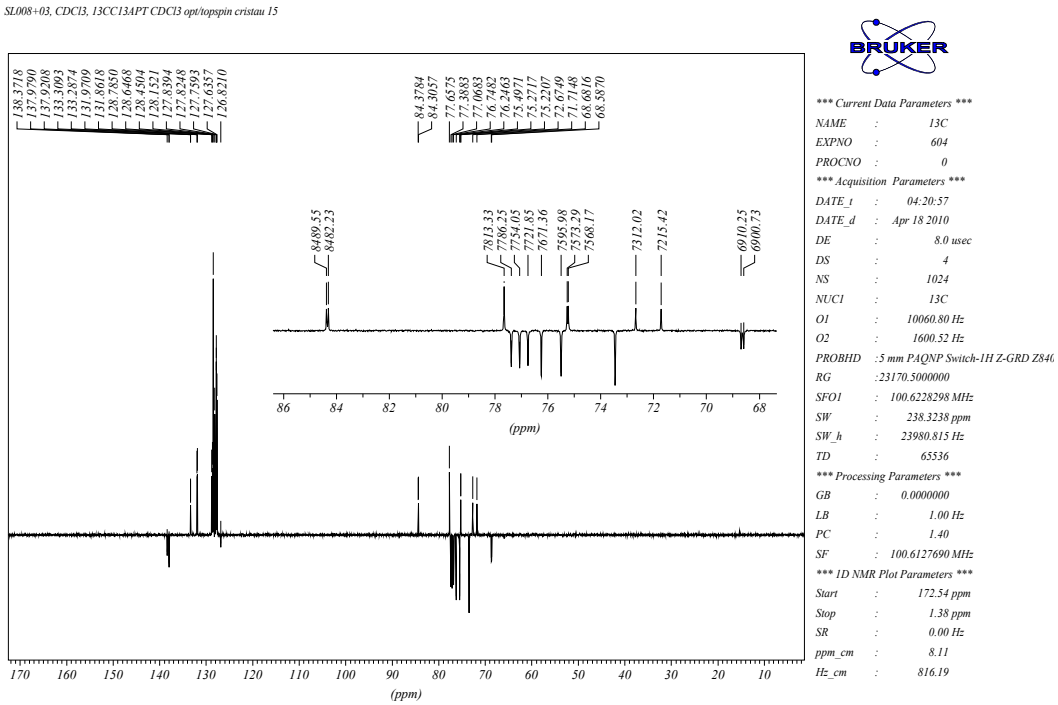
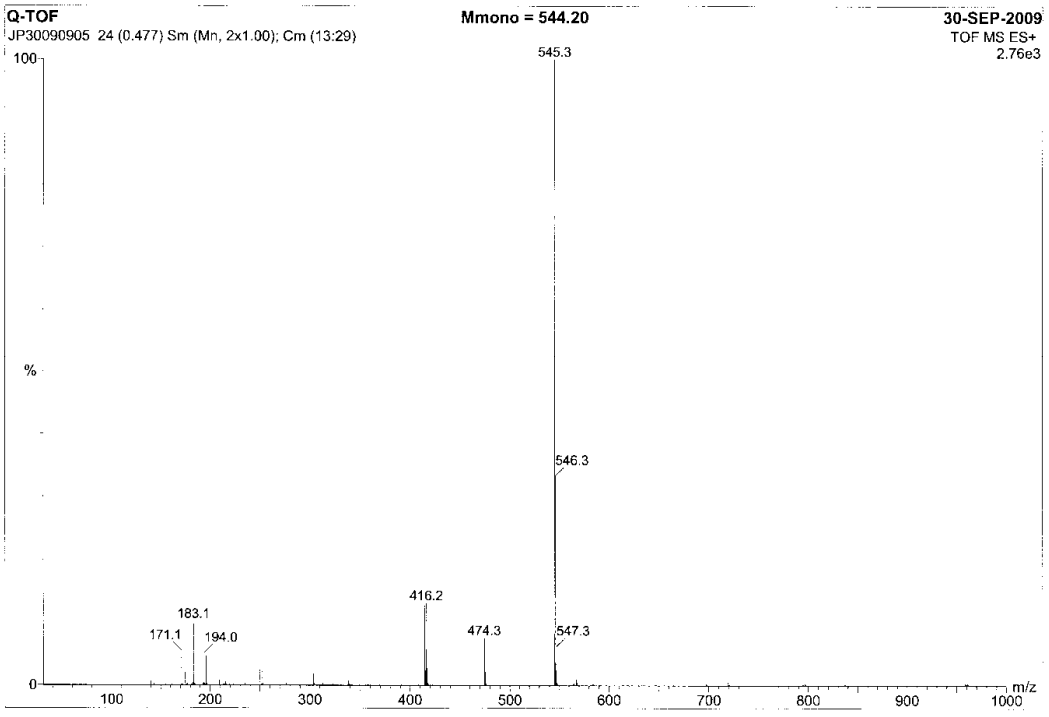
Stop : 3.42 ppm
SR : 42.97 Hz
ppm_cm : 0.09
Hz_cm : 34.21

^{13}C NMR – $CDCl_3$



ES+-MS

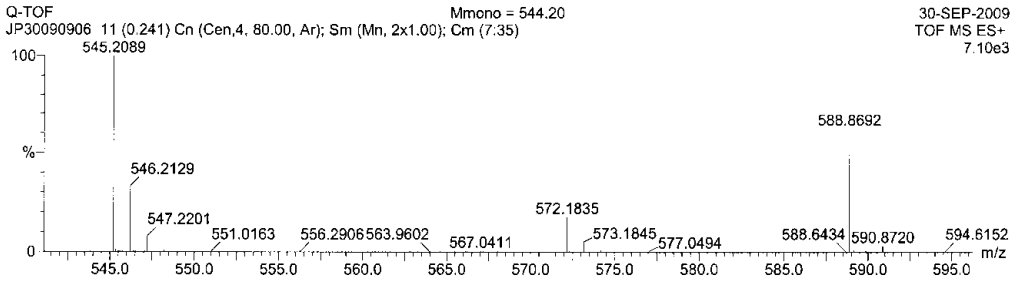


HRMS

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 3.0 mDa / DBE: min = -10.0, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
36 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)



Minimum:				-10.0		
Maximum:		3.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
545.2089	545.2093	-0.4	-0.7	16.5	1	C32 H34 O6 P

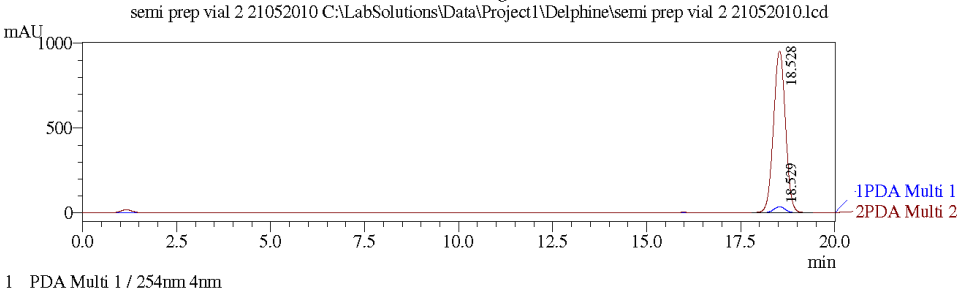
Analytical HPLC

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\Delphine\semi prep vial 2 21052010.lcd

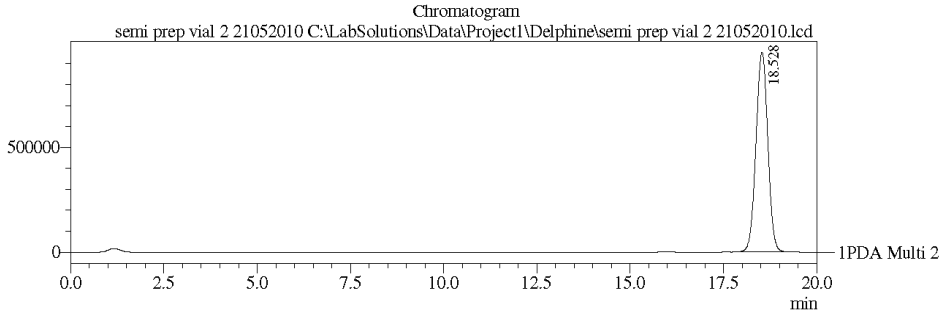
Acquired by	: Admin
Sample Name	: semi prep vial 2 21052010
Sample ID	: semi prep vial 2 21052010
Tray#	: 1
Vail #	: 23
Injection Volume	: 20 uL
Data File Name	: semi prep vial 2 21052010.lcd
Method File Name	: isocratique 63-C- 20 min.lcm
Batch File Name	: semi prep 63C-26052010-1.lcb
Report File Name	: delphine report.lcr
Data Acquired	: 26/05/2010 10:51:22
Data Processed	: 07/02/2011 11:46:46

Chromatogram
semi prep vial 2 21052010 C:\LabSolutions\Data\Project1\Delphine\semi prep vial 2 21052010.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram
semi prep vial 2 21052010 C:\LabSolutions\Data\Project1\Delphine\semi prep vial 2 21052010.lcd



1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	18.528	951996	21043034	100.000	100.000
Total		951996	21043034	100.000	100.000

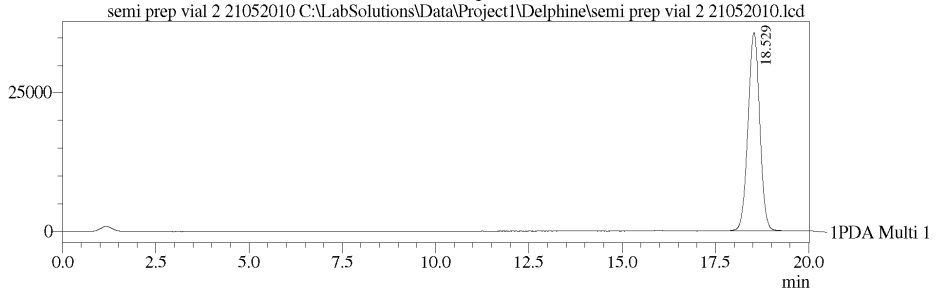
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	18.529	35833	778565	100.000	100.000
Total		35833	778565	100.000	100.000

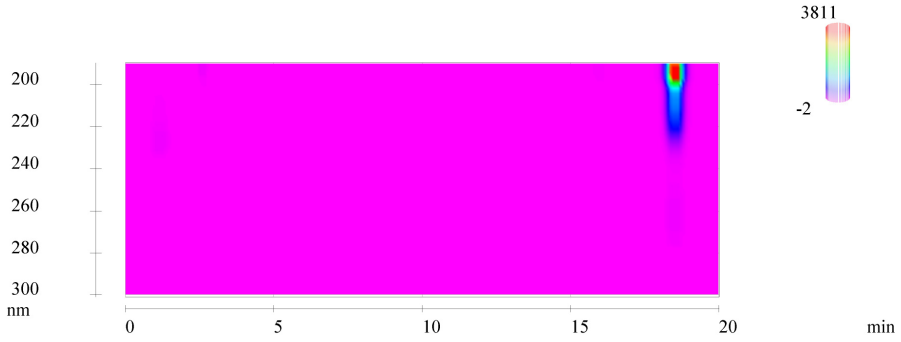
Chromatogram

semi prep vial 2 21052010 C:\LabSolutions\Data\Project1\Delphine\semi prep vial 2 21052010.lcd



1 PDA Multi 1 / 254nm 4nm

Contour

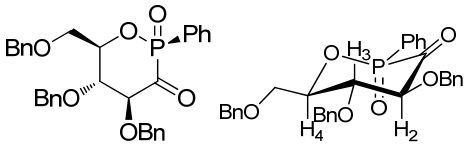


Method

<<LC Program>>

Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
20.00	Controller	Stop		

Preparation of (R_P)-4,5-bis-benzyloxy-6-benzyloxymethyl-2-phenyl-2-oxo-2λ^5-[1,2]oxaphosphinan-3-one 7:

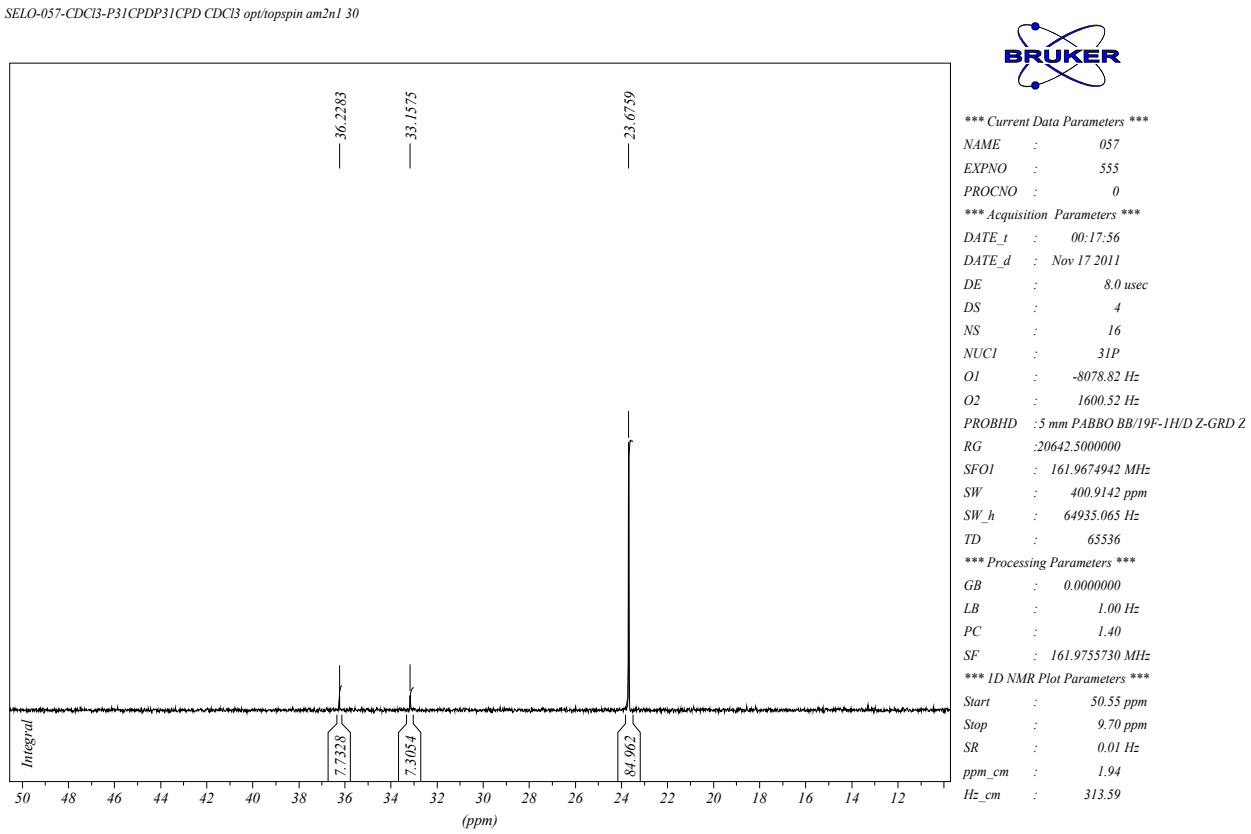


Dess-Martin periodinane (0.956 g, 2.25 mmol) and *tert*-butanol (0.167 g, 0.215 mL, 2.250 mmol) were added to a solution of a mixture of **3**/**4** (40/60, 0.408 g, 0.750 mmol) in dichloromethane (20 mL). The reaction mixture was stirred at room temperature for 6 h, and then dichloromethane (10 mL) was added. The reaction mixture was filtrated through celite, organic layer was washed with an aqueous solution of sodium sulfite (20 mL, 20%), followed by an aqueous solution of carbonate sodium (20 mL, 20%). The organic layer was dried over magnesium sulfate and filtered. The solvent was evaporated to give an oil (0.4 g, 89%, which was used directly without further purification.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 23.64 (s); ^{1}H NMR (400.13 MHz, $CDCl_3$): 4.18 (t, $^3J_{HH}$ = 9.6 Hz, 1H, PCCCH); HRMS m/z (MH^+) 543.1934 (calcd for $C_{32}H_{32}O_6P$: 543.1937).

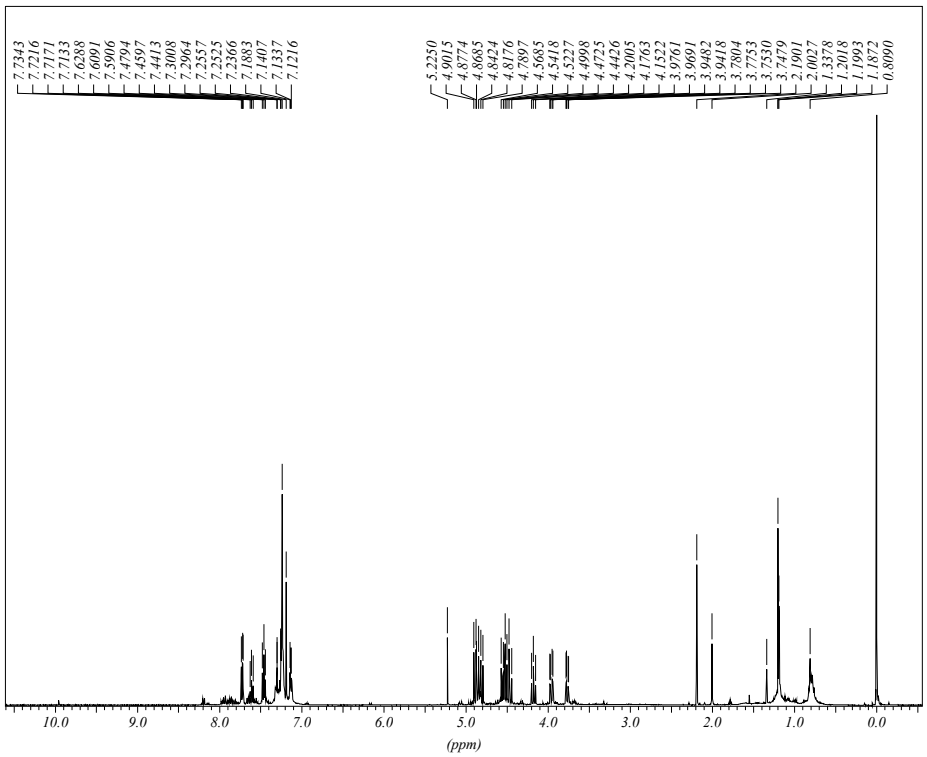
The ^{1}H NMR data of compound **7**, showed trans di-axial vicinal coupling constants between protons H_3/H_2 ($J_{H3\text{-}H2}$ = 9.6 Hz) and protons H_3/H_4 ($J_{H3\text{-}H4}$ = 9.6 Hz) which confirmed a chair structure for compound **7**.

^{31}P NMR spectrum of **7**.



^{1}H NMR spectrum of **7**.

SELO-057-protondecP31-CDCl3PROP31DEC CDCl3 opt/topspin am2n1 5



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DATE_d : Nov 17 2011
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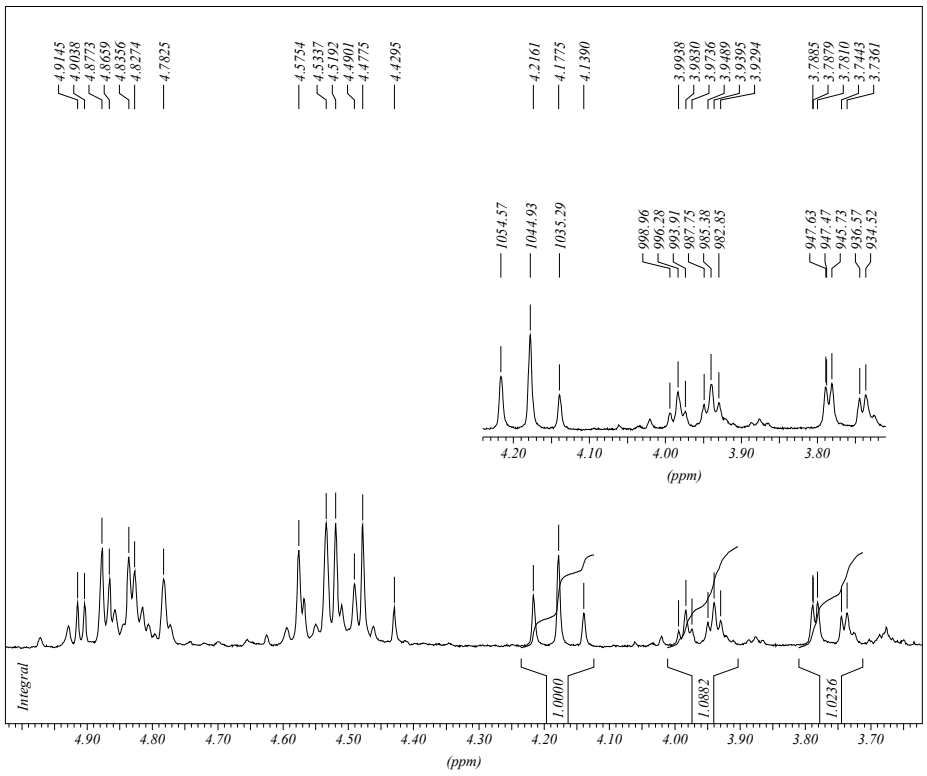
O2 : 491.83 Hz
PROBHD :5 mm PABBO BB/19F-1H/D Z-GRD Z
RG : 90.5000000
SFO1 : 400.1325018 MHz
SW : 20.8264 ppm
SW_h : 8333.333 Hz
TD : 32768
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.40
SF : 400.1300383 MHz
*** 1D NMR Plot Parameters ***
Start : 10.61 ppm
Stop : -0.55 ppm
SR : 38.32 Hz
ppm_cm : 0.53
Hz_cm : 211.68

SELO-057-proton-CDCl3



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NUC1 : 1H
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O2 : 1544.66 Hz
PROBHD :5 mm QNP 1H/13C/31P/19F Z-GRD Z
RG : 512.0000000
SFO1 : 250.1315447 MHz
SW : 20.6930 ppm
SW_h : 5175.983 Hz
TD : 65536
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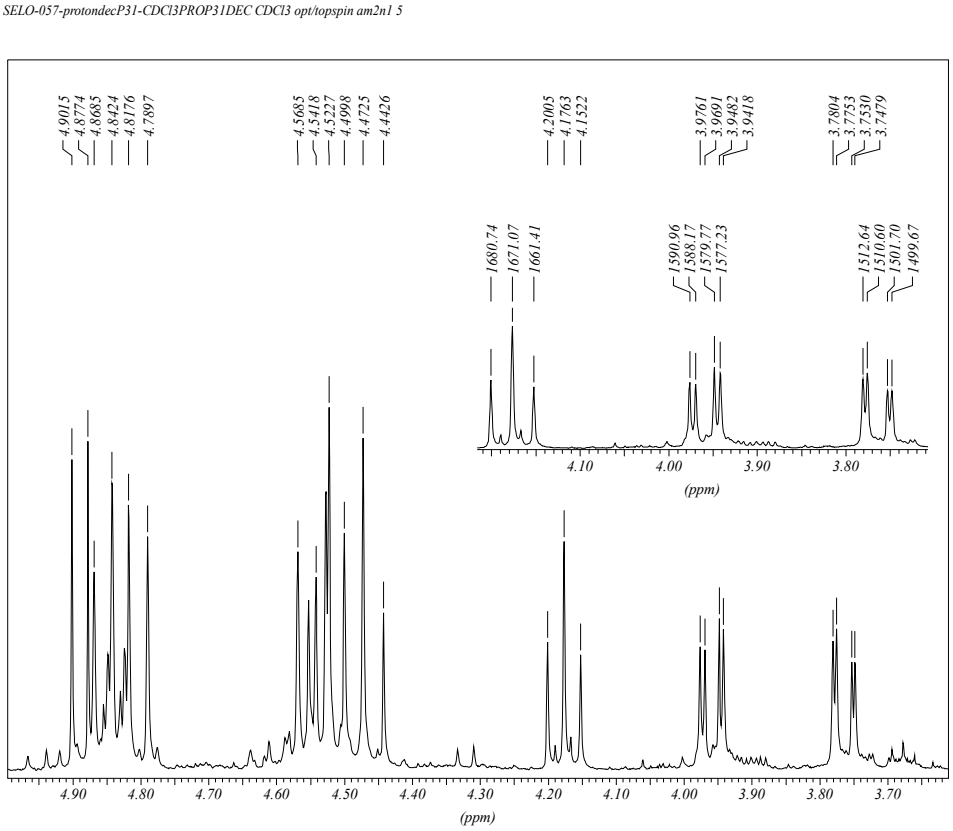
PC : 1.00
SF : 250.1300187 MHz
*** 1D NMR Plot Parameters ***
Start : 5.03 ppm
Stop : 3.62 ppm
SR : 18.74 Hz
ppm_cm : 0.07
Hz_cm : 16.65

^{1}H NMR spectrum of **7** (Proton with Phosphorus decoupling).



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NUC1 : 1H
O1 : 2501.84 Hz
O2 : 491.83 Hz
PROBHD : 5 mm PABBO BB/19F-1H/D Z-GRD Z
RG : 90.5000000
SFO1 : 400.1325018 MHz
SW : 20.8264 ppm
SW_h : 8333.333 Hz
TD : 32768
*** Processing Parameters ***
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LB : 0.10 Hz
PC : 1.40
SF : 400.1300383 MHz
*** 1D NMR Plot Parameters ***
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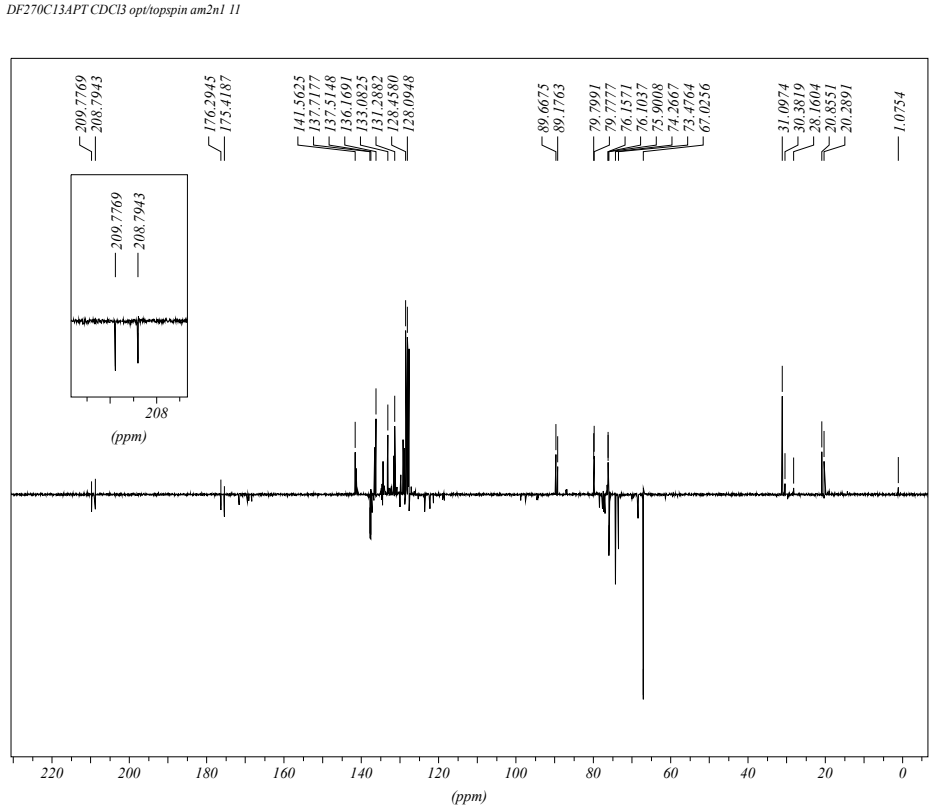
Stop : 3.61 ppm
SR : 38.32 Hz
ppm_cm : 0.07
Hz_cm : 26.29

^{13}C NMR spectrum of **7**.



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DATE_d : Jun 02 2010
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NUC1 : 13C
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O2 : 1600.52 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z84(
RG : 16384.0000000
SFO1 : 100.6228298 MHz
SW : 349.9332 ppm
SW_h : 35211.268 Hz
TD : 65536
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PC : 1.40
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*** 1D NMR Plot Parameters ***
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Stop : -6.53 ppm
SR : 0.00 Hz
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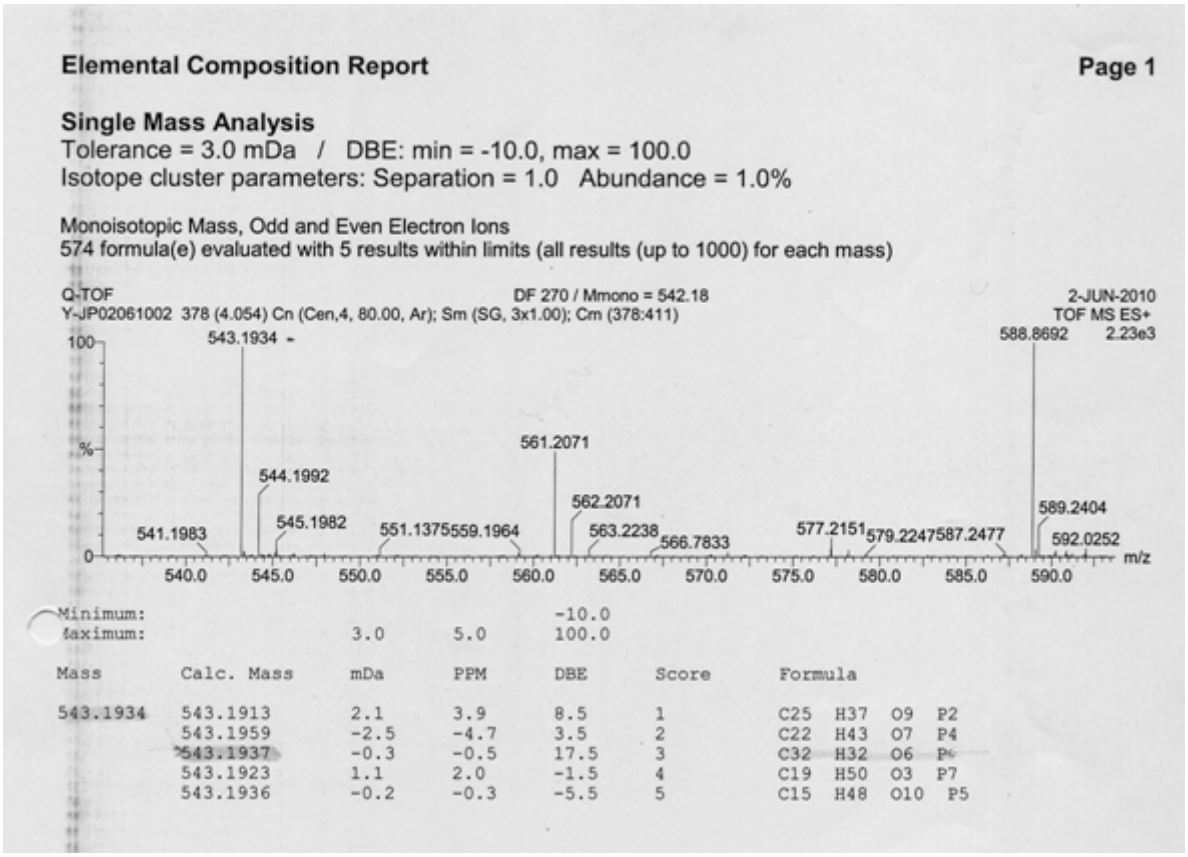
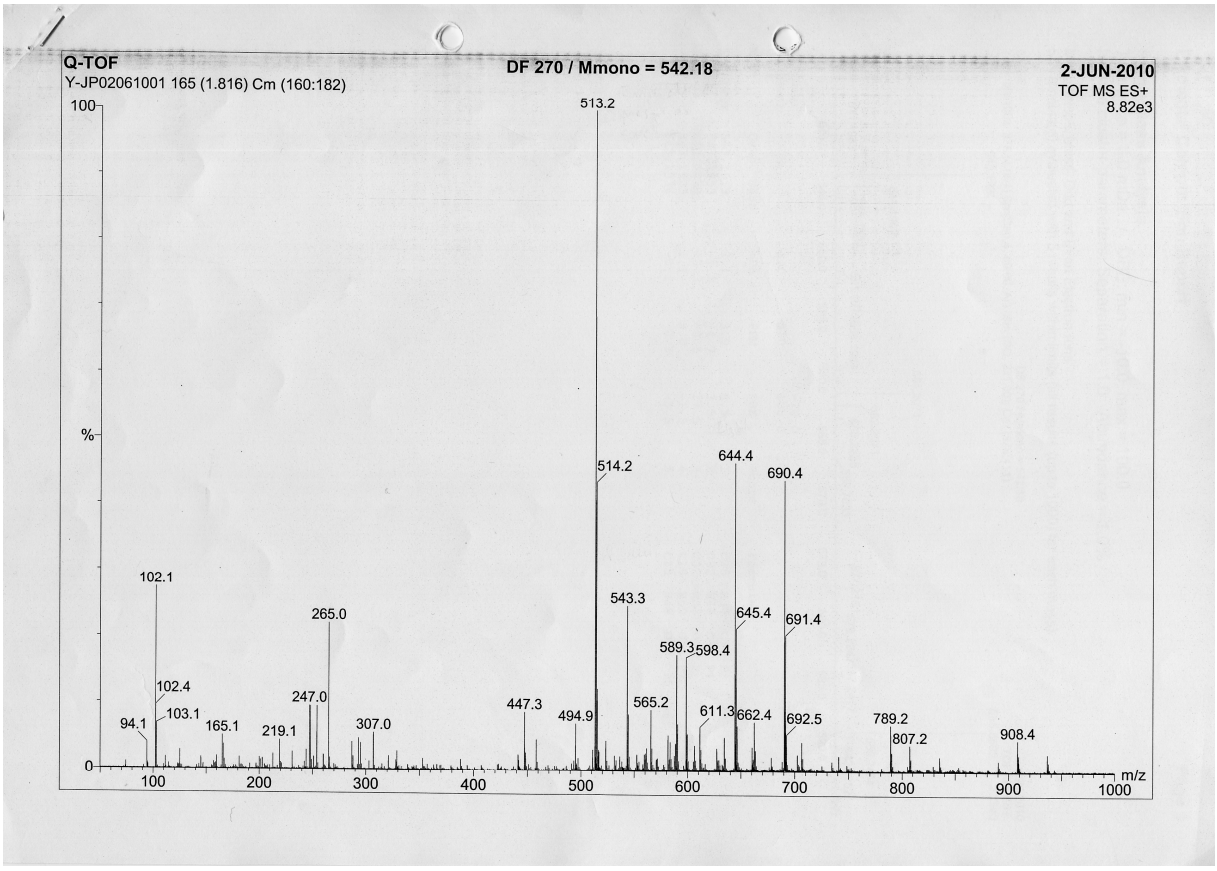
Hz_cm : 1130.79

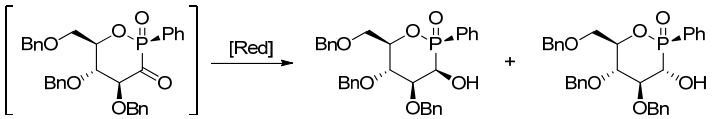
HRMS of **7**



MS ES+ of **7**



IV. Diastereoselective reduction of the α–ketophosphinate 7



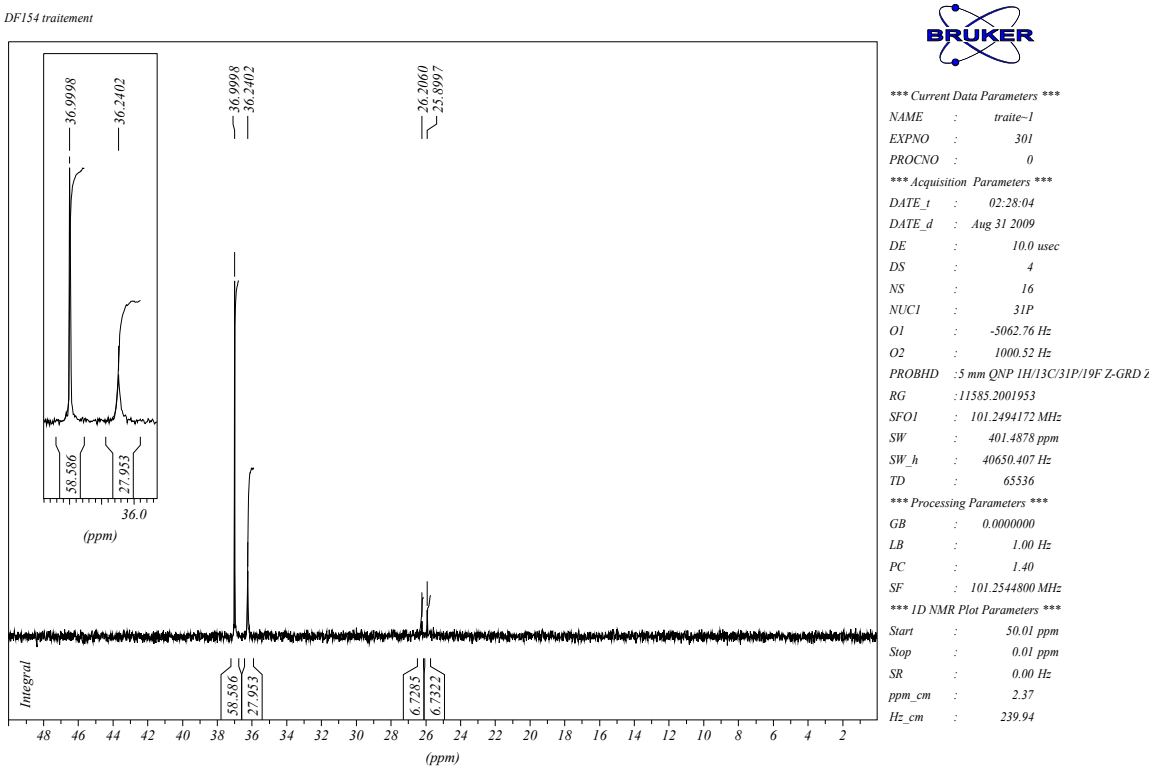
3 4

Entry 1. $NaBH_4$

Sodium borohydride (16.8 mg, 0.442 mmol) was added to a solution of **7** (0.200 g, 0.368 mmol) in THF (8 mL). The reaction mixture was stirred for 5 h, and then solvent was evaporated. The residue remaining was diluted with ethyl acetate (15 mL) and organic solution was washed with a saturated aqueous solution of sodium carbonate (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 37.00 (s), 36.24 (s).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 1. $NaBH_4$

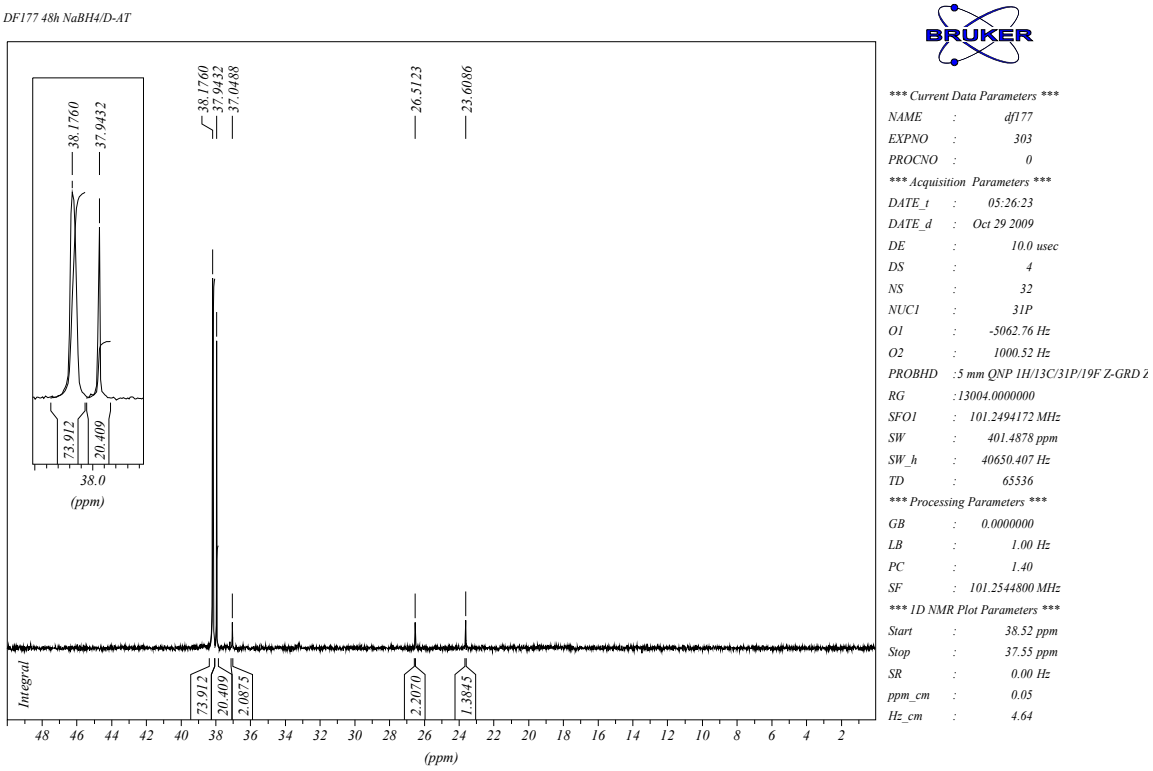


Entry 2. $NaBH_4$/(*S,S*)-tartric acid

Sodium borohydride (56.2 mg, 1.48 mmol,) was added to a solution of (*S,S*)-tartaric acid (0.222 g, 1.48 mmol) in THF (8 mL). The reaction mixture was stirred to reflux for 4 h. At -30 °C, a solution of α-ketophosphinate (0.200 g, 0.37 mmol) in THF (2 mL) was added and the mixture was stirred for 24h at - 30 °C. The solvent was evaporated and the residue remaining was diluted with ethyl acetate (15 mL). The organic solution was washed with an aqueous solution of hydrochloride (10 mL, 1M). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 38.17 (s), 37.94 (s).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 2. $NaBH_4$/(*S,S*)-tartric acid.

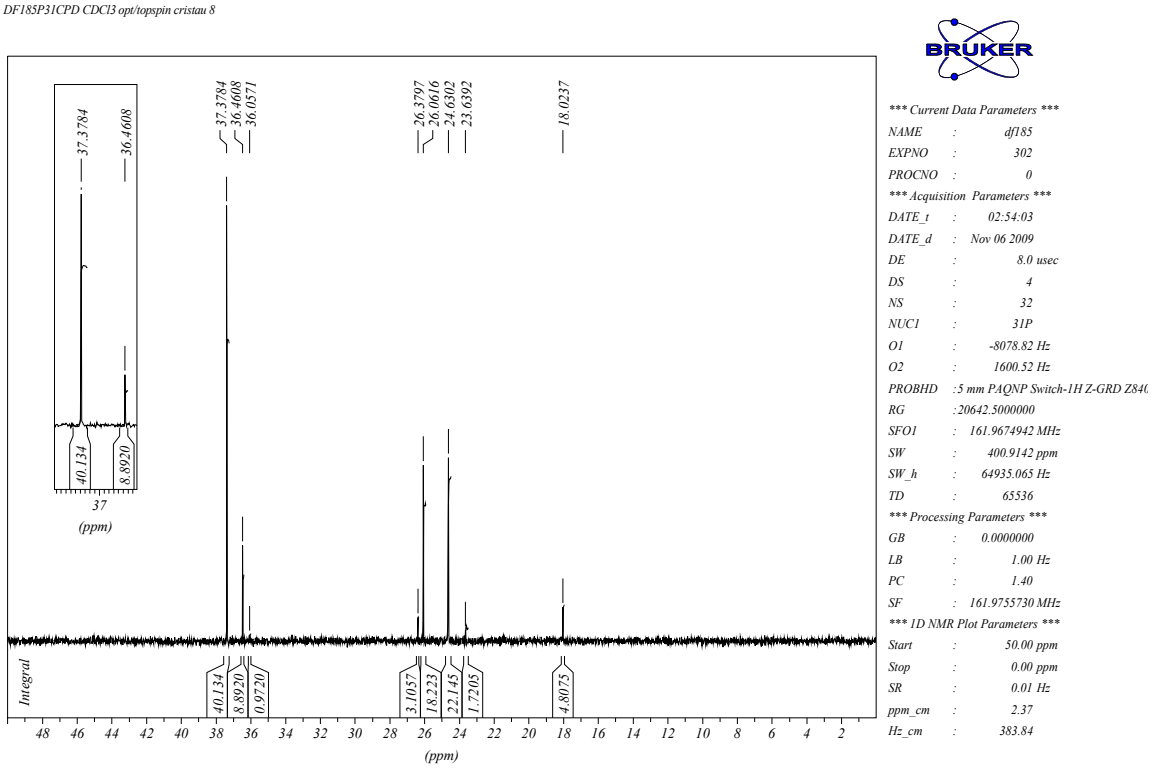


Entry 3. $NaBH_4$/(*R,R)*-tartric acid

Sodium borohydride (56.2 mg, 1.48 mmol,) was added to a solution of (*R,R*)-tartaric acid (0.222 g, 1.48 mmol,) in THF (8 mL). The reaction mixture was stirred to reflux for 4 h. At - 30 °C, a solution of α-ketophosphinate (0.200 g, 0.37 mmol,) in THF (2 mL) was added and the mixture was stirred for 24h at - 30 °C. The solvent was evaporated and the residue remaining was diluted with ethyl acetate (15 mL). The organic solution was washed with an aqueous solution of hydrochloride (10 mL, 1M). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 37.38 (s), 36.46 (s).

^{31}P NMR spectrum of **3** and **4:** Table 1, entry 3. $NaBH_4$/(*R,R)*-tartric acid.

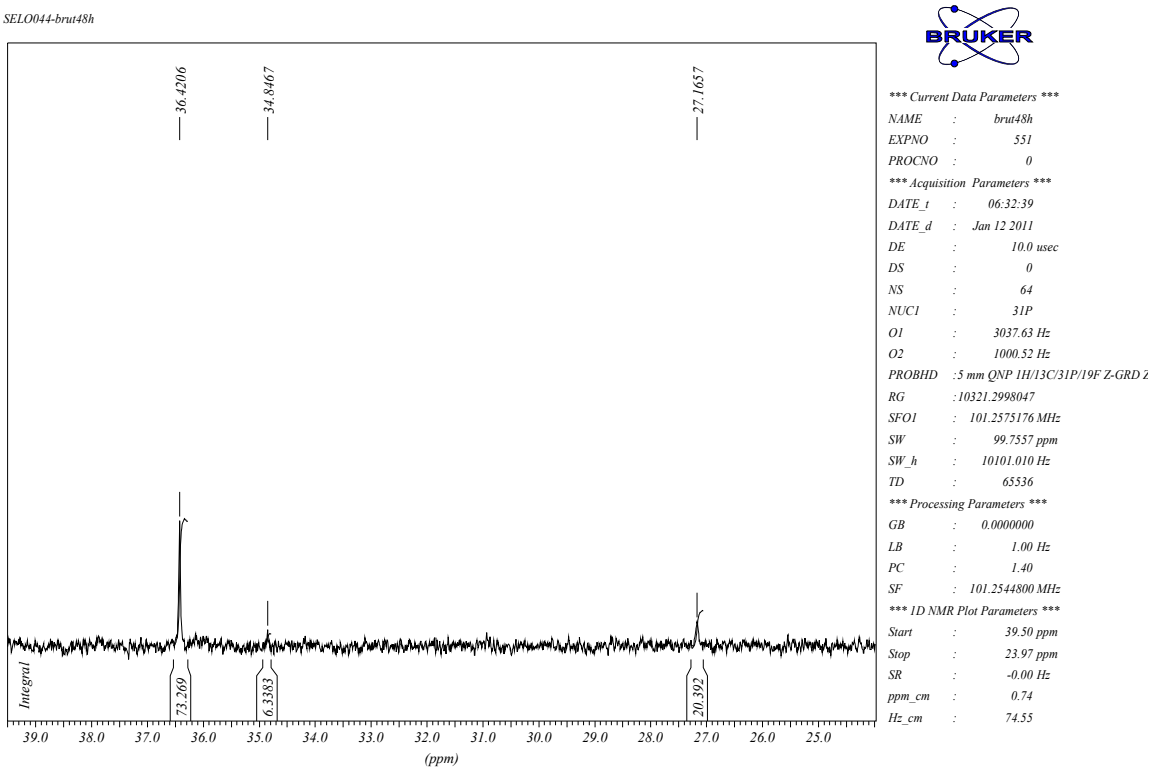


Entry 4. $NaBH_4/CeCl_3.7\ H_2O$

Sodium borohydride (8.2 mg, 0.22 mmol) was added to a solution of ketophosphinosugar (0.100 g, 0.18 mmol) and cerium (III) chloride heptahydrate (60.6 mg, 0.162 mmol) in THF (5 mL). The reaction mixture was stirred for 48h at room temperature, and then the solvent was evaporated. The residue remaining was diluted with dichloromethane (10 mL) and the organic solution was washed with an aqueous saturated solution of ammonium chloride (5 mL). The organic layer was dried over magnesium sulfate, filtrated and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 36.42 (s). Analytical HPLC (Column: Waters SunFire™ C18, 5µm, 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 $mL.min^{-1}$): Retention time = 16.35 (95%), 19.02 (5%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 4. $NaBH_4/CeCl_3.7H_2O$.



HPLC chromatogram of **3** and **4**: Table 1, entry 4. $NaBH_4$ / $CeCl_3$,7 H_2O

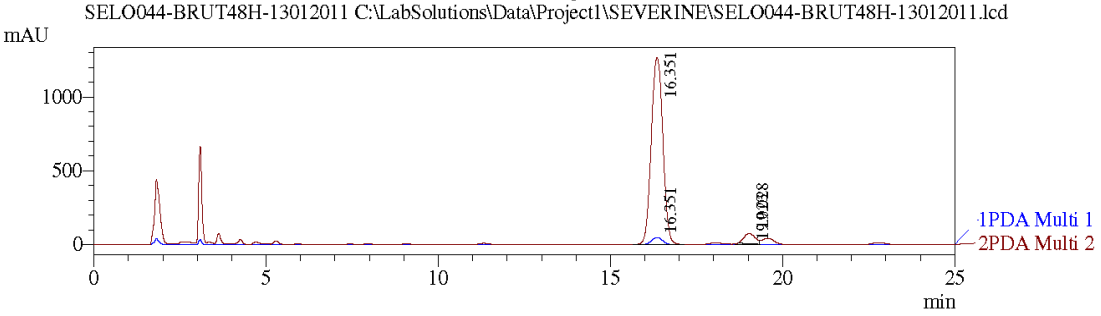
==== Shimadzu LCsolution Analysis Report ====

C:\...\Data\Project1\SEVERINE\SELO044-BRUT48H-13012011.lcd

Acquired by	: Admin
Sample Name	: SELO044-BRUT48H-13012011
Sample ID	: SELO044-BRUT48H-13012011
Tray#	: 1
Vail #	: 21
Injection Volume	: 20 uL
Data File Name	: SELO044-BRUT48H-13012011.lcd
Method File Name	: isocratique 63-C- 25 min.lcm
Batch File Name	: 13012011-SELO044-brut48h-63C-1.lcb
Report File Name	: delphine report.lcr
Data Acquired	: 13/01/2011 11:04:06
Data Processed	: 15/02/2011 13:58:10

Chromatogram

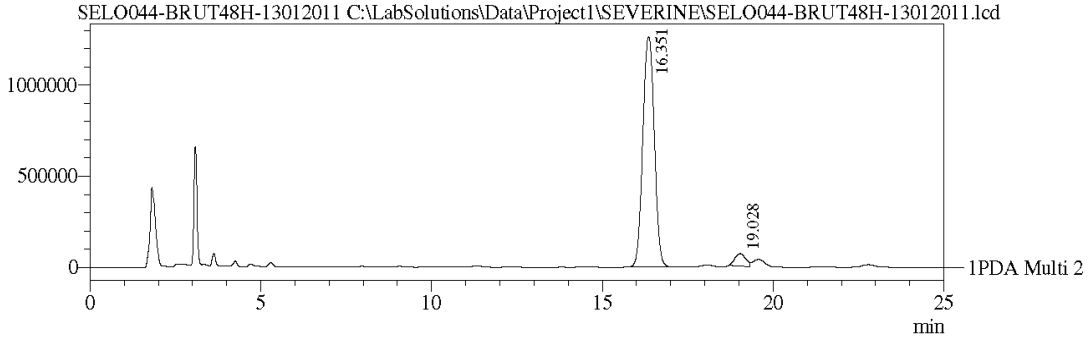
SELO044-BRUT48H-13012011 C:\LabSolutions\Data\Project1\SEVERINE\SELO044-BRUT48H-13012011.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram

SELO044-BRUT48H-13012011 C:\LabSolutions\Data\Project1\SEVERINE\SELO044-BRUT48H-13012011.lcd



1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	16.351	1262542	29487300	94.844	95.040
2	19.028	68637	1539025	5.156	4.960
Total		1331179	31026326	100.000	100.000

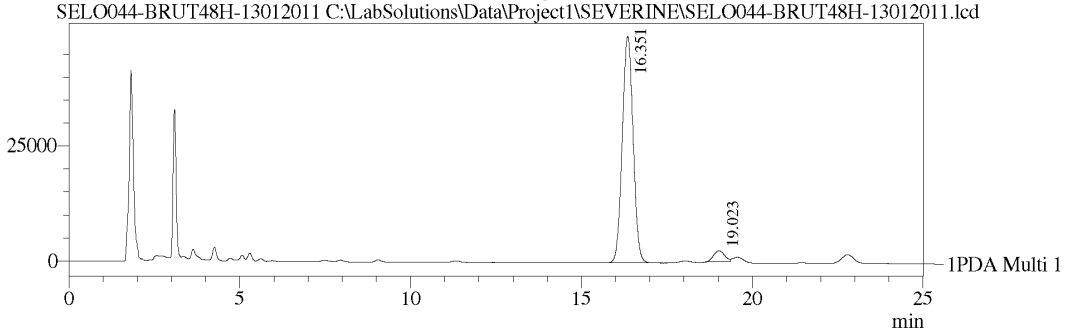
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	16.351	49378	1084069	95.320	95.140
2	19.023	2424	55379	4.680	4.860
Total		51802	1139448	100.000	100.000

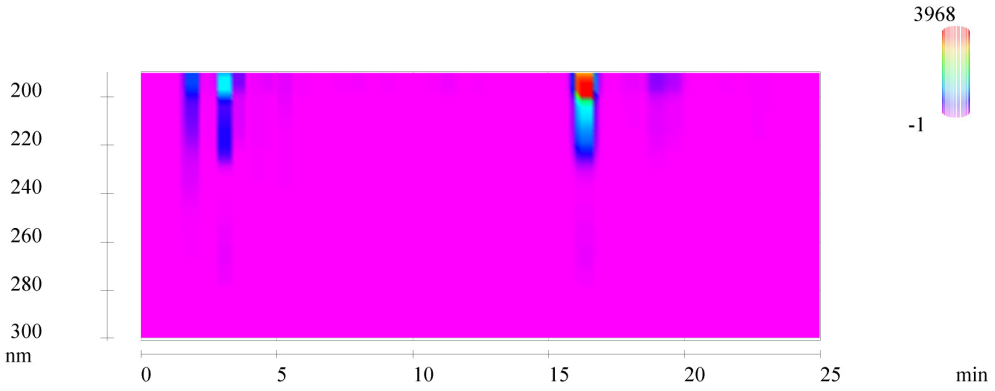
Chromatogram

SELO044-BRUT48H-13012011 C:\LabSolutions\Data\Project1\SEVERINE\SELO044-BRUT48H-13012011.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

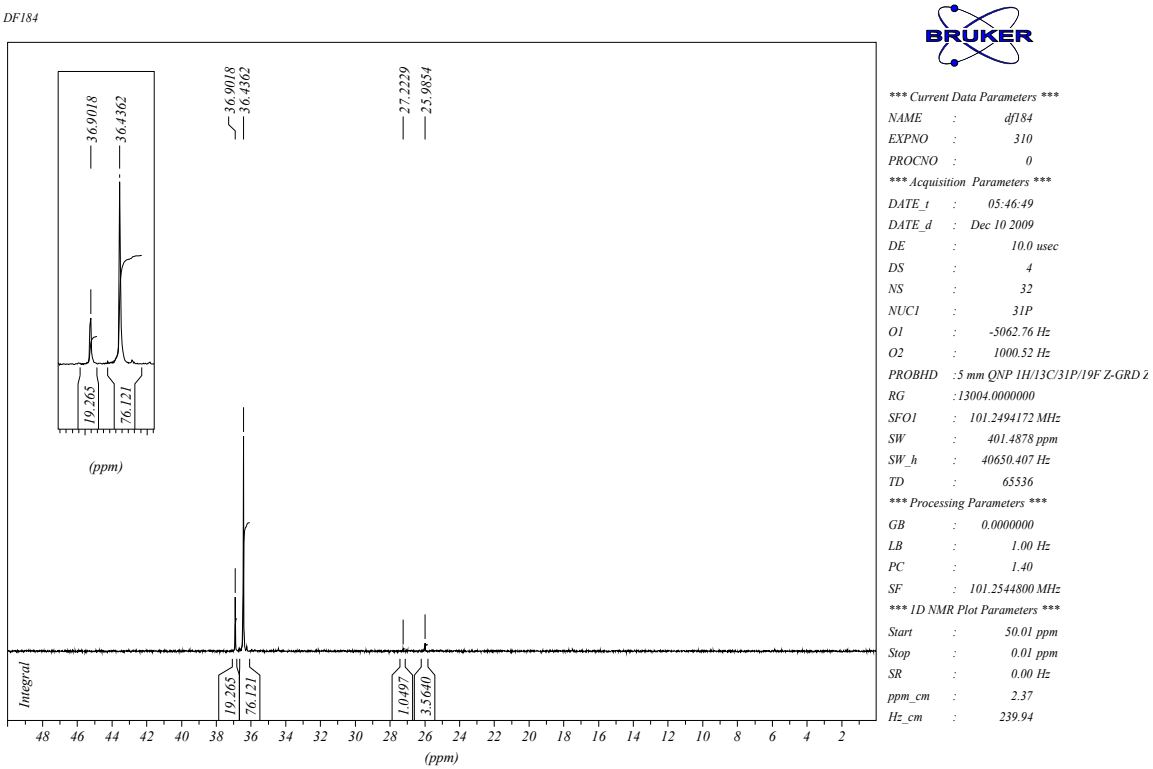
Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
25.00	Controller	Stop		

Entry 5. $NaBH_4$/*L*-proline

Sodium borohydride (21.1 mg, 0.55 mmol) was added to a solution of *L*-proline (63.9 mg, 0.55 mmol,) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.200 g, 0.37 mmol) in THF (1.2 mL) was added. The mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 36.42 (s)

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 5. $NaBH_4$/*L*-proline.

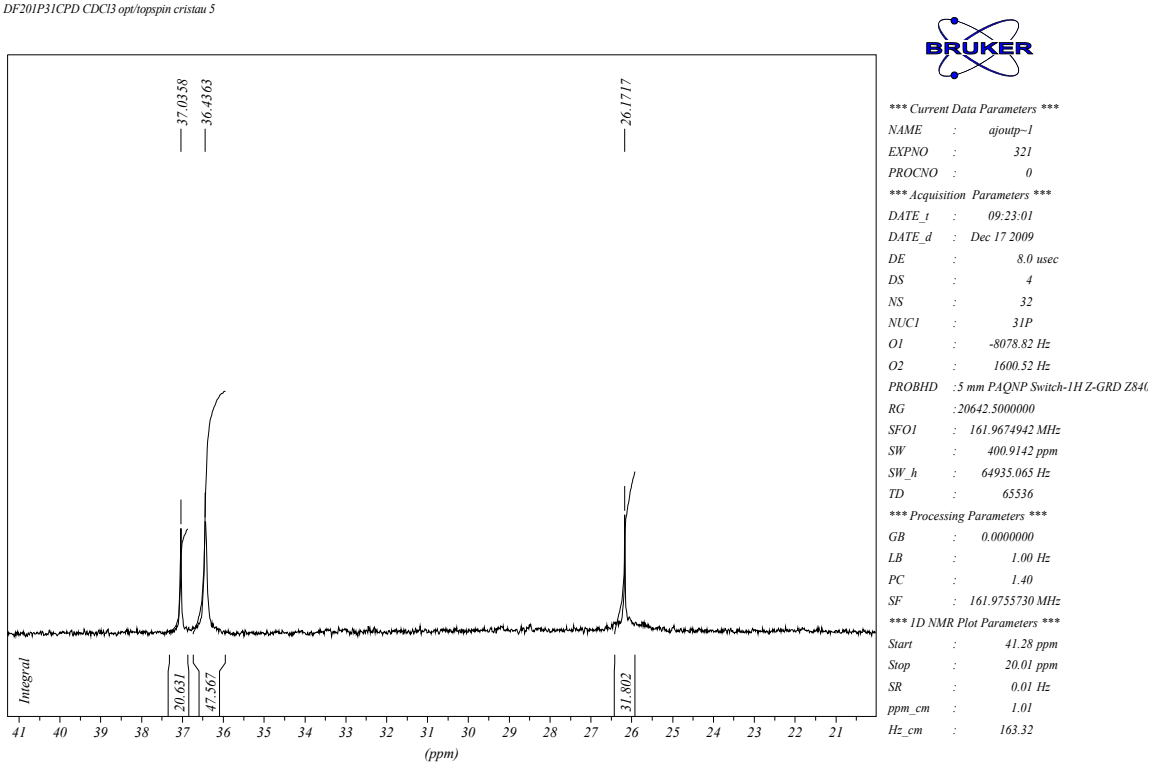


Entry 6. $NaBH_4$/*D*-proline

Sodium borohydride (0.55 mmol, 21.1 mg) was added to a solution of *D*-proline (63.9 mg, 0.55 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.37 mmol, 0.200 g) in THF (1.2 mL) was added. The reaction mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride solution (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 36.83 (s), 36.54 (s).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 6. $NaBH_4$/*D-proline*.

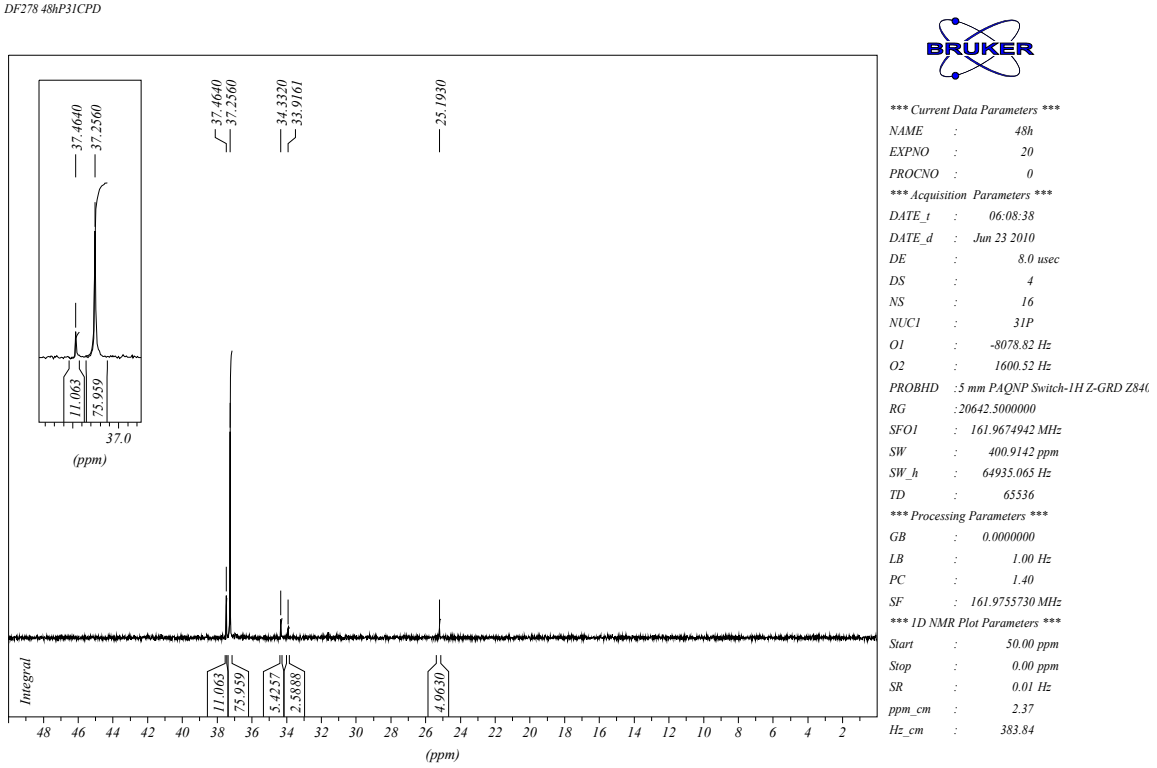


Entry 7. $NaBH_4$/*L*-proline/$MgBr_2$

Sodium borohydride (20.0 mg, 0.525 mmol) was added to a solution of *L*-proline (60.4 mg, 0.525 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.375 mmol, 0.203 g) and magnesium bromide ethyl etherate (0.375 mmol, 97.0 mg) in THF (1.2 mL) was added. The reaction mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 37.46 (s), 37.26 (s); Analytical HPLC (Column: Waters SunFire™, C18, 5 µm, 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 16.68 (13%), 19.46 (87%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 7. $NaBH_4$/*L*-proline/$MgBr_2$



HPLC chromatogram of **3** and **4**: Table 1, entry 7. $NaBH_4$/*L*-proline $MgBr_2$

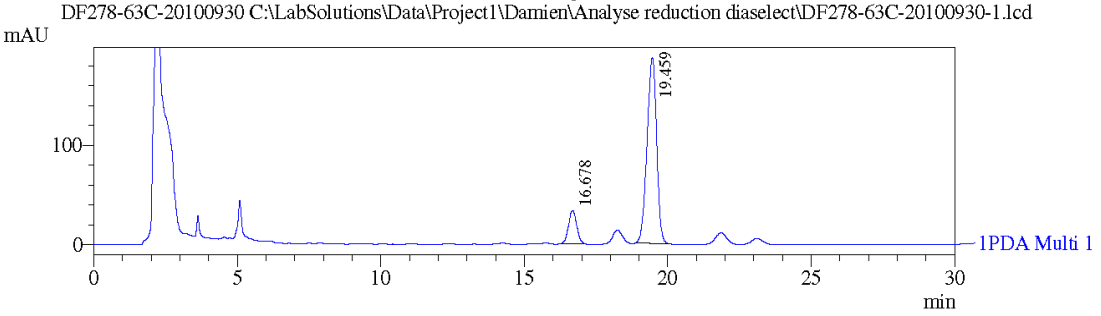
==== Shimadzu LCsolution Analysis Report ====

C:\...\Damien\Analyse reduction diaselect\DF278-63C-20100930-1.lcd

Acquired by	: Admin
Sample Name	: DF278-63C-20100930
Sample ID	: DF278-63C-20100930
Tray#	: 1
Vail #	: 46
Injection Volume	: 20 uL
Data File Name	: DF278-63C-20100930-1.lcd
Method File Name	: isocratique 63-C- 30 min.lcm
Batch File Name	: 30092010-Analyses dia278-279-1.lcb
Report File Name	: delphine report.lcr
Data Acquired	: 30/09/2010 14:48:53
Data Processed	: 15/02/2011 14:08:56

Chromatogram

DF278-63C-20100930 C:\LabSolutions\Data\Project1\Damien\Analyse reduction diaselect\DF278-63C-20100930-1.lcd



1 PDA Multi 1 / 254nm 4nm

Chromatogram

DF278-63C-20100930 C:\LabSolutions\Data\Project1\Damien\Analyse reduction diaselect\DF278-63C-20100930-1.lcd

PeakTable

PDA Ch2

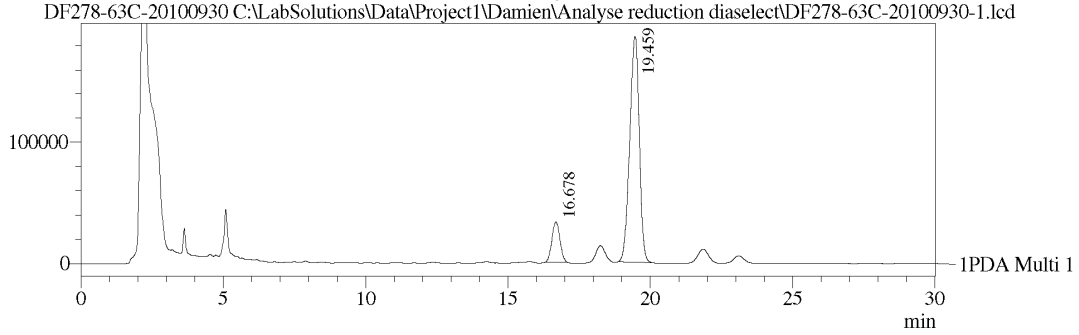
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	16.678	33304	651184	15.144	13.050
2	19.459	186609	4338793	84.856	86.950
Total		219912	4989977	100.000	100.000

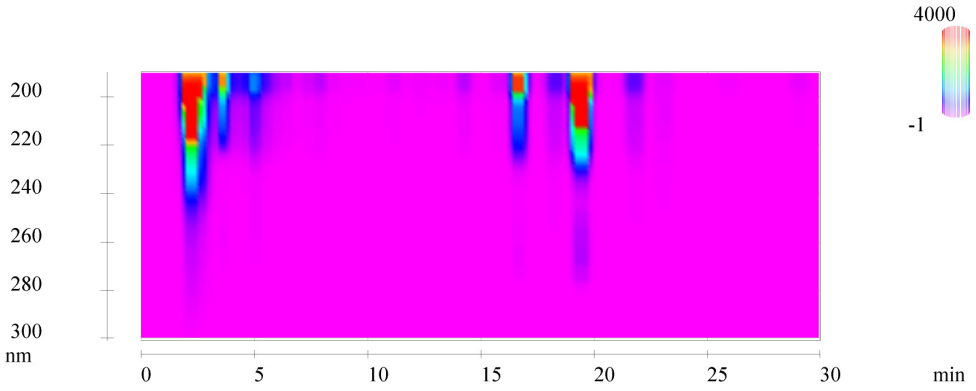
Chromatogram

DF278-63C-20100930 C:\LabSolutions\Data\Project1\Damien\Analyse reduction diaselect\DF278-63C-20100930-1.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

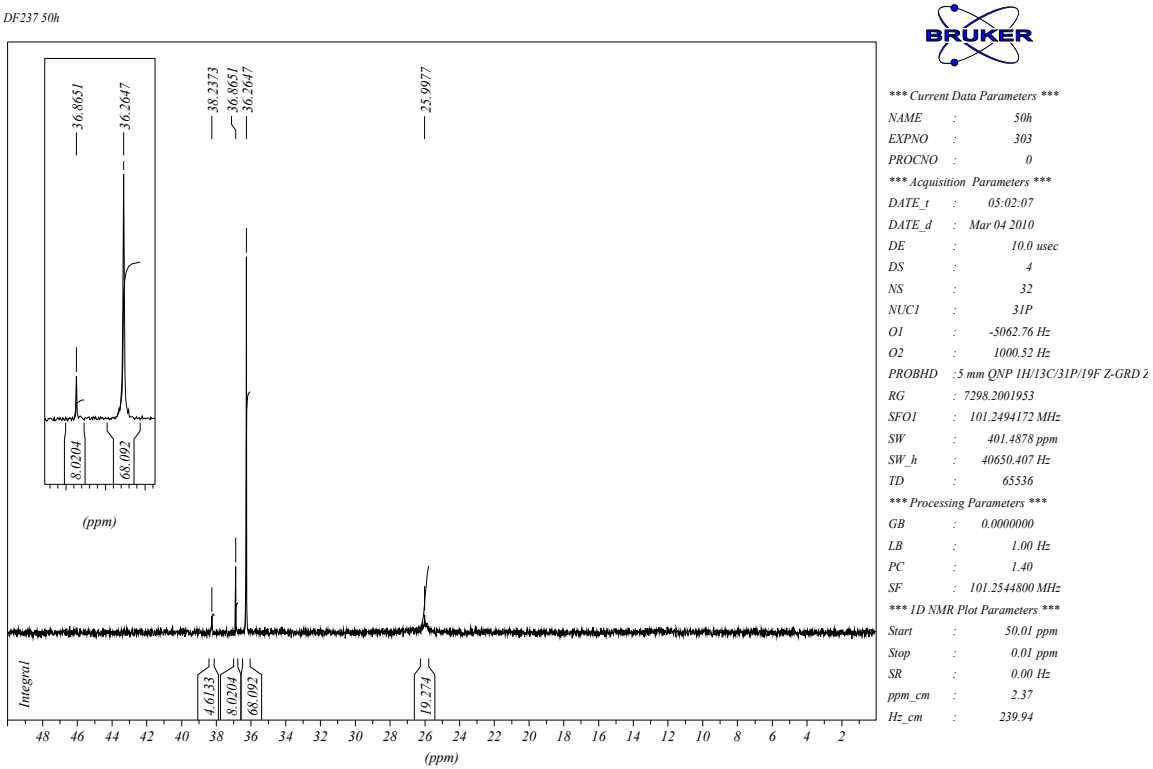
Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
30.00	Controller	Stop		

Entry 8. $NaBH_4$/*L*-proline/$LiClO_4$

Sodium borohydride (20.0 mg, 0.525 mmol) was added to a solution of *L*-proline (60.4 mg, 0.525 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.203 g, 0.375 mmol) and lithium perchlorate (0.375 mmol, 40 mg) in THF (1.2 mL) was added. The reaction mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 36.86 (s), 36.26 (s); Analytical HPLC (Column: Waters SunFire™ C18, 5 µm, 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 15.92 (12%), 18.48 (88%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 8. $NaBH_4$/*L*-proline/$LiClO_4$



HPLC chromatogram of **3** and **4**: Table 1, entry 8. $NaBH_4$/*L*-proline/$LiClO_4$

==== Shimadzu LCsolution Analysis Report ====

C:\...\Damien\Synthese diaselect\DF237_isocratique 63-C- 20 min.lcd

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Sample Name	: DF237
Sample ID	:
Tray#	: 1
Vail #	: 58
Injection Volume	: 20 uL
Data File Name	: DF237_isocratique 63-C- 20 min.lcd
Method File Name	: isocratique 63-C- 20 min.lcm
Batch File Name	: Synthese diastereoselective Batch1.lcb
Report File Name	: Default.lcr
Data Acquired	: 18/05/2010 16:47:00
Data Processed	: 18/05/2010 17:53:37

Chromatogram
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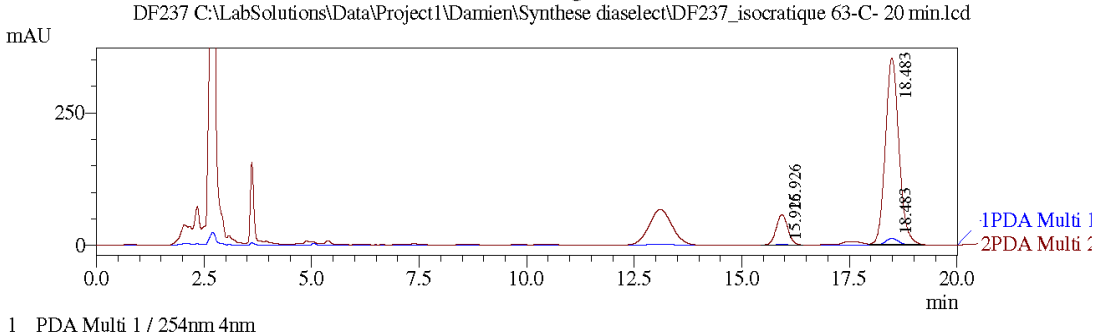
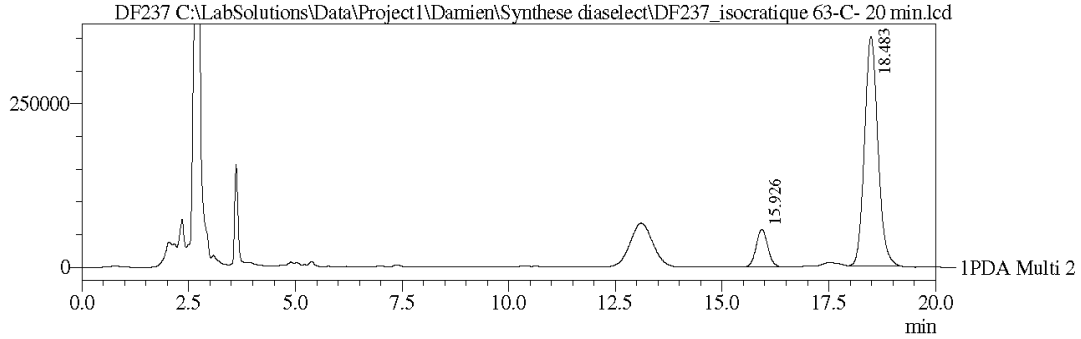


1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram
DF237 C:\LabSolutions\Data\Project1\Damien\Synthese diaselect\DF237_isocratique 63-C- 20 min.lcd



1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	15.926	57440	1076651	14.104	12.379
2	18.483	349813	7620754	85.896	87.621
Total		407253	8697405	100.000	100.000

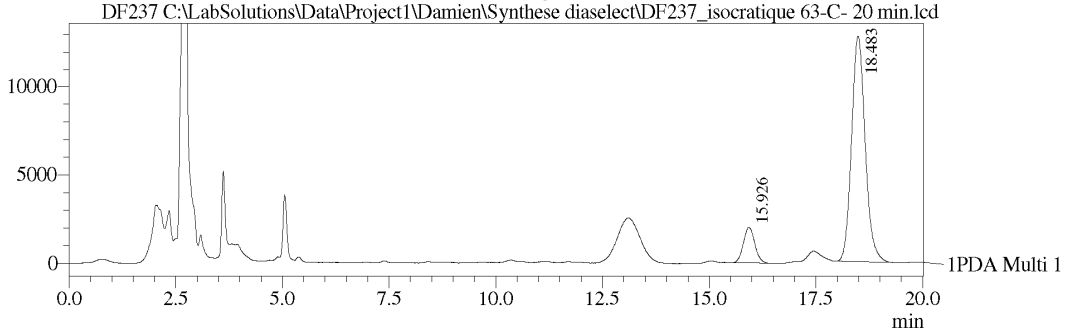
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	15.926	2007	37081	13.553	11.587
2	18.483	12804	282951	86.447	88.413
Total		14811	320032	100.000	100.000

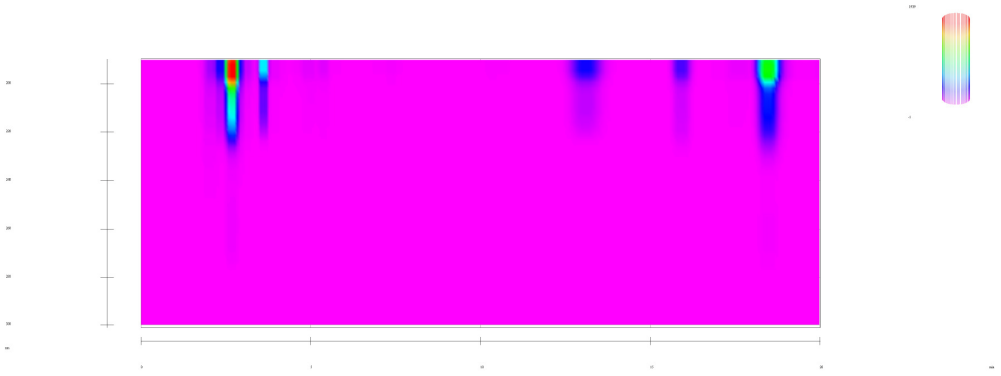
Chromatogram

DF237 C:\LabSolutions\Data\Project1\Damien\Synthese diaselect\DF237_isocratique 63-C- 20 min.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

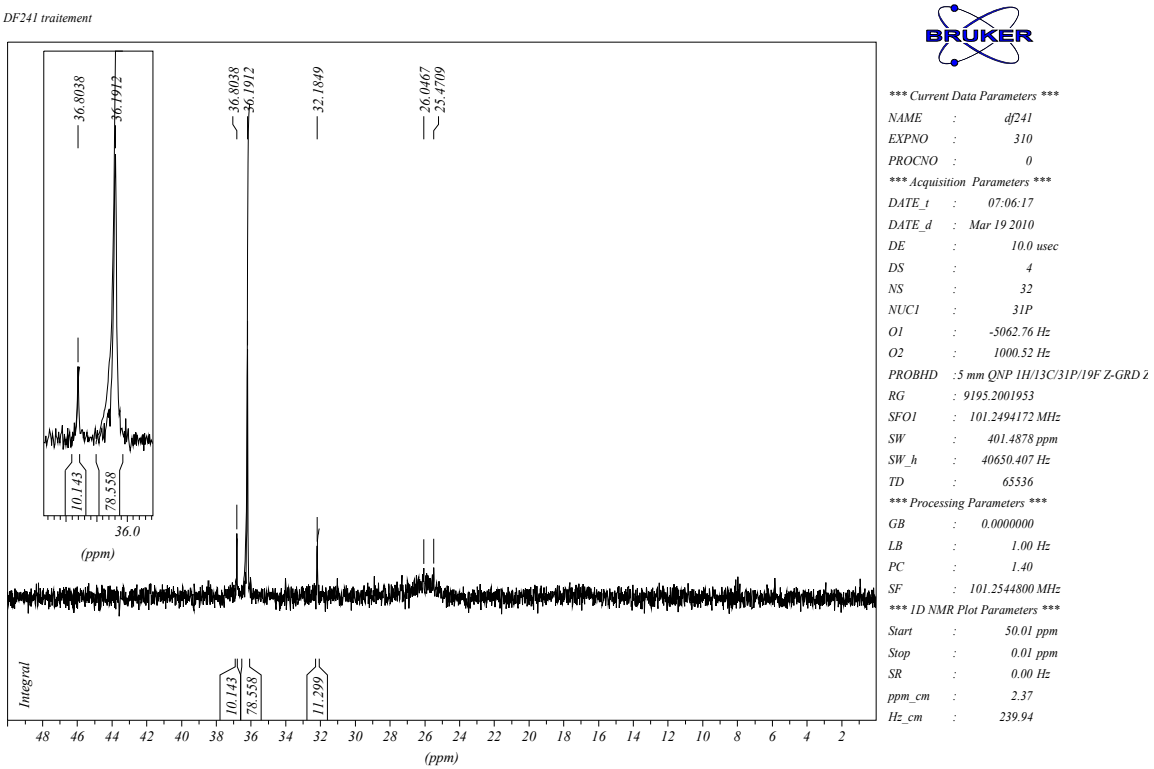
Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
20.00	Controller	Stop		

Entry 9. $NaBH_4$/*L*-proline/$ZnCl_2$

Sodium borohydride (20.0 mg, 0.525 mmol) was added to a solution of *L*-proline (60.4 mg, 0.525 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.375 mmol, 0.203 g) and zinc chloride (0.375 mmol, 51 mg) in THF (1.2 mL) was added. The reaction mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, $CDCl_3$): δ (ppm): 36.80 (s), 36.19 (s); Analytical HPLC (Column: Waters SunFire^{TM} C18, 5 µm, 4.6×250 mm; Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 15.91 (12%), 18.47 (88%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 9. $NaBH_4$/*L*-proline/$ZnCl_2$



HPLC chromatogram of **3** and **4**: Table 1, entry 9. $NaBH_4$/*L*-proline/$ZnCl_2$

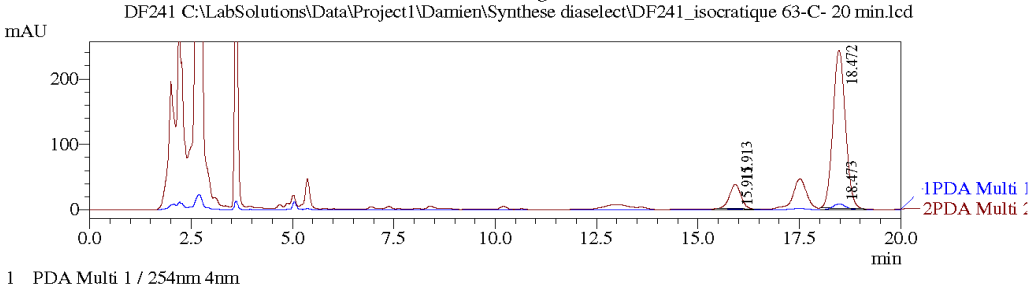
==== Shimadzu LCsolution Analysis Report ====

C:\...\Damien\Synthese diaselect\DF241_isocratique 63-C- 20 min.lcd

Acquired by	: Admin
Sample Name	: DF241
Sample ID	:
Tray#	: 1
Vail #	: 57
Injection Volume	: 20 uL
Data File Name	: DF241_isocratique 63-C- 20 min.lcd
Method File Name	: isocratique 63-C- 20 min.lcm
Batch File Name	: Synthese diastereoselective Batch1.lcb
Report File Name	: Default.lcr
Data Acquired	: 18/05/2010 16:26:32
Data Processed	: 18/05/2010 17:51:05

Chromatogram

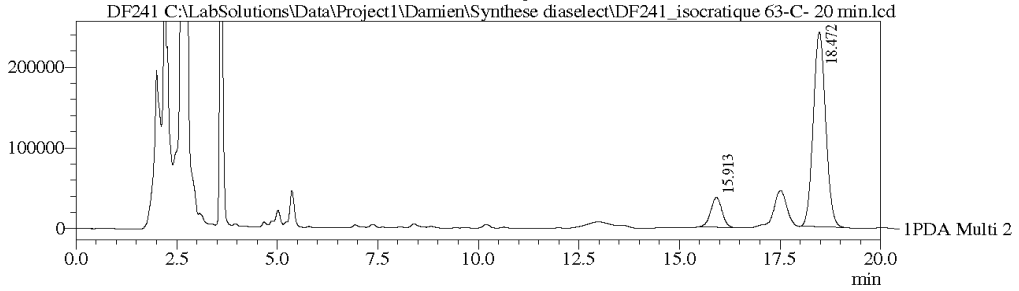
DF241 C:\LabSolutions\Data\Project1\Damien\Synthese diaselect\DF241_isocratique 63-C- 20 min.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram

DF241 C:\LabSolutions\Data\Project1\Damien\Synthese diaselect\DF241_isocratique 63-C- 20 min.lcd



1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	15.913	37023	714353	13.326	12.208
2	18.472	240794	5137198	86.674	87.792
Total		277816	5851552	100.000	100.000

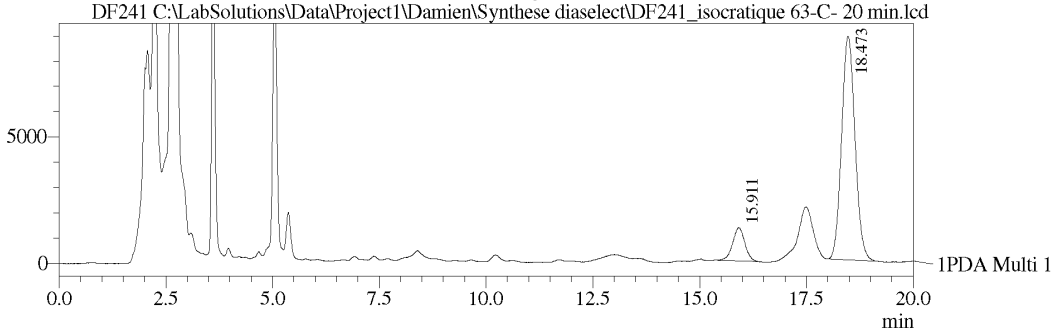
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	15.911	1309	25945	12.889	11.873
2	18.473	8850	192579	87.111	88.127
Total		10160	218523	100.000	100.000

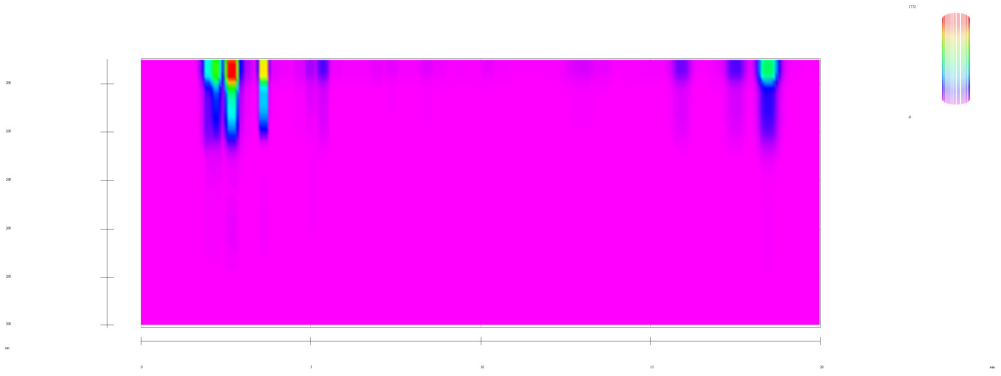
Chromatogram

DF241 C:\LabSolutions\Data\Project1\Damien\Synthese diaselect\DF241_isocratique 63-C- 20 min.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

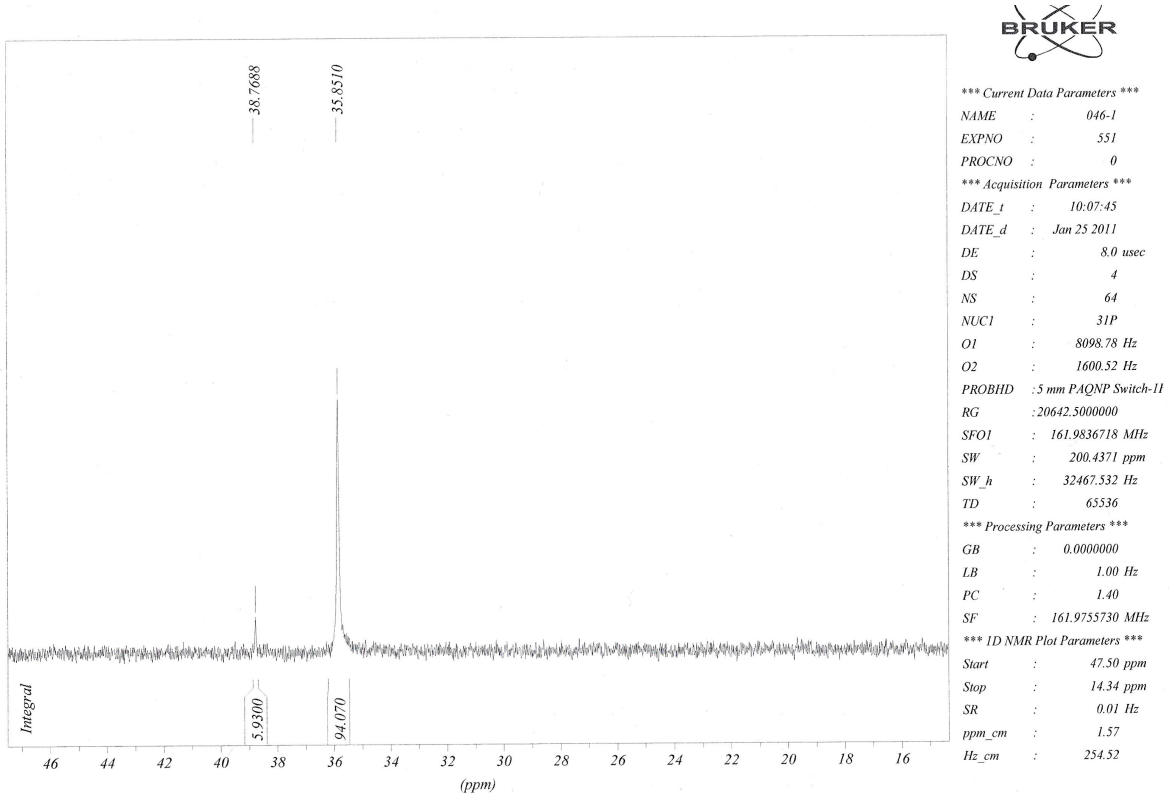
Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
20.00	Controller	Stop		

Entry 10. $NaBH_4$/*L*-proline/$CeCl_3$.7 H_2O

Sodium borohydride (20.0 mg, 0.525 mmol) was added to a solution of *L*-proline (60.4 mg, 0.525 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.375 mmol, 0.203 g) and cerium (III) chloride heptahydrate (0.375 mmol, 140 mg) in THF (1.2 mL) was added. The mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtrated and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, DMSO-d6): δ (ppm): 38.79 (s), 35.85 (s); Analytical HPLC (Column: Waters SunFire^{TM} C18, 5 µm 4.6×250 mm, Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 16.26 (7%), 18.96 (93%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 10. $NaBH_4$/*L*-proline/$CeCl_3$.7 H_2O



HPLC chromatogram of **3** and **4**: Table 1, entry 10. $NaBH_4$/*L*-proline/$CeCl_3.7\ H_2O$

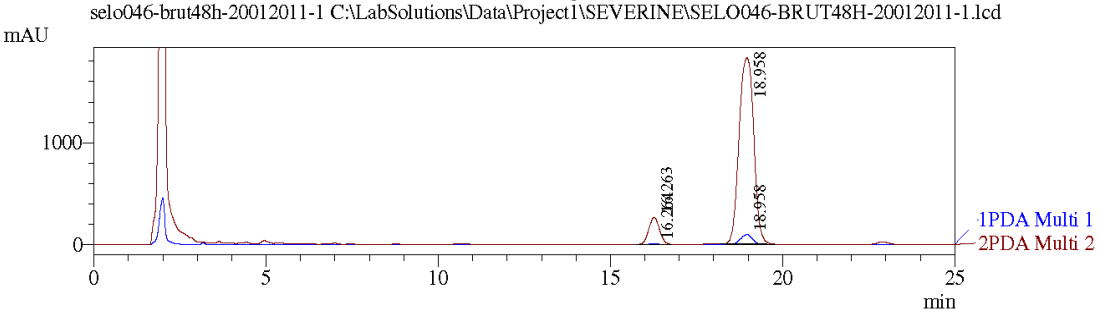
==== Shimadzu LCsolution Analysis Report ====

C:\...\Data\Project1\SEVERINE\SELO046-BRUT48H-20012011-1.lcd

Acquired by	: Admin
Sample Name	: selo046-brut48h-20012011-1
Sample ID	: selo046-brut48h-20012011-1
Tray#	: 1
Vail #	: 24
Injection Volume	: 20 uL
Data File Name	: SELO046-BRUT48H-20012011-1.lcd
Method File Name	: isocratique 63-C- 25 min.lcm
Batch File Name	: 20012011-SELO046-brut48h-63C-1.lcb
Report File Name	: delphine report.lcr
Data Acquired	: 20/01/2011 14:47:59
Data Processed	: 20/01/2011 15:34:01

Chromatogram

selo046-brut48h-20012011-1 C:\LabSolutions\Data\Project1\SEVERINE\SELO046-BRUT48H-20012011-1.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram

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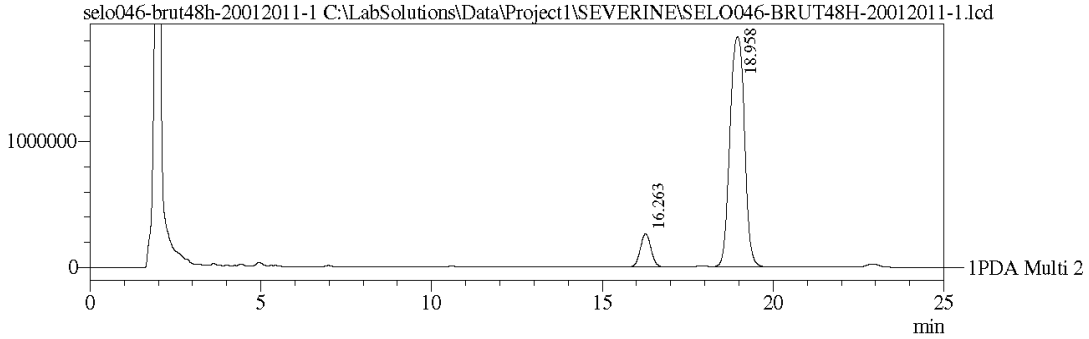


1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	16.263	263436	5655557	12.603	9.476
2	18.958	1826784	54029712	87.397	90.524
Total		2090220	59685269	100.000	100.000

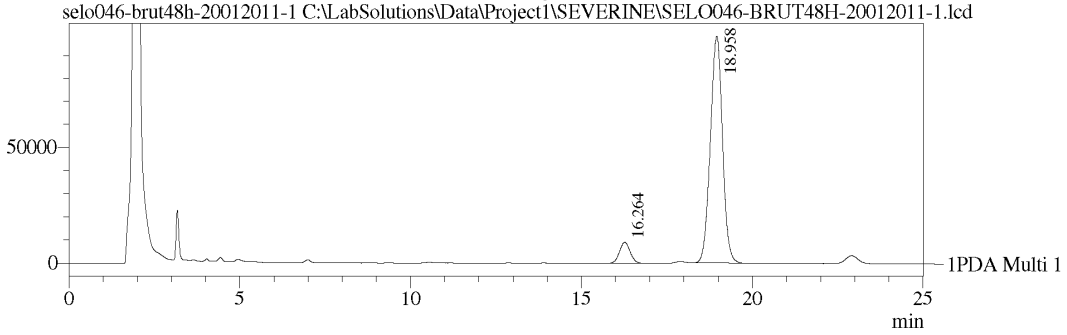
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	16.264	9040	194293	8.418	7.416
2	18.958	98351	2425708	91.582	92.584
Total		107391	2620000	100.000	100.000

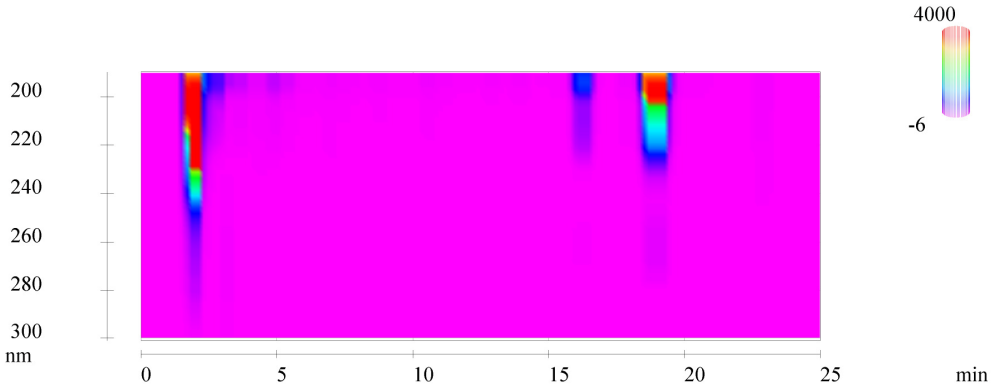
Chromatogram

selo046-brut48h-20012011-1 C:\LabSolutions\Data\Project1\SEVERINE\SELO046-BRUT48H-20012011-1.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

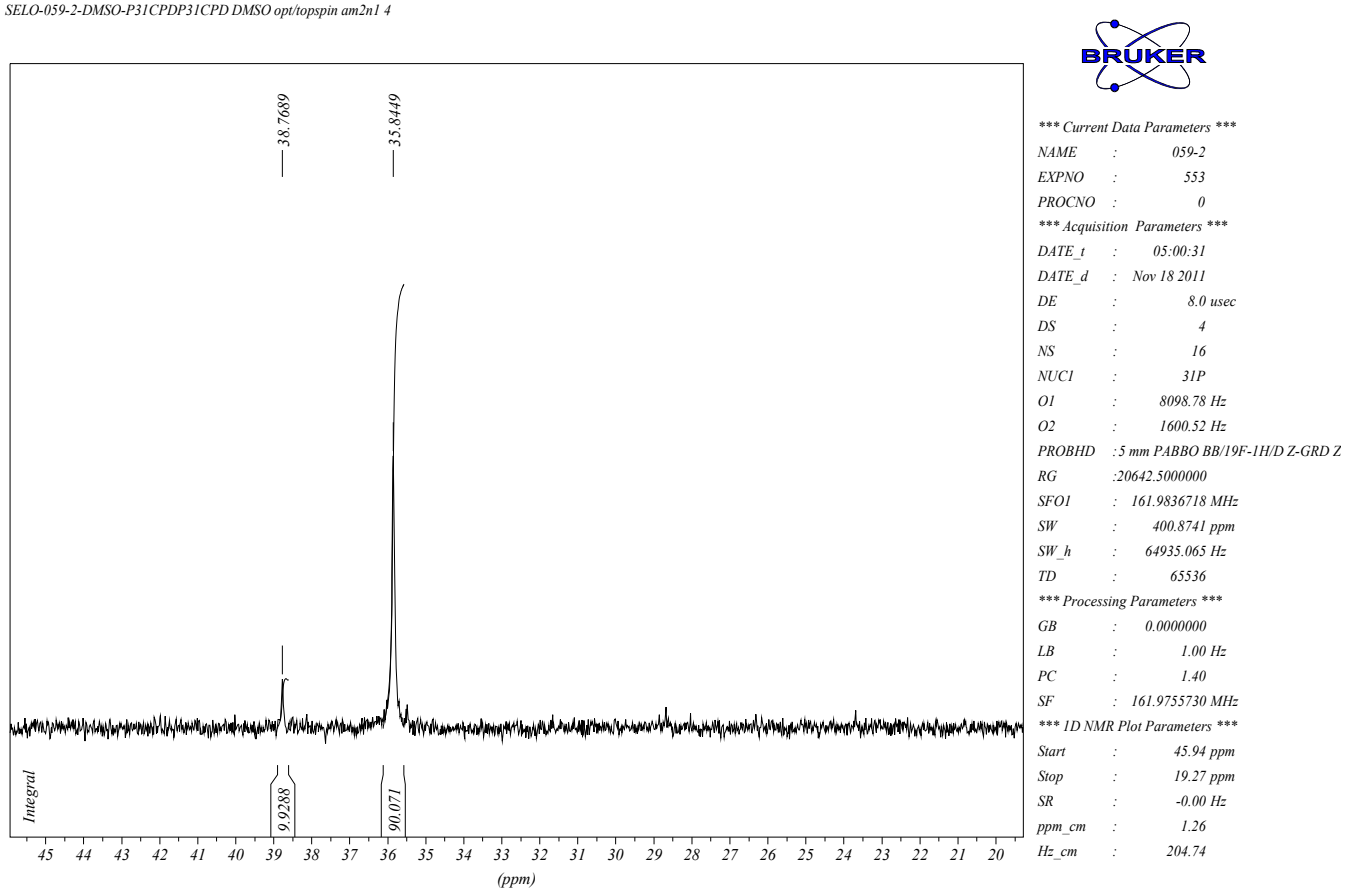
Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
25.00	Controller	Stop		

Entry 11. $NaBH_4$/*D*-proline/$CeCl_3.7\ H_2O$

Sodium borohydride (20.0 mg, 0.525 mmol) was added to a solution of *D*-proline (60.4 mg, 0.525 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 60 h, and then a solution of α-ketophosphinate (0.375 mmol, 0.203 g) and cerium (III) chloride heptahydrate (0.375 mmol, 140 mg) in THF (1.2 mL) was added. The mixture was stirred for 48 h at room temperature and solvent was evaporated. The residue remaining was diluted with dichloromethane (20 mL) and organic solution was washed with a saturated aqueous solution of ammonium chloride (10 mL). The organic layer was dried over magnesium sulfate, filtrated and concentrated under vacuum to give yellow oil.

^{31}P NMR (161.97 MHz, DMSO-d6): δ (ppm): 38.77 (s), 35.84 (s); Analytical HPLC (Column: Waters SunFire™ C18, 5 µm 4.6×250 mm, Eluent: acetonitrile/water (63:37); Flow: 1 mL.min^{-1}): Retention time = 16.26 (7%), 18.96 (93%).

^{31}P NMR spectrum of **3** and **4**: Table 1, entry 11. $NaBH_4$/*D*-proline/$CeCl_3.7\ H_2O$

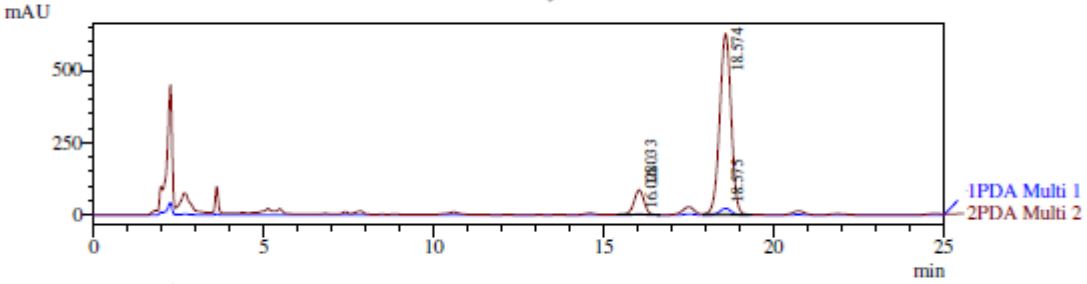


==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\SEVERINE\SELO059-18112011-1.lcd

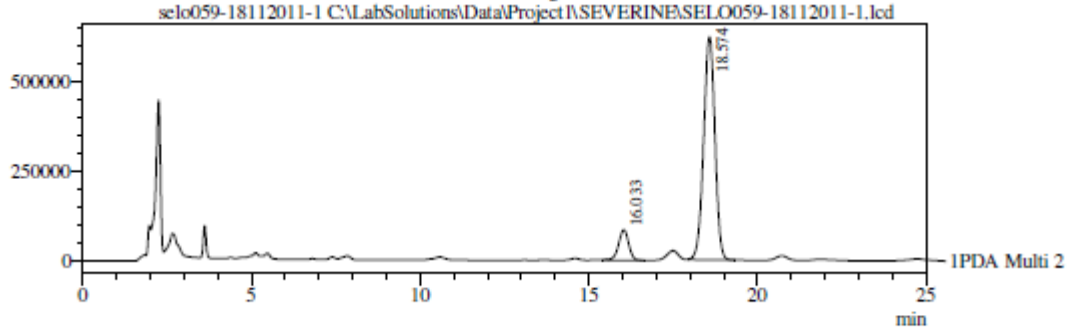
Acquired by	: Admin
Sample Name	: selo059-18112011-1
Sample ID	: selo059-18112011-1
Tray#	: 1
Vail #	: 18
Injection Volume	: 20 uL
Data File Name	: SELO059-18112011-1.lcd
Method File Name	: isocratique 63-C- 25 min.lcm
Batch File Name	: 18112011-SELO059-48h-63C-1.lcb
Report File Name	: delphine report.lcr
Data Acquired	: 18/11/2011 15:35:12
Data Processed	: 18/11/2011 16:03:25

Chromatogram
selo059-18112011-1 C:\LabSolutions\Data\Project1\SEVERINE\SELO059-18112011-1.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 214nm 4nm

Chromatogram
selo059-18112011-1 C:\LabSolutions\Data\Project1\SEVERINE\SELO059-18112011-1.lcd



1 PDA Multi 2 / 214nm 4nm

PeakTable

PDA Ch2 214nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	16.033	84940	1745518	11.982	10.722
2	18.574	623984	14534831	88.018	89.278
Total		708924	16280349	100.000	100.000

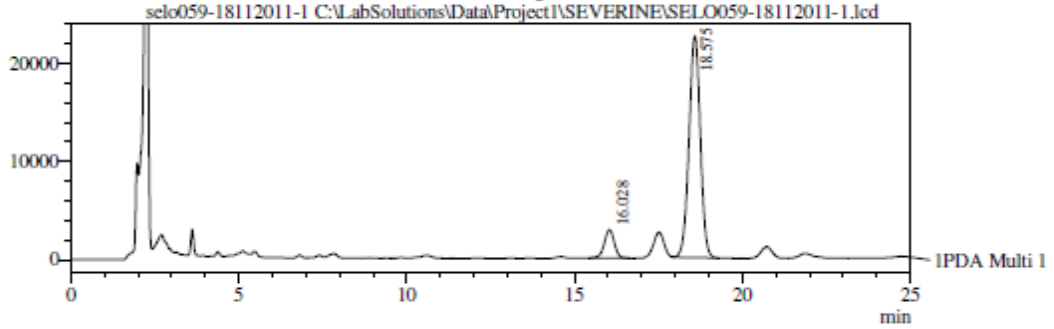
PeakTable

PDA Ch1 254nm 4nm

Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	16.028	2882	59941	11.322	10.217
2	18.575	22570	526726	88.678	89.783
Total		25452	586667	100.000	100.000

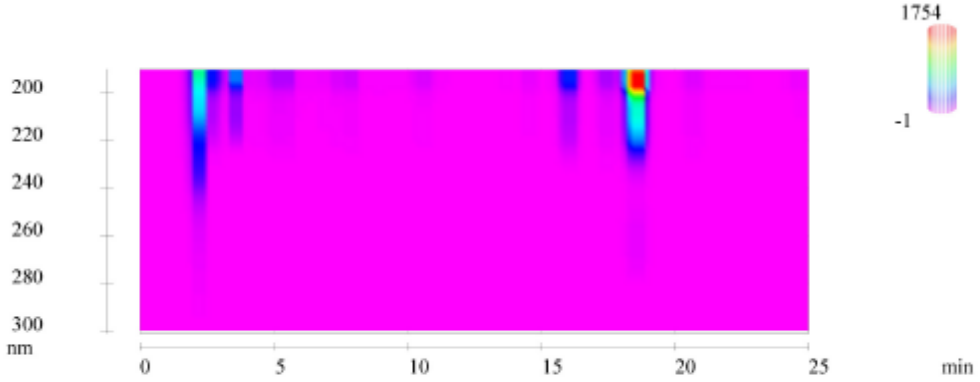
Chromatogram

selo059-18112011-1 C:\LabSolutions\Data\Project1\SEVERINE\SELO059-18112011-1.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



Method

<<LC Program>>

Time	Unit	Command	Value	Comment
0.01	Pumps	C.Conc	63	
0.01	Pumps	T.Flow	1	
25.00	Controller	Stop		